Episode 155 Transcript

00:00:00:00 - 00:00:08:19
Mark Newman
That's the whole point, is we want something that's going to move with the clinical picture that we can hang our hat on to say, did I do what I'm trying to do?

00:00:08:20 - 00:00:34:04
Dr. Jaclyn Smeaton
Welcome to the DUTCH podcast, where we dive deep into the science of hormones, wellness and personalized health care. I'm Doctor Jaclyn Smeaton , chief medical officer at DUTCH. Join us every Tuesday as we bring you expert insights, cutting edge research, and practical tips to help you take control of your health from the inside out. Whether you're a health care professional or simply looking to optimize your own well-being, we've got you covered.

00:00:34:06 - 00:00:53:02
Dr. Jaclyn Smeaton
The contents of this podcast are for educational and informational purposes only. This information is not to be interpreted or mistaken for medical advice. Consult your health care provider for medical advice, diagnosis and treatment. Hi and welcome to this week's episode of the DUTCH podcast. Now, today's a little bit of a special day because we have two guests on the show.

00:00:53:08 - 00:01:18:12
Dr. Jaclyn Smeaton
I've got Mark Newmann, founder of the DUTCH Test, and I've got Doctor Mark Holthouse, MD, who has been practicing in men's health and is really thought of as one of our premier testosterone experts. We're going to have a dialog about the recent publication that we had just put out in Frontiers in Reproductive Health. It's titled Alternatives to Serum Testing for Transdermal Testosterone Monitoring A Review of Clinical Data and Correlation with Clinical Response.

00:01:18:15 - 00:01:40:18
Dr. Jaclyn Smeaton
You can find a link to our open access paper in the show notes. If you want to pull that open. And there's also a link there to the blog that we wrote that summarizes it, because it is a very meaty review. Now, essentially with this review, what we did was we wanted to see what evidence is out there in regards to monitoring testosterone

replacement therapy using different techniques and media.

00:01:40:19 - 00:02:02:16
Dr. Jaclyn Smeaton
So we looked at serum, we looked at saliva, we looked a little bit at dried blood spot and a little bit of urine. And what we really found and what we published in this review, is that the predominance of evidence really is for serum only. And in fact, one of the reasons why we wanted to talk about this with saliva in particular, is that it's highly it's used regularly to monitor saliva, is used to monitor testosterone.

00:02:02:18 - 00:02:17:23
Dr. Jaclyn Smeaton
And a lot of providers have done that for so long. We wanted to see what the data said about that. And in the end, we could not find any papers that showed correlation with clinical symptoms. And that was actually a surprise to us as well, because we thought there would be some body of research that we would be comparing it to.

00:02:18:01 - 00:02:50:14
Dr. Jaclyn Smeaton
So ultimately, this is an open invitation for dialog. And we really wanted to hear how this plays out. And Doctor Holthouse is practice because he's doing so much testosterone replacement therapy. And ultimately, this paper was kind of a tough one to publish because we didn't want it to offend anyone who has been using salivary practices. I mean, we haven't published the serum in this a live research, but we felt it was really necessary and part of the process of challenging what we think we know and advancing science and integrative medicine to have an honest conversation about where we're at today with the evidence.

00:02:50:16 - 00:03:14:06
Dr. Jaclyn Smeaton
So let's go ahead and dive in. I want to first introduce doctor Mark Holthouse As I mentioned, he's a medical doctor, and he's practiced family and functional medicine for over three decades, specializing in men's and women's hormones and peptides and longevity medicine. He was one of the first cohort to receive IFM certification in functional medicine, and he's taught the men's Hormone advanced module for 14 years.

00:03:14:08 - 00:03:41:05
Dr. Jaclyn Smeaton

He's also served as a faculty member at Loma Linda University School of Medicine, where he taught preventive cardiology. His integrative approach combines peptide therapy, lifestyle foundations, hormone optimization, and cardio metabolic health into a comprehensive longevity program. He currently sees clients full time and serves as the Chief Medical Officer at the Functional Medicine Institute. And outside of his clinical role, he continues to teach and educate colleagues and patients alike.

00:03:41:06 - 00:04:07:09
Dr. Jaclyn Smeaton
We are lucky to have him. Let's go ahead and get started. Thanks for joining me. We're going to try our best to keep the two of you straight in the podcast. For people who are just listening today. Mark Newman, for providers who are newer to the testosterone monitoring debate, then we're going to be talking about today. Can you briefly describe, like, what is the core disagreement that we see clinically and we see these people that are using kind of different approaches in the integrative medicine world?

00:04:07:14 - 00:04:13:02
Dr. Jaclyn Smeaton
Why and why do you think it's become contentious, and why did we have to do this formal review?

00:04:13:04 - 00:04:14:22
Mark Newman
Yeah. Yeah. It's a.

00:04:15:00 - 00:04:21:13
Dr. Jaclyn Smeaton
It's such a, you know, it's a big question, but I think it's like, I'm gonna start here because I know I understand your intent with this, and we want to.

00:04:21:15 - 00:04:41:20
Mark Newman
In there. I think it's easier for me to start with, like, where there's agreement. So what you can show in the literature is if Doctor Holthouse takes a guy and gives him a testosterone injection and then, you know, he's really good friends with lots of lab people. So he gets lots of free testing and he monitors blood and urine and saliva.

00:04:41:22 - 00:05:01:19

Mark Newman
Over time, what the literature shows is this track pretty well, like they tell a similar story. So then we can have this interesting debate about, you know, serum versus urine and what it has to offer and then versus saliva and how that might track a little bit better with free testosterone. But you can get a pretty decent window of free testosterone from serum.

00:05:01:19 - 00:05:25:20
Mark Newman
And you can have that conversation, but they dance together with each other. And so it's a different conversation. So then as soon as you take a hormone cream or gel and you put that on a patient, now we have this like pretty wild discrepancy. Where you have, 50mg is always the place I send people, at 50mg, the serum in the urine.

00:05:25:20 - 00:05:39:06
Mark Newman
If you take a guy at, say, a serum of, you know, 300 or 290 or something, you say, hey, that's that's not getting the job done for him. And then, of course, there's free testosterone. But if you're in that neck of the woods and you use 50mg, generally they're going to jump up to and totally jump in there.

00:05:39:07 - 00:06:01:10
Mark Newman
Correct me if I'm wrong, Mark. Probably 450, 500. Maybe you get them to 600 with 50mg. Maybe not whatever. But it's a modest increase and you see an analogous change in most people in urine. And then the saliva at that point depends on when you test. But generally speaking, they're in a whole other stratosphere, like you're sending the let me put it this way.

00:06:01:15 - 00:06:19:23
Mark Newman
If you match that saliva number with an injection, you'd be giving them an injection about ten times higher than you wanted, and you would never do that. So then we all pause and we say, Holy cow, this is really, really different. Like, which one makes sense? And so the history of how we got here is a long story.

00:06:19:23 - 00:06:44:08
Mark Newman
And it might be worth telling, to give some context to this, but that is the discrepancy

is the increase. This is not controversial. The increase in serum and urine compared to saliva is vastly different when it's, cream or a gel put on the skin. And we all have been sorting through that since two, you know, the early 2000s.

00:06:44:08 - 00:07:14:18
Mark Newman
There's been lots of confusion over that. And so, you know, for me, I was trained in the world of saliva testing and taught that, hey, these big numbers, they're the ones that matter. And we need to titrate to those numbers. And as I dug into the data, I realized, oh, I the clinical data tells a very different story and is in more alignment, particularly for testosterone and estradiol, with what's going on in blood or urine, although there are some caveats to that as well.

00:07:14:20 - 00:07:35:08
Mark Newman
And so, so just to give more of a short answer, that's the issue is that while discrepancy, which one tells a better clinical story is something I've been digging into, I mean, and really digging into for the last 15, 20 years. And it's a fascinating story, but it changes people's habits of how they treat patients fairly dramatically.

