A Better Way To Treat Pain

Jonathan Tait, D.O.

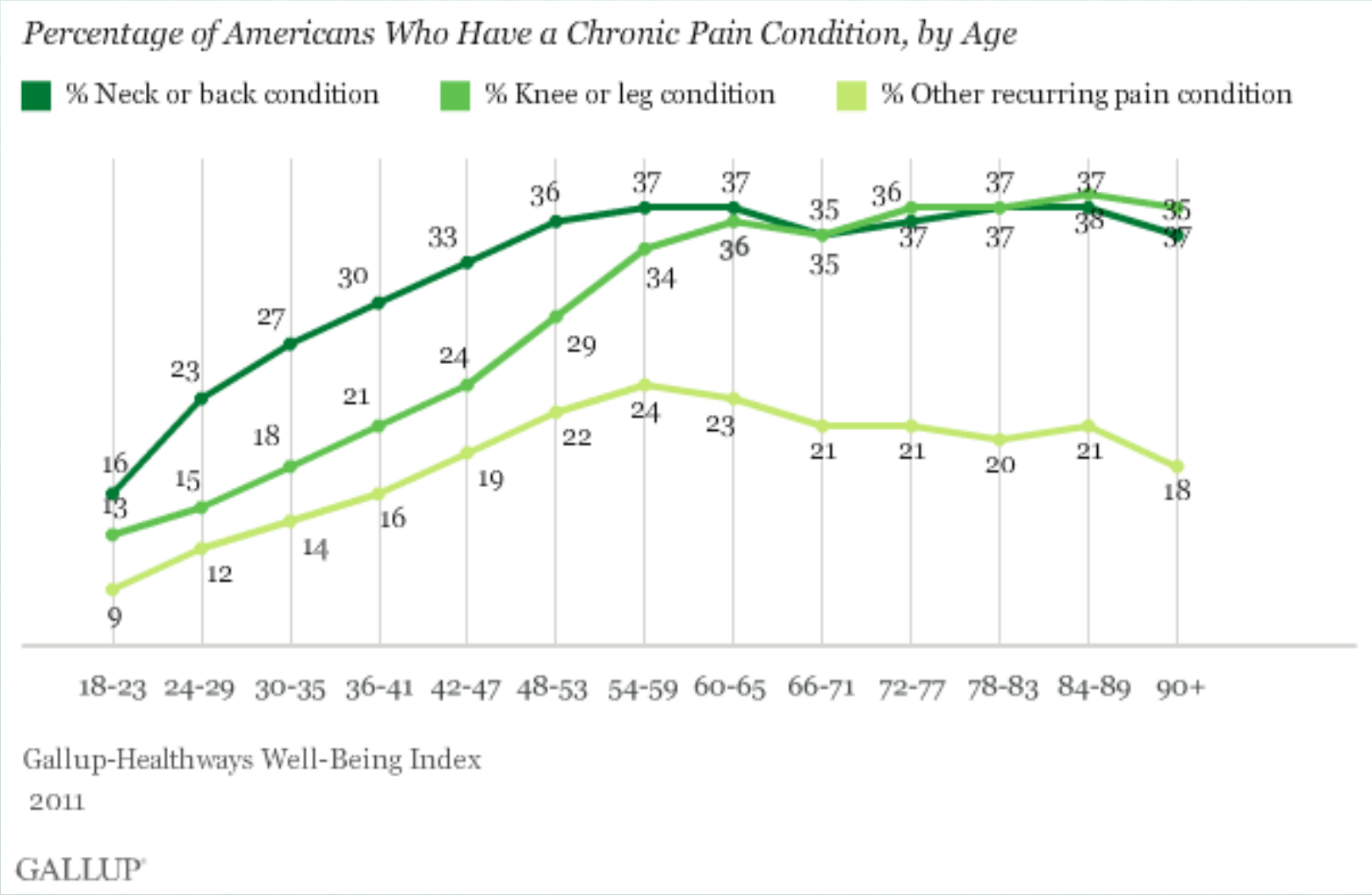
Physical Medicine and Rehabilitation
Sports Medicine
Pain Medicine

Rejuv Medical Southwest
Tucson, AZ

“The doctor of the future will give no medications, but will interest his patients in the care of the human frame, diet and in the cause and prevention of disease.”

- Thomas A. Edison

Chronic pain in the U.S.



Chronic Pain and Income

Chronic Pain Condition Self-Reports for 2011, by Annual Income

	% Neck or back condition	% Knee or leg condition	% Other recurring pain condition
Less than $36,000	37	32	23
$36, 000-$90, 000	29	23	16
$90, 000 or more	26	19	13

Gallup-Healthways Well-Being Index
2011

GALLUP

Chronic Pain and Obesity

Chronic Pain Condition Self-Reports for 2011, by BMI Group

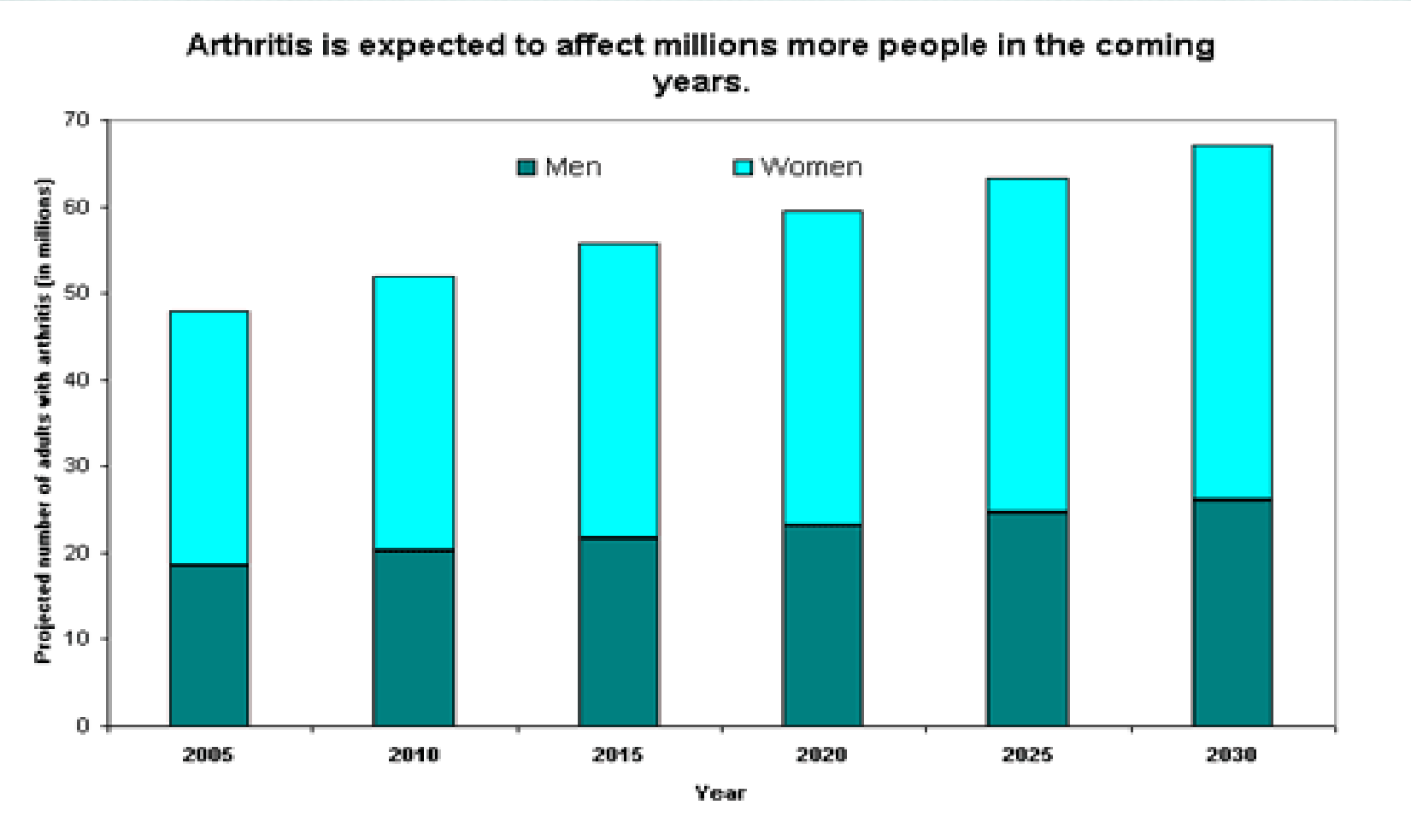
BMI GROUP	% Neck and back condition	% Knee and leg condition	% Other recurring pain condition
Underweight	28	20	18
Normal weight	27	19	15
Overweight	31	25	17
Obese	37	36	24

Gallup-Healthways Well-Being Index

2011

GALLUP

OA rates in the U.S.

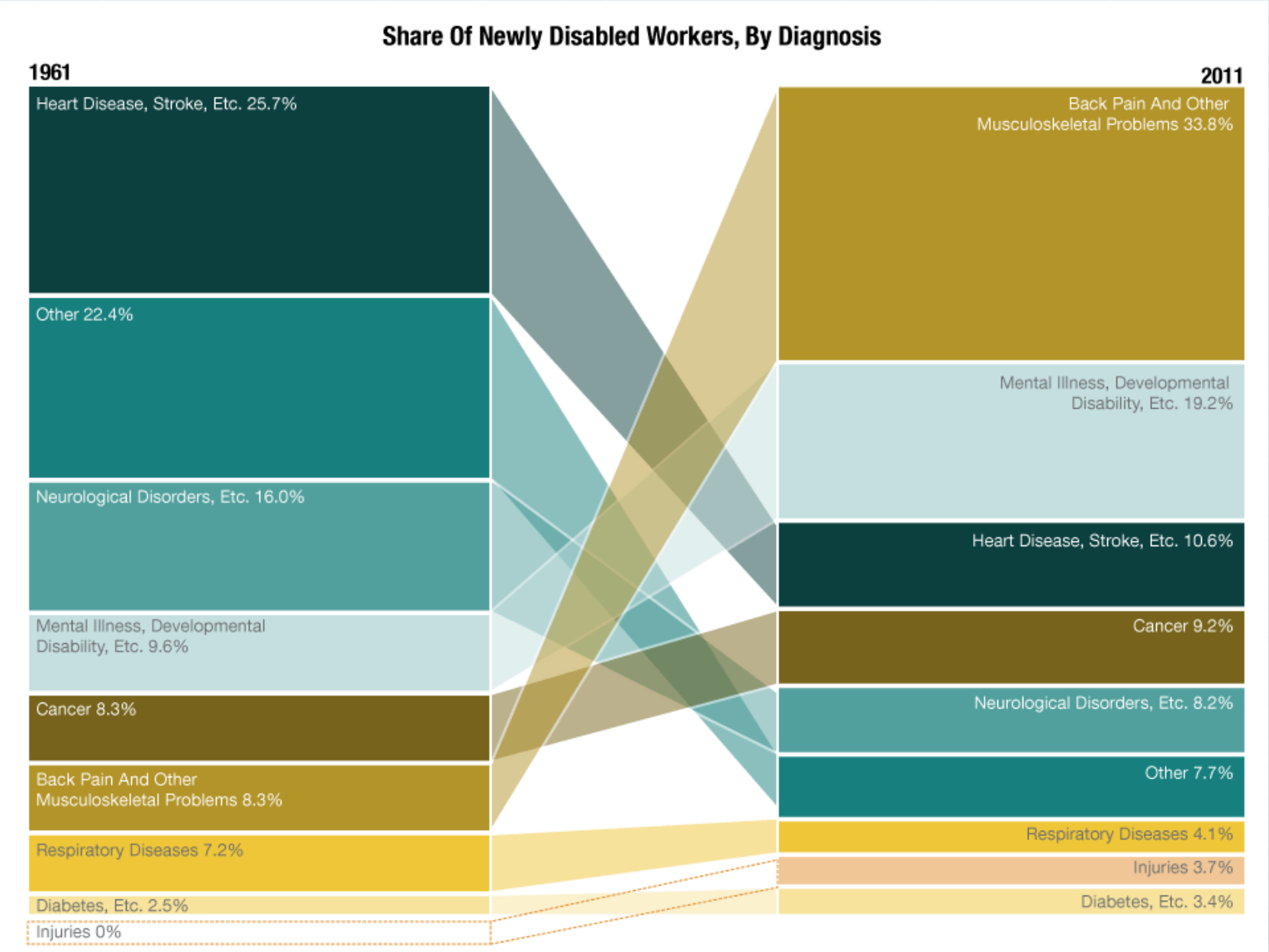


cdc.gov

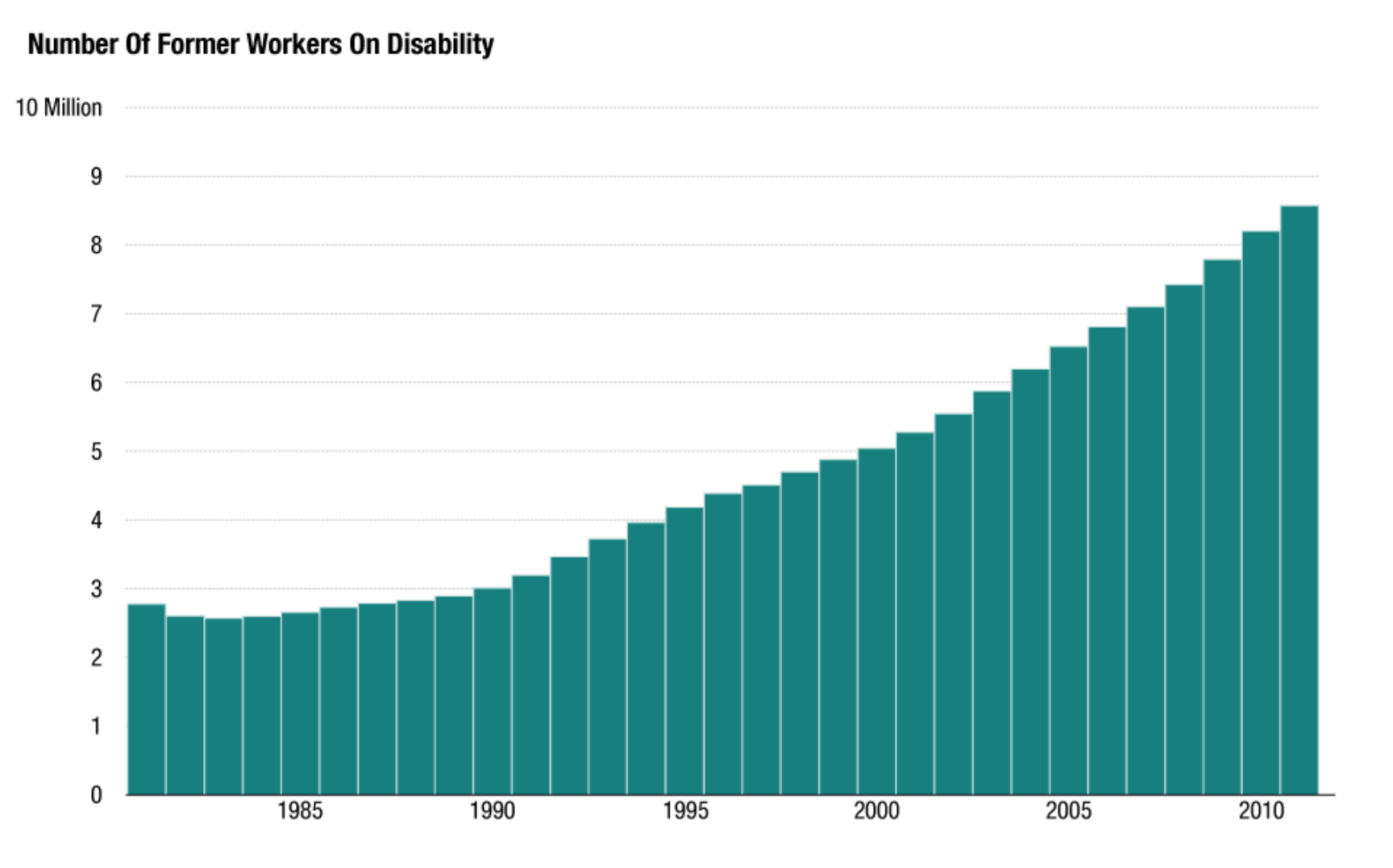
Low Back Pain

- Leading cause of disability in the world
- More than 632 million people (1 in 10) worldwide suffer from low back pain.
- 1/3 of all work-related disability
- "With aging and growing populations, low back pain is an enormous burden in developing countries", "This is predicted to grow substantially over coming decades and will likely have an enormous impact on individual livelihoods, health care systems, and economies."

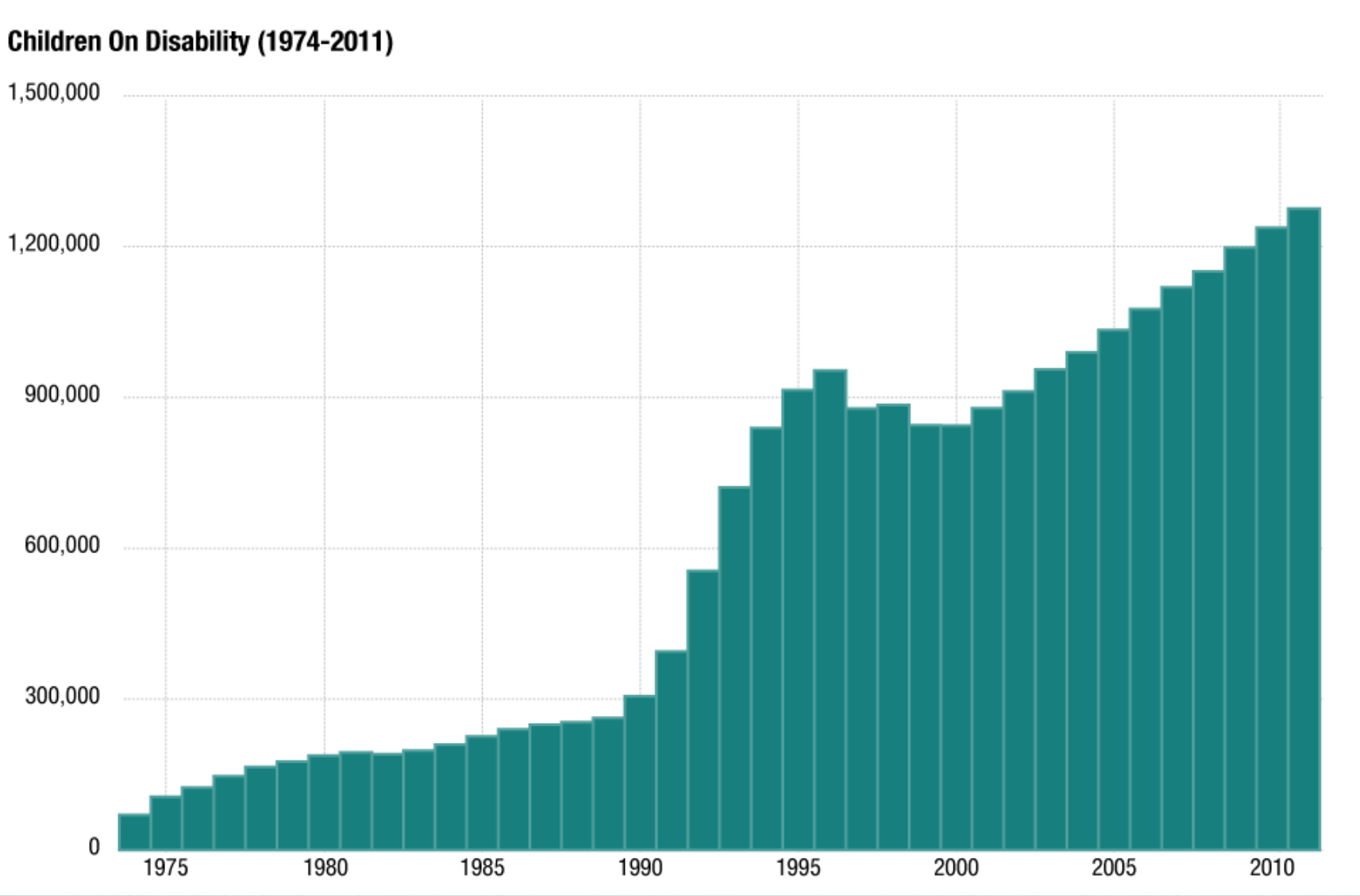
Hoy, D et al. Annals of the Rheumatic Diseases. March 2014



Source: Social Security Administration

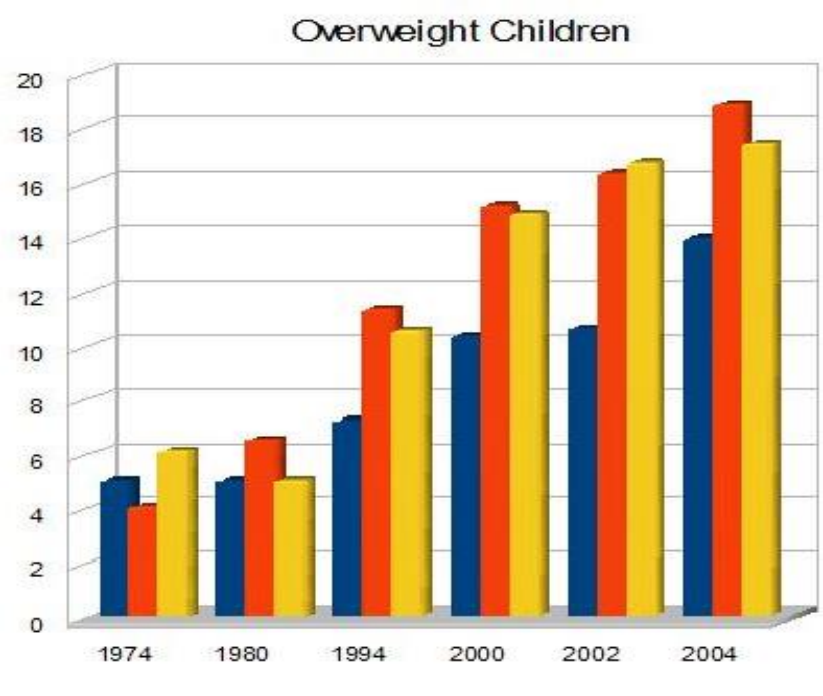


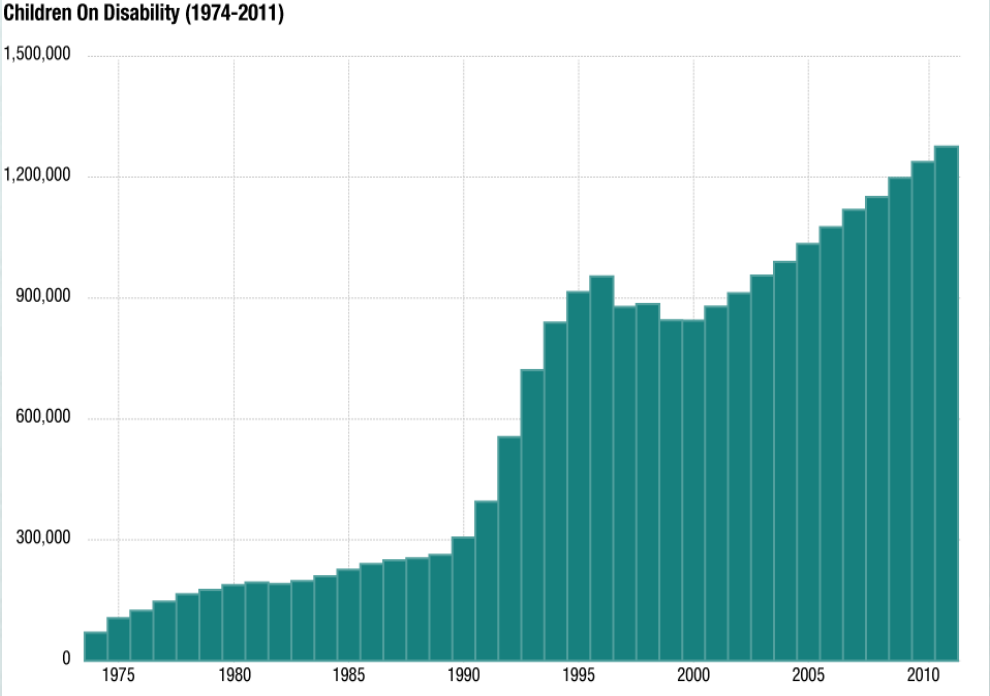
Source: Social Security Administration



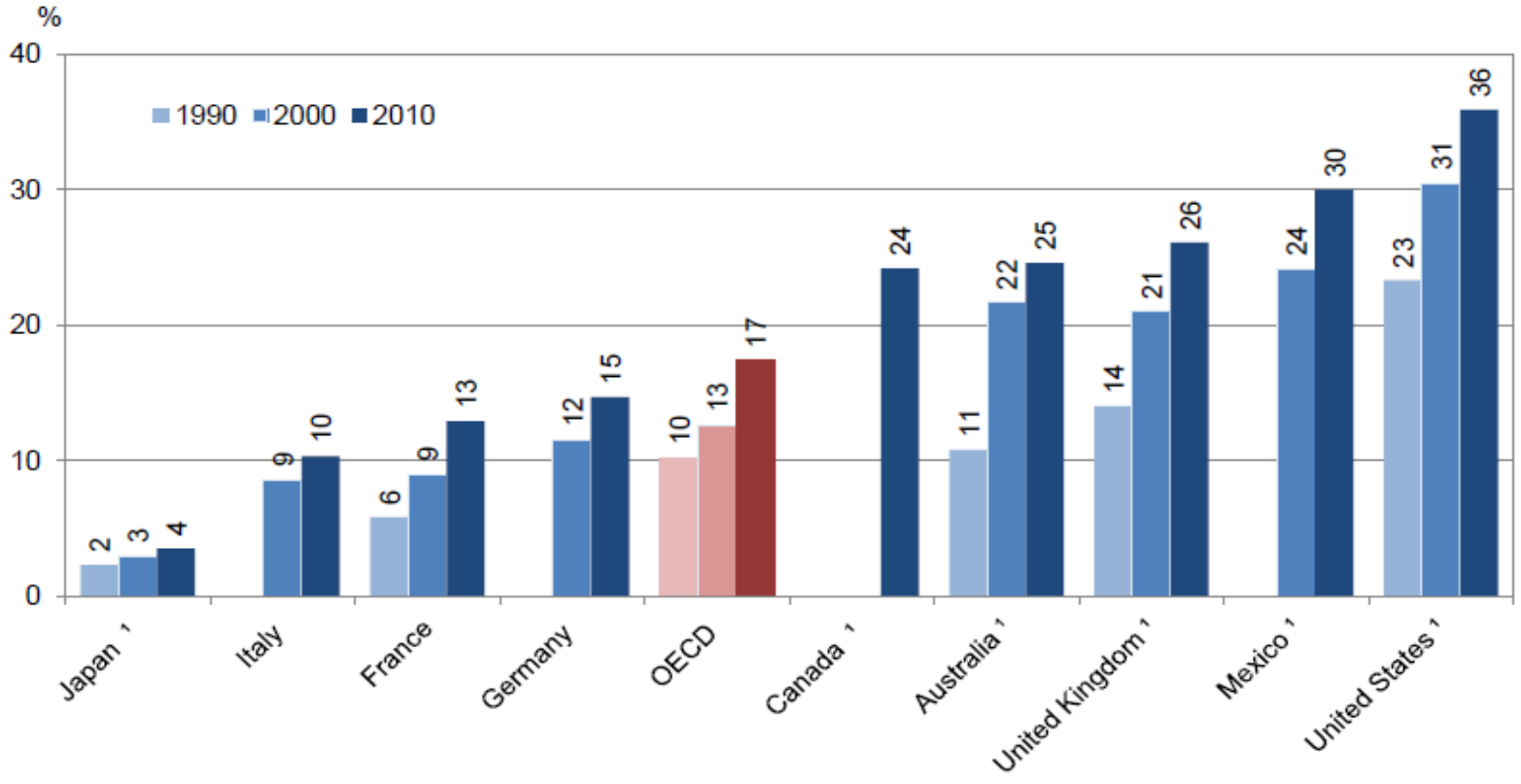
Source: Social Security Administration

Are we going to see an increasing trend with obesity and disability?



