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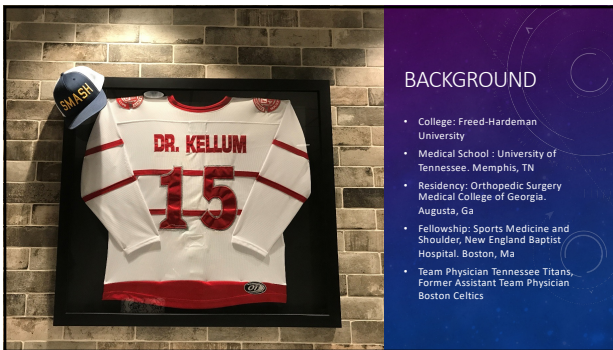
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THINGS THAT GOT ME THINKING

- Marathon runner
- Arthroscopic meniscectomy
- A reps mom

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THE PROBLEM

- What is problem
- Why must is be addressed
- Why does the problem exist
- My line in the sand

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THE BASICS...



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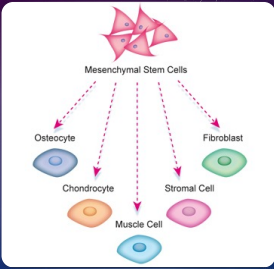
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WHAT IS REGENERATIVE MEDICINE

- Stem cells
- Growth Factors



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WHAT IS AN ADULT STEM CELL?

- Simple
  - An undifferentiated cell that's held in reserve until replacement or repair is needed.
  - It can turn into many cell types
  - It can orchestrate a repair response

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# STEM CELLS

- 1960's discovery- bone marrow cells
- Since then- ESC, FSC, and ASC
- ASC- mesenchymal stem cell

```
graph TD; A[Stem Cells] --> B[Adult]; A --> C[ESC]; A --> D[FSC];
```

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**REMEMBER WHEN YOU COULD REFER TO YOUR KNEES AS RIGHT AND LEFT?**

# STEM CELLS

- -Control Inflammation
- -Modulate the Immune System
- -Stimulates Regeneration

**INSTEAD OF GOOD AND BAD.**

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# SOURCES OF STEM CELLS

- Bone marrow
- Adipose
- Amniotic, peripheral blood
- Umbilical, Placental

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**HOW DO THEY WORK**

- Immunomodulatory- t cell, dendritic cells, monocytes
- Growth factors secretion for local cells
- Differentiation to those cells

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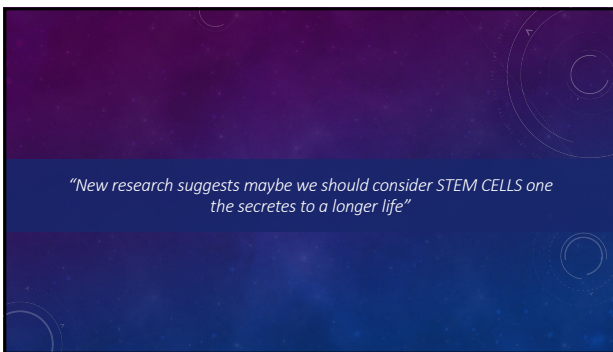
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*"New research suggests maybe we should consider STEM CELLS one the secretes to a longer life"*

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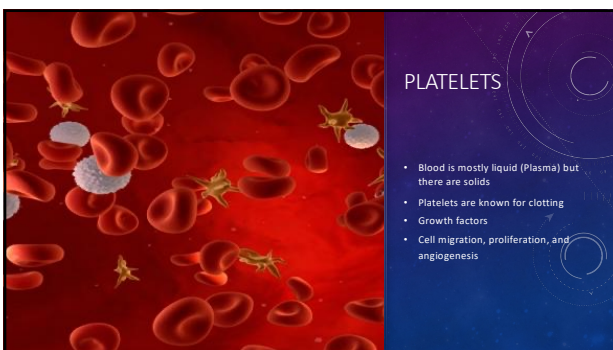
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**PLATELETS**

- Blood is mostly liquid (Plasma) but there are solids
- Platelets are known for clotting
- Growth factors
- Cell migration, proliferation, and angiogenesis

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### GROWTH FACTORS

- **AZM**
  - Binds to IL-1, IL-6 and TNF
  - Eliminates proteases that cause osteoarthritis
  - Stops degeneration/osteoarthritis disease complex
- **PRP**
  - Controls inflammation
  - Contains higher vesicles/exosomes for regeneration
  - 30 years and younger

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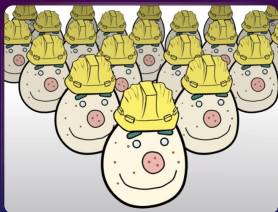
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- To use a construction site metaphor:
  - Platelets are like espresso shots given to the workers to help them work harder and faster.
  - Stem cells are a curious mix of a general contractor who can recruit more sub-contractors and who can also turn into the bricks and mortar.