00:07:35:11 - 00:07:48:04
Mark Newman
So it's important that we know what's true and what's not true and what's still unknown. And we are pursuing, you know, truth and best practices together. And that's, you know, the reason for this conversation. And I think it's a really important one.

00:07:48:06 - 00:08:15:02
Dr. Jaclyn Smeaton
Yeah. You know, one thing that you I've heard you say, but it's stuck with me. You'll be glad to know your words. Stick with me for sure. Is that research sometimes can't prove what's right, but it can certainly prove what's not right. And, I think that that really, that sentiment is really an interesting one that usually we get to truth in physiology and medical practice by like one by one kind of filtering off hypotheses that we can't bear out in clinical research.

00:08:15:02 - 00:08:29:19
Dr. Jaclyn Smeaton
So I do think it's worthwhile for you to share a little bit about that background that

you have, like starting in saliva. And because it's the inception of the DUTCH test really comes from that number one. So if you use a DUTCH test today, it's just an interesting, interesting story about how the company was founded and where it came from.

00:08:29:21 - 00:08:58:04
Dr. Jaclyn Smeaton
But the other thing that I think is really important from my point of view is that I liked learning about you, that you believed one thing, and then you kept looking at data and then it changed your understanding. And now you believe something different, because I think that that is what science is. And I think in our industry sometimes with clinicians, we train under someone and it's almost like a guru type environment and it becomes dogma.

00:08:58:07 - 00:09:11:22
Dr. Jaclyn Smeaton
And I just my caution as a clinician for all clinicians listening is like, we don't act on dogma. Dogma doesn't work in medicine. We have to apply science and evolution. And I just think the story of that would be interesting for you to share if you're open to it.

00:09:12:02 - 00:09:34:19
Mark Newman
Yeah, yeah. I mean, and there really are two different channels of that story, like the DUTCH test at its heart was about taking hormones, taking the measurement of hormones and adding the measurement of metabolites and opening up that, that picture and moving it from kind of a two dimensional story to a three dimensional story. And that centered really around a non HRT scenario of, hey, here's this cortisol story.

00:09:34:19 - 00:09:57:15
Mark Newman
And when we add the metabolites, we get a richer understanding of what's going on. And there's a parallel story for estrogen and metabolites and androgen and metabolites and then once we started the company, then I kind of went back to that HRT conversation and went, okay, where does this test that we have to tell a story that seems to be true and is helpful for clinicians, and where does it not?

00:09:57:15 - 00:10:20:07

Mark Newman
And let's try to educate around that. And, and then this like for us, if saliva told a unique story like it tells a unique cortisol story, which is why we have the DUTCH Plus, because that opens up a window that we want to see. And if it told a uniquely true story about HRT, then we would look at commercializing our our saliva tests for estradiol, testosterone and progesterone.

00:10:20:07 - 00:10:46:09
Mark Newman
So the origin of this to me, and I think it comes from even people I really disagree with, I think a very genuine place of just trying to find truth for your patients. So if you go back to, I don't know, the late 1990s, early 2000s, the story really started with progesterone, I think. And, and the there's a confusion there that some of it can and some of that can't be applied to testosterone, which is what makes this so confusing.

00:10:46:09 - 00:11:05:21
Mark Newman
But if you give a woman topical progesterone, a lot of them feel better. And then you go, okay, well that's interesting. What happens at the lab tests and what you find with topical progesterone is it doesn't push urine. It doesn't. But more importantly, it doesn't push serum levels up. So then you get this confused group of people, like rightfully so.

00:11:06:00 - 00:11:24:09
Mark Newman
In the early 2000, right when I was starting to get into this industry, going like, what the heck do we do with this? Because, so if you take a woman, I would imagine a woman with PCOS who's got estrogen levels that are a little dominant to progesterone. She might legitimately feel much better if you give her topical progesterone.

00:11:24:11 - 00:11:45:09
Mark Newman
And and then if you go try to monitor that what you find is you find the serum really doesn't move and you go well that doesn't tell me a story that's helpful. And the saliva is sky high. So you're like, well I guess that tells me a story that like jives with reality. And it's a it's a confusing story because yes, women feel better on topical progesterone often.

00:11:45:15 - 00:12:02:14
Mark Newman
But then when you say, okay, let's go to its most common use case, which is I have hormones up here, I hit menopause and estrogen and progesterone drop. I give her estrogen. Now I know I've got to give her progesterone. And you say, well, how should I do that? And if you use topical progesterone the serum doesn't move.

00:12:02:14 - 00:12:29:00
Mark Newman
And you say, well that doesn't work. And then the saliva goes sky high and you say, well, does it work? And the thing that's confusing is there are split studies on that. The Leonetti study says, yes, it does work. Even when serum doesn't go up. And people responded to that one study. And it really is the genesis point, I think, of almost all of this movement and model around saliva testing.

00:12:29:02 - 00:12:49:04
Mark Newman
The thing is, the two other studies that are bigger and longer studies, show that it doesn't actually work. And the study actually said, hey, we have saliva, progesterone values that are very elevated and the uterus isn't protected in these cases. So right there we got to pause and go, Holy cow. This is really confusing. We've got to figure this out.

00:12:49:04 - 00:13:16:04
Mark Newman
But a fraction of our industry just really ran with that message of look this is free hormone. Saliva is a tissue surrogate. And so it speaks for tissue in this case, which is why it goes up and serum doesn't. And they and they really ran with that. And and from there there are layers to this that get really confusing because progesterone doesn't go up when you give it topically in serum, but testosterone and estrogen do.

00:13:16:09 - 00:13:37:05
Mark Newman
So they go up right. And the saliva goes much, much higher. And so that's not to get into. I mean, there are other layers of this that we need to unpack, but that I think is really the genesis point of this. And there and, and even from there, there are lots of confusing points. So people will say, when you take topical hormones, it doesn't show up in serum.

00:13:37:07 - 00:14:02:00
Mark Newman
And that is relative. I would say that is true of progesterone, but for estrogen and testosterone, it's not true. They do go up. They do scale with dosing. And then we get to this all important question of like, okay, if both numbers move, which one is dancing with the clinical outcomes. And that's why for us we started with testosterone, not with this case.

00:14:02:00 - 00:14:22:16
Mark Newman
We've been making this case for progesterone, for estradiol, for testosterone, for years. This process of this paper we just published was taking that case and putting it through the peer review process so that we can contribute to this dialog. So for testosterone, we know clinical endpoints. We know about muscle mass increase. We know about LH suppression. We know about erythrocyte ptosis.

00:14:22:16 - 00:14:46:14
Mark Newman
All the things that happen when you take testosterone. And if you follow the clinical data, it looks a certain way. If you're giving too much testosterone and it looks a certain way when you have insufficient testosterone, and it looks a certain way when you get it right, and so then you can go and overlay the saliva data and the serum data with that and say, hey, which is dancing more with like in concert with the clinical data.

00:14:46:14 - 00:15:10:18
Mark Newman
And what we found is that for every single clinical endpoint that we could find, there's a pretty good alignment with what happens in serum. And that's in disillusionment with the salivary testing. And so that's that was our attempt is to really lay that out for people, so that we can make some sense of this. And again, just continue to pursue best practices and things that seem to align with reality.

00:15:10:20 - 00:15:37:12
Dr. Jaclyn Smeaton
Yeah, absolutely. Well, before we get into the paper, Doctor Holthouse, you've been in functional and integrative medicine for literally three decades and such a highly respected person in this field. And we're really grateful for you joining our conversation today. Can you talk a little bit about how saliva fit into your practice

when you first got into training, when it came to hormones, and was there something in your patient experience that kind of shifted or made you question that saliva first model?

00:15:37:14 - 00:16:06:14
Dr. Mark Holthouse
Absolutely glad to be here, you guys. You know, it was kind of simultaneous. I think, with the, dried blood spot that I was I was seeing people largely coming to the practice with these really elaborate printouts, beautiful colors. And, you know, you have a little bit of imposter syndrome when you first get into this field and you see an unfamiliar test and you feel like, oh, my gosh, I need to know more than the person sitting in front of me, you know?

