Costly and/or Complex

Orthopedic Surgeries

Goals for Today

1. Understand the problem;
2. Identify the most common orthopedic problems affecting commercial groups; and,
3. Describe the effectiveness of “traditional” and newer treatments.

Which Joints, What Causes

1. In commercial populations, the commonest joints requiring intervention are shoulder and knee;
2. Wrist and back are also impacted; and,
3. “Overuse” injuries are common.
4. Elevated BMI and diabetes can be contributing factors;
5. “Overuse” injuries often become Worker’s Comp or long-term disability issues.

Extent of the Problem - Prevalence

Hip Replacement

	Women	Men	
< 50	0.1%	0.1%	
50 - 59	0.8%	1.0%	75,000
60 - 69	2.1%	2.1%	
70 - 79	4.4%	3.8%	
80 - 89	6.3%	4.8%	
90 +	6.1%	4.8%	

2,500,000 individuals living with hip Implants

Knee Replacement

	Women	Men	
	0.1%	0.1%	
	1.8%	1.2%	366,600
	5.5%	3.6%	
	10.1%	7.3%	
	11.0%	8.8%	
	7.4%	7.4%	

4,700,000 individuals living with knee Implants

Extent of the Problem - Cost

Description	Total* Cost
Carpal tunnel syndrome, w/o surgery	$374
Carpal tunnel syndrome, with surgery	$4,183
Surgery Cost	**$3,809**
Joint degeneration, localized - knee & lower leg, w/o surgery	$780
Joint degeneration, localized - knee & lower leg, with surgery	$15,720
Surgery Cost	**$14,940**
Joint degeneration, localized - shoulder, w/o surgery	$839
Joint degeneration, localized - shoulder, with surgery	$15,024
Surgery Cost	**$14,185**
Joint degeneration, localized - back, w/o surgery	$1,353
Joint degeneration, localized - back, with surgery	$19,592
Surgery Cost	**$18,240**

* Allowed amount

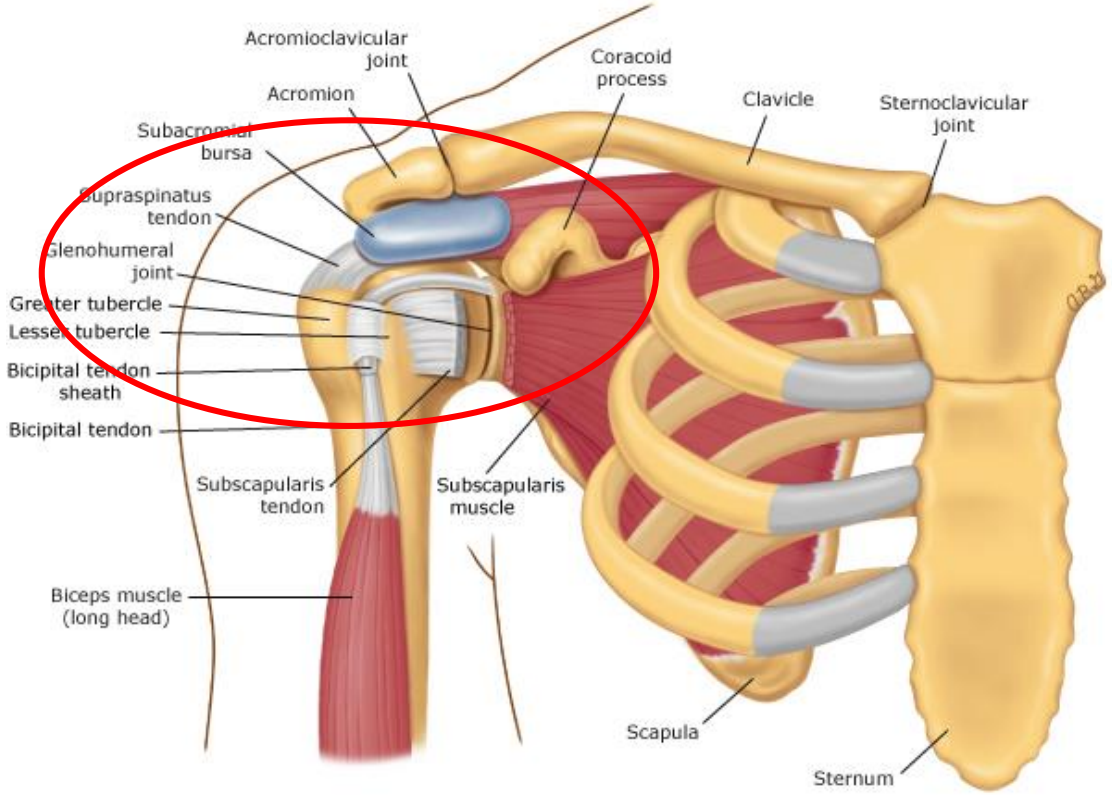
Costs- The High End

Costs for complex surgeries (for example, “redos”) can easily reach $75,000 - $100,000 (in addition to the cost(s) of a first therapy.

