



Gynecologic Oncology: HPV Related Cancers

Hosted by: Steven Gore, MD

Guest: Elena Ratner, MD, Associate Professor of Obstetrics, Gynecology and Reproductive Sciences; Co-Chief, Section of Gynecologic Oncology, Yale School of Medicine

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Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about gynecologic oncology and HPV-related cancers with Dr. Elena Ratner. Dr. Ratner is an Associate Professor of Obstetrics, Gynecology and Reproductive Sciences at Yale School of Medicine and Co-Chief in the Section of Gynecologic Oncology. Dr. Gore is a Professor of Internal Medicine and Hematology at Yale and Director of Hematologic Malignancies at Smilow Cancer Hospital.

Gore GYN cancers, it seems to me like a lot of women know they are supposed to be seeing their GYN for reproductive health, hopefully everybody knows that, and I wonder how many of the patients, how many healthy women understand exactly what they are being screened for in terms of normal GYN health? Obviously, people get Pap smears, we all know that, and then they get all these kind of unusual physical exams, what are people being screened for cancer-wise?

Ratner That's actually an excellent question because we frequently have women asking exactly that. So, yes, it is imperative for women to see their gynecologist because so much right now in gynecologic cancers is about prevention. We do not even talk about treating cancers or even finding them early anymore. The future and the present is about cancer prevention. When a woman sees her gynecologist, her gynecologist can screen her for cervical cancer and that is why Pap smears come into play and we will talk a little bit more later today about checking HPV as part of that workup, but that is not the only thing. Additionally, women also have a good pelvic exam that looks for any cysts or any masses in the ovary or any masses in the pelvis or any abnormalities with the uterus. So, even though we do not really have screening tests for uterine cancer or ovarian cancer, a pelvic exam serves as that.

Gore How common are those cancers in patients who are otherwise healthy? Are we talking about women of reproductive age or post-reproductive age and is this something people should be worried about?

Ratner Yeah absolutely. Endometrial cancer is the most common gynecologic cancer. In the United States, there is an epidemic of endometrial cancer partly because of obesity. Obesity increases risk of endometrial cancer. The good thing with endometrial cancer is that there are symptoms and there are signs, and so much of what we do is awareness for women to know that if they have bleeding after they have reached menopause, that that is not normal. And once they have the bleeding, go see their

gynecologist. Usually, these cancers are diagnosed very early and they are completely curable. This is where prevention comes into play and in this case prevention is awareness, just knowing that once you reach menopause and you no longer get your periods, if you start bleeding, that that is not normal and that you need to see your provider.

Gore But not every bleeding postmenopausal is cancer right?

Ratner I was just going to say that. Absolutely not all bleeding, actually most bleeding postmenopausally will not be cancer. There are so many reasons polyps, there is atrophy, there are all kinds of benign things. But the key is it is never normal and always see your provider because they can see why the bleeding is happening.

Gore I am clearly not a woman and I never had a pelvic exam, it might surprise you, but it is true. But I know that it is not something women traditionally look forward to, and I know obviously there is ultrasound and CT scans and MRIs and biomarkers, so is there still really a role for a physical exam, shouldn't we just be scanning everybody yearly or something like that?

Ratner That's a wonderful question as well. We all are so tempted to just order a test but in gynecology, nothing is as important as a physical exam. There is nothing that is better than your fingers when you feel for these cysts or nodularity, there is nothing that is better. CAT scans are not better, ultrasounds are not better. Currently, there are guidelines that are changing in Pap smear screening. As of just a couple of months ago there are new screening guidelines that instead of Pap smears, you can just have an HPV test. HPV test is very easy, it is like a Pap smear and the reason we do that is because we know that for cervical cancer, HPV is the definitive test. A great, great majority of cervical cancers and pre-cancers are HPV related. So, if a woman does not have HPV, then her risk of cervical cancer or ovarian cancer is significantly lower. And now, because of that and because of all this literature and because of cost savings, these kinds of tests can be done once every 5 years. But it is so important and this is why I am bringing up at this juncture that we do not confuse guidelines for Pap smear or guidelines for cervical cancer screening with the need of still seeing your gynecologist once a year.

Gore I see. And is this screening – the screening for the Papillomavirus, is that done with the cervical swab or is it a blood test or how do you do that?

Ratner At this time, it is a swab that you do kind of just like a Pap smear and there are different ways of getting it done, and once this test is negative, then depending on your age – women do not have to get it repeated for 3-5 years.

