When NSAIDs make pain worse
by Ross Hauser, MD, caringmedical.com

In our practice we see patients of all ages. We see the high school athlete, we see the great-grand parent. If both have knee problems – from sports related injury or age deterioration, both prior to their visit with us, they will likely be prescribed an NSAID. Why? Because doctors believe that NSAIDs can offer the best of both worlds – an anti-inflammatory medication and a pain reliever.

However, NSAIDS have significant side effects beyond gastrointestinal distress – these medications PREVENT healing and ACCELERATE osteoarthritis and joint deterioration.

Research from January 2015 is "alarming." Doctors note that due to the high risk of life-threatening side effects, non-steroidal anti-inflammatory drugs (NSAIDs) are not favored for treating persistent non-cancerous pain in the elderly.

> Now listen to these staggering numbers – between 2000 and 2007 there were 206 MILLION doctor visits recorded for patients with an average age of 75. Most of the NSAIDs users had Medicare (75%), and about 25% were prescribed with adjuvant medications considered inappropriate for their age. Compared to men, women were 1.79 times more likely to be prescribed NSAIDs. The researchers of this study concluded: "We recommend investigating the appropriateness (or inappropriateness) of the high prevalence of NSAIDs use among older patient.1

- Update: Patients with or at risk of cardviovascular disease are advised against taking Nonsteroidal Anti-inflammatory Drugs in research from May 2015. Researchers call the overuse of NSAIDs in these patients "a significant public health concern." 2

Treating or Suppressing Joint Pain?

The American medical care system is focused on providing relief of symptoms, rather than prevention or treating the underlying causes. Thus when a patient presents with an acute sports injury, or chronic pain, the first thing they do is prescribe non-steroidal anti-inflammatory drugs (NSAIDs) under the assumption that quelling inflammation assists recovery.

Mostly because of a lack of adequate information provided by the prescribing physician, many patients are under the mistaken impression that these drugs not only reduce pain, but also promote healing. Nothing could be further from the truth. As every Prolotherapist (but apparently very few orthopedic and family physicians) knows, inflammation resulting from injury is an integral part of the healing process. So it may not be so wise to interfere with it.

Furthermore, no available evidence suggests that NSAIDS are able to promote the healing process independent of the body's inflammatory reaction.

- Nonsteroidal anti-inflammatory drugs (NSAIDS) include examples such as Ibuprofen, Piroxicam, Flurbiprofen and Indomethacin. One of the damaging side effects of NSAIDS is the inhibition of the healing process of soft tissues. The long term detrimental effects far outweigh the temporary positive effect of decreased pain.
- NSAIDs inhibit proteoglycan synthesis – a component of ligament and cartilage tissue regeneration and repair.

Non-steroidal anti-inflammatory drugs all inhibit release of prostaglandins and the healing process of soft tissues.

> When a ligament or tendon is injured, prostaglandins are released which initiate vasodilation in non-injured blood vessels.

This enables healthy blood vessels to increase blood flow and immune cell flow to the injured area to begin the repair process.

The use of anti-inflammatories inhibits the release of prostaglandins thus ultimately decreasing the blood flow to the injured area.

Proteoglycans are essential for the elasticity and compressive stiffness of articular cartilage and suppression of their synthesis has significant adverse effects on the joint.

The key question regarding the healing of any injury is, "What exactly does any therapy do to the fibroblastic cells that actually grow the ligament and tendon tissue?" Treatments that stimulate fibroblast proliferation will cause ligament and tendon repair and will help with healing (Prolotherapy). Therapies that interfere with or destroy fibroblastic growth will be detrimental to the healing (NSAIDS).

NSAIDs prevent soft tissue healing.

As far back as 1995, a study from the University of North Carolina, School of Medicine, Division of Orthopaedic Surgery, Sports Medicine section found how detrimental NSAIDs use was in healing soft tissue. They separated study patients into groups:

- Group I was the control in which no treatment was done;
- Group II- the tendons were exercised;
- Group III- the tendons were exercised and anti-inflamed with Indomethacin; and
- Group IV- the tendons were just anti-inflamed with the Indomethacin.

All the tendons underwent injury through repetitive motion, similar to what would happen to an athlete in training. Seventy-two hours after the injury, it was noted that compared to controls the only group that showed increased levels of prostaglandins (inflammation) was the exercised group. The group that was exercised and received the NSAID, as well as the NSAID group, had statistically significant lower levels of prostaglandins (specifically Prostaglandin E2) in the tendons.

