Clomid vs Enclomiphene: Which Is Better for Fertility? Transcript

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Why TRT Affects Fertility

If you are a man and If you are a man and have been interested in testosterone replacement have been interested in testosterone replacement therapy therapy therapy, you have, you have probably read somewhere probably read somewhere that it can reduce that it can reduce your fertility. This is your fertility. This is true. You may true. You may also have heard of two also have heard of two other options other options designed to designed to address this same address this same problem in a completely problem in a completely different way: different way: clomiphene and clomiphene and enclomiphene. Both enclomiphene. Both can can can boost your boost your testosterone testosterone testosterone by boosting by boosting your your your body's own signal, rather than body's own signal, rather than replacing replacing replacing it from outside. And it from outside. And the difference between these the difference between these two drugs is not as big two drugs is not as big as you probably as you probably think. Welcome think. Welcome back to Dr. Greg Jones' Optimization Academy.

Dr. Greg Jones' Optimization Academy. I'm Dr. Greg Jones, a I'm Dr. Greg Jones, a naturopath and naturopath and founder of the Center for founder of the Center for Innovative Innovative Innovative Health here in Health here in Phoenix, Arizona. I have been treating. I have been treating men with low men with low testosterone for years.

testosterone for years. And I don't start And I don't start treatment without treatment without discussing the different discussing the different options for optimizing options for optimizing testosterone and testosterone and preserving preserving preserving fertility. So, fertility. So, by the end of this video, by the end of this video, you will understand why you will understand why ZTT affects ZTT affects fertility, how these fertility, how these two compounds can two compounds can help help help preserve it, what preserve it, what mechanisms mechanisms mechanisms distinguish them, and what clinical studies clinical studies in humans have actually found.

in humans have actually found. Finally, we'll Finally, we'll look at the honest look at the honest tradeoff between tradeoff between cost and access, cost and access, as this is rarely as this is rarely mentioned. Now, a mentioned. Now, a quick note quick note before we before we begin. This is not begin. This is not medical advice or a medical advice or a recommendation about recommendation about what you should or should what you should or should not take.

not take. Please Please Please discuss your discuss your own case and own case and your tests with your your tests with your doctor. So, doctor.

How the HPG Axis Works

So, let's start with the problem that this let's start with the problem that this entire entire entire video answers. Why does video answers. Why does treatment that treatment that corrects low corrects low testosterone testosterone testosterone also also also compromise your compromise your fertility? Your fertility? Your body controls body controls testosterone production through a testosterone production through a feedback loop called the hypothalamic-pituitary- gonadal axis, or gonadal axis, or HPA axis. Your brain HPA axis. Your brain sends a signal, and sends a signal, and your testicles respond to it your testicles respond to it. Here's what's. Here's what's really happening. Your really happening. Your hypothalamus is constantly hypothalamus is constantly reading your overall hormone levels. When you hormone levels. When you inject testosterone inject testosterone or apply or apply it from an external it from an external source, your brain source, your brain takes it as a signal that you have that you have plenty of it. So it plenty of it. So it reduces its own reduces its own signal, GnRH, or signal, GnRH, or gonadotropin- gonadotropin- releasing hormone, which releasing hormone, which will lead to a reduction in will lead to a reduction in other signals other signals called LH and FSH, or luteinizing, or luteinizing hormone and hormone and follicle-stimulating follicle-stimulating follicle-stimulating hormone. LH and FSH are hormone. LH and FSH are not just background not just background chemistry. These are real chemistry. These are real messages that messages that tell your testicles tell your testicles to produce both to produce both testosterone and testosterone and sperm. When you sperm. When you reduce these signals, reduce these signals, sperm production sperm

production drops with them.

drops with them. So, if you've heard So, if you've heard the phrase that HRT can the phrase that HRT can affect affect affect or or or harm your fertility and harm your fertility and never never never delved deeper into delved deeper into the statement, the statement, this is the mechanism behind this is the mechanism behind it. But here's it. But here's something you should know something you should know before we before we move on.

move on. One of these two never One of these two never actually made it actually made it past the finish past the finish line with the FDA, and it's line with the FDA, and it's probably not the one probably not the one you thought of. We you thought of.