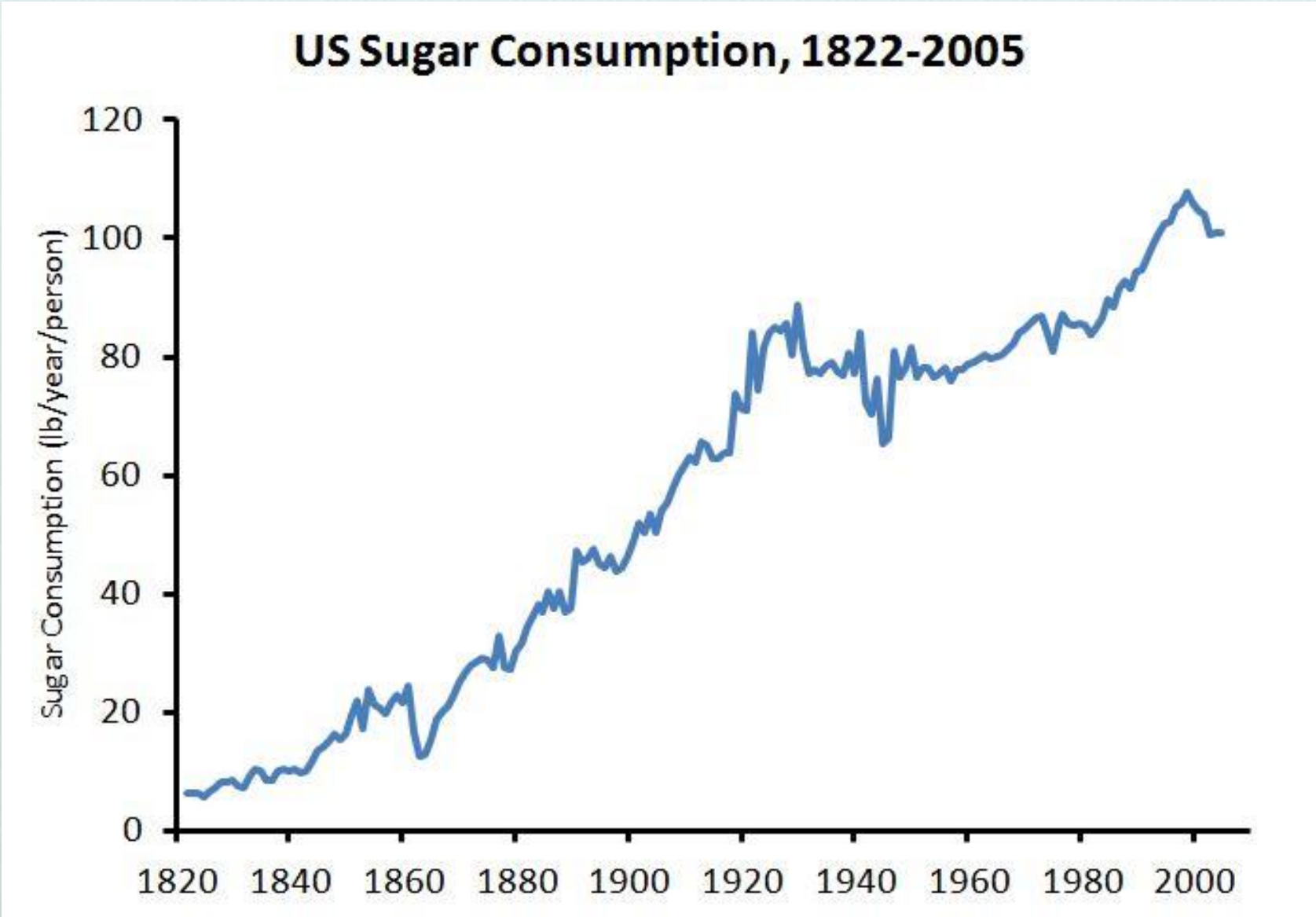


Obesity rates have increased substantially over the past 20 years and are highest in the US



1. Data are based on measurements rather than self-reported height and weight.
Source: OECD Health Data 2012.

“We’re lovin’ it”


US Sugar Consumption, 1822-2005
Sugar Consumption (lb/year/person)
120
100
80
60
40
20
0
1820
1840
1860
1880
1900
1920
1940
1960
1980
2000

Economic Burden of Pain in the U.S.

- > 100 million adults affected by chronic daily pain
- Many have functional limitations restricting their ability to work
- Annual economic costs are staggering
  - Medical care
  - Indirect costs due to lost wages, disability days, fewer hours worked.
- The cost of pain:
  - Work days missed $11.6-12.7 billion
  - Hours of work lost $95.2-96.5 billion
  - Lower wages $190.6-226.3 billion
  - Medical care $150-$300 billion

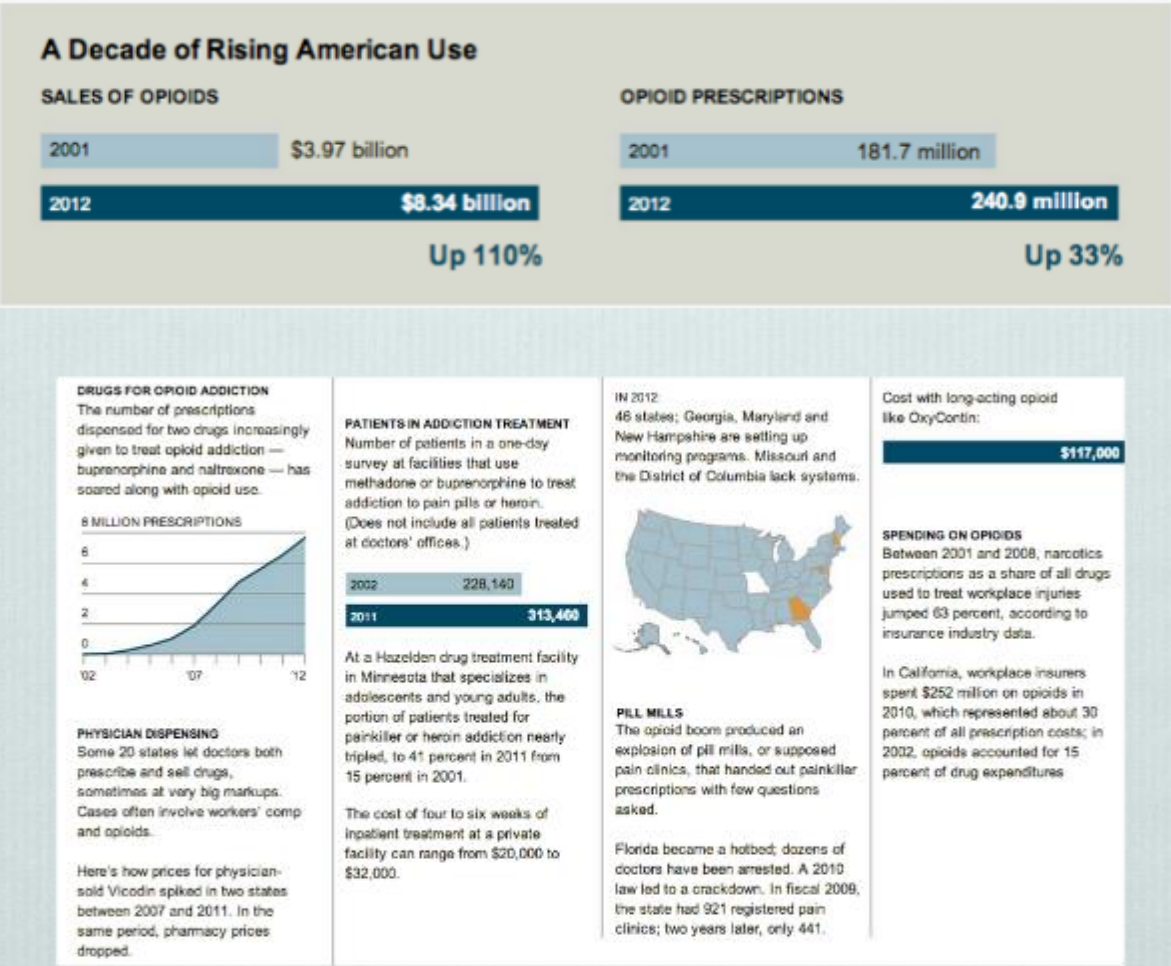
DJ Gaskin, P Richard. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. National Academies Press. 2011

Economic Burden of Pain in the U.S.

- Annual Cost of Pain
  - Work days missed $11.6 -12.7 billion
  - Hours lost work $95.2 - 96.5 billion
  - Lower wages $190.6 - 226.3 billion
  - Medical care $150 - $300 billion
  - **TOTAL $560 - 635 billion**
- Annual Cost of Other Conditions
  - Heart Disease $309 billion
  - Cancer $243 billion
  - Diabetes $188 billion

DJ Gaskin, P Richard. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. National Academies Press. 2011

Do we have an opioid epidemic?



Original Article: Barry Meier and Bill Walsh. New York Times. June 22, 2013. Sources: IMS Health Data; Frost & Sullivan; California Workers' Compensation Institute; Workers Compensation Research Institute; Centers for Disease Control and Prevention; Drug Abuse Warning Network; Substance Abuse and Mental Health Services Administration; Accident Fund Holdings, Lansing, Mich.; PDMP Center for Excellence, Brandeis University; Florida Department of Health

Do we have an opioid epidemic?

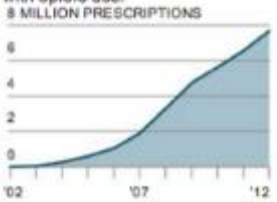
More Pills, More Business ...

DRUG-SCREENING TESTS
Many of these tests check the urine of patients taking opioids, looking for abuse of those drugs. In 2013, workers' compensation insurers in California will spend about $100 million on tests, up 200-fold since 2002.

Estimated size of the U.S. screening industry:

2000 $800 million
2013 $2 billion

DRUGS FOR OPIOID ADDICTION
The number of prescriptions dispensed for two drugs increasingly given to treat opioid addiction — buprenorphine and naltrexone — has soared along with opioid use.



PHYSICIAN DISPENSING
Some 20 states let doctors both prescribe and sell drugs, sometimes at very big markups. Cases often involve workers' comp and opioids.

Here's how prices for physician-sold Vicodin spiked in two states between 2007 and 2011. In the same period, pharmacy prices dropped.

More Hospitalizations ...

U.S. EMERGENCY ROOM COSTS
Cases in which an opioid other than heroin was cited as a reason for an emergency-room treatment:

2004 299,498
2011 885,348

OVERDOSE DEATHS
Where prescription opioids were involved:

1999 4,030
2010 16,651

PATIENTS IN ADDICTION TREATMENT
Number of patients in a one-day survey at facilities that use methadone or buprenorphine to treat addiction to pain pills or heroin. (Does not include all patients treated at doctors' offices.)

2002 228,140
2011 313,460

At a Hazelden drug treatment facility in Minnesota that specializes in adolescents and young adults, the portion of patients treated for painkiller or heroin addiction nearly tripled, to 41 percent in 2011 from 15 percent in 2001.

The cost of four to six weeks of inpatient treatment at a private facility can range from $20,000 to $32,000.

More Legal Expenses ...

MONITORING "DOCTOR SHOPPING"
Most states have databases of prescriptions to flag patients trying to get additional opioids.

IN 2002:
16 states with monitoring.

IN 2012:
46 states; Georgia, Maryland and New Hampshire are setting up monitoring programs. Missouri and the District of Columbia lack systems.

PILL MILLS
The opioid boom produced an explosion of pill mills, or supposed pain clinics, that handed out painkiller prescriptions with few questions asked.

Florida became a hotbed; dozens of doctors have been arrested. A 2010 law led to a crackdown. In fiscal 2009, the state had 921 registered pain clinics; two years later, only 441.

More Workplace Costs

INSURANCE CLAIMS FOR TIME LOST
Workers' compensation costs include treatment expenses and lost wages. The stronger the opioid, the higher the expense.

Average claim cost without use of opioids:
$13,000

Cost with short-acting opioid like Percocet:
$39,000

Cost with long-acting opioid like OxyContin:
$117,000

SPENDING ON OPIOIDS
Between 2001 and 2008, narcotics prescriptions as a share of all drugs used to treat workplace injuries jumped 63 percent, according to insurance industry data.

In California, workplace insurers spent $252 million on opioids in 2010, which represented about 30 percent of all prescription costs; in 2002, opioids accounted for 15 percent of drug expenditures

Original Article: Barry Meier and Bill Walsh. New York Times. June 22, 2013. Sources: IMS Health Data; Frost & Sullivan; California Workers' Compensation Institute; Workers Compensation Research Institute; Centers for Disease Control and Prevention; Drug Abuse Warning Network; Substance Abuse and Mental Health Services Administration; Accident Fund Holdings, Lansing, Mich.; PDMP Center for Excellence, Brandeis University; Florida Department of Health

Rx Abuse - The "Silent" Epidemic

- In November 2011, the CDC reported that deaths from Rx pain relievers have reached **epidemic proportions**
  - Rx pain reliever deaths are greater than heroin and cocaine combined
  - Drug poisoning **deaths have surpassed motor vehicle deaths**
  - **~40 deaths per day** and ~15,000 per year (2008) – a **3 fold increase** since 1999
  - **Half a million ED visits** per year for misuse and abuse (2009)
- There was a **4 fold increase** in the quantity of Rx pain relievers sold in the U.S. in the last decade
  - Enough Rx pain relievers were prescribed in 2012 to medicate every Arizona adult around-the-clock for **more than two weeks.**
  - In some areas of Arizona, this is **as high as 4 weeks**

Courtesy of Shana Malone, County Level Strategies. Arizona Criminal Justice Commission, Statistical Analysis Center. www.azcjc.gov

Do we have an opioid epidemic in AZ?

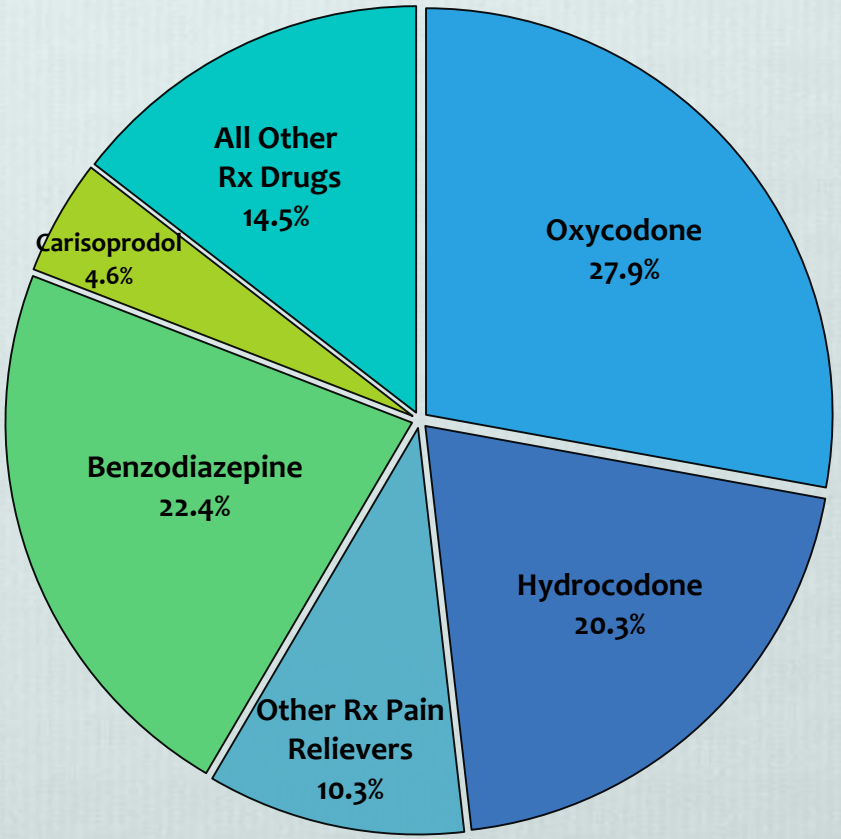
- **~ 585 million** Class II-IV **pills** were prescribed in Arizona in 2012

- **Pain relievers** had the highest % of Rx's, pills and average number of pills per day; accounting for **58.5%** of all pills prescribed

- **Hydrocodone** and **Oxycodone** accounted for 82.4% of all pain relievers prescribed in Arizona

- Why it matters = probability and **access!**

Percentage of Pills by Drug Type in Arizona
(2012)



Courtesy of Shana Malone, County Level Strategies. Arizona Criminal Justice Commission, Statistical Analysis Center. www.azcjc.gov

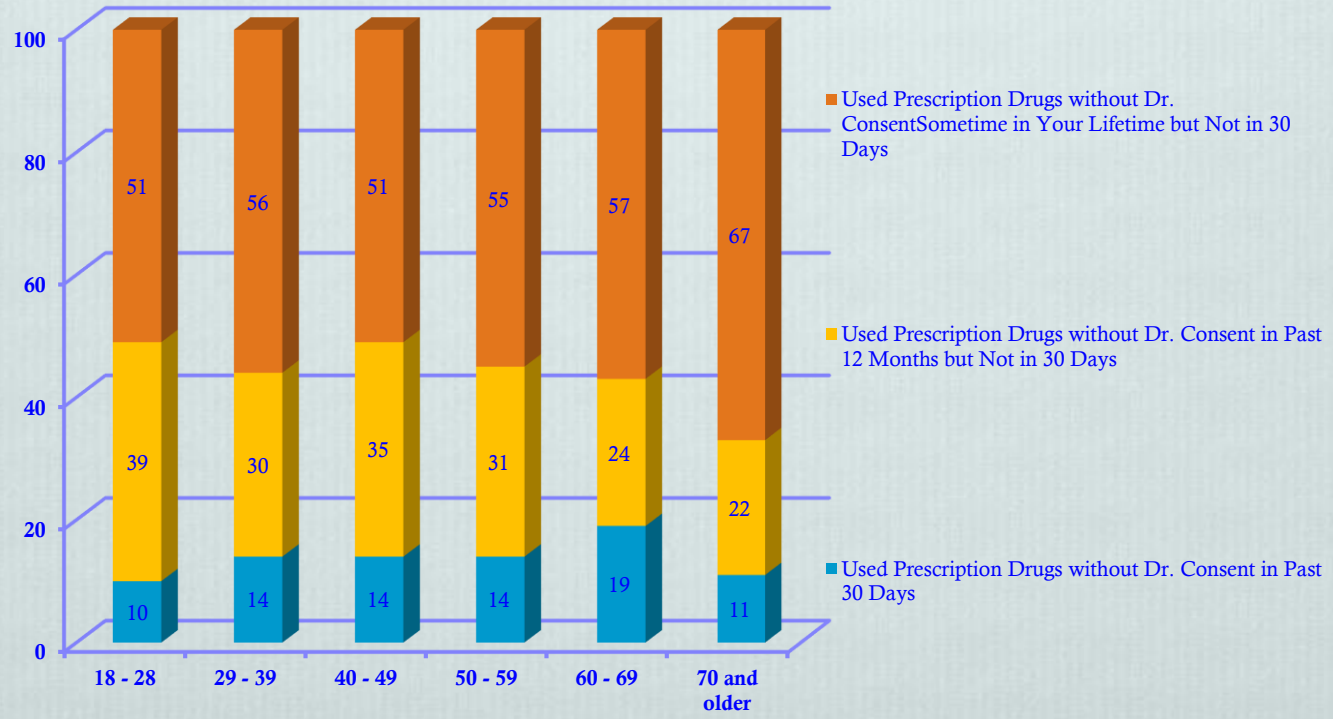
Who Is It Affecting?

ARIZONA ADULTS

In 2010, **~50%** of adults reported Rx drug misuse in the past 12 months

13% reported misuse in the past 30 days

- 47% of Rx abusers reported misusing **pain relievers**, 32% sedatives and 3.3% stimulants



Courtesy of Shana Malone, County Level Strategies. Arizona Criminal Justice Commission, Statistical Analysis Center. www.azcjc.gov

Who Is It Affecting?

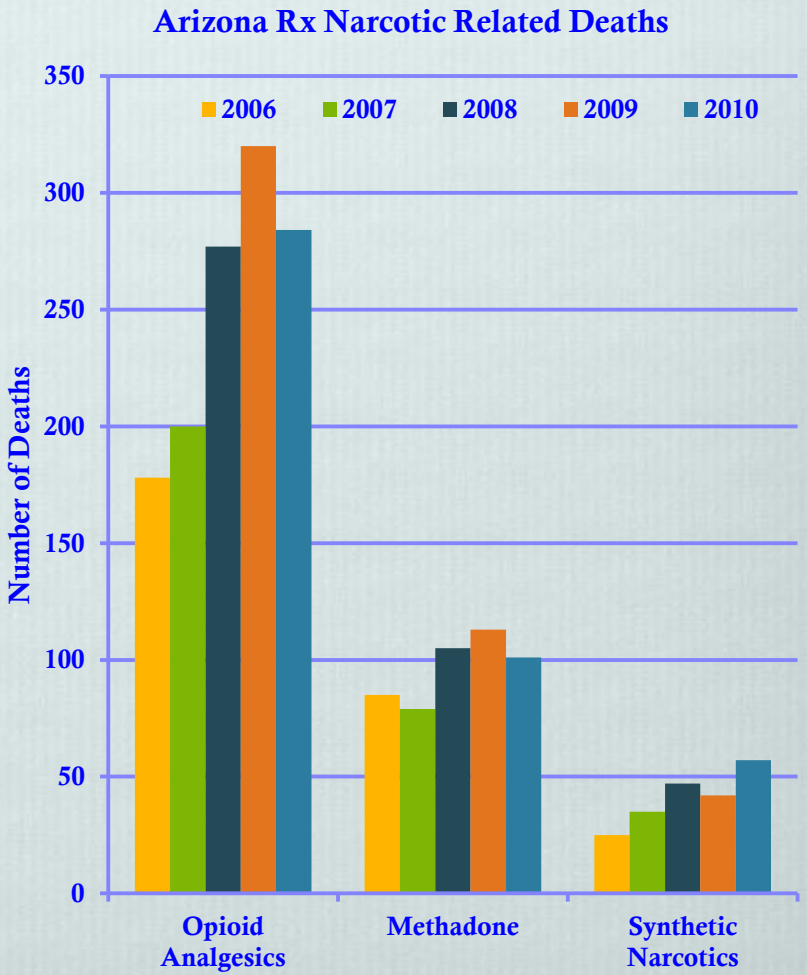
ARIZONA YOUTH

- **In 2012, 7.9% of AZ youth reported current Rx drug misuse (the most commonly used substance after alcohol, tobacco and marijuana)**
  - Though a moderate decrease occurred between 2010 and 2012, **Arizona remains the 6th highest state in the country for Rx drug misuse among individuals 12+ years**
  - While rates of Rx type use were comparable to national levels for sedatives and stimulants, Arizona youth in all grades reported higher rates of **Pain Reliever misuse**
  - The **majority** of youth (91.9%) reported **obtaining** them **from everyday sources** (e.g. friends and family/home)

Courtesy of Shana Malone, County Level Strategies. Arizona Criminal Justice Commission, Statistical Analysis Center. www.azcjc.gov

What Is It Costing Us?

- Mortality & Morbidity
  - Opioid-related cases in the **ED** have consistently **increased 86% between 2008 and 2011**
  - 490 **deaths** involved Rx narcotic drugs in AZ in 2010, **increased 53.3% between 2006 and 2010.**
    - 11% were youth & young adults between 15-24 years
    - **Opioid Analgesics accounted for 64.3%**
- Increase in Crime
- Increase in DUI-D
- Increase in babies born with NAS



Courtesy of Shana Malone, County Level Strategies. Arizona Criminal Justice Commission, Statistical Analysis Center. www.azcjc.gov

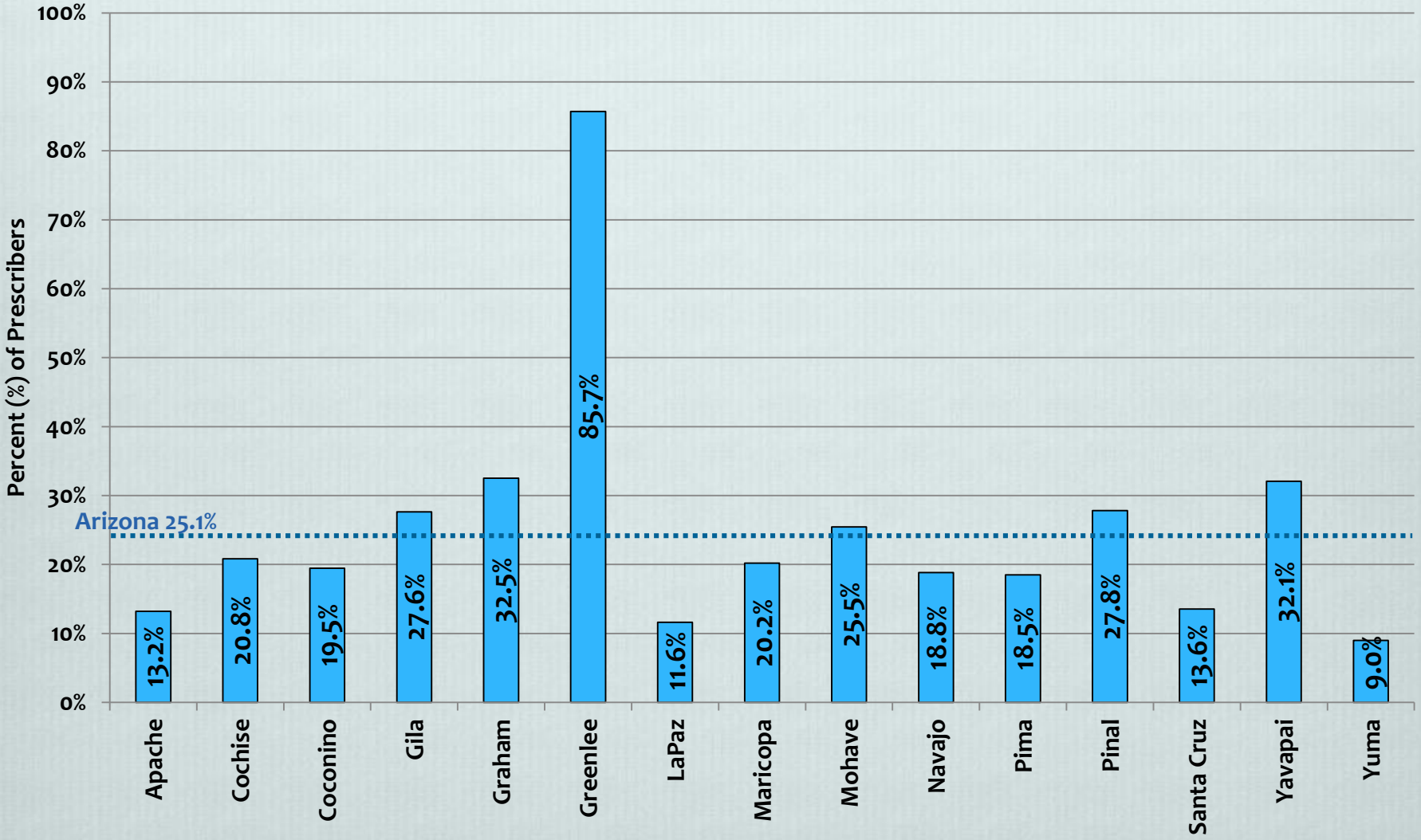
What Is Amplifying The Problem?

i.e., What Can We Change?

- Social acceptance and the **perception of "safety"** by parents, youth, health consumers and some medical professionals
  - Lack of proper disposal and storage
  - Lack of understanding about risks
- **Only 25%** of AZ prescribers are using the Prescription Drug Monitoring Program (PDMP) – as low as 9% of prescribers in some counties
- Lack of **education and inconsistent prescribing guidelines** for Rx narcotics – prescribers were told a little over a decade ago that they weren't assessing pain well enough
- **Unrealistic expectations of the health consumer** for zero pain and immediate gratification
- **Diversion Crimes:** it's a high demand market and lucrative business

Courtesy of Shana Malone, County Level Strategies. Arizona Criminal Justice Commission, Statistical Analysis Center. www.azcjc.gov

Percentage of Prescribers Signed Up to Use the PDMP (11/2013)



Courtesy of Shana Malone, County Level Strategies. Arizona Criminal Justice Commission, Statistical Analysis Center. www.azcjc.gov

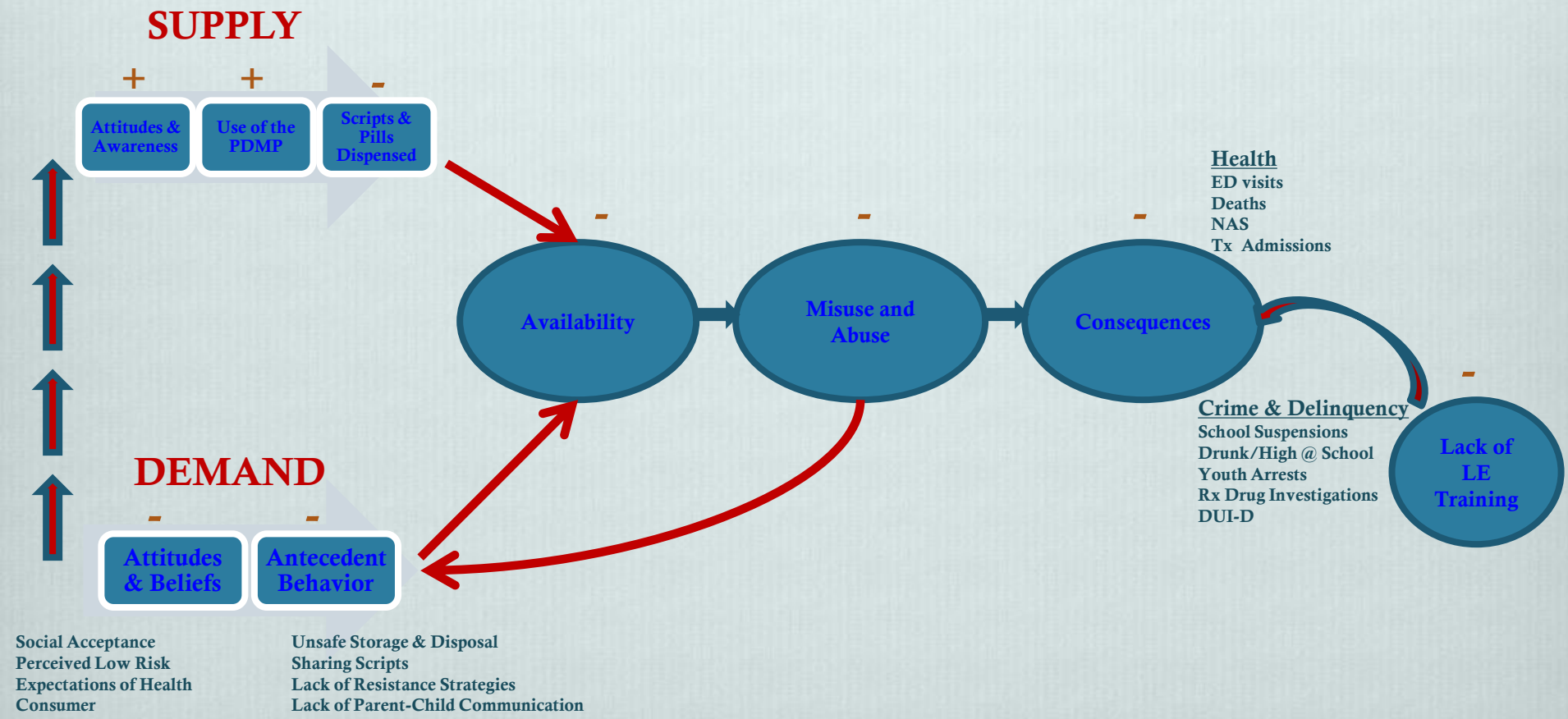
Food for Thought

- How much pain could be considered self-inflicted?
- Do we have a medical/legal/ethical obligation to intervene when we are witness to lifestyle choices and negative behavior that directly contribute to painful conditions?
- Are we enabling poor lifestyle choices by over-utilizing powerful pain medications and procedures?
- Where does this end for our patients, us and the health care system?