Gore And if it is positive, does that mean they have cancer?

Ratner No, not at all. HPV, human papillomavirus is very, very common. There are certain ages where 80-90% of women have it. HPV virus by itself actually does not cause too much trouble. It is only the HPV virus that does not clear itself. So, we never check HPV virus in young women. We never check it in women younger than 30 because so many of them will have it and so many of them, the majority of them will clear it. So, those HPV viruses do not matter. The ones that we watch a little closer are the ones that persist after age 30 and those are the women that need that tests and their Pap smear being done more frequently than 3-5 years.

Gore So they still get regular Pap smears – the people who are HPV positive?

Ratner Correct.

Gore What about the stigma associated with HPV? I mean traditionally it is a sexually transmitted virus, we still have a bit of a puritanical culture in many parts of our country, do you have a problem getting women past that?

Ratner Yes, it is very much an issue that comes up and the question that comes up and most importantly, it comes up with vaccination. As you know, we have had this Gardasil vaccine that has now been out probably 10 years if not more and it has been incredibly, incredibly successful in decreasing rates of HPV and hence decreasing rates of pre-cancer to cancer. It is incredible. It is what we have always looked for. We have always dreamt of it, and as a physician who deals with this all the time, I actually see this on a daily basis. It is a dream, it is what we dream for all cancers, but the truth remains that a lot of states and some women do not vaccinate their children because of the stigma that this carries. There is no stigma and there shouldn't be a stigma. This is a very prevalent, very common virus that is very, very contagious, it is very easy to get, a lot of women and a lot of men have it and there shouldn't be stigma. It really should just be a way for prevention and cure of this cancer so that cervical cancer should not exist in the future.

Gore Why are you letting the fathers off the hook?

Ratner Not at all, not at all. Not the fathers, not the boys, I have 2 older boys who both got this vaccine. I think this is something that is prevalent and everybody should be vaccinated. HPV does not just cause cervical cancer, it causes vaginal cancer, it causes vulvar cancers. For men, it causes anal cancer and for women it causes anal cancer. It

can cause throat cancer. So, this is not something that women should be singled out and again, this is an opportunity not just for women but also for men not to have to deal with cancers in the future.

Gore I think it is important for people to know about the head and neck cancer in men; again when you start talking about anal cancer, we are not talking about puritanical feelings about sexuality in general but then we have this whole issue about how comfortable people are with acknowledging that they do not know whether the boys eventually will be heterosexual or homosexual, I mean this part of changing society, although I think it is getting better.

Ratner Coming just from a conference in Europe, it is so not even a conversation in Europe and it continues to be a conversation here. But yes, I agree with you. I think we are now seeing the fruits of the first batch of these vaccinations. We are now seeing much less of this pre-cancer and cancers and not just as physicians I think as women, as patients, we see this. So, I think this is the fruits of the labor.

Gore Yeah, it is terrific. And do you think that pediatricians are, I do not know how to put this, are pediatricians doing their job in promoting the vaccinations?

Ratner I do, I certainly do. I mean, at least here in Connecticut, it is super, super rare that I see a young girl, woman now, who has not had the vaccine.

Gore So, the uptake is pretty good around here?

Ratner Absolutely.

Gore We were very excited when our son was just about the right age when they approved it for boys. I think we might have even done it before for boys because we just knew that was the right thing to do, and it has always been my hope as a parent that my children will have a healthy sexual life when they are adults, right? Seriously, the fact of life is that in our society, sexuality is not one partner the rest of your life often for many people.

Ratner Of course, and again, we shouldn't look it as that, we should look at this as cancer prevention. It is not about values or our future hope, this is truly singly cancer prevention.

