

[MUSIC PLAYING]

**KATHLEEN
HWANG:**

So thanks today for coming to listen to a quick chat about some concepts about managing male reproductive and sexual health. I spend most of my time at Magee, but I also spent some time at Presby as well, where I focus on both the male reproductive and sexual health here at UPMC. Just a quick disclosure; I have a grant from NICHD.

So our first half of our talk is really going to focus on the male reproductive half. We'll kind of go through the different thoughts that go through my mind when I see these consultations and work with our male reproductive patients and couples to help them figure out how they can conceive.

As a brief background, so I always remind our couples, right, as a fertility fact, I always remind my colleagues and my trainees, this is not an inconvenience. This is not a woman's problem. This is something where we have to keep in mind that in approximately 40% of infertile couples, there's either a sole male factor and/or a contributing cause of infertility where there's both a male and a female factor.

Just like any other patient that walks in the door, We do a very thorough evaluation with a history and a physical exam. There's laboratory evaluation, there's imaging.

But there are some detailed history questions that probably don't normally factor into your average evaluation if you're not focusing on their fertility status. Sexual history is really important. Pregnancy history, current therapy, childhood diseases, medical and surgical history, as well as gonadotoxic exposure. These are six things that we always focus on, I'm always harping on with trainees as well. But these are kind of the things that we have sort of come to the head where we're realizing there's a lot more within these three that we have to ask about.

This is an algorithm that was recently published by our joint guidelines from our AUA, as well as the ASRM. You can read through it yourself. But the real take home messages are that the male and the female partner do need to be evaluated in parallel. And the end goal is we want both of them to end up at the finish line together, so we have outcomes directives treatments all tacked away and done ready for that.

In order to start a male factor evaluation, it starts with the cornerstone of a semen analysis. Semen analysis is a snapshot, and we're going to go through a little bit more detail later in the presentation, but it's just a snapshot into the sperm factory to get an idea for what types of sperm numbers and quality are being generated. We often recommend at least two.

A semen analysis is a really subjective test. It can be very stressful for the individual, kind of an awkward collection, so we always want two to make sure that they're consistent. The recommendation is that they have at least two to three days of abstinence leading up to the collection.

And what's sort of really become more evident is we need to ask about supplements. We need to talk about supplements. And unless you specifically ask patients about it, they really don't think that it's part of their fertility course and their fertility journey, and won't think it's relevant, and it really is.

We're finding that of all of the infertile couples who are coming in, about 15% to 20% of them, we have men who are on exogenous androgens and don't even know that is contributing to their concerns about their sperm production. So always ask.

Now pregnancy history is really important too, and this is how we define primary versus secondary infertility, what potentially could be contributing to these challenges of conceiving. Repeated miscarriages is also a really important thing. This really sets this couple aside, and different evaluation, different treatments become more relevant to these couples.

Now I flash all these up on the screen because I keep wanting to harp on the fact that all administered testosterone needs to be considered as a form of a male contraceptive. Whether it's a transdermal, whether it's a pellet implant, or an old-fashioned IM injection, every single one of them is going to interfere with that hypothalamic gonadal axis, and downstream have a very negative impact on spermatogenesis.

Childhood diseases is incredibly important too to ask; what sort of unilateral problems potentially could have a bilateral effect on sperm production. We ask about histories of torsion; histories of trauma; histories of potential tumor, even; Undescended history, varicocele history, and recognizing that many of these may be childhood exposures, and they have to dig deep and ask family members and parents about this.

Preserving fertility is also something we're always going to be very, very vocal about. It's really important that all patients be offered sperm banking prior to any gonadotoxic therapy. Now obvious ones are chemotherapy, radiation therapy. Less obvious ones or things like exogenous testosterone. But these are all toxic to the sperm factory and testicular function that is endogenous, so this discussion needs to be had.