Common Injuries: Common Factors

1. Involve complex joints;
2. Primary issue is pain;
3. Significant treatment failure rates historically, especially for back, knee and shoulder;
4. “Overuse” injuries are common.
5. Elevated BMI and diabetes are contributing factors;
6. “Overuse” injuries often become Worker’s Comp or long-term disability issues; and,
7. Tendency for injuries to become “chronic:

Commonest Structures Involved: Shoulder

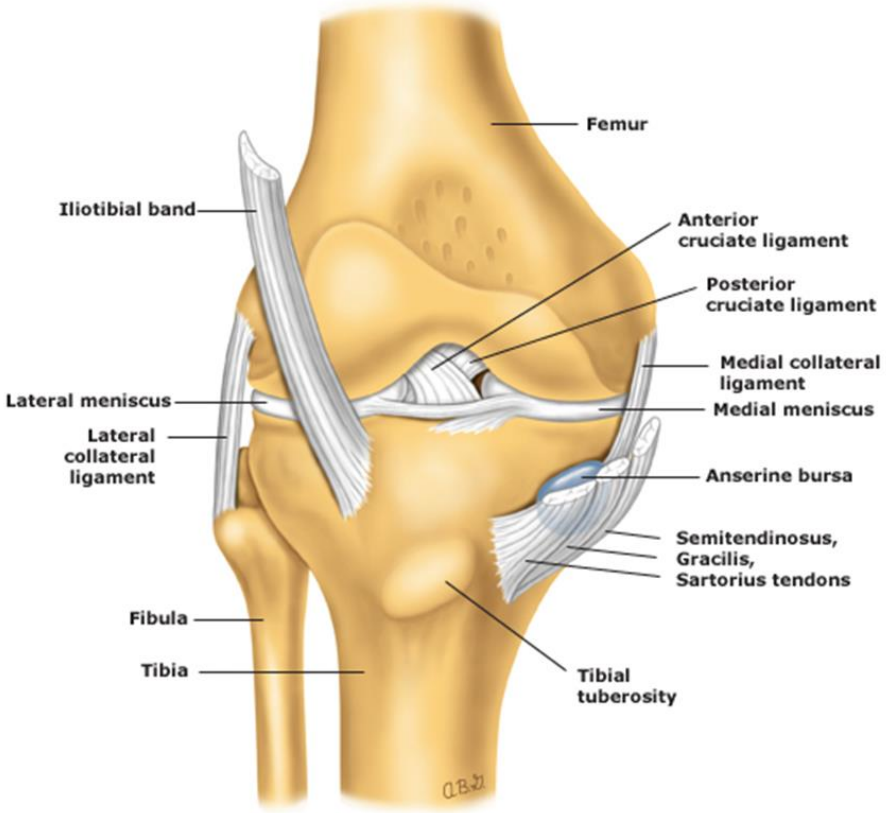


1. Commonest injuries are to the Glenohumeral joint and tendons associated with the rotator cuff.
2. Both are associated with overhead lifting or other over-the-head work.
3. 250,000 repairs annually.

Traditional Treatment- Shoulder

1. Initial treatment is usually non-surgical.
2. Failure rates can be as high as 85%!
3. When conservative care is ineffective, a variety of surgeries can (usually tendon transfer)are employed.
4. Surgical “Failure” rates can be as high as 90%.
5. Failure is often due to the lack of “regrowth” of the bone-tendon connjection.

Commonest Structures Involved: Knee



1. Commonest injuries are to the menisci, ACL and patellar tendon (not shown here).
2. Both are associated with improper lifting mechanics, “weekend warrior” behavior, and elevated BMI; and,
3. 200,000 ACL reconstructions at a cost of $2 - $3 billion annually.

Traditional Treatment- Knees

1. For incomplete ACL tears, traditional treatment has been conservative (physical therapy and pain medications or surgical; results in less severe cases have been good.
2. For more severe tears, if left untreated, 66%-85% of individuals will continue to have pain and instability resulting in significant long-term issues;
3. Definitive treatment is surgical tendon transplant; the procedure has a 25% failure rate.

Traditional Treatment: Back Disorders

1. Treatment of back disorders follows a similar pattern with conservative care early on wiith surgical repair reserved for individuals with chronic issues or who meet certain clinical criteria.
2. Epidural or facet joint steroid injections (long a staple of therapy) have recently been shown to lack long-term effectiveness.
3. National guidelines no loner recommend early complex imaging or surgery because of their ineffectiveness;
4. Even when surgery is performed, failure rates are high; and,
5. Individuals failing surgery often become chronic pain patients with attendant problems of disability and opioid abuse.

Administrative Solutions- Not the Answer

MCOs have tried several solutions:

1. Bundled pricing- savings are minimal and long-term outcomes are not improved;
2. Utilization management techniques (such as preapproval) do not change outcomes or materially impact costs; and,
3. “Centers of Excellence”- performing a fundamentally ineffective treatment well does not make it effective.

