Testosterone & Testosterone Replacement Therapy (TRT) | Dr. Peter Attia & Dr. Andrew Huberman

I love to talk a little bit about hormone replacement therapy in men Um When one looks on social media and the internet there seems to be a younger and younger cohort of guys and people in their teens and twenties showing up to the table thinking uh that injecting testosterone cate or taking Anno VR or whatever it is is going to be the right idea They mainly seem to be focused on cosmetic effects I'm not a physician So I can't say whether or not they were actually hypogonadal et cetera But it seems to me again correct me if I'm wrong But it seems to me that similar to the Aia's rule as it relates to longevity that we could come up with a broad contour rule in which if a male of any age is not trying to get decent sleep exercise appropriately appropriate nutrition minding their social connections et cetera et cetera The idea of going straight to testosterone seems like a bad idea that said just like with depression and antidepressants there is a kind of a cliff after which uh low enough testosterone or low enough serotonin prevents people from sleeping exercise social connection et cetera So I do wanna acknowledge that But with that in mind how do you think about and perhaps occasionally prescribe uh and direct your patients in terms of hormone replacement therapy in men person in their thirties person in their forties who's doing almost all the other things correctly Uh What sorts of levels do you think are meaningful Because the range is tremendous in terms of blood tests 300 nanograms per deciliter I think on the low end now in the US all the way up to 900 or 1200 that's an enormous range What are some of the other hormones you like to look at estrogen DH D and so on So um uh you know a lot a lot to unpack there So um let's start with the ranges right So um the the the ranges you gave her for total testosterone of course and we don't spend a lot of time looking at that Uh the way we use the way we you know I used to spend more time looking at total and free when I had when I used more tricks to modulate it So I I'm actually far more simple in my manipulation of testosterone today than I was six or seven years ago six or seven years ago I mean we were you know we would use a micro dose of Anavar to lower SHBG in a person who had normal testosterone but low free testosterone what what was um a low dose of Anavar in that context 10 mg sub 2 to 3 times a week and of our basically being DH T oxandrolone And again we're not recommending this is actually if you're playing a competitive sport can

get you banned from that sport It can it can also get you banned from having Children if you do it incorrectly So a micro dose of this has to be small enough that it doesn't impair your body's ability to make testosterone But Anavar has such a high affinity for SHBG that it basically distracts your shbd from binding your testosterone freeing up testosterone That's exactly right So so the goal was how do I just give you more free testosterone So if if a patient shows up and they've got a a total testosterone of 900 nanograms per deciliter which would place them at you know depending on the scale you look at the scale we look at that would place you at about the 70th percentile but your free testosterone is you know eight nanograms per deciliter So that's pretty bad That means you're less than 1% free A guy should be about 2% free t so that dude should be closer to 16 to 18 nanograms per deciliter So in that situation that I just gave you his SHBG is really high His SS Hbg is probably in the 80 to 90 range That's very high because I think the upper range is somewhere around 5556 So we would first backs stall for what's driving is SHBG So there's basically three hormones So genetics plays a huge role in this There's no question that just out of the box people have a different like set point for SHBG Mine is incredibly low My SHBG is like kind of in the thirties twenties to thirties Um But from a hormone perspective there's basically three hormones that run it So estradiol being probably the most important insulin and thyroxine So we're gonna look at all of those and decide if any of those are playing a role So insulin suppresses it So this is actually the great irony of helping a person get metabolically healthy is in the short run you can actually lower their free testosterone all things equal because as insulin comes down SHBG goes up and if testosterone hasn't gone up with it you're lowering free testosterone So somebody who goes on a very low carbohydrate diet and attempt to drop some water and drop some weight is going to increase their shb GB up testosterone less free testosterone Um I can I can tell the carnivore diet people are going to be coming after me with um with bone marrow in hand But then again that after this discussion extends a little further I'm sure the vegans will be coming after me with celery stock So it's a uh so then the same is with estra dial So except in the opposite direction So higher estra dial is higher SHBG Um So again occasionally you'll see a guy with incredi normal testosterone but he's a very high aromatase activity person So he has a lot of the enzyme that converts testosterone into estradiol You can lower estradiol a bit with an aromatase inhibitor and that can bring down SHPG Now again these things individually are rarely enough to move the needle Uh The last is is thyroxine So if you

