How Old is "Too Old" for Fertility?

Every woman feels the pressure of time when she has trouble getting pregnant, and running out of time keeps her worrying. The impact of age on fertility is a truth to reckon with, and age related fertility might be a factor for you. But this does not stop you from having a child.

Groundbreaking and fast paced advancements in the field of reproduction and fertility has helped women in later years become mothers successfully.

Rajo Devi 70 years of age, gave birth to her first child in 2008 in India via in vitro fertilization (IVF).

Celebrities like Halle Berry and Kelly Preston are examples of women who chose to have their babies in their later years. We are diving deep with Dr. Richard Paulson, embryo implantation and fertility preservation expert, to understand how old is too old for fertility, and learn the latest treatments in the field.

Full Transcript:

Priya Menon – Good evening and welcome to CureTalks. I am Priya Menon, Scientific Media Editor of CureTalks, joining you from India; and this is CureTalks' 104th episode. Today, we are talking about fertility and reproduction. Before we begin with today's talk details, I would like to take a few minutes to talk about the new study CureTalks is involved with. The study called America Walks is the first mobile app study on walking. It is sponsored by Trialx.com and is led by Dr. Chintan Patel. The purpose of the study is to determine your walking pattern and how much you are actually walking. You can also compare your walking habit with that of your friends and peers in your state as well as in your country. To participate in the study, all you need to do is download the app on your iPhone or android. Details are available at trialx.com/americawalksstudy. So, come on, let's get America walking!

Priya Menon – Coming to today's talk which is part of a popular talk series on fertility and reproduction, we will be discussing How Old Is Too Old For Fertility. I will now hand over to Shweta to begin with the discussion. Thank you, everyone. Shweta, over to you.

Shweta Mishra – Thank you, Priya, and good evening, everyone. This is Shweta Mishra, and I welcome you all to this 104th episode of CureTalks where we are discussing How Old Is Too Old For Fertility. The question of carrying a successful pregnancy and reaching motherhood over the age of 40 or 45 is a delicate

and complex one and has been intensely debated medically as well as socially; however, according to the statistics shared by CDC, birth by women 50 to 54 years old rose by more than 165% between the years 2000 to 2015. Rajo Devi of India gave birth to her first child in 2008 at 70 years of age via IVF, and actresses like Halle Berry and Kelly Preston are a few successful examples of celebrities who have showed the way. Much of the rise in fertility in older women is owed to the groundbreaking advances like in vitro fertilization, aided embryo implantation, and the use of donor eggs. Some of the latest developments in the field of infertility treatments in older women are egg rejuvenation and ovarian rejuvenation. So, amidst all these treatment…., treatment options available, actually how old is too old for fertility. Today, we are talking to our eminent guest and expert, Dr. Richard Paulson, who specializes in embryo implantation and fertility preservation to get the answer and also to discuss about the challenges of conceiving and carrying a pregnancy beyond a certain age. On our last show, we discussed recurrent miscarriages with Dr. Kristin Bendikson.

Shweta Mishra – Our expert today, Dr. Richard J. Paulson, is the holder of Alia Tutor Chair in Reproductive Medicine and is the Professor and Vice-chair, Department of Obstetrics and Gynecology, the Chief of the Division of Reproductive Endocrinology and Infertility at the Keck School of Medicine, University of Southern California. He has been the Director of the fertility program since 1986. Dr. Paulson is the President elect of American Society of Reproductive Medicine and serves as an Associate Editor of Fertility and Sterility. Dr. Paulson has authored over 150 scientific articles and chapters and has received more than 35 research awards for scientific publications. His major research interest is reproductive aging with a particular emphasis on human embryo implantation and fertility preservation. Thank you for…, for finding time for us, Dr. Paulson. Welcome to the show.

Dr. Richard J. Paulson – Thank you very much. Its a great pleasure to be here. I am looking forward to it.

Shweta Mishra – Thank you, doctor, and on the panel we have with us today Gray-Haired Mom and Alia Paige. Gray-Haired Mom, in her own words, is literally a gray-haired mom. She gave birth at 51 to her only son after donor egg IVF treatment. Since 2011, she has written her blog, grayhairedmom.com, to share her experiences as an IVF patient, an older pregnant woman, and a geriatric new mom; and she has been thrilled to have been contacted by so many other hopeful gray-haired moms to hear their stories. She lives with her husband and a now 5-year-old bundle of joy in New York City. We also have Alia Paige who is the author of her blog, expirationdate. Alia is a speaker and blogger, working to educate women about their reproductive lifespan and how to beat their expiration date. Alia and her friends who have personal experiences with assisted reproductive technology procedures and selecting a fertility center started this blog to provide friendly and easy-to-understand information about preserving female fertility. They advise couples in managing their fertility journey with their job and family and aim to educate people from the girlfriend's perspective. I welcome you to the show, Gray Mom and Alia. I extend a warm welcome to all our listeners; and before we begin, we…, I would like to remind the listeners that we will be discussing questions sent in via email at the end of the show. So, you can mail your questions to priya@trialx.com; and if you want to ask the question live, please press 1 on your keypad and we…, we will bring you on air to ask them or you can simply post your questions on the CureTalks' website as you listen to the show.

Shweta Mishra – So, Dr. Paulson, we have come a long way in fertility-related science, but one thing that really stands out in bold letters is still the age of the woman as the biggest risk factor of infertility and you have treated and helped many women of different ages in your practice. So, please paint the real picture for us here, doctor. How old is actually too old?

Dr. Richard J. Paulson – Well, thanks for having me on and thanks for asking that question. So, let me set the stage by talking about the biological clock which is really what we are talking about here. The biological clock in women is a reality; and if there is nothing else that we take from this show today it is that the biological clock is an extremely important aspect of the human infertility, not just female fertility but human fertility in general and it is basically the observation that women have good fertility potential until about 35 which is at…, at which point it starts to diminish and by the time the women reach about age 45, that potential for conception, I am speaking about natural conception now, is near zero. So, from…, up to 35 its pretty flat

and then from 35 to 45, it drops and after 45, there is a few anecdotal pregnancies, but really for the most part fertility is pretty much gone. One of the main myths that is propagated and misconceptions about fertility is that as long as women are menstruating regularly that this means that they have good eggs and that they are able to conceive and this, of course, is not true. So, a majority of women at the age of 45 still have regular periods and yet the vast majority are infertile. So, the menstrual history does not necessarily predict that the patient is going to be able to get pregnant; and we know that this fact, this diminishment in fertility, is due primarily to the age of the egg and this was discovered, of course, as a result of egg donation. So, let's talk about egg donation kind of quickly.