We have an amazing fertility preservation program here at UPMC, and so there are many coordinators waiting just to be asked to talk to patients for you. The important part when we talk about folks who have been exposed to chemotherapy and/or radiation, the patients and the couple should not be trying to conceive for at least one year after any type of toxic therapy has been completed. There's many, many level 1 evidence studies showing that genetic changes, molecular changes, particularly aneuploidies, are still going to be present even up to 18 months after they've been completed.

No looking at the physical exam, this is a very targeted physical exam. We are focusing on things that we know can impact testicular health, testicular function, and so hormonal imbalances, we're going to be looking for gynecomastia. The genital exam is really kind of like that cornerstone. We're looking at the meatus, the testis size, consistency, location, presence and absence of the varicocele, looking for scars, looking for whether or not the vas is present or not, the epididymis status.

And we still often will even sort of use the digital rectal exam; not for necessarily prostate health or screening for cancer, but rather to try to delineate if there are midline prostatic cuticles, cysts, that may contribute to an obstructive process; something that's going to cause a plumbing issue.

So when we talk about a varicocele, the ultrasound tends to have been something that everybody, once they get to me, has already had an ultrasound. By ultrasound criteria, it's incredibly sensitive, but the definition is it has to have at least 3 millimeters of diameter and a reversal of flow with valsalva. So if you see this initially, asking the patient to valsalva generates this kind of picture.

Now this here, I always kind of lovingly sort of refer to it as the Holy Trinity for us, right? So the hypothalamus, the pituitary, and the gonad. This is really the axis that generates all of testicular function. We have FSH, which we have LH that stimulates, respectively, the Sertoli cells and sort of manning spermatogenesis, as well as LH, which stimulates the Leydig cells to produce testosterone.

There's negative feedback that gets built in, and it's this tight circuit of communication that really determines testicular function. Often I'll describe this to patients as saying, your testicle only has two jobs. It's make testosterone and make sperm, but it generally won't do anything unless given direction by the brain. So this communication and anything that interferes with it downstream interferes with testicular function.

So we talk about hormonal production, and endocrine evaluation is very algorithmic for reproductive health. We always start with an FSH, we talk about getting an LH and testosterone, and this reflects your testicular production. Prolactin is another hormone that we're going to use when we have high concern that the testosterone panels are incredibly low and we suspect that there's a central issue going on.

Now however, the initial endocrine evaluation really does not get triggered. It's not done in everybody unless their sperm concentration, meaning their sperm factory, is not able to generate more than 10 million sperm per milliliter of ejaculate, and/or if they have clear symptoms suggestive of a hormonal imbalance, clear sexual dysfunction. Other suggestive findings are someone walking in and saying, listen, I don't really have peripheral vision. Something has changed. Then we have to worry quite a bit.

Now focusing on the testis, this is a nice cross-section of the seminiferous tubule. You start at the periphery, you move towards the end, and you're looking at how sperm is produced.

So semen analysis; this is really the only test that we have to really get a snapshot into it, get an idea of what's happening. But what's really adequate for pregnancy? Our World Health Organization has published many journals and directives on how to delineate, what's in theory, normal. The fifth edition, which came back out in around 2010, is what is the most updated version, sort of generating these reference ranges that we are all using now. The sixth edition actually just came out this year in July. It doesn't change any of the reference ranges, so we're going to continue talking about these fifth edition ranges.

These ranges were the first ever to really be generated based on actual evidence versus expert opinion. These are about 1,900 semen samples from recent fathers, so fertile men, time to pregnancy all within the past year across multiple countries in different continents. And so this was very strict in how they looked at it.

They determined that looking across the different centiles of these numbers from those particular men we just described, they determined the fifth centile. This is the lower limit of what's considered, you should be able to generate this if you're going to be able to father a child.

Now having said that, a semen analysis is genuinely just a snapshot. It does not equal fertility; It does not equal infertility. And I have to remind patients of that because they get very panicked when any range, any parameter, falls out of that reference range.