have a person whose thyroid is out of whack you have to fix that before you If their T four is out of whack you're gonna interfere with HPD There are also some supplements which I I think you've probably talked about these on the podcast I feel like I've heard you talk about these on the podcast Yeah there are a few that will adjust you know there is this idea Now there's a much better review that just came out I'll send it to you I'd love your thoughts on it and I've been perusing it line by line Um But I love input from experts like you on um the use of Tonga Ali for reducing SHPG In my experience it does free up some testosterone by which mechanism It isn't exactly clear and the effects aren't that dramatic right They're probably multiple effects Uh for all we know it increases libido and it does generally by way of increasing estrogen slightly which can also increase libido in some individuals So we don't know the exact motive of action So we've talked about a few the one that a few years back people were claiming could reduce SHPG was um uh stinging nettles um stinging nettle Well just urine seems to be urinating seems to be coming out multiple times on this podcast for whatever reason Uh stinging nettle extract I took the the the uh most pronounced effect of that was you could basically urinate over a car and when taking SHBG what the underlying mechanism of that was I do not know I took it for a short while It didn't drop my SHBG very much Um but it did drop by DH T sufficiently so that I stopped taking it I do not like anything that impedes DH T I I don't care if my hairline retreats I don't care about any of that DH T to me is something to be um coveted and held on to because you feel so much better when your DH T is in the appropriate range and love your thoughts on that I guess it really depends on the guy and it depends on what risk you're trying to manage Right So prostate size starts to become one of the issues with DH T Luckily my prostate p antigen is low Um And DH T um the things that I know can reduce it are things like Finasteride Propecia things like right things to that people take to try and avoid hair loss can dramatically reduce DH D and lead to all sorts of terrible sexual side effects mood based side effects et cetera But um yeah so I'm not aware of anything that can be taken in supplement form that can really profoundly drop shp Don't spend much attention on it anymore Basically I used to have a much more complicated differential diagnosis eight years ago Like I I mean it was I would drive patients nuts with the whiteboard diagrams I would draw for them And in the end I think they were just like dude just what do I need to take Um Today we take a much more simple approach So the first question is should you or should you have your free

testosterone being higher That's the metric I care about is free testosterone is the first most important The second most important is estradiol and sorry to interrupt you You said if you look at your total testosterone you want the free tea to be about 2% of your it should be So I can't I might not change that anymore So in other words if a guy is at 1% then I know I to really boost his total testosterone If he's only going to get 1 to 1.5% of it converted to free I need to boost him And that's why I don't care if he's outside the range Like I'll have a guy who's free tea I might have to get a guy's total tea up to 1500 to get his free tea to 18 I see So free tea is the target I like to see And do you still use antibiotics Uh um sorry to try and lower SHBG because it's too potent No because it's just too complicated for patients You know You know it's a it's a it's a drug that can't be taken orally So you have to take it under the tongue like a or something But then you know I had one patient once who even though we told him about 87 times that he was like swallowing the anti vs and his liver function and he was like we're talking 10 mg three times a week is a tiny dose and three months of him or whatever two months of him swallowing that every time tripled his liver function test So it's like it's just I was like you know it's just not worth the hassle of doing this Um for you know perfection Uh in reality we can fix this another way So so the first order question is do we believe clinically you will benefit from normalizing your free testosterone or taking it to a level that's called it 80th to 90th percentile So upper normal limit of physiologic ranges Um That's the first order question and that's going to come down to symptoms and that's going to come down to some biomarkers I think there's um two years ago Was it two years ago or maybe a year ago Very good study came out that looked at prediabetic men You've probably talked about this study and looking at insulin resistance and glucose uh disposal with and without testosterone And the evidence was overwhelmingly clear Um testosterone improves uh glycemic control testosterone improves insulin signaling This shouldn't be surprising by the way given the role muscles play as a glucose reservoir and a glucose sink So now I include that as one of the things that we will consider as a factor for using testosterone Now again it's not the only one So you can accomplish that with exercise you can accomplish that with these other things But then you get into a little bit of the vicious cycle of will having a normalized testosterone facilitate you doing those things better So uh let's just assume we come to the decision that this this this person is uh a good candidate for for testosterone replacement therapy The next question is what's the method we're going to do it Are we going to do it indirectly or