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### Knee Osteoarthritis



### OA OF THE KNEE- THE NUMBERS

- 27 million Americans with Knee OA
- 89.1 million US dollars
- 4<sup>th</sup> leading cause of disability world wide
- Treatment- Visco, Steroids, nsalds, TKA

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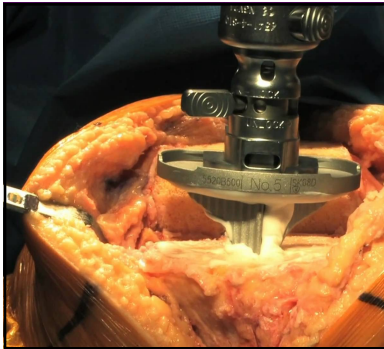
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**TKA**

- 600 k TKA done a year in the US
- Done before age 65, revision rate increases 2.5
- Revision rate will grow by 600% by 2030
- Great surgery but..... 20 % continue to have pain and significant problems. 2% have complications as PE, infections and death

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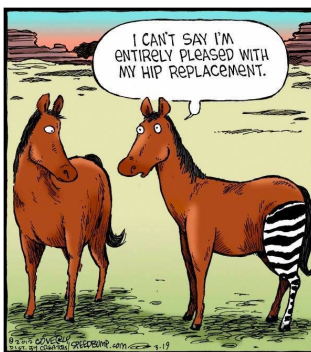
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I CAN'T SAY I'M ENTIRELY PLEASSED WITH MY HIP REPLACEMENT.

**DATA WITH STEM CELLS**

- Patient cohort of 339 patients
- 70% were told they needed TKA
- Treated with one stem cell injection, at one yr's time only 6 % went on to need a total knee. Unpublished data-this has gone out to about 4-5 yrs and the conversion rate is about the same
- 60 % of patients had greater than 50% pain relief and 40% of patients had greater than 40% pain relief

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**STEM CELLS VS. SURGERY- BEDELL**

Joint Replacement vs Stem Cell Projective Study

- **446 Patients**
  - 223 Surgery
  - 223 Stem Cell
- **Costs**
  - \$40k-\$70k Surgery
  - \$10-\$15k Stem Cell
- **Complications**
  - 10-20% Surgical
- **Success Rates**
  - 50% Surgery
  - 90%+ with Stem Cell



<https://stemcellcollege.files.wordpress.com/2019/05/berkeleybedellwhywecantweuseourstemcells.pdf>

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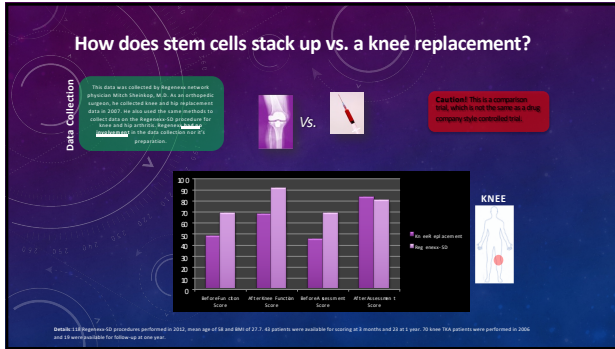
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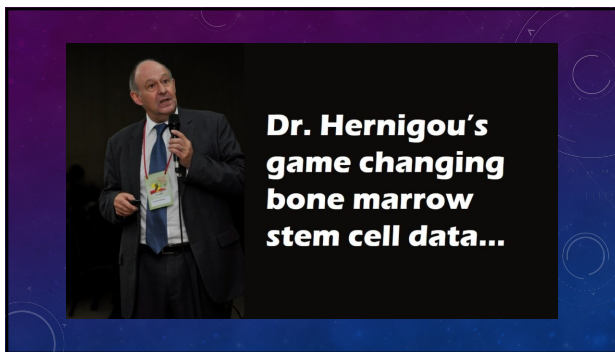
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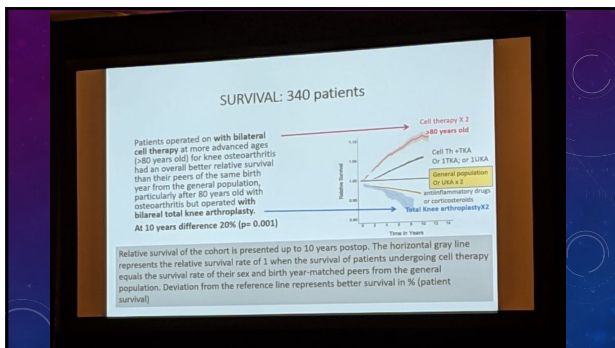
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Regenexx