Dr. Richard J. Paulson – IVF began in 1978 with the birth of Louise Brown and five years later in 1983 was the first report of an egg being successfully donated from one woman to another. For us at our center, it began in about '86, right around the time that I started in this field, 30 years ago, and we noticed pretty quickly that the active egg donation where we got eggs from young volunteers and then transferring them to the recipient was actually very successful and the patients that we were treating at the beginning were all typically young and with premature ovarian failure. We thought they…, that was the correct group to be a recipient's egg donation and as time went along, we noticed that as these women, that is to say the recipients, became older that the probability of their pregnancy did not diminish and this was the aha moment, the realization that women over the age of 40 could be recipients of egg donation and that they would have the same success as young women who were recipients of egg donation. That was clearly not the case with fertility of women using their own eggs; and so, by comparing two groups, it became obvious that all of the aging that we observe between 35 and 45 is concentrated in the age of the egg. So, when someone asks the question, how old is too old for fertility, I always think to myself, we really need to divide that into two groups because the woman's contribution to the fertility equation is two fold, one is in the provision of the egg and the second one is in carrying the pregnancy. So, to answer the first part of the question, how old is too old for women's own eggs, I think the answer is about 45. So, there are pregnancies that happen for women on their own and there was recently a report of somebody getting pregnant with IVF at the age of 46 and even another one at the age of 50, but these are isolated cases, so typically, most programs do not treat women with IVF beyond the age of 45 or perhaps 46.

Dr. Richard J. Paulson – The second part of the equation, which is, how old is it…, is a woman…, is it too old to carry the pregnancy. That is a more complicated question because it seems like the uterus does not lose its receptivity. We noticed in our studies receptivity was the same all the way up until about age 55 and so the…, the…, the rate-limiting step is not the ability of the uterus to tolerate the implantation, but rather the…, the patient being healthy enough to be able to carry the pregnancy and so that's where you run into that second half of the equation, at what point is it simply too risky for the woman to carry the pregnancy or are the complications too frequent.

Dr. Richard J. Paulson – So, we have looked at this in a number of studies. We looked at obstetrical outcomes; and the obstetrical outcomes in women over the age of 50 were generally good, but there is no question that there was an increase in preeclampsia, that is to say, pregnancy-associated high blood pressure beyond the age of 50 and this was dramatically increased for women over the age of 54 where the risk of preeclampsia in our relatively small series because there are not that many women beyond 54 getting pregnant, but the risk of preeclampsia was 60% and so we thought that perhaps 54 or 55 was around the age of the physiological limit and that indeed is what has recently been published by the ethics committee of the American Society for Reproductive Medicine, who has agreed now that it is ethically acceptable for women in their early 50s to be able to be recipients of egg donation, but that going beyond 55 is probably not advisable and for women in their early 50s that this would have to be qualified for women that do not have any underlying vascular disease, high blood pressure for example, or kidney disease or any of those things. So, a woman who wants to be a recipient of egg donation could probably do it safely up until the age of 50 if she has medical problems. If she is healthy and has no medical problems and perhaps as high as 54 or 55 and beyond that I think we are getting into a…, into a territory where if the person wants to become a parent, that I think a gestational surrogate should probably be…, be utilized.

Shweta Mishra – Okay. Thank you, doctor. So, you mentioned that the receptivity is still okay at the age of

65, but what about the low estrogen and breastfeeding, hip pain, and other general body changes that the women experience as they age and more importantly, what are the effects of age on the fetuses or the babies born to the women…, to women of age?

Dr. Richard J. Paulson – That's a great question, and I think its important to realize that the pregnancy actually makes it own hormones. So, in order to get someone pregnant, to get the pregnancy started, the recipients do have to take a regimen of estrogen and progesterone which imitates what their own ovaries would normally be making, but the reality is after the trimester they don't need anymore steroid supplementation. They don't take anymore estrogen or progesterone. The pregnancy makes all of that. So, as far as the fetus is concerned, the fetuses' experience is, it doesn't know how old the mom is. I… My impression is, is that the fetus that is born to a woman at the age of 52 is exactly like a fetus that's born to a woman at the age of 42 or 32. There is no evidence that there would be really any difference in terms of their experience.

Shweta Mishra – Okay, but I read it somewhere, fused labia, is that a problem? I read it somewhere, some babies having that problem, in babies who are born to women beyond 50?

Dr. Richard J. Paulson – You mean, female babies that are born would be born with fused labia?

Shweta Mishra – Yes, yes.

Dr. Richard J. Paulson – Is that what you mean? Yeah, that would be a problem if too much androgen in the pregnancy and that would not be associated with women over the age of 50 because again the hormones that are normally produced by the pregnancy are produced by…

Shweta Mishra – Right.

Dr. Richard J. Paulson – …the placenta and the placenta is primarily a fetal tissue. I mean its half fetal and half maternal, but…, but that is not…, that is not a case and that is not a specific association with women over the age of 50. It is fair to say that women over the age of 50 do have their vascularity, their blood supply to the uterus is perhaps not as good as that of younger women and so that is why you have earlier deliveries, the high blood pressure that's associated with pregnancy, and even gestational diabetes. So, these kind of obstetrical complications, yes, those are increased over the age of 50, but fused labia or abnormal hormones and so forth, that is not associated.

Shweta Mishra – Okay. All right. Thank you so much for answering my question, doctor, and with this, I will take this discussion forward by inviting the panelists. I'll first invite Gray Mom to ask her questions. Gary Mom, its a pleasure to have you here with us. Thank you for coming out and sharing with us. Please ask your questions.

