

Side Effect of opioids and painkillers – low testosterone levels

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Many men may find themselves in a situation where they are on prolonged opioid use to manage their chronic pain. They are being pain managed until they can decide on surgery or choose to remain on painkillers to get them through their day or their job or their activities. A growing concern is what are these opioids doing to these men's testosterone levels? The concern is well-founded.

In this article, we will see how opioids cause joint destruction by impacting and causing reduced testosterone levels.

The discussion points of this article:

Part 1: The ability to heal and the impact of hormones

- The patient is concerned about their testosterone levels: "I need to work, I need to play, I need to be active."

- Low testosterone is present among approximately 63% of male patients on chronic opioids.
- Physicians might not believe patients who claim that a standard opioid dosage is an ineffective treatment.
- The incidence of opioid-induced androgen (testosterone) deficiency (OPIAD).
- Research has shown that Testosterone has a direct effect on cartilage growth. If the testosterone levels are low, so is the body's ability to regrow damaged cartilage.
- The loss of muscle function despite testosterone replacement.
- Different opioids may affect men differently.
- But what about my daily aspirin and over-the-counter anti-inflammatories?

Part 2: Painkillers, low testosterone symptoms: Erectile dysfunction

- Research: Painkillers cause erectile dysfunction – 53.3% to 81.7% of patients who were opioid-dependent (addicted) had problems with sexual dysfunction.
- Does aspirin prevent erectile dysfunction?
- No erectile dysfunction in aging and older rats on aspirin.
- Ibuprofen can suppress the production of testosterone.
- Taking prescription painkillers is clearly associated with a higher risk of needing medications for erectile dysfunction or testosterone replacement.
- Painkillers are causing Erectile Dysfunction. Now men are taking medicine for their pain and asking for prescriptions for their erectile dysfunction.
- The management of male patients with pain should include a review of their sexual health history.
- Testosterone does repair joint damage.
- The answer is not a balance of painkillers and erectile dysfunction medications: the answer is to fix the joint and get rid of the painkillers and the need for erectile dysfunction medications.
- Strengthen and stabilize joints with Prolotherapy injections.

The patient is concerned about their testosterone levels: “I need to work, I need to play, I need to be active.”