directly Now uh we used to use a lot of Clomid in our practice Um And have you talked about on the phone I talk too much about it I'm um no we talked a little bit about the fact that some people taking things like an Astros all to reduce aromatase activity run can potentially run into trouble because they think oh well more testosterone good lower estrogen bad And then they end up with issues like joint pain memory issues and severe drops in libido And I think a lot of the reason even fat accumulation So if estrogen is too low you you'll you can develop adiposity in a way that you wouldn't Otherwise there's a great new England journal paper It's probably 10 years old now that looked at five I believe it was five different doses of testosterone cypionate So these men were chemically castrated and divided into 10 groups It's pretty remarkable Signed up for this study So you were with and without an astro and five doses of testosterone So now you basically had five testosterone levels plus or minus high or low estradiol And the results were really clear that the higher your testosterone and the more your estradiol was in kind of that 30 to 50 range the better you were So if estrogen was too low even in the presence of high testosterone the outcomes were were were uh less significant and this is 30 to 50 nanograms per de or not 30 to 50% of your of one's testosterone Ok Great Um So we haven't talked but Clomid is no we have not talked a lot about Clomid I'd love to get your thoughts on Clomin So Chloe is a fertility drug It's a synthetic hormone It's actually two drugs M Chloe and I forget the other one and it tells the pituitary uh to secrete FSH and LH So uh you and and so the advantage of of Clomid is it's oral and it's meant to be taken orally So you know a typical starting dose would be like 50 mg three times a week And if you do that you'll notice in most men especially young men FSHLH goes up in any man the FSH and LH go up But if a man still has testicular reserve he'll make lots of testosterone in response to that Um because that's the first order question we're trying to answer is do you is your failure to make testosterone central or peripheral Yeah And I think uh just one point out again correct me if I'm wrong But my understanding is that a lot of the drugs that we're talking about um the synthetic compounds testosterone estrogen things uh related to growth hormone et cetera were discovered and designed in order to treat and excuse me in order to isolate and treat exactly these kinds of syndromes Whether or not it was the hypothalamus the pituitary or the target tissue the o the ovaries or the or the testes Correct Yeah I mean I think the easiest way to go about doing this is just give the hormone that's that's missing without attention to where it's where the deficiency is Why this becomes relevant is if you have a

35 year old guy whose testosterone is low but you can demonstrate that it's low because he's not getting enough of a signal from the pituitary Why would you bother giving him more testosterone when he has the capa he has the latest cells and the Cerulli cells to make testosterone he just needs the signal Um Sometimes though not always just a course of Clomid can wake him up and he's he's back to making normal testosterone So he'll do this three times a week 50 50 mg three times a week for a short course And then we would do it for 8 to 12 weeks and then we re evaluate and estrogen and testosterone will increase in in parallel Yes And again it depends you know aromatase activity is dependent on how much body fat you have and genetics Um And if estradiol gets too high we think if it gets over about 5560 we will give micro doses of an astro zole but it has to be real micro doses I mean you cannot pound people with an astro zole to to give you perspective the the the sort of on label use like if you just go to a pharmacy and order an astra zole you're gonna get 1 mg tablets Like we can't give anybody a milligram they'll feel like garbage We we have to have it compounded at 0.1 mg and we might give a patient 0.12 to three times a week That would be a big dose of an astro zole Yeah I think that the typical T RT clinic out there is giving 200 mg per meal one mil 200 mg of testosterone once every two weeks and then hitting people with um multiple milligrams of an astro zole and they're all over the place I I I've never really understood I mean I guess I shouldn't be surprised but it's kind of blows my mind that these T RT clinics are up all over the place given how bad I mean I see the results because I have patients that come from them and I don't understand like why they're so incompetent I actually think it's worse than that I think that they simply don't understand and don't care because it's a um pill mill and it's a money mill I think that nowadays it seems almost everybody who's doing T RT is taking lower doses more frequently every other day or twice a week dividing the dose and being very very careful with these estrogen or aromatase blockers Um We we we most of our patients do not take aromatase inhibitors It's not needed It's really only the high aromas that need it Um And so yeah when we'll talk about testosterone we'll talk about dosing there because I agree the more frequently you can take it the better and and frankly you don't need to go more frequently than twice a week because half the half life of the drug is is I think it's about 3.5 days is the plasma half life or something like that It could be off a little bit But but twice a week dosing is is really nice So if you're if if you if if you go to like uh you know uh a testosterone clinic that's giving you 200 every two weeks 50 twice a week is the same total dose

which by the way is a physiologic dose that's not going to give somebody any of the side effects You would see you're not gonna get acne with that you're not gonna get gynecomastia you're not gonna get anything The only real side effect you get from that is you will get testicular atrophy