

RICE: The End of an Ice Age

Posted on April 4, 2014 by Joshua Stone

"Coaches have used my "RICE" guideline for decades, but now it appears that both Ice and complete Rest may delay healing, instead of helping." – Gabe Mirkin, MD, March 2014



In 1978, Gabe Mirkin, MD coined the term RICE.

Health care practitioners to laypersons are quick to recognize RICE as the 'gold standard' treatment option following injury. Followers of my blog know my stance against ice and now there is support from the physician who coined the term. Yes, the very same physician, Dr. Gabe Mirkin, who coined RICE, is now taking a step back. I reached out to Dr. Mirkin and asked for permission to share his story. As you will read below in Dr. Mirkin's full post, the lack of evidence for cryotherapy is something we must listen to.

This is a controversial topic. My blog [Why Ice and Anti-inflammatory Medication is NOT the Answer](#) sparked a lot of debate. I had nearly 30,000 page hits per day for several weeks. I recently received a tweet from a peer (@AlanMRussell) who attended a presentation by Cindy Trowbridge from the University of Texas-Arlington refuting many of my comments. The debate continues, but given the evidence – or lack thereof – I stand by my thoughts that ice does not facilitate tissue healing.

I recently had the pleasure of connecting with Nichan "Nick" Zourikian a physiotherapist and researcher at Sainte-Justine University Hospital Center in Quebec. Nick published a study with Angela Forsyth, DPT (Rush University Medical Center) that led to a unique, in-journal debate among experts. The original review article published in Haemophilia, challenged the effectiveness of ice (1). This led to a "Letter to the Editor" rebuttal published one year later (2), which led to a rebuttal to the rebuttal published in the same journal (3). Why is this such a hot topic? Nick summed it up perfectly in an email:

"There clearly exists a dogmatic polarization on the use of ice in our physiotherapist/athletic therapist communities! Old habits die hard. Many colleagues (even in our hemophilia community) still insist on using ice...despite the current scientific evidence available." Nick is spot on, RICE is an old habit that is dying hard.

I have long said modalities are overused and exercise is under used. [Ice: The Overused Modality](#) was my first post to make this point. I have added several posts that demonstrate the need for exercise and the positive effect mechanical load has on tissue healing and repair. See my posts on [Mechanotransduction](#), [Achilles Tendinopathy](#) and [reversibility](#) as these explain more.

The NATA's position statement in August 2013 on management of ankle sprains would support my anti-ice case. The researchers for the NATA position statements take years to critically appraising data to make conclusions. They comb over all the data and rate evidence from best "A" to worst "C". In this particular position statement cryotherapy was overall a C rating for evidence (4). The article says "*Strong clinical evidence for advocating cryotherapy is limited*". The evidence that had the better ratings: functional rehabilitation, proprioception, balance, and range of motion (note: these are all tissue loading exercises) (4). What's interesting is many of the readers to my blog are athletic trainers, physical therapists, and physiotherapists. Yet, they are the ones who think I am nuts. Your own organization has a comprehensive position statement that supports my thoughts. Am I that crazy?

I read a piece on Medscape the lead author of the NATA position statement, Thomas W. Kaminski, PhD, ATC, said that he believes that many practitioners are still following the prescription too closely (5). The article goes on to quote Dr. Kaminski: "*I wish I could say that what we found is what is really being done in a clinical setting.*" There is another quote: "*Maybe our European colleagues know something we don't..." "there is very little icing over there.*" (5)

Despite the lack of evidence advocating the use of ice the debate continues. Peers continually challenge me and would like to see me hung, drawn, and quartered for suggesting no ice. 'My gosh, you mean I shouldn't take 30 ice bags out to the baseball field wrap shoulder and elbows? You're insane!' A shift in paradigmatic treatment is on the horizon. Exercise is heating up and ice is melting down. Below is the full article from [Dr. Mirkin's website](#), which will only fuel the end of the ice age.

Why Ice Delays Recovery

March 20, 2014

by Gabe Mirkin, MD

When I wrote my best-selling *Sportsmedicine Book* in 1978, I coined the term **RICE** (**R**est, **I**ce, **C**ompression,**E**levation) for the treatment of athletic injuries (Little Brown and Co., page 94). Ice has been a standard treatment for injuries and sore muscles because it helps to relieve pain caused by injured tissue. Coaches have used my "RICE" guideline for decades, but now it appears that both Ice and complete Rest may delay healing, instead of helping.