How Do We Turn This Around?

AZCJC - Conceptual Framework

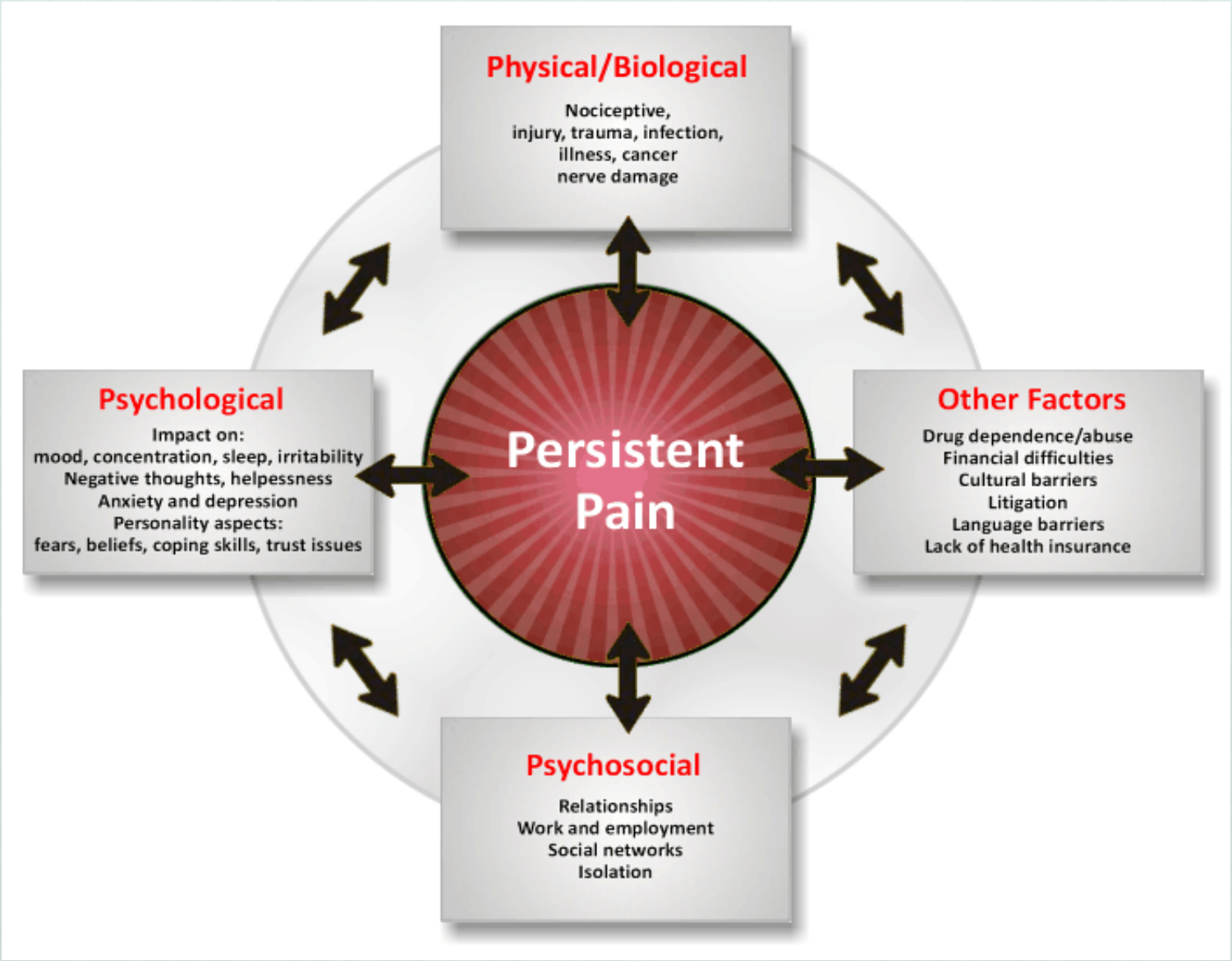
Targeted Increases (+) and Decreases (-)

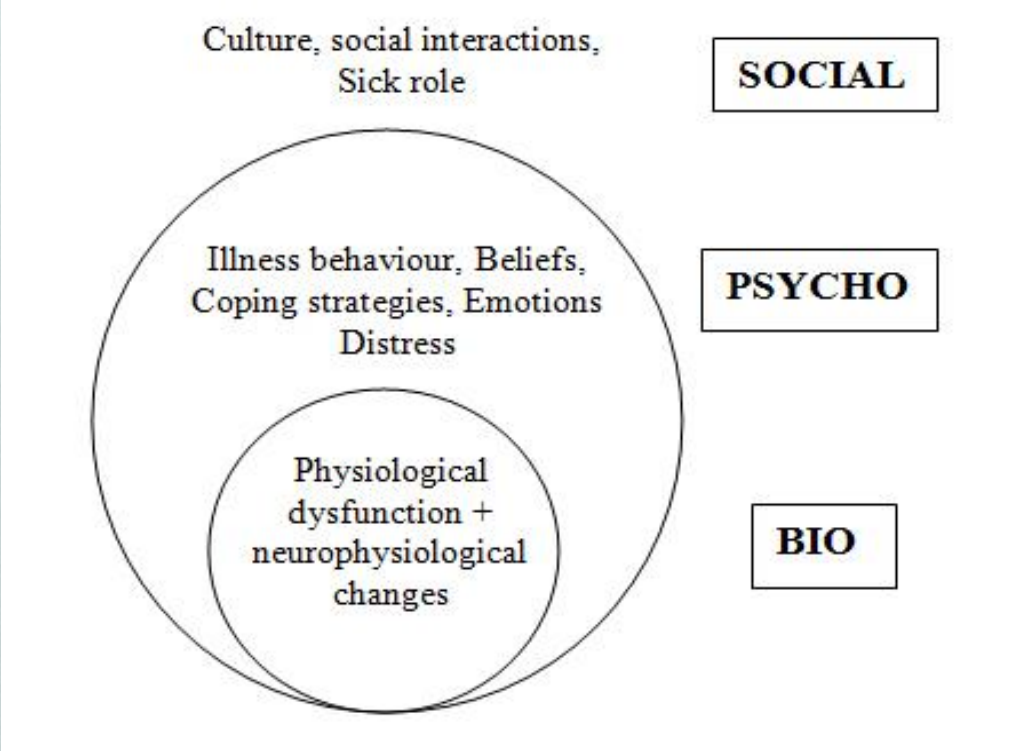


Courtesy of Shana Malone, County Level Strategies. Arizona Criminal Justice Commission, Statistical Analysis Center. www.azcjc.gov

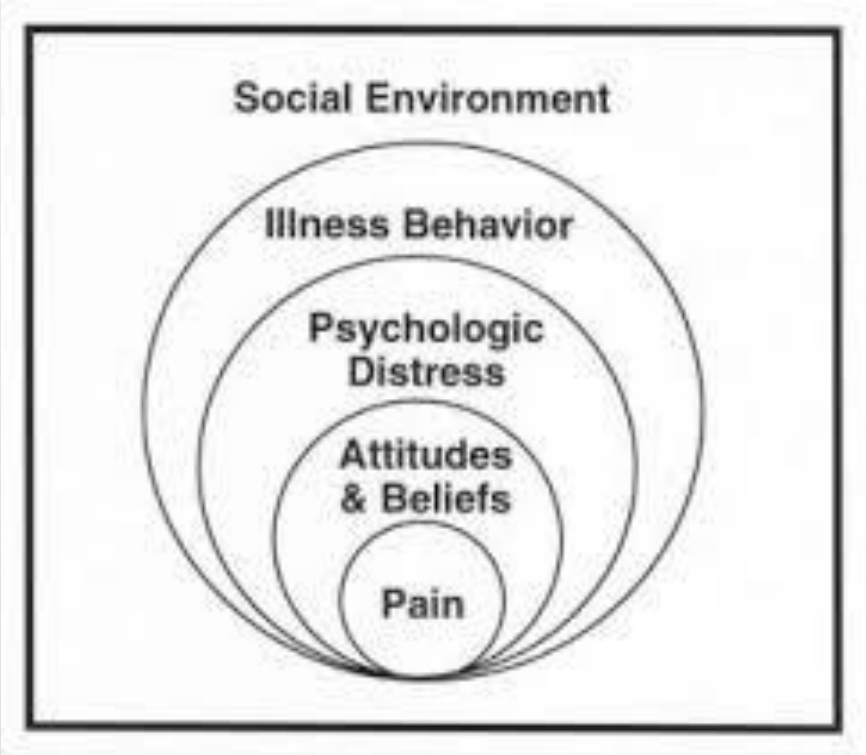
Is There A Better Way To Treat Pain?

- **Objectives:**
  - Review the depressing pain statistics for the U.S.
  - Briefly discuss the government's role in treatment of pain
  - Blow the dust off the biopsychosocial model of care and put it to use
  - Learn about Medical Fitness and Nutritional Coaching programs and their role in treatment of pain
  - Introduce Functional and Regenerative Medicine as the future of treating pain


Physical/Biological
Nociceptive,
injury, trauma, infection,
illness, cancer
nerve damage
Psychological
Impact on:
mood, concentration, sleep, irritability
Negative thoughts, helpessness
Anxiety and depression
Personality aspects:
fears, beliefs, coping skills, trust issues
Persistent Pain
Other Factors
Drug dependence/abuse
Financial difficulties
Cultural barriers
Litigation
Language barriers
Lack of health insurance
Psychosocial
Relationships
Work and employment
Social networks
Isolation



www.lakewoodfrp.com



www99.mh-hannover.de

Biopsychosocial Model of Chronic Pain

CURRENT	FUTURE
MEDICATIONS TARGETING SYMPTOMS	FUNCTIONAL MEDICINE
BARIATRIC SURGERY MEDICAL "WEIGHT LOSS" CLINICS	NUTRITIONAL COACHING MEDICAL FITNESS
PAIN MEDICATIONS (NSAID, OPIOIDS)	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
CORTICOSTEROID INJECTIONS	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
SPINAL SURGERY / FUSIONS	STEM CELL THERAPY
TOTAL JOINT REPLACEMENT	STEM CELL THERAPY
MASK AND MITIGATE SIGNS AND SYMPTOMS	**TREAT ROOT CAUSE TO REBUILD, RESTORE, AND REJUVENATE PATIENT HEALTH**

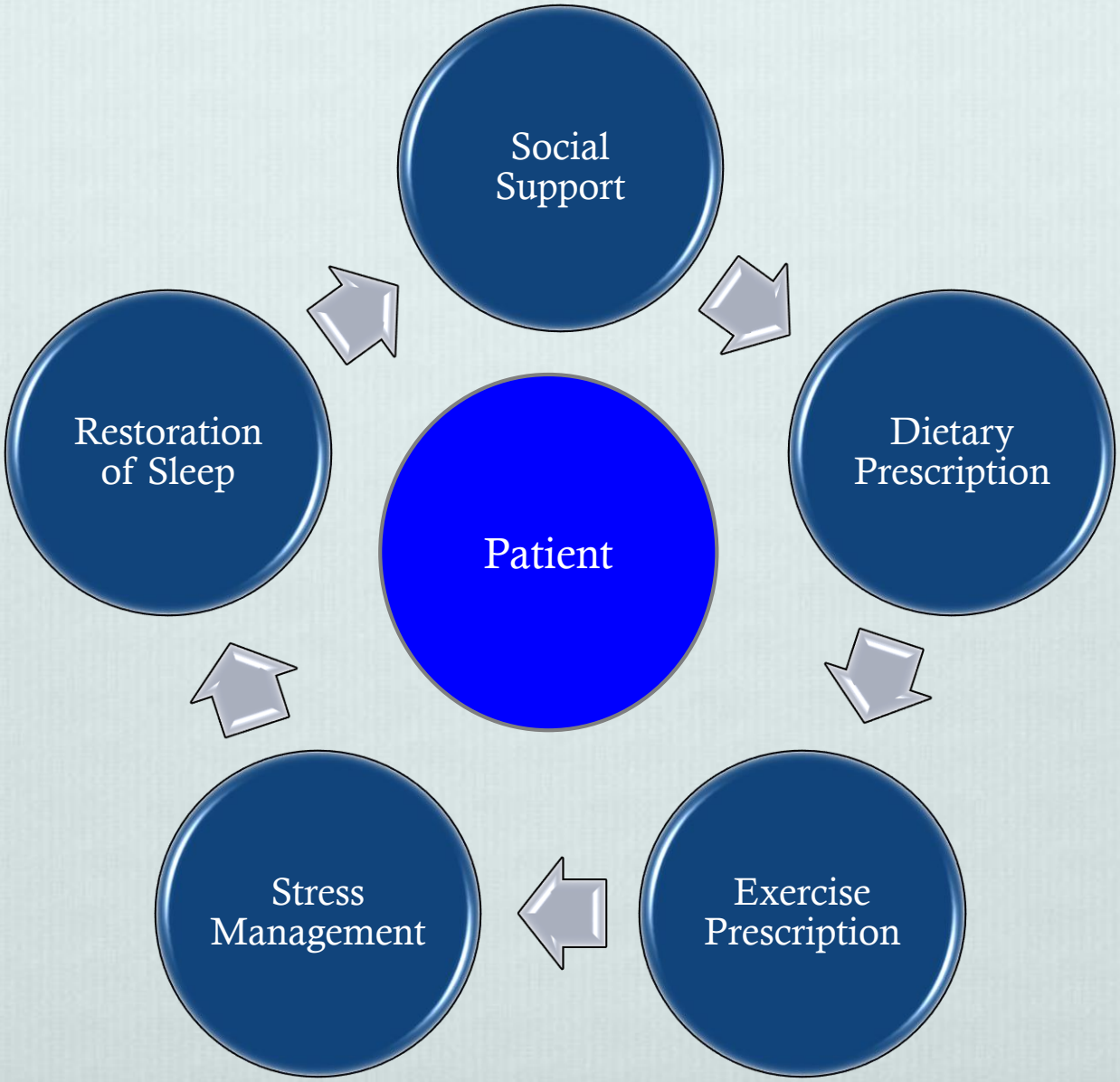
What is Functional Medicine?

- A broad category of medicine that engages both patient and practitioner in a therapeutic partnership that seeks to determine and address underlying causes of disease using a systems-oriented approach.

- The patient is empowered to take ownership for their health and healing.

Core Principles of Functional Medicine

- Biochemical individuality based on genetic and environmental uniqueness.
- Patient-centered rather than disease-centered approach to treatment
- Search for dynamic balance among internal and external factors in a patient's mind, body, and spirit.
- Understanding of web-like interconnections of internal physiological factors
- Identify health as positive vitality and vigorous physiology, not merely the absence of disease
- Promotion of "organ reserve" to enhance the health span of each patient.


Social Support
Dietary Prescription
Exercise Prescription
Stress Management
Restoration of Sleep
Patient

Restoration of Sleep

- Growth hormone (GH) production peaks during sleep.
- Actions of GH
  - Triggers serotonin release within the gut
  - Critical action in the repair of damaged tissue
  - Carbohydrate metabolism
  - Regulation of mood
  - Increases Dehydroepiandrosterone (DHEA) levels, a biologic intermediate of androgen and estrogen sex hormones
- The National Heart, Lung, and Blood Institute recommendation for adults is 7-8 hrs/night.

Stress Management

- The cumulative catabolic load on the immune system from sustained stress will undermine response and effectiveness of treatment.
- Smoking is of course a poor coping strategy.[1] In addition to having no positive benefit on health:
  - May increase inflammatory pain via inhibitory action on leukotriene A4 hydrolase (LTA4H)[2]
  - Systematic review by Leboeuf-Yde et al illustrated most studies showed positive association between smokers and increased back pain.[3]

1. Patterson, Al et al. Smoking cigarettes as a coping strategy for chronic pain. The J of Pain, vol 13, 2012; 285-292
2. Smith, HS.Smoking-Induced Nocieption.Pain Physician 2011; 14:E1-E4.
3. Leboeuf-Yde, C. Smoking and low back pain. A systematic literature review.Spine 1999;24:1463-1470

Social Support and Social Worth

- Many patients have dysfunctional, or nonexistent, support systems.
- Poor job/life satisfaction
- Support through office encounters, email interactions, or social media engagement is critical for success of treatment

CURRENT	FUTURE
MEDICATIONS TARGETING SYMPTOMS	FUNCTIONAL MEDICINE
BARIATRIC SURGERY MEDICAL "WEIGHT LOSS" CLINICS	NUTRITIONAL COACHING MEDICAL FITNESS
PAIN MEDICATIONS (NSAID, OPIOIDS)	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
CORTICOSTEROID INJECTIONS	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
SPINAL SURGERY / FUSIONS	STEM CELL THERAPY
TOTAL JOINT REPLACEMENT	STEM CELL THERAPY
MASK AND MITIGATE SIGNS AND SYMPTOMS	**TREAT ROOT CAUSE TO REBUILD, RESTORE, AND REJUVENATE PATIENT HEALTH**

Diet and Nutritional Coaching

“People are fed by the food industry, which pays no attention to health, and treated by the health industry, which pays no attention to food.”

– Wendell Berry

"Specific diets can support the reduction in inflammation."

(Reference: Stendell-Hollis NR et al. J Womens Health. 2012)

"Dietary inflammation can worsen diabetes and microvascular complications such as neuropathy."

(Reference: Nguyen DV et al. Front Endocrinology. 2012)

"Diet can lower concentrations of markers of coronary risk."

(Reference: Guallar-Castillon P et al. Atherosclerosis. 2012)

"Tendons and ligaments can be damaged by metabolic disorders worsened by poor diet."

(Reference: Abate M et al. Rheumatology. 2013)

"Nutritional interventions can prevent and treat osteoarthritis."

(Reference: Lopez HL. PMR. 2012)

"Manipulation of dietary fatty acids can decrease pain associated with rheumatoid arthritis."

(Reference: Kremer JM et al. Lancet. 1985)

Metabolic Syndrome Markers

- Fasting blood sugar
  - < 100 mg/dL
- Triglycerides
  - < 150 mg/dL
- HDL
  - Women >50 mg/dL
  - Men >40 mg/dL
- BP
  - <130/85
- Waist circumference
  - Women < 35”
  - Men < 40”

Pro-Inflammatory Markers

Anthropometrics

- Body Mass Index
  - Normal 18.5-24.9
  - Overweight 25-29.9
  - Obese >30
- Waist/hip ratio for women (risk factor for DM)
  - Low risk < 0.80
  - mod risk 0.81-0.85
  - high risk > 0.85
- Waist/hip ratio for men (risk factor for DM)
  - Low risk < 0.95
  - mod risk 0.96-1.0
  - high risk > 1.0

Labs

- hs-CRP (mg/L)
  - Normal < 1.o
  - moderate 1.0-3.0
  - high > 3.0
- 25-Hydroxy Vitamin D
  - Goal > 40 ng/mL
- Fasting triglycerides
  - < 90 mg/dL
- 2-hour postprandial glucose
  - Normal < 140 mg/dL
  - Prediabetes 140-190 mg/dL
  - Diabetes > 200 mg/dL

Seaman DR. An Anti-Inflammatory Diet for Pain Patients. Prac Pain Mgmt. Nov 2012

Reactions to Food = Dietary Injuries

- Allergy
  - Involves immune system
  - Antibodies form towards offending food (and other foods through cross-reactivity)
- Intolerance
  - Does not involve immune system directly
  - Can involve enzyme deficiency
- Sensitivity
  - Does not involve immune system directly
  - Food causes negative reaction of some type

Symptoms of Repetitive Dietary Injury

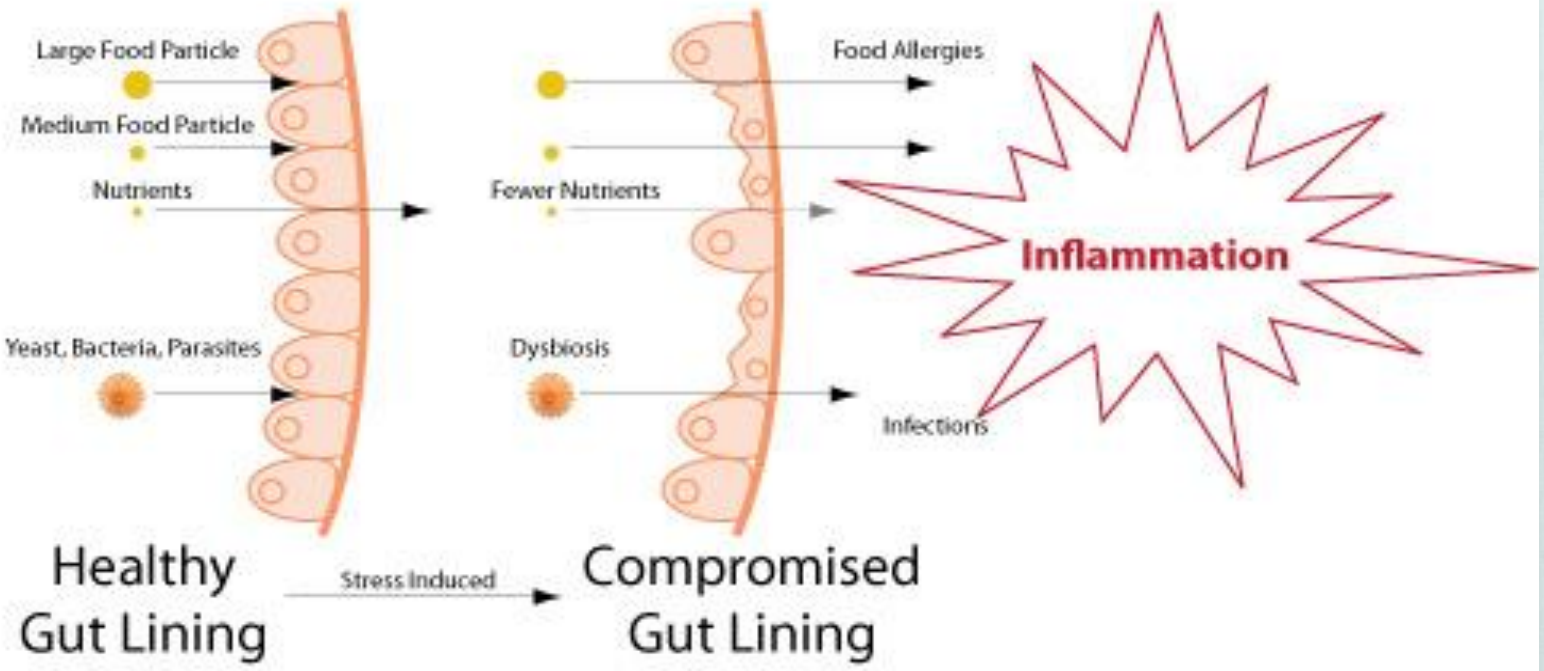
- Digestive problems
- Slow healing/recovery
- Chronic pain
- Fatigue
- Decreased libido
- Poor sleep quality
- Irritability
- Anxiety
- Depression
- Cognitive dysfunction

Pathophysiology of a Dietary Injury

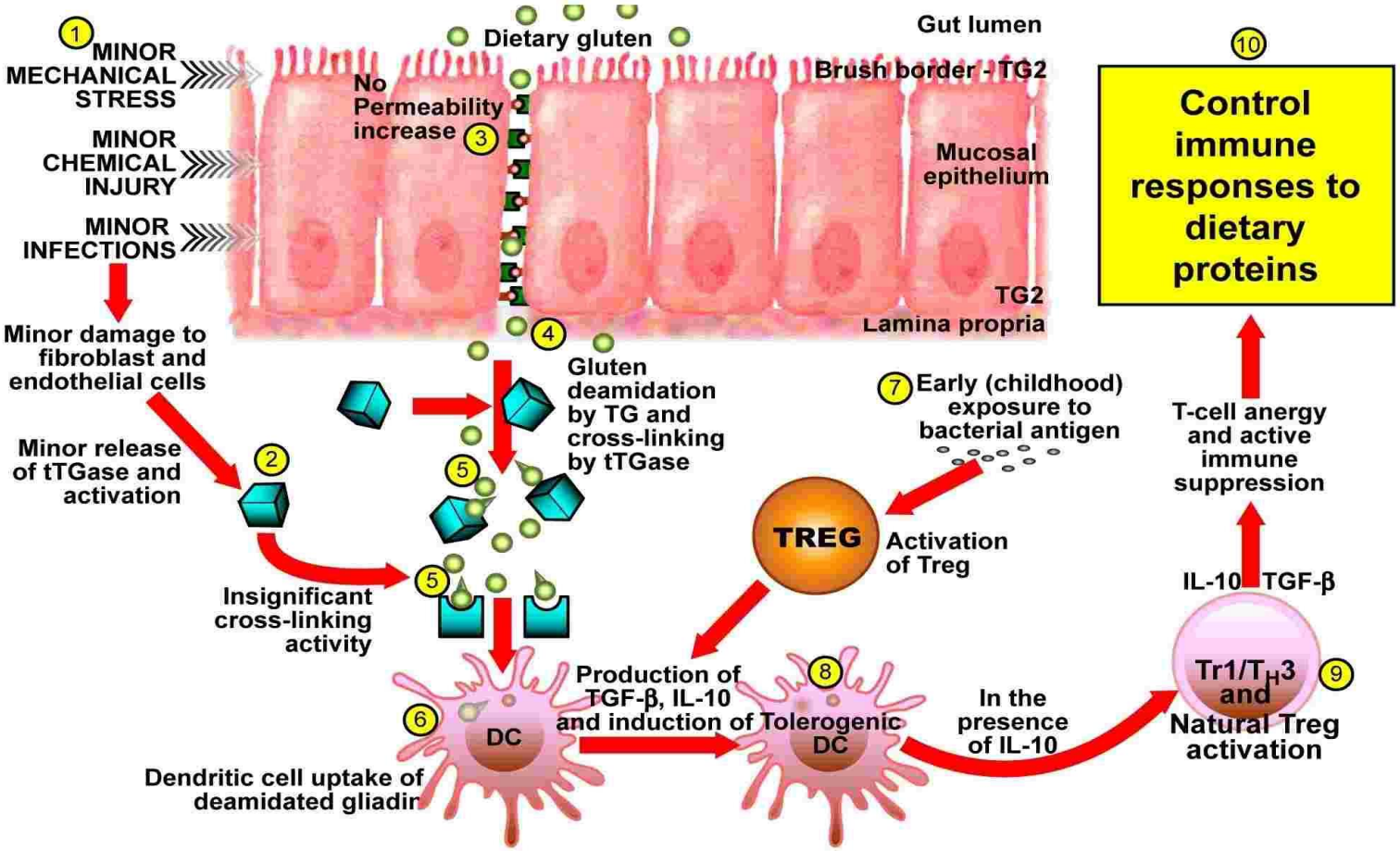
What's really going on under the hood?

- Intestinal Permeability
  - Tight cellular junctions of the gut lining become compromised
  - Zonulin upregulation
- Dysbiosis
  - Food is not digested effectively
  - Balance of good bacteria in the gut is upset
  - Overgrowth of bacteria and yeast
  - Increased permeability of the gut lining
  - Larger undigested food particles (containing toxins), bacteria, viruses, and yeast are allowed entry to the bloodstream.

Food Allergy and Leaky Gut Inflammation



Stress deteriorates the gastrointestinal lining over time causing Leaky Gut. This triggers additional food allergies and inflammation.

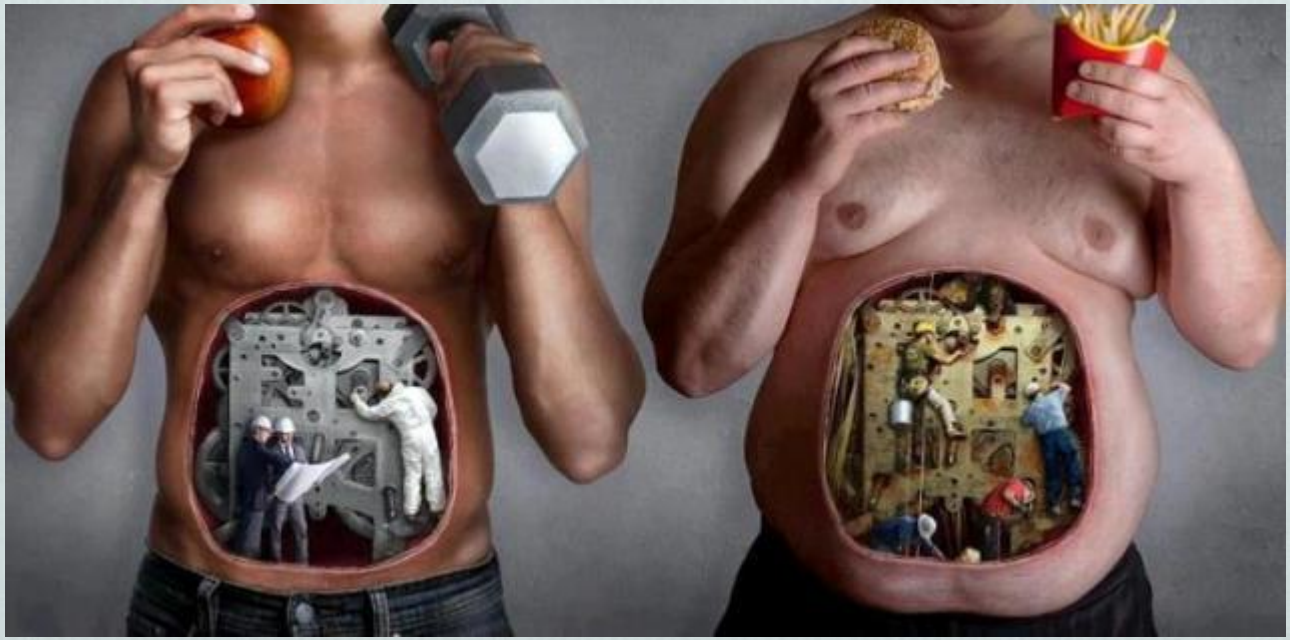


Cellular and molecular induction of immune tolerance to dietary proteins (gliadin).

