Fighting Polycystic Ovary Syndrome (PCOS) - New Developments in Symptoms Management & Treatment

PCOS is a little understood life changing syndrome. What we know about PCOS are the disturbing symptoms it creates in our bodies, but we only know the tip of the iceberg when it comes to reasons behind why these symptoms occur. Moreover, almost 70% of teenage girls/women remain undiagnosed mainly because they dont understand their symptoms and avoid discussing them. We are talking to Dr Carolyn Alexander of Southern California Reproductive Center, about new developments in PCOS symptom management & treatment and PCOS updates from recently held #ASRM2019 Conference. Dr. Alexander has conducted extensive research on PCOS and specializes in the treatment of patients facing the diagnosis of PCOS and infertility. Guiding the discussion from the patient panel will be Ashley Levinson @PCOSgurl who has been advocating for PCOS since the last 20 years. Dr Michelle Shwarz, a PCOS patient and researcher, will also be on the panel to discuss about funding and gaps in research in the field of PCOS.

Full Transcript:

Shweta Mishra: Good evening and welcome to CureTalks. This is Shweta Mishra, your host and today we are going to discuss about new developments in the management of polycystic ovary syndrome, a disorder which affects one in five girls and women with disturbing symptoms like excessive hair growth, acne, male pattern baldness, mood swings and infertility. Our eminent expert for today's talk is Dr. Carolyn Alexander of Southern California Reproductive Centre, who has done extensive research on PCOS and specializes in dealing with patients facing infertility as a result of PCOS. Welcome to the show, Dr. Alexander, it's a pleasure to have you with us today.

On the patient panel, we have Ashley Levinson and Michelle Schwarz. Ashley has been very actively advocating for PCOS for the last 20 years and sits on the patient advisory board for PCOS Challenge, the largest nonprofit support and advocacy organisation globally for people with PCOS. Michelle on the panel, is a PCOS patient as well as PCOS researcher. She's an epidemiologist in the pharmaceutical industry, and currently on the patient advisory board and co-chair of the research committee of for PCOS Challenge. I welcome you both to CureTalks, Ashley and Michelle. I also want to welcome our audience to the talk and want to inform that we will be discussing questions sent in via email at the last 10 minutes of the show. So you can email your questions to shweta@trialx.com or you can post your questions on the website curetalks.com as you listen to the talk. We'll try our best to answer them as time permits.

So Dr. Alexander, welcome to the CureTalks once again and I want to begin this discussion by asking a question which is very basic, but also about which most of the mothers of teenage girls are confused about as their daughters start to menstruate at the age of 11 to 13. And that is, how early should a girl be screened for polycystic ovary syndrome? And at what age? Does early diagnosis mean that severity of the disease, say for example, PCOS leading to excessive hair growth or acne or infertility can be controlled? What do recent studies tell us?

Dr Carolyn Alexander: So, it's really important to recognise early signs of polycystic ovary syndrome including early breast development, especially around age eight or younger that's extremely early. And an early underarm hair can also be a signal, it can be familial, in some families, women get earlier hair growth but it's important to alert the paediatrician as well. And typically we wait for two years from the first period before we label a young girl as irregular periods because it takes anyone whose hypothalamic pituitary ovarian starts, when they when they get their first period, it does take about two years before the traditional flow each month can occur and so we tend to give it a little bit of time hoping it will regulate. But in terms of chin hair or thickened sideburns or upper abdomen, abdominal hair, and lower back hair, if it's black and

dark hair, it can be important to at least get some evaluation and talk it over with the paediatrician as well.

Shweta: Sure, thank you for that answer Dr. So I know all of us with PCOS, as we reach our teenage and then adolescence and adulthood, we have a variety of symptoms and I want to give you a background of this PCOS tracker app, which is now being used by more than 6000 anonymous women and helping them track their daily and monthly PCOS symptoms and seeing their monthly menstrual pain, their intensity of flow, hair growth intensity, acne problems and mood swings. All these symptoms are being tracked. And we did a bit of an analysis on the data that was shared via this PCOS tracker. And one of the things we found was that irregular periods or irregular menstrual cycles was the main symptom that makes women think that they may have PCOS and 60% of women chose irregular periods as their predominant symptom.

So my question to you is on the association of irregular periods and infertility issues, first of all, what causes irregular periods in PCOS? And then have you found in your research or have research studies shown that women who have irregular menstrual cycles as a predominant symptom, tend to have more infertility problems than women who don't have irregular menstrual cycles and still diagnosed with PCOS, because we have women in our circle who have regular cycles with other PCOS symptoms, still having a hard time getting pregnant.

Dr Carolyn Alexander: I think it's a great question. I think all that information from those women is so important and vital. And I think it's fantastic that you guys are collecting that data. It's very interesting that a most common reason that patients come in is that their periods not coming every month. And it's really frustrating because all their friends are in college, their roommate is getting their period every month and they're just waiting for their period and sometimes it takes a few months.