In a recent study, athletes were told to exercise so intensely that they developed severe muscle damage that caused extensive muscle soreness. Although cooling delayed swelling, it did not hasten recovery from this muscle damage (*The American Journal of Sports Medicine*, June 2013). A summary of 22 scientific articles found almost no evidence that ice and compression hastened healing over the use of compression alone, although ice plus exercise may marginally help to heal ankle sprains (*The American Journal of Sports Medicine*, January, 2004;32(1):251-261).

Healing Requires Inflammation

When you damage tissue through trauma or develop muscle soreness by exercising very intensely, you heal by using your immunity, the same biological mechanisms that you use to kill germs. This is called inflammation. When germs get into your body, your immunity sends cells and proteins

into the infected area to kill the germs. When muscles and other tissues are damaged, your immunity sends the same inflammatory cells to the damaged tissue to promote healing. The response to both infection and tissue damage is the same. Inflammatory cells rush to injured tissue to start the healing process (Journal of American Academy of Orthopedic Surgeons, Vol 7, No 5, 1999). The inflammatory cells called macrophages release a hormone called Insulin-like growth Factor (IGF-1) into the damaged tissues, which helps muscles and other injured parts to heal. However, applying ice to reduce swelling actually delays healing by preventing the body from releasing IGF-1.

The authors of one study used two groups of mice, with one group genetically altered so they could not form the normally expected inflammatory response to injury. The other group was able to respond normally. The scientists then injected barium chloride into muscles to damage them. The muscles of the mice that could not form the expected immune response to injury did not heal, while mice with normal immunities healed quickly. The mice that healed had very large amounts of IGF-1 in their damaged muscles, while the mice that could not heal had almost no IGF-1. (*Federation of American Societies for Experimental Biology*, November 2010).

Ice Keeps Healing Cells from Entering Injured Tissue

Applying ice to injured tissue causes blood vessels near the injury to constrict and shut off the blood flow that brings in the healing cells of inflammation (*Knee Surg Sports Traumatol Arthrosc*, published online Feb 23, 2014). The blood vessels do not open again for many hours after the ice was applied. This decreased blood flow can cause the tissue to die from decreased blood flow and can even cause permanent nerve damage.

Anything That Reduces Inflammation Also Delays Healing

Anything that reduces your immune response will also delay muscle healing. Thus, healing is delayed by:

- cortisone-type drugs,
- almost all pain-relieving medicines, such as non-steroidal anti-inflammatory drugs like ibuprofen (Pharmaceuticals, 2010;3(5)),
- immune suppressants that are often used to treat arthritis, cancer or psoriasis,
- applying cold packs or ice, and
- anything else that blocks the immune response to injury.

Ice Also Reduces Strength, Speed, Endurance and Coordination

Ice is often used as short-term treatment to help injured athletes get back into a game. The cooling may help to decrease pain, but it interferes with the athlete's strength, speed, endurance and coordination (*Sports Med*, Nov 28, 2011). In this review, a search of the medical literature found 35 studies on the effects of cooling . Most of the studies used cooling for more than 20 minutes, and most reported that immediately after cooling, there was a decrease in strength, speed, power and agility-based running. A short re-warming period returned the strength, speed and coordination. The authors recommend that if cooling is done at all to limit swelling, it should be done for less than five minutes, followed by progressive warming prior to returning to play.

My Recommendations

If you are injured, stop exercising immediately. If the pain is severe, if you are unable to move or if you are confused or lose even momentary consciousness, you should be checked to see if you require emergency medical attention. Open wounds should be cleaned and checked. If possible, elevate the injured part to use gravity to help minimize swelling. A person experienced in treating sports injuries should determine that no bones are broken and that movement will not increase

damage. If the injury is limited to muscles or other soft tissue, a doctor, trainer or coach may apply a compression bandage. Since applying ice to an injury has been shown to reduce pain, it is acceptable to cool an injured part for short periods soon after the injury occurs. You could apply the ice for up to 10 minutes, remove it for 20 minutes, and repeat the 10 minute application once or twice. There is no reason to apply ice more than six hours after you have injured yourself.