Healthy Gut

A Gut Feeling

- Nearly 95% of serotonin is produced in the gut via enterochromaffin cells
- A healthy gut effects how we feel and function.



The Gut: Your Second Brain

- Role of serotonin:
  - Release of Growth Hormone (GH)
  - Mood regulation
  - Appetite
  - Sleep quality
  - Memory and Learning
- Role of GH:
  - Repair of damaged muscle tissue
  - Carbohydrate metabolism
  - Regulation of mood
  - Increases DHEA (dehydroepiandrosterone)
  - Sleep quality

Immune Response to Eating

- Foods that trigger the original dietary injury, as well as others not involved, can be seen as foreign invaders.
- Immune and non-immune system mediated reactions can occur with repeat exposure
- Cyclically, the gut function and immune system become more compromised
- The body has a limited capacity to extract vital nutrients from even healthy foods being consumed
- Systemic inflammation develops

One man's food is another man's poison.

-Lucretius

Allergenic and Inflammatory foods

Account for 90% of food allergies

- Milk
- Wheat gluten
- Eggs
- Peanuts
- Tree nuts
- Fish
- Crustacean shellfish
- Soybeans

Allergenic and Inflammatory foods

Most Inflammatory Foods

- Refined Foods (C.R.A.P.)
- Sugar
- Dairy
- Wheat gluten
- Soy

Allergenic foods

- Trigger immune and non-immune system mediated reactions increasing inflammation within the gut
- Autoimmune response may develop
- Result - widespread inflammation within the GI system, eventually having a more systemic effect on the entire body

Fatty acid deficiency and health

- An overabundance of omega-6 FA's, or a deficiency in omega-3 FA's can promote inflammation.[1]
- Traditional "western diet" can contain a ratio of 20-30:1 omega-6 to omega-3.[2,3]
- Ideally the ratio should be *no more than 4:1*, and ideally 1:1 for optimal health. [4,5]

1. Kremer JM, et al. Effects of manipulation of dietary fatty acids on clinical manifestations of rheumatoid arthritis. Lancet. 1985
2. Domei T, et al. Ratio of serum n-3 to n-6 polyunsaturated fatty acids and the incidence of major adverse cardiac events in patients undergoing percutaneous coronary intervention. Circ J. 2012
3. Kashiyama T, et al. Relationship between coronary artery plaque vulnerability and serum n-3/n-6 polyunsaturated fatty acid ratio. Circ J. 2011
4. Simoppulus AP. The importance of omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. Exp Biol Med. 2008
5. Sierra S, et al. Dietary fish oil n-3 fatty acids increase regulatory cytokine production andexert anti-inflammatory effects in two murine models of inflammation. Lipids. 2006

The Skinny on Fatty Acids(FA's)

- Composed of triglycerides or phospholipids
- Named according to the number of carbon double bonds
  - Saturated – no carbon double bonds and so are *saturated* with hydrogen atoms
  - Monounsaturated – contain one carbon double bond
  - Polyunsaturated – contain multiple carbon bonds
- FA's vary in length of carbon tail
  - Short chain FA – less than 6 carbons
  - Medium chain FA – 6-12 carbons
  - Long chain FA – 13 carbons
  - Very long chain FA – More than 13 carbons

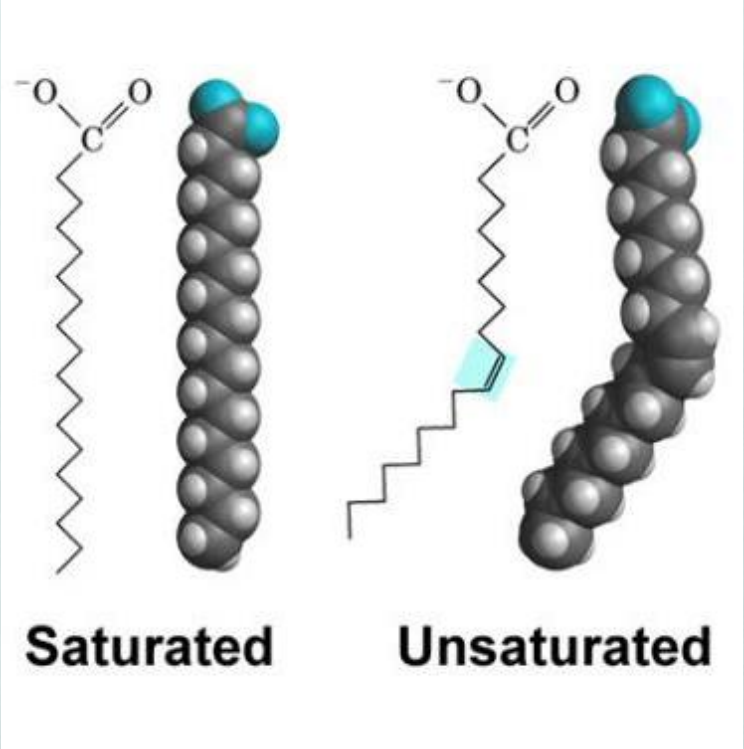
The Skinny on Fatty Acids

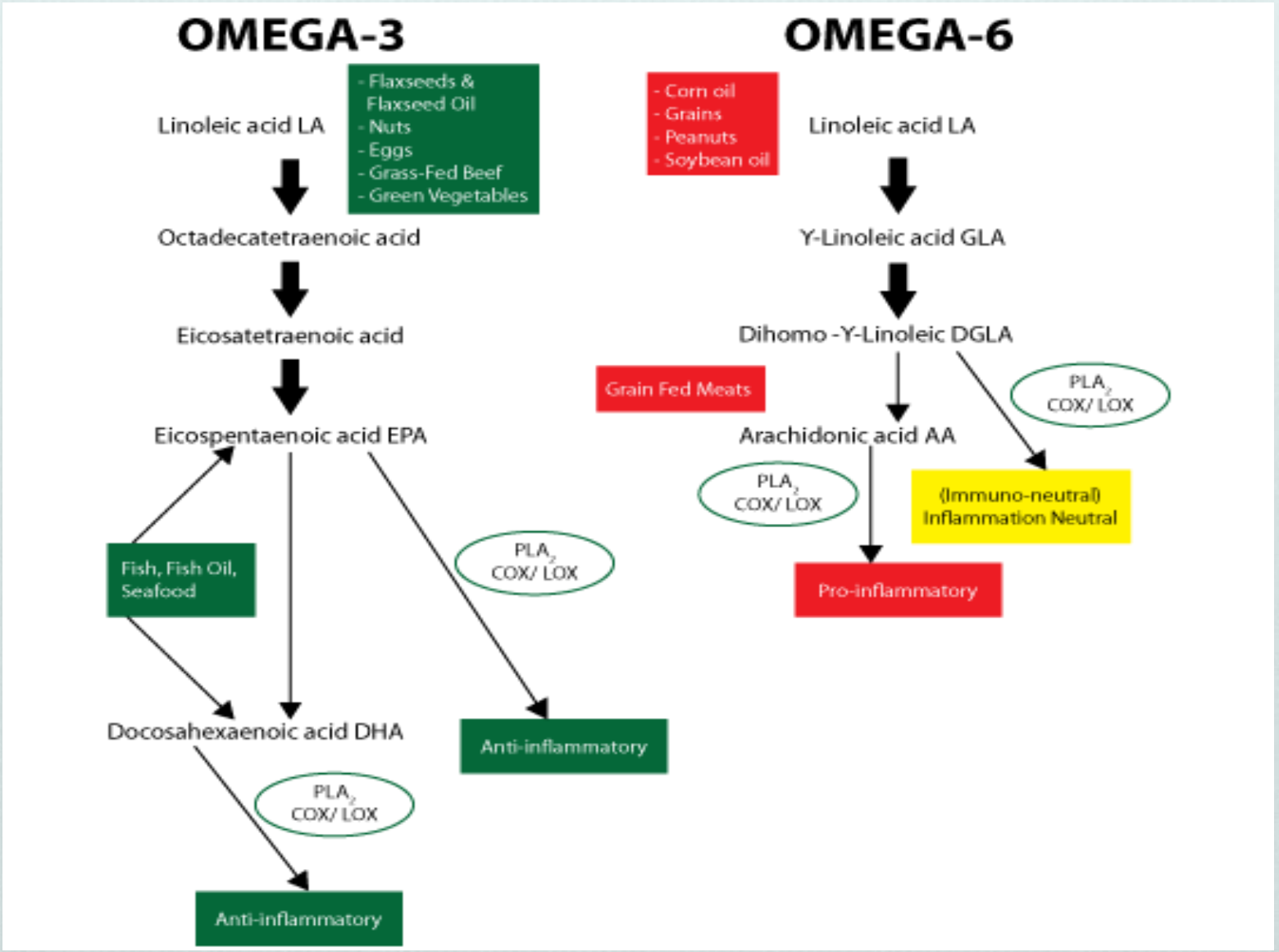
- PUFA's are further classified according to the position of the last double bond
  - Long chain, or omega-3 FA (n-3)
  - Functional, or omega-6 FA (n-6)
  - omega-9 FA (n-9)

- Under heat, saturated fats are much more stable than PUFAs
  - Translation – healthier and less inflammatory
  - Use saturated fats (coconut oil, butter from grass fed cows, and red palm oil) for high temperature cooking

The Skinny on Fatty Acids

- Omega-9
  - Nuts, Olive oil, Avocado
- Omega-6
  - Vegetable Oils (soybean, safflower, sunflower, corn)
  - Nuts and seeds
  - Grains
  - Grain-fed meat
  - Soy
- Omega-3
  - Fish oil, krill oil, algae oil
  - Flaxseed, nuts
  - Eggs
  - Grass-fed beef




OMEGA-3
- Flaxseeds & Flaxseed Oil
- Nuts
- Eggs
- Grass-Fed Beef
- Green Vegetables
Linoleic acid LA
Octadecatetraenoic acid
Eicosatetraenoic acid
Eicospentaenoic acid EPA
Fish, Fish Oil, Seafood
PLA2 COX/ LOX
Docosahexaenoic acid DHA
Anti-inflammatory
PLA2 COX/ LOX
Anti-inflammatory
OMEGA-6
- Corn oil
- Grains
- Peanuts
- Soybean oil
Linoleic acid LA
Y-Linoleic acid GLA
Dihomo -Y-Linoleic DGLA
Grain Fed Meats
PLA2 COX/ LOX
Arachidonic acid AA
PLA2 COX/ LOX
(Immuno-neutral) Inflammation Neutral
Pro-inflammatory

FA's and the "evolution" of OA

- Normal cartilage should have a higher ratio of n-9 than n-6.[6]
- Over 35 years ago, Bonner et al. demonstrated that the ratio of fatty acids within cartilage changes with age.[7]
- Comparisons of osteoporotic and osteoarthritic cancellous bone show very different n-6 composition.[8]
  - OA – very high
  - OP – very low

6. Adkisson HD et al. Unique fatty acid composition of normal cartilage:.FASEB J. 1991
7. Bonner VM et al. Changes in the lipids of human cartilage with age. Arthritis Rheum. 1975
8. Plumb MS, Aspden RM. High levels of fat and (n-6) fatty acids in cancellous bone in osteoarthritis. Lipids Health Dis. 2004

Radicalization of OA

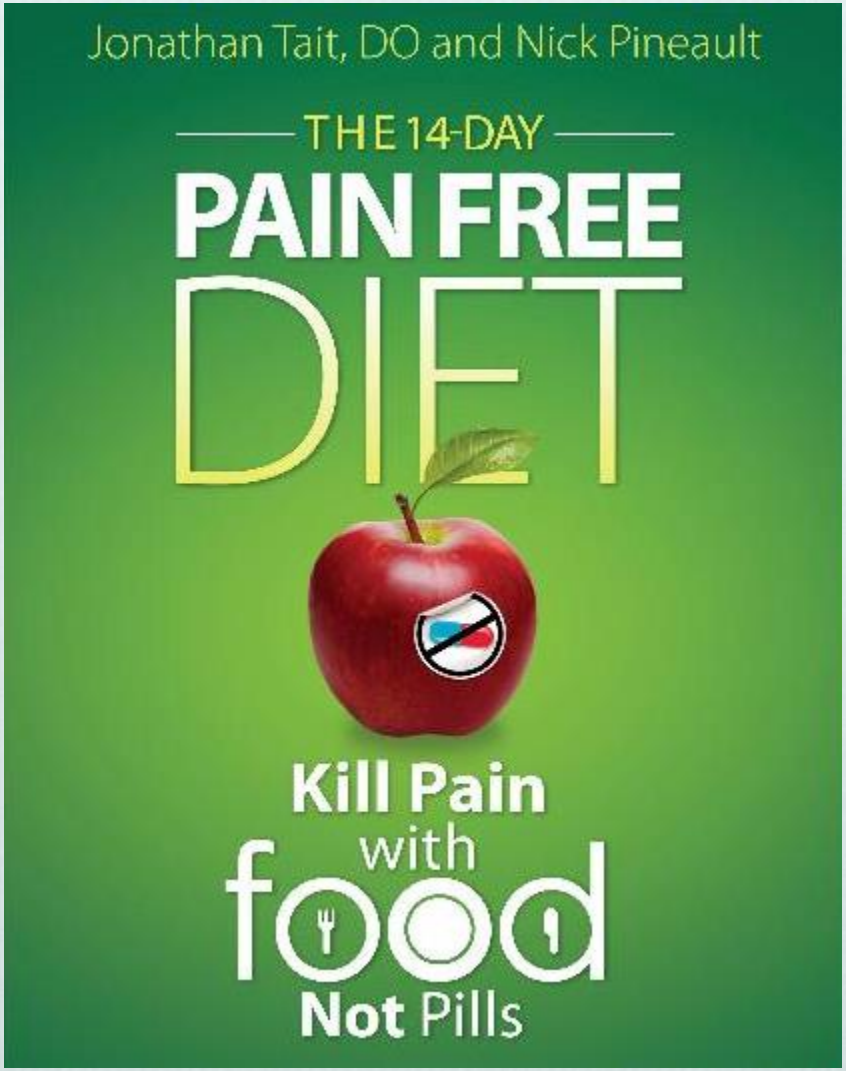
- Oxidative stress has a major role.[9]
- Decreased joint fluid antioxidants in OA joints. [10]
- FA's in fish oil (EPA and DHA) are showing promise in treatment of OA and other chronic pain syndromes. [11]

9. Goldring MB, Otero M, Tsuchimochi K, et al. Defining the roles of inflammatory and anabolic cytokines in cartilage metabolism. Ann Rheum Disease. 2008
10. Regan EA, et al. Joint fluid antioxidants are decreased in osteoarthritic joints. Osteoarthritis Cartilage. 2008
11. Ramsden CE, et al. Do omega-6 and trans fatty acids play a role in complex regional pain syndrome? A pilot study. Pain Med. 2010

Big-Boned or Bound for Bone Problems?

- Severity of OA can be accelerated by mechanical overload.
- Obesity, as a component of metabolic syndrome, is contributing directly to the progression of joint disease in OA.[12,13]
- Obesity itself has a bearing on the amount of reported pain, often very disproportionate to duration of disease or severity of radiographic findings.[14]

12. Scotece M, Conde J, Gomez R, et al. Beyond fat mass: Exploring the role of adipokines in rheumatic diseases. Sci World J. 2011
13. Otero, M et al. Leptin, a metabolic hormone that functions as a pro-inflammatory adipokine. Drug New Prospect 2006
14. Stone, AA, Broderick JE. Obesity and pain are associated in the United States. Obesity. 2012



www.thepainfreediet.com

Phase 1 -Simplify The Diet by Removing

-CRAP foods

- Inflammatory foods

-Potentially allergenic foods

- Genetically modified (GM) foods

Phase 2 - Optimize the Diet

- Organic sources of the "dirty dozen"

- Eating ample amounts of the "clean 15"

Phase 3 - Systematic Reintroduction

- Healthy foods

- Potentially allergenic foods

Phase 2: Optimize with "Healthy Foods"

- **The Dirty Dozen**
  - Apples
  - Apricots
  - Cantaloupe (from Mexico)
  - Celery
  - Cherries
  - Cucumbers
  - Grapes
  - Green beans
  - Peaches
  - Peppers – red and green bell
  - Spinach
  - Strawberries
- **The Clean 15**
  - Asparagus
  - Avocadoes
  - Cabbage
  - Cantaloupe
  - Corn (Non-GM)
  - Eggplant
  - Grapefruit
  - Kiwi
  - Mango
  - Onions, sweet
  - Pineapples
  - Peas, sweet
  - Potatoes, sweet, yams
  - Watermelon

Monitor: Signs and Symptoms

- General – Fatigue, malaise
- Joints – Increased inflammation, pain, swelling, or stiffness
- GI – stomach upset, heartburn, reflux, bloating, nausea, diarrhea
- Neurological – headaches, mood changes, fatigue, sleep disturbance
- HEENT – nasal congestion, thickened mucus, runny nose, watery eyes

Let food be thy medicine, and let thy medicine be food.
- Hippocrates

"Specific diets can support the reduction in inflammation."
(Reference: Stendell-Hollis NR et al. J Womens Health. 2012)

"Dietary inflammation can worsen diabetes and microvascular complications such as neuropathy."
(Reference: Nguyen DV et al. Front Endocrinology. 2012)

"Diet can lower concentrations of markers of coronary risk."
(Reference: Guallar-Castillon P et al. Atherosclerosis. 2012)

"Tendons and ligaments can be damaged by metabolic disorders worsened by poor diet."
(Reference: Abate M et al. Rheumatology. 2013)

"Nutritional interventions can prevent and treat osteoarthritis."
(Reference: Lopez HL. PMR. 2012)

"Manipulation of dietary fatty acids can decrease pain associated with rheumatoid arthritis."
(Reference: Kremer JM et al. Lancet. 1985)

Diet is a BIG deal

- Mounting research is showing that our food sources may be contributing to the escalation of disease in the U.S.
- There is a link between dietary consumption, inflammation, and pain.
- Skin allergy testing (IgE, acute phase) is insufficient to determine the reactivity of foods.
- Each individual must take a systematic approach to determine potentially problematic foods

One quarter of what you eat keeps you alive, the other three-quarters keeps your doctor alive.

– Ancient Egyptian Proverb

CURRENT	FUTURE
MEDICATIONS TARGETING SYMPTOMS	FUNCTIONAL MEDICINE
BARIATRIC SURGERY MEDICAL "WEIGHT LOSS" CLINICS	NUTRITIONAL COACHING MEDICAL FITNESS
PAIN MEDICATIONS (NSAID, OPIOIDS)	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
CORTICOSTEROID INJECTIONS	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
SPINAL SURGERY / FUSIONS	STEM CELL THERAPY
TOTAL JOINT REPLACEMENT	STEM CELL THERAPY
MASK AND MITIGATE SIGNS AND SYMPTOMS	**TREAT ROOT CAUSE TO REBUILD, RESTORE, AND REJUVENATE PATIENT HEALTH**

Metabolic Syndrome Markers

- Fasting blood sugar
  - < 100 mg/dL
- Triglycerides
  - < 150 mg/dL
- HDL
  - Women >50 mg/dL
  - Men >40 mg/dL
- BP
  - <130/85
- Waist circumference
  - Women < 35”
  - Men < 40”

Pro-Inflammatory Markers

Anthropometrics

- Body Mass Index
  - Normal 18.5-24.9
  - Overweight 25-29.9
  - Obese >30
- Waist/hip ratio for women (risk factor for DM)
  - Low risk < 0.80
  - mod risk 0.81-0.85
  - high risk > 0.85
- Waist/hip ratio for men (risk factor for DM)
  - Low risk < 0.95
  - mod risk 0.96-1.0
  - high risk > 1.0

Labs

- hs-CRP (mg/L)
  - Normal < 1.o
  - moderate 1.0-3.0
  - high > 3.0
- 25-Hydroxy Vitamin D
  - Goal > 40 ng/mL
- Fasting triglycerides
  - < 90 mg/dL
- 2-hour postprandial glucose
  - Normal < 140 mg/dL
  - Prediabetes 140-190 mg/dL
  - Diabetes > 200 mg/dL

Seaman DR. An Anti-Inflammatory Diet for Pain Patients. Prac Pain Mgmt. Nov 2012

What Is Medical Fitness?

- Medically directed and supervised exercise and nutritional coaching programs
  - Comprehensive intake
  - Baseline labs, EKG, stress testing
  - Metabolic testing (Indirect calorimeter)
  - Functional Movement Screen (FMS)
  - Nutritional coaching

FMS
Functional Movement Systems

What Is Medical Fitness?

- Mapping out the road to optimal health, vitality and function.
- Social Support
- Classes
  - Individual
  - Small group
  - Bootcamps

Exercise – ACSM Recommendations

- Cardiorespiratory Fitness
  - Adults - 150 minutes of moderate-intensity exercise per week
  - Continuous session and multiple shorter sessions (of at least 10 minutes) are both acceptable to accumulate desired amount of daily exercise
  - Gradual progression of duration, frequency, and intensity is recommended to decrease injury risk
  - If unable to meet goal of 150 minutes, any activity is still beneficial

American College of Sports Medicine – Physical Activity Guidelines for Americans

Exercise – ACSM Recommendations

- Resistance Exercise
  - Major muscle groups should be trained 2-3 days/week
  - Light intensity is best for older person starting exercise
  - 2-4 sets of 8-10 repetitions for each exercise will improve strength and power
  - 48 hour recovery interval between strength workouts

American College of Sports Medicine – Physical Activity Guidelines for Americans

Exercise – ACSM Recommendations

- Flexibility
  - Adults should perform flexibility exercises 2-3 days/week
  - Each stretch held for 10-30 seconds, repeated 2-4 times, accumulating 60 seconds per stretch
  - Combination of static, dynamic, ballistic and Proprioceptive Neuromuscular Facilitation (PNF) stretches are all effective
  - Most effective after warm-up or incorporated into progressive warm-up prior to longer duration aerobic or strength training workouts.

American College of Sports Medicine – Physical Activity Guidelines for Americans

Exercise – ACSM Recommendations

- Neuromotor Exercise (Functional Fitness Training)
  - 2-3 days/week, 20-30 minutes
  - Involves motor skills (balance, agility, coordination, and gait), proprioceptive exercise training (tai chi or yoga) for fall prevention and to improve physical function

American College of Sports Medicine – Physical Activity Guidelines for Americans

Exercise ≠ Torture

- Should be enjoyable to limit cortisol elevation that can negate benefits*

Lovallo WR, et al. Cortisol responses to mental stress, exercise, and meals following caffeine intake in men and women. Pharmacol Biochem Behav. 2006 March; 83(3): 441–447.

CURRENT	FUTURE
MEDICATIONS TARGETING SYMPTOMS	FUNCTIONAL MEDICINE
BARIATRIC SURGERY MEDICAL "WEIGHT LOSS" CLINICS	NUTRITIONAL COACHING MEDICAL FITNESS
PAIN MEDICATIONS (NSAID, OPIOIDS)	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
CORTICOSTEROID INJECTIONS	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
SPINAL SURGERY / FUSIONS	STEM CELL THERAPY
TOTAL JOINT REPLACEMENT	STEM CELL THERAPY
MASK AND MITIGATE SIGNS AND SYMPTOMS	**TREAT ROOT CAUSE TO REBUILD, RESTORE, AND REJUVENATE PATIENT HEALTH**

The Downhill Slide of Life?

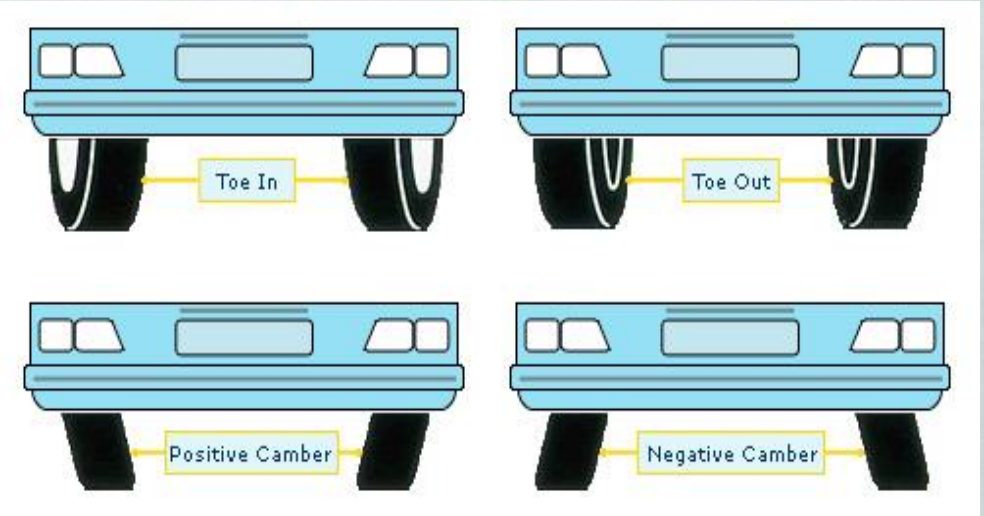
- Why do we lose function and hurt as we age?
  - Environmental Factors (nurture)
  - Genetic Factors (nature)
  - Lack of scheduled regular maintenance (nurture)
- What is the underlying problem?
  - Cellular Health
    - Nutritional Deficiencies
    - Lack of Exercise or Fitness
    - Hormonal Imbalances
  - Joint Integrity/Stability/Mobility
    - Stability
    - Articulation
    - Neuromuscular
    - Symmetry

Service Engine Soon

- For many patients pain is the signal light on the dashboard that has been on for several years
  - Treatment Option #1 – The “Pop a pill”, “Pop my back”, “Shoot it up” approach
  - Treatment Option #2 – Determine diagnosis, deliver appropriate restorative treatment, and then educate patient on sustainable maintenance plan

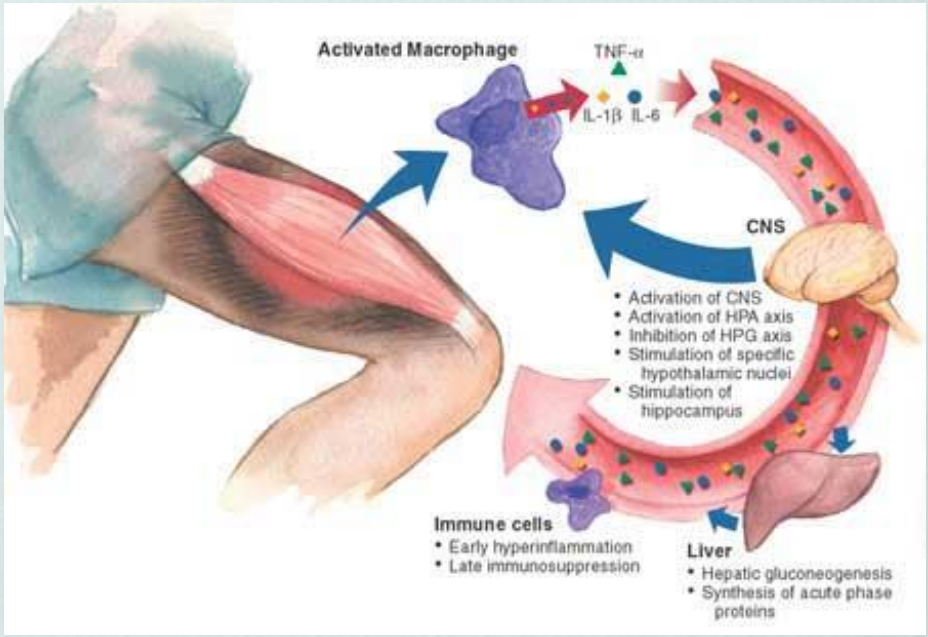
Symmetry in Form and Function

- Alignment
- Kinetic chain
- Gait and Mobility dysfunction
- Balance and Coordination
- Neuromuscular Control
- Restoration of Function
  - OMT
  - PT
  - Corrective Exercise
  - Movement Maintenance



Immune System and Inflammation

- Immune system response:
  - Injury*
  - Emotional Trauma
  - Infections
  - Toxins*
  - Allergy*
  - Total Nutritional State*