00:16:06:14 - 00:16:36:18
Dr. Mark Holthouse
So you learn these tests, you get these vendors at, at the, conferences to, to get you up to speed. And what I learned right off the bat was that there was just this, this inconsistency with, not just, monitoring and results, but actual clinical endpoints, how they felt. You know, largely with the discussion of progesterone, it's largely a symptom treatment, drug, as far as I'm concerned.

00:16:36:18 - 00:17:13:22
Dr. Mark Holthouse
And it's very difficult to monitor, but with testosterone and estrogen, it was just apparent early on that it was it was tough to have the validity and the reproducibility even within the same patient using saliva and then expanding that to the dried blood spot later on to get any kind of, conscious, meaningful discussion with the client when they would see these results and they would have symptoms and they would look at where they were and where they are, it was just it was hard to make sense of it.

00:17:14:00 - 00:17:42:08
Dr. Mark Holthouse
And that's where I really started focusing on, on, urine and, and serum serum because it's covered by insurance. Got all these, all this data. And that was a low point of entry for patients. So that was my experience early on. And honestly, it was probably two years of hardcore really trying to make that work. You know, you go to these conferences and you'd hear what Mark just laid out beautifully and, and, that was the dogma.

00:17:42:10 - 00:17:59:22
Dr. Mark Holthouse
And and then when I went to apply it, this is a men and women, it was it was just not like that. So my, my reality with my practice and implementing and what I was being taught back in those days was, was very different.

00:18:00:00 - 00:18:09:08
Mark Newman
Can I, can I lay out for you what I would say is the average patient in that world and see if that kind of aligned with your experience.

00:18:09:10 - 00:18:10:05
Dr. Mark Holthouse
Absolutely. Yeah.

00:18:10:05 - 00:18:34:13
Mark Newman
So the average patient, as I, as I sort of look at all the data, is the guy that comes to you that has a serum testosterone of 300 and has symptoms of low testosterone, like, okay, this is a guy I can help. Right? So if, if you put him on ten milligrams of testosterone, the average saliva value goes way outside of the young, healthy norm.

00:18:34:15 - 00:18:56:15
Mark Newman
And if and that's and that's considered a pretty low dose, and then the blood spot value on average goes with ten milligrams, I think, to about 1200. So so it creates this nice space to go. Okay. It's a pretty good learning environment because the serum results imply and in the urine that a transdermal gel is going to absorb at about 10%.

00:18:56:17 - 00:19:18:18
Mark Newman
So if I give you ten milligrams I'm giving you a higher level female dose and an almost negligible dose for a minute. Okay. And then if I look at the blood spot, or saliva, I get these really high values. And, and they're usually collected 24 hours after. So you're ready for the next dose. So this is the low point.

00:19:18:20 - 00:19:43:02
Mark Newman
Like if you tested at 12 hours or 8 hours, those numbers would be about 2 to 20 times

higher. So these are really hefty values that tell you hold on. This ten milligrams is actually a pretty hefty dose. Like you might want to scale it back because you're being super aggressive. But that patient that's coming in at ten milligrams is giving you on the higher end of where you'd want to go in blood spot and even higher in saliva.

00:19:43:05 - 00:20:08:08
Mark Newman
And then if you push towards 25 and 50mg and 50mg is what the data says works. At that point those values are just in the stratosphere. So on average, so I'm just curious for you is which doses did you try and and what's sort of just general numbers did you get in. Does that does that jive with kind of what the sort of aggregate data says in terms of what you experienced?

00:20:08:09 - 00:20:37:07
Dr. Mark Holthouse
Exactly. You know, I started off with much higher doses with guys than ten. You know, I was used to looking at serum, and I was used to looking at at published dosing and what worked for people and, you know, anywhere, anywhere from 25 to 50mg was, was where I was hanging out. And so, yeah, I was getting I was getting stuff that was 20, 50 fold higher in the saliva, sometimes higher.

00:20:37:09 - 00:20:45:16
Dr. Mark Holthouse
I mean, I was seeing tent readings in the tens of thousands. It was just like, what is going on here? I thought for sure there was a contaminant.

00:20:45:18 - 00:20:53:07
Dr. Jaclyn Smeaton
You know, I don't know how concerning that would be to a clinician thinking contaminant or way you're way over dosing that patient.

00:20:53:09 - 00:21:18:00
Dr. Mark Holthouse
Well, what I was told by the experts when I called on this, I called, the vendors for these labs and said, what what am I measuring here? And well, oh, well, that's that has to be somebody that has done a finger stick with the same finger that they used to put the cream on, or, you know, the saliva must, be measuring somebody who put the, you know, they put the topical cream on their jaw or on their neck.

00:21:18:00 - 00:21:38:19
Dr. Mark Holthouse
And I said, now they're not doing any of those things. And so despite getting that kind of feedback, you know, I just was never able to justify going back to the client and saying, hey, did you did you maybe do this with your collection? And it was like, no, I did exactly what you said. And these are the kind of results that I'm getting.

00:21:38:21 - 00:22:05:04
Dr. Mark Holthouse
And even worse, when we would use the same dose on the same client, putting it on exactly the same way, looking every three months, trying to make some sense of trending. There was a lack of it just didn't make intuitive sense with where I was going with my dosing escalating or de-escalating. I would often see opposite reactions, and that's what really did it for me.

00:22:05:04 - 00:22:34:04
Dr. Mark Holthouse
And I was like, this just makes no sense that we dropped your dose 50% and your, your thinking about dried urine, dried blood spot in particular went went up. How does that even happen? So, you know, the, the, the rationale that I was given was that somebody had there was a contaminant in the way it was collected, but, no, that's exactly my understanding is that about 10% is absorbed topically.

00:22:34:04 - 00:22:44:11
Dr. Mark Holthouse
And that's what you're going to get in, in the serum and, and see reflected and, and with these, these other ways of measuring it, it was just it was very inconsistent.

00:22:44:13 - 00:23:09:04
Dr. Jaclyn Smeaton
Mark Newman, a question for you here. So I mean, I think one of the things that may be surprising to people reading this paper or maybe who haven't read the full paper, but like, we're not selling dried urine testing for testosterone dose monitoring in that paper. You know, we're not really promoting that as the primary means. And if you've ever trained with dots, if you're a listener, if you're a provider, we recommend serum testing to get the dose right.

00:23:09:04 - 00:23:35:08
Dr. Jaclyn Smeaton

With testosterone, there is a complementary, amount of information that can come from the test from a primary point of view, like DUTCH is not the hammer for all the nails, and this is a case where serum is really the best standard. Do you want to speak at all to that? Or maybe just briefly around why this issue mattered to us, even though it's not really something that directly affects us as a business.

00:23:35:10 - 00:23:41:03
Dr. Jaclyn Smeaton
And I think secondarily, like, how is DUTCH supportive when it comes to testosterone replacement?

00:23:41:05 - 00:23:56:16
Mark Newman
Yeah, I mean your in testing has kind of two potential uses when it comes to HRT. The first question that people want to ask is did I get my dose right. And I am in perfect alignment with you, doctor. Hotels when it comes to progesterone is when you say, how did I get my progesterone dose right?

00:23:56:18 - 00:24:21:04
Mark Newman
The labs don't help. It's a it's a complex question because it's a different reason why they don't work for oral progesterone and why each test doesn't work for oral progesterone and why they don't work for vaginal progesterone. But if if progesterone was given as an injection, for example, the labs would probably be somewhat helpful. But it isn't, and it just so happens that you need to track what the literature says works and how your patient's doing.

00:24:21:07 - 00:24:47:17
Mark Newman
And that's the best you can do. And it's better to know that than to spend your life trying to jam square pegs into round holes. So when it comes to testosterone, the first question is how do I get my dose right? And then another question is like, what about the rest of the story? And so, so for me, I think when you give topical estrogen to a woman, the urine value has some value in saying like, hey, am I giving her the dose?