If the injury is severe, follow your doctor's advice on rehabilitation. With minor injuries, you can usually begin rehabilitation the next day. You can move and use the injured part as long as the movement does not increase the pain and discomfort. Get back to your sport as soon as you can do so without pain.

I want to thank Dr. Mirkin for allowing me to share his article. I really appreciate his continued contributions to health and wellness.

Until next time –

Josh

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5. http://www.medscape.com/viewarticle/823217_1 – accessed April 9, 2014.

Why Ice and Anti-inflammatory Medication is NOT the Answer

Posted on November 7, 2013 by Joshua Stone



In July I posted a blog discussing [the overuse of cryotherapy](#). The controversy surrounding the topic made it one of the most popular blogs I've written. What is surprising to me is that a controversy exists at all. Why, where, and when did this notion of anti-inflammation start? Ice, compression, elevation and NSAIDs are so commonplace that suggesting otherwise is laughable to most. Enter an Athletic Training Room or Physical Therapy Clinic nearly all clients are receiving some type of anti-inflammatory treatment (ice, compression, massage, NSAIDs, biophysical modalities, etc). I evaluated a client the other day and asked what are you doing currently – "Well, I am taking anti-inflammatories and icing." Why do you want to get rid of inflammation and swelling? I ask this question for both chronic and acute injury!

The Stigma of Inflammation

Editor in Chief of The Physician and Sports Medicine Journal (Dr. Nick DiNubile) once posed this question: "Seriously, do you honestly believe that your body's natural inflammatory response is a mistake?" Much like a fever increases body temperature to kill off foreign invaders; inflammation is the first physiological process to the repair and remodeling of tissue. Inflammation, repair, and remodel. You *cannot* have tissue repair or remodeling without inflammation. In a healthy healing process, a proliferative phase consisting of a mixture of inflammatory cells and fibroblasts naturally follows the inflammatory phase (1).

Researchers headed by Lan Zhou, MD, PhD, at the Cleveland Clinic, found that in response to acute muscle injury, inflammatory cells within the damaged muscle conduct phagocytosis, contribute to accumulation of intramuscular macrophages, and produce a high-level of Insulin-like growth factor 1, (IGF-1) which is required for muscle regeneration (3). IGF-1 is a primary mediator of the effects of growth hormone and a stimulator of cell growth and proliferation, and a potent inhibitor of programmed cell death. Similarly, in 2010, Cottrell and O'Conner stated "overwhelmingly, NSAIDs inhibit or delay fracture healing" (2). And you want to stop this critical process of healing by applying ice, because inflammation is "bad"?

The Anecdotal Rationale for Ice

Somewhere along the line the concept that ice facilitates healing became conventional wisdom. Sorry, that wisdom is wrong. I had someone tell me the other day, "We need to ice, because we need to get the swelling out." Really? Does ice facilitate movement of fluid out of the injured area? No, it does not. The lymphatic system removes swelling. The Textbook of Medical Physiology says it best:

"The lymphatic system is a 'scavenger' system that removes excess fluid, protein molecules, debris, and other matter from the tissue spaces. When fluid enters the terminal lymphatic capillaries, any motion in the tissues that intermittently compresses the lymphatic capillaries"

propels the lymph forward through the lymphatic system, eventually emptying the lymph back into the circulation."

Lymphatic drainage is facilitated by contraction of surrounding muscle and changes in compressive forces that push the fluid back to the cardiovascular system. This is why ankle pumps work so well and removing swelling accumulation.

Besides, since when is inflammation a bad thing? Inflammation is a necessary component in the first phase of the healing process. Swelling is controlled by the body's internal systems to attain homeostasis. If swelling is accumulated it is not because there is excessive swelling, rather it is because lymphatic drainage is slowed. The thought that ice application increases lymphatic flow to remove debris makes no sense. Gary Reinl, author of "[Iced! The Illusionary Treatment option](#)" gave me a good analogy. Take two tubes of toothpaste, one is under ice for 20 minutes, the other is warmed to 99 degrees. In which tube will the toothpaste flow fastest? It does not take an advanced physics degree to know that answer.

