



SCIENCE

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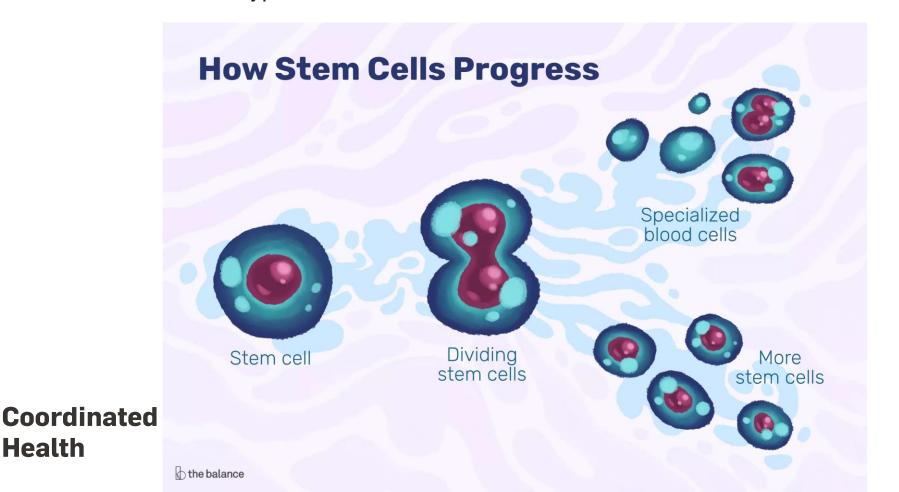
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Stem Cells-Definition

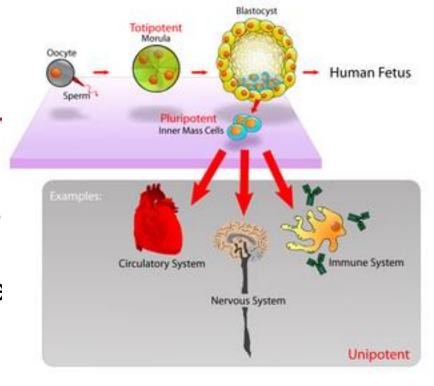
Cells- can differentiate into other types of cells, and can also divide in self-renewal to produce more of the same type of stem cells.



Health

Stem Cell Types

- 1. Embryonic Stem Cells- require destruction of embryo
 - Many nations currently have <u>moratoria</u> or limitations on either human ES cell research or the production of new human ES cell lines.
 - Currently no approved treatments using ES cells.



2. Adult Stem cells- Adipose, Bone Marrow, Blood
Stem cells, are cells which maintain and repair the tissue in which they are found. [26]



Stem Cell History

- 1998- Isolated human embryonic stem cells
 - 2010 1st human trial
- 2006- Adult stem cells could be reprogrammed
- 2008 no SC clinics
- 2019 > 700 clinics
- FDA- only oversees Drugs....but 2017-Fat Stem Cells are DRUGS
- Argument- Stem cells manipulated w drugs/enzymes
- Until 2020- licensed and FDA Approved Clinics
- Where are we now?--- WILD WILD WEST!



Stem Cell Basics I.

- Stem cells are unspecialized. -Sleeping- long time-til needed
 - The primary roles of adult stem cells in a living organism are to maintain and repair the tissue **in which they are found.**
- Scientists are just beginning to understand the signals inside and outside cells that trigger each step of the differentiation process.



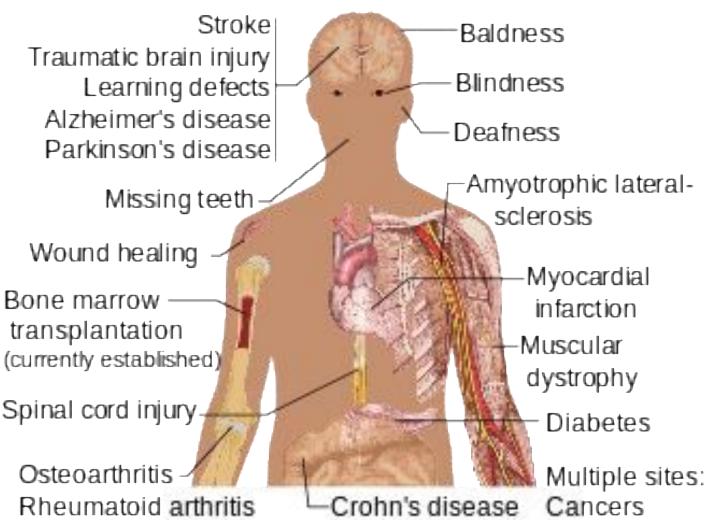
Problem

- Need lots Stem Cells to treat problems- millions and millions
- Not many MSC- (adult stem cells in Fat or Bone Marrow)-least amt-RARE
- Very Hard to grow in Lab- unlike ESC
- Turn into other tissues—tumors???? We dont know signals to turn into specific tissues
- Isolating these cells from an adult tissue is challenging,
- methods to expand their numbers in cell culture have not yet been worked out.