00:24:47:17 - 00:25:07:09
Mark Newman
I think I'm giving her? Is it absorbing in like the like, am I helping with bone or do I need more, or do I need to back off because she's absorbing too much? Like that's a

question that a lab test can potentially help you. And then the secondary question, which is where we really like the urine story for testosterone, is what else is going on.

00:25:07:09 - 00:25:26:12
Mark Newman
So if you raise a man's testosterone, I like serum to hang your hat on and say, did I get my dose right? Or it may be someone who uses pellets. The question might be, am I ready for another dose? Those types of questions the values seem to like do best with serum. Okay, then you have other questions of one.

00:25:26:14 - 00:25:52:06
Mark Newman
I would imagine doctor hold tests if a guy comes to you and he has a kind of low testosterone and he's stressed out of his mind getting rid of low testosterone symptoms. If you don't deal with the HPA axis, anxiety, stress is also going to be difficult. That's a great use case for what we do. Secondarily, if too much of that testosterone is spilling over into estrogen, that's a question you can ask with serum or urine.

00:25:52:06 - 00:26:16:02
Mark Newman
But urine goes further to say, how is this phase one metabolism houses methylation? Like, how is you processing that estrogen? We actually just print I published a case study that was a tracking of that of the elevation of testosterone and too much estrogen and crappy metabolism. And then we address the metabolism step by step. And it pulled that estrogen down into range.

00:26:16:02 - 00:26:37:11
Mark Newman
So you have this sort of better picture. So it's what are you doing with testosterone DHT production, estrogen production, estrogen phase one and estrogen methylation. And what's going on with, the HPA axis. And then of course, we've got some of those other ancillary pictures of oxidative stress and melatonin and some of those other things that fit into the whole person.

00:26:37:11 - 00:26:58:05
Mark Newman
But they don't they don't speak as directly to the hormone story. But so that's for us, is the DUTCH test. It has more of a complementary, nature when it comes to its best

use case for androgen therapy. But our goal for this is to really help people get it right, because we've just seen, you know, people like you that have come through.

00:26:58:07 - 00:27:15:16
Mark Newman
I mean, you were educated really well, on parts of this and then got exposed to this argument. So it's a little easier, I think, for you to sort of tease through it. And yet it took some time. Right? Yeah. And if someone lays because if you went to the literature before this paper, no one is laying out in the literature.

00:27:15:18 - 00:27:36:00
Mark Newman
You know, the case for like, how well do these different tests seem to go up and down with the clinical, utility of the test? Like there's a really nice paper combination of papers that we reference where there are two different testosterone that are used topically. One of them absorbs a little bit better than the other. And there are two studies that used each of these products.

00:27:36:06 - 00:28:00:06
Mark Newman
And they're both following sexual side effects related to testosterone. And in one of them, the serum went up into that target range. And the the the sexual side effects were relieved better than placebo. And then the other one, it went up, but not into that target range. It was too mild of an increase in serum. And wouldn't you know, it failed for the sexual side effects.

00:28:00:08 - 00:28:23:00
Mark Newman
And the frustration with all these studies is nobody's bothering. And I mean, I don't blame the researchers, but if they had looked at saliva in those men, what they very likely would have found is in both studies, the saliva is high. Like, holy cow, high, right? Like really, really high. And then you would say, oh, well that doesn't in that second study, the saliva is really, really high.

00:28:23:00 - 00:28:45:05
Mark Newman
And the serum is lagging. And the serum correlates better to the sexual side effects than does the saliva. But and this has been part of what I consider my job for the industry is okay. What we have to do is grab the saliva values out of different studies

and overlay them with what these studies say. Not because that's ideal, but because that's all we have, because nobody's doing this.

00:28:45:05 - 00:29:09:07
Mark Newman
The only study to date where people have taken serum, saliva and clinical outcomes in the same study is that Rand study clear back in I think right now maybe it is early 2000. Yeah. And they said, yeah, when the saliva climbs we don't see the clinical outcome, but nobody's looking at a comprehensive lab story, when it comes to those clinical outcomes.

00:29:09:07 - 00:29:27:20
Mark Newman
Because it's it's I mean, there really isn't you can justify not doing it because there's no data that says you should. But but that's where all that a lot of the confusion comes from. And what we tried to do here is take all the data that's available and overlay it and say, where do we see coherence and where do we see, you know, a lack of coherence.

00:29:27:20 - 00:29:39:00
Mark Newman
And that's so that's was the goal of this. And again, the point is let's pursue, you know, best practices together to the best degree that we can.

00:29:39:02 - 00:29:42:18
DUTCH Podcast
We'll be right back with more.

00:29:42:20 - 00:30:22:02
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00:30:22:04 - 00:30:29:02
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00:30:29:04 - 00:30:48:00
Dr. Jaclyn Smeaton
So, Doctor Holthouse I want to kind of get your experience so that other clinicians might be listening, be like, oh yeah, I find I'm finding that's happening. And you've covered this a little bit, but I want to just reinforce, like when you first started in practice, you were using saliva and dried blood spot when patients came to you and they'd been managed on that type of testing.

00:30:48:02 - 00:30:53:14
Dr. Jaclyn Smeaton
What were you seeing clinically and how were they feeling? And what did their testosterone levels like actually look like?

00:30:53:16 - 00:31:20:04
Dr. Mark Holthouse
Yeah. So the testosterone levels were, you know, depending on the technology, they were consistently super physiologic. I mean, that's across the board. Progesterone was a unique, critter. As Mark alluded to. And it was it was pretty much something that I learned early on, even before I learned from Mark and David Zaslav and some of the experts in the field.

00:31:20:06 - 00:31:53:09
Dr. Mark Holthouse
You know how that's different from testosterone and estrogen, because that's not something, as a clinician, I'd ever heard before. I learned it was a it was really most prudent to follow progesterone with symptoms. And whether it was topical, there's a little bit of nuance with the oral, which is by far my preference, but it was it was a super physiologic, lab result that I was seeing across the board, especially with progesterone and with, testosterone, estrogen, maybe not as big of an issue.

00:31:53:09 - 00:32:11:17
Dr. Mark Holthouse
And one of the things that I think you mentioned, Mark, in your blog, was that estrogen is not quite as labial as testosterone, at least not when it's given in a cream

or topical form. When you're looking at saliva, it's it's kind of got this up and down thing that you describe. And that's actually what I saw clinically.

00:32:11:19 - 00:32:37:17
Dr. Mark Holthouse
It was the the bookends were progesterone and testosterone. We saw the outliers and these super physiologic things. And where that became a problem was my postmenopausal gang that was on systemic HRT that for whatever reason, they didn't want to take oral P4 microRNAs, progesterone, at 100 or 200mg orally to protect the uterus from over estrogen ization.

00:32:37:19 - 00:33:14:09
Dr. Mark Holthouse
They were coming to me. And this is really what started my whole journey in this. What is really going on query. How am I knowing that these super physiologic progesterone doses are protective and and in fact, I had heard of some cases in California where I was practicing at the time, where there were some practitioners that had gotten into real trouble with and any mutual hyperplasia over using this combination of systemic, HRT in combination with either imaginal or at that time it, which is still kind of controversial, but at that time it was actually just a topical, progesterone.

00:33:14:11 - 00:33:38:16
Dr. Mark Holthouse
And they were using saliva to manage the dose, the therapeutic tissue levels because. Right. We were all trained that represents free tissue hormone. Right. And so that was kind of my first wake up call that maybe that wasn't true. And here was a population of people that really you can't afford not to get it right. You could be, you know, causing cancer.

00:33:38:16 - 00:34:05:19
Dr. Mark Holthouse
And so that, that was, that was really the starting point. So, it was it was not long after that realizing these super physiologic representations were not representative clinical results. On the guy's side, it was certainly, this serum, because I started experimenting and doing other ways to monitor, not just diagnosed, but then to monitor. And it was a consistency with this serum.

00:34:05:19 - 00:34:14:12

Dr. Mark Holthouse
It was an inconsistency with these other two modalities that I mentioned. So that was really the evolution is was nothing more complex than that.