This showed that the NSAID blocked the inflammatory healing of even the tendon injuries that were exercised or rehabilitated. The tendonitis that was treated with just the NSAID had almost no prostaglandins in the sample, signaling a complete inhibition of the inflammatory healing process. The effect was even more pronounced at 108 hours.

The researchers also measured DNA synthesis in the fibroblasts (repair mechanism). This showed which fibroblasts were proliferating. Again, the exercised group was the only group that exhibited elevated levels of DNA synthesis in the fibroblasts. Compared to the control group there was 100 percent more growth of fibroblasts in the exercise group. The tendons treated with Indomethacin had no DNA synthesis noted.

This showed there was no fibroblastic growth occurring. The group that exercised and took the NSAID showed a little bit of growth. The paper also stated a fact that many researchers in this field are wondering, "Despite the lack of scientific data, NSAIDs are widely used, often as the mainstay of treatment."3 **Twenty years later – little has changed.**

NSAIDs and the RICE treatment nearly eliminate the body's ability to heal.

NSAIDs have been shown to delay and hamper the healing in all of the soft tissues, including muscles, ligaments, tendons, and cartilage. Anti-inflammatories can delay healing and delay it significantly, even in muscles with their tremendous blood supply. In combination with RICE

therapy (Rest, Ice, Compression, and Elevation) NSAIDs will nearly eliminate the body's ability to heal itself.

In one study on muscle strains, Piroxicam essentially wiped out the entire inflammatory proliferative phase of healing.4 In a study in The Journal of Hand Surgery, it was found that the ibuprofen doses used in the study caused the strength of the flexor tendons to decrease.5

NSAIDS diminish the healing ability of the injured soft tissue

From the above studies, it is clear that NSAIDs inhibit the fibroblastic growth process and thus diminish the individual's chance of healing. NSAIDs are used because they decrease pain, but they do so at the expense of hurting the healing of the injured soft tissue. A good example of this is a study on the use of Piroxicam in the treatment of acute ankle sprains in the Australian military.

Compared with the placebo group, the subjects treated with Piroxicam had less pain, were able to resume training more rapidly, were treated at lower cost, and were found to have increased exercise endurance on resumption of activity. At first glance in reviewing this study, NSAIDs appear to be great, but the real question is…did they help the ligament injury heal?

To test ligament healing, the ankles were tested via the anterior drawer test. During this test the ankle was moved forward to determine the laxity in the ligaments. In this study, at every date of testing after the initial injury, days three, seven, and fourteen, the Piroxicam-treated group demonstrated greater ligament instability.

At the time of the initial injury the ligament instability in the Piroxicam group and the control group were exactly the same. This study showed that the NSAID stopped ligament healing, yet the person felt better. The authors noted, "This result is of concern in that it may reflect a paradoxically adverse effect of the NSAID-derived analgesia in allowing subjects to resume activity prematurely."6

In research from 2014 , doctors tried to make the case that injecting Piroxicam and Hyaluronic Acid in combination reduced inflammation and acted effectively against knee osteaorthritis.7 This is effectively argued against in the companion paper Hyaluronic Acid Injections for knee osteoarthritis.

NSAIDS and the acceleration of the arthritis process

NSAIDs are truly anti-inflammatory in their mechanism of action. Since all tissues heal by inflammation, one can see why long-term use of these medications will have harmful effects. Osteoarthritis and other chronic pain disorders are not an ibuprofen or other NSAID deficiency. Their chronic long-term use will not cure, and will actually hamper soft tissue healing and accelerate the arthritic process.