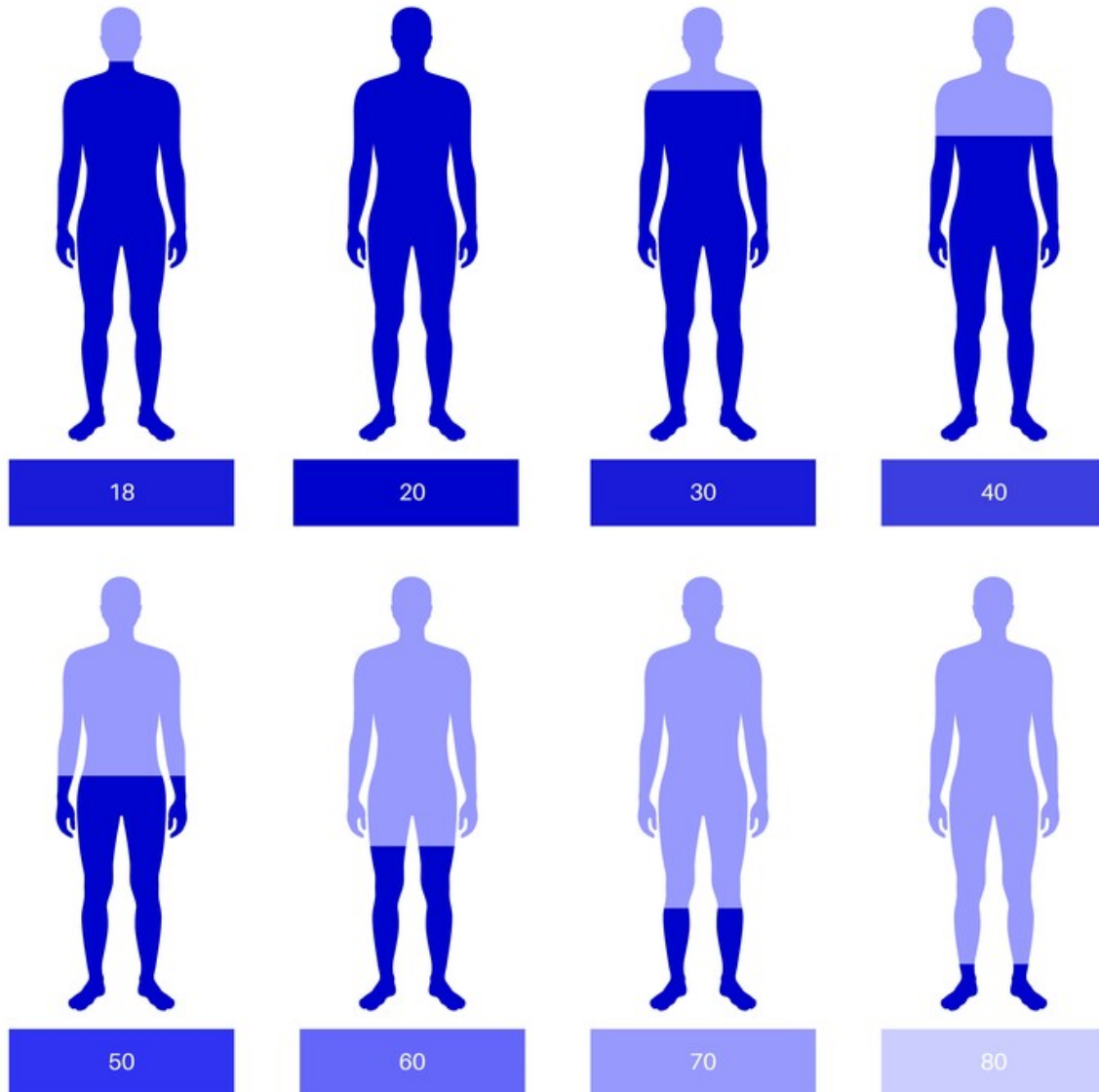
As you are reading this article, the need to work, play, and be active are likely the main reasons why you are looking up chronic pain and your concerns about testosterone levels and that you are becoming or are “Low-T.”

In our patient population, we see many men who tell us that they use **painkillers** and **anti-inflammatory medications** following any activity that is considered physically demanding or requires more than the usual physical exertions. Depending on their level of exertion, they may double up on normal doses to get them through whatever it is that they are doing. The men we see at our center have come to an understanding that if they continue on painkillers

they will ultimately need a joint replacement. Some have even come to the realization that if they continue on painkillers, they will have well-known and documented symptoms and conditions related to low testosterone levels.

As you can see in the chart below, men already face problems of declining testosterone as they age.

TESTOSTERONE LEVEL BY AGE



Low testosterone is present among approximately 63% of male patients on chronic opioids

Possibly accelerating their decline in testosterone in opioid use. An April 2020 study in *The Journal of Clinical Endocrinology and Metabolism* (1) makes these very real observations after monitoring the patients in their study many men have low testosterone following continuous use of painkillers.

- Hypogonadism or testosterone deficiency is present among approximately 63% of male patients on chronic opioids.
- Hypocortisolism (adrenal insufficiency) is present in 15% to 24% of patients of both genders.
- In addition, hyperprolactinemia (increases in prolactin levels – responsible for breast development) common feature in chronic opioid users.

Physicians might not believe patients who claim that a standard opioid dosage is an ineffective treatment. Is the problem in their low hormone levels?

In 2015, noted researcher and physician Forest Tennant, MD, wrote in the journal *Pain Medicine* (2) about hormone abnormalities in patients with severe and chronic pain who fail standard pain management treatments. Here are the learning points.