00:34:14:14 - 00:34:35:15
Dr. Jaclyn Smeaton
I want to just kind of wrap that thought on the right and on the progesterone, cause I think whenever we talk about progesterone for post-menopausal women, I like to make sure we leave listeners with crystal clear guidance, which is our point of view. It doesn't differ from that of, you know, menopause society on this one, you want to be using 100 or 200mg of OMV, not using transdermal for endometrial protection.

00:34:35:15 - 00:34:57:00
Dr. Jaclyn Smeaton
If you have a perimenopausal woman who needs help with sleep or something like that, that's fine. But if they're on an estrogen replacement therapy or you're looking for endometrial protection, you have to go with those trusted, validated, clinically validated doses. And we agree, like testing does not help. In that case, the vaginal progesterone does have some research now where we we think that's a pretty good alternative for women who don't tolerate the oral.

00:34:57:00 - 00:35:05:14
Dr. Jaclyn Smeaton
But you're right. The body of evidence is not the same for that when it comes to safety. So you have to like really have informed consent with your patient. One.

00:35:05:14 - 00:35:32:08
Mark Newman
One if we're being fair to that, to the use of transdermal, progesterone is some people do have the practice of using relatively low dose of estrogen and then adding endometrial surveillance. And if you add endometrial surveillance, then that is a route, that you can go, but if you're, if you're not, then. Yeah, I think the, the evidence of protection, it's not high enough to just give the hormone and then trust that it's going to work.

00:35:32:08 - 00:35:35:20
Mark Newman
So I think in terms of your practice, I think that makes a lot of sense what you're doing, doctor.

00:35:35:21 - 00:35:36:10
Dr. Jaclyn Smeaton
Definitely.

00:35:36:10 - 00:35:51:19
Dr. Mark Holthouse
Yeah. A lot of people that are using the, you know, the vaginal, progesterone, in that case, they have in-office ultrasounds. So it totally makes sense. And yeah, if you know what you're doing, you know, you're watching for for the endometrial thickness. Totally responsible.

00:35:51:21 - 00:36:11:13
Mark Newman
Yeah. One of the, one of the things that was kind of an early tip to me in terms of the fact that saliva didn't make sense in an intuitive sense, is that if you think about the vaginal tissue, it's very vascular, right? It's going to you would guess that that tissue would absorb hormone better than the skin, which is meant to be a barrier.

00:36:11:15 - 00:36:29:12
Mark Newman
Right. And if you move the hormone from the skin to the vaginal tissue at the same dose, you would think, oh, I'm probably going to absorb more. And what you find in the, the urine and the serum is that it goes up like five x, something like that. I would don't quote me on that, but it goes up.

00:36:29:13 - 00:36:52:00
Mark Newman
It's definitely up. Right. And then if you take the same exact scenario, the saliva values when you move from the skin to the vaginal tissue is about ten times less, which then tells you the message, hey, the skin is a much better way to get the same dose into your patient than the vaginal tissue. And if you just say that out loud several times, you go, wait, hold on.

00:36:52:02 - 00:37:10:02
Mark Newman
Like that doesn't make any sense. The vascular tissue that you would think. So that was one of the things for me that maybe go like, hold on. Like something's not telling the right story here. And the and the outlier, if you look at the data, actually, if you

give vaginal hormones, there's one study where they looked at serum and saliva.

00:37:10:04 - 00:37:29:01
Mark Newman
It's a very similar story, like the magnitude of the increase in saliva and serum is fairly similar there. And then you move it to the skin and that's where you get this huge discrepancy. And, so it was that I thought was a pretty good tell that like, this is not these values are not reflecting, you know, what's going on systemically when it's on the skin.

00:37:29:05 - 00:37:52:19
Dr. Mark Holthouse
When it's on the skin. Yeah. That's a really good point actually clinically because in, in practices I'm involved with right now. And what the contemporary teachers are sharing. More there's more and more of a leaning towards using vaginal applications of hormones, in particular progesterone. I like it. Obviously we like it for the pregnant alone effect.

00:37:52:19 - 00:37:58:02
Dr. Mark Holthouse
We want that first phase metabolism because they sleep so amazing. They love you after work.

00:37:58:03 - 00:37:59:11
Mark Newman
Meaning that's why you like oral.

00:37:59:11 - 00:38:23:05
Dr. Mark Holthouse
It's why I like the oral microRNA. Exactly. So there's very rarely in my practice there is. Is there really an indication to to go vaginal progesterone or topical creams in a combo because they, they get so much better symptom relief within so many these patients that are, you know, needing HRT have sleep disorders. So it's it's just a better way to go.

00:38:23:07 - 00:38:53:02
Dr. Jaclyn Smeaton
Well, I want to talk a little bit about the clinical impact of potentially deciding to dose testosterone off these super physiological levels. You know, the typical clinical

response would be reduced the true dose, and that could be reducing it to a level that's below what's been demonstrated to have clinical efficacy. That's ultimately the big concern here. So this study highlights that this sub therapeutic serum testosterone is associated with a failure to achieve protection for things like bone mineral density, muscle mass, sexual function.

00:38:53:04 - 00:39:14:13
Dr. Jaclyn Smeaton
These are all areas where, like Mark alluded to before, a minimum serum threshold is required to confer benefit. So I think it's really important for clinicians to be thinking about what does it look like, not on the labs, but in your patient when they have inadequate dosing of TRT. Can you talk about like what are the symptoms and what's the clinical picture that you see coming in.

00:39:14:18 - 00:39:27:16
Dr. Jaclyn Smeaton
And if you had to see a patient and you could say that it looks like things are adequate now versus probably not, we should double check their levels. What are the indicators to you? What are they telling you or how are they feeling? Or what are you seeing on a clinical exam.

00:39:27:18 - 00:39:32:16
Dr. Mark Holthouse
Yeah, this has so many tempting Jaclyn you got to keep me on track here because.

00:39:32:18 - 00:39:34:09
Dr. Jaclyn Smeaton
I'll try my best.

00:39:34:11 - 00:40:02:20
Dr. Mark Holthouse
You know, I'm thinking about the differences with Coloma Thien and Clomid seen in hCG with the answer to that, which there's all kinds of layers to this discussion clinically, which is really fun. But we won't go there, I swear. But, no, it's it's it's the lack of, reduction in central obesity that often. I'll see. It's the lack of improvement in insulin sensitization that we often see with adequate doses of testosterone.

00:40:02:22 - 00:40:26:01
Dr. Mark Holthouse

So it really comes down to, not just the structural concerns of bone loss and estrogen, obviously, being a huge player as well in men with maintaining good bone health. But it's really about these people that have got fatty liver that are metabolically ill. The the new book Good Energy talks about this. And so many of our clients are suffering from these areas.

00:40:26:01 - 00:40:56:12
Dr. Mark Holthouse
And this is as big of, a reason in my practice where I'm using it as much as sexual function. Maybe even more now is with fatty liver, with insulin resistance syndromes. Mets in pre-diabetic type twos, people that cannot lose central obesity, people on Dexa scans who their body composition just shows persistent visceral obesity where we're trying to to to move these things, especially in guys but also in women when it's dosed appropriately.

00:40:56:13 - 00:41:31:18
Dr. Mark Holthouse
So I often will see a failure to meet these end points. Mark mentioned bone density. So yeah, you will see it in in lean skeletal muscle mass, not just lean mass but actually skeletal muscle mass in pounds. We see when we don't meet the mark. By under dosing, it's obviously the other thing is true too. If you're overdosing, especially in women, you can precipitate a lot of anger and hostility and and just really irritable people, that are getting do getting overdose.

00:41:31:18 - 00:41:56:14
Dr. Mark Holthouse
So I think as we move testosterone out of, the arena of a fear of prostate cancer and coronary heart disease being provoked, and now we're knowing that after the traverse trial in July of 23, hey, it looks like actually it's safe and it's effective. And we've got all this data now that shows it's actually a therapeutic for things like insulin resistance.