In our own research article The Acceleration of Articular Cartilage Degeneration in Osteoarthritis by Nonsteroidal Anti-inflammatory Drugs, we noted: "For those using NSAIDs compared to the patients who do not use them, joint replacements occur earlier and more quickly and frequently. Massive NSAID use in osteoarthritic patients since their introduction over the past forty years is one of the main causes of the rapid rise in the need for hip and knee replacements, both now and in the future."8

Other authors agree:

- "NSAIDs have been one of the most frequently used drugs for over 30 years with 80% of rheumatologists prescribing NSAIDs for symptomatic osteoarthritis."9

- "It has been questioned whether there is a correlation between the sudden increase in OA: with replacement surgeries between 1997 and 2005 significantly rising: knee replacement's climbing by 69%, hip replacements by 32% and spinal fusion surgeries increasing by 73%."10
- Another group investigated the association of non-steroidal anti-inflammatory drugs (NSAIDs) and the risk of atrial fibrillation in a prospective study of elderly individuals, and found that the use of NSAIDs was associated with an increased risk of atrial fibrillation.11

Our research continues, "Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used drugs in the world for the treatment of osteoarthritis (OA) symptoms, and are taken by 20-30% of elderly people in developed countries. Because of the potential for significant side effects of these medications on the liver, stomach, gastrointestinal tract and heart, including death, treatment guidelines advise against their long-term use to treat OA. One of the best documented but lesser known long-term side effects of NSAIDs is their negative impact on articular cartilage."8

The following human study demonstrates the impact of NSAIDs on the acceleration of the progression of OA of the knee and the radiological deterioration of joint space:

"After 1 year of treatment with indomethacin compared to placebo on 376 patients: the indomethacin group showed 47% progression of radiographic modifications of osteoarthritis, while placebo demonstrated only 22%." Of 170 available patients at the 3rd interim analysis, 40 of 85 receiving indomethacin had deteriorated compared to 19 of 85 receiving placebo, a statistically significant difference. Indomethacin increased the rate of radiological deterioration of joint space in patients with OA of the knee."12

Prolotherapy, because it stimulates inflammation, helps the body heal. Prolotherapy stops the arthritic process and helps eliminate the person's chronic pain, often permanently. NSAIDs should not be taken while undergoing Prolotherapy because they inhibit the inflammation caused by the treatment. For that matter, anyone with chronic pain should seriously consider stopping NSAIDs and starting Prolotherapy.

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The NSAIDs Crisis
by Dr. Rick Marinelli

News reports the last few months on the increased cardiovascular risks associated with taking NSAIDs is hardly a news flash for those progressive doctors doing prolotherapy and other cutting edge pain therapies. Ever since Merck took rofecoxib (Vioxx) off the market in September, it seems one carboxylic derived NSAID after another has fallen as evidence of or suggestion of injury has been associated with their use including voldecoxib (Bexstra), celecoxib (Celebrex), and now naproxen (Naprosyn, Aleve). The public and uninformed doctors are now scrambling for alternatives to taking these drugs when the answers have been before us for a long time.

The primary reason knowledgeable doctors have not wanted their patients taking these NSAIDs is the inhibiting effect of these drugs on healing ligaments, tendons, cartilage. While not all NSAIDs are created equal there is significant animal data to indicate a general inhibition in wound repair and collagen synthesis in the presence of these drugs. Ligaments have been shown to have less tensile strength, articular cartilage is less robust, and tendon strength is inhibited when chronically exposed to NSAIDs in these classes or when these NSAIDs are taken after an acute injury. Collagen synthesis and remodeling of wounded areas is how our bodies have such remarkable self-healing capabilities. If this becomes unbalanced, as with the inhibition of collagen synthesis in the presence of carboxylic derived NSAIDs, then this lack of healing quickly gives way to accelerated tissue breakdown of the collagen matrix, leading to degeneration of the tendons (tendinopathy), of the cartilage (osteoarthritis), and of the surrounding ligaments (joint instability). In part this occurs because there is now an imbalance of the collagen remodeling with a definite trend toward collagen breakdown instead of repair and regeneration. To be sure this may be associated with injury, age, osteoarthritis, or an immune-mediated type of collagen vascular disease like rheumatoid arthritis as well as nutrient deficiencies and other metabolic disturbances.

So what are we to do? There is also an increasing body of evidence to support the long known effects of diet, nutritional supplements, herbal medicine, and exercise on the healing of collagen and specifically on osteoarthritis. Let's just briefly mention the best studied of these.

Glucosamine sulfate: Ever since the Lancet study in 1999 on oral glucosamine for knee osteoarthritis, it has been clear that our observations were correct. Many doctors have been using glucosamine for years prior to this study showing that not only are functional symptoms greatly improved (e.g. pain-free walking time) but in some cases cartilage regrowth and an increase in thickness of the cartilage was able to be seen on xray. Similar results have been associated with the oral ingestion of other GAGs (glycosaminoglycans) such as chondroitin (more chondroprotective than regenerative), bovine trachea cartilage, green-lipped muscle, etc.