“Some patients with severe and chronic pain fail to obtain adequate pain relief with standard pharmacologic treatment agents, including low to moderate dosages of opioids. Understandably, physicians might not believe patients who claim that a standard opioid dosage is an ineffective treatment. These patients may be severely impaired, nonfunctional, and bedridden or housebound.”

To help show doctors that these patients may not be responding to typical doses of painkillers because their hormone levels were so low, Dr. Tennant suggested that these patients be characterized by their hormonal problems, and then, based on this information, doctors could develop treatment strategies for them.

- In this study: a serum hormone profile consisting of
 - adrenocorticotropin (ACTH),
 - cortisol,
 - pregnenolone,
 - progesterone,
 - dehydroepiandrosterone (DHEA),
 - and testosterone was obtained on 61 chronic pain patients who failed standard treatments.
- 49 patients (80.3%) demonstrated more than one hormone abnormality defined as a serum concentration or level above or below the normal range.

Dr. Tennant suggested hormone serum abnormalities are biomarkers of severe, uncontrolled pain, and, in a patient who has failed standard treatment, they are an indicator that enhanced analgesia (the patient may need more painkillers) is required and that hormone replacement may be indicated.

More painkillers are given as a suggestion in some patients. That you are reading this article is likely an indication that you want to solve your problem of needing more painkillers. Let's continue on.

The incidence of opioid-induced androgen (testosterone) deficiency (OPIAD).

Let's advance that 2015 to 2018. A 2018 paper from Rutgers University Medical School published in the journal *Sexual Medicine Reviews* (3) noted the non-coincidental rise in the incidence of opioid-induced androgen (testosterone) deficiency (OPIAD) and the "epidemic" of prescription painkiller usage. To combat testosterone deficiency and the health impacts it creates the researchers suggested men:

- Stop using opioids.
- Use short-acting opioids.
- Consider testosterone replacement therapy (TRT).

Further: "The patient and physician should weigh the risks and benefits of testosterone replacement therapy against more conservative approaches. Options such as clomiphene (an infertility drug for women often prescribed to men in an "off-label" or not-originally intended use) and anastrozole (a drug used to decrease estrogen in women with breast cancer) are available for patients (men) who wish to preserve fertility." In other words, if you are a younger man and more children are in your future, you may be recommended to this class of drugs to maintain fertility.

In the conclusion to this research Rutgers's doctors said: "Because opioid-induced androgen (testosterone) deficiency (OPIAD) is an underappreciated and underdiagnosed consequence of chronic opioid abuse, healthcare providers should be particularly vigilant for signs of hypogonadism in this patient population. It is reasonable for pain specialists, urologists, and primary care physicians to closely monitor patients on prescription opioids and discuss available options for treatment of hypogonadism."

Further, a study published in October 2020 by the California Institute of Behavioral Neurosciences & Psychology (4) describes the problems of painkillers and low testosterone levels:

"it is crucial to focus on the adverse effects of narcotics, and one of the lesser-known side effects is hypogonadism (low testosterone). Opioids act on the hypothalamus, pituitary, and directly on gonads affecting serum testosterone levels. Narcotic-induced androgen

insufficiency contributes to sexual dysfunction, infertility, hyperalgesia, and involving various body functions overall, affecting the quality of life.”

Continuing this line of research, German doctors wrote in August 2022 in the German language medical journal *Schmerz (Pain)* (5): “Androgen insufficiency under treatment with opioids, antidepressants, and anticonvulsants in chronic pain diseases is a side effect with a high prevalence. It can lead to clinical metabolic alterations, adynamia (the mental inability to start or finish an activity), stress intolerance, anemia, or osteoporosis and has a significant impact on the quality of life. Opioids, antidepressants, and anticonvulsants affect (sex hormones.) A urologist, andrologist or endocrinologist should be involved in the treatment at an early stage. . . Awareness of this side effect of an otherwise (interventional) medicinal pain therapy must be sharpened and compulsory included in the differential diagnostic considerations.” In other words, treatment should be initiated.

Research has shown that Testosterone has a direct effect on cartilage growth. If the testosterone levels are low, so is the body’s ability to regrow damaged cartilage.