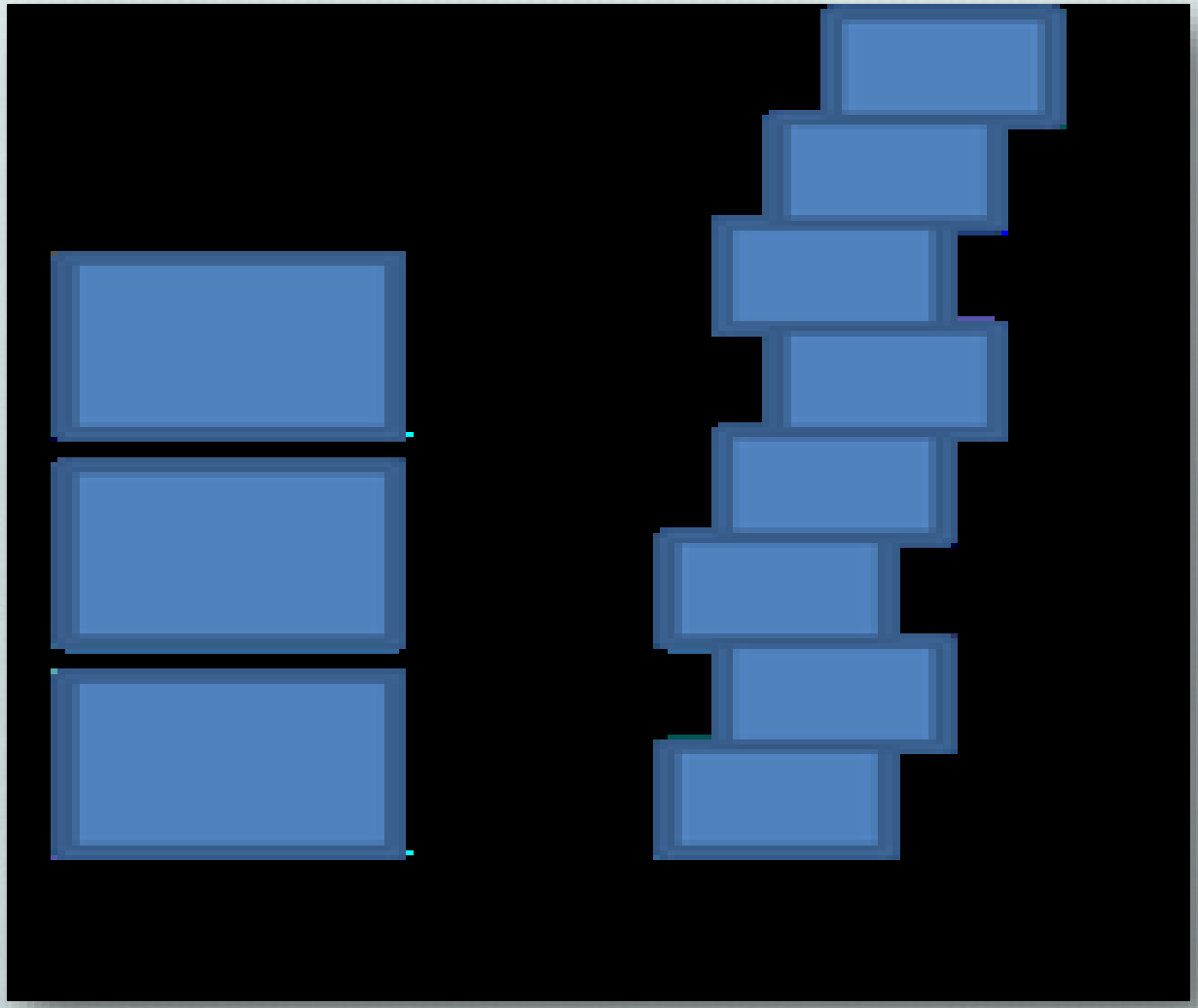
www.mdsystems.com

*Significantly impacted by dietary choices

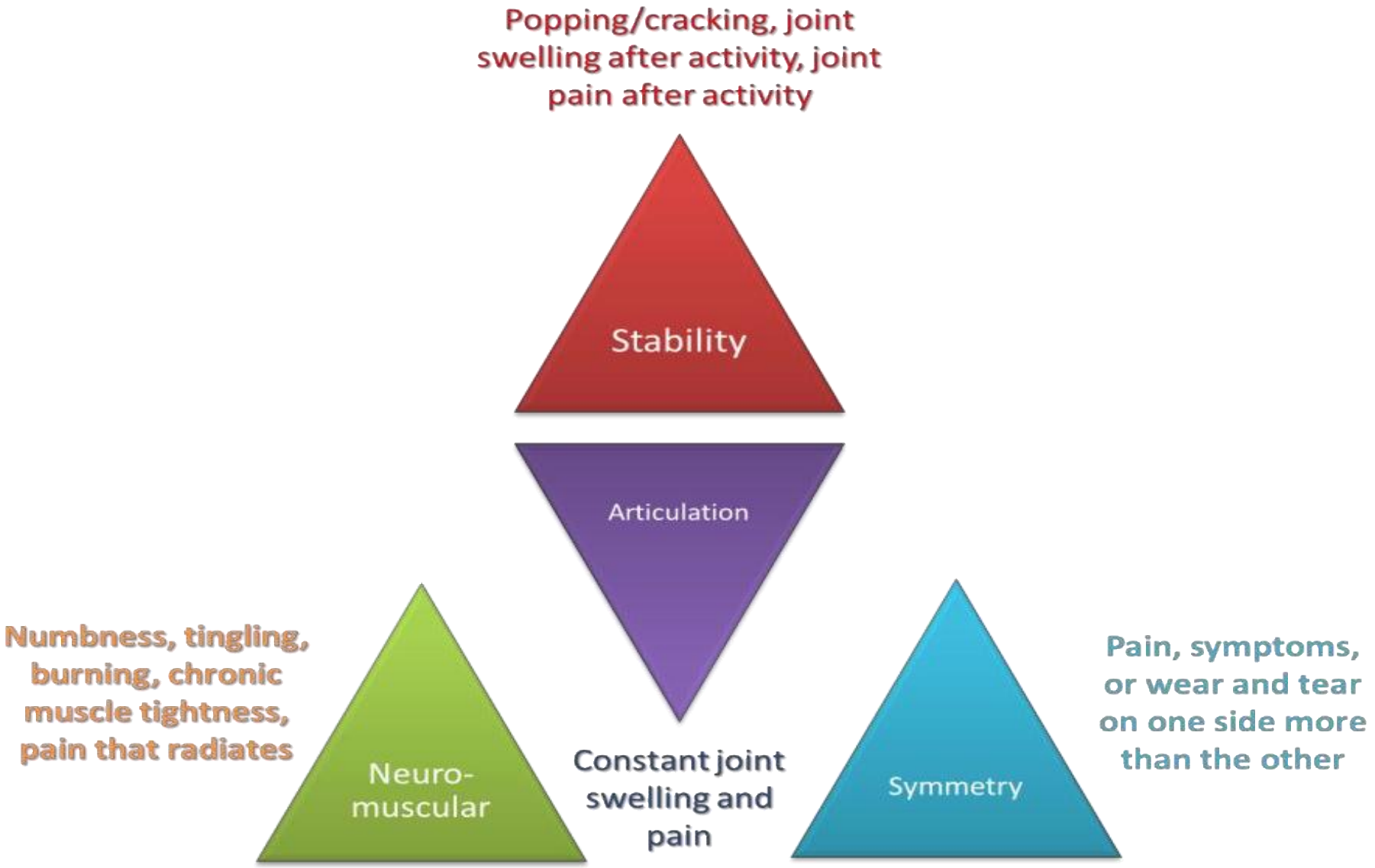
Form and Function

- Stability
- Articulation
- Neuromuscular Control
- Symmetry

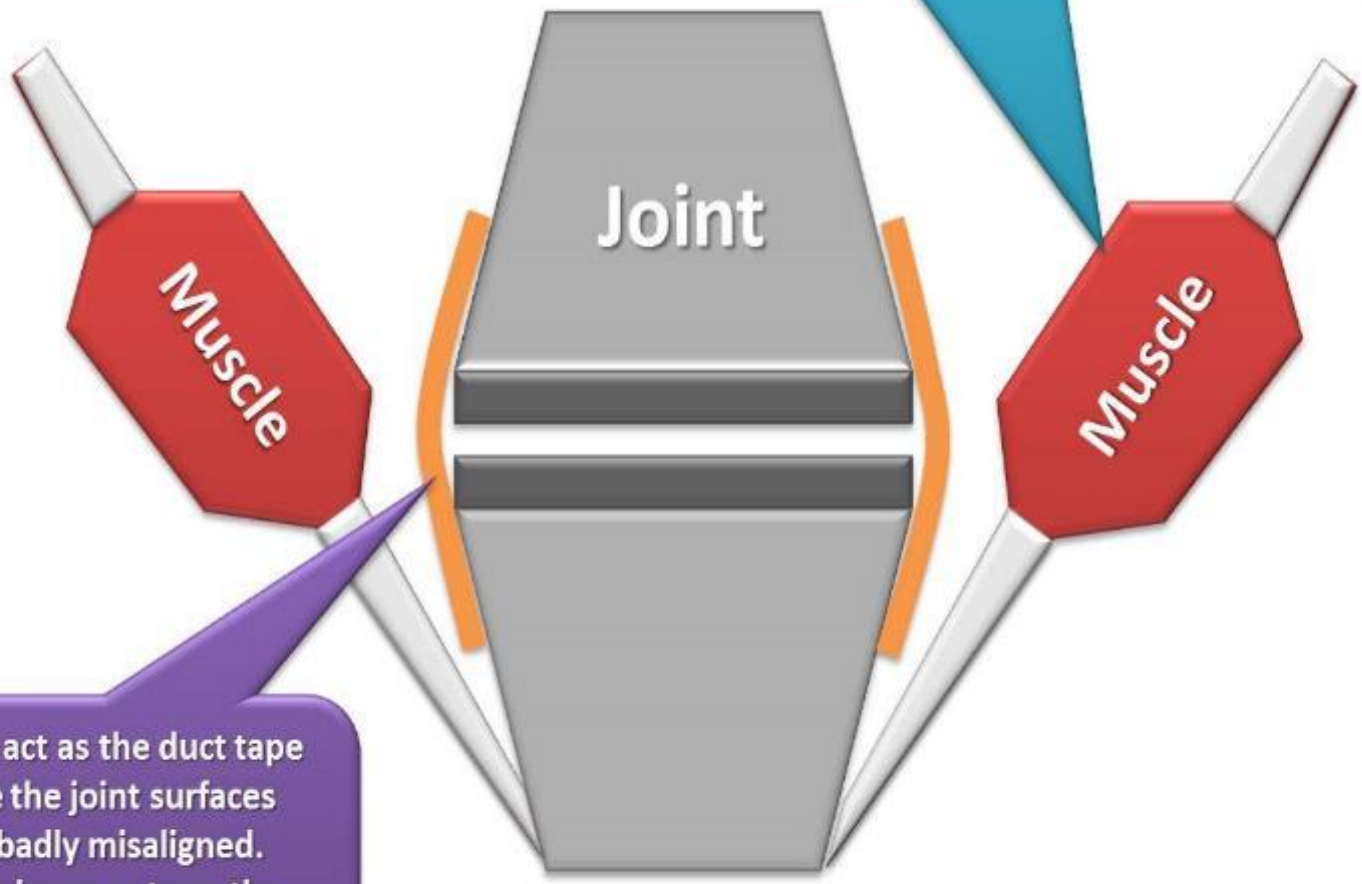
Which is more stable?



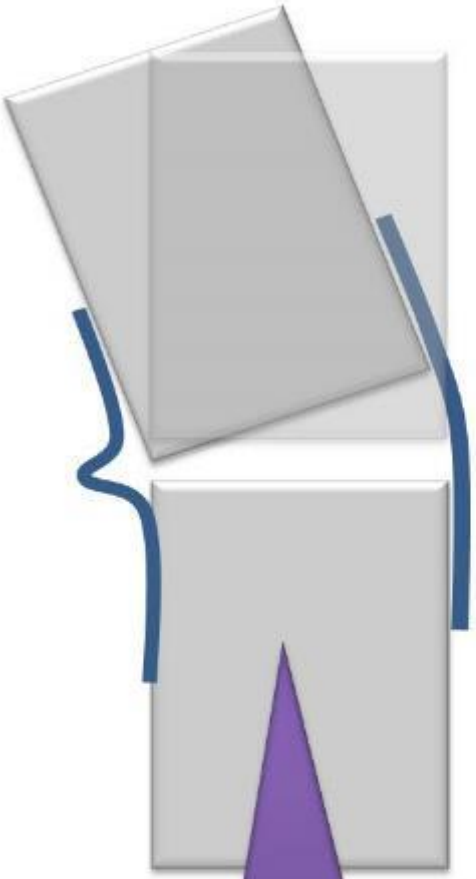
Theory of Functional Degeneration



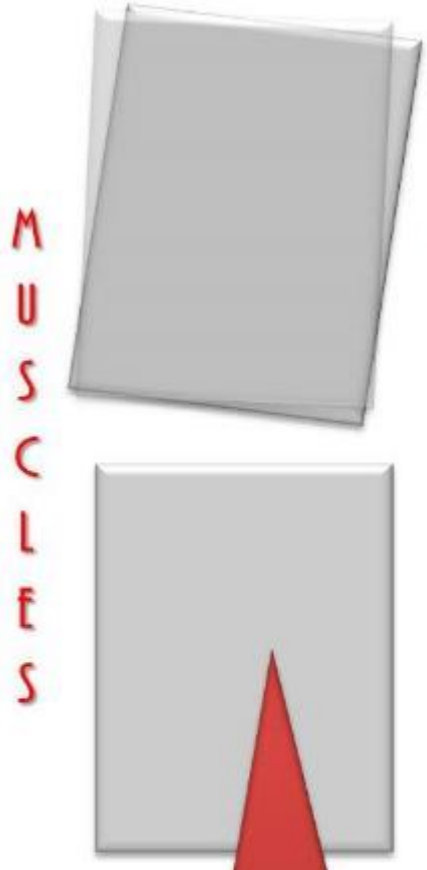
Stability


The muscles help keep the joint properly aligned during movement. This happens with micrometer precision. Problems in the muscles such as trigger points lead to bad stability and increased joint wear.
Joint
Muscle
Muscle
The ligaments act as the duct tape that male sure the joint surfaces can't become badly misaligned. When they are loose or torn, the joint undergoes much more wear and tear.

Muscle vs. Ligament Stability



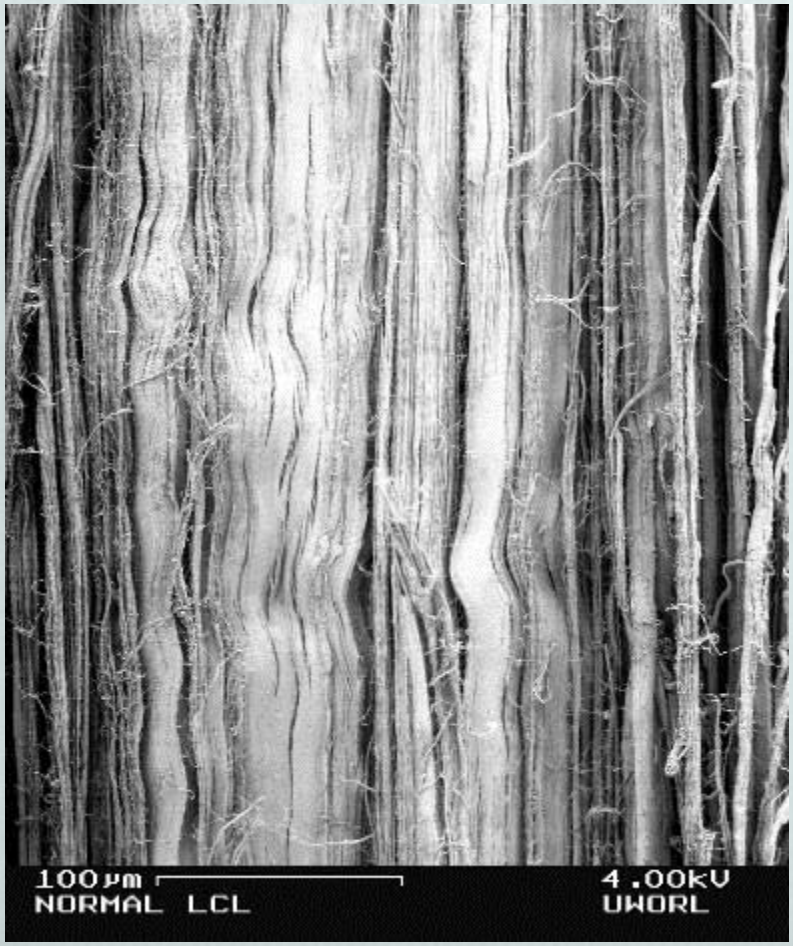
Ligaments keep the joint from moving too badly out of alignment. They kick in when the joint goes to the end limits of motion.



Muscles help make the small adjustments that keep the joint precisely aligned with movement.

Ligaments

Normal Ligament



Damaged Ligament

Spinal Instability

Injury, Aging or Overuse

↓

INSTABILITY

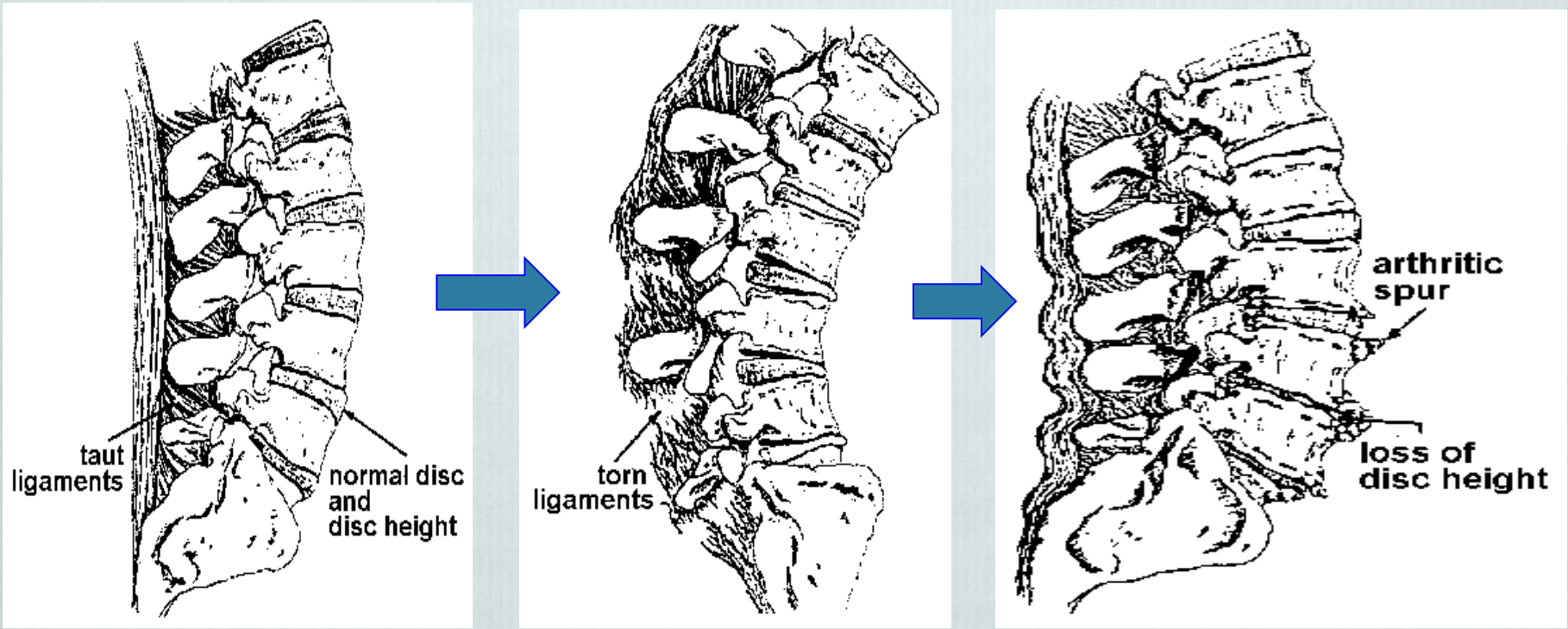
↓

Dysfunctional Movement

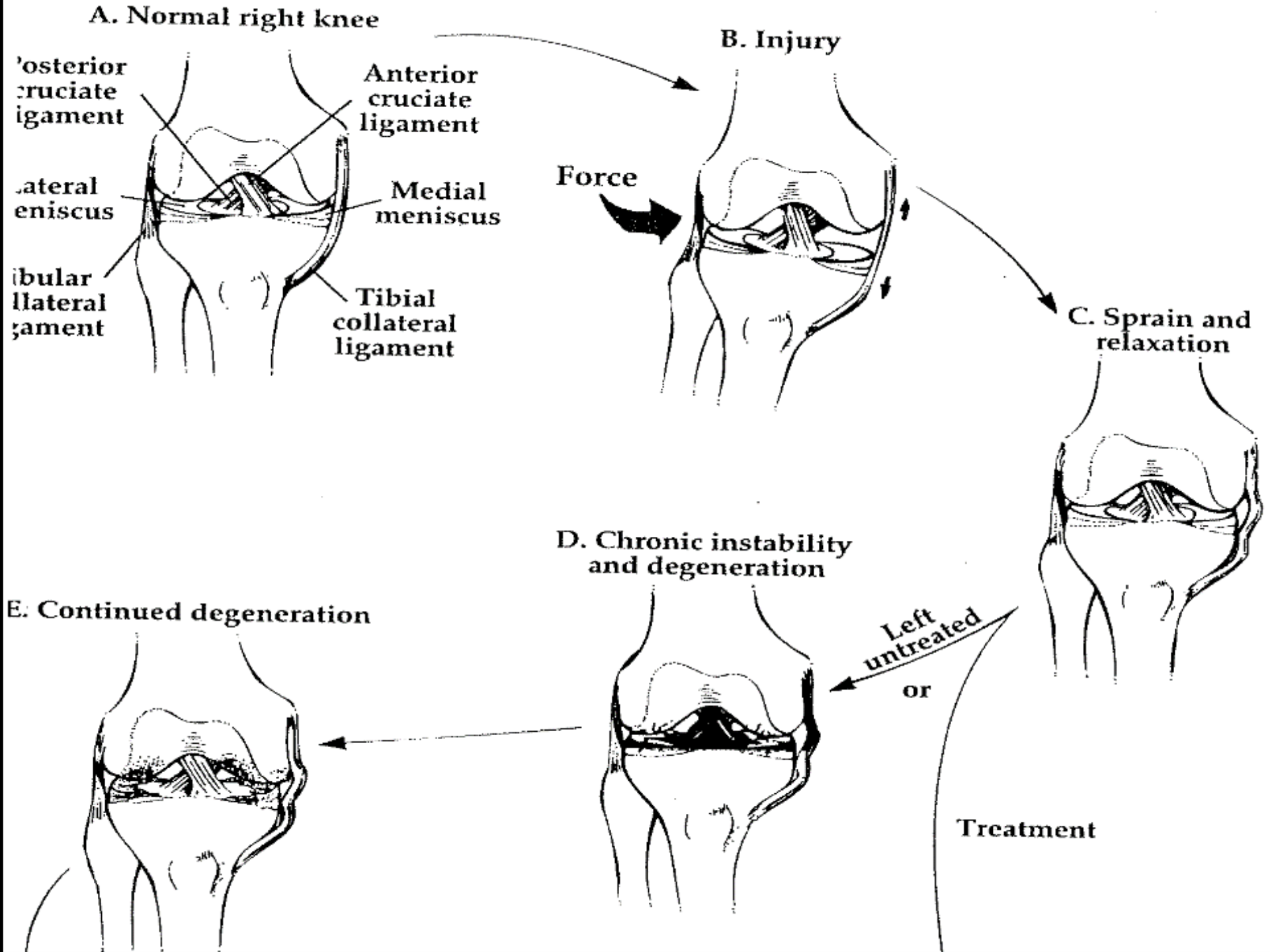
↓

Arthritis and Disc Disease

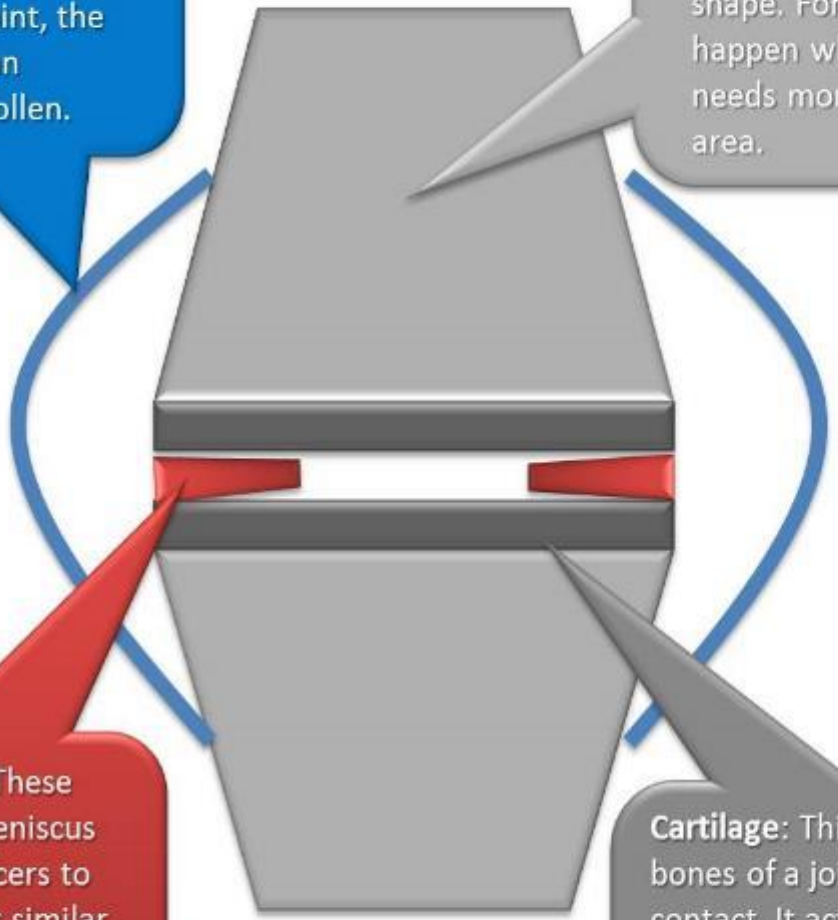
Can We Reverse Spinal Degeneration?



REGENERATIVE MEDICINE


A. Normal right knee
'osterior
cruciate
igament
Anterior
cruciate
ligament
ateral
eniscus
Medial
meniscus
ibular
llateral
gament
Tibial
collateral
ligament
B. Injury
Force
C. Sprain and
relaxation
D. Chronic instability
and degeneration
E. Continued degeneration
Left
untreated
or
Treatment

Articulation



Joint Capsule: The living outer covering of the joint that keeps the joint fed and determines in which directions it can safely move. In an arthritic joint, the inside of the capsule can become chronically swollen.

Bone: Usually thought of as the body's inert cement, it's actually living tissue that reacts to forces by getting stronger and changing shape. For example, bone spurs happen when the bone detects it needs more of itself in a certain area.

Spacers and stabilizers: These tissues such as a knee meniscus can act as important spacers to help absorb shock. Other similar tissue such as a hip or shoulder labrum can help keep a ball and socket joint aligned.

Cartilage: This living tissue lines all bones of a joint that come in contact. It acts as a shock absorber to protect the bone and it it's slippery surface allows the joint to move smoothly. In arthritis, the cartilage can become damaged and worn out.