There's kind of two schools of thought of why polycystic ovary syndrome occurs. Some people think that LH pulsatility is too frequent more frequent so there's an LH, chronic LH elevation and so there isn't the traditional cycle where women ovulate one egg and have a peak LH surge at the mid cycle and allow the egg to pop out so that they can make progesterone in the latter part of the cycle, so that they can get an actual period when the corpus luteum dissolves and causes progesterone withdrawal, and then that causes a period to come out.

Dr Carolyn Alexander: Other people think that there's this chronic insulin elevation that leads to the ovaries having theca-cell hyperplasia, which are the cells in the ovary that make testosterone so T for theca makes testosterone and that makes a micro environment around the ovary that causes the follicles to be in a halted state. And so instead of allowing the follicle to develop in a proper manner, they may or may not ovulate, and perhaps it even can be an immature egg like a smaller follicle with the egg that perhaps can't get fertilized, which kind of rolls into why irregular periods may also impact why women try for many months and are trying to time their ovulation, but can't quite figure out when their LH surge is going to happen.

And so, the premise of it is that irregular periods can mean irregular ovulation. And so the ovulation may not be at a traditional time point so that in unprotected intercourse can cause fertilisation at the timing that traditionally we see.

Shweta: Alright, so we do have studies showing that more irregular cycles means more infertility issues, compared to the one to the women who have regular cycles, right? Alright. Thanks. That's helpful. With that, I guess I'll bring on the panel in this discussion. We have Ashley Levinson with us. Ashley, you're on air. Can you briefly introduce yourself and then go on to ask your questions, please.

Ashley Levinson: Absolutely. Thank you so much for having me this evening. My name is Ashley Levinson. Most people know me on social media as PCOS Girl. I have been a PCOS patient advocate for over 20 years. And in those 20 years, there have been a lot of advances a lot of changes in how we perceive what PCOS is what causes PCOS. But many people who have the condition when they go to see their doctor don't understand exactly what it is. Because you see people that have lean PCOS, you see obese women that have PCOS, and there even is an expanded definition to now include female to male transgender. So

my question is, how do you define PCOS to your patients? What are some of the signs you look for in making a diagnosis with all this diversity?

Dr Carolyn Alexander: So I take a detailed history, especially including family history, there seems to be an interesting finding that it's not only from like our mom's side that genes can pop up that cause polycystic ovary syndrome, there seems to be also a family history of the father's side having diabetes, or early balding, and then there can be also, if he has dyslipidemia, or cholesterol problems, there can be some of those genes that manifest in her. And I think it's important to really tease out when the symptoms started in terms of the hair growth and making sure to evaluate the ovaries for any uncommon things that look like polycystic ovary syndrome, but could be different like high prolactin or thyroid issues or something called non-classical adrenal hyperplasia and as well as Cushing syndrome, which can cause obesity, as well as like a high blood pressure, and some of those young girls are misdiagnosed as polycystic ovary syndrome, but they actually may have something else that can be a little bit different to deal with as well.

And so I think a detailed history looking at the family history, I tend to tell patients it's not anything you specifically did, because I noticed, especially when patients come in with their parents or a sibling or someone they'll say like, yeah, they're eating different or they're doing something different than everybody else in the family and it's not necessarily anything the person's really doing that causes per se over a summer to gain weight or their periods to become irregular.

It's very poly genetic. So it's multiple different genes that click on in place. There's some evidence about in during foetal programming, when she was in her mom's tummy, that maybe there's epigenetic changes that happened during that time that may manifest when puberty starts. And it's again, nothing this person specifically did. So I tend to say it's a poly genetic issue, but that there's a couple ways we tackle it so that as best as we can, we can control the symptoms and protect from long term consequences that can happen.

Ashley: Well, then my next question is, once we know that we have PCOS, what types of options are available to treat PCOS? I know that ASRM had recently a conference and there were some updates on new developments about management of the condition. Can you talk a little bit about what options are available or what new management techniques might be available?

Dr Carolyn Alexander: Sure, I think traditionally most people talk about a birth control pill. But others I see a lot of women, especially in Los Angeles here that want to be natural and try non-birth control many options and we can use cyclical progesterone and it can be a non-synthetic progesterone that we can use that they take for 12 days of the month. And that does bring on their period and keep the periods regular, but it is not contraception. So if it's a young woman who's not ready to start a family that won't protect her from ovulating and getting pregnant. So we kind of discuss, specifically what their hopes are, do they need contraception? Are they really focused on that on the male pattern hair growth, it's really frustrating to see that. For them do we need to block the testosterone so that they can stop having as much mood swings, because sometimes when the testosterone seems to be quite high, I've noticed is that they have some mood swings and we use non-traditional things in our armamentarium including acupuncture, meditation, yoga, to help those things.