Fish oil: Type in fish oil on the query line of the National Library of Medicine (Pub Med) and you get almost 10,000 hits. To say there are many articles on the benefits of taking fish oil as a supplement is a gross understatement. In addition to its well-recognized effects on cardiovascular risks (decreases in strokes, blood pressure, blood viscosity, triglycerides, vascular inflammation), you will find studies suggesting benefits in osteoarthritis, soft tissue pain and inflammation, and reduction of the breakdown of the collagen matrix we have been talking about.

Antioxidants: Despite recent flawed studies on the negative effects of antioxidants, the majority of studies show an overall reduction in cancer, degenerative diseases, and cardiovascular mortality from the use of antioxidant supplements. Clinically, this is especially apparent in osteoarthritis. Whole food antioxidants such as fish, green tea, berries, chocolate, garlic, and nuts are especially easy additions to one's diet.

Herbal medicine: Historically, in traditional herbal medicine many formulae have been successfully used. Prominent among these are those containing the herbs ginger, boswellia, angelica dahurica, salvia, atractylodes, lycium, bupleurum, poria, etc. The complexity of these herbal medicines and the lack of research funding has hampered understanding from a scientific perspective. These herbal

medicines will gain prominence in use as they are better understood. Many important discoveries in pharmacology have been associated with the study of traditional herbal medicine prescriptions.

Exercise: The lack of exercise in our culture is certainly a huge problem with soaring rates of obesity, cardiovascular mortality, and diabetes as a result. This is hardly news to prolotherapy doctors who along with others have been advocating and prescribing exercise to their patients from the beginning. In older athletic patient, or with "weekend warriors" there are greater challenges with optimizing the amount of exercise. Many of these folks also have excessive collagen breakdown due to exceeding their bodies' repair abilities. This repair function is often improved with the addition of glucosamine, fish oil, antioxidants, and herbal medicine and a more reasonable and varied exercise approach. Often, there are deficiencies of anabolic repair (hormones such as testosterone, growth hormone, thyroid) inhibition by metabolic factors (excess sugar intake, insulin resistance, cytokine imbalance) or a combination of these factors. An experienced practitioner can help to sort these out. Overall though, more exercise is better!

Conclusion: From the preceding discussion, I think it is clear there are many good natural alternatives to the use of NSAIDs. If you are a patient, seek out those practitioners who have experience in these areas. If you are a doctor that would like to use these approaches but have little experience, please seek out some of the excellent continuing education courses offered. Your patients will be glad you did.

NSAIDs May Hinder Not Help Sore Muscles
by S.B. Leavitt, MA, PhD, updates.pain-topics.org

Many persons experience muscle pain after heavy exercise, which may persist for some time. Taking nonsteroidal anti-inflammatory drugs (NSAIDs) to ease the discomfort is common practice; however, new research suggests that this may not be beneficial. In fact, the pain may be prolonged with NSAIDs.

At the latest annual meeting of the European League Against Rheumatism (EULAR 2012), Matthias Rother, MD, PhD — of International Medical Research in Graefelfing, Germany — and colleagues presented research examining the effects of two NSAIDs with different anti-inflammatory potency on muscle soreness due to strenuous exercise. They conducted two randomized, placebo-controlled studies of similar design in which muscle soreness was induced by having healthy subjects walk down stairs, the exact number of which was determined by body weight, but similar to walking down from the top of a 100-story building.

Here is a summary of the 2 studies and their outcomes:

- STUDY 1 — subjects were randomly assigned to either twice daily celecoxib 200 mg (N=40) or placebo (N
- STUDY 2 — subjects in this study were randomly assigned to either twice daily ketoprofen 100 mg (N=24) or placebo (N=48) for 7 days following exercise. Ketoprofen administration resulted in pain reduction in calf and thigh muscles as compared with placebo during the first 24 hours of treatment; however, considering the full 7- day observation period, the ketoprofen group actually showed higher pain scores as compared with placebo (P=0.024). Also, maximum pain and time to maximum pain relief were numerically higher for the ketoprofen group. Evaluation of all parameters indicated that most of the negative effect of oral ketoprofen was caused by a significant delay of time to full recovery (P<0.005) — discomfort ended at about 5 days (122 hrs.) in the ketoprofen group versus roughly 4 days (105 hrs.) in the placebo group.