Now as a quick review in terminology: when we say oligospermia, the sperm count needs to fall below 15 million per mL. Severe oligospermia of the sperm is when it falls below five. And the distinction is made because below 5 million is what triggers a genetic evaluation below 5 million, up to 15% of the patients presenting to us in this room will have a genetic abnormality.

And this can include something within a numerical thing, such as Klinefelters, which we're going to identify on a karyotype or a chromosome analysis, and/or something like an AZF deletion, a Y chromosome deletion. There's a certain segment there that we're going to be looking at.

Azoospermia, zero sperm in the ejaculate. And this is on that initial wet mount. But standard protocol suggests that if there's no sperm seen initially, what will happen is the specimen is then centrifuged down to a pellet. And the pellet is then analyzed.

If sperm is found in the pellet, and oftentimes you'll see on these analyses that, say, after pelleting on a frosted slide, they saw nine sperm. And that's genuinely. It's like single digit numbers.

But this falls into a different category and this is called cryptospermia. Asthenospermia, abnormal sperm motility. Teratospermia, they're funny looking, right? So different shapes.

When we talk about assisted reproductive techniques, This is a brief overview very, very simplistic. But timed intercourse with or without female stimulation. So timed intercourse generally has to be timed, right? We need to know when their ovulation is happening, when that ovulatory window is.

And the female stimulation comes into ovarian stimulation, where they're on medical stimulation to induce more than one egg being released from the ovary.

Intrauterine insemination, IUI is commonly known as the turkey baster method, right? Really easy to understand for patients, really a natural step above timed intercourse. And the way that I describe it is all we're doing is we're putting the sperm and the egg in the same room.

IVF is getting a little bit more fancy. It's in vitro fertilization. If you look at the diagram on the right, it'll show you the difference between plain IVF as well as IVF with ICSI, which is intracytoplasmic sperm injection. This is the most advanced technique that we have to help couples conceive. And the difference being you're taking a single sperm and injecting it into a single oocyte with ICSI.

With IVF, plain IVF, the semen sample and sperm itself is placed in a dish with the oocyte and allowed to penetrate and fertilize on its own. But both of these are happening in vitro outside of the body in a lab setting.

Now other aspects of a semen analysis that you may see, and we wonder what's going on, is we'll have a whole parameter called round cells. And this is the initial indicator to say, maybe we need to delve further into seeing if are these leukocytes. Round cells can be really two things. They're either baby sperm that have leaked out from the seminaries tubule and this is very common, and/or other leukocytes, which is an indicator that there might be an inflammatory and/or infectious process ongoing.

These are specific antibodies that we use, and the key with this slide is to recognize that your basic, standard semen analysis will not tell you if there leukocytes. All they will tell you is that they're round cells. In order to determine the difference between a baby germ cell and a leukocyte, you have to specialty order a next-level test to do the staining.

Now there are specific tests of sperm function. There are tests of sperm function that go as far as their computer assisted analyses, there's hypo-osmotic swelling test, there's acrosomal staining. There's even sperm penetration assays. Really, most of these are at this point relatively historical. But the end goal is to determine if fertilization will happen if the sperm actually gets into the oocyte.

Now Kruger morphology is what we use to describe the shape of the sperm. And you can see how ridiculous they get, where they're measuring the shape of the head, the neck piece, as well as the tail.

Now when you see morphology reported on a semen analysis, very often it's going to be red flagged, because there aren't that many folks who have very normal sperm shapes that are not flagged. And this is the reason why. This is such strict criteria that the reality is it needs this smooth, oval head, acrosome has to be 40% to 70% of the head volume, there can't be any abnormalities. And so these are really strict.

And what that turns out to is that most folks will have a lot of abnormal sperm. But that does not equal not having the ability to conceive, but rather we worry that maybe if the sperm head is misshapened enough, that the ability to penetrate the egg is absent.