Dr Carolyn Alexander: But it's important to also look at the hormones and try to balance that. I think at the ASRM there was really an interesting discussion in terms of in the future but not quite now have an LH blocker that is a medication, it's an oral medication that was initially used for hot flashes, but that they were mentioning that maybe it'll actually block this chronic LH elevation in some young women and help regulate the menstrual cycle. And so they don't have a name for it, but it was a neurokinin B-receptor antagonist. And it was an interesting discussion. It's this still the party line is 5% body weight loss if the women have a BMI over 30 – that is probably the best thing we can do to help our patients with PCOS in terms of strategy.

Ashley: Wonderful. With PCOS often, a lot of patients are focused on infertility or weight loss in immediate results. And often once those results are met, or they're into a pattern, they don't consider that there may be some future risks with that. So my question is, what are some of the risk factors associated with PCOS?

Dr Carolyn Alexander: Traditionally, I think of it as a young woman, it's the two Ps – periods and pregnancy. So if the periods are not regular, there's a concern that the build-up of the endometrial uterine lining can thicken and can actually have unopposed oestrogen, which is like a Ying Yang and if there's too much oestrogen there can get pre-cancer cells, which doesn't happen quickly, but in some younger patients over the last 15 years, I have seen that younger women can get a pre-cancer, especially if their periods are irregular. And so it's really important with one of the Ps is to try to keep your periods regular least have a discussion with your doctor on how to tackle that.

Dr Carolyn Alexander: And then the other P is pregnancy. And so if they are having irregular periods we can discuss ovulation and timing; we can be as natural as possible with just ultrasounds to see when the body is making the big follicle and helping them, guiding them to timing intercourse. Or it can be medication such as Letrozole or Clomid, which have been around for some time, and they work as an anti-oestrogen to tell the brain Oh my gosh, there's no oestrogen. So then the pituitary gland sends FSH – Follicle Stimulating Hormone to the ovary, to excite the ovary and make a follicle or an egg which is in the follicle pop up and become ready for fertilisation with the sperm. And so there's kind of a few ways.

Dr Carolyn Alexander: But the long term consequences which we don't use fear factor to scare anyone we just talk about it is, we check cholesterol fasting every other year. We check for diabetes every year. We check for in terms of if they snore, then I send them to discuss sleep apnea. Some younger women snore and it can be a risk for pulmonary hypertension, and sleep apnea which can be risky when we get older and as well as mood issues if they need to talk out, if they're having some mood disorders and we can talk that out and see, we use a multidisciplinary approach. And then the last one is something called non-alcoholic non alcoholic steatorrhea so it can be early fatty liver of the liver and that is important to talk to their primary care doctor about.

Ashley: Great! So with all these different issues that can occur, how often should someone with PCOS see their provider?

Dr Carolyn Alexander: Every year for liver, kidney, anaemia check as well as a check for diabetes. And then usually every other year we look at the lipids to keep an eye on the cholesterol and things like that. But I think it's important and if their periods are irregular, they need to see their doctor sooner.

Ashley: Right. And why do you think so many with PCOS are still undiagnosed, are misdiagnosed?

Dr Carolyn Alexander: I think that's a great question because I was thinking about that. And I see a lot of women coming in saying I'm like, so frustrated, no one's listening to me. I feel like I've just been on my own battling my issues and stuff like that. I think it's kind of complex in a sense is that a lot of the time is someone's BMI is high, we tend to just hope or some physicians, they will try to lose some weight and let's reevaluate, right and then over time, how many times can you get told that without getting a full hormone panel, especially if there can be a correlation with PCOS with high prolactin which can also lead to irregular periods and maybe if that's remedied that might make their periods better? And there can be other kind of hormone imbalances. I think it's also the fact that the woman is so young, nothing's really wrong with her so that there's a little bit of confusion but I think it's important to really be careful with irregular periods because of the risk for those pre-cancer cells that can pop up in the lining.

Ashley: Wonderful. I thank you so much for taking the time to answer these questions. I really appreciate it.

Dr Carolyn Alexander: Thank you, I love your tweets.

Ashley: One of my partners in crime someone that I absolutely adore that's been part of the PCOS community as long as I have and who has done some tremendous work and tremendous activism, Michelle Schwarz is here and I know she has a couple of questions that she wanted to ask as well. Michelle, if you could introduce yourself.

Michelle Schwarz: Yes, thank you, Ashley, for that very kind introduction. And thank you so much for having me on your show. I'm as Ashley said, a PCOS researcher. I'm currently an epidemiologist. In my research, I have studied the knowledge of mental health providers PCOS specifically and psychologists and psychiatrists, and what we needed to do to increase their knowledge and have them screen and refer their patients for PCOS treatment. So given that I was wondering Dr. Alexander if you could maybe tell us a little bit about your previous PCOS research and what you learned and maybe what new questions your research sparked?