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- Gore Right. And back to the whole exam thing, the vaginal or vaginorectal exams, I think it is important for women to know, that your risk of cancer does not stop when you are in the post-reproductive ages, post menopause or if you are not sexually active, am I correct there?
- Ratner That's exactly correct. On contrary, most of our cancers do appear later in age, in women in their 60s, late 50s, mid 60s. So, yes you are absolutely correct; once women reach menopause and go through menopause, this is very much the time not to stop seeing their providers. It is very much the time to continue.
- Gore I have heard recently on the radio, I don't if it is a book or if it's a documentary about Gilda Ratner, the great comedian, who unfortunately died of very early ovarian cancer, think of that as being a reminder, my guess she was getting good medical care, who knows?
- Ratner We talked a little bit ago about uterine cancer and I mentioned how the good thing about uterine cancer is that there are signs and symptoms and that is why the great, great majority of these cancers are diagnosed early and are cured. Ovarian cancer unfortunately is not like that. We call ovarian cancer – the cancer that whispers because they are so few signs and symptoms. However, we actually do not think that is true anymore. We do not necessarily think that ovarian cancer is whispering, we just think that nobody is listening.
- Gore Typical man.
- Ratner And women. It goes both ways. But we do actually think that even women with ovarian cancer do have symptoms and do have early symptoms, and so much of this again is just education about awareness.
- Gore Well we are going to want to pick up on that after the break.

Medical Minute

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This is a medical minute about melanoma. While melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths. When detected early, however, melanoma is easily treated and highly curable. Clinical trials are currently underway to test innovative new treatments for melanoma. The goal of the Specialized Programs of Research Excellence in Skin Cancer or SPORE grant is to better understand the biology of skin cancer with a focus on discovering targets that will lead to improved diagnosis and treatment. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

Gore Welcome back to Yale Cancer Answers. This is Dr. Steven Gore and I am joined tonight by my guest, Dr. Elena Ratner and we are discussing gynecologic oncology and HPV-related cancers. Elena, just before the break, you said something I found very interesting that ovarian cancer used to be thought of as, the silent cancer. They didn't cause symptoms because where the ovaries sit and all that, but you are saying that now you are recognizing that there are symptoms oftentimes?

Ratner There have been some studies and some really good studies that show that even at early stages, women do have symptoms – some bowel symptoms, some bladder symptoms, clothes not fitting very well, not eating great and in the older days, like 5 years ago, it used to be checked up as just menopause, this was the common thing, women would go see their providers and pretty much be told, this is just normal hormonal changes, and you know, that is probably true and for a great majority of women this is just normal menopausal changes. What separates women who actually have something that needs to be looked at closely from those who just have hormonal changes is that in women with ovarian cancer, these symptoms happen every single day for 2 weeks versus women with hormonal changes, it just comes and goes. But again, the gynecological cancer landscape is so different now, it is really drastically changing; so much is about awareness and educating women about what is normal and what is not normal, and you know, also not taking no for an answer. The current studies say that women right now who get diagnosed with ovarian cancer, has probably had this cancer for 18-24 months and she usually has seen 6 providers before the cancer gets diagnosed. I usually say, women know their bodies better than anybody, you are your best advocate; you know something is wrong, you go and you get the answer and you don't say no, you don't accept this is normal until you are satisfied.

Gore I will take my bad marks as a male physician because over the years my wife was worried when she was having maybe some constipation symptoms or something, the first thing she thinks about is, I hope I don't have ovarian cancer and I am thinking, okay, come on I mean what is the chance, but you know the truth is, what you are saying is, it is not the craziest thing to worry about and of course get yourself checked out and she is fine as far as we know of course, but I dismissed her. I apologize.

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Ratner The key is exactly what you just said. Ovarian cancer is not common, we have got to remember that there is a 1.4% chance of having ovarian cancer, so yes, the great majority of women do not have ovarian cancer and will not have ovarian cancer, but it is all about awareness, it is all about knowing when something does not feel right, just go to your provider, that's all it takes, and having a good exam and then that's that.

Gore Is an exam sufficient, a vaginal exam by a good GYN?

Ratner Yeah, we do not call them vaginal exams, pelvic exams.

Gore I'm sorry.

Ratner Having a good exam by your provider would tell you whether you need anything else and that something else would be an ultrasound. Sometimes, we get ultrasounds, coming back to the beginning of our conversation, and the reason why ultrasound is not enough is that ultrasound by itself actually is not great, but ultrasound together with a good pelvic exam would be a very good assessment and would be sufficient.

Gore Gotcha. It is certainly interesting and what I wonder about is hormones, for a long time many women were put on estrogen replacement, of course some still are for postmenopausal symptoms, and then for a while that was seen as potentially contributing to cancers I recall, and I think there has always been some concern about oral contraceptives, where are we at with hormonal therapies, both contraceptives and menopause treatment and the causation of cancer?

Ratner You really brought up a very important and very divisive question. Birth control pills unquestionably reduce your risk of ovarian cancer.