Peripheral Joint Instability

Trauma / Overuse

↓

Ligament damage

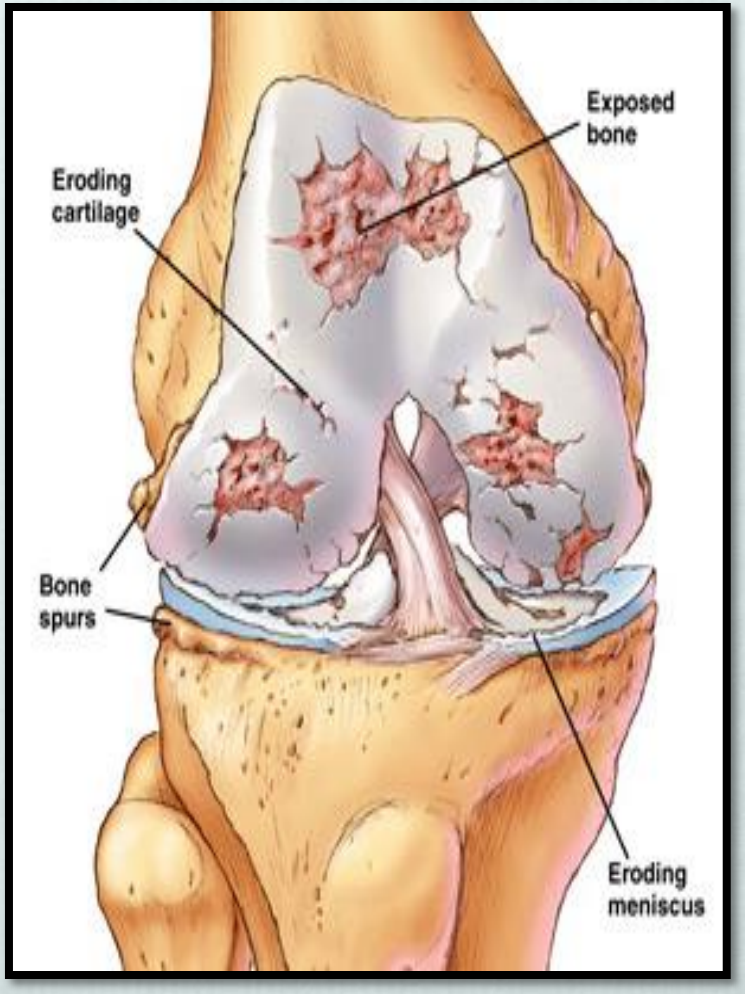
↓

Instability

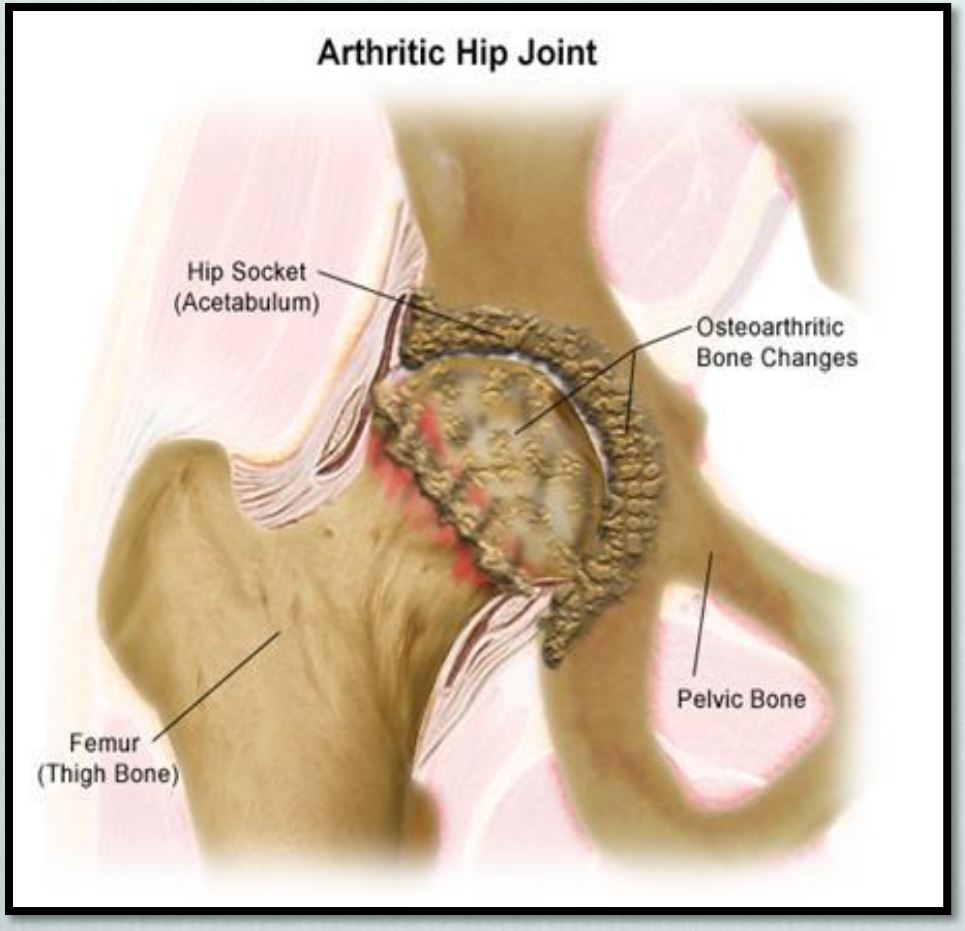
↓

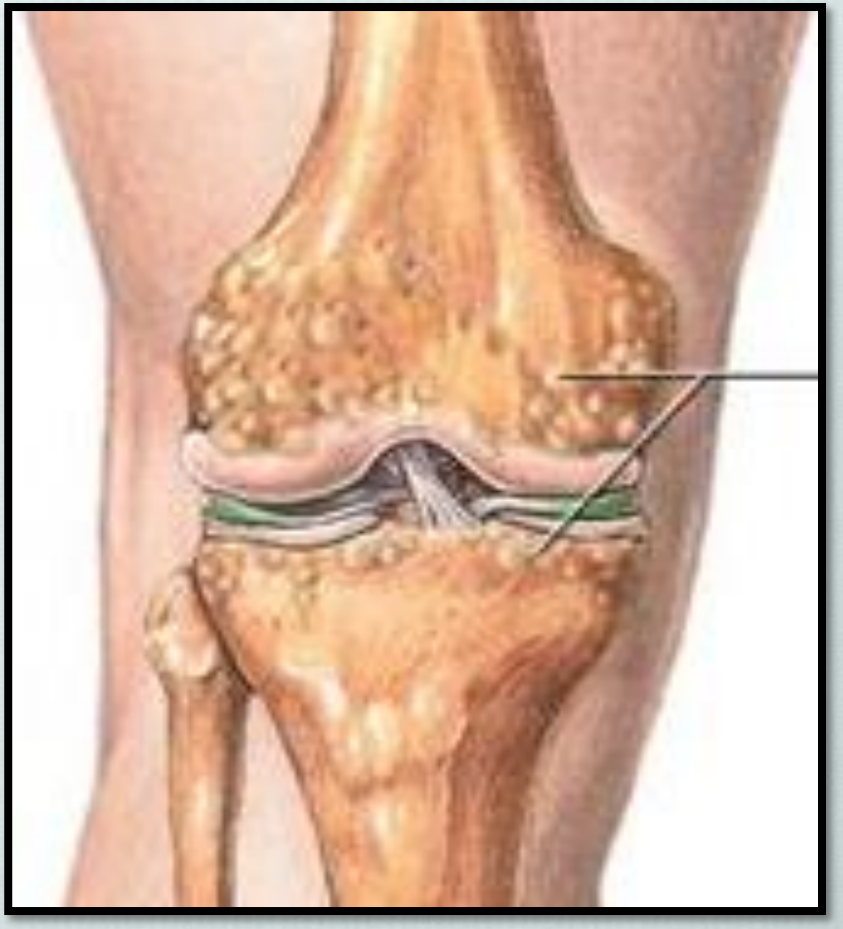
TENDINOSIS

ARTHRITIS

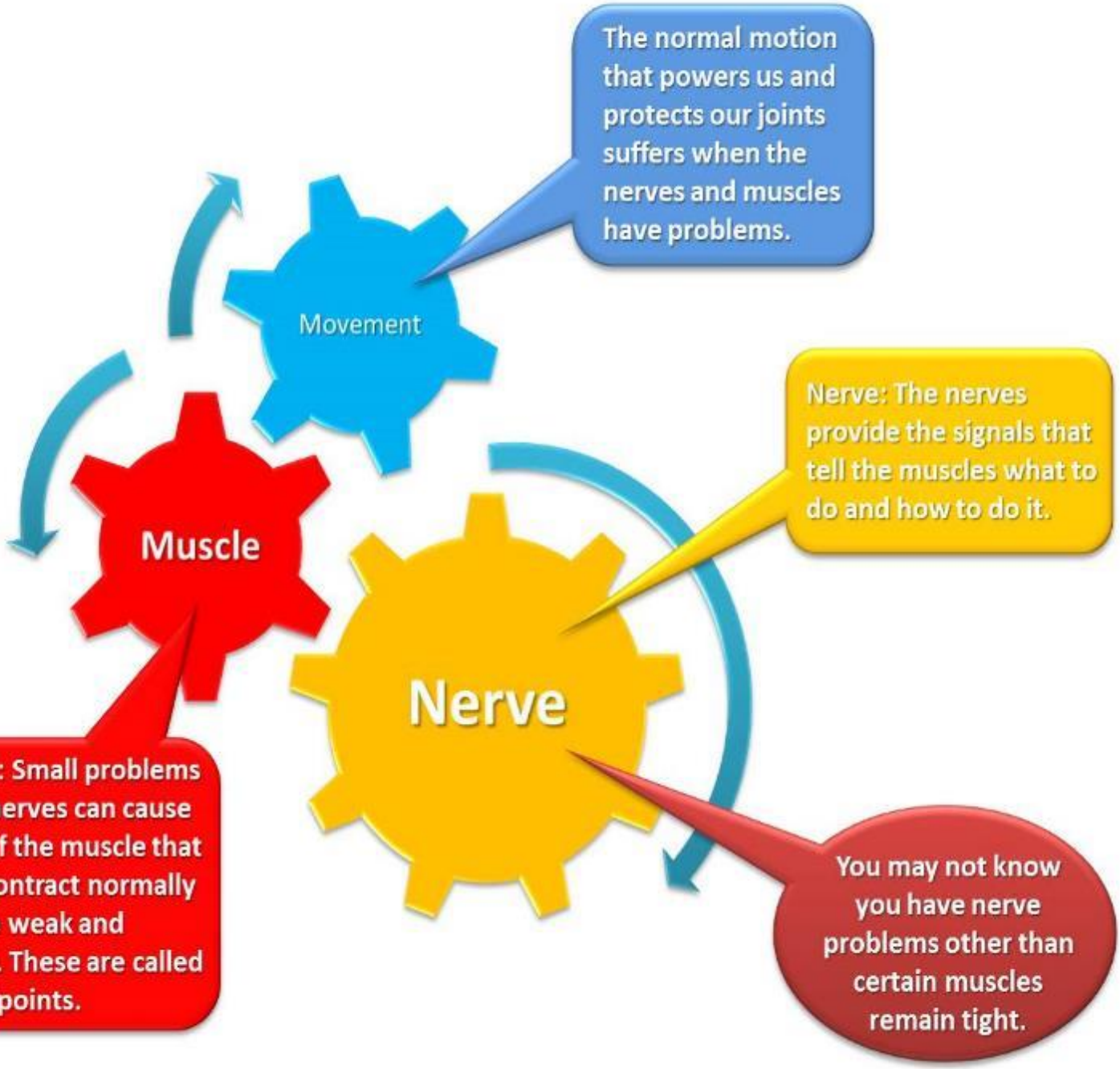


Articulatory Degeneration



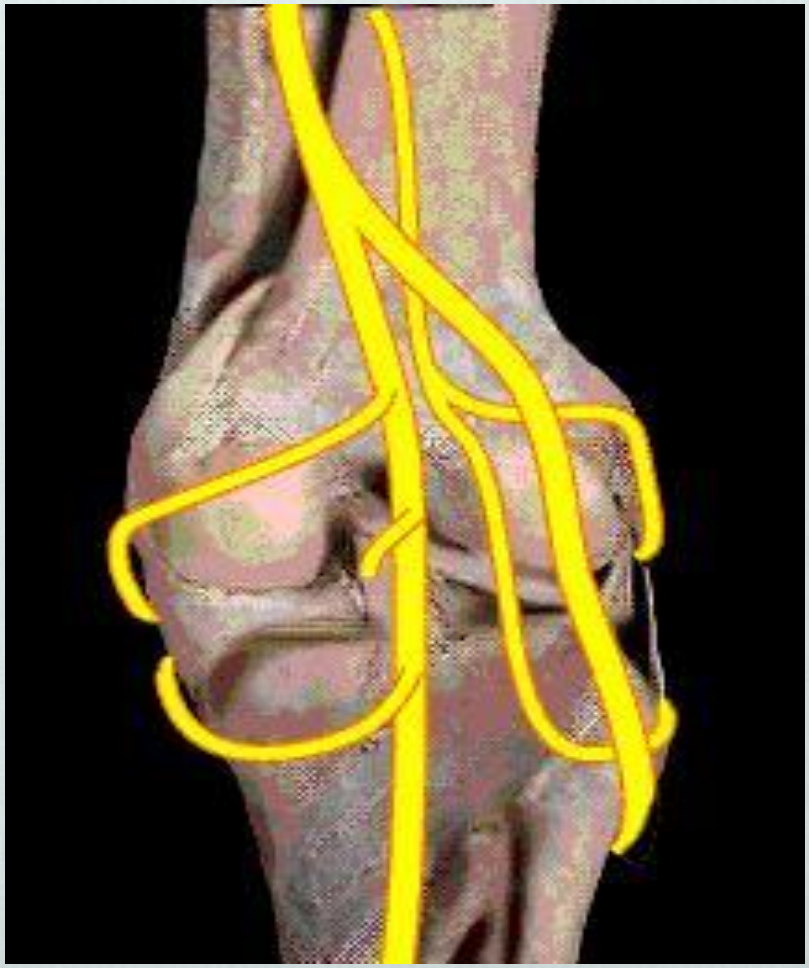


Neuromuscular

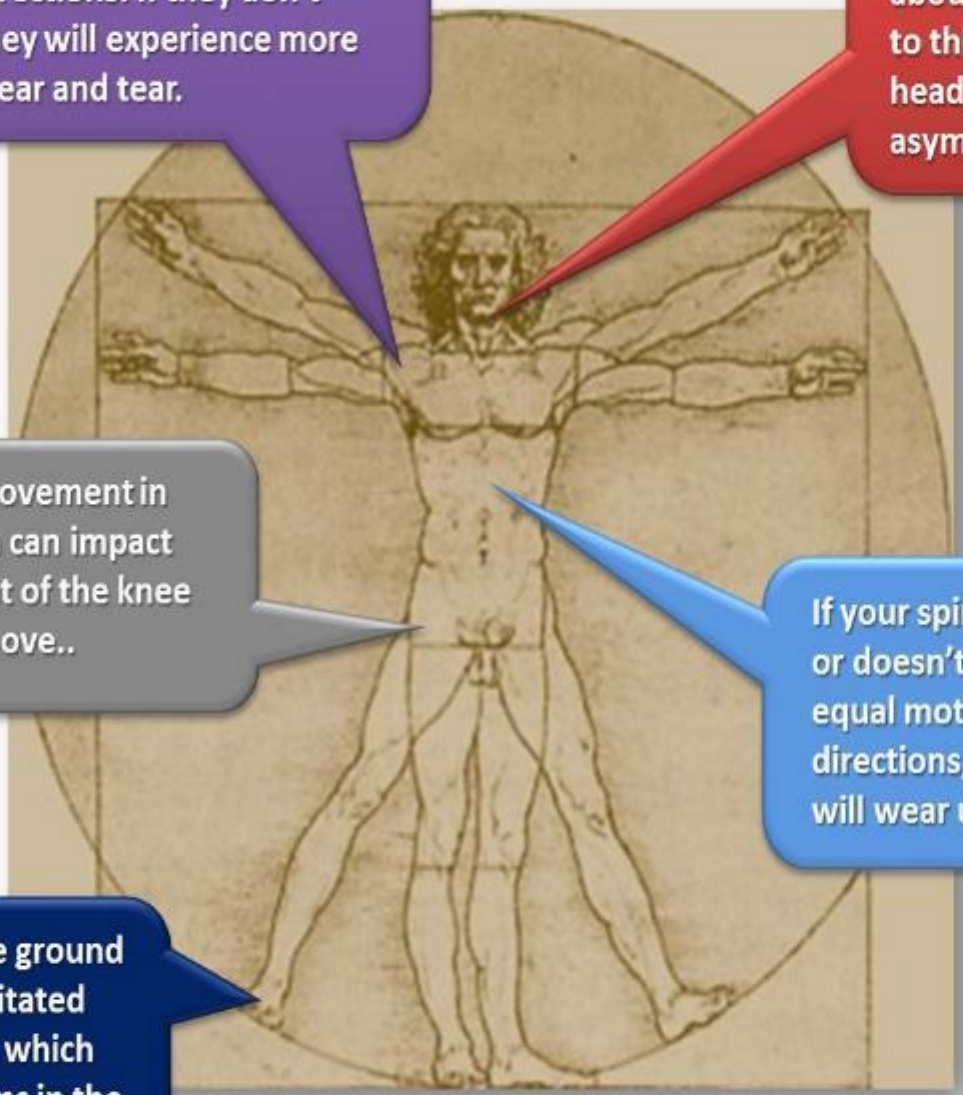


Neuromuscular Control

- Complex interrelationship between nerves, muscles, joints, vessels and skin.
- Pain can be a manifestation of dysfunction or imbalance in any component of the system.
- Functional movement restoration must be achieved to correct neuromuscular deficits and effectively turn off the pain generator(s).



Symmetry



Your individual joints need to have the same amount of full motion in all directions. If they don't they will experience more wear and tear.

The upper neck supplies information to the brain about body position. Injury to this area can cause headaches and body asymmetry.

Loss of hip movement in one direction can impact the alignment of the knee cap in it's groove..

If your spine isn't straight, or doesn't have full and equal motion in all directions, then your joints will wear unevenly.

The foot can hit the ground unevenly due to irritated nerves in the back, which can lead to problems in the knee and hip.

What is Regenerative Medicine?

"The process of repairing, replacing or regenerating human cells, tissues or organs to restore or establish normal function."

What is Regenerative Medicine?

- **The Idea -** Fusion of cutting edge technology with innate healing capacity
- **The Focus -** To repair damaged tissue by stimulating the body's own repair mechanisms to heal previously irreparable tissues or organs
- **The Goal -** Accelerate healing without subjecting the patient to significant risk

Regenerative Medicine: Theory & Conceptual Model

- **RESTORE**
  - Homeostasis of intra- and inter-cellular activity
  - Lost functional and fundamental movement patterns
- **REBUILD**
  - Damaged cells and tissues with healthy constituents
  - Diseased tissues to restore tissue function and optimize growth
- **REJUV**
  - Rejuvenation of the innate healing capacity of the body
    - Optimal nutrition
    - Cellular health and function through diet and movement
    - Sleep quality
    - Stress mitigation
    - Social worth and connectivity

Regenerative Medicine: Epidemiology

- Globally increased incidence of chronic and degenerative diseases
  - **1 in 2 Americans have a chronic medical condition (DM, HTN, CAD, CHF)**
- Symptoms can be managed, but the underlying causes remain leading to complications or sequelae
- Current evidence based and palliative treatments (medications, surgery, devics) are unable to keep pace with aging population

Regenerative Medicine: Epidemiology

- According to the World Health Organization (WHO):
  - Musculoskeletal injuries are the *most common cause* of severe long-term pain and physical disability

  - Soft tissue injuries, including tendon and ligament trauma, represent 45% of all musculoskeletal injuries in the U.S.

Why Regenerative Medicine?

- Steroids have side effects:
  - Tissue degradation
  - Cartilage deterioration in animal models
  - Reduced ability of bone stem cells to make new bone
  - Systemic SIDE EFFECTS

Why Regenerative Medicine?

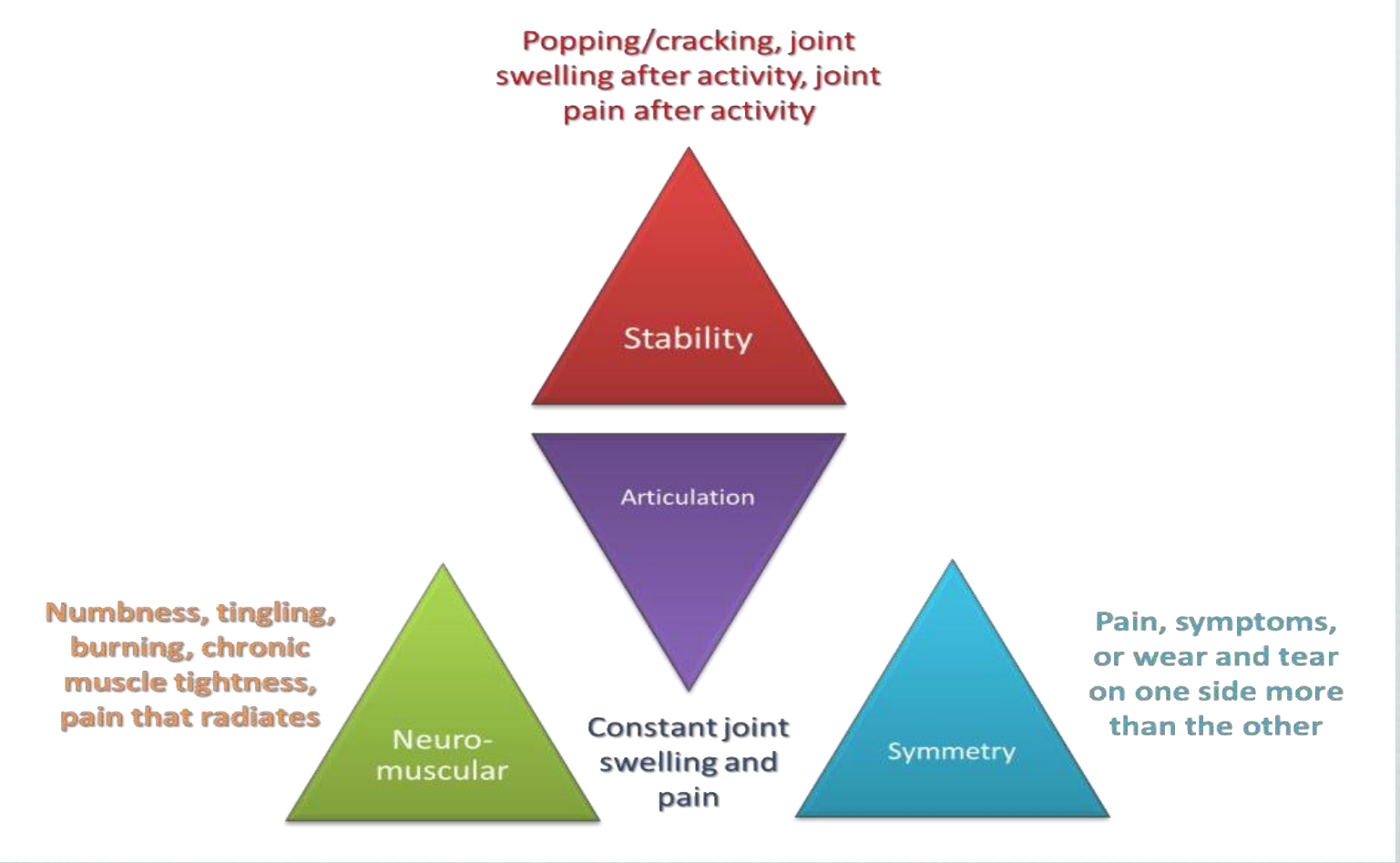
- Depending on the diagnosis, a less invasive alternative to spine or joint surgery

- Avoid known surgical risks :
  - DVT, PE
  - Hardware infection
  - Metal toxicity
  - Pain despite joint replacement or fusion
  - Painful recovery period of several months
  - Permanent decrease in range of motion, strength, and/or activity level

Regenerative Medicine Treatments

- Prolotherapy
- Platelet Rich Plasma (PRP)
- Nerve Blocks
- Stem Cells

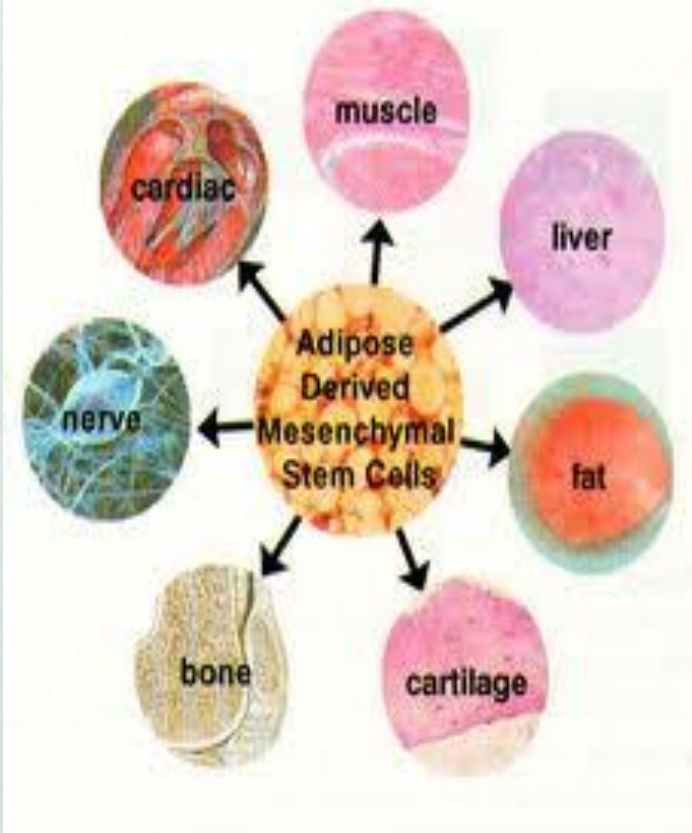
Regenerative Medicine: Addresses Underlying Cause of Dysfunction



Regenerative Medicine: The Future…

- Holds the promise of definitive, affordable, non-surgical solutions to allow the body to heal from within.

- Potential to heal damaged tissues thought to be beyond repair



Prolotherapy

Prolotherapy

- Definition – The rehabilitation of an incompetent structure, such as ligament or tendon, by the proliferation of new cells.
- Involves injecting an otherwise non-pharmacological and non-active irritant solution (dextrose)
- A “controlled injury” to trigger the inflammatory cascade.
- Purpose – To strengthen weakened connective tissue and alleviate musculoskeletal pain

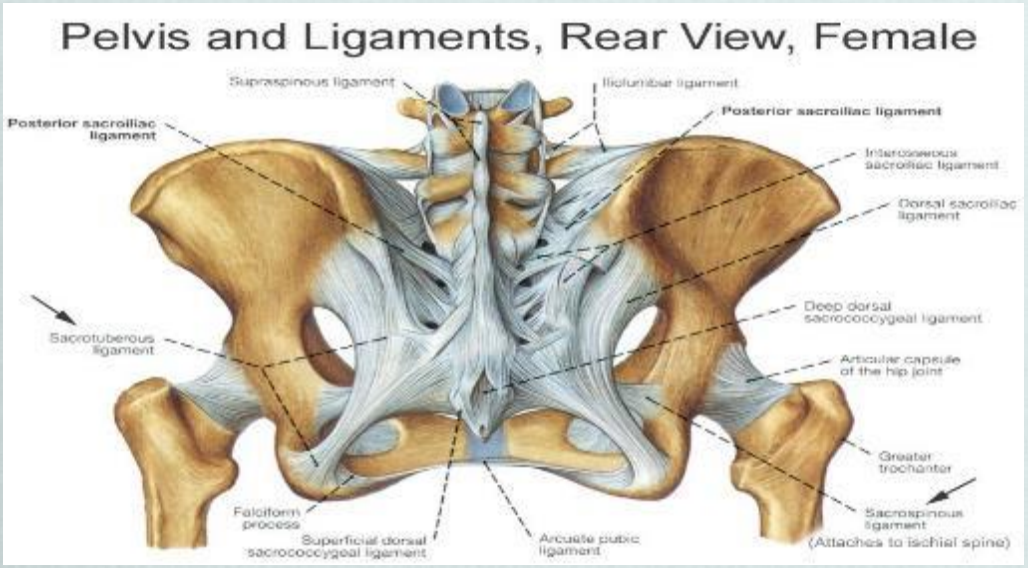
Prolotherapy Agents

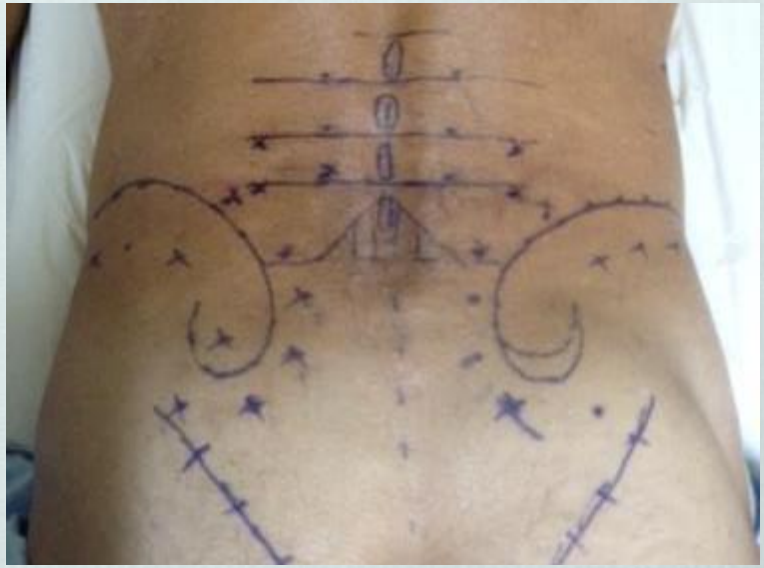
- Hyperosmolar Dextrose
  - 25% intra-articular
  - 15% extra-articular
- Glycerine
- Phenol
- Sodium Morrhuate

Phases of Injury Healing

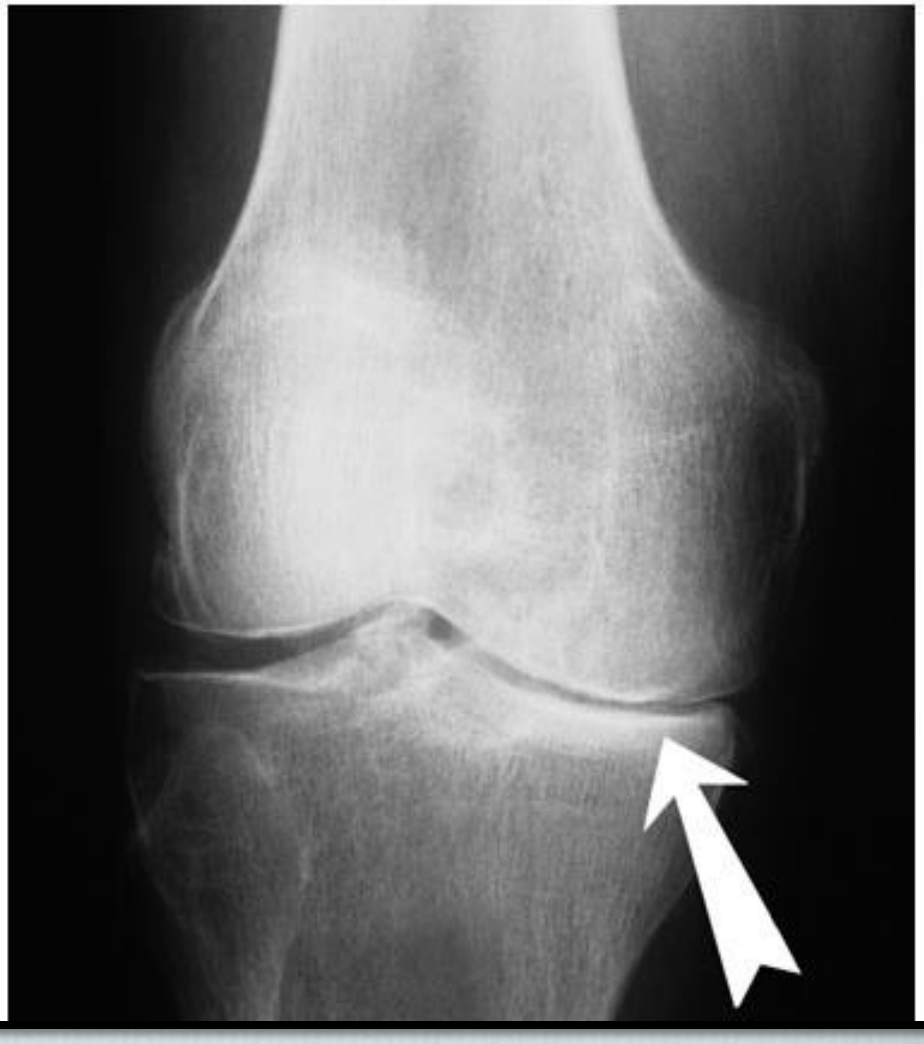
- Inflammatory Phase* (Day 0 – 7)
- Proliferative Phase (Day 2 – 42)
- Remodeling Phase (Day 42 - to a year+)

Prolo – Lumbar spine, SI region





2003
Reeves



Before

After

Is Prolotherapy effective?