Dr Carolyn Alexander: Yeah, I think when I was at Cedar Sinai, I worked closely with Dr. Ricardo Aziz and Martha Darzi on some looking carefully at genetics of PCOS and we were initially hoping to find a link between the different types of PCOS and kind of a unified genetic complement of things that could lead to it. We looked carefully at the FSH receptor. We looked at the LH receptor, we looked at different genes that bind to the androgen or kind of male hormone receptors. And really what was kind of interesting is because we see such different ethnic backgrounds and different phenotypes, it wasn't anything specific of one gene that we could kind of say, yeah, this is the culprit, and maybe we could create medications or something that could sort of battle that issue. So I think the thing that popped up in my mind which was helpful is that how important it was to get a detailed family history from the father's side because I think we always ask how did your mom's periods go, how's your aunts and sort of that sort of thing, but from the dad's side, there were a lot of interesting remarks that they had a strong family history of diabetes or obesity or something like that.

Dr Carolyn Alexander: And then the questions that sparked is really what was interesting is the foetal programming or the actual reasons in the developing foetus of that person that led to maybe those epigenetic changes, which are different than the actual genetic mutation, that maybe we could help counsel the next generation of people so that when they're pregnant, maybe they could avoid those issues. I think it does seem that three months before we ovulate, our healthy eating matters and taking vitamins, and there's a lot of new interesting information about probiotics, helping, especially the obese PCOS patient. But that's my answer.

Michelle: Wow, that's really fascinating, and the new questions really deserve some attention. And I guess, that was the next question as to why are there so many gaps in PCOS research that are keeping us for finding out more?

Dr Carolyn Alexander: Yeah, I think it was kind of complex to have the strict criteria to allow the patients into the study because I think, really lumping together lean and obese PCOS and the women who have really cystic acne on their back, versus women who have all the male hair on their chin or their upper belly, it's kind of harder to lump everybody together, because probably they're a little bit different. And so I think that was part of why the research projects to really hone down things why they're not all similar variables in the group. But that's and also, you know, this, getting women to get involved with researchers. We did it. We worked really hard at the time to do lots of research with them, but it was harder.

Michelle: Understandably, I think we have key US researchers have had a lot of difficulty getting funding for research. And I think it's certainly one of the biggest reasons why we have gaps in the research. I looked into the current state of research endeavours and right now there are less than 40 active studies on PCOS in the United States and almost none of them are NIH funded. So in your opinion, what do you think we can do to increase PCOS funding and research?

Dr Carolyn Alexander: I think it all starts with the NIH and awareness and what they I think they set specific goals like sometimes it's maternal health so that there's less mortality in pregnancy for that's a big topic right now. And especially, there's a lot of research in men and like prostate and those kinds of things. So I think it's at the level of sort of our government officials and things like that, that maybe if they had more awareness that it's such a big, it really is one in eight or even more than more frequently than that that we do see this issue. So I think what you're doing is amazing and really important to bring about awareness of the issue.

Michelle: Great, thanks. While looking at clinicaltrials.gov I noticed that there were currently a handful of studies underway in PCOS for medications that are FDA approved for other condition so for example, Orilissa which is an endometriosis drug and Byetta, which is a diabetes drugs, and though oral contraceptive pills Metformin, Letrozole, Spironolactone are among the more common although unapproved medical treatments for PCOS. Do you ever go out of the box and prescribe those newer medications to women with PCOS and just interested if you have which ones you've tried and what the results have been, and if you may be looking for certain factors in certain women, so like age or PCOS phenotype or other considerations when you think about using these other treatment options?

Dr Carolyn Alexander: Yeah, I think there's a couple important like the last 10 years has changed a bit. So in the past, we really were limiting Metformin to women with an HbA1C or a blood test that showed that their average glucose over the last three months was showing that it was high or if they had signs of acanthosis nigricans which is kind of a darkening of the skin, between the thighs or at the neck, we were really super proactive to make sure to talk about the medication and encourage women to take it. There's newer studies showing that lean PCOS patients that may not have those issues actually may benefit as well for risk of gestational diabetes or diabetes in pregnancy and things like that. The one medication that I've used outside the box and I keep a list of the women I have on it is called Finasteride or Proscar and it works really well and women who cannot tolerate Spironolactone for acne or the male pattern hair growth and they're really frustrated because nothing's making their testosterone stop making those hairs grow or cystic acne.