Gray Mom – Hi! Thank you. Its a pleasure to be here. So, I began my treatment at age 48; and I was treated by Dr. Mark Sauer at the Center for Women's Reproductive Care, Columbia, and because I was approaching 50, we were given a long list of pre-treatment tests that I had to complete and I was wondering if the doctor could talk a little bit about some of the pre-treatment tests he recommends for women, women of age…

[00:15:45] Dr. Richard J. Paulson – Certainly. Certainly. So, Mark Sauer was my partner when we started this work in the 1980s and he went to Columbia in 1995. So, he and I are very much of the same mindset and we were…, we were very excited about the possibility of making pregnancy possible beyond the age of 45 and even beyond the age of 50, but we were very cautious at the same time and so we made up an admittedly arbitrary list of tests which included EKG and chest x-ray and for women over the age of 50, we recommend actually a treadmill test and for us it was the analogy of saying if somebody came to you and said I would like to start running a marathon or start training for a marathon, what kind of tests would you do on that person because we've figured that a pregnancy is a pretty stressful time for the cardiovascular

system. So, we made up all of these tests and…, and wanted all of the patients to pass and I am thinking that that is what you are talking about and I have to tell you that we have been criticized by some of the perinatologists saying that its probably unnecessary, but I would really rather err on the side of caution, to be honest with you, and if we should discover something ahead of time that…, that somebody should have known about, I…, I feel like that's still the right thing to do. So, if you are going to take pregnancy beyond the age where someone becomes pregnant on their own, then I think its worth doing that. So…, so, that's what we are talking about and these are general health tests. So, blood count, blood chemistry, EKG, chest x-ray, and a stress treadmill and for women over the age 50 now, of course, we recommend a colonoscopy and not that that has anything to do with fertility, but, of course, it has everything to do with somebody being healthy and somebody being around to be able to take care of their baby.

Gray Mom – Yeah, I think the…, it was a really daunting list when we first saw it and I think the most difficult one personally for me was the treadmill test and not just passing it from a health standpoint but even getting insurance to pay for it. That was one of our…, our big obstacles as we completed our list. I was also wondering if you make any recommendations about the age of the father or sperm donor because I know there's been a lot of press recently about advanced paternal age contributing to perhaps conditions like autism in offspring.

Dr. Richard J. Paulson – Yes, I appreciate you say that and I want you to know that we are very empathetic about the insurance question that you brought up. That's pretty difficult. So, I have got somebody who is 50 years old and she says, I just finished running my marathon last month and you want me to go do a stress treadmill and its going to cost me 1,000 dollars out of pocket. Yes, we have made exceptions in some of those kind of situations, but to answer your second question about the paternal age, you know, most people arrive as couples and so we are trying to make fertility an option for these couples and so we…, we don't rule someone's health. We do caution them that once men get past the age of 50, there is an association with new mutations such as dwarfism, for example, and with the kinds of diseases that we don't really understand their genetic origin, but they do seem to be associated with advanced paternal age, advanced age of the father, like autism spectrum diseases, schizophrenia and so forth. So, we caution them about it, but these numbers.., the…, the absolute numbers are still quite small. So, if you take a disease that has a very low incidence and you double that incidence even twice or three times, its still relatively low. So, the… So, so, its not thought to be prohibitive in other words. Its not the case if somebody comes in and says, I have got a 70-year-old husband, we say, oh, no, you can't use him. You have to get a younger donor. That is not the case. You can indeed use the sperm from a 70-year-old.

Gray Mom – Thank you. My next question is about actually your experiences with women and…, and their experiences in childbirth and, you know, obviously there has been a lot of data about older mothers, but what my doctor recommended was or at least warned me about was the higher risk of emergency C-section. Usually that older mothers do quite well during the labor stage, but then maybe by the delivery stage are either too tired to…, to complete the natural childbirth and in my case, I had to schedule C-section medically necessary for other reasons, so I was wondering if you could talk a little bit about your mother's experiences in…, in childbirth?

Dr. Richard J. Paulson – Certainly. Certainly. I think it to be fair to say that there are as many stories of childbirth as there are individuals. I think everyone approaches it with different mindsets and so forth. We do know that statistically speaking that incidental cesarean section is much higher for women over the age of 45 and much higher over 50 and our series even for the singletons, of course, all the twins are delivered by cesarean section, but the singletons were I think experienced about 72% incidence of cesarean section, so obviously, the vast majority. The problem with trying to look at the data is…, is to try to isolate exactly why that is. So, is it the nervousness of the obstetrician who is nervous because the mom has gray hair or is it that the…, they are nervous and so they induce labor and when you induce labor, of course, there is a much higher incidence of cesarean section or is it partly elective. Somebody says, you know, I have been pushing long enough and I really…, I went to a lot of trouble to have this pregnancy and I am okay having a C-section.

Dr. Richard J. Paulson – So, we don't know if they really…, if you were really to control the…, the situation

very carefully, whether a healthy 50-year-old would really have a harder time pushing out of pregnancy than someone who is younger. We certainly don't think that there is any physiological difference in terms of the uterus not being able to contract quite as well or that the pelvis changes shape. None of that is the case. So, from all of those perspectives, I suspect that the vast majority of reasons for why women deliver by cesarean section are not specifically inherent to their age and inability to push the baby out, but that they have to do it. People being nervous and maybe some comorbidities, like, for example, without going into detail but you had a reason for a cesarean section and those reasons might increase for women over the age of 50, let's say somebody's got a fibroid in the lower uterine segment and that's not going to allow the baby to come out. The fibroids are more common in women who are older. So, you see what I mean. All of these little factors, I think, add up to increase the C-section rate, but I…, I am not sure that the older women…, I…., I wouldn't want to go and say, I think the older patient is just not going to be able to push the baby out and they should just schedule a C-section, I don't think that is okay.

Gray Mom – Thank you. The other question I had was about your standards. I know Dr. Sauer had rules around the number of the embryos transferred at one time. Do you have a number or limit of transfers and does that change with a women's age, a younger woman to an older woman?