The other thing we always review is that in order to do these calculations, the algorithm actually only requires the techs to count 400 sperm, which is infinitely much lower than what your average semen analysis is going to hold. So on average, I just sort of mentioned, a normal count is above 15 million sperm per milliliter of ejaculate. A tech would be there for years doing that if they tried to measure it. So 400 sperm, which is a very small representation of the rest of the specimen.

Now when we talk about other forms of avenue of testing, we can actually test the sperm DNA integrity directly. Now why do we test this? Well, the sperm of infertile men have certainly been shown to have higher levels of DNA damage. DNA damage, unfortunately, is also associated with impaired post fertilization embryo cleavage. And all that means is once it's fertilized the embryo will not develop well, and oftentimes will halt development, usually around day three.

This oftentimes is seen as an unexplained infertility, repeated early miscarriage, and again, this falls into that couple where they're having recurrent IVF failures, recurrent pregnancy losses. And so this is when DNA integrity does become relevant.

Now how do we utilize imaging? We don't actually utilize a ton of imaging. Really, ultrasound is the one that is probably utilized the most, and this looks at the testicular architecture, looking at the presence of epidermal abnormalities, presence or absence of internal testicular concerns, the ones that are not palpable.

We will also use them for renal ultrasound in cases of congenital bilateral and/or unilateral absence of vas. So these are folks born without vas deferens, and what they've known is that congenital absence also portends a risk of having a unilateral absence of a kidney. So these are folks who will have solitary kidney units.

The ejaculatory ducts is important because this is where we're going to find a lot of the obstructive processes. So if you have someone who's azoospermic, with no sperm in their ejaculate, it's either going to be a plumbing issue or a production issue. And looking at these ejaculatory ducts, the seminal vesicles, is going to help you distinguish between those two.

This is a textbook, literally a textbook, picture of what a vasogram is. So there really, unfortunately, is no imaging modality that's going to be able to tell you if the vas deferens itself, the ampulla of the vas, the seminal vesicles themselves are pinged. They won't be able to tell you dynamically if they're obstructed.

So in order to do that, we proceed with something called a vasography. And this is an intraoperative test because we actually have to deliver the vas deferens, open it up, and inject contrast directly.

And you can see here in the picture, that's contrast getting into the bladder after the vas has been instilled with contrast dye. And you can follow all these different sites where it's going to the ampulla, the vas, the seminal vesicle, the ejaculatory ducts. And this is not done that often, but we'll do this in the OR.

Now a transrectal ultrasound is very helpful as well if we have high suspicions for an obstructive process. So when we perform these, are often in times when we have normal-sized testicles, normal FSH level, suggesting that sperm production is happening.

Now in order to do this, oftentimes there's going to be a dilated seminal vesicle that we're going to find, and/or a midline prostatic utricle. And here are just minimal measurements that we're looking for.

This is also something that I would do independently in the clinic, and if there are dilations that we find in the seminal vesicle and/or a utricle cyst, I will aspirate it to confirm presence of sperm.

Now here is a very humbling kind of table, right? And this is old, but the reality is it hasn't changed in the past two to three decades. You can see when we distinguish between the different etiologies of why male fertility is presenting to clinic, look at how many go undiagnosed, right?

So almost over 20% of the males presenting for evaluation are idiopathic. We don't know. We've done everything we think we know, and we still can't give them a reason why we're seeing these struggles to conceive.

However, what we're trying to do is to reduce. That, we want to reduce that percentage and that's going to happen with a better understanding of the genetics. There is a huge gap of knowledge in the genetics of male fertility. We very much need to put more focus on an identification of reproductive health hazards, right?

Getting better at preconception counseling; educating the masses of what sort of exposures put you at risk for harming or reducing your fertility capacity; development of new tests to identify abnormal sperm function; and realistically, develop more sensitive biomarkers, right? So semen analysis is actually a pretty poor biomarker for sperm health, but it's the best thing that we have so far.