Dr Carolyn Alexander: And a very low dose of Finasteride has been shown to help with those situations. I think there are some studies looking at it for the long run also for lipid or cholesterol because if you can block the androgens or the male hormones, then maybe we'll have a better cholesterol profile and things like that. But we're very careful to use that in women who are not trying to get pregnant right now. My colleague does use Byetta, she's a medical endocrinologist that I work closely with. But I tend to be a little more cautious if they're pre-pregnancy like in a year or two, they may try to get pregnant because the long term safety data is not really there for that. And so I think it's a little bit we have to walk cautiously on things like that because I don't know the ramifications unless she's post having her family then maybe because Byetta has been shown to improve the weight and that can be improving the other metabolic issues too.

Michelle: Great thanks! And so in my line of research, especially amongst psychiatry, what my findings were that they prefer to treat the conditions that are presented to them so they have a woman with PCOS, they'll treat the depression or anxiety or bipolar disorder, and they tend not to give consideration to the effect of the treatments to the PCOS. So I was wondering what advice you can give other practitioners, especially in other specialties, about working with women with PCOS, and what you would want them to know about PCOS?

Dr Carolyn Alexander: I think I just want to re-echo that if the periods are really irregular, that it's important, at least to get evaluation for that, and not let it go. Because that's like one of the things that we really have to be cautious about as well as checking for diabetes each year, because that can pop up in thinner, overweight women very kind of relatively quickly in some situations. But I think one thing and because I really get intimate and talk to patients so closely, and for such a long time, and I have patients who been around under my care for a long time is that I've noticed that there is these moments of rage and I don't know when they're untreated and not on medications and things and I think it can be in women who are very mild mannered, and it's just these moments and I feel like, from my side of it, I'm trying to tackle it from the hormone side. But I think there's probably other ways that the cognitive behaviour therapy or the psychiatrist can use other tools to help with that sense of being a little bit out of control of the mood, because it's a repetitive thing I hear, but I don't know if it's anything, you know, specific, but that's what I hear from clinical like seeing the patient.

Michelle: Great.

Shweta: Thanks. Thanks a lot, Michelle, for your wonderful questions. And it was really wonderful listening to your discussion with Dr. Alexander. Before I move on to the audience questions now. I have one question for all three of you. How do you think citizen science can help in accelerating the process to find a cure for

PCOS that is upsetting the lives of one in five women? Do you think if we keep track of our symptoms on daily and monthly basis with the help of the health apps like the PCOS tracker, will it help inform the doctors and researchers better and help accelerate cure? Dr. Alexander you can start and then Michelle and Ashley can follow.

Dr Carolyn Alexander: Yeah, I think knowledge is power and so having that real life-real patients information is very valuable, especially if there's a pattern or something with puberty so that paediatricians can recognise earlier signs and perhaps intervene because when the hair especially on the face or in different parts of the body terminalises or becomes that darker, thicker hair, it's hard to turn back time to when it was a little bit less. And that is it's such a vital time in that time window and as well as, diet modifications, increasing exercise in those kinds of things to counsel people. So I think that information is so valuable and helpful. In terms of, like infertility as well to guide women to seek help, sooner than to just wait and be frustrated and then time goes by, and it starts to become a bigger issue, perhaps at least popping up the discussion of talk about it with a physician…so those are my thoughts.

Shweta: Okay, thanks. Michelle, you want to comment on it?

Michelle: Sure. Absolutely. I think citizen science is where we need to go right now when we're dealing with a condition that is so overlooked by funding. And it's a wonderful resource for hypothesis generation. In fact, the industry is now really relying on real world evidence and post marketing studies for drugs, I don't know why we can't start there to generate ideas as to what's causing PCOS. We have some great ideas that we're not sure. We also can start seeing and maybe better putting into categories the types of PCOS that are out there and more information is better, especially in the age of big data and where you have advocates like Ashley and myself and we're now becoming the first line of advocacy and push for additional research, this is a great way to start and maybe we're onto something new. This hasn't been done before, and maybe PCOS could be the condition that starts this new trend of citizen science, where we're saying what we want done and how we want done and push for that cure. Having this certainly will make us not ignorable.

Shweta: Sure, yeah. Okay, Ashley, do you have any comments on this question?

Ashley: Just briefly echoing what Michelle said. Citizen science really is an extension of activism. It gives everyone in our community a chance to participate, to show evidence and to drive the research and funding towards the research. So I think it's vitally important. A lot of people always ask, what can I do, how can I get people to understand by participating in these research studies and citizen science – That's a way that everyone can raise their voice and let researchers and providers know that that we need to be heard and that this is a condition that cannot be ignored anymore.

Shweta: That's right. Okay. Thank you so much for your answers everyone. Without further delay, I think I'll just move on to the audience questions. We have quite a few number of questions coming in. I'll just go ahead first with this one – does acupuncture work as a treatment for PCOS? And so there are a couple of them – does losing weight cure PCOS, or eliminate the symptoms and how can lab work return as normal yet PCOS symptoms persist or exist?