Dr. Richard J. Paulson – I must admit that it does and I wish I could tell you that we had a very specific rule. We…, we…, we do have a rule that women over the age of 50 only get one embryo put back at a time, and we must remember that these are donor egg embryos. So, each embryo has really a very high chance of implanting. These…, these are really good embryos. They are 50% plus per embryo implantation rate. So, when we put back two, we realize that we are taking a chance on…, a very real chance on having twins and we really are not comfortable with that for women over the age of 50, but really how much difference is there between 49 and 50. So…, so, as of the last time that…, that this happened to me I think last week, I think at age 48, I think if the patient requests two embryos and says, I really would to have twins. I am…, I am 48 years old and I don't have much time and if I have two babies, I will think that this is a blessing and then…, then we can send them for the increased risk of obstetrical problems with twin gestations, but we will let them have two embryos and, of course, we would never transfer 1 and 2.

Shweta Mishra – All right. Thank you, Gray Mom, for your questions and I guess I want to invite in Alia Paige at this point. Alia, are you there?

Alia Paige – I am here.

Shweta Mishra – All right. Please come in with your question.

Alia Paige – Thank you so much for inviting me today, Shweta. I really appreciate it. Dr. Paulson, I actually started my journey to maintain my fertility back in 2011 when I decided at that point in time to freeze my eggs and I am really very thankful and very happy to tell you that about five years later now I just delivered twin baby girls and its been really really exciting and also just very personal, lot of ups and down during my journey, but one thing I think is really important to speak to…, is to also speak to women of all ages and so the first question I will ask you is at what age do you think that a young woman should take advice from a reproductive endocrinologist if she is concerned about maintaining her fertility?

Dr. Richard J. Paulson – Alia, well I am so happy to hear your story. That's fabulous. That's…, that's a…, that's a great story. I… Would you be willing to share with us how old you were when you froze your eggs or are we…, are we going a little too personal?

Alia Paige – Absolutely. No, I would be happy to. Yeah, so I was 38 years old when I froze my eggs and at a time really, you know, prior to a lot of discussion about egg…, egg freezing was really quite popular or at least a heck of a lot more popular than it was back in 2011 and so essentially I froze my eggs. I was able to freeze eight eggs and then we decided to use them approximately two years later and when they wanted to thaw all eight of the eggs, only two of them thawed well and I was also able to produce seven additional eggs. They fertilized the seven that I created and the two that thawed. The two that thawed did not make it to

day 3 and so my first, I actually went through two different cycles of IVF and two different cycles of IUI. I initially tried IUI for the first time and I was not successful, I decided to go straight to IVF at first cycle, that's when they thought all eight of the eggs were able to unthaw. They did not make it to day 3, but I was able to produce seven additional eggs. They put two of the embryos in and unfortunately it was not successful. I went through a second round of IVF. I was also able to produce eight additional eggs. Of those eight, two more fertilized, we placed those back in and I was unsuccessful unfortunately and then we decided just to take a break and our doctors said, hey, you know what, let's just try few more IUIs. We did the first IUI and we were successful. That was last June and I just…, I just delivered the girls a month ago, March 7th.

Dr. Richard J. Paulson – Congratulations! That's a wonderful story that has a…, that has a happy end and also I think shows that the…, the…, the path is not always…, always straight. Sometimes it takes twists and turns, but let's go back to your original question and that is, how old women should be. So, our oldest patient that I had successfully frozen her eggs and then returned and had them transferred, then had a baby, was 40 at the time that she froze her eggs and she was 47 when she came back and had them thawed and had a successful pregnancy and has a baby boy and I think is coming back for her second pregnancy soon. She was 40. I think that's pushing your luck a little bit. Even 38 is really not optimal.

Dr. Richard J. Paulson – We know that fertility starts to go downhill at 35, and that is a statistical statement. So, I…, I think that…, that somewhere between 30 and 35 is the correct age and maybe a better way to say it would be that women should at the age of 30, if they are concerned about their own fertility, look around and say, I am 30 now. Am I in a position now to start having a family and will I be done having my family by the time I am 35 and if the answer is yes, then great, then get on with it and do it. If the answer is no, my life is not in a position where I think I am going to have my children by the time I am 35, then I think its very reasonable for those women to go in and to freeze her eggs and, of course, the younger your are, the better quality those eggs are going to be and the more you are likely to put away. So, you only put away eight eggs during your one cycle. Our 40-year-old actually had very good ovarian reserve, and I think she put away about 17 or 18. So, that gives you more options and you are, of course, more likely to be able to put 17 or 18 eggs away in one stimulation if you are younger rather than older. So, I…, I don't think there is a specific line, I would say between 30 and 35 is the time to obtain that consultation and to think of it, but certainly if somebody is not pregnant by the age of 35, then that would be the age that I would say, yes, go in and freeze your eggs.

Alia Paige – Okay. So, that, you know, help us…, helps women…, future generations of women kind of keep hope alive here, but what advances are on the horizon that future generations of women would be able to take advantage of to maintain their fertility into advanced maternal age?

Dr. Richard J. Paulson – So, great question! We are currently and…, and I'll try to answer it both sort of scientifically as well as maybe metaphysically. So, on a scientific basis at the present time in 2016, the only technology that we have available is the cryopreservation of reproductive tissue. So, that means you either freeze eggs or you freeze embryos, you can…, men can freeze sperm and so forth and we are very good at that now. We know how to do it. The…, the…, the reproductive tissues survive well. They seem to retain their youth. They don't seem to deteriorate and so forth. So, this is fabulous.