Now here are a few take-home messages for patients. And this is really straightforward advice that we give all the time. Use sperm friendly lubricant. There really aren't that many. Preseed is one that's sitting right next to all the other lubricants in your average pharmacy, and is the same price, but this was one that was developed for couples trying to conceive.

Always recommend for the male partners to take a daily multivitamin. They've actually done clinical trials looking at primary outcomes of looking at sperm health. And this is an easy thing to do. Generic daily multivitamin, they shouldn't be doing it.

Immediate smoking cessation. Of all of the toxic exposures, environmental, lifestyle, smoking is the one that we have the most level 1 evidence on suggesting the more you smoke, the worse your sperm gets. The less you smoke, the faster you quit, it improves.

And the last thing is just talking to your couples about timed intercourse and what that means versus unprotected intercourse. Understanding the timing of ovulation, and recommending the use of ovulation detection kits. There are many out there on the market. Some are incredibly expensive; some are actually fairly affordable.

There are different methods. The urine dip test is one I recommend the most. There are basal body temps, there is apps that they can use. Anticipating ovulation is a good recommendation, and our recommendation for our couples from the male half is every other day, timed intercourse during this ovulatory window.

Not multiple times a day; not once a week. Every other day tends to generate consistent numbers of sperm that are emitted and ejaculated with each timed intercourse throughout that ambulatory window. Basically it doesn't deplete your storage of sperm within the epididymis too quickly. We want to evenly distribute the exposure of sperm throughout that ovulation window.

And then the last point is to always reassure that it's actually fairly normal for couples to take up to 12 months of timed intercourse, timed intercourse, to conceive. And certainly I've had many couples present who have just been having unprotected intercourse for years, and as soon as we redirect them to actually timing it, they're conceiving without much difficulty.

All right so that wraps the half of reproductive health, and now we're going to switch gears to go into sexual health. So with erectile dysfunction, this is our top chief complaint that we have coming into the Men's Health Center.

ED traditionally is defined as the inability to attain and/or maintain a penile erection sufficient for satisfactory sexual performance. The prevalence is huge. It's not surprising.

This is the Massachusetts Male Aging Study. It's really old, but this also hasn't really changed. And the whole point is to reassure your patients that, really, men between the ages of 40 to 70 years old, over 50% of them have some form of ED. And whether it's mild, moderate, or severe, it's present across all of these years.

And this sometimes is enough to reassure your patient that they're not alone, because this is a lot on their anxiety and stress. So I often reference this, and say, listen, actually over half of the men in your age group will have some form of ED. Nothing to be embarrassed about.

Now, most men with ED actually don't receive treatment. Only about a quarter, a quarter of men polled, actually have received treatment. 3/4 of men were untreated, which is a lot. And in a population-based study of men over 40, again, 3/4 of men not really even treated or offered to have a PDE5 inhibitor.

Now potential reasons, they're not asking. They're not asking for help. Turns out that men are really bad at asking for help. So offering and asking gives them an opportunity to just say, yes I actually am struggling with this.

Now what are the etiologies of ED? These are very clear, different categories. The psychogenic is going to be part of every single individual asking about ED. As soon as your body doesn't do something that you expect it to do in the sexual function realm, your own stress and anxiety about it becomes very powerful. So I always counsel patients that it's always going to be multi-factorial, right?

Now someone who's clearly just had a robotic prostatectomy for prostate cancer, we know why their erections are struggling. But these are clear categories that we have to think through about why someone struggling with erections.

Now with diagnosis, it's pretty algorithmic as well. If someone is able to self-report it, we talk about their medical and psychosexual history, partner status. You talk through what their concerns are. And most of the time patients actually have a pretty poor grip on exactly what ED is, versus ejaculatory dysfunction, versus Peyronie's disease. So sometimes it takes some help to tease out what their concerns are.

A very focused physical exam looking at penile deformities, their prostatic state, signs of hypogonadism, symptoms, their cardiovascular and neuro status is important as well. And there are some laboratory tests, right? Glucose, lipid. We're always working with their primary care physicians. We're always working with-- actually, if they have a cardiac health the cardiologists as well.