Dextrose Prolotherapy for Knee Osteoarthritis: A Randomized Controlled Trial

David Rabago, MD[1]
Jeffrey J. Patterson, DO[1]
Marlon Mundt, PhD[1]
Richard Kijowski MD[2]
Jessica Grettie, BS[1]
Neil A. Segal, MD, MS[3]
Aleksandra Zgierska MD, PhD[1]

[1]Department of Family Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

[2]Department of Radiology, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

[3]Departments of Orthopaedics & Rehabilitation, Epidemiology, and Radiology, The University of Iowa, Iowa City, Iowa

ABSTRACT

PURPOSE Knee osteoarthritis is a common, debilitating chronic disease. Prolotherapy is an injection therapy for chronic musculoskeletal pain. We conducted a 3-arm, blinded (injector, assessor, injection group participants), randomized controlled trial to assess the efficacy of prolotherapy for knee osteoarthritis.

METHODS Ninety adults with at least 3 months of painful knee osteoarthritis were randomized to blinded injection (dextrose prolotherapy or saline) or at-home exercise. Extra- and intra-articular injections were done at 1, 5, and 9 weeks with as-needed additional treatments at weeks 13 and 17. Exercise participants received an exercise manual and in-person instruction. Outcome measures included a composite score on the Western Ontario McMaster University Osteoarthritis Index (WOMAC; 100 points); knee pain scale (KPS; individual knee), postprocedure opioid medication use, and participant satisfaction. Intention-to-treat analysis using analysis of variance was used.

RESULTS No baseline differences existed between groups. All groups reported improved composite WOMAC scores compared with baseline status ($P < .01$) at 52 weeks. Adjusted for sex, age, and body mass index, WOMAC scores for patients receiving dextrose prolotherapy improved more ($P < .05$) at 52 weeks than did scores for patients receiving saline and exercise (score change: 15.3 ± 3.5 vs 7.6 ± 3.4, and 8.2 ± 3.3 points, respectively) and exceeded the WOMAC-based minimal clinically important difference. Individual knee pain scores also improved more in the prolotherapy group ($P = .05$). Use of prescribed postprocedure opioid medication resulted in rapid diminution of injection-related pain. Satisfaction with prolotherapy was high. There were no adverse events.

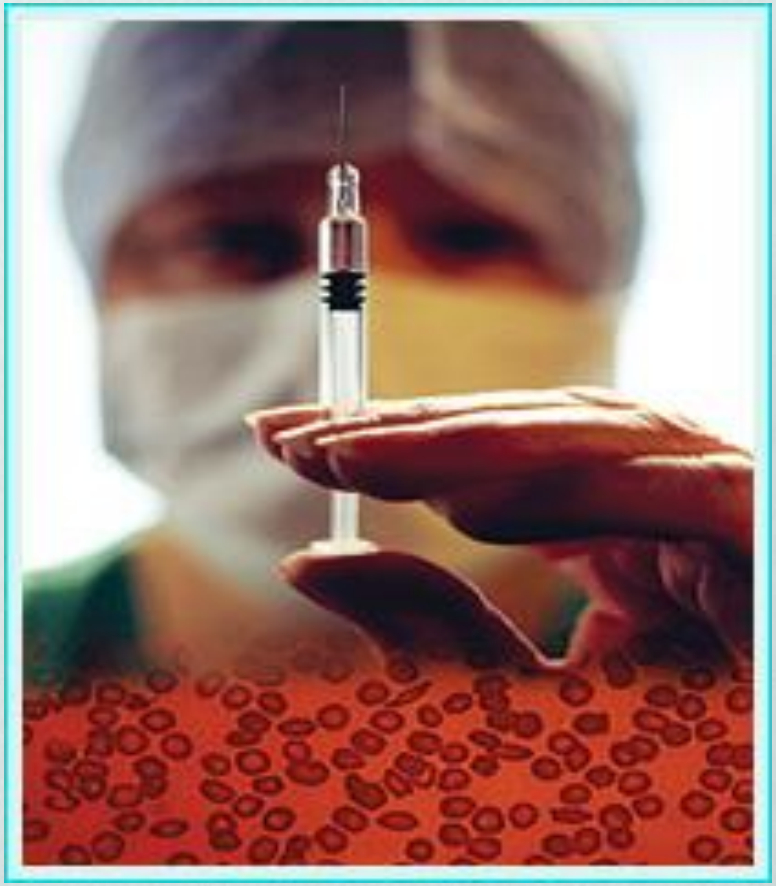
CONCLUSIONS Prolotherapy resulted in clinically meaningful sustained improvement of pain, function, and stiffness scores for knee osteoarthritis compared with blinded saline injections and at-home exercises.

Ann Fam Med 2013;11:229-237. doi:10.1370/afm.1504.

Platelet Rich Plasma (PRP)

What is Platelet Rich Plasma (PRP)?

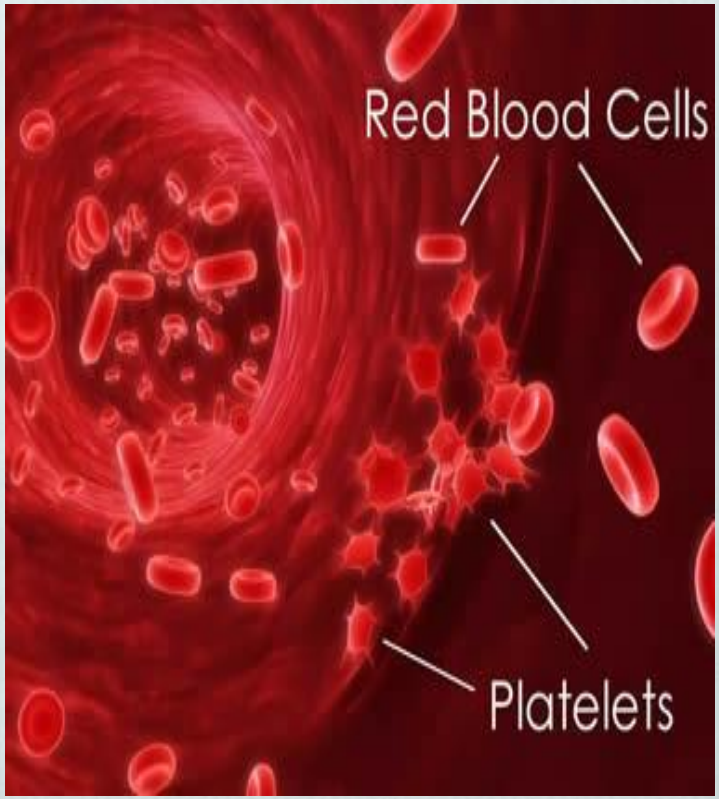
- Autologous blood plasma with concentrations of platelets in a given volume above the concentration found in whole blood.



Arnoczky et al, JAAOS 2010

Composition of Whole Blood vs. PRP

- **Whole Blood**
  - 45% RBCs
  - 1% Platelets
  - 1% WBCs
  - 55% Plasma



- **PRP**
  - 94% Platelets and Plasma
  - 5% RBCs

Sampson et al, Curr Rev Musculoskelet Med. 2008

Blood Constituents:

- **Plasma**
  - Liquid component of blood
  - Made mostly of water
  - Acts as a transporter for cells
  - Contains fibrinogen
    - Protein that acts like a net and catches platelets at a wound site to form a clot
- **RBC**
  - Facilitates oxygen exchange and delivery
  - Removes carbon dioxide
- **WBC**
  - Fights infection
  - Kills germs
  - Carries off dead blood cells
- **Platelets**
  - Responsible for hemostasis
  - Construction of new connective tissue
  - Revascularization

Blood Constituents

Platelets

- Small, non-nucleated bodies in peripheral blood
- Assist in clot formation
- Contain a number of proteins, cytokines, and other bioactive (growth) factors that initiate and regulate basic aspects of wound healing
- Normal platelet count in blood (150,000/μL – 350,000/μL)

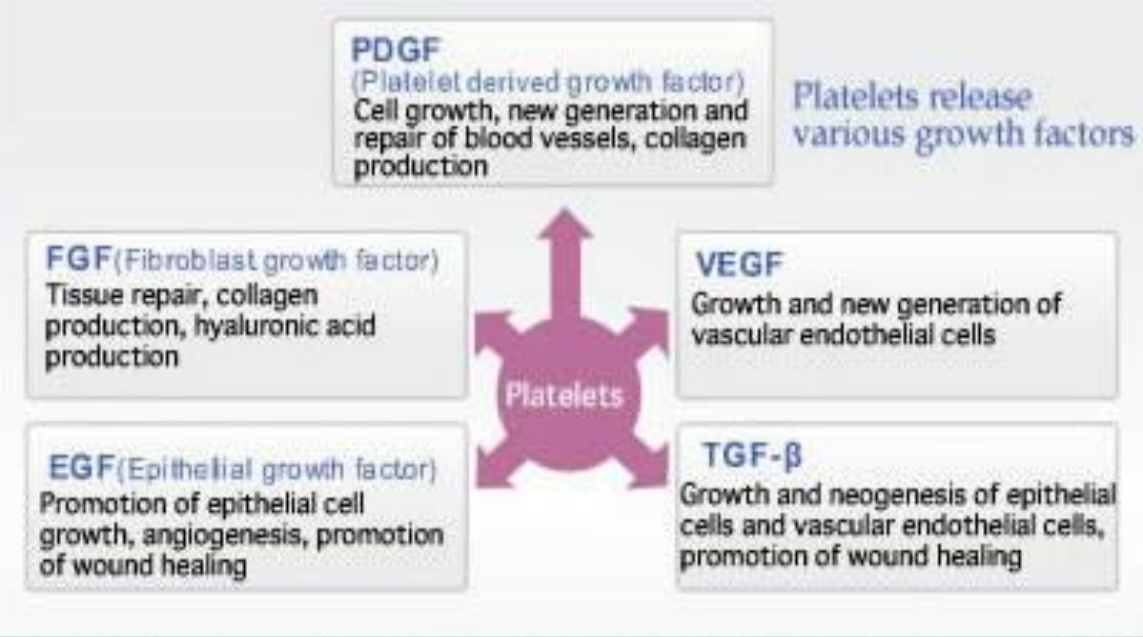
Plasma

- Fluid portion of blood
- Transport medium
- Contains clotting factors, other proteins and ions

Platelet Rich Plasma (PRP)

- Platelet concentration of at least 1,000,000 platelets/μL in 5 mL of plasma
- Contains a 3-5 fold increase in growth factors

Biologically Active Growth Factors



History

- For **>20 years**, PRP has been used in many applications:
  - Dentistry
  - ENT
  - Maxillofacial surgery
  - Neurosurgery
  - Ophthalmology
  - Urology
  - Wound healing
  - Cosmetic surgery
  - Cardiothoracic surgery
  - **Orthopedics and Sports Medicine**

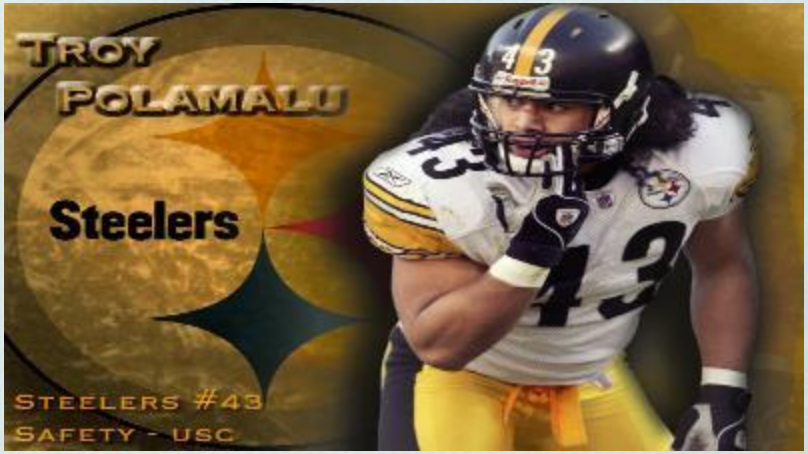
History of PRP

- First introduced in the 1980's for the treatment of cutaneous ulcers.[1]

- Use expanded in the 1990's for the maxillofacial and plastic surgery fields.[2]

1.Margolis et al, Diabetes Care 2001
2.Marx, *J Oral Maxillofac Surg* 2004

Use in MSK injuries

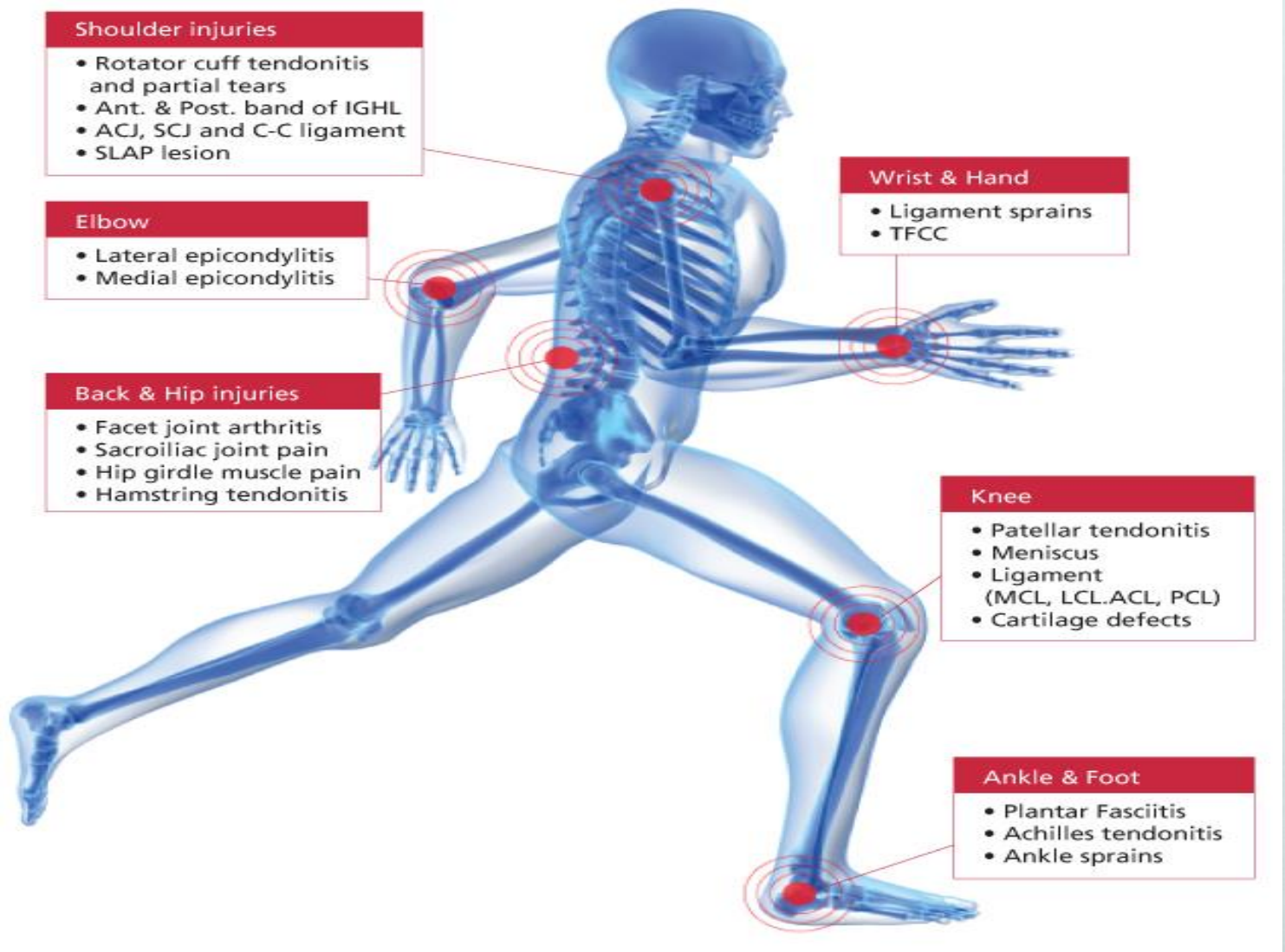


Use in MSK injuries

How Does PRP Work?

- Mechanism of action:
  - Similar to prolotherapy
  - Provides additional growth factors
  - Can further stimulate tissue repair
  - Revascularization? -

Conditions Treated with PRP



Basic Science of PRP

Healing Stages:

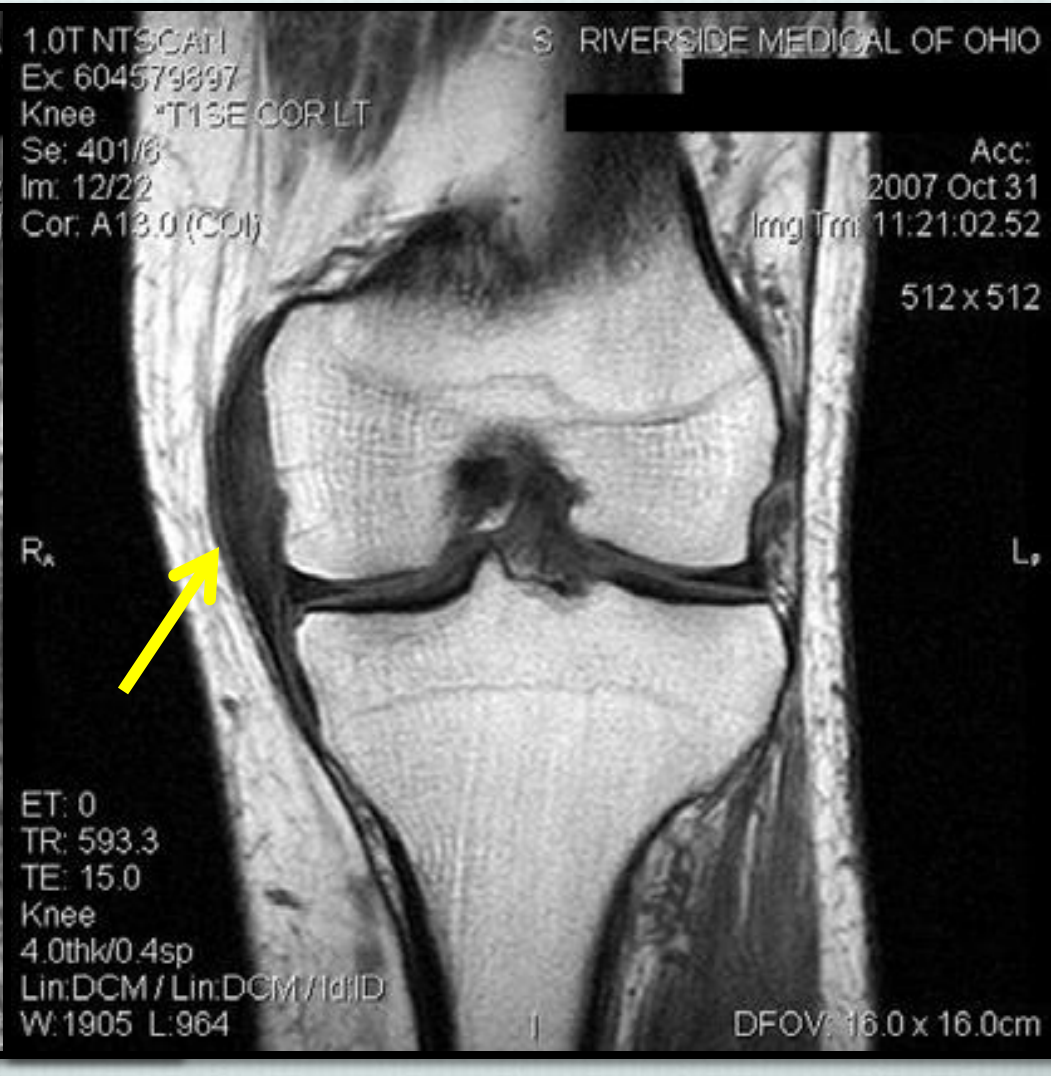
- **Inflammation**
  - Growth factors (PRP)
- **Cellular and matrix proliferation**
  - Growth factors (PRP)
- **Tissue formation**
- **Tissue maturation and remodeling**
  - Conductive matrix (PRP)
  - Mechanico-biological signaling (PRP)

Platelet Actions

- Initially thought to act exclusively with clotting
- PRP literature continues to investigate other actions of platelets resulting from release of bioactive proteins:
  - Attracting macrophages
  - Stem cell signaling
  - Osteoclast/osteoblast balance
- Not only promotes removal of necrotic tissue, but also enhances tissue regeneration and healing

PRP for Chronic MCL Tear

BEFORE



AFTER

Technique: Extraction of Blood

Technique: Blood Sample

Technique: Centrifugation

Technique: Platelet Rich Plasma Isolate

Technique: Syringe Preparation

Technique: Activation With Thrombin or Calcium Chloride

PRP Activation

- Combining the PRP isolate with 10% calcium chloride and/or thrombin initiates platelet activation, clot formation, and growth factor release
- 70% of stored growth factors are released within 10 min and nearly 100% are released within 1 hour.

Foster et al, Am J Sports Med 2009

Technique: Injection of PRP Utilizing Ultrasound Guidance

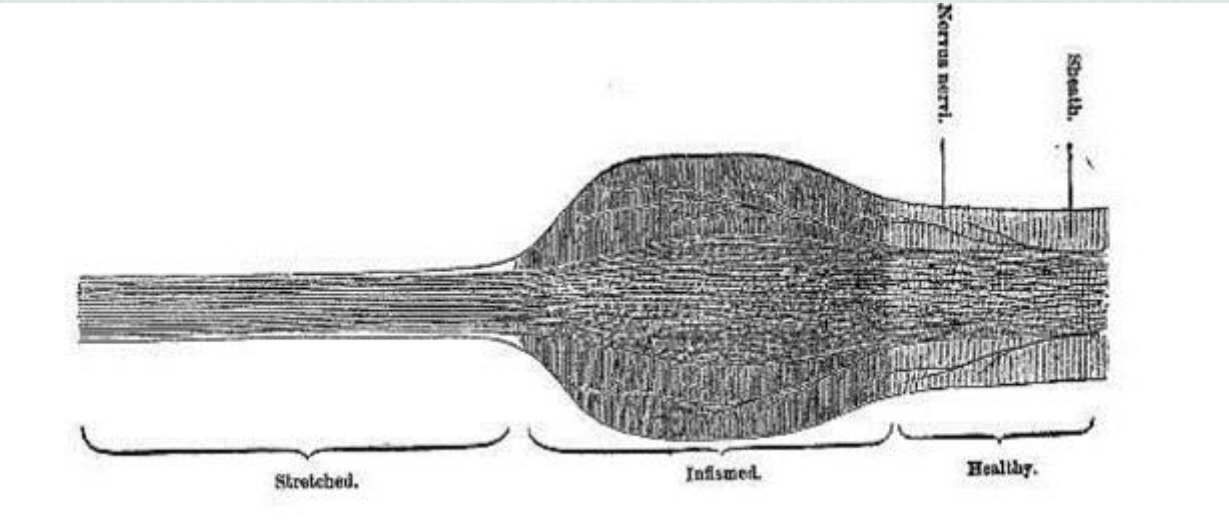
Safety of PRP

- NO studies have documented any cases of hyperplasia, carcinogenesis, or tumor growth.

Mehta, S et al. J Orthop Trauma.2008

Neural Injections

Neuroanatomy & Physiology



- "Neuropathic pain results from dysfunction within the nervous system without regard for sit of origin or etiology"

Fields HL. Pain. New York, NY: McGraw Hill; 1987:133-169

Nerve Injury: Overview

Damage to neural structures

↓

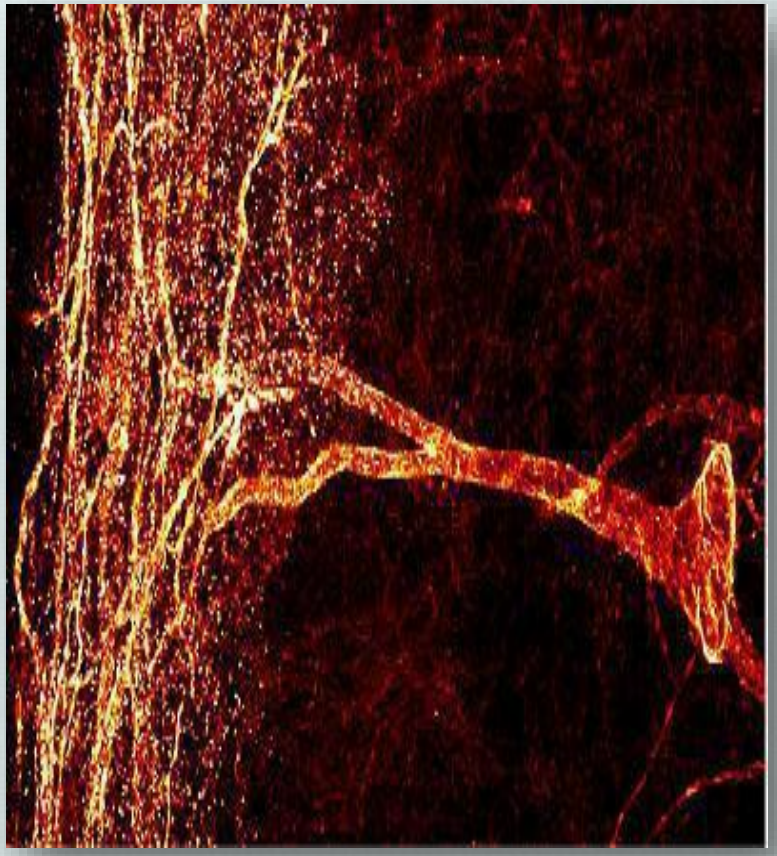
Release of TRPV1 Agonists
(CGRP, Substance P)

↓

Neurogenic Inflammation (Pain)

↓

Tissue and Joint Degeneration



Degenerative Effects of Neurogenic Inflammation

CGRP

- Neovascularization - Pain
- Collagenolysis - Tendon Breakdown
- Calcification - Calcific Tendonosis / Spurs
- Osteoclast activity - Stress Fractures

Substance P

- Post vasodilation - Varicosities
- Edema with increased permeability - Protein Leakage / Swelling
- Neuropathic pain - Hyperalgesia / Allodynia
- Depression, anxiety, fatigue and stress - Adrenal Fatigue

Neurogenic/Neuropathic Pain

- " a TRPV1 dependent pain state"
- TRPV1 regulates:
  - Tissue homeostasis
  - Neurogenic inflammation
  - Neuropathic pain
  - Immune modulation
  - Thermal regulation
  - Kinesis
- "Full and effective regeneration of the peripheral nervous system usually extinguishes the pain."