What might surprise you is that ice actually *reverses* lymphatic drainage and pushes fluid back to interstitial space. A study published in 1986 (yes, 1986, is old, but this is a foundational study) found when ice is applied to a body part for a prolonged period of time; lymphatic vessels begin to dramatically increase permeability. As lymphatic permeability increases fluid will pour from the lymphatics into the injured area, increasing the amount of local swelling (5). Ice can *increase* swelling and retard debris removal!

Load Facilitates Repair

The acronym RICE is bogus in my opinion. Rest is not the answer. Rest does not stimulate tissue repair. In fact rest causes tissue to waste. The other reason RICE is bogus is obvious, ice. Evidence has shown that tissue loading through exercise or other mechanical means stimulates gene transcription, proteogenesis, and formation of type I collagen fibers (See studies by Karim Khan, Durieux, Mick Joseph, and Craig Denegar). Ice does nothing to facilitate collagen formation.

Our body has all types of cells. When a cell is born it has no clue what type of cell it will eventually become. This infancy cell – for lack of a better term – is called a progenitor cell. Progenitor cells can be changed to a specific cell type. Load in tendon tells our body to turn a progenitor cell into a tenocyte. Load in bone tells a progenitor cell to become an osteocyte. Ever wonder why myositis ossificans (calcification or bone growth in muscle) develops? The direct, repeated trauma turns progenitor cell currently living within muscle to an osteocyte. Subsequently, we develop bone growth within muscle.

Ice will not influence progenitor cells development. Ice does not regenerate tissue. Ice does not facilitate healing – it inhibits natural healing process from occurring. Ice does not remove swelling; it increases swelling and lymphatic backflow.

Closing thoughts

Bottom line, ice and NSAIDs are over utilized. I am not saying never, but I am saying ice is not a magical cure all that fixes everything and is required for healing. It is not the gold standard that it has come to be. My goal with this blog is to get individuals to stop and think before immediately turning to ice and NSAIDs. Is it really the best option? Is it necessary for this injury at this stage? I understand it is not the only form of treatment clinicians use, but ice certainly is the most heavily used. My goal is to get this trend reversed one clinician and one patient at a time. Have you seen [the video discussion](#) between Kelly Starrett, DPT and Gary Reinl? If not I recommend you watch it. It's fascinating. I am glad to have expert minds like Kelly and Gary in this fight with me.

I ask health care professionals to do one thing, just try it. Pick one client with chronic musculoskeletal pain, skip the ice, skip the NSAIDs and try to use light exercise as a repair stimulus. Then, try skipping the ice on a client with an acute mild injury. The outcomes might surprise you.

Great Thought Provoking Reads

- NATA 2013 Meeting. **If you have access – read these**
 - Selkow, NM, Pritchard, K. CRYOTHERAPY FOR THE 21ST CENTURY: UPDATED RECOMMENDATIONS, TECHNIQUES, AND OUTCOMES. NATA 2013 Annual Meeting.
 - Dolan. New Concepts in the Management of Acute Musculoskeletal Injury. NATA 2013 Annual Meeting.
 - Johnson, M, Denegar, C. Mechanobiology, Cell Differentiation and Tendinopathy – From Bench to Bedside. NATA 2013 Annual Meeting.
- Articles and Peer-Reviewed Literature
 - William JR, Srikantaiah S, Mani R. Cryotherapy for acute non-specific neck pain (Protocol). Cochrane Database of Systematic Reviews 2013, Issue 8.
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Update:

I've had an enormous amount of feedback for this post. I greatly appreciate all of it – good and bad. I am adding this note in regards to an overwhelming amount of questions / comments about acute injury and other treatment options.

In regards to acute injury, my response is yes, in many cases I would skip the ice for acute injuries as well!! Why do you feel like we must ice an acute injury but not ice the chronic? What is the benefit to halting the healing process of an acute injury? To prevent hypoxic death or to reduce pain? We'd have hypoxia with or without ice. The body will remove dead cells and replenish with

new. I agree, ice has pain modulating effects. But to this I ask, at what cost are we reducing the pain? Is a temporary (30 minutes) pain reduction more important than healing? Theoretically, pain can increase after icing secondary to the back flow of lymphatic drainage that may further increase post-ice swelling.