This is an algorithm put out by the AUA and you can read it yourself. But the most important thing to me for this is shared decision making. This is really different, and you'll find that like men presenting for sexual function have very different expectations.

Even if you have the same person with the same complaint, they will want different things. And so it's really important to specifically talk to the individuals about what their goals are, what is your priority and what are you hoping to achieve with this consultation.

Now, ultrasounds. We can do what's called a color doppler ultrasound of the penis. This is very helpful as a dynamic test. The downside is this requires a penile injection with the vasodilator to induce an erection, and we're monitoring blood flow in the cavernosal artery. We're documenting arterial flow. We're checking peak systolic velocities and diastolic velocities.

And this is very helpful in someone who has a pure suspected psychogenic problem. This very quickly will prove to them that their vasculature, which is really the driving force with good erections, is intact and doing just fine.

These ultrasounds are also very helpful when we're surgical planning for Peyronie's disease; scar tissue; looking at the depth and calcification status of scars within the penis. So this is something that we will use selectively for specific patients.

There is a clear correlation between ED and cardiovascular disease. The prevalence of silent coronary artery disease in patients with ED is like a huge range, tons of different studies being put out by this.

Mulhall, who was a really, really well-established sexual medicine expert, demonstrated that 20% of patients with vasculogenic ED, they have an abnormal cardiac stress test. And this has been drilled into us as sexual health experts, they should be stratified for cardiovascular disease, right?

So if you have a young gentleman coming in and it's not purely psychogenic, you have to start talking to them about what their family histories are, what their cardiovascular status is. And I work very closely with a lot of cardiologists, who I will refer to often, to do a cardiometabolic evaluation for me.

Now, erectile dysfunction treatment is very tiered. It is very algorithmic, and I describe it to patients pretty much like a ladder. In the first rung on the ladder are these phosphodiesterase type 5 inhibitors. These are the Viagra type meds, and that's the first rung. The higher you get up on the ladder, the more aggressive the treatment is, but the more effective it becomes as well.

But what's overwhelmingly important before any of these treatments is the discussion about how do we correct why we think you're here. I am almost always going to sit down and talk to them and say, listen, there's two different opportunities here. One, we can treat you to figure out how to get your erections functioning now. But the more important part is, how can we get you into a healthier state to prevent any of this from worsening?

And so they don't love it when I tell them they have to lose weight. They don't love it when I tell them they have to stop smoking. But it is definitely a conversation that happens with every single patient presenting for ED.

Now when we look at the current ED treatment approaches, oral therapies are really first line, and about 75% of people treated for ED will be on these alone. And these are often prescribed by just about anybody.

And they're out there. They've become more accessible. Viagra is now generic. And there are compounded versions of others as well. When you get into the urethral suppositories, injectable, vacuum pumps, implants, and corrective vascular surgery, that's more often generated and directed by urologists.

Now many of us are often going to be prescribing these type medications. It's worth reviewing though what's on the market and when they've been out. There are four that are on the market. Viagra is the oldest; Sildenafil. It's from 1998. It's been out for a long time, and hence, it's now generic. Levitra came out afterwards, Cialis very quickly after that, and Avanafil is the most recent one, which came out in 2014.

Now if we look at the three older ones, looking at Sildenafil, Tadalafil, and Vardenafil, they're very similar as far as onset of action. Sildenafil and Vardenafil are the closest. They're roughly the same. Tadalafil is a popular PDE5 inhibitor just because it has a longer half life. It lasts longer and it is the only one that you don't have to worry about whether you have eaten or not.

Sildenafil and Vardenafil are always going to be counseled to patients that they should be taking it on an empty stomach. Any level of fatty food in the stomach will reduce its efficacy. Avanafil is the newest kid on the block. The claim to fame with a vanity bill is that it has the fastest onset of action. And so what we find is that we are seeing feedback from patients that they can take it within 15 to 20 minutes and they'll start to see development of an erection.