00:41:56:14 - 00:42:20:01
Dr. Mark Holthouse
And, certainly maintaining good bone health and mood and sexual dysfunction and men and women that we really have to get the dosing in the monitoring spot on so that we're giving people their best attempt. They're paying a lot of money in the case of pellets and some of these, these, modalities. And so I think it's really important to get the monitoring piece correct.

00:42:20:04 - 00:42:39:07
Mark Newman
So you said two things that like, we're kind of, really helpful for me in the literature when you talk about bone and you talked about signs of women having too much testosterone. What I love what they do in studies. Not not because it's the best way to do a study. It's just best for my brain is when you use doses until it fails.

00:42:39:09 - 00:43:00:18
Mark Newman
It's so handy in terms of understanding what's going on. So the because the one one study, in our paper that we reference, I think it's Sattler. I forget the author. It was on bone. And what they found is they found success at 50mg. They barely succeeded at 25mg. And then they failed at 12.5mg. They said that is insufficient.

00:43:00:23 - 00:43:18:21
Mark Newman
And that is so instructive to say, great, because if I take that dose that I know, I now know is heading towards a female dose and is insufficient for a man, and I give it to a population of people, I have that data, and it says that the saliva data is sky high. You know, for those men.

00:43:18:21 - 00:43:42:18
Mark Newman
And then I'm able to go, oh, okay. Then that value like totally conflicts with the clinical data. And on the other side of it, I'm able to say, okay, if I go down from 12.5mg just a bit to ten milligrams, if that's a male dose of hormone, right. If saliva and blood sputter saying, hey, this ten milligrams, it might be too much for a man, I can go, oh, okay.

00:43:42:20 - 00:43:54:16
Mark Newman
Well then what happens when I give that to a woman? Because if you shift over to injections and you take a male dose of injections and you give it to a female, you're going to get symptoms that she doesn't want.

00:43:54:16 - 00:43:56:05
Dr. Mark Holthouse
Shaving the next morning.

00:43:56:07 - 00:44:21:05
Mark Newman
Yeah. Unless. Good. In all seriousness, you're talking about trans men. And there is really good data that says, look, when we give 5 to 10mg transdermal as a chemist, I'm not saying that's the right dose. I'm not saying that's the wrong dose. But if you look at every single study where they've given that dose to women, you never see high testosterone symptoms except in the rare cases when what?

00:44:21:08 - 00:44:42:05
Mark Newman
When the serum level goes outside the range towards the male range. And then one of the things we did in this paper is then we shifted our attention to the body of literature on trans men, where the goal is to take a biological female and accomplish those high testosterone symptoms. And you ask the question, well, okay, what did it take to do that?

00:44:42:10 - 00:45:10:20
Mark Newman
And what they say is even with 25mg of a of a gel, like you get mild symptoms of excess testosterone, and only if you push the serum into those male ranges do you start to see what you call in this. It's in this sense excess. And so when you add all those up you go. Oh, so the very simple truth that I have here is the saliva values for those people are very high values that have nothing to do with the clinical reality.

00:45:10:22 - 00:45:48:12
Mark Newman
And the serum data seems to speak well for what's going on clinically. And that's the whole point, is we want something that's going to move with the clinical picture that we can hang our hat on to say, did I do what I'm trying to do? Which is either to take a woman who's low and make her normal, or take a biological female and put her in the male range, or take a male who's insufficient and put him in the range where he's going to see the bone increase, like, and those things to the bone and the, the females with, symptoms of excess testosterone were two really good, points in this paper that we

00:45:48:12 - 00:46:02:10
Mark Newman
were able to point to, to say we see really good congruence between what's going on

with serum, and what's going on with the clinical picture. And we see a contrast when we look at those other, lab types of saliva and dry blood spot.

00:46:02:12 - 00:46:22:08
Dr. Jaclyn Smeaton
Yeah, yeah. I love that you bring up. I mean, I think we have such an interesting body of literature when it comes to like, looking at the, trans male population. It is a unique opportunity for us to see that, like titration of dose and the impact in a biological female. And it's very interesting to have that data to be able to reference.

00:46:22:08 - 00:46:44:10
Dr. Jaclyn Smeaton
I think that's one of the most interesting aspects of the research that we did. With this review. Now, doctor, whole House, I think one of the things that would be helpful to cover, because we're talking a lot about getting into this target threshold serum range. And I think one of the challenges when it comes to testosterone is that, like the generally accepted range of normal is like 300 to 1000 nanograms per deciliter.

00:46:44:10 - 00:47:07:04
Dr. Jaclyn Smeaton
It is so huge. Some actually labs report up to 1200 nanograms per deciliter as normal. So we have like that kind of endocrine society. They say normal lower limit of normal is about 260. On target therapy ranges you see 400 to 700. There is the Framingham Heart Study. We have all these studies that point to different targets clinically in your own practice.

00:47:07:06 - 00:47:23:20
Dr. Jaclyn Smeaton
Can you tell me what you look for and how do you blend? Because I mean, it's really interesting how sometimes you'll see men come in and you're just doing routine screening and their testosterone is like 250, but they report no symptoms of low testosterone. Yeah. And then other times you have men like treated. And they're at eight 900 and they're still feeling low.

00:47:23:20 - 00:47:26:19
Dr. Jaclyn Smeaton
So how do you wrangle that clinically.

00:47:26:21 - 00:47:51:20

Dr. Mark Holthouse
Yeah I think it's largely a function of inflammation and cortisol. So many I tell guys that cortisol is the great Kryptonite to, symptom relief from testosterone replacement. You know, whether it's central obesity and their aromatase thing like crazy. I always say you've got to be careful with the people I train, the body that you're putting the testosterone into.

00:47:51:20 - 00:48:19:10
Dr. Mark Holthouse
What's it going to do? What's that body going to do with the enzymes and the terrain. You know, so these, these folks that have got a lot of central obesity and a lot of aromatase activity. So you have to be wary of that. And that's what I actually appreciate about the DUTCH test is that you've got that cortisol piece HPA axis kind of built in to, to what's needing to be part of the bigger conversation.

00:48:19:12 - 00:48:43:06
Dr. Mark Holthouse
I ideally would love to have every man's baseline at 25 when they walk in. What were you at your peak? And unfortunately, 90% of the time we just don't have that unless they've been with me forever as a client. And so that would be wonderful because some of these guys were 800, 1200 when they're a 25 years old and peaked.

00:48:43:06 - 00:49:36:01
Dr. Mark Holthouse
And, you know, before they got comorbid diseases, which we know has a huge correlation with promoting hypogonadism. You know, they were in a, in a different place. Now they're just walking in at 40 and they're at 550 and they've got symptoms. What do you do? Well, you you have to look at that bigger picture knowing that 1720 lace that moves you from the pregnant alone progesterone family over to the androgen precursors, knowing that aromatase and knowing that five alpha reductase are all influenced by things like insulin resistance, stress, oxidative, oxidative stress, inflammation, you have to understand all of those things about this guy to know what's happening with testosterone, which is just

00:49:36:01 - 00:50:04:10
Dr. Mark Holthouse
sitting kind of in the middle of all this, this noise, and things are metabolizing it away. And things that are inhibiting or supporting its production, or not. So I'm always thinking of it in that bigger context of how did they get there with that number that

I'm seeing on a two dimensional page? And really, I tell guys, I'm going to treat you as a person, as the first priority as opposed to any lab result.

00:50:04:12 - 00:50:36:16
Dr. Mark Holthouse
And I say the same thing to women because these reference ranges, especially for women, are fairly ridiculous when it comes to managing optimization. But I usually look for something north of five 5600. There's some data out there that suggest there might be, increased all cause and even cardiovascular mortality in folks that are even less than, you know, or six that six hundreds and that 650 should be kind of our, our benchmark for optimization.

00:50:36:18 - 00:51:10:16
Dr. Mark Holthouse
Androgen, you know, the androgen stuff that you see with FDA and Endocrine Society, is out there. But then there's the real application. I have many guys that don't feel great until they're up around 1800, you know, and if there's if they're desiring, you know, fertility in the near term and or using HCG or something, and, you know, they're they're younger still, we can get them up in the 800, nine hundreds pretty easily with those non testosterone products.