How SERMs Restore the Signal

We will find out what exactly this will find out what exactly this drug is and why it is drug is and why it is still important. So, still important. So, if adding if adding testosterone from outside testosterone from outside suppresses the signal or turns it off completely, what does turns it off completely, what does its its its restoration look like? This is where restoration look like? This is where Clomid Clomid Clomid and Enclomiphene come in. So and Enclomiphene come in. So how do SERMs restore a how do SERMs restore a signal instead of signal instead of replacing it?

replacing it? Clomid and enclomiphene Clomid and enclomiphene belong to a class of belong to a class of drugs drugs drugs called SERMs, which stands for selective selective estrogen estrogen receptor modulators. So receptor modulators. So imagine your imagine your hypothalamic- hypothalamic- pituitary axis as a pituitary axis as a thermostat. TZT is thermostat. TZT is like manually like manually heating a room with an heating a room with an electric heater.

electric heater. The thermostat senses The thermostat senses heat and never heat and never tries tries tries to turn on the boiler on its to turn on the boiler on its own. SERMs work own. SERMs work differently. It increases differently. It increases the sensitivity of the sensitivity of the thermostat itself, so it the thermostat itself, so it turns on the boiler itself.

turns on the boiler itself. Namely, these drugs Namely, these drugs block estrogen block estrogen receptors in your receptors in your hypothalamus and hypothalamus and pituitary gland. Your brain pituitary gland. Your brain perceives this as perceives this as low low low estrogen levels, which estrogen levels, which matches the data matches the data it receives when it receives when overall overall overall hormone production is truly hormone production is truly low. So it low. So it increases your levels of GnRH, increases your levels of GnRH, LH, and FSH, and your LH, and FSH, and your testicles respond by testicles respond by producing more producing more testosterone and testosterone and sperm.

sperm. sperm. Using the Using the body's own resources instead of an body's own resources instead of an external source. external source. And this is the mechanism that underlies what we are we are talking about now.

talking about now. Signal restoration, Signal restoration, not not not hormone replacement. If hormone replacement. If explaining the feedback mechanism seemed complicated, here is the seemed complicated, here is the short version. The TTC short version. The TTC turns off the signal. SERM turns off the signal. SERM turns it on again.

turns it on again.

Clomid vs Enclomiphene Chemistry Explained

Same axis, but moving in Same axis, but moving in opposite opposite opposite directions. That's the directions. That's the mechanism. mechanism. mechanism.

Let's get Let's get into the details, as into the details, as Clomid and Clomiphene are Clomid and Clomiphene are

two names that are often two names that are often used used used interchangeably, although interchangeably, although this is not the case at all.

this is not the case at all. Many present the Many present the confrontation between confrontation between confrontation between clomiphene and Clomid clomiphene and Clomid as a competition with a as a competition with a clear winner. This is simply not true. And. This is simply not true. And to understand why, it's to understand why, it's worth turning to worth turning to one chemical one chemical fact. Clomiphene fact. Clomiphene citrate, the drug citrate, the drug known as Clomid, known as Clomid, is actually a is actually a fixed mixture of fixed mixture of two isomers, that is, two isomers, that is, two mirror-image two mirror-image versions of the same versions of the same molecule. Although 62% of this molecule. Although 62% of this mixture is mixture is enclomiphene, the remaining 38% is zuclomiphene.

is zuclomiphene. Enclomiphene is the exact Enclomiphene is the exact isomer that isomer that does the job we described does the job we described : blocks the : blocks the estrogen estrogen estrogen receptor and restores receptor and restores the signal. Zuclomifene, the signal. Zuclomifene, on the other hand, on the other hand, behaves like a behaves like a weak estrogen and weak estrogen and is eliminated from the is eliminated from the body much body much more slowly. The half- more slowly. The half- life of life of life of enclomifene enclomifene enclomifene is about 10–12 hours, while 10–12 hours, while zuclomifene and its zuclomifene and its metabolites can metabolites can remain in remain in the body for weeks, the body for weeks, causing causing it to accumulate in it to accumulate in the system upon repeated administration, which enclomifene does not the system upon repeated administration, which enclomifene does not do.

do. do. So if you read So if you read that Clomid causes that Clomid causes more visual more visual disturbances or disturbances or mood swings than mood swings than enclomiphene, enclomiphene, enclomiphene, this this this slower- slower- slower- release isomer is the release isomer is the most cited most cited mechanistic mechanistic mechanistic reason for this. It's not that reason for this. It's not that enclomiphene enclomiphene is an improved version and Clomid is outdated.

and Clomid is outdated. It's one molecule It's one molecule split into two split into two halves, and halves, and enclomiphene isolates the enclomiphene isolates the part that actually part that actually does the work. So, this does the work. So, this is the is the difference in mechanism. The difference in mechanism. The real question is real question is whether it works the whether it works the same in humans, and that's what trials are being conducted for. I trials are being conducted for. I understand. Choosing understand. Choosing dietary supplements dietary supplements can be difficult.