Enormous Potential!!!

Potential uses of **Stem cells**





Reality

Stem Cells

'Stem Cells' From FAT





1:1000 to 1:1,000,000



Bone Marrow Stem Cells







Blood, Bone Cartilage



Fat Stem Cells







Fat Cells,insulate Store food





Dedifferentiation

AAOS-2018

Misrepresentation of Uncharacterized and Unproven Minimally Manipulated Products as **Stem Cells** May Erode Public Trust and Compromise Development of Legitimate Cell Therapies

- AAOS
- National Institutes of Health (NIH),
- American Orthopaedic Society for Sports Medicine,
- Arthroscopy Association of North America,
- International Cartilage Regeneration and Joint Preservation Society,
- Keynote speakers
 - National Institutes of Standards and Technology,
 - Stanford Center for Innovative Study Design
 - FDA.



Recommendations

- Stem cells have unique characteristics that are not met by minimally manipulated cell-based therapies being widely marketed in the United States
- Problematic, confusion for patients, physicians, and the general public.
- ALL current cell therapies offered in the US for musculoskeletal conditions involve the transplantation of adult cells obtained through harvest and minimal manipulation of native tissues
- Term stem cell has been overused, misused
- CALL IT: cell therapy and that the untested and uncharacterized nature
 of these treatments be clearly understood by practitioners and clearly
 communicated within the profession, to patients, and to the public.



NEWS | STEM CELL THERAPIES | DECEMBER 20, 2018

FDA Clamps Down on Unapproved Stem Cell Therapies

Genetech warned its umbilical cord blood-derived cellular products are not FDA cleared





PROBLEM \$\$\$\$\$\$\$\$

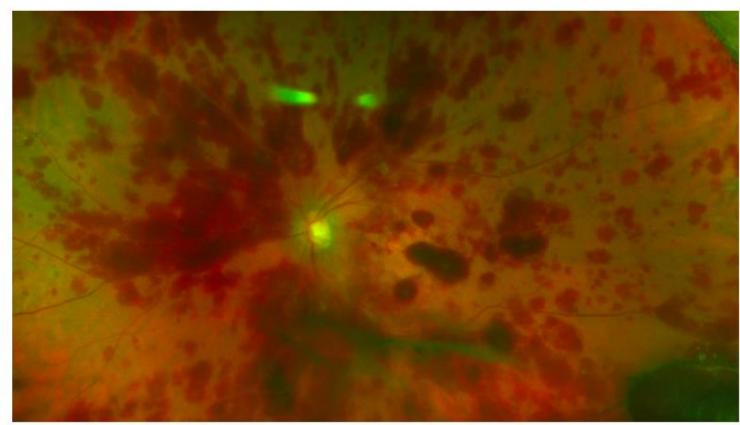
"This is not an industry that's just going to melt away overnight," Turner said. "It may be a prolonged battle. There's just too much money caught up in this marketplace." Bioethicist

None of the therapies they offer have FDA approval. The clinics use a variety of stem cell products, including those from fat tissue, along with cells from bone marrow and from birth tissue like the placenta and umbilical cord.

"At best, these clinics are selling bogus treatments that cost patients thousands of dollars, say industry critics; at worst, the therapies can cause permanent harm."



This clinic's experimental stem cell treablinded patients. Years later, the govern still trying to stop it.





A picture of a patient's eye one week after receiving stem cell injections from U.S. Stem Cell in 2015 shows widespread retinal hemorrhages, according to ophthalmologist Thomas Albini. He said the patient suffered significant loss of vision. (Thomas Albini)

Criticism: FDA-Not great track record!!!

- If the FDA had done something meaningful around 2009 and these businesses hadn't proliferated there wouldn't be this huge regulatory challenge facing the FDA
- Hundreds of these businesses and they say they can't possibly regulate them all, so they have to prioritize their resources and just pick the most outrageous ones.
- "The FDA is part of the very problem they're now responsible for addressing.
- They did very little for years
- If they had done a better job of it over the last seven or eight years, we'd be in a very different place."



Excitement

- Stem cell research is one of the most fascinating areas of contemporary biology,
 - BUT-- research on stem cells raises scientific questions as rapidly as it generates new discoveries.



Patients w (OA) that eventually fail conventional nonsurgical therapies lead to chronic pain, disability, and difficulty with self-care and activities of daily living.

-

Patients vulnerable to unsubstantiated claims in direct-to-consumer advertising.4,5











Dr. ---proudly offers advanced regenerative medicine in the form of stem cell treatment. An injection of a patient's stem cells reduces inflammation and promotes healing by triggering the growth of muscle, cartilage, and bone.