00:51:10:18 - 00:51:38:23
Dr. Mark Holthouse
But if they if they get their numbers up with those products, sometimes they don't feel the same symptomatically as they do. When I've used a testosterone product and gotten them to that exact same threshold. So even using different modalities of getting their total testosterone to the same number, and I can't explain that exactly. I think probably there's some estrogen things at play with the with the sperm, with the Clomid in particular, but.

00:51:39:01 - 00:51:59:05
Mark Newman
Meaning meaning that the because Clomid works on the estrogen receptor that maybe it's it's also doing something to symptom symptoms. Do you do you find it. And we're getting off topic which is totally fine with me. HCG doesn't do that. And and Clomid thing does hit on that estrogen receptor. Do you find between those two that you get better.

00:51:59:07 - 00:52:05:01

Mark Newman
You get better symptom relief from the same testosterone level from HCG which doesn't hit the receptor?

00:52:05:01 - 00:52:32:19
Dr. Mark Holthouse
Yes. We kind of in the biz, we're thinking of hCG and testosterone replacements as equal in that fact, where sometimes Clomid they'll have the same number. And because it's it's pumping FSH and LH, not just LH, you'll, you'll see that now the in column a thing compounded isomer of that has pretty much solved for that. It seems to it, it does not have that same estrogen zation effect.

00:52:32:21 - 00:53:01:19
Dr. Mark Holthouse
And so I, I pretty much exclusively am using that over the standard often citrate. Yeah. Yeah. But so I, you know, to your point, Jaclyn, I think, you know, I don't treat to a threshold per se as much on this topic as I would say for estradiol in a postmenopausal female where I'm trying to maintain bone and get them above 60, I have colleagues that are really respect that think that that's probably somewhere more like 40.

00:53:01:19 - 00:53:17:09
Dr. Mark Holthouse
You don't need that many picograms. But, suffice it to say, with testosterone, I'm going to go after the symptoms. As as my number one goal with these guys. And that's, that's, after all, what's going to bring them back?

00:53:17:11 - 00:53:43:16
Mark Newman
I, I feel better. One of the things I think is challenging about estrogen is if one of your key things is bone is you can't just ask, you know, your 60 year old female patient, like, how are your bones doing? Obviously there are some some additional testing that you can do that speaks into that. But, you know, because what I've noticed from the literature is if you give someone a placebo, it's half the effect on hot flashes that that a proper dose of iron is.

00:53:43:22 - 00:54:03:00
Mark Newman
So you have to be careful about saying like, do you feel better? Yes, I have fewer hot

flashes. That doesn't necessarily mean you're sufficient. I think one of the things that is challenging about estradiol is in this whole argument that we're having, I can just hear some people saying, hey, listen, you're wrong. Like when I give estrogen, I don't see it in the serum.

00:54:03:00 - 00:54:27:07
Mark Newman
And I think there is a difference between estrogen and testosterone. And that is that when you give a man testosterone on average, it's a gentle, up and down pattern throughout the day. And when you give a cream or a gel of estradiol, it's actually relatively rapid. So it is easy to test in serum. And not see it even if it's there, not because it's not there, but because it's fast.

00:54:27:11 - 00:54:52:17
Mark Newman
And so and that's where we've said, I think an area where urine can be helpful is that you want to test that captures over time. Urine is set up very well for that to sort of integrate the area under the curve. So I just want to like I just want to acknowledge that people do have to be careful that if you set a target in your mind for estradiol and you go chase it with a patch in serum, that's not a bad approach because it's a pretty flat pattern.

00:54:52:17 - 00:55:27:22
Mark Newman
But if you go chase that target number with a cream or a gel, it can exceed that number. And before you test, come back down. So you have to be really careful. I don't think serum is a great option for gels and creams of estrogen because you can end up overdosing again, not because it's there, but because it goes up and down so fast and then and this is where all this gets confusing is on top of that, what you just alluded to is there is also then a good faith debate about whether the impact you see from 20 to 40 in serum or 40 to 60 or even above 60 when you start

00:55:27:22 - 00:55:47:15
Mark Newman
talking about cognitive benefits and some of these other things, I would say that's not a debate that's settled is where that target really is optimized. And and of course, it's it's going to be an individual, you know, game that you're playing with a particular patient. So it's it's this 3 or 4 dimensional picture that is confusing. You have these up and down patterns.

00:55:47:20 - 00:56:13:04
Mark Newman
You have confusing targets as to where you should really be shooting for. And then you do have some differences, not just between progesterone and these hormones, but also between estradiol and testosterone that can confuse that. So and this is where we really love to have people like you when we have conferences lay out for people not only what the literature says, but also just very practically, what actually works in practice for getting the dose right.

00:56:13:07 - 00:56:21:05
Mark Newman
And then also looking at some of these confounding factors of metabolism, HPA axis, etc., which is what also makes it all interesting.

00:56:21:07 - 00:56:44:10
Dr. Jaclyn Smeaton
Totally. I mean, if you're interested in so estrogen, you know, we don't have time to talk about that in today's podcast. That's a whole nother subject that Mark just tapped into. But we do have a lot of resources on that. So if you want information on estradiol monitoring or our point of view on it, or how urine LCMs might be a really nice way to monitor, I'd encourage you to come to doctor's dot com and check out the education that we have.

00:56:44:10 - 00:57:06:11
Dr. Jaclyn Smeaton
There's a lot of free education, and if you're a provider, you can get access to our behind the scenes portal, where we have even a full 6 to 8 hour course on HRT that's unbranded. It's not much promoting, it's just the evidence on it. So I just highly recommend those resources. Doctor hold House, I want to speak to one of the things that you also said about testing men at 25.

00:57:06:12 - 00:57:24:20
Dr. Jaclyn Smeaton
Yeah. I think it's so important. And I'm, you know, I hope that we have a lot of, like, younger people listening. I feel like now, you know, no people in our generation didn't get interested in hormones until, like, they were gone. Really. But I think younger generations are just engaging in their health so much more proactively. And that goes for men and for women.

00:57:24:20 - 00:57:53:22
Dr. Jaclyn Smeaton
So if you're one of those people listening, I think this is where getting that baseline is so important. Your baseline for metabolic health, cardiovascular health, hormone health, liver health do that screening. And I now that there's all these direct to consumer serum testing companies that can be very inexpensive to get this broad swath of data. And even if you don't know what to do with it today or if things look great, it's just nice to have that to compare it to decade by decade, so that you can see how you're changing.

00:57:53:22 - 00:58:08:15
Dr. Jaclyn Smeaton
And one of the things I think about a lot and I talked I talked about this a lot with thyroid health in my practice because the normal range for thyroid for T, as H is like 0.5 to 4 or 5, depending upon the lab you're using, and sometimes women feel terrible at 3.

00:58:08:15 - 00:58:09:10
Mark Newman
A.m..

00:58:09:12 - 00:58:25:20
Dr. Jaclyn Smeaton
And you're like, where are you? You're in the normal range. Are you okay or not? Okay. And so I think one thing, the baseline is great to compare it. How is it changed. But I always used to say to patients, you know, the normal range for a shoe size for a woman is like a five and a half to a ten.

00:58:25:22 - 00:58:47:21
Dr. Jaclyn Smeaton
You know, if you are a size nine foot and you put on a size six shoe, it's going to be uncomfortable. And likewise, if you're a size seven and you wear a size ten shoe, it's not going to be a fit. And I think we have to keep that in mind when it comes to normal ranges is that when we are measuring ourselves or our patients, there is a large section of the normal range that's abnormal for that particular individual.

00:58:47:21 - 00:59:05:02
Dr. Jaclyn Smeaton

So just keep that in mind. And it's like you always have to treat the person and have the labs support. And I think that now that we have the advent of all these like self-directed tools and algorithms that are interpreting our labs, you can really lose that. You can lose that nuance. I think it's just so important to capture that.