The second set of comments I receive are regarding topics like heat, other modalities, what would I do in situation x, or ice is not all we do. I understand this, but these are beyond the scope of this blog. If I wrote to each point I'd be authoring a textbook rather than a blog post. Hopefully, I can touch on these topics in later posts.

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2. Cottrell, and O'Connor, P. Effect of Non-Steroidal Anti-Inflammatory Drugs on Bone Healing. Pharmaceuticals, Vol 3, No 5, 2010.
3. Haiyan Lu, Danping Huang, Noah Saederup, Israel F. Charo, Richard M. Ransohoff and Lan Zhou. Macrophages recruited via CCR2 produce insulin-like growth factor-1 to repair acute skeletal muscle injury. The FASEB Journal. Vol. 25 no. 1 January 2011. 358-369.
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6.Ice: The Overused Modality?

7. Posted on July 3, 2013 by Joshua Stone
8. Many years ago I got tired of watching my athletes roll in to the

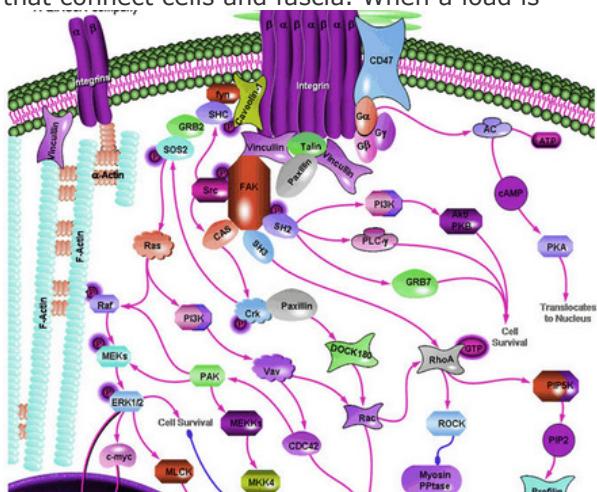


athletic training room and slap on ice. These athletes are in a drug-like induced state of ice addiction. Their athletic trainers keep feeding the disease, by recommending cold treatment and doing the easy – here's ice, shut-up, leave. I felt I was doing a disservice to my athletes and asked myself, "Why are we icing this injury?" I never had an answer that was supported by evidence. So I began my own case study.

9. I took 9 Division I athletes (6 patellar tendinopathy, 2 bicipital tendinopathy and 1 subacromial impingement) and had the athletes cease all cryotherapy and electrical stimulation.
10. *Warning: Telling an athlete not to ice brings about a firestorm from all angles. Coaches, parents, the athletic director, the family friend chiropractor, the great aunt who is a dentist, and even mom the real estate agent will question your motives. It is possible you will be hung, drawn, quartered, and undoubtedly face major scrutiny. Your athletes will*

whine, piss, and moan the day you stop allowing ice. Your athletes may befriend a student athletic trainer to do the dirty deeds. You must have the scientific facts to fight all naysayers.

11. I then put the athletes on a rehabilitation only protocol. My results, all 6 patellar tendinopathy issues resolved. 1 biceps tendon resolved, the other was later found to have a SLAP tear. The subacromial had no change. Why did this work? Because I followed the science, used common sense, and challenged traditional thought. The NATA and the BOC have emphasized the importance of Evidence Based Practice. As clinicians we will have better outcomes if we listen to the evidence.
 12. During the NATA conference I was glad to see lectures supporting my thoughts and the evidence. I tweeted my thoughts and had an immediate response of "what?" "Really?" "Why?" There is lack of evidence to support utility of cold for healing. Inflammation is the initiation of healing, so why do we stop the healing process? Inflammation occurs within seconds after injury. Why allow inflammation to start then stop the process? Imagine cars on a busy freeway as cells moving to a location. Then, suddenly a roadblock is applied and only some of the cells make it to the site. How are you supposed to heal and repair if the body is not allowed to do its job? Let's use the analogy of baking a cake. You go to the store, buy ingredients, come home mix all the ingredients, but I won't let you bake the cake. Now you have a bunch of material that you created, that is now wasted and no longer useful. Doesn't make sense does it?
 13. It is true we want to limit excessive inflammation and we want to facilitate removal of inflammatory byproducts from the injury site. However, ice / cold does not do this. Ice prevents movement and removal. In the case to limit excessive inflammation and remove inflammatory byproducts, use compression, elevation, and massage, not ice.
 14. We often sue the term "tendonitis". However, the "itis" is not really true. Tendon is not really inflamed, rather it is deranged (Tendiopathic / tendinopathy). When tendon is deranged you should apply the theories of mechanobiology, cellular signaling, and mechanotransduction to repair tissue. If you want [more info on mechanotransduction](#), I have written a blog dedicated just to that.
 15. Evidence has shown that tissue loading through exercise or other mechanical means stimulates gene transcription, proteogenesis, and formation of type I collagen fibers (See studies by Karim Khan, Durieux, Mick Joseph, and Craig Denegar). Ice does nothing to facilitate collagen formation. Tenocytes are spread out and have octopus like tentacles that connect cells and fascia. When a load is