Dr. Richard J. Paulson – In the future, I think that stem cell technology is going to make it possible for people to be able to generate sperms certainly. I think again the men are going to get off, you know, more easily because sperm is just so much simpler than the complex egg, but I think that we will reach the point where we will be able to generate eggs in the laboratory by stem cell technology from other cells. So, it will not be necessary for someone to cryopreserve their eggs; and if they are unable to get pregnant naturally, they will be able to go in and have the, you know, generate a rejuvenated egg, but I'd like to answer the question also little bit from a psychosocial perspective, which I think is always important to maintain. One of the benefits I think of being aware of the biological clock is that our society is becoming aware of the fact that this is an important thing and its a reality and we can't just sweep it under the carpet and say for the sake of egalitarianism, we allow men to work themselves to death from the time they are 20 until the time they are 50 and if women want to be at that same level, they too need to work themselves to death from the age of 20

to age 50 and then…, maybe then start thinking about having babies. Maybe our society should look around and say, you know what, there are more important things in life or there should be a way for us to set up our corporate or our employment structure in such a way that people can take time off when they are 30 so they can have the babies, both for biological reasons as well as I think for energy reasons. If you want to be chasing around behind your…, your kid at…, at the American, you know, Youth Soccer Organization, it will be easier when you are 35 than when you are 55 for sure.

Alia Paige – Oh, I can definitely co-sign that, that's for sure. (Laughter) I'll ask you this question then. You know, what is the number one reason that women are telling you, you know, day in and day out that's the way you are going to have children. Is it for corporate or professional reasons or…, or what…, what are they reporting to you?

Dr. Richard J. Paulson – Another great question and I have to tell you that I think its changing. I think that it was corporate and that it was job and it was career and I would say that gradually over the last five, maybe not 10 years, but five years, the people are…, young people are not pairing up. They are not pairing up. I…, I think in the old days they would still have gotten married in their late 20s, but both the husband and the wife worked and they worked and worked and this is not a good time and we are starting a business and now they come in at age 45 and they say, okay, we got our business started, we are ready to have babies and we say, you know, its…, now you are at advanced maternal age, but I am not sure that's happening anymore. I think a lot of women are aware of this and they would just as rather have babies in their early 30s, but they are not pairing up. The…, the…, the young people today, as near as I can tell, are…, are not really interested and they don't even think about marriage until they turn 30, then they start thinking maybe its time to get married and they get married at…, at maybe 35 or 36 and so, that I…, my perception is, again this is in my little corner of the world, is that that is going to be an increasing reason for people delaying fertility is because there is no one in their life and they would like to have a family. They don't just want to be single parent. They would like to have a family and so…, so its taking a longer time to get the…, the family infrastructure to get the husband and the wife in the house and so forth to get that started. That's my impression.

Alia Paige – Thanks so much, doc. I appreciate it.

Dr. Richard J. Paulson – My pleasure.

Shweta Mishra – Well, thank you, Alia. Dr. Paulson, with so many mind blowing advances in this field, I am wondering are there any tests available to tell a young couple how much time do they have before they can successfully build a family?

Dr. Richard J. Paulson – So… Excellent question and the answer is yes and no. So, the… So, the…, the question is, can you measure someone's ovarian reserve or someone's ability to become pregnant and the answer is yes and this is called ovarian reserve testing. An ovarian reserve testing is done on the female partner, and it involves assessing her age and then do…, we do three measurements. Two measurements are blood tests and that is a blood test for the hormone FSH, follicle-stimulating hormone, and a serum follicle-stimulating hormone level should be obtained on the third day of menstrual bleeding. This gives us a good sense as to the…, the quality of the eggs and the other blood test is called AMH or anti-mullerian hormone and a serum level of anti-mullerian hormone that's above 2 is a normal value. So, AMH is produced by the ovary and so higher levels are good. FSH, follicle-stimulating hormone, is produced by the pituitary and so higher levels are bad. So, you want a low FSH and a high AMH. So, those are two of the tests and the third test we do is an ultrasound where we count the number of follicles that are in the ovaries, and young women typically have at least 10 follicles on each side and what a follicle is is the…, is a little fluid-filled structure that contains the egg and the number of these fluid-filled follicles on each ovary correlates nicely with both the number of eggs you are likely to get in a…, in an ovarian stimulation, for example, and also with fertility potential, in general. So, the answer is yes, you can assess someone's fertility potential.

Dr. Richard J. Paulson – The second twist to the question, the way you phrased it, Shweta, is that can you predict how much time the couple has, this we do not know.

Shweta Mishra – Yes. All right

Dr. Richard J. Paulson – So…, so, there is not the long-term followup to say, "Oh, if your AMH is now 1.1, then you've got 5 years or 10 years or…," we just don't know. So, we can do a snapshot and tell you where you are now and in general, if you have better ovarian reserve, we are thinking of more time, but there is…, we don't have that information. So, it is not really predictable and I would not want people to say, "Oh, I went and I had ovarian reserve testing and it was really good. So, I got plenty of time." I think that would be…, that would be incorrect.

Shweta Mishra – Right and talking about AMH, doctor, you know, can it also fluctuate back up in couple years because you know what happened. I got my AMH tested, say, three years back and then after a year later, it was up, you know, my levels became normal. It was not normal and now they became normal. Can it happen or was it a wrong testing?

Dr. Richard J. Paulson – Yeah, well, we don't know. So, AMH is a relatively new test and…, and just like… I have to tell you one of the advantages of having been around for 30 years is I have seen all of these tests come and go and whenever a new test comes out, it is always the greatest and it is the most reliable and everything like that and so…, so when…, when FSH first came out, everybody thought that was the greatest thing and then everybody saw that that was fluctuating and sometimes it will be high and sometimes it will be low and so when AMH came out, same thing. Oh, AMH is the greatest and you can measure it even if somebody is on birth control pills or even if they are pregnant, it doesn't matter. Its always…., but that is not the case. So, clearly it does fluctuate and clearly it does…, does vary with age and that makes you wonder how reliable is it really in terms of predicting thing. All of these tests should be realized that these are statistical statements, so the number can give you a statistical probability. You are in a better category than that person, but in terms of your own, individual potential, obviously there is no guarantee.

Shweta Mishra – All right. Okay. The next thing that I wanted to talk to you about is egg rejuvenation technique. What is your opinion about this technique, doctor, and how long will it be before it becomes available to the patients in clinic?

Dr. Richard J. Paulson – So, egg rejuvenation is.., is one of those terms that you have to be very careful about and people talk about egg rejuvenation by, for example, taking medications. So, those…, some of your listeners may have heard about CoQ10, for example, which is thought to rejuvenate the egg because…

Shweta Mishra – Yeah.