STEM CELL THERAPY IN PITTSTON

The future is now! You can now harvest your cells and store them for future use through Cells on Ice.

(570) 569-2250

ARE STEM CELLS SAFE?

Stem cells are harvested under sterile conditions using a special "closed system" technology so that the cells never come into direct contact with the environment throughout the entire process from removal to deployment. Sterile technique and antibiotics are also used to prevent infection.

Patients have their fat harvested in our special sterile treatment facility under a local anesthetic. The fat removal procedure lasts approximately twenty minutes. Specially designed equipment is used to harvest the fat cells and less than 100cc of fat is required. Post operative discomfort is minimal and there is minimal restriction on activity.

No. Only adult "mesenchymal" stem cells are used. These cells are capable of forming bone, cartilage, fat, muscle, ligaments, blood vessels, and certain organs. Embryonic stem cells are associated with ethical considerations and limitations.



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Mesenchymal stem cells for cartilage regeneration in osteoarthritis

Baldur Kristjánsson, Sittisak Honsawek

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Research

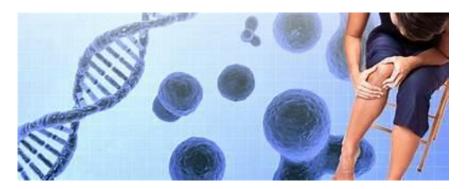
- MSCs have also been found to have no capability for cartilage regeneration after articular cartilage damage.
- Another study found that patients' age and stage of OA also affected the differentiation capability and expression of stemness genes of localized adipose-derived MSCs[17].
- More shockingly, recent study reported that synovial fluid from OA patients inhibited the *in vitro* chondrogenic differentiation in MSC cultures of healthy donors[18].
- Cell based tissue engineering for OA have been used with varying results for over two decades. <u>Autologous chondrocyte implantation</u> (ACI) is a cell based technology wherein the cultured chondrocytes are applied on the injured area for regenerating and repairing cartilage[20]



Clinical Study

- 1. India- 10pts ADSC +PRP
- 2. China –Rat study
- 3. Korea- symptomatic improvement
- 4. Korea- review
- 5. British review article
- 6. Basic Science- no ref
- 7. Vietnam- ADSC +PRP—21 pts
- 8. European study- no ref





- •As promising as the field is, **stem cell treatments still are unproven**, and they often have high rejection rates.
- •The cost also can be prohibitive for many patients, with a single treatment costing well into the thousands of dollars, (\$4000-\$12,000) as of 2018.

Stem cell clinicians will admit they don't have the broad, controlled studies to prove injected stem cells are safe and effective.

For today, however, we remain in murky medical waters. Stem cells are a high-priced treatment backed by insufficient research, and they can be administered by any physician willing to take a weekend course and accept cash or charge.



Summary

Meanwhile, the FDA has given the industry at large until 2020 to comply with the new rules. So far, few companies have made any move to do so, FDA officials said.

- International scientific groups,
- Leading stem cell researchers
- American Lung Association
- American Academy of Ophthalmology



'Although stem cells may eventually be used to treat many diseases, the research is in its early stages, they said, and the therapies at cash-based clinics are unproven and premature.'



Stem Cells



OR



?

BOTH



PRP



OR



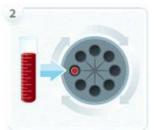


PRP-Definition

- Platelet-rich plasma (PRP)--is a concentrate of platelet-rich plasma protein derived from whole blood, centrifuged to remove red blood cells.
- PRP contains several different growth factors
- Tentative evidence supports its use in osteoarthritis (OA) of the knee. [7][8]
- PRP was "a promising, but not proven, treatment option for joint, tendon, ligament, and muscle injuries". [9]



Collect Blood 30-60ml of blood is drawn from the patient's arm.



Separate the platelets The blood is then placed in a

The blood is then placed in a centrifuge. The centrifuge spins centrifuge. The centrifuge spins and separates the platelets and separates the platelets

Extract platelet-rich plasma



Inject injured area with PRP

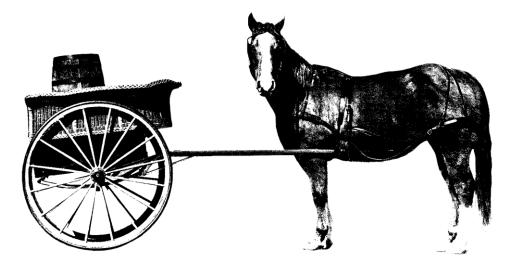
Using the concentrated platelets, we increase the growth factors up to eight times, which promotes temporary relief and stops inflamation.