can be difficult. There are hundreds of There are hundreds of brands, conflicting brands, conflicting claims, and it's impossible claims, and it's impossible to figure out what's to figure out what's actually beneficial actually beneficial and what will truly and what will truly improve your improve your health. That's why I health. That's why I created the created the Dr. Supplement Store. John's. Every Dr. Supplement Store. John's. Every product in the store product in the store for energy, for energy, gut health, gut health, sleep, hormonal sleep, hormonal optimization, optimization, optimization, recovery, and more is recovery, and more is personally reviewed, tested, and, tested, and recommended. These are the recommended. These are the formulas I formulas I use and use and recommend to my recommend to my patients, friends, and patients, friends, and family. So go family. So go to drjoesupplements.com, to drjoesupplements.com, sign up for the sign up for the newsletter, and you'll newsletter, and you'll get 10% off your get 10% off your first order. You will first order. You will also receive also receive exclusive exclusive exclusive protocols and tips protocols and tips that I share only that I share only with my community.

with my community.

What the Clinical Trials Show

So discard the unnecessary and So discard the unnecessary and choose what choose what actually works. actually works. Now let's Now let's back up back up everything we've just everything we've just discussed with numbers. In an discussed with numbers. In an early early early “proof of concept” study, 12 “proof of concept”

study, 12 men were switched from men were switched from testosterone testosterone testosterone gel to continued gel to continued gel therapy or to gel therapy or to oral oral oral enclomiphene. After 6 enclomiphene. After 6 months, both groups months, both groups achieved similar achieved similar testosterone levels.

testosterone levels. The difference was manifested in The difference was manifested in the number of the number of the number of sperm. sperm. sperm. Every man who Every man who took enclomiphene— seven out of seven after seven out of seven after three months and six out of three months and six out of six after six six after six months—retained months—retained months—retained normal normal normal sperm counts.

sperm counts. None of the men None of the men who remained who remained on testosterone on testosterone gel alone achieved this. gel alone achieved this.

I know this is a small I know this is a small trial, only 12 trial, only 12 men in total, and it's men in total, and it's worth mentioning the worth mentioning the number, but the results were number, but the results were consistent with what larger larger studies later found. A larger studies later found. A larger randomized randomized phase II trial found the same phase II trial found the same pattern.

pattern. pattern. Enclomiphene Enclomiphene Enclomiphene increased increased increased testosterone, testosterone, testosterone, estradiol, and LH levels estradiol, and LH levels almost as almost as effectively as effectively as testosterone gel, while, while preserving preserving preserving sperm production, sperm production, which the gel simply which the gel simply could not do could not do structurally.

structurally. structurally. Two Two Two placebo- placebo- controlled phase controlled phase controlled phase III trials were then conducted in overweight men with overweight men with secondary secondary secondary hypogonadism hypogonadism hypogonadism for 16 weeks, and for 16 weeks, and they found the same thing they found the same thing on a larger scale.

on a larger scale. Enclomiphene restored Enclomiphene restored normal levels of normal levels of testosterone, LH, and testosterone, LH, and FSH. Sperm concentration FSH. Sperm concentration remained within remained within normal limits, while normal limits, while testosterone gel, again,, again, caused a marked caused a marked decrease in decrease in sperm production. This sperm production. This study study study was conducted was conducted was conducted specifically with overweight and overweight and obese men obese men suffering from suffering from hypogonadism. So, it hypogonadism. So, it would be fair to would be fair to say that this say that this applies to this applies to this group of group of study participants, not study participants, not all men.

all men. The authors of the latest The authors of the latest study study study call their call their finding " recovery," not " replacement." And those replacement." And those were four words that were four words that summed up the entire summed up the entire video. I want to video. I want to make sure we do make sure we do this again.

this again. These are comparative These are comparative trials of trials of trials of enclomiphene versus enclomiphene versus testosterone testosterone testosterone gel. No direct gel. No direct comparative comparative comparative trials of trials of trials of enclomiphene versus enclomiphene versus Clomid have yet Clomid have yet been conducted.

been conducted. The explanation about The explanation about isomers a minute isomers a minute ago was based on ago was based on generally accepted generally accepted generally accepted pharmacology, not pharmacology, not comparative comparative comparative clinical clinical clinical studies. And that's why studies. And that's why we expect a we expect a difference, but that's not difference, but that's not proof that the proof that the study study study recorded one. So, recorded one.