Dr. Richard J. Paulson – …it helps the energy production from the mitochondria and this has been shown to work very nicely in the mouse model, but it has not been demonstrated in the human model and the CoQ10…

Shweta Mishra – Okay.

Dr. Richard J. Paulson – …theory followed after a previous theory which was acetyl-carnitine. Acetyl-carnitine is another chemical that's involved with the energy production in the mitochondria and it was touted as the…, as the latest thing, I would say, about 15 or 20 years ago. That also did not prove to be correct and so the medications that are out there, that are supposed to improve or rejuvenate eggs, whether it is CoQ10 or acetyl-carnitine or DHEA or any of these other medications, none of those unfortunately have panned out and there are anecdotal reports, but those are not…, those are not real science and…, and…

Shweta Mishra – All right.

Dr. Richard J. Paulson – …there is no…, there is no oral supplement that has been shown to do that. So, then the second thing, the other kind of egg rejuvenation is supposed to be what you can do in the laboratory and there is a pretty good theory about mitochondrial, either transfusions…

Shweta Mishra – Injections..

Dr. Richard J. Paulson – …or swapping out the mitochondria and the egg and that this is going to be helpful and I, for one, am optimistic that this is going to be helpful, but it has…

Shweta Mishra – Okay.

Dr. Richard J. Paulson – …not been shown to be a reality as yet. The…, the…, the first group that is going to be able to take advantage of the mitochondrial swapping out are women who have mitochondrial disease and I think if we can show that…, that it works and that it is safe in this group, then I think the next step would be to try it in older patients and see if the.., if the younger mitochondria might be able to rejuvenate the egg and might be able to help women get pregnant with their own genetic. My own belief is that the stem cell technology and the…, and the production of…, of oocytes, of egg cells in the laboratory from somatic cells, from other kinds of cells, I think is probably going to end up being easier and quicker than…

Shweta Mishra – Right.

Dr. Richard J. Paulson – …egg rejuvenation. So, a long-winded answer, there is currently no technique that works to rejuvenate eggs. There are techniques on the horizon which are promising and that there are at least two of them, one of them is this, that's the egg rejuvenation and then the other one, which I mentioned previously, is the generation of eggs in the laboratory from…

Shweta Mishra – Right.

Dr. Richard J. Paulson – …other stem cells.

Shweta Mishra – All right and what is the difference between ovarian rejuvenation and the egg rejuvenation? Is it a…, is it a different procedure, I mean technique?

Dr. Richard J. Paulson – Yeah, well, these are…, these are just sort of hypothetical procedures. One with the…, one with the ovarian rejuvenation techniques was…, was very interesting and…, and very kind of avant-garde where they would actually take the ovary out and they would chop it up into very small pieces and then bring it back together, the theory being is that as the ovary ages that there is scarring and that there are actually mechanically forces that are preventing the follicles from being able to grow and that if you…, if you cut the ovary into very small pieces, that you are actually going to be able to get a better response from the tissue that remains. Again, this is just hypothesis and that is the only kind of ovarian rejuvenation that I have heard of and it is not being a practice, so its not currently a reality. It is…, its a scientific hypothesis, which is interesting, but…, but again quite unproven.

Shweta Mishra – All right. So, while we are talking about this, there is one listener's question on stem cells. So, the person is asking, how is stem cell science expected to help women of advanced maternal age conceive with their own egg? What exactly would be the treatment and how long before this science is available for the patients?

Dr. Richard J. Paulson – Well, so…, so stem cells… So, let's…, let's quickly just review what stem cells are. We know that all of the cells in our body are…, are mortal, they will die, and our skin cells, for example, are constantly being sloughed off and so new cells are being generated from skin stem cells and analogously there are stem cells in our thyroid and in our liver and so forth and for women there are…

Shweta Mishra – Right.

Dr. Richard J. Paulson – …stem cells in the uterus and so forth. It is controversial as to whether there are or are not stem cells in the ovary, but it looks plausible that you could take stem cells from one tissue type and convince them to become another tissue type. In other words, if you could take a skin cell, reprogram it to be

a…, a pluripotential stem cell and then…

Shweta Mishra – Right.

Dr. Richard J. Paulson – …differentiate and you can get that stem cell to go and become an egg cell and that is the technique that I have been talking about all along and saying that I think stem cell technology is going to help us. The logic…, logical extension of that is is that that means that eggs could be produced for anyone, if people that don't have ovaries, for example. So, could that mean that you could potentially make an egg cell for somebody who is male and the answer is yes. So, you could take a male cell which has the wrong chromosomes with its XY, of course, and then you would have to eliminate the Y chromosome, but that's okay because egg cells only have half of the chromosomes. So, you could actually take a male individual and make an egg cell, an oocyte, from a male and so hypothetically, you could have two men who wanted to have a baby together and one of them would…, would donate cells that would be turned into an oocyte and the other one which produced the sperm, they would be able to co-mingle their genes together. So, these are the kinds of….

Shweta Mishra – Wow!

Dr. Richard J. Paulson – …science fiction kind of things that might be possible. I think that it is still a little ways out, people are very nervous about introducing stem cell kinds of, you know, into the reproductive equation because whatever you have introduced is going to stay in the gene pool for ever. Its not just a repair on an existing person. So, I don't think its around the corner, but, you know, stem cells have made huge advances that have…, that have I think outpaced the anticipation of most of us. So, I would say that in the next 5 to 10 years that technology might be here.

Shweta Mishra – Wow! So, that's a…, that's a very interesting scenario which you just talked about, doctor, that would help gay couples having…, have their own babies. Well, I think we have time for one more round for panelists. Gray Mom, do you have another question for the doctor?

Gray Mom – I do. I was wondering what sort of information the doctor would give to a patient concerned about maybe the longer term of sex on her health from hormone use, both the donors and…, and the birth mothers.