AAOS

The clinical use of biologics such as platelet-rich plasma (PRP) and cell-based therapies to treat orthopaedic complications has greatly outpaced the evidence.

CARTBEFORETHEHORSE





Proponents

 Proponents of PRP therapy have argued that negative clinical results are associated with poor-quality PRP produced by inadequate <u>single</u> <u>spin devices</u>.





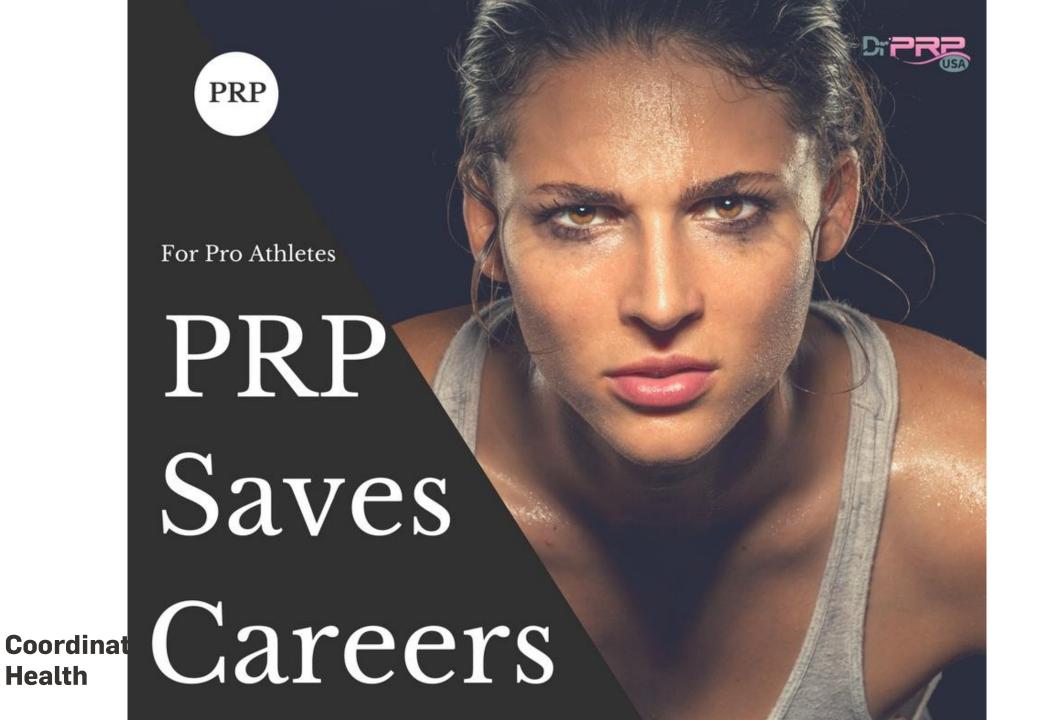


Good News

 There are no studies to date that have reliably documented adverse effects associated with PRP treatment

Treatment of knee OA with PRP and minimally manipulated autologous cells are already widely used in the United States. The existing studies do not show that these therapies are associated with substantial risk of harm. 12,39





21 Biggest American Pro Athletes Who've Had PRP In 2016

This USA-only list is not all-inclusive and I'm sure we have omitted a lot. But this list should give you an idea of how popular this treatment really is.

- 1. As we mentioned above, Garrett Richards had platelet-rich plasma injection for healing the pitcher's partially torn elbow ligament. He's confident of his comeback without Tommy John.
- 2. Stephen Curry had Platelet-Rich Plasma for a grade 1 MCL sprain during Game 4 of the team's first-round series
 against the Houston Rockets in 2016.
- 3. In November, Los Angeles Lakers' D'Angelo Russell got a platelet-rich plasma injection to alleviate pain in his left knee.
 After having the injection on Nov 23, he missed 11 games to pave way for full recovery.
- 4. Philadelphia 76ers Jerryd Bayless also got his PRP to heal his wrist in November. But one thing he didn't do after
 Platelet-Rich Plasma was rest. He continued playing so healing didn't happen. And he was under immense pressure to
 stop the season and do surgery to get well for the next season, which is what he eventually did in December.
- 5. New York Mets catcher Travis d'Arnaud received a platelet-rich plasma injection in his ailing right shoulder. His was a strained rotator cuff. Today, word is out that he is 0-for-5 in his attempt to throw out base stealers this season.



Platelet-Rich Plasma Cuts Downs Healing Time By 50%

We've had physicians who say they're seeing hamstring strains that typically has about a six-week healing window heal completely in three-weeks. They are astounded. Typically natural treatments should have LONGER healing window than traditional treatments. But here, we're talking about hundreds of cases where it's actually cut down by 50% or more – and this is the most natural (and simple) of all treatments.

PRP just concentrates the body's own healing resources to where needs it most!