The authors conclude that, the more potent anti-inflammatory drug ketoprofen appears to cause unfavorable effects on recovery from muscle soreness induced by strenuous exercise, as compared with less potent celecoxib. Neither NSAID was superior to placebo and the results of their studies could imply that the inflammatory reaction following muscle injury induced by exercise is an essential part of recovery. Therefore, since even the benefits of celecoxib were only modest and not

significant, the use of NSAIDs for the treatment of exercise induced muscle soreness cannot be recommended.

CLINICAL CONCEPTS: These studies were published as abstracts at a clinical conference, so their data and conclusions should be considered as preliminary until publication in a peer-reviewed journal. The trial designs were straightforward; however, the studies were only modestly powered statistically and generalization of the outcomes, which focused on only two NSAIDs, to the whole class of NSAID analgesics is questionable at this time.

The implication is that inflammation in certain acute pain situations has a beneficial role in resolving the discomfort, and that attempts to suppress this process may lengthen the time to recovery. For example, muscle pain after heavy exercise is natural and may be healthy, and taking anti-inflammatory drugs for normal soreness could be deleterious. Conjecture regarding other pain conditions, including more chronic musculoskeletal pain, was not discussed in the present research.

Unfortunately, from the limited information available at this time it is unknown what the researchers might recommend as a better approach for dealing with acute musculoskeletal discomfort. In the present studies, the maximum pain was moderate — reaching about 5 on a 0-to-10 scale — and there was no evidence of traumatic injury; so, advising patients to merely endure the soreness for several days might be acceptable. In other cases, this may not be the most prudent or preferred approach.

REFERENCE: Rother M, Seidel EJ, Fischer A, et al. Is the inflammatory reaction an essential part of recovery after muscle injury? Presented at EULAR 2012, abstract FRI0457; also in Ann Rheum Dis, 2012;71(Suppl3):469 [abstract here]. Also reviewed in MedPage Today, June 11, 2012 [here].

NSAIDs Hamper Ligament and Tendon Healing
by Ross Hauser, MD www.caringmedical.com

The following statement comes from a well-known sports medicine book that has gone through five printings. "In spite of the widespread use of NSAIDs there is no convincing evidence as to their effectiveness in the treatment of acute soft tissue injuries." (Bruckner, P. Clinical Sports Medicine. New York City, NY: McGraw-Hill Book Company, 1995, pp. 105-109.)

This is a true statement, but definitely not strong enough. More appropriate would be something like. In spite of the widespread use of NSAIDs there is substantial evidence that they hamper soft tissue healing.

NSAIDs have been shown to delay and hamper the healing in all the soft tissues, including muscles, ligaments, tendons, and cartilage. Anti-inflammatories can delay healing and delay it significantly, even in muscles with their tremendous blood supply. In one study on muscle strains, Piroxicam essentially wiped out the entire inflammatory proliferative phase of healing (days 0-4). At day two there were essentially no macrophages (cells that clean up the area) in the area and by day four after the muscle strain, there was very little muscle regeneration compared to the normal healing process. The muscle strength at this time was only about 40 percent of normal.(Greene, J. Cost-conscious prescribing of nonsteroidal anti-inflammatory drugs for adults with arthritis. Archives of Internal Medicine. 1992; 152:1995-2002.)

The authors concluded that NSAIDs might delay muscle regeneration, when their study did in fact show delayed muscle healing. But you know politics...

Another study confirmed the above by showing that at day 28 after injury the muscle regenerative process was still delayed. The muscles of the group treated with Flurbiprofen (NSAID) were significantly weaker. The muscle fibers were shown under the microscope to have incomplete healing because of the medication. (Almekinders, L. An in vitro investigation into the effects of repetitive

motion and nonsteroidal anti-inflammatory medication on human tendon fibroblasts. American Journal of Sports Medicine. 1995; 23:119-123.)

The key question regarding the healing of sports injury is, "What exactly does any therapy do to the fibroblastic cells that actually grow the ligament and tendon tissue?" Treatments that stimulate fibroblast proliferation will cause ligament and tendon repair and will help the athlete heal. Therapies that kill or hamper fibroblastic growth will be detrimental to the athlete.