Dr Carolyn Alexander: Yes. So sometimes at the especially with the male pattern hair, it can be the specific sensitivity to testosterone or di-hydro testosterone to actually make those hairs grow. So it may not be and it may be ethnic specific. So some ethnicities, we were using a little bit of a lower testosterone to say that's abnormal versus others, because we're putting everybody in one category, but maybe in some specific people, the normal blood tests may not be normal for them specifically, but in terms of I am a big believer in acupuncture, I found it to be very valuable when I was trying to get pregnant. I think also, it does, definitely lower cortisol, which can be high, which is our stress hormone. And so I think there's something to actually lean to in all the important Eastern medicine techniques they use, so I do find it valuable. I think, definitely there's a lot of evidence about the 5% body weight loss in women with a higher BMI, that that's been shown to improve ovulation as well as regular menstrual cycles and improving metabolic function in the system.

Shweta: Sure, okay. I think there's a third question which also asked how can lab works return normal, yet PCOS symptoms exists? So what is your answer to that?

Dr Carolyn Alexander: There may be a specific type of receptor in that person that the blood tests look normal, but for them the endogenous testosterone still causing issues.

Ashley: Can I comment on that also, I should ask – a lot of providers that I've talked to about this situation say that sometimes the ranges are set a little too low or a little too high. And with PCOS, you have to look at things as a bigger picture, rather than just looking at things that fall within the ranges because there are a lot of nuances. And also with, like, TSH, sometimes they might do a basic TSH instead of looking for free testosterone or things that again, require a little more nuanced. I mean, Dr. Alexander, what do you feel about that as far as the range is concerned.

Dr Carolyn Alexander: That's true, I think that's really well said, Yeah, I totally agree with that. That's why we look at the whole detailed history and talk it over versus just kind of quickly saying that looks fine and nothing's wrong. So we look at everything in peace.

Shweta: Sure, alright, so the next is – I was diagnosed 12 years ago. I have been on Metformin for 12 years. Nothing seems to work except expensive shots to get me ovulate properly and I recently lost a hundred pounds with a keto diet. I still have been unable to conceive. Are there any new, inexpensive treatments to help conceive?

Dr Carolyn Alexander: Yeah, that one's a little bit harder to, I would encourage diet and exercise because I think that also sounds like you're in an amazing job you're doing with that. Traditionally, the medications are a little bit more costly. At some pharmacies, you can save a bit of costs for especially if oral tablets are not working to help you ovulate versus the medications that are injectable medications, but nothing specific other than potentially in a few years if this newer oral medication is available that maybe it'll help lower the LH which lowers the likelihood of properly ovulating. So maybe there's things on the horizon but not right now.

Ashley: Now also, I mean, I know that I've seen that a lot of doctors will turn to using Clomid and Metformin. What is your feeling about the Letrozole because I know there have been studies in which it shows the Letrozole has been more effective for people with PCOS who are facing infertility?

Dr Carolyn Alexander: Letrozole is not an anti-oestrogen at the uterine lining. And so Clomid has a tendency to be an anti-oestrogen at the uterine lining and causes a thinning of the lining and so that can also lead to a difficulty for the embryo to stick inside the uterus for some people taking Clomid over and over and saying why isn't the Clomid working, I'm for sure oscillating. And the nice thing about Letrozole is that it actually is an anti-oestrogen at the pituitary. So it helps work in a similar way. But it also is not an anti-oestrogen that the uterine lining so people tend to get pregnant a little more easily, as well as we're seeing less twins with Letrozole versus Clomid when we used to cause more twins, which has a higher risk for the pregnancy. And so we're really finding that Letrozole has been shown in especially in women with PCOS to be beneficial and more successful in general and less side effects.

Shweta: Alright, thanks. Thanks for that answer. Dr. The next question is on diet. So the person writes a little bit about the keto diet that she's been following and she says a low carb diet under hundred carbs a day or even ketogenic diet with return to saturated fats and animal proteins with no grains, no sugar and starchy vegetables, low sugar fruits eaten on occasion would perhaps prevent or reverse PCOS rather than manage or treat it with drugs for life. Would you agree to that?

Dr Carolyn Alexander: I think it's a little bit hard because again it depends on the other issues the person may have like their BMI and cholesterol and things like that to look at the whole picture as well as their HbA1C which is the sign of pre-diabetes or real diabetes. So I think it's and I tend to be a moderate kind of person in terms of extreme diets because I get worried that it's so hard to maintain such a low carb thing

and then suddenly when they're pregnant, we're letting them just eat regularly and it starts to become like a big yo-yo in the system. But I think if a person is at a higher BMI and really needs to strategize to work hard on it, I think that's reasonable, but then I think if they're more of in the middle of the road, it's harder for me to encourage such limitation, especially in the younger women.