The growth factors and other cytokines present in PRP include

- platelet-derived growth factor
- transforming growth factor beta
- fibroblast growth factor
- insulin-like growth factor 1
- insulin-like growth factor 2
- vascular endothelial growth factor
- epidermal growth factor
- Interleukin 8
- keratinocyte growth factor
- connective tissue growth factor



Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Metaanalysis of Randomized Controlled Trials. Arthroscopy 2017

CONCLUSIONS:

Current evidence indicates that, compared with HA and saline, intra-articular PRP injection may have more benefit in pain relief and functional improvement in patients with symptomatic knee OA at 1 year postinjection.

This study suggests that PRP injection is more efficacious than HA injection and placebo in reducing symptoms and improving function and quality of life.

Knee Surg Sports Traumatol Arthrosc. 2016



Not all PRP's created equal

- Different concentrations WBC, Platelets, Fibrin
- Most research- white papers by companies
- No significant peer review comparisons

PLATLET RICH FIBRIN 10 cc of blood centrifuged for 10 minutes Acellular Plasma Layer Platelet Rich Fibrin Layer Red Blood Cell Layer



PRP



OR



- Neither-if honest
- Does no Harm
- May accelerate soft tissue healing
- As good or better than HA
- BUT- NO INSURANCE





SCIENCE

Costly Joint-Pain Injections Replaced By New \$2 Pill

New pill boosts the same lubricating joint fluid as expensive and painful injections - without using a needle. Users report dramatic relief from swelling, pain and stiffness without side effects and expense.

Health News Syndicate

HNS—A popular needle injection for people with joint pain is now available in an inexpensive nonprescription pill. The breakthrough came when researchers discovered a way to deliver the injected "relief molecule" through the digestive system.

Top US clinics have used these needle injections for years because they deliver powerful relief. Unfortunately, the shots are painful and expensive. They also only work on the joint being treated.

The new pill, called Synovia, delivers the same "relief nolecule" as the injections. dowever, it has some noressive advantages. irst, it's inexpensive and onprescription. Also, relief delivered to every joint in e body because it enters e bloodstream through the gestive system.

This gives it the ability to duce a much wider variety pain. Users report greater



NO MORE NEEDLES: A popular needle injection pain-killer for joint pain is being replaced. The key molecule in these injections can now be delivered by taking a new low-cost pill called Synovia.

Impressive Clinical Results

Leading clinics use injection therapy because it works. Recent clinical trials show the pill form also delivers major relief.

One example is a landmark study out of Europe. In the study the active ingredient in Synovia was compared to a popular NSAID pain reliever.

roles: lubrication and giving the cartilage the nutrients it needs."

Approved By Leading Doctors

The new delivery system for this molecule has caught the attention of leading medical doctors.

"Needle injections for joint"



UNHEALTHY: No lubricating fluid or cartilage leads to painful bone-on-bone rubbing.



HEALTHY: Synovia's active ingredients lubricate joints and nourish cartilage!





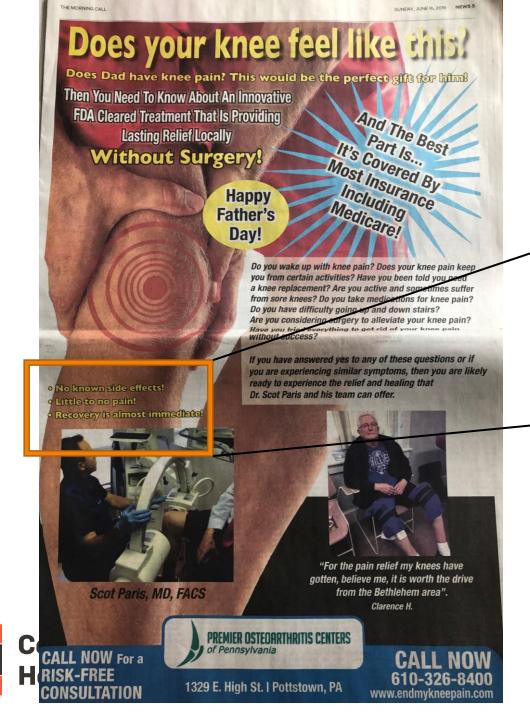


Boswellia serrata: Boswellic acids – the active components – have strong anti-inflammatory and analgesic properties. They also may help prevent cartilage loss and inhibit the autoimmune process, making Boswellia a potential therapy for RA, too.

- **2**. **Capsicum Annuum:** capsaicin reduces substance P, a pain transmitter.
- **3**. **Curcuma longa:** Curcumin blocks inflammatory cytokines and enzymes, including cyclooxygenase-2 (COX-2), the target of celecoxib.
- **4. Zingiber officinale:** ginger has been shown to have anti-inflammatory properties similar to ibuprofen and COX-2 inhibitors. Ginger also suppresses leukotrienes (inflammatory molecules) and switches off certain inflammatory genes, making it potentially more effective than conventional pain relievers.