### MENISCAL TEARS

- 4 large randomized controlled trials now show that knee arthroscopy to treat a meniscus tear is no better than placebo surgery

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### MENISCAL PATHOLOGY

- Lets say meniscus tear/OA vs PT- no diff
- Lets say meniscus tear no OA vs sham surgery- no diff
- Framingham study found that middle aged and more senior saints have meniscus tears without pain

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### THE STRUCTURAL PAIN MODEL ISN'T ACCURATE

- While some MRI results show the cause of why a joint hurts, most do not:
  - Based on the OAI and Framingham knee arthritis studies, cartilage loss on a knee MRI is not associated with pain
  - Meniscus tears in middle aged and older people are commonly seen in pain free patients



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SO THE 50 YEAR OLD THAT EXPERIENCES SUDDEN KNEE PAIN WHILE SKIING AND THE MRI SHOWS A MENISCUS TEAR:

- The meniscus tear was likely there before the pain episode and likely has nothing to do with why the knee hurts
- Hence operating on the meniscus tear is not the right move



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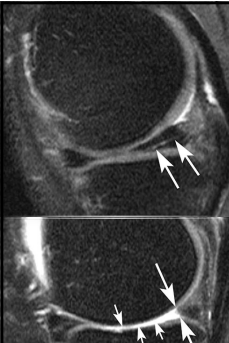
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RSNA 2014 100% VS 59%

\*"We found that patients without knee osteoarthritis who underwent meniscal surgery had a highly increased risk for developing osteoarthritis and cartilage loss in the following year compared to those that did not have surgery, regardless of presence or absence of a meniscal tear in the year before," Dr. Roemer

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SO IS THERE A BETTER WAY?

- Let's stop cutting stuff out and use precise image guided injections of agents that can help tissues heal



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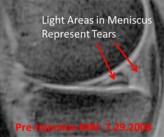
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TRETMET WITH STEM CELLS


Pre-Injection MRI: 7.29.2008



Light Areas in Meniscus Represent Tears

Pre-Injection MRI: 7.29.2008

Post-Injection MRI: 2.25.2011



Darker Areas in Meniscus Represent Healing

Post-Injection MRI: 2.25.2011

**\*\* IMPRESSION \*\*:**  
 1. Improved appearance of the known complex tear of the posterior horn medial meniscus. Lateral meniscus and remainder of the tendons/ligamentous structures are unremarkable.

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Kellum Stem Cell Institute  
Knee

Patient ID	Pain Level	4 weeks	8 weeks	12 weeks	16 weeks
M8774	8	5	5	4	1
M4243	9	3	3	1	0
J4650	10	3	0	0	0
D2670	10	6	0	0	1
S2582	9	4	2	2	1
K7478	10	2	0	1	1
M2729	10	1	0	2	2
B8254	10	6	2	0	0
J2637	9	5	1	0	0

\*results were taken from Bellingham location at random

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JOURNAL OF PAIN RESEARCH  
 ANTERIOR CRUCIATE LIGAMENT TEARS TREATED WITH PERCUTANEOUS INJECTION OF AUTOLOGOUS BONE MARROW NUCLEATED CELLS: A CASE SERIES