This, however, also has an impact of you have to take it on an empty stomach if you want this to be as optimized for you. And again, about 15 to 30 minutes prior to intercourse. This is the newest, this is the most expensive. There are no compounded versions of this one.

Now intra-cavernosal injection therapy sounds terrifying to most patients when you introduce this concept to them. My goal is when we talk about ED is I introduce these concepts early. Just because it's helpful for them to hear about it before hearing my recommendation that this is what's really going to work, and so it's more familiar.

But you can look at the cross section. You can see the corpora cavernosa, you can see the urethra, and the inferior aspect of the cross section. The end goal is you need to inject the needle and the medication directly into the corpora, one side. There are bridges between the two, allowing a unilateral injection, but allows bilateral effect.

The medications we use are all vasodilators. They started model therapies on Alprostadil. Branded comes with Caverject and EDEX. But then when we get compounded medications, is when we start getting fancier.

The advantages of penile self-injection is that it works really well. It's obviously easy for diabetics because they're really familiar with these U-100 needles. The disadvantages is nobody wants to think about injecting their penis.

This does have a realistic side effect profile of having a priapism. And if your technique of injection, you're not clean about doing it, you're repetitively injecting the same side, you can develop scarring and fibrosis. And this is also fairly expensive to some degree, if you compare it to the generic version of Sildenafil.

If you look at the left half, we just talked about a monotherapy without Alprostadil. Then we start blending medications. There's BiMix, there's TriMix, And there's even QuadMix. And even amongst those three categories, there's super versions of each, where we up the dosages of one or two of the medications within the blend.

MUSE is a different version of a localized therapy, right? So penile self-injections is localized. You're injecting directly into the penis. You don't have to wait for absorption. It's going directly into the corpora itself.

Muse as a branded name. This is all prostital urethral suppository. It comes with this little kit that you see there. It's a little applicator. But you're basically sliding the tip of the applicator into the meatus, into the urethra. You plunge the button down and it drops off a little suppository. Kind of looks like a tic tac, but it instantaneously starts to dissolve as soon as it touches the mucosa within the urethra.

Now MUSE itself, this is the kind of technique. Once you drop off the suppository, you do a little massage and it'll start to get absorbed. It definitely is effective. It promotes nitric oxide synthesis. It generates an erection pretty well. The advantages are you don't have to inject anything. There's nothing sharp. It works fairly often.

But the disadvantages are very real, and I would say about 50% to 60% of all patients using this have some significant discomfort the urethra is really not forgiving. It doesn't like having anything stuck in there.

And so putting even a small suppository in there, it's just not it's not comfortable and patients will give you that feedback. It's also not cheap. This very rarely is covered by insurance, so this is not something we've been able to get for patients as often.

The vacuum erection device, this is ideal for a patient who has contraindications; a bad cardiac status, contraindications of any sort of like vasodilator medication, it's purely mechanical. It is a cylinder that you slide over the penile shaft. A vacuum is created, either manually or electrically, and then that vacuum pressure pulls blood into the penis, stretching and generating rigidity.

You will need to use this in combination with a penile constriction ring because the cylinder gets the blood there, the ring will keep the blood there, and it generates a rigidity that patients can use for penetration and function.

The advantages are sometimes it's covered by insurance, that's becoming less and less, but it works in just about everybody. But the disadvantages are it's a little bit clumsy. The dexterity is important.

The constriction can be very tight and uncomfortable. But once someone, as a patient, figures it out and appreciates the mechanics of this, is the only thing they'll ever need to continue to be functional.

Now the goal is, our target population for any of those that we've just described, is people who failed oral therapies. In penile self-injections, it works. It's really effective. Now, the key is there, as I mentioned, there's many tiers of different types of medication you inject, and so the patients need to be made aware that there is a trial. There's a trial period to figure out what works for them.