- . Glucosamine sulfate: Glucosamine produced in the body provides natural building blocks for growth, repair, and maintenance of cartilage. Like chondroitin, glucosamine may lubricate joints, help cartilage retain water and prevent its breakdown. Similar to NSAIDs for its effectiveness of easing osteoarthritis symptoms.
- 6. Methylsulfonylmethane: MSM is an organic sulfur compound. Sulfur is needed to form connective tissue. MSM also seems to act as an analgesic by lessening nerve impulses that transmit pain.
- 7. Willow Bark: Willow bark contains a chemical called salicin that is similar to aspirin. It eases pain and reduces inflammation.







- o No known side effects!
- · Little to mo pain!
- · Recovery is almost immediates

Common side effects of Synvisc include:

- •injection site reactions (pain, swelling, warmth, stiffness, puffiness, or fluid buildup in or around the knee),
- •muscle pain,
- trouble walking,
- •fever,
- •chills,
- •nausea,
- numbness or tingly feeling,
- headache,
- dizziness,
- tired feeling, or
- •itching or skin irritation around the knee.

Tell your doctor if you have serious side effects of Synvisc including:

- back pain,
- •severe headache, or
- •fast or pounding heartbeat.
- •Synvisc may cause an allergic reaction.



Pt Complaints:

I had one synvisc injection. Within 24 hours my knee had doubled in size. My Ortho had to drain my knee two days later. The pain was intense and continued for weeks. I'm still dealing with pain two months later.

I had the series of three shots and a small reaction after the third one....Dr recommended Synvisc one and it was a nightmare....huge swelling...could not bend our move my right knee at all...got so sick and dizzy I ended up in er ...had horrible results in blood work...it even affected my liver....er dr aspirated three times....now most of swelling is down but my knee it's so stiff and painful I'm in tears at times...is there a class action against Synvisc somewhere?

I have had the same bad reaction and now I am going to have my knee "washed" out as my orthopedic Dr calls it after the sinvisc injection missed work and working out it's been a month. I am for a class action LS.



Introducing Dr. Scot Paris



Dr. Scot Paris received a BA in Psychology from Emory University in Atlanta, GA in 1987. He then received his Medical Degree from UMDNJ/Robert Wood Johnson Medical School in Piscataway, NJ in 1991. Dr. Paris completed a Residency in General Surgery at Mercy Catholic Medical Center in Darby, PA in 1996, and then completed a Fellowship in Colon and Rectal Surgery at UMDNJ/Muhlenberg Hospital in 1997.

Currently, Dr. Paris practices General and Colorectal Surgery in private practice in Pottstown, PA and is the Chairman of the Department of Surgery at Pottstown Memorial Medical Center in Pottstown.

Dr. Paris joins Northeast Spine and Wellness Center as the Medical Director. Dr. Paris has taken an interest in the treatment and prevention of chronic back pain and other musculoskeletal conditions. He is currently receiving training in minimally invasive pain management techniques and provides and performs surgical expertise for pain management physicians that perform techniques that require surgical intervention. In addition, Dr. Paris plans to obtain certification



with the American Academy of Pain Management.