Testosterone is an anabolic hormone. An anabolic hormone is a “builder upper,” its characteristics are well known as a hormone that promotes the repair and growth of soft tissue, including muscle and cartilage growth.

Many people believe that testosterone is only a male hormone, research over the years shows testosterone also plays a pivotal role in female body chemistry. Male or female, if one has a low testosterone level, then he/she will likely experience more difficulty healing.

In our article: **Hormone replacement therapy and Osteoarthritis – degenerative joint disease**, we discuss this subject further.

Opioids impact serum testosterone levels



Testosterone does repair joint damage.

- An Australian study published in the *Annals of the Rheumatic Diseases* examined the role of low circulating testosterone in men facing total knee replacement and found that low testosterone impacted cartilage tissue loss and bone loss. **(6)**

In this study, 28 men (average age 52) had a knee MRI. Then two years later they had another MRI of the same knee. By measuring testosterone levels and examining the MRIs, the researchers found a reduction in tibial cartilage (shin bone). This tibial cartilage loss was associated with serum-free testosterone levels.
- In one landmark study from St Bartholomew's Hospital Medical College in London, doctors showed how testosterone reversed cartilage damage and reduced proteoglycan (the stuff of connective tissue) loss. It was suggested that testosterone replacement therapy in patients with low testosterone levels may help prevent joint damage and disability. **(7)**

- Doctors of the Research Program in Men’s Health: Aging and Metabolism, Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston University School of Public Health, and the University of Pittsburgh School of Medicine found that men with androgen deficiency (low testosterone) brought on by overuse of painkillers and other pain medications, showed improvements in pain, sexual desire, body composition, and aspects of quality of life when put on a testosterone replacement program. (8)

The loss of muscle function despite testosterone replacement

A March 2022 paper in the journal *Andrology* (9) comes to us from the University of Southern Denmark and Odense University Hospital Denmark. The research team writes that “Chronic pain and opioid treatment are associated with increased risk of male hypogonadism and subsequently decreased muscle function. A diagnosis of hypogonadism is based on the presence of low total testosterone and associated symptoms. The effect of testosterone replacement therapy on muscle function in men with chronic pain and low total testosterone remains to be investigated.” In men on opioids, it is not just loss of muscle that is the concern, it is also the loss of muscle function or weakness that medical professionals are being confronted with by their patients. In this study, the objective was: “To investigate the effects of testosterone replacement therapy on muscle function and gait performance in men treated with opioids for chronic non-cancer pain.”

- This was a double-blind, placebo-controlled study.
- Forty-one men (over 18 years old) with opioid-treated chronic pain and low serum total testosterone were divided into groups of 24 weeks of testosterone replacement therapy (testosterone undecanoate injection three times/6 months, total 20 injections) or placebo injections (total 21 injections).
- At baseline, the average age was 55 years old and BMI was 30.7 (obese).
- After testosterone injections, muscle function and gait performance were similar between testosterone replacement therapy and placebo. However lean body mass was significantly higher following testosterone replacement therapy compared to placebo.

Discussion: “Testosterone replacement therapy, compared to placebo, did not improve muscle function or gait performance despite increased lean body mass. Changes in body composition did not infer any changes in muscle function.”

Different opioids may affect men differently – research on painkillers that may cause low testosterone

A January 2022 paper in the *Drug Design, Development and Therapy* (10) wrote: “The degree of hormonal (testosterone) deficiency may depend on the individual opioid used. In (previous research), the odds of (testosterone) deficiency were higher in men using fentanyl, methadone, or oxycodone as compared with individuals using hydrocodone. Some reports

indicated that buprenorphine and tapentadol may have less of an effect on the levels of sex hormones. The risk of opioid-induced low testosterone is higher with higher opioid doses (more than 100 mg morphine equivalent daily dose) and the use of long-acting opioids as compared to short-acting.”