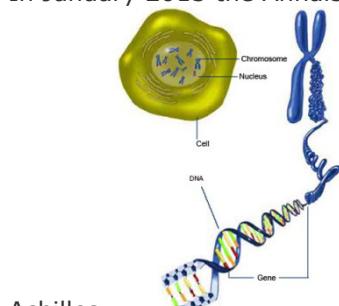
MLCK
MKK4
Myosin PPase
Dawkins

applied to a tenocyte the force is transmitted to neighboring cells. The neighboring cells receive the signal through receptors called integrins. The integrins then carry the signal from the outside of the cell to the inside. This signal is then carried down actin filaments to the cell nucleus, where transformation occurs. See the image to right for a visual.

16. Our body has all types of cells (osteo, white, red, fibro, etc.). Stem cells are cells that have no idea what they will be in the future. Then there are [progenitor cells](#). These cells have some idea what they will be, but can still be manipulated and changed to a specific cell type. So a progenitor cell can become an osteocyte, chondrocyte, tenocyte, etc. Load in tendon tells our body to turn a progenitor cell in to a tenocyte. Load in bone tells a progenitor cell to become an osteocyte. Why do bone stimulators work? Because we are loading bone by using sound waves to apply a mechanical force on bone. Similarly, tendon is thicker and more dense in athletes, because they load tendon more.
17. The acronym RICE is bogus in my opinion. Rest is not the answer. Rest does not stimulate tissue repair. In fact rest causes tendon to waste. You may say, "yeah but this is an overuse injury, you must rest." True, overload does cause tendon thickening and tendon stiffness, but rest is not the answer. Appropriate load IS the answer as it stimulates metabolic processes of repair.
18. The other reason RICE is bogus is obvious, as the blog title indicates, ice. Evidence shows that cryotherapy slows metabolic processes and nerve conduction velocity. Metabolic pathways are necessary for human function. Cells are supposed to produce catabolic and anabolic reactions. This is a constant process in all humans. During healing we breakdown and rebuild tissue. Cold inhibits this function, so in a sense we are slowing the necessary catabolic and anabolic pathways.
19. I heard a great discussion at the NATA conference discussing ice and stim. Ice is designed to reduce pain by decreasing nociceptor fiber response and slow nerve conduction velocity. Stim (IFC / Premod / Biphasic waves) is designed to pump impulses at a high frequency to stimulate large diameter nerve fibers and override pain fibers. But if Ice slows nerve velocity, then why do we combine cold with high frequency stim? Is this not counterproductive? What happened to good ole rehab? Why use modalities and rest when you can rehabilitate. And don't use the argument for a time crunch as I already wrote a blog on creating a beneficial [rehabilitation program in 15 minutes](#).
20. It just makes no sense. The NATA and BOC are emphasizing clinicians use evidence base practice. If you are a clinician, use the evidence and steer away from traditional thought if it does not work.