Zochodne, D. Neurobiology of Nerve Regeneration. Cambridge University Press.2008

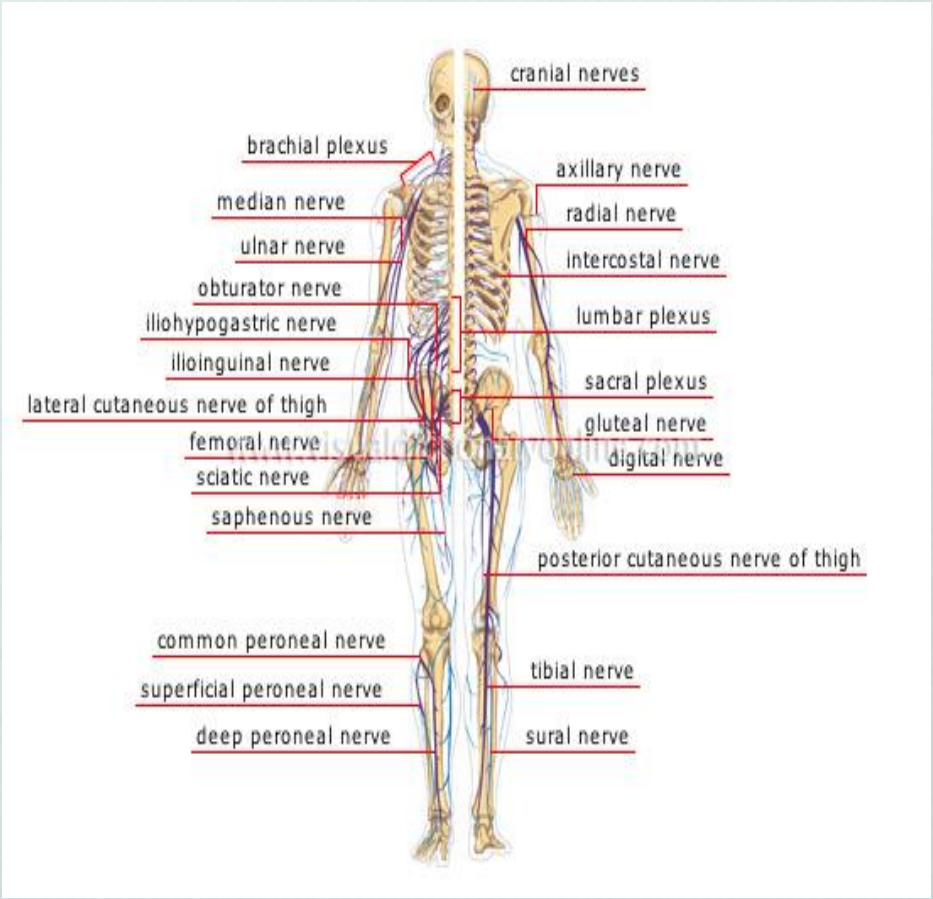
Nerve Block Injections

- **Block** the effects of TRPV1
- **Reverse** the degenerative effects of CGRP and SP
- Injectates (sugar analogues) utilized act as **<u>TRPV1 Antagonists</u>:**
  - Dextrose
  - Mannitol
  - Glycerine

Nerve Block Injections

Procedure:

- Identify and palpate source of pain
- Inject superficially along course of the nerve
- Ultrasound guidance for deeper nerves

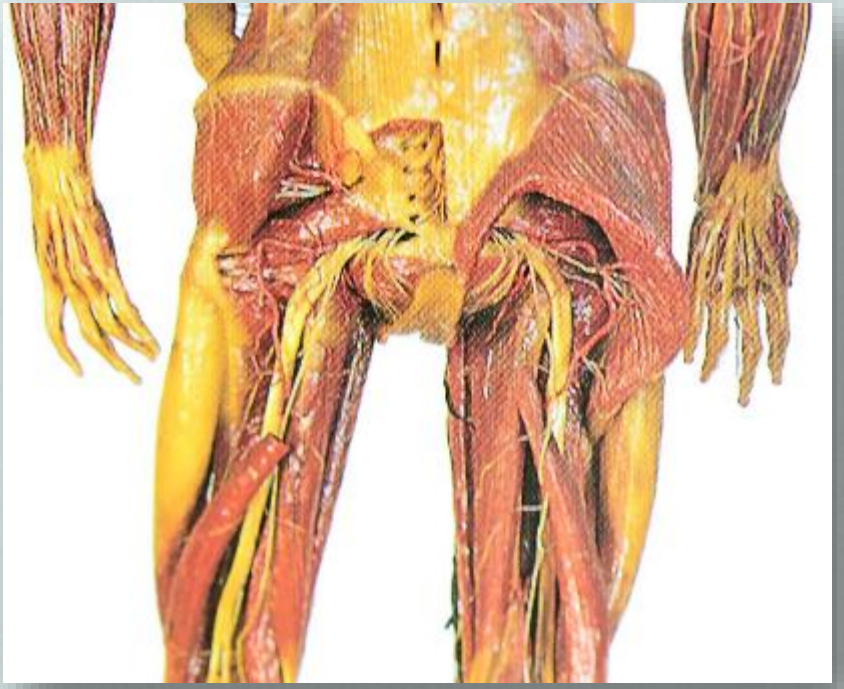


Nerves Treated: Face and Upper Extremities

- Facial
- Trigeminal
- Occipital
- Supraclavicular
- Brachial Plexus
- Cervical Plexus
- Suprascapular
- Axillary
- Radial
- Median
- Ulnar

Nerves Treated: Pelvis and Lower Extremities

- Cluneal
- Sciatic
- Pudendal
- Lumbar Plexus
- Lumbar Roots
- Femoral
- Tibial
- Sural
- Plantar
- Calcaneal

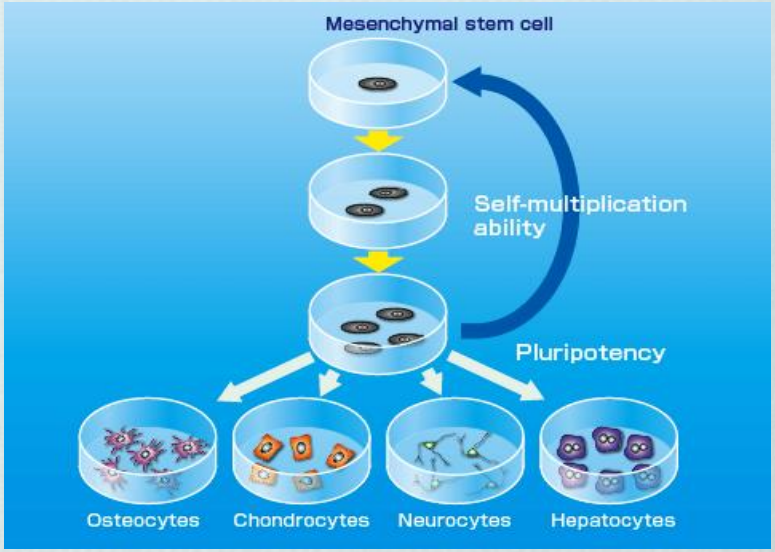


CURRENT	FUTURE
MEDICATIONS TARGETING SYMPTOMS	FUNCTIONAL MEDICINE
BARIATRIC SURGERY MEDICAL "WEIGHT LOSS" CLINICS	NUTRITIONAL COACHING MEDICAL FITNESS
PAIN MEDICATIONS (NSAID, OPIOIDS)	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
CORTICOSTEROID INJECTIONS	REGENERATIVE MEDICINE (PROLOTHERAPY, PRP)
SPINAL SURGERY / FUSIONS	STEM CELL THERAPY
TOTAL JOINT REPLACEMENT	STEM CELL THERAPY
MASK AND MITIGATE SIGNS AND SYMPTOMS	**TREAT ROOT CAUSE TO REBUILD, RESTORE, AND REJUVENATE PATIENT HEALTH**

Stem Cell Therapy

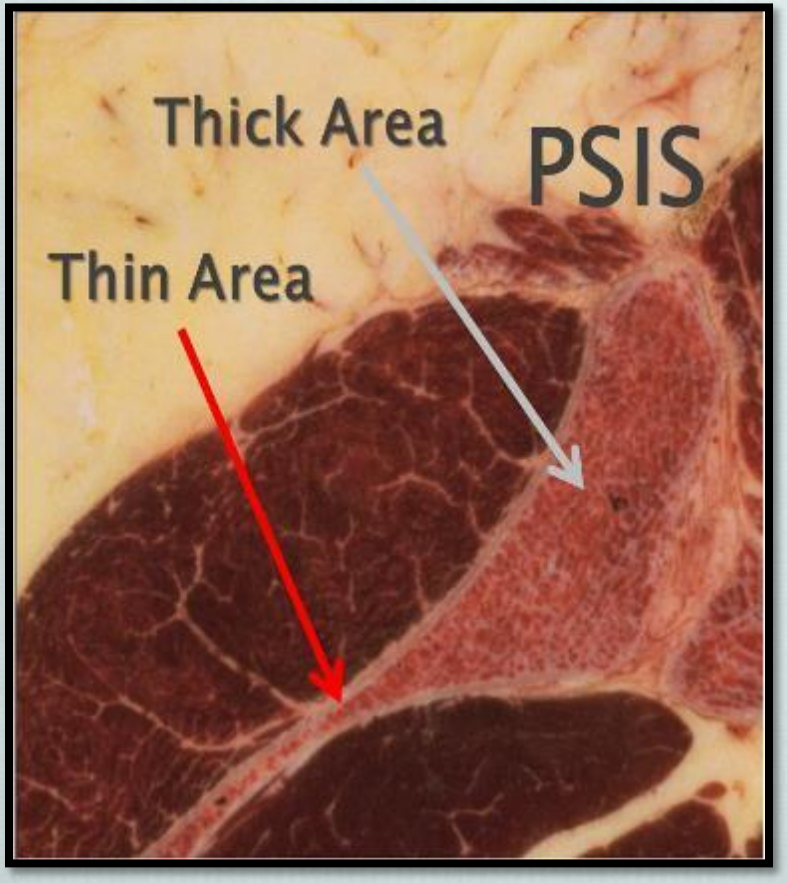
Mesenchymal Autologous Stem Cells

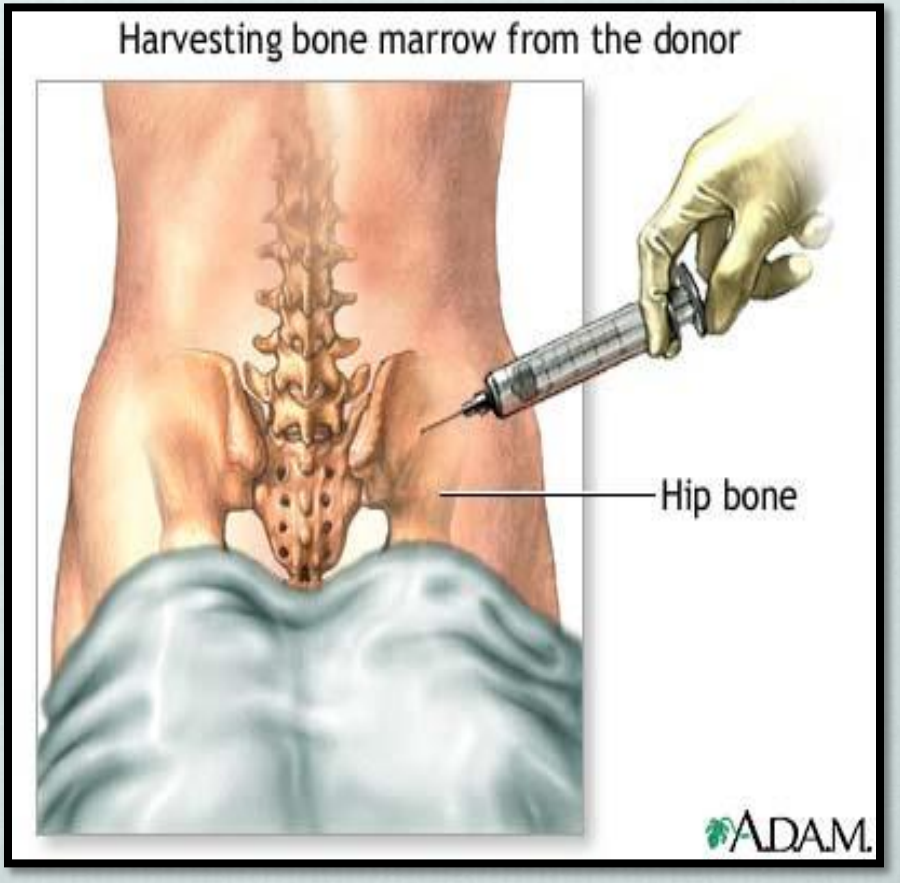
- Autologous
  - Derived from own body
- Mesenchymal
  - Pluripotent
    - Can differentiate into bone, cartilage, skin, muscle, vessels, nerve

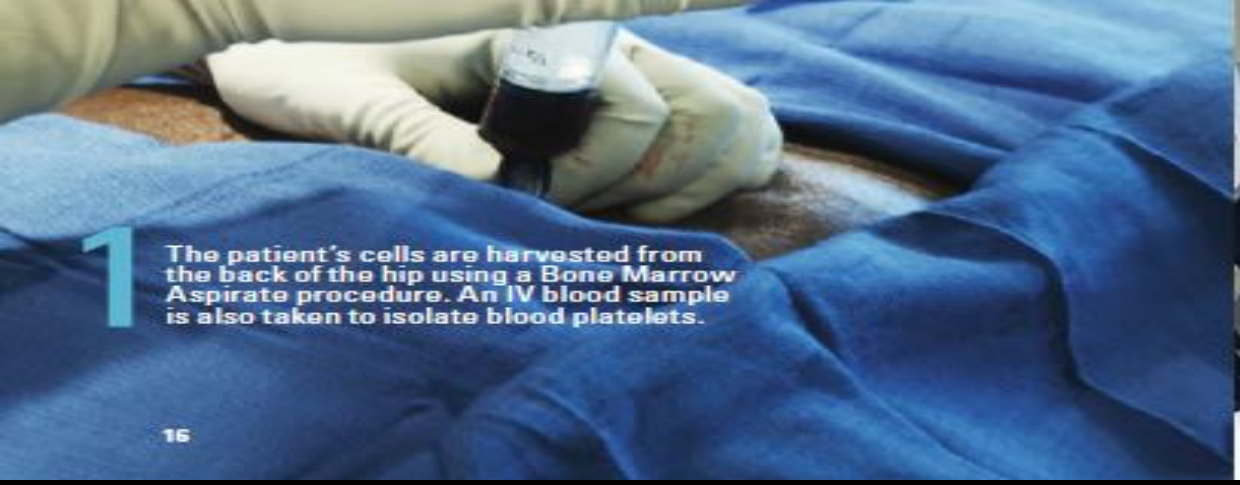


Stem Cells

- Harvested from the Pelvis

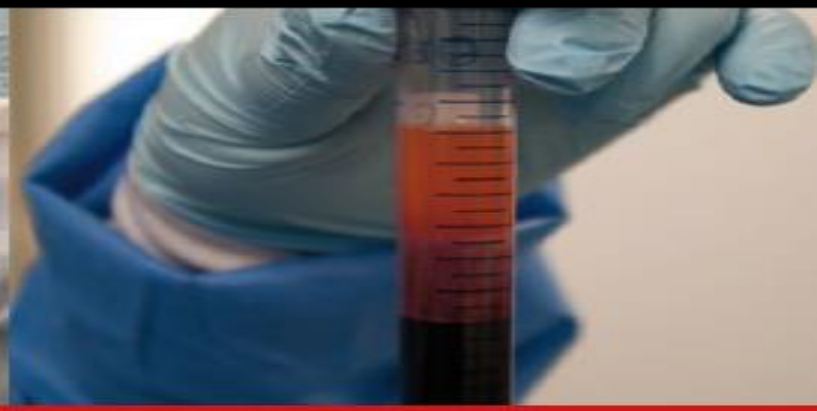


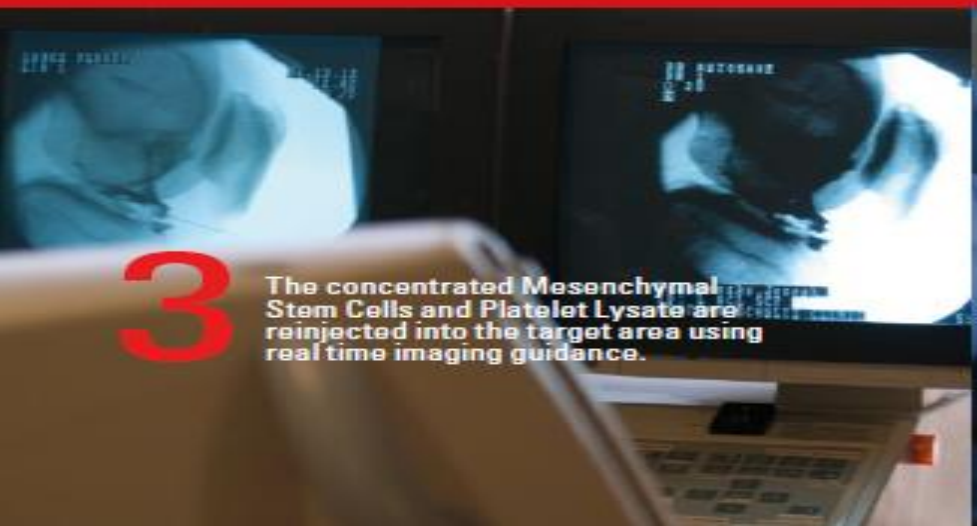




1 The patient's cells are harvested from the back of the hip using a Bone Marrow Aspirate procedure. An IV blood sample is also taken to isolate blood platelets.

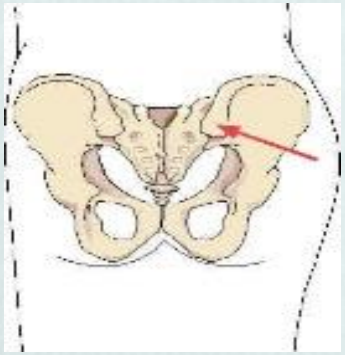
2 Mesenchymal Stem Cells are isolated from the bone marrow, while blood platelets are separated from the blood sample.



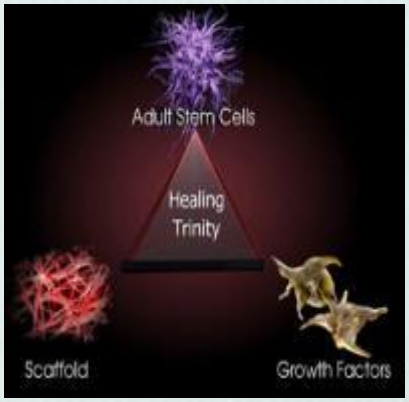


3 The concentrated Mesenchymal Stem Cells and Platelet Lysate are reinjected into the target area using real time imaging guidance.

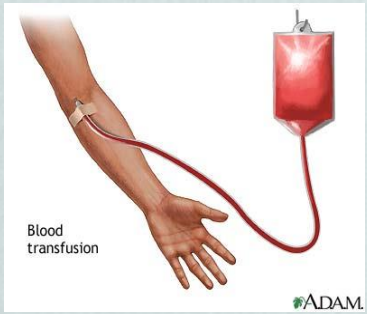
Bone Marrow Aspirate



Cells harvested (bone marrow aspirate, adipose)



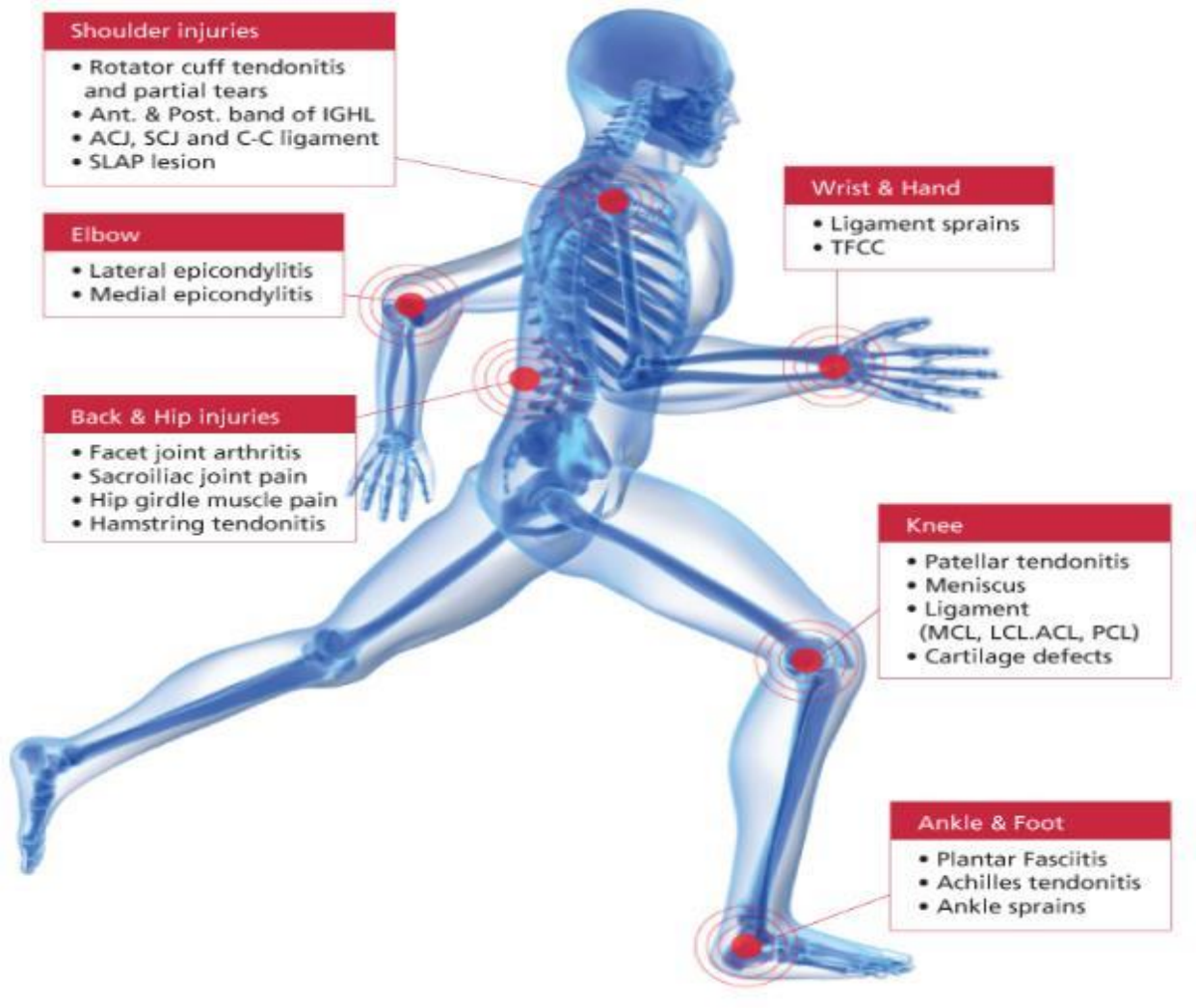
MSC's isolated by lab



IV blood sample taken to isolate PRP and platelet lysate

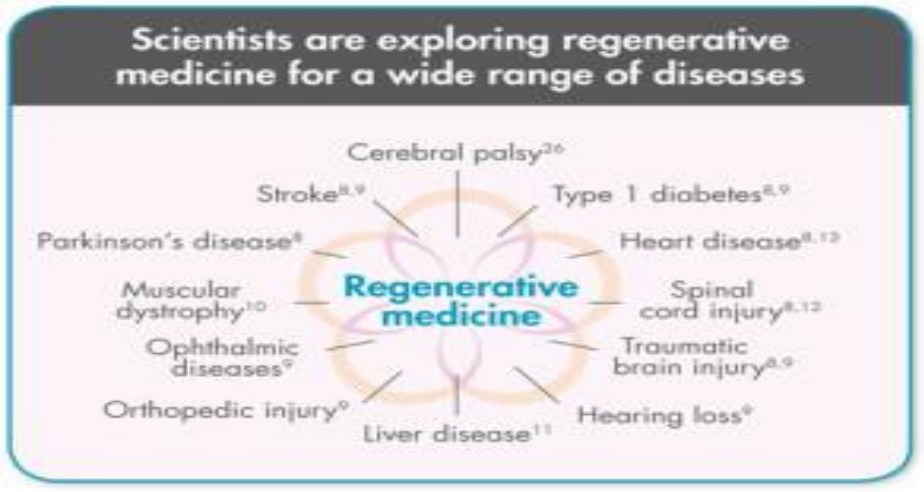
Injected same day

Stem Cell Indications:



Stem Cell Therapy: Conclusion

- Wide range of clinical studies are being conducted expanding the study of Regenerative Medicine, particularly as it relates to stem cell therapy.



Regenerative Medicine: Conclusion

- **REGENERATIVE MEDICINE** offers a safe, convenient, and effective therapeutic option for individuals who have pain from joint and spine degeneration or neuropathic pain
- Review of literature indicates effectiveness for tendon, ligament, bone and cartilage disorders
- Coupled with lifestyle interventions (nutritional coaching, medical fitness, sleep enhancement, stress mitigation, and social empowerment) the paradigm shift in treatment is to restoring optimal health

Is There A Better Way To Treat Pain?

- **Regenerative Medicine** offers a safe, convenient, and effective therapeutic option for treatment of painful joint or spine conditions, as well as neuropathy.
- **Functional (Lifestyle) Medicine** must be used in tandem to achieve optimal results.
  - Nutritional coaching
  - Medical fitness
  - Sleep enhancement
  - Stress mitigation
  - Social engagement
- Paradigm shift must occur with a focus on restoring health, not simply masking symptoms or managing disease state.

Nothing of any real positive social value has ever been achieved from the top down; it's always been achieved from the bottom up.

- Howard Zinn

Adding life to your years,
not just years to your life.

REBUILD. RESTORE. REJUV.

Rejuv
MEDICAL
SOUTHWEST

www.RejuvMedicalSW.com

References

Mishra A, Woodall J, Vieira A. Treatment of Tendon and Muscle Using Platelet-Rich Plasma. *Clinics in Sports Medicine.* 2009;28: 113-125

de Vos R, Weir A, van Schie H, Bierma-Zeinstra S, Verhaar J, et al. Platelet-Rich Plasma Injection for Chronic Achilles Tendinopathy. *JAMA*.2010;303(2):144-149.

Arnoczky S, Fu F, Mishra AK, Hannafin JA. Platelet-rich plasma: Clarifying the issues. *JAAOS*. 2010;9:1-5.

Foster TE, Puskas BL, Mandelbaum BR, et al. Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med.* 2009;37:2259-2272.

Lopez-Vidriero E, Goulding KA, Simon DA, et al. The use of platelet-rich plasma in arthroscopy and sports medicine: optimizing the healing environment. *Arthroscopy.* 2010;26:269-278.

Hall MP, Band PA, Meislin RJ, et al. Platelet-rich plasma: current concepts and application in sports medicine. *J Am Acad Orthop Surg.* 2009;17:602-608.

Gaweda K, Tarczynska M, Krzyzanowski W. Treatment of achilles tendinopathy with platelet-rich plasma Int J Sports Med.. 2010;31:577–583

Marx R. Platelet-rich plasma: evidence to support its use. *J Oral Maxillofac Surg*. 2004;62(4):489-496.

Sánchez M, Anitua E, Azofra J, Aguirre JJ, Andia I. Intra-articular injection of an autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study. *Clin Exp Rheumatol.* 2008;26(5):910-913.

References

Bennet NT, Schultz GS. Growth factors and wound healing: biochemical properties of growth factors and their receptors. Am J Surg. 1993; 165(6):728-737.

Sanchez M, Anitua E, Azofra J, Andia I, Padilla S, Mujika I. Comparison of surgically repaired Achilles tendon tears using platelet rich fibrin matrices. *Am J Sports Med. 2007;35(2):245-251.*

Kasemkijwattana C, Menetrey J, Bosch P, et al. Use of growth factors to improve muscle healing after strain injury. *Clin Orthop Relat Res.* 2000;370:272-285.

Kajikawa Y, Morihara T, Sakamoto H, et al. Platelet rich plasma enhances the initial mobilization of circulation-derived cells for tendon healing. *J Cell Physiol.* 2008;215(3):837-845.

Haynesworth SE, Kadiyala S, Liang LN, et al: Mitogenic stimulation of human mesenchymal stem cells by platelet release suggest a mechanism for enhancement of bone repair by platelet concentrates. Presented at the 48th Meeting of the Orthopedic Research Society, Boston, MA, 2002

Peerbooms J, Sluimer J, Bruijn DJ, Gosens T. Positive Effect of an Autologous Platelet Concentrate in Lateral Epicondylitis in a Double-Blind Randomized Controlled Trial: Platelet-Rich Plasma Versus Corticosteroid Injection With a 1-Year Follow-up. *Am J Sports Med* 2010 38: 255

Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med*. 2006;34:1774–1778.

Eppley BL, Woodell JE, Higgins J. Platelet quantification and growth factor analysis from platelet rich plasma: implications for wound healing. *Plast Reconstr Surg*. 2004;114:1502–1508.

Radice F, Yánez R, Gutiérrez V, et al. Comparison of magnetic resonance imaging findings in anterior cruciate ligament grafts with and without autologous platelet-derived growth factors. *Arthroscopy.* 2010;26:50-57.

References

de Jonge S, de Vos RJ, Weir A, et al. Platelet-rich plasma for chronic Achilles tendinopathy: a double-blind randomised controlled trial with one year follow-up. *Br J Sports Med*. 2011;45:e1. doi:10.1136/bjsm.2010.081554.40.

Barrett SL, Erredge SE. Growth factors for chronic plantar fasciitis? *Podiatry Today.* 2004;17(11):37-42.

Sampson S, Gerhardt M, Mandelbaum B. Platelet rich plasma injection grafts for musculoskeletal injuries: a review. *Curr Rev Musculoskelet Med*. 2008 Dec;1(3-4):165-74

O' Malley M. Platelet-rich plasma (PRP) in managing Achilles tendinosis
2010 Annual American Orthopaedic Foot & Ankle Society (AOFAS) Meeting.

Lui Y, Kalen A, Risto O, et al: Fibroblast proliferation due to exposure to a platelet concentrate in vitro is pH dependent. Wound Repair Regen 10:336, 2002.

Randelli PS, Arrigoni P, Cabitza P, et al. Autologous platelet rich plasma for arthroscopic rotator cuff repair: a pilot study. *Disabil Rehabil*. 2008;30:1584-1589.

Castricini R, Longo UG, De Benedetto M, et al. Platelet-rich plasma augmentation for arthroscopic rotator cuff repair: a randomized controlled trial. *Am J Sports Med*. 2011;39:258-265.

Kon E, Filardo G, Delcogliano M, et al. Platelet-rich plasma: new clinical application: a pilot study for the treatment of jumper's knee. *Injury.* 2009;40:598-603

References

Virchenko O, Aspenberg P. How can one platelet injection after tendon injury lead to a stronger tendon after 4 weeks? Interplay between early regeneration and mechanical stimulation. *Acta Orthop Scand*. 2006;77:806–812.

Creaney L, Hamilton B. Growth factor delivery methods in the management of sports injuries: the state of play. *Br J Sports Med.* 2008;42:314-320.

Ljungqvist A, Schwellnus MP, Bachl N, et al. International Olympic Committee consensus statement: molecular basis of connective tissue and muscle injuries in sport. *C lin Sports Med*. 2008;27:231-239, x-xi.

Borrione P, Gianfrancesco AD, Pereira MT, Pigozzi F. Platelet-rich plasma in muscle healing. *Am J Phys Med Rehabil*. 2010 Oct;89(10):854-61

Mehta S, Watson TJ. Platelet rich concentrate: basic science and current clinical applications. *J Orthop Trauma*. 2008;22:432-438

Margolis DJ, Kantor K, Santanna J, Strom BL, Berlin JA. Effectiveness of platelet releasate for the treatment of diabetic neuropathic foot ulcers. *Diabetes Care.* 2001;24(3):483–488.

Lyras DN, Kazakos K, Verettas D, et al. The influence of platelet-rich plasma on angiogenesis during the early phase of tendon healing. *Foot Ankle Int.* 2009;30(11):1101-1106.

de Mos M, van der Windt A, Jahr H, et al. Can platelet-rich plasma enhance tendon repair? A cell culture study. *Am J Sports Med*. 2008;36(6):1171–1178.

Anitua E, Sánchez M, Nurden AT, et al. Platelet-released growth factors enhance the secretion of hyaluronic acid and induce hepatocyte growth factor production by synovial fibroblasts from arthritic patients. *Rheumatology (Oxford).* 2007;46(12):1769-1772.