Conclusion: “Supplementation with sex hormones may improve sexual functioning and should be considered under close specialist supervision whenever opioid dose reduction or opioid cessation is not feasible. Of interest, hormone supplementation may reverse hyperalgesia (hyper-pain) and improve pain control in patients treated with opioids.”

But what about my daily aspirin and over-the-counter anti-inflammatories?

Ibuprofen can suppress the production of testosterone

A 2018 study ([11](#)) from a team of European researchers published in the *Proceedings of the National Academy of Sciences of the United States of America* reported: “Ibuprofen use results in selective transcriptional repression (destructive interference) of endocrine cells (which produce sperm/fertility and testosterone) in the human testis. This repression results in the elevation of the stimulatory pituitary hormones (which can suppress the production of testosterone), resulting in a state of compensated hypogonadism (“Low-T”).”



To be fair, there is a lot of controversy surrounding the use of **Non-steroidal anti-inflammatory drugs (NSAIDs)** and aspirin and the NSAIDs and aspirin effect on erectile dysfunction.

In July 2018, Urologists published research in the journal *Medicine* (**12**) which outlined these controversies:

- “There are various etiologies of erectile dysfunction (ED), including endothelial dysfunction (degeneration or failure of the inner lining of small arteries throughout the body including the penis), atherosclerosis (clogged arteries), and chronic inflammation.
- Aspirin has a protective role against endothelial dysfunction and atherosclerosis, whereas all non-steroidal anti-inflammatory drugs (NSAIDs) are known for their anti-inflammatory properties.
- However, the association between the use of aspirin or non-aspirin NSAIDs and ED is controversial.”

Comment: On the surface, it would appear that NSAIDs would help ED as an anti-inflammatory and aspirin would help ED as it may help clear clogged arteries. So why the controversy? Because many researchers think the opposite. This is the concluding statement from this research:

“Most clinical trials indicated an association between aspirin or non-aspirin NSAIDs and ED, but other studies reported inconstant results, ranging from beneficial effects to marginal/moderate risk. These diverse clinical consequences may come from various study designs, population samples, dosages, or medical indications.”

Aspirin and NSAIDs while shown to cause erectile dysfunction – may help others with their ED. The evidence according to this research team is inconclusive.

Part 2: Painkillers, low testosterone symptoms: Erectile dysfunction

Research: Painkillers cause erectile dysfunction – 53.3% to 81.7% of patients who were opioid-dependent (addicted) had problems with sexual dysfunction.

Men do not like to go to the doctor, this is well documented. Men will finally go to the doctor when erectile dysfunction is involved. This was documented by researchers at Brown University who wrote in the *Asian Journal of Andrology* (**13**):

“Erectile dysfunction is estimated to affect more than 30% of men between the ages of 40 and 70. As a result of an improved understanding of the disorder and improved treatment options, an increasing number of men are going to the doctor with Erectile dysfunction

concerns. In fact, **many of these men are visiting their health care professional for the first time with ED as their primary complaint.**”

But what is causing their erectile dysfunction? While there are many causes of erectile dysfunction, this article will concentrate on the relationship between low testosterone, joint pain, and opioid or painkiller use.

A recent study from Tagore Medical College in India ([14](#)) begins with this statement: **“The relationship between opioid use and sexual problems among males is a complex one, as some are using opioids to increase their sexual performance while others are suffering from sexual problems due to its use.”**

The big problem is this research from Tagore Medical College is suggesting that 53.3% to 81.7% of patients who were opioid-dependent (addicted) had problems with sexual dysfunction.

Does aspirin prevent erectile dysfunction?

This is a controversial subject with little research to support findings one way or the other. A May 2019 paper in the journal *Science Reports* ([15](#)) examined the effects of long-term aspirin administration on erectile function in old and aging rats. Here are the summary learning points:

The association between aspirin and erectile function is still controversial however this animal study confirmed that aspirin did not alter erectile function. The researchers suggested that long-term aspirin administration had no impact on erectile function.