In 1993 at the University of North Carolina School of Medicine, Division of Orthopaedic Surgery, Sports Medicine section, Dr. Louis Almekinders and associates studied human tendon fibroblasts to determine the effect of exercise and the NSAID Indomethacin on fibroblasts. Group I was the control in which no treatment was done; Group II-the tendons were exercised; Group III-the tendons were exercised and anti-inflamed with Indomethacin; and Group IVùthe tendons were just anti-inflamed with the Indomethacin. All the tendons underwent injury through repetitive motion, similar to what would happen to an athlete in training. Seventy-two hours after the injury, it was noted that compared to controls the only group that showed increased levels of prostaglandins was the exercised group. The group that was exercised and received the NSAID, as well as the NSAID group, had statistically significant lower levels of prostaglandins (specifically Prostaglandin E2) in the tendons. This showed that the NSAID blocked the inflammatory healing of even the tendon injuries that were exercised or rehabilitated. The tendonitis that was treated with just the NSAID had almost no prostaglandins in the sample, signaling a complete inhibition of the inflammatory healing process. The effect was even more pronounced at 108 hours.

The researchers also measured DNA synthesis in the fibroblasts. This showed which fibroblasts were proliferating. Again, the exercised group was the only group that exhibited elevated levels of DNA synthesis in the fibroblasts. Compared to the control group there was 100 percent more growth of fibroblasts in the exercise group. The tendons treated with Indomethacin had no DNA synthesis noted.

This showed there was no fibroblastic growth occurring. The group that exercised and took the NSAID showed a little bit of growth. The authors concluded, "Motion and prostaglandin release in Group II were associated with increased DNA synthesis. Inhibition of prostaglandin by Indomethacin also coincided with a decrease in DNA synthesis... Inhibition of prostaglandin synthesis, and thereby DNA synthesis, may not be desirable during the proliferative stage of a soft tissue injury, when DNA synthesis for cell division of fibroblasts is needed to heal the injury to the tendon." The paper also stated a fact that many researchers in this field are wondering, "Despite the lack of scientific data, NSAIDs are widely used, often as the mainstay of treatment." (Almekinders, L. An in vitro investigation into the effects of repetitive motion and nonsteroidal anti-inflammatory medication on human tendon fibroblasts. American Journal of Sports Medicine. 1995; 23:119-123.)

Another study was done on the use of perhaps the most popular anti-inflammatory medication used in sports medicine, ibuprofen, in the treatment of tendon injuries. It was found that only thing the ibuprofen doses used in the study caused the strength of the flexor tendons to decrease. A decrease in strength of the flexor tendons of 300 percent was observed at four weeks. The peak force of the flexor tendons of controls was 12.0 newtons, whereas in the Indomethacin group it was an average of 2.5 newtons. Extensor tendon analysis showed similar results, with controls having a breaking strength of 12.0 newtons and the tendons treated with the NSAID, 3.5 newtons. The authors noted, "Examination of the data reveals a marked decrease in the breaking strength of tendons at four and six weeks in the ibuprofen-treated animals....This difference was statistically significant." (Kulick, M. Oral ibuprofen: evaluation of its effect on peritendinous adhesions and the breaking strength of a tenorrhaphy. The Journal of Hand Surgery. 1986; 11A:100-119.)

From the above studies, it is clear that NSAIDs inhibit the fibroblastic growth process and thus diminish an athlete's chance of healing. NSAIDs are used because they decrease pain, but they do so at the expense of hurting the healing of the injured soft tissue. A good example of this is a study on the use of Piroxicam (NSAID) in the treatment of acute ankle sprains in the Australian military.

Compared with the placebo group, the subjects treated with Piroxicam had less pain, were able to resume training more rapidly, were treated at lower cost, and were found to have increased exercise endurance on resumption of activity. The conclusion of the study was that NSAIDs should form an integral part in the treatment of acute ankle sprains. (Slatyer, M. A randomized controlled trial of Piroxicam in the management of acute ankle sprain in Australian regular army recruits. American Journal of Sports Medicine. 1997; 25:544-553.) At first glance in reviewing this study, NSAIDs appear to be great, but the real question is did they help the ligament injury heal?