Dr. Richard J. Paulson – So, the…, the… Let's see the egg donors first. We…, we have not been able to find any adverse effect of ovarian stimulation on the egg donors or for that matter on the women that undergo ovarian stimulation for the purpose of getting pregnant themselves and let's remember that worldwide there are about 5 million babies born after IVF and that probably represents about 15 to 20 million IVF treatment cycles, given the current rate of success that have been performed and so I think if there were to be a problem, I think we would have…, we would have tripped across it by now and remember when we get eggs from an egg donor, we are not taking eggs that she needs for the future. We are really only harvesting those eggs that the body would normally have thrown away that particular month. So, we don't think that there is a negative effect on the egg donor.

Dr. Richard J. Paulson – Now, the recipients taking the hormones that you are talking about, you know, the reality is is that pregnancy seems to have positive effects on women rather than negative effect, particularly than early in life. So, early pregnancy, for example, protects against breast cancer, pregnancy protects against ovarian cancer, protects against uterine cancer. All of these things seem to be improved in the aftermath of a pregnancy. So, how do you put that together with the fact that you are using what would be called super physiological levels of estrogen and progesterone. I mean, they are much higher than would normally be in a menstrual cycle and my impression is is that whatever negative…, negative effect would come from the estrogen and progesterone I think would be balanced by the positive effect of the pregnancy, assuming of course that the patient doesn't have an underlying medical disease which would her at high risk for some bad thing happening during pregnancy.

Dr. Richard J. Paulson – So, for example, pregnancy is a…, is a time of very high risk for thrombosis, for having a blood clot in your leg. In older women that might already have some amount of abnormality of those blood vessels, to use medical speak, I would say who already have some pathology, who have already some…, some vascular disease, they would be at higher risk for that. So, if you have a blood clot and that blood clot then migrates and goes to your lung, it gives you a pulmonary embolus, a blood clot in your lung, that would be very bad for your health, but assuming that you are healthy and that you go through pregnancy okay and you have the baby, my impression is is that the pregnancy is a very…, tends to impart very, very positive things on the person who carries the pregnancy. So, I think we are going to be okay. I…, I think we are okay as long as we make sure that we don't do any harm to somebody by having them go through pregnancy at a time in their life when perhaps they are not healthy enough to do it. So, that gets back to the question that you and I talked about at the beginning and that is, why do you need to be doing all of these…, these silly cardiovascular tests to make sure that everything is okay.

Gray Mom – Thank you.

Dr. Richard J. Paulson – Sure.

Shweta Mishra – All right. Alia, do you have any other questions for the doctor?

Alia Paige – I do. I do. I have another more of a historical question, Dr. Paulson. So, you know, you have the women's suffrage movement or the women's liberation movement, which really changed opportunities for women, but in your opinion, what historical event or events attributed to the delay in childbearing that we see in women today and that…, that's part a and part "b" is, do you think that that delay will continue with…, with future generations of women?

Dr. Richard J. Paulson – Okay. Let me just polish up the crystal ball and try for the second part of the question. The first part of the question I think is, you know, society moves forward in…, in…, in weird ways. Its not a linear movement. Its kind of we go this way and then we zig this way and then we zag that way and…, and…, and all of these things and you think you…, you make things better by making a change and then you have the law of unintended consequences and something else happens. So, my impression is is that the desire…, when we think back on the 50s and sort of the 60s and the desire to make opportunities equal for women so that they could go and…, and have equality in the work place, I think…, I think it worked and I think, not to say that its perfect, but it certainly made more opportunities for women in the work place and so they were able to go to work and they were allowed to work themselves to death just like the men. So, they would start working at 20 and work continuously for the next 20 years and then suddenly realize that I am 40 years old and I wanted to have children and so that I think was the initial push and so now, as we discussed earlier, I think that these things are kind of balancing out a little bit.

Dr. Richard J. Paulson – Is it going to continue? I…, I really don't know. I…, I am encouraged that people are living longer, but, you know, I…, I have been in this field for 30 years, so I am getting along also and…, and even though I think we are healthier at an advanced age, we are still aging and so if anything, I am hoping that the society will recognize the existence of the biological clock and will recognize the importance of allowing couples, really not just women, but women and men, to have children earlier in their lives so that they are able to…, to enjoy them or to have the children at a time when physiologically we are better equipped to do it, to run behind your…, your son or daughter at AYSO and to…, and to be around and…, and maybe to get to experience grandchildren and…, and…, and go to their college graduation as well. So, I…, I am hoping that all of this stuff and all of the science has raised our consciousness to understand that some of these things simply cannot be reversed and even though we can get around them and even though we have got high-tech fertility that will help us to get around them, its still really nicest to get pregnant naturally and to have children at a time naturally when we are best equipped to do so. So, I am hoping that society will…, will move in that direction and…, and will allow our children and our grandchildren to have…, to have babies at an age where we can still sort of enjoy them.

Alia Paige – Okay. Well, I…, I totally agree with that, having experienced what I have experienced, but now I

have one last question. I know that you shot down DHEA CoQ10, but I do want to know, Dr. Paulson, do you think that there…, is there anything that women can do to sort of or even if there is some micronutrients that you do believe in or is there anything that women can do to naturally maintain their fertility?

Dr. Richard J. Paulson – Well, I mean and I don't mean to be shooting these down. All I want to say is that there is not adequate scientific evidence to warrant any of these and I have to tell you, Alia, I have seen so many of these things come and go and…, and…, and they were touted as the be all. I still have in my drawer, in my desk drawer at work, I think about 10 bottles of the acetyl-carnitine because I was going to do a perspective randomized trial. This acetyl-carnitine, that was the last CoQ10. That was the last medication that was going to rejuvenate eggs and really rejuvenate the whole body and my father at the time, I think, was buying it on the internet because he thought it was going to make him younger, but, you know, it didn't and so we are all looking for the fountain of youth and the fountain of youth I think is not going to be in a pill. I think the fountain of youth is going to be in a general healthy lifestyle and avoiding those kinds of things that are unhealthy for you and avoiding the toxins that you get, whether its in the form of air pollution, smoking. There's lots of toxins out there that are bad for us and I…, I am hoping that the…, the other part that I am hoping that our society will do is will realize that we are also putting into the environment so…, so I am sorry to make it be a negative instead of a positive thing, but the negative thing is is that our environment is absolutely filled with plastics that…, that look like estrogen and…, and pesticides that…, that kill the pests that have unknown reproductive effect on men and women and so I am hoping that our consciousness is going to be raised to that and that rather than thinking that we are going to reverse all of the toxins of the world with simply one food supplement or one micronutrient, I think we should just avoid those toxins in the first place.