SEVEN OF TEN PATIENTS SHOWED IMPROVEMENT IN AT LEAST FOUR OF FIVE OBJECTIVE MEASURES OF ACL INTEGRITY IN THEIR POST PROCEDURE MRIS. IN THE ENTIRE STUDY GROUP, THE MEAN GRAY VALUE, MEDIAN, RAW INTEGRATED DENSITY, AND MODAL GRAY VALUE ALL DECREASED TOWARD LOW-SIGNAL ACLS (P<0.01, P<0.02, P<0.002, AND P<0.05), INDICATIONS OF IMPROVED LIGAMENT INTEGRITY. SEVEN OF TEN PATIENTS RESPONDED TO THE SELF-RATED METRICS FOLLOW UP. THE MEAN VAS CHANGE WAS A DECREASE OF 1.7 (P<0.25), THE MEAN LEFS CHANGE WAS AN INCREASE OF 23.3 (P<0.03), AND MEAN REPORTED IMPROVEMENT WAS 86.7%.

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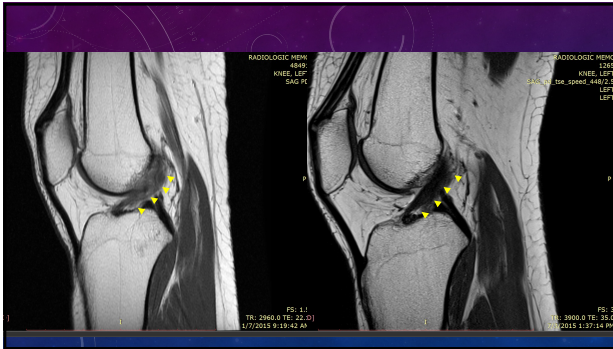
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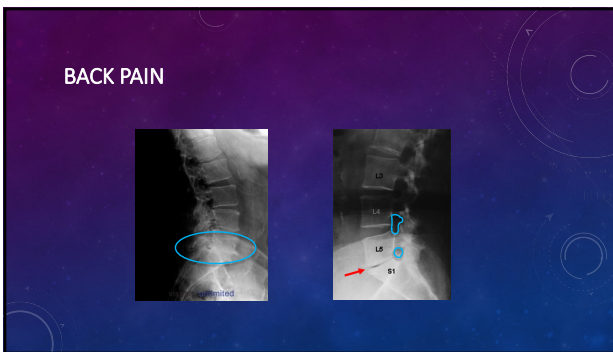
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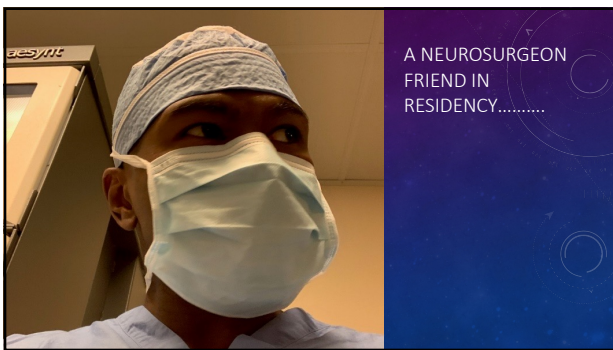
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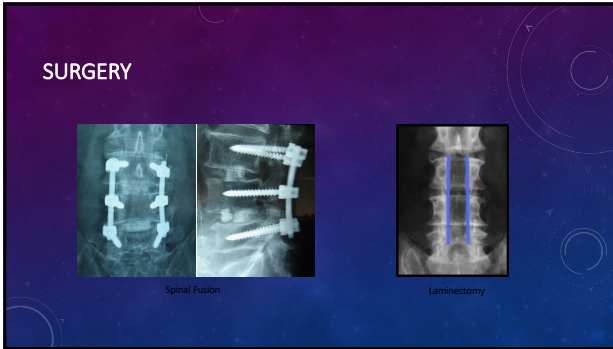
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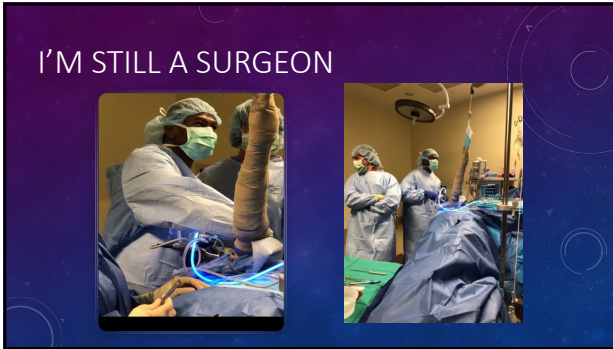
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Lee, W. S., Kim, H. J., Kim, K. I., Kim, G. B., & Jin, W. (2019). Intra-Articular Injection of Autologous Adipose Tissue-Derived Mesenchymal Stem Cells for the Treatment of Knee Osteoarthritis. A Phase I/II, Randomized, Placebo-Controlled Clinical Trial. *Stem cells translational medicine*, 8(6), 504–511. <https://doi.org/10.1002/sctm.18-0122>