21. Why Does Rehabilitation Work?

22. Posted on March 22, 2013 by Joshua Stone
23. You have an athlete with a stress fracture. The physician prescribes active rest and places the athlete in a non-weight bearing boot. Sound familiar? Suppose I told you the better option is to place some load on that bone and non-weight bearing is not recommended. Would you think I am nuts? Maybe I can convince you otherwise. Let me explain but, before you read the next paragraph and decide to leave the page, bear with me. What follows this introductory piece may provide insight to further understanding of injury pathophysiology and could revolutionize the future of rehabilitation science.
24. In January 2013 the Annals of Human Genetics published an article that demonstrated



Tendinopathy is associated with gene polymorphism (Abrahams, et al., 2013). I am not a geneticist by any stretch of the imagination, so pardon my basic explanation. COL51A is a gene that encodes the development and organization of Type V collagen. Type V collagen is a collagen that is distributed in tissues

as a component of extracellular matrix and composed of one pro alpha 2 (V) and two pro alpha 1 (V) chains. This collagen can be found in ligaments, tendons, and connective tissue. COL51A plays an integral role in development and maintenance of connective tissue. Abrahams, et al. (2013) demonstrated that polymorphisms occur in the COL51A gene causing altered structure of collagen resulting in tendonopathy.

25. I state the aforementioned because it is time for athletic trainers to begin taking a deeper look at pathophysiology and more importantly, to utilize this understanding in the development of our rehabilitation and treatment guidelines. Some of you may already be cognizant of this, but these revolutionary approaches to treatment and rehabilitation are already coming to light. Let me introduce the concepts of cellular signaling, mechanotransduction, and mechanotherapy.
26. *Mechanotransduction and the Processes of:*
27. Mechanotransduction (described by Khan 2009) is the process whereby mechanical load initiates biochemical signals that leads to gene upregulation, protein synthesis and ultimately structural change (Khan 2009). Load causes perturbation to cells that initiates signaling pathways, where mRNA is sent to the endoplasmic reticulum for gene encoding. If you recall from college physiology, proteins are created by ribosomes following this transcription. These proteins are the new collagen and are extruded from the extracellular matrix and delivered to the damaged tissue. This is why eccentric training heals tendinopathy.
28. This process is not limited to damaged connective tissue. The mechanical load induces cellular signaling in all tissue – nervous, muscular, connective, bone and cartilage (Khan, 2009). In muscle, load stimulates upregulation of mechano-growth factor and ultimately hypertrophy. Chondrocytes are sensitive to load and are fed through load. Load applied to osteocytes deep within bone stimulates bone lining cells and facilitates healing to expedite fracture repair.
29. *Review of cool supporting studies:*
30. Joseph, et al., (2012) stated that tendinopathic tendon is less stiff and loses ability to transfer energy. Joseph goes on to state that load creates a viscoelastic response in the Achilles tendon that increases stiffness and decreased hysteresis. Fragala et al., (2011) demonstrated leukocyte β_2 -adrenergic receptor expression changed in response to heavy resistance exercise. Flück, et al., (2008) evaluated tenascin-C, a protein responsible for tissue remodeling that is expressed only in damaged tissue and regulated by mechanical load. They found that mice deficient of tenascin-C had diminished muscle tissue healing and conclude that tenascin-C is needed for reducing and healing of musculoskeletal injuries.
31. Scott, et al., (2008), demonstrated physiological load induces an osteogenic response that stimulates anabolic cellular activity in bone. In the Journal of Sport Rehabilitation – published by the one and only Human Kinetics – stated “the notion that deep friction massage may provide mechanical stimulation for healing is intriguing, especially given the context in which Cyriax, advocated this “mechanotherapy” as early as 1984.... While this is difficult to study in a human model, there is some poignant animal evidence that tendon massage indeed stimulates tissue adaptation at the cellular level.” (Joseph, et al., 2012). Durieux, et al., (2009) assessed regulation of focal adhesion kinase in mechano-regulated differentiation of slow-oxidative muscle. Focal adhesion kinase initiates cellular signaling and ultimately migration of cells and is required during development. The authors found that focal adhesion kinase is part of the signaling pathway that governs repair of striated muscle.
32. *Conclusion:*
33. Is a non-weight bearing walking boot the best treatment option for a stress fracture? It appears it is not. Based on the data discussed here, the practitioner must utilize an intricate balance between rest and mechanical loading of bone to obtain optimal healing. In

order to heal damaged tissue we must use exercise as a repair stimulus – mechanotherapy.

34. The body of evidence exists and is continuing to grow. It is recommended athletic trainers and rehabilitation specialists take time to understand the pathophysiology of injury and the biochemical processes that elicits healing. In the very near future you will need to understand the biochemical events that promote tissue repair. The knowledge gained will dictate rehabilitation protocols needed for specific injuries.

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