A September 2020 paper in the *American Journal of Men’s Health* ([16](#)) suggested with admitted skank evidence that aspirin could have a significant effect on the improvement of erectile function however, limited research supported this. However, the researchers did conclude that: “Aspirin needs to be considered by practitioners when prescribing drugs for vasculogenic erectile dysfunction.”

Taking prescription painkillers is clearly associated with a higher risk of needing medications for erectile dysfunction or testosterone replacement.

A study in the medical journal *Spine* ([17](#)) examined over 11,0000 men with back pain who were taking painkillers. What they found was that medication prescriptions for erectile dysfunction or testosterone replacement were significantly associated with both the dose (the number of painkillers you took) and duration (how long men were on painkillers) of opioid therapy. The more you took, the longer you took it, the greater the chance you would be given erectile dysfunction medications.

For patients receiving high-dose long-term opioids, **over 19% had such evidence of sexual dysfunction.** Both long-term use of opioids and high-dose opioid therapy were associated with roughly 50% greater odds of using medications for erectile dysfunction or testosterone replacement.

Painkillers are causing Erectile Dysfunction. Now men are taking medicine for their pain and asking for prescriptions for their erectile dysfunction

Listen to what researchers in the *Journal of Sex Medicine* (**18**) had to say. “Long-term opioid therapy has been found to have a strong impact on the hypothalamic-pituitary-gonadal axis that can be manifested clinically by sexual dysfunction. **This event is rarely reported and thus unnoticed and undertreated.**”

- So a man goes into the doctor’s office. He has chronic joint or back pain but desires to have the ability to be able to sexually perform. He is given painkillers.
- A man goes back to the doctor and says, his problem now is that he cannot perform sexually NOT because of pain, he cannot perform sexually because he is on painkillers. Now he gets a prescription for erectile dysfunction.
- The man and his doctor are not aware of this usually unnoticed connection between painkillers and erectile dysfunction.

The management of male patients with pain should include a review of their sexual health history

A second study, published in February 2017 (**19**) by the same team of researchers, this time appearing in the journal *Clinical Medicine*, made these findings:

- Erectile dysfunction was observed in 27.6% of patients on opioids.
- Treatment for Erectile Dysfunction:
After 6 months, 42% of those patients showed a significant improvement after being treated with iPDE5 – Viagra (48.5%) and/or testosterone gel (81.8%).
- Erectile function and quality of sexual life, as well as anxiety, improved in patients treated chronically with opioids after administering andrological (testosterone) treatment. The management of patients with pain should include a review of their sexual health history given the significant emotional impact posed to the patient, the impact on their overall quality of life, and its good clinical response to an interdisciplinary treatment.

The use of testosterone gel should be discussed with your healthcare provider.

The answer is not a balance of painkillers and erectile dysfunction medications: the answer is to fix the joint and get rid of the painkillers and the need for erectile dysfunction medications

The summary of research and concerns about low testosterone in men who routinely take painkillers can be seen in October 2018 research published in the *Journal of Endocrinological Investigation*. ([20](#))

“Opioid-induced androgen deficiency is a common adverse effect of opioid treatment and contributes to sexual dysfunction, impairs pain relief, and reduces the overall quality of life. The evaluation of serum testosterone levels should be considered in male chronic opioid users and the decision to initiate testosterone treatment should be based on the clinical profile of individuals, in consultation with the patient.”

The answer is not a balance of painkillers and erectile dysfunction medications: the answer is to fix the joint and get rid of the painkillers and the need for Viagra.