Impibits Cancer Cell growth

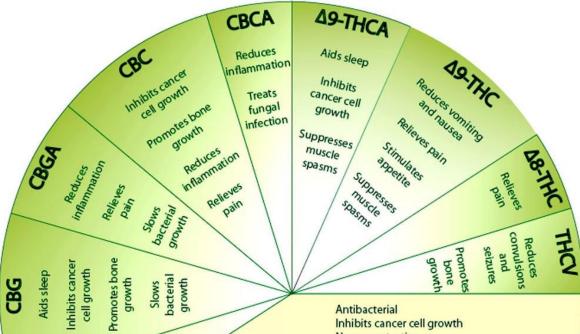
CBD

Reduces Inflamma

CBDA

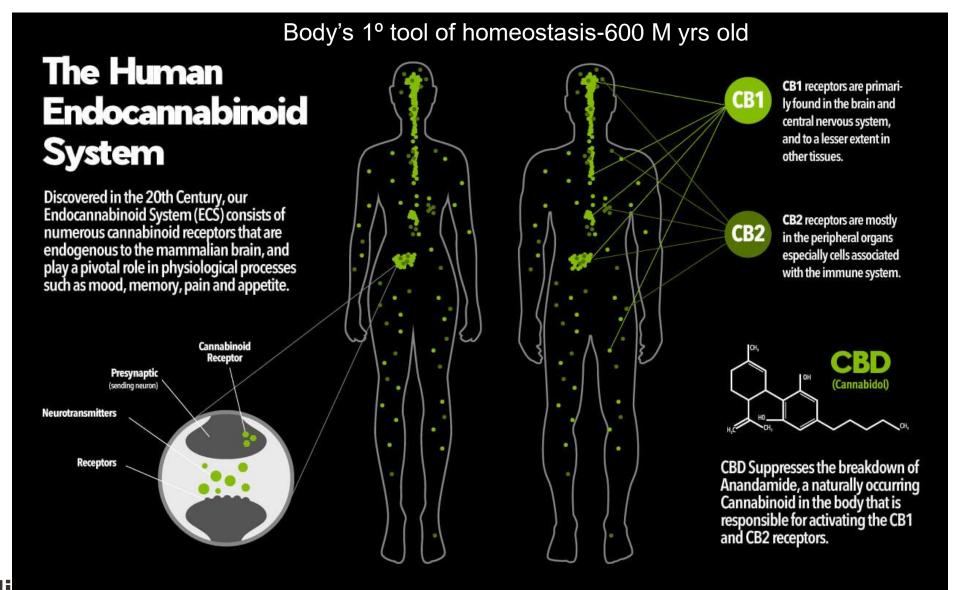
CBD





Inhibits cancer cell growth Neuro-protective Promotes bone growth Reduces seizures and convulsions Reduces blood sugar levels Reduces function in the immune system Reduces inflammation Reduces risk of artery blockage Reduces small intestine contractions Reduces vomiting and nausea Relieves pain Relieves anxiety Slows bacterial growth Suppresses muscle spasms Tranquilizing Treats psoriasis Vasorelaxant







Basic Science Facts- Endocannabinoid System

- Humans and animals synthesize endocannabinoids- same receptors as exogenous plant based CBD/THC
- Crucial for bioregulation and unique/ubiqutous cell signaling: PAIN-Acute, Chronic Inflammatory, Neuropathic
- Anti- inflammatory effects of most spices –mediated thru CB2 receptors
- Derived from FFA in cell membranes-similar to Omega 3/6
- May help normalize sleep, improve appetite PO TJA
- US Dept HHS- owns patent on use CBD as Anti-Ox & Neuroprorectants
- Significant 'cross-talk' betwn opioid & EC receptors- dec dose response curve
- CB 1-2 receptors may-decrease cartilage destruction inhibitting chondrocyte expression of cytokines



Basic Science Facts- Endocannabinoid System

 Ibuprofen, Ketorolac, Acetaminophen, Cox-2 – all have a cannabinoid MOA for analgesia

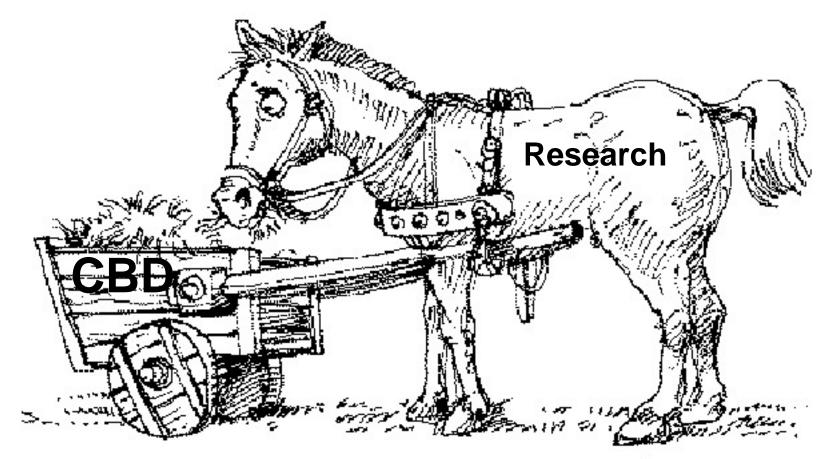
 EC system in widely distributed in body. Main function is cellular homeostasis.

Understanding is emerging, incomplete, complex-

exciting!!







PUTTING THE CART BEFORE THE HORSE









Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Primary Arthroplasty

Should Cannabinoids Be Added to Multimodal Pain Regimens After Total Hip and Knee Arthroplasty?



Thomas R. Hickernell, MD, Akshay Lakra, MD *, Ari Berg, MD, Herbert J. Cooper, MD, Jeffrey A. Geller, MD, Roshan P. Shah, MD

Department of Orthopedic Surgery, Center for Hip and Knee Replacement, NewYork-Presbyterian Hospital/Columbia University Medical Center, New York. New York



Since All pain is ultimately transmitted through inflammatory mediators......