FDA Approval and Access Differences

So, this mechanism this mechanism is confirmed in is confirmed in real real real tests. What is much less talked about is what you you you are actually signing up for are actually signing up for when you choose any of when you choose any of these options.

these options. Let's figure this out Let's figure this out. Clomid. Clomid has been FDA-approved since 1967 has been FDA-approved since 1967 for a completely different for a completely different indication—female indication—female indication—female infertility—and its infertility—and its use in use in men is “off-label,” men is “off-label,” but it is an inexpensive and but it is an inexpensive and widely available widely available widely available generic. Now about generic. Now about enclomiphene, enclomiphene, enclomiphene, developed under developed under the name Androxal, which the name Androxal, which never received never received FDA approval as a FDA approval as a stand-alone drug.

stand-alone drug. Its development was Its development was effectively discontinued in effectively discontinued in 2021, and at the time of 2021, and at the time of this video, this video, it is only available it is only available through prescription through prescription pharmacies that pharmacies that make make custom-made drugs and custom-made drugs and is prescribed “off-label.” So does this mean that.” So does this mean that Clomid is the better choice?

Clomid is the better choice? Not necessarily. A Not necessarily. A fair compromise fair compromise is to choose between a is to choose between a cheaper, cheaper, cheaper, FDA-approved but off- FDA-approved but off- label label label option and a option and a more expensive, more expensive, unapproved but unapproved but purer purer drug. And that's drug. And that's a conversation for you and a conversation for you and your doctor, where you your doctor, where you weigh cost, weigh cost, availability, availability, availability, monitoring, and your own fertility plans, not a fertility plans, not a topic for a YouTube video. In any case,. In any case, both options both options require require require blood tests before starting blood tests before starting and periodically afterwards.

and periodically afterwards.

Clinical Applications and Combination Protocols

Testosterone, Testosterone, Testosterone, estradiol, and, depending estradiol, and, depending on your goals, a on your goals, a semen analysis. So, semen analysis. So, let's summarize.

let's summarize. TTZ and these two TTZ and these two drugs do not drugs do not compete for the same compete for the same task. task. task. Traditional HRT Traditional HRT replaces the hormone and replaces the hormone and turns off your own turns off your own signal. Clomid and signal. Clomid and enclomiphene again enclomiphene again amplify your amplify your own signal, so own signal, so sperm production sperm production is maintained is maintained while taking them, which while taking them, which does not happen with does not happen with HRT. The difference between them is not a not a contrast between contrast between contrast between old and new or old and new or worse and better. And what do worse and better. And what do I do in clinical I do in clinical practice? Clomid is practice? Clomid is again cheaper again cheaper and more accessible, but and more accessible, but I have had patients I have had patients complain of complain of mood swings while mood swings while taking it. Not all, taking it. Not all, but some. On the other but some. On the other hand, enclomiphene hand, enclomiphene has proven effective has proven effective for many of my for many of my male patients male patients without significant mood side effects. And since mood side effects. And since it's a it's a custom- custom- custom-made drug, I can made drug, I can combine it with combine it with other substances that other substances that enhance endogenous enhance endogenous testosterone production, such as testosterone production, such as DHEA and pregnenolone.

DHEA and pregnenolone. In addition, there are In addition, there are situations when I situations when I prescribe both testosterone and Clomid testosterone and Clomid or enclomiphene to patients at the same time. This or enclomiphene to patients at the same time. This often happens when often happens when Clomid does not Clomid does not achieve the achieve the achieve the optimal optimal optimal testosterone levels we are testosterone levels we are seeking. But these are seeking. But these are always individual always individual cases and protocols.

cases and protocols.

Which Option Is Right for You

And again, this is not a And again, this is not a discussion about what is discussion about what is right or right or wrong, but about what is right for wrong, but about what is right for you you. And before you. And before you ask, “What about ask, “What about HCG?” This is something I want HCG?” This is something I want to discuss in the to discuss in the next video, next video, comparing HCG and comparing HCG and Clomid, but today Clomid, but today we are focusing on these we are focusing on these two. So, if you two. So, if you were told that HRT is were told that HRT is the only way to the only way to increase increase increase testosterone levels, and testosterone levels, and fertility was not fertility was not discussed, there are discussed, there are alternatives that are alternatives that are worth discussing with your worth discussing with your doctor before doctor before agreeing to anything. And agreeing to anything. And if this analysis was if this analysis was useful to you, please like useful to you, please like it, it, it, subscribe to new subscribe to new research on research on hormones, peptides, and hormones, peptides, and longevity medicine, longevity medicine, and share and share this video with those who this video with those who might need it.

might need it. Thank you for watching. Thank you for watching. Dr. Greg Jones was with you Dr. Greg Jones was with you, see you in the, see you in the