Dr Carolyn Alexander: It's like early college students, it's I think that's not fair to say everybody else is sort of eating, so I tend to say nutrition is over seven days. And it over the seven days try to be super vigilant with five or six of the days and one of the days you can have kind of a normal weekend day to be just normal, whatever, within reason, of calories and stuff like that. But so I don't know if that exactly answered the question. But that's the way I approach it.

Shweta: Right, right. Absolutely. Thank you so much for that input. Dr. The next question is actually a concern. She says my main concern is not being able to conceive or having any trouble in the future to conceive a baby. I have had several cyst ruptures and the biggest one I have had was about the size of a mandarin fruit. So what do you have to say to her?

Dr Carolyn Alexander: Unruptured follicle is very frustrating. So that tends to be a follicle which holds the microscopic egg inside of it. And it just never gets the proper signal from the pituitary gland in the brain to actually ovulate and so it can become a very large cyst. I had a very big cyst as well, I mean, it just sometimes when even when people are very stressed out, their body won't ovulate and then this follicle becomes this kind of bigger problem for us. So I think it's very important to monitor your menstrual cycles with a menstrual calendar. And if the person sensing that their periods are going past 35 days apart, they really need to get evaluated so that that means the egg never really came out. And so that can lead to unruptured cysts, which can then rupture later, which can be quite painful.

Dr Carolyn Alexander: In some circumstances, though, I know it's not always the best answer to say in some circumstances, we see a benefit in taking a low dose birth control pill because in those patients, we tend to avoid making cysts. And so if they're not ready to try to start a family, it's useful because it's contraception as well as lowering testosterone, as well as kind of regulating the menstrual cycles and there tends to be less cysts, but in terms of trying to conceive, you'd work closely with either your ob-gyn or fertility specialist to really tailor the care to make sure to avoid cysts.

Shweta: Okay. Thanks for the answer Dr. The next question is, again, I think about lifestyle and diet and the person says that is there such a thing as unmanageable PCOS? You see, I have a pituitary tumour and I'm starting to suspect my symptoms could be due to that instead of PCOS. If it is not possible at the moment to have a cure for PCOS, I wish there was at least a definite test available for it. That would save us a lot of confusion.She said that she has been following a healthy lifestyle and diet with best metabolic profile, possible insulin resistance, no cholesterol, no inflammation yet, despite all this symptoms,…

Dr Carolyn Alexander: So I think that's a really good question. I also really feel I wish there was kind of, the Europeans are leaning towards using one blood test called AMH – anti-müllerian hormone. And they've had papers saying anyone with an AMH over eight usually has PCOS. I think it's a little confusing here because sometimes we'll have people with a high AMH, but they may have non classical adrenal hyperplasia. And we have to be very careful to not just quickly say, yeah, based on one easy test, the person has polycystic ovary syndrome when they may have something else going on. But in my mind, the way is really the two out of three criteria. So irregular menstrual cycles, the blood tests so we do a full panel of androgens and check everything, as well as the ultrasound and if a person has two out of three that tends to lean to us diagnosing PCOS and we do check pituitary hormones in those blood tests to tease out the people who have prolactin, or prolactin pituitary tumours versus other issues versus PCOS, but I completely agree. I wish there was like one quick test but the only one I can think of is AMH. And again, the Europeans are kind of using that as a tool too.

Shweta: So the next question is in line with what Michelle was talking about – psychologists and psychiatric. So the question is, the person says four out of five clinical psychologists are women and this person is from

the UK. One in five women have PCOS and this means at least one in 10 clinical psychologists have PCOS, so many women with PCOS have experienced psychological issues like anxiety and depression. So why are so few clinical psychologists interested in PCOS?

Dr Carolyn Alexander: I think that's really a great question because I was trying to think how often we work really closely with our psychologists in the area, like, I'm always talking to them on the phone and stuff to talk about different patients. But I think it's a little bit of denial to is like, oh, people are just hormonal, we all get PMS a little bit too. Like we all get a little bit of hormonal things. And so sometimes it's just because society sort of says, it's that time and people get hormonal. And so I think it's important to recognise the bigger picture and look at everything very carefully, especially for quality of life for that individual and helping them get the best they can be and stuff like that, but I don't know if that exactly answers it, but that's my thoughts on it.

Michelle: I would love to chime in as well. I've actually collected data around this and it's important to make a distinction between a psychologist which is the one with like a PhD, and the psychiatrist who is a medical doctor. I found that psychologists, it's not that they're not interested, it's that learning about medical conditions in their degree isn't necessarily part of the curriculum. It's something they have to like maybe get through continued education. And in my research, I found that clinical psychologists are incredibly receptive to learning about PCOS but it's not necessarily knowledge they come into their practice with. So it's something that the patient will have to bring to the psychologist to get attention unless they happen to be familiar with it. So if we do a better job educating them, they're definitely more receptive to knowing and treating their patients with PCOS and anecdotally, after my after my study, I had a couple of psychologists reach out to me and thank me for letting them participate because they were able to make the connection and pick up on some symptoms in their patients and help them go on screen for and get treated for PCOS.