NEUTRACEUTICALS TO HELP OPTIMIZE SURGICAL OUTCOMES

- Omega-3 (Fish Oil)-1000-3000mg
- Turmeric/Curcumin(700-1500)
- -ASA 81mg
- Bromelain (100mg bid)
- Vit D3 (5000mg)
- Vit E (400-800mg)
- Vit C (2000mg)
- Mg+ (400-800mg)
- CoQ10 (100-200mg)
- Zn(50mg)
- Selenium (200mcg)
- Resveratrol (250mg)
- L-Arginine (1500mg)

Green/Black Tea

Carotenoids

Black Pepper-peppercorns

Cinnamon

Clove

DHEA (25-100mg)

Tart Cherry

Avocado

Pomegranate

Ginger

Quercetin (250mg)

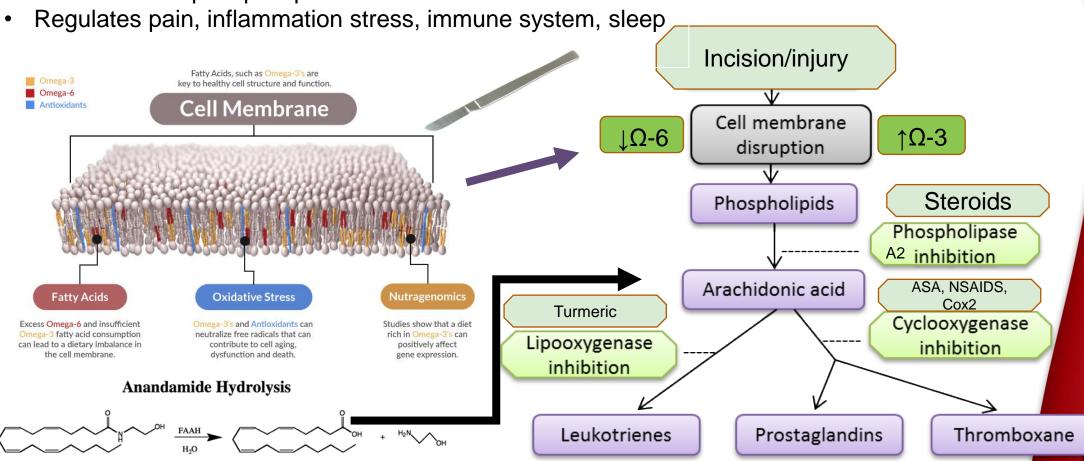


Hemp- CBD!!!

Anandamide (endocannabinoid-'CBD')- produced on demand from phospholipids in cell membrane

Arachidonic Acid

Ethanolamine



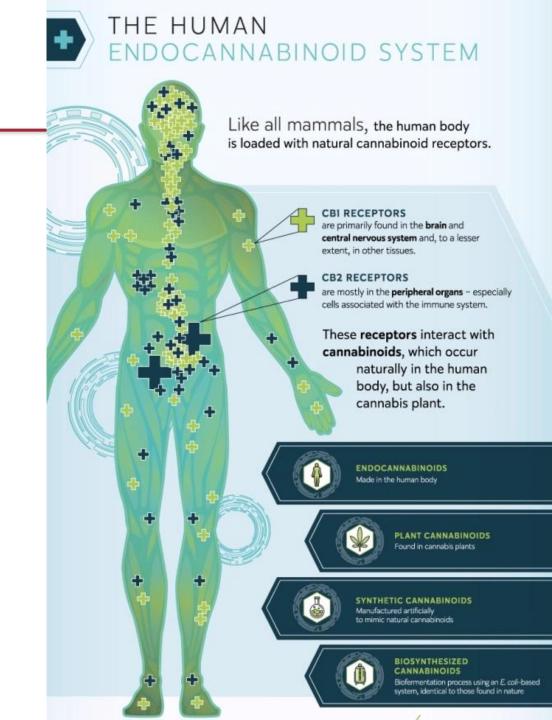




The Endocannabinoid System, Cannabinoids, and Pain

- Modulate Pain and Inflammation
- Anti-Nausea
- Tissue healing
- No respiratory depression
- No fatalities reported directly related to toxicity
- 600 million y.o. system & thousands yrs. social/medicinal use
- Pain related medical service = \$1Trillion USA
- Stay tuned- 31 states approved
 - Overdose Rx deaths decreased 25%







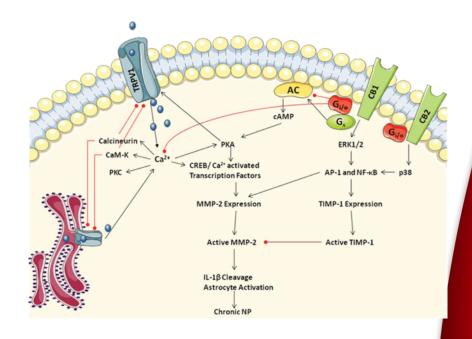
CBD



BOTH







THANKYOU