In reviewing the study, the answer is a resounding NO! To test ligament healing the ankles were tested via the anterior drawer test. During this test the ankle was moved forward to determine the laxity in the ligaments. This study was published in 1997, and the author stated that this was the first time the clinical measurement of the anterior drawer sign had been used in a clinical trial. It meant that all the studies done prior to this one, in assessing whether anti-inflammatories helped with ankle sprains, did not test whether the ligaments healed. In this study at every date of testing after the initial injury, days three, seven, and fourteen, the Piroxicam-treated group demonstrated greater ligament instability. At the time of the initial injury the ligament instability in the Piroxicam group and the control group were exactly the same. This study showed that the NSAID stopped ligament healing, yet the person felt better. The authors noted..."This result is of concern in that it may reflect a paradoxically adverse effect of the NSAID-derived analgesia in allowing subjects to resume activity prematurely." (Slatyer, M. A randomized controlled trial of Piroxicam in the management of acute ankle sprain in Australian regular army recruits. American Journal of Sports Medicine. 1997; 25:544-553.)

Do you see the difference between pain relief and healing? The athlete needs healed tissue. Up until the present, too many studies were advocating NSAID use when it came to ligament injuries, because they were such great pain-relievers, when in fact they were and are stopping the healing mechanisms of the body. Any technique or medication that stops the normal inflammatory process that helps heal the body must have a long-term detrimental effect on the body.

BY TABATHA ELLIOTT, PHD

ANOTHER REASON TO AVOID NSAIDs

Regular M&F readers already know that we warn against taking non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen for delayed-onset muscle soreness, the pain that follows intense workouts. NSAIDs work mainly by inhibiting an enzyme present in muscle cells called cyclooxygenase (COX) that initiates inflammation and pain following a muscle injury, such as after a hardcore training session.

While it would seem like a good idea to inhibit COX, inflammation is actually a necessary component of muscle growth. In fact, **research shows that NSAIDs decrease muscle protein synthesis and muscle growth.** And if that's not enough to deter you from taking NSAIDs, new research from Appalachian State University (Boone, North Carolina) may. Scientists found that taking NSAIDs before exercise increases oxidative stress following a workout. Such an increase can have negative implications on not only muscle recovery but also your health.

Don't stress on it

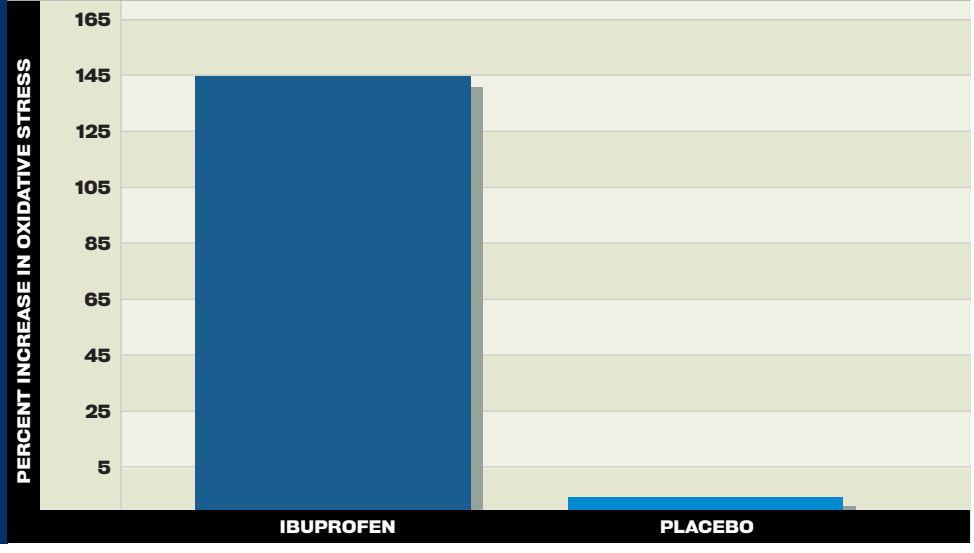
Oxidation Overload | The researchers had 54 ultramarathoners take either ibuprofen or a placebo on the day before and the day of an ultramarathon race. They collected samples of the runners' blood and urine the morning before the race and immediately afterward to measure indices of oxidative stress. Racers who took ibuprofen were found to have significantly higher levels of oxidative stress.