Dr. Richard J. Paulson – So, I am, you know, wondering were there people who really want to have babies, should they be really advised to only eat organic food, that is…, that does not have any of these artificial pesticides in it. So, we don't know and…, and I don't want to go on record as saying that that I advised that, but I think that the equation is a little more complicated than one micronutrient. So, live healthy, exercise everyday. The…, the antioxidants, I think, are very reasonable and avoid those kinds of things that we know to be toxic, you know, smoking and air pollution is bad. Air pollution is bad for you, so support clean air and clean water. I think those are all very important.

Alia Paige – Great advice, Dr. Paulson. Thank you so much. I appreciate that. Dr. Paulson…

Gray Mom – Hear, hear!

Alia Paige – Who knew! Who knew! Great advice!

Shweta Mishra – Well, thank you so much, Alia, for your question. I think now its time for the listener's question and, Dr. Paulson, you have already answered a few of them, but still few of them are left. I'll just read it out. One question says, what percentage of the miscarriage risk in 40+ women is from the problem apart from egg embryo quality and what are the potential problems likely to be? For example, uterine, etc. And a second part of the question, it says, what can be done before an embryo is transferred to detect any of these other potential problems in advance so that they can be mitigated to the degree possible to give a 40 pluser the best possible chance of success with what could be her only healthy embryo?

Dr. Richard J. Paulson – Yeah, right. So…, so that points out really a very relevant aspect about this and that is that even though we can circumvent the biological clock in a 40-year-old with a…, with a donor egg for example, we are not going to circumvent the fact that…, that the rest of her reproductive tract is also aging and so she is more likely to have fibroids in her uterus or other sorts of abnormalities that as near as we can tell, the primary reason for miscarriages is in the embryo and the reason we know that is because you can look at the miscarriage rate in somebody who is 30 and/or 35 and 40 and you can see that increase and almost all of that is due to the age of the egg. We know the older egg is more likely to make mistakes and have chromosomally abnormal pregnancies and the vast majority of those are lost as miscarriages. So, the miscarriages are primarily because there is something wrong with the embryo and that is why its miscarried.

Dr. Richard J. Paulson – Now, the second part of that question is how can you make sure that the uterus is optimized? I think you can do imaging of the uterus. In our practice, for example, we really like saline injection sonography, its called saline injection sonography or some people call it hydrosonography or some people call it as sonohysterography.

Shweta Mishra – Right.

Dr. Richard J. Paulson – I don't know why we have so many names, but you inject saline into the uterus and then you can see if there is a polyp or a fibroid in the uterus and make sure that those are all gone before you put somebody through the fertility treatment. If you do that and the uterine cavity is normal and if you also look at the uterine lining thickness and the thickness is more than 7 mm, then its very difficult to show any other diminution or any other problem that would then increase the miscarriages. So, so we think that the miscarriage of 30%…, miscarriage rate is about 30% in women at the age of 40, for example. We think that's primarily due to the age of the egg and to make sure that you are not making it any worse for the uterus, you should make sure that the uterine cavity is normal, that there are no fibroids or polyps inside the cavity and of course monitor the ultrasound, the.., the uterine lining thickness to make sure that its thick enough to…, to be able to receive and…, and successfully implant the embryo.

Shweta Mishra – All right. Thank you, doctor. There is another question. I think somebody wants to know that chronic diseases like preeclampsia and gestational diabetes, do they become permanent once they set in during pregnancies or can they be cured once the pregnancy is over in advanced maternal age?

Dr. Richard J. Paulson – In advanced maternal age, so, actually its a great question and I don't…, I… So, we know that if somebody has preeclampsia, so preeclampsia specifically is pregnancy-associated high blood pressure. So, by definition…

Shweta Mishra – Right.

Dr. Richard J. Paulson – …it is only present during the pregnancy and then once the pregnancy goes away, it should go away. Now, the reality is if somebody has preeclampsia and you look at that population and compare it in the women who do not develop preeclampsia, those that do develop preeclampsia are at high risk for developing high blood pressure later on in life. Now, whether that would still be the case at the age of 50 or not, I don't know. I don't think we have had enough followup to say whether over the age of 50 that would still be true. So, the disease does not have to be cured because its only particular to the pregnancy, but it does make you be at higher risk for developing high blood pressure later on in life. So…, so, sum of each.

Shweta Mishra – All right. Thank you so much, Dr. Paulson. I think you have answered so many of our questions and you have given us so important…, such important take-home messages to us today, like the biological clock is a reality, menstrual history does not predict fertility, and most importantly, you are saying that people should be finding time out to start a family early on because of biological as well as energy reasons and I really like your saying, fountain of youth is not in a pill but in general good health.

(Laughter)

Shweta Mishra – So, thank you so much, Dr. Paulson. Yeah.

Dr. Richard J. Paulson – My pleasure.

Shweta Mishra – It was a wonderful discussion. Yeah… and its just our pleasure… Pleasure is all ours, doctor, to have you here today with us and thank you so much for finding time out. Alia and Gray Mom, thank you so much for your time and your insightful questions and I hope this discussion will be helpful to many who are looking to educate themselves about fertility in older age or were planning to start a family late; and audience, I thank you for your support and we look forward to having you all join us on our next CureTalks

on modern women and family building with Amy Demma in July. I will be announcing the date and time soon on social media. For more information on this show and other upcoming shows, visit our website, www.curetalks.com or you can also mail priya@trialx.com. The link for today's show will be sent in via email to all the participants; and before you log off today, please don't forget to check out the details of the America Walks study at trialx.com/americawalksstudy. So, until the next show, thank you so much, everyone. Bye, bye.