00:59:05:04 - 00:59:41:22
Dr. Mark Holthouse
Yeah. To Mark's point, I think that we have we owe it to our clients to evaluate tissue, efficacy, you know, and I think we've got ways to do that, whether it's, you know, body composition analysis, whether it's looking at LH face, FSH suppression, whether it's looking at, you know, bone density, you know, these are these are things that I think we owe it to our clients to be evaluating and even, you know, having an ultrasound available and, you know, it's it's a noninvasive way to evaluate what you're doing to a woman's uterus.

00:59:42:00 - 01:00:06:21
Dr. Mark Holthouse
Chemically, you're chemically. You know, I have the landscaping analogy where the estrogen is the fertilizer for the lawn and the mower is the progesterone, and the dose of progesterone is the mower deck. How how low you're going. Don't scalp the lawn. It'll bleed. And don't do too little. It'll get too much fertilizer and it'll bleed that way. So it's it's this bigger art that we're trying to betray.

01:00:06:21 - 01:00:33:13
Dr. Mark Holthouse
And, this, this, this very tunnel visioned approach and move towards where it is truly the art of medicine. Hormone hormones are truly the art of functional medicine. In my mind. You have to understand all of these moving parts. The lab piece is probably the last thing to really come into the to focus for me. And I think for a lot of clinicians, it's incredibly confusing.

01:00:33:13 - 01:01:08:04
Dr. Mark Holthouse
Even in my own AFM teaching faculty, we have disagreements and that's okay. But sometimes it really impacts how your how your treatment goes. I think that's probably why I've gravitated towards patches and, and serum for monitoring and doing some of these things where I'm getting away from some of the pitfalls that Mark alluded to with overdosing, with using serum and topical estrogen, for example, and then using oral progesterone.

01:01:08:04 - 01:01:30:09
Dr. Mark Holthouse
So it's there's like an easy way to do it. And then there's a hard way to do hormone replacement therapy and monitoring and monitoring is, is, is is where the art is. Anybody can identify symptoms and initiate treatment. I think, it's the safe and efficacious, monitor that separates the men from the boys, so to speak.

01:01:30:11 - 01:01:32:02
Dr. Mark Holthouse
In my mind.

01:01:32:04 - 01:01:52:17
Dr. Jaclyn Smeaton
That's great. Well, as we wrap Mark, can you really just share? I mean, one of the things that we did, we wrote we wrote this blog when we released the paper, and it really wrapped with this open invitation in a call for discussion and feedback, because that's ultimately what we wanted was to put information forward, to stimulate feedback and discussion that can help move us forward from a clinical perspective.

01:01:52:19 - 01:02:01:10
Dr. Jaclyn Smeaton
Can you wrap us with just what your hopes are with this publication, and what practitioners and what our industry might do with it?

01:02:01:12 - 01:02:37:06
Mark Newman
Yeah, I mean, it really is the the pursuit of, you know, best practices for all of us. And there's, there's probably a little component of, like, myth busting in there. And, and when it comes to that, there, there are two different sides of any of those issues. And one of the things that is sort of passively pointed out by our paper is that people have been supporting, and I think, in good faith, supporting a particular model for now, 20 years, without like any data that's been through the peer reviewed process that actually supports that model.

01:02:37:06 - 01:03:02:16
Mark Newman
And I think that's a problem with just our industry can't work that way. And one of the things that's actually in the paper that sort of is kind of quietly in the paper is there's

new publication in that that shows women who are on topical testosterone, who have elevated saliva values, and they do not have a higher frequency of high testosterone symptoms than women who are on topical testosterone, who do not have high saliva values of testosterone.

01:03:02:16 - 01:03:40:02
Mark Newman
So when we have a model that we think like, does something prove something, show something, and it's a provable claim, then it really is, I think, important for us in the industry to be putting data forward that supports that. And, and there's there's silence on that front for 20 years. And so I think what people do from that is, is in this, I think effort to be kind and to be Switzerland ish is you just say, well, perhaps this model is out ahead of the research, but the point of this paper is there's a lot of research that actually evaluates that claim.

01:03:40:04 - 01:04:09:18
Mark Newman
I would say sort of indirectly. And the point of the paper is when you indirectly evaluate that claim with the available data, where there's there is a lot of data, it all falls in one camp. I mean, I would be honest with you, when I started this journey, I went into this with an open mind. I mean, at least from my own perspective, and said, okay, I've been told both things are true and I'm going to go dig into the data, and I'm going to find every paper that supports this claim and every paper that supports sort of the opposite position.

01:04:09:23 - 01:04:32:04
Mark Newman
And what I thought I would end up with is a short stack of papers over here, and a big stack of papers over here. And then I would weigh the evidence, and what I ended up with is zero. When it comes to testosterone and estradiol, I will say the lie in any study stacks on this side that says serum didn't go up and the symptoms exceeded what you would predict from serum.

01:04:32:08 - 01:04:57:05
Mark Newman
And that's the central question that I'm asking. Can I find evidence where the clinical response exceeds what serum or urine would predict in these scenarios? And for estradiol and testosterone, the stack is dozens and dozens deep on the side that says no. And and the side that says, yeah, there's an issue here. And maybe saliva has

something to offer.

01:04:57:07 - 01:05:15:02
Mark Newman
That's a unique message that we should listen to. I haven't found a single set of data that supports that, and it is an open invitation to say, look, if there's evidence for this other this model that says the opposite of the direction we're sort of headed, then let's get it out in the literature so we can add it to the dialog.

01:05:15:07 - 01:05:41:13
Mark Newman
Otherwise all you end up with is conjecture and anecdotes on this side, and you can stack those in creative ways where people think there's evidence. And that's what I'm saying is there isn't evidence. So one like let's let's bring evidence forward that helps us understand that. And let's also be honest with the fact that if there isn't, then let's discard models that aren't consistent with the data, because even what is consistent with the data has a lot of confusion in it.

01:05:41:13 - 01:06:04:01
Mark Newman
With urine testing and serum testing and different pharmacokinetic patterns and metabolism and different routes of administration like this isn't easy stuff. So we've got to take the things that aren't consistent with reality and discard them as we continue to pursue that. But yeah, it's an open invitation to say take things that are meaningful, get them in the peer reviewed literature.

01:06:04:01 - 01:06:15:11
Mark Newman
So this is a conversation that's like a validated conversation and not one that just relies too much on conjecture and theory and and anecdotes.

01:06:15:12 - 01:06:33:18
Dr. Jaclyn Smeaton
Well, thank you both so much for joining me for this thoughtful conversation today. I mean, I think that we need to be having these tough conversations more in our industry, and it's not. And going into it with an open mind, I mean, there's no like winner and loser here other than our patients. So let's make sure that we're talking about the decisions we make being in the best interest of our patients.

01:06:33:18 - 01:06:54:14
Dr. Jaclyn Smeaton
And I would just encourage on the place we started with the dogma is that as clinicians, we're called to be scientists and to make sure we're consistently applying the science and and sometimes it can be really hard to think that you maybe made the wrong decisions for patients in the past. And it's hard to challenge what we're doing today because we're accustomed to it.

01:06:54:18 - 01:07:16:15
Dr. Jaclyn Smeaton
It's part of our clinical workflows, etc. but it's really important for us to be open minded in adapting our clinical practices into best practices, which will continue to evolve because we're still from an integrative and functional perspective, a relatively new field of practice. So, thank you guys all so much for listening. And Mark and Doctor Holthouse I really appreciate you both being with me today.

01:07:16:17 - 01:07:18:18
Dr. Mark Holthouse
Honored. Thank you.

01:07:18:20 - 01:07:36:01
Dr. Jaclyn Smeaton
If you enjoyed this conversation and you want to hear more like it, I just want to remind you that we release a new podcast episode every Tuesday. You can follow us and subscribe at any of the places that you are streaming the podcast right now. And also just to remind you, we do have really great dialog like this on all of the social media channels.

01:07:36:01 - 01:07:41:04
Dr. Jaclyn Smeaton
So I encourage you to follow us at DUTCH Test. I hope to see you with me next week.

01:07:41:06 - 01:07:53:23
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