Michelle: Psychiatrists on the other hand, they have a little bit of a cognitive dissonance, meaning that I asked them and they correctly said that about one in 10 women have PCOS. And then I asked them, well, how many women in work practice have PCOS, and they said less than 1%. So there's definitely a connection between their knowledge and what their what they think they're seeing in their practice. So again, it relies on us to go in and make a change of conception. So I think with psychologists they're willing if we just open the door for them, and I think psychiatrists also need help from some other specialists, some other positions. But we need to do a better job of treating our patients as a whole and not just their parts, not their moments.

Ashley: And I just wanted to add one more thing to this – mood disorders in women with PCOS is quite often really kind of brushed under the rug, which I don't understand because there are about 45% of women who present with anxiety that have PCOS, there are 34%. In the studies that show women have depression, higher rates of suicide, sleep disorders, binge eating, it's something that should be focused on more. I know that there is a gentleman in the UK that is doing research on mood disorders associated with PCOS. And I think it's really important that these providers are brought into this, someone who is wonderful that I recommend to everyone – Christina – She has PCOS, she is also a provider. And I think that the key is for providers to kind of train other providers in these areas. So much has been put on the patients, it has been our onus to kind of figure out what PCOS is, tell the doctors what the symptoms are. And I think it's time that the providers get interested enough in doing the research and meeting the patient halfway.

Shweta: So, yeah, thanks for the answer to that question. Dr. Alexander, Michelle, and Ashley, the next question – I think this is the last question that we have right now before we wind up the talk. The person asks, can you suggest me how to cure my PCOS? What are the most important few things that a person newly diagnosed with PCOS should start doing so that she can control the symptoms of a disease to a good extent?

Dr Carolyn Alexander: I think that's a great question. Keep a menstrual diary. So keep track of your periods. I think it's very important to see a physician to get the panel blood tests that we traditionally do to look into which vitamins may help, as well as which possible medications, if they're necessary, can benefit

your overall health as well as the long term health. We could traditionally do an ultrasound to make sure the ovaries specifically don't have any cysts or any issues as well as talk about exercise and increasing your heart rate past 135 for at least 20 minutes every other day to really amp up your cardio so that the heart, which is a muscle pump and improves your circulation, which then can improve your overall health as well as the weight issue is if there is one. And then what I've seen is, it depends on the different metabolic types of people, some people really do well with no food 830 to 730 in the morning to 8pm sort of to 7am and that tends to help their body and some people it doesn't work for them from work, they get in traffic and they can't get home and those kinds of things. So we look at which type of a diet works; Mediterranean style diet is more, what I believe helps especially pre pregnancy because it has colourful vegetables and lower carb fruits and lean meats and I think that's helpful. But there's no one size fits all like for me versus my own sister, like our body types are totally different. And so everybody has to figure out what works for them. But that would be my advice.

Shweta: All right, thank you. Thank you so much, Dr. Alexander, for wonderful advice that you have given us in the last one hour. I think we will have to wind up our talk now, it's or already the end of the hour now. PCOS is disturbing the lives of one in five women yet it remains a little understood disorder, it's still hard for doctors to treat it and help their patients manage the symptoms. We just heard Dr. Carolyn Alexander of Southern California Reproductive Centre discuss what best can be done to deal with various symptoms of PCOS and share about the latest ongoing research that may become helpful for disease patients and managing their disease in the future.

We hope to see a speedier advancement in PCOS research so we have better solutions for us and our daughters and the upcoming generation of PCOS sufferers. Dr. Alexander, thank you so very much for your time today and educating us on a disorder that is affecting millions daily. Ashley and Michelle, thanks for your participation and your insightful questions that really brought out a very informative discussion. Audience I thank you for your overwhelming response and your questions.

And I want to share with you all our **PCOS tracker that is helping more than 6000 women now to keep track of their daily and monthly PCOS symptoms and it is available on iOS and Google Play stores.** Please see if you'd like to track your symptoms with the PCOS tracker, and any of your reviews and feedback will only help us help you better.

And if you wish to participate in clinical trials related to PCOS please visit our page curetalks.com and click on Find PCOS trial. And if you're in Philadelphia, the Penn PCOS Centre at the University of Pennsylvania is conducting a six month research study to compare the effects of medications on metabolic risk factors for women with PCOS and the study is called the **COMET PCOS study** and if interested, you can take the pre-screening survey at **tinyurl.com/cometpcos** or you can call them at 215-662-7727 to get more info.

Please write to me at shweta@trialx.com about your feedback on Cure Talks and suggestions on topics that you would like to be covered on the show. The link for today's show will be sent via email to all the participants. So until next time, thank you and have a great day everyone.