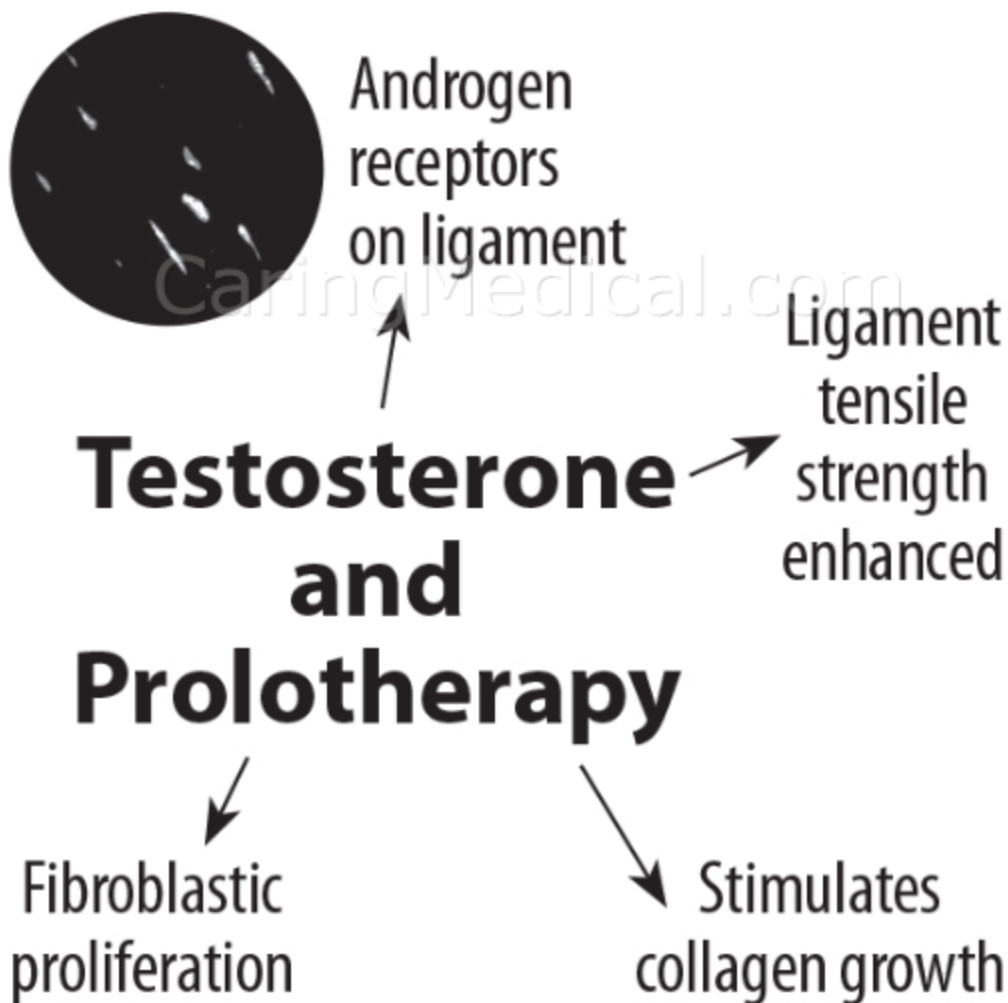
Strengthen and stabilize joints with injections

Throughout this article, we offered research to suggest that prolonged use of painkillers can cause erectile dysfunction and other symptoms common to low testosterone, including loss of muscle, energy, libido, weight gain, etc. At our center, we treat the cause of the pain and try to eliminate the need for painkillers. **Prolotherapy is an in-office injection treatment** that research and medical studies have shown to be an effective, trustworthy, and reliable alternative to surgical and non-effective conservative care treatments. In our opinion, based on extensive research and clinical results, Prolotherapy can be superior to many other treatments in relieving the problems of chronic joint and spine pain and, most importantly, in getting people back to a happy and active lifestyle.

As briefly demonstrated in this graphic. Prolotherapy injections share many of the healing characteristics of testosterone. We mention that both Prolotherapy and testosterone help fibroblasts (connective tissue cell that produces collagen and other fibers to proliferate and subsequently produce strong ligament strength.

Testosterone–Prolotherapy

connection. Both Prolotherapy and testosterone help fibroblasts proliferate and subsequently produce strong ligament strength.



As briefly demonstrated in this graphic. Prolotherapy injections share many of the healing characteristics of testosterone. We mention that both Prolotherapy and testosterone help fibroblasts (connective tissue cell that produces collagen and other fibers to proliferate and subsequently produces strong ligament strength.)

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