JUST SAY NO

The take-home message from these studies on NSAIDs is simply that you should avoid taking them whenever possible. Of course, there are times when NSAIDs are helpful and even necessary, such as when you have a headache that won't quit or an injury that's inflamed. At those times when you must take an NSAID, consider taking it with an antioxidant supplement such as 500–1,000 mg of vitamin C.

NSAIDs, ENOUGH SAID

This graph shows the percent greater increase in oxidative stress after the race compared to before the race in ultramarathon subjects taking ibuprofen vs. a placebo.



Graph created using data from McAnulty, et al, 2007.

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From Medscape Medical News > Neurology

All Nonsteroidal Anti-Inflammatory Drugs Have Cardiovascular Risks

Allison Gandey

January 12, 2011 — New data showing nonsteroidal anti-inflammatory drugs (NSAIDs) have cardiovascular risks are putting the well-known pain relievers back in the headlines. Investigators evaluating available evidence report they have found little to suggest that any of the investigated options are safe.

Regulatory agencies have already pointed to cardiovascular signals with NSAIDs, but these concerns are based mainly on observational evidence. This new study provides a comprehensive analysis of all randomized controlled trials of the drugs.

During an interview with *Medscape Medical News*, senior investigator Peter Jüni, MD, from the University of Bern in Switzerland, said his team expected to see an increased risk but was surprised by the magnitude of the signal. "We never thought we'd see 2- and 4-fold increased risks," he said. "The doses were admittedly high," he pointed out, "however, this is clearly clinically relevant."

Several earlier meta-analyses were unable to resolve the debate over risk because they failed to include all randomized evidence in 1 study. This new network meta-analysis, published online January 11 in *BMJ,* includes all available evidence.

The team led by Sven Trelle, MD, also at the University of Bern, included 31 trials and 116,429 patients taking naproxen, ibuprofen, diclofenac, celecoxib, etoricoxib, lumiracoxib, rofecoxib, or placebo.

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Misusing Painkillers Can Prove Deadly, FDA Warns

Associated Press

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WASHINGTON -- Too many Americans unwittingly overdose on over-the-counter painkillers, or take the wrong ones. Now the government is warning consumers that following the directions can mean the difference between feeling better or suffering severe, even lethal, side effects.

Topping the warning list is the popular painkiller acetaminophen, best known by the Tylenol brand but present in more than 600 products that treat pain, coughs, cold and flu. Taking too much can poison the liver.

More than 56,000 emergency-room visits a year are due to acetaminophen overdoses, and about 100 people a year die after an unintentional overdose of the drug, according to Food and Drug Administration estimates.

Sometimes consumers swallow extra pills in hopes of faster pain relief. Others unknowingly ingest too much by taking more than one acetaminophen-containing remedy.

Most acetaminophen products are nonprescription, but there are some prescription ones, such as Vicodin. Often the ingredient is listed only in the label's fine print or, for prescription drugs, with the confusing abbreviation APAP.

In drugstore brochures and public-service ads unveiled Thursday, the FDA is urging consumers to check which products contain acetaminophen and carefully follow dosage instructions.

It's not the only over-the-counter drug getting attention: FDA's campaign also will warn that certain patients are at increased risk of other side effects from different painkillers -- such as aspirin, ibuprofen, naproxen or ketoprofen -- called NSAIDs, or nonsteroidal anti-inflammatory drugs.

Those side effects include stomach bleeding and kidney problems.

In addition to dosage warnings, FDA's new campaign says:

- The risk of liver damage increases if you have three or more alcoholic drinks while using acetaminophen.
- It's rare for stomach bleeding to occur with NSAIDs using over-the-counter doses for short periods of time. Risk increases, however, for people who are over 60; take prescription blood thinners or steroids; have a history of stomach bleeding or other bleeding disorders; or have three or more alcoholic drinks a day.
- NSAIDs also can cause some reversible kidney problems; people most at risk are those who are over 60, have pre-existing kidney disease or take blood-pressure medicine known as diuretics.

Some 100 million people a year take acetaminophen, and serious liver damage is very rare, manufacturers insist. Still, McNeil Consumer

& Specialty Pharmaceuticals, the manufacturer of Tylenol, voluntarily upgraded warnings on its acetaminophen-containing products to explain the liver risk -- and has begun listing the ingredient's name in large type on the box front of multi-ingredient products like Tylenol Cold.

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