12 patients underwent autologous adipose-derived MSC treatment, injected intra-articularly into 12 knees.  
 12 knees were injected with saline, acting as the control.  
 A single injection led to significant WOMAC improvement at 6 months.  
 There was no significant WOMAC improvement in the control group.  
 There was no significant change in cartilage defect for the MSC group after 6 months while there was a significant increase in defect for the control group after 6 months.  
**This study demonstrates that intra-articular injections of MSCs for knee osteoarthritis significantly improves pain scores and prevents continued cartilage defect**

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Chan, C. F., Hu, C. C., Wu, C. T., Wu, H. H., Chann, C. S., Hsiao, Y. P., Tsai, C. C., & Ohano, Y. (2021). Treatment of knee osteoarthritis with intra-articular injection of allogeneic adipose-derived stem cells (ADSCs) FLEXCYTES. A phase III, randomized, active-control, single-blind, multi-site-center clinical trial. *Stem cell research & therapy*, 12(1), 562. <https://doi.org/10.1186/s13287-021-02631-z>

57 subjects were randomized into 4 different groups: one group receiving a hyaluronic acid control and 3 groups receiving doses of adipose derived stem cells.  
**At the week 24 follow up, both groups had improvements in WOMAC score but the stem cell group also had significant improvements after 4 weeks.**  
 The stem cell group pain scores after 48 weeks suggest a longer duration of effectiveness compared to the HA group

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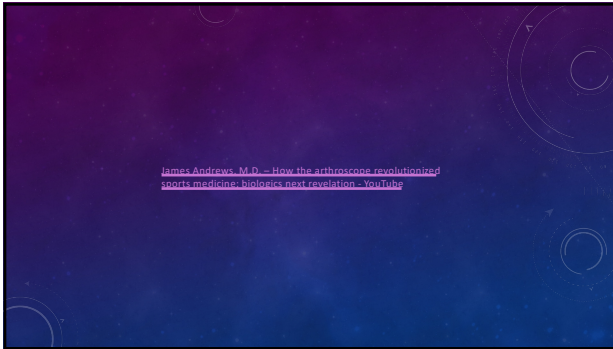
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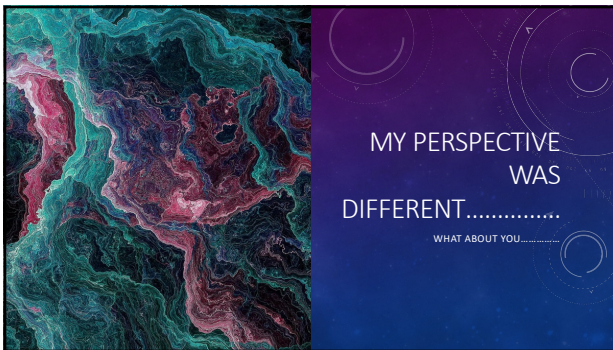
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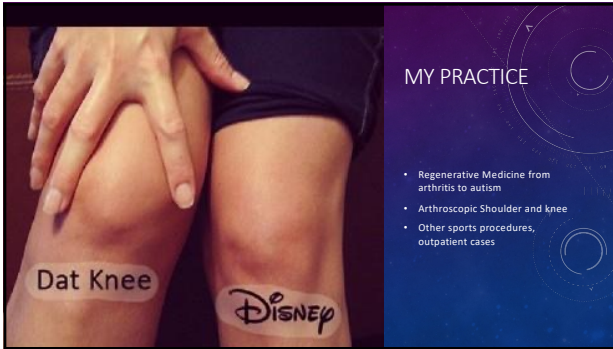
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