MUSE which is that Alprostadil urethral suppository; effective, but can cause discomfort. The VED can be great if you're willing to do it. The adverse effects are real as well. And these are all part of the counseling that we tell patients.

Now important safety information. Do not administer these phosphodiesterase type 5 using any form of nitrates. This is kind of well established. We can potentially get hypertensive effects.

You also want to be cautious about co-administering with alpha blockers. A lot of our patients are going to be on alpha blockers for lower urinary tract symptoms, and most of them are going to be taking them at night before they go to bed. And so if you are talking to your patient and cautioning about this, there is that risk that they will feel even more hypertensive and get lightheaded.

And so what we've counseled our patients is to not take them at those same time frames, right? Either shift your alpha blocker to a different time, which you can do, and/or change the time of intimacy. And what we've sort of cautioned patients is the reality is the best time for intimacy in anyone who's struggling with good consistent erections is morning, first thing when you wake up.

You're the most well-rested, your hormones are naturally the highest, you have an empty stomach already, so anything you would need to take that would require that is already established. And so you would get the best efficacy during that time frame. And so folks kind of look at me like I'm crazy when I tell them to shift their intimacy time frame, but folks, once they experience the better outcomes recognize that, OK, maybe it's worth it to do this.

These are folks who we don't recommend. Anyone who's had a serious cardiovascular event, I'm almost always going to be in communication with their cardiologist to review this. Resting hypertension, uncontrolled hypertension, angina, and those with any sort of hereditary retinal disorders. This is the most concerning when we have folks with Viagra.

I talked to many of our patients' cardiologists. They're probably sick of me asking questions, but I always want and prefer to have a discussion and clearance so that they're aware that we're sort of embarking on different treatments so that everyone who's involved in these patients' care know what we're planning on doing.

OK. So as a summary for erectile dysfunction overall ED is definitely a progressive disease. It's increasing in prevalence with age. And it's shocking to me how we have patients who come in who have had the worst cardiovascular history, very complicated medical history, and will genuinely look at me and say, I don't know why I have ED. I have no idea why my erection isn't working. And very, very few patients have that insight to say I need to be better about stuff.

However, they should certainly all have a cardiovascular assessment, as it's often simultaneously present. Patients have been very thoughtful and say, listen, my cardiologist tells me that since I've had very, very bad coronary artery disease that I'm high risk for ED and all those type of things, and vice versa. And so that's always nice to hear, when they're well aware of that.

The PDE5 inhibitors are certainly considered effective first line therapies for ED. What I can tell you is Sildenafil now is generic. It is relatively cheap. We actually have been encouraging our patients to use Good RX coupons, because that allows them to actually achieve consistent usage of these medications for actually a very affordable sort of price out of pocket.

They know it's out of pocket, but we can get these 20 milligram tablets for less than \$0.30 a pill. We're able to get 100 milligram tablets for about \$1 a pill. And so it opens certain doors.

Tadalafil and Levitra have compounded versions that you can work with your patients to get compounded versions that are also much more affordable. They're still branded, and the branded versions are still extremely expensive.

Patients not responding to PDE5 inhibitors can either be referred to a urologist, and/or second line therapies utilized can be the things that we just talked about. The penile self-injections, to give you a rough idea, compounded version of TriMix, for example. TriMix is compounded. It's not going to be covered by insurance, But you can prescribe a kit to specific compounding pharmacies.

The patient will get 500 units of medication with the needles and alcohol swabs, and it costs roughly about \$100 to \$125 per kit. It's not cheap, but it certainly is something that people should be aware of. It's not something that is limiting for everyone.

The vacuum is also available. It's sometimes covered by insurance. If not, there are medical grade ones that are available for roughly about \$200 out of pocket. The intra-urethral suppositories are also there, and these are prescribed through your commercial pharmacies. The branded name is MUSE. But this can also be very effective.

All right. That was it that was male reproductive and sexual health in a short little presentation. Thank you for listening.