Orthobiologics

An answer?

Evolution of treatment

Rationale

2nd generation platelet products contain growth factors that stimulate tissue regeneration;

If injuries are severe, these preparations may be ineffective; and,

The optimal method of preparation has not been determined.

Bone marrow stem cell preparations contain growth factors and cells that can "rebuild" tendons, muscle and bone.

Danger: Unapproved Products

FDA 12/2019 –"Public safety alert due to marketing of unapproved stem cell and exosome products."

Proliferation of clinics using unapprovedand unproven platelet-rich plasma and other biologics (for example "exosomes").

This is an international ("medical Tourism") problem.

A Reliable Alternative?

Regenexx is a BAN partner:

1. National chain of clinics providing advanced orthobiologic treatments (platelet lysates and bone marrow stem cells.
2. Treatments are recognized by the FDA and supported by medical evidence.
3. Utilization management techniques (such as preapproval) do not change outcomes; and,
4. “Centers of Excellence”- performing a fundamentally ineffective treatment well does not make it effective.

Case Study: Outcomes

Regenexx is a BAN partner:

1. Manufacturing Company;
2. 1,486 covered lives;
3. Costs typically 1/3 of surgery.
4. Employer Statement:

8 cases referred to Regenexx from June – December 2019 have avoided surgery, recovered extremely well, and
returned to work within 7 days or less. The other tangible cost is the savings we are achieving in our
productivity. Typically, these cases would be out of work for 6-8 weeks, and at lost production time
of $82.00 per hour, per employee,

How it works

All components of treatment are outpatient;

Platelets are obtained from blood or bone marrow aspirates;

The injectables are prepared in the laboratory;

The preparations are (needle) injected into the site of injury.

Significant cost advantages over surgeries.

Conditions Treated and Network

1. Nationwide network;
2. All common orthopedic conditions treated.
3. Convincing peer-reviewed medical evidence available for knees, shoulders, and backs.
4. Long-term success rates are superior to surgery.

Coverage

1. Most suited for self-insured groups. MCOs consider these techniques “experimental” and they are usually not covered in a fully-insured scenario.
2. We expect coverage rules to change for Orthobiologic treatments

Public Safety Alert Due to Marketing of Unapproved Stem Cell and Exosome Products

[Posted 12/09/2019]

AUDIENCE: Health Professional, Patient, Consumer, Risk Manager

ISSUE: FDA is informing the public, especially patients, health care practitioners, and clinics, of multiple recent reports of serious adverse events experienced by patients in Nebraska who were treated with unapproved products marketed as containing exosomes. FDA is carefully assessing this situation along with our federal and state partners. Certain clinics across the country, including some that manufacture or market illegal "stem cell" products, are now also offering exosome products to patients. They deceive patients with unsubstantiated claims about the potential for these products to prevent, treat or cure various diseases or conditions.

BACKGROUND: As a general matter, exosomes used to treat diseases and conditions in humans are regulated as drugs and biological products under the Public Health Service Act and the Federal Food Drug and Cosmetic Act and are subject to premarket review and approval requirements. Clinics may claim that they these products do not fall under the regulatory provisions for drugs and biological products – that is simply untrue. There are currently no FDA-approved exosome products.

The clinics currently offering these products outside of FDA's review process are taking advantage of patients and ultimately puts patients at risk by either delaying treatment with legitimate and scientifically sound treatment options, or worse, posing harm to patients, as evidenced by these recent reports of adverse events.

RECOMMENDATION: Patients considering treatment with exosome products in the United States should:

- Ask if the FDA has reviewed the treatment.
- Ask the clinical investigator to give you the FDA-issued Investigational New Drug Application (IND) number and the chance to review the FDA communication acknowledging the IND. Ask for this information before getting treatment and follow up with your personal health care provider to confirm this information.

- Sign a consent form. Because there are no approved products, patients must sign a consent form to participate in a clinical trial that requires an IND application. The consent form also identifies the Institutional Review Board (IRB) that assures the protection of the rights and welfare of human subjects. Make sure you understand the entire process and known risks before you sign. You also can ask the study sponsor for the clinical investigator's brochure, which includes a short description of the product and information about its safety and effectiveness.

If you are considering treatment using an exosome product in another country you should:

- Learn about regulations that cover products in that country.
- Know that FDA does not have oversight of treatments done in other countries. FDA typically has little information about foreign establishments or their products.
- Be cautious. If you're considering an exosome product in a country that may not require regulatory review of clinical studies, it may be hard to know if the experimental treatment is reasonably safe.

FDA remains committed to protecting patients. Our work to ensure compliance with the law does not take away from our firm commitment to advance an efficient path for the safe and effective development of novel regenerative medicine therapies and to help foster beneficial new innovations.

Health care professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report online (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm).
- Download form (https://www.fda.gov/safety/medical-product-safety-information/medwatch-forms-fda-safety-reporting) or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

[12/06/2019 – Public Safety Notification (https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products) - FDA]