Gore Reduce?

Ratner Absolutely, the best protection besides awareness and besides knowing your family history and knowing if you are at higher risk in terms of genetics, but besides that the best thing that every women could do for herself to decrease her risk of ovarian cancer is to take birth control pills. Any women who takes birth control pills for 5 years, decreases her risk by 50%.

Gore That's amazing.

Ratner The other way you can get the reduction is to have 5 children and to breast feed each one of them for 1 year. That's the plan I wanted. I am working on that plan. But most other people go with birth control pills. And of course, birth control pills, you cannot
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take if you had a history of blood clots, it is not for everybody and it is very much an individual decision, but this is again -- the present and the future is personalized care and really listening to everybody and understanding their history and understanding their risks and then understanding how you can mitigate those risks, how those risks can be reduced. Birth control pills unquestionably decrease your risk significantly. And these birth control pills do not have to be taken at the same time, it could be 2 years here, 2 years there – it is a cumulative benefit. So, I always tell all my friends, all my girlfriends, try to get in 5 years of birth control pills during your lifetime so that your risk of ovarian cancer is decreased significantly.

Gore Fascinating.

Ratner Hormone replacement therapy is the more difficult discussion. Yes, you were absolutely correct; in the older days, everybody, every woman pretty much who reached menopause would be placed on hormone replacement for her symptoms, and then studies came out including the nurses' study that showed that these women had a higher risk of breast cancer, and at that point everything stopped and pretty much all women were taken off, some of the providers in the community always tell me stories how the morning after that study was published, they could not even get into their office because their phones were just ringing because everybody was so afraid and everybody was taken off. But that is also not the case. We again know much better about understanding who needs it, who does not need, what are the risks, what are the benefits; in particular, I do a lot of surgeries for women who have genetic mutations where they go into menopause at a young age, let's say this woman unquestionably needs hormone replacement, it is not detrimental to them, it is beneficial, it is detrimental for them not to have hormone replacement and we have many, many studies that show that it is completely safe. So, we know now that estrogen by itself is much safer than we thought, so we no longer say yes or no - this is again very much an individualized decision. It matters how old the woman is, what her risks are and what her benefits are and what her symptoms are, but certainly even myself as an oncologist, I routinely use hormone replacement therapy in my practice.

Gore You know, that's really good to hear or to know about because the scare was pretty big for a long time. When you talk about these surgeries for genetic problems, are you talking about prophylactic surgery for women who are at risk of ovarian cancer and breast cancer?

Ratner Exactly. This kind of adds on the conversation on prevention where we mentioned previously that the most important aspect of this is to know your risk. We really need

to understand who are the women who are at increased risk of developing this cancer – ovarian cancer and breast cancer in particular. With these cancers, there are certain genetic mutations that we are always looking for – some of them are called BRCA mutations. This is the mutation that Angelina Jolie wrote about and what actually made it kind of common place is her New York Times articles.

Gore And she had bilateral mastectomies prophylactically right?

Ratner And she had ovaries removed prophylactically. It is challenging information to have, but knowledge is power – once you know you are able to prevent cancers and make sure they do not happen.

Gore Such a tough decision, I imagine.

Ratner It is a difficult decision, but it is a much better decision than having to deal with cancer. So much is available right now for prevention and it is not just hysterectomies or removing ovaries or mastectomies, there is so much more, there is just closer screening, there are more tests, there are closer exams, and of course, this kind of genetic testing is not for everybody. This is really for women who for whatever reason are considered to be high risk, which would mean that they have a number of family members who have had ovarian cancer or breast cancer, but I certainly do not want all the women to worry whether they have this gene or not. This gene is not very common, especially not in the Jewish Ashkenazi population.

Gore It is common among Ashkenazi Jews?

Ratner It is more common in the Ashkenazi Jews and again in the older days, we used to say, if you are not Ashkenazi Jewish, then you do not have to worry, but it is totally not the case. There are Italian women, there are Mexican women, there are all kinds of populations that also carry these mutations, but again, for the general population, this is not for everybody, this is just for women who have a strong family history of these cancers.

Gore What is considered a strong family history – one first-degree relative with breast cancer, two – who should be worried, a lot of women have breast cancers?

Ratner Breast cancer is common and yeah, uterine cancer is common. Uterine cancer is actually not a genetic cancer for the most part. The women we worry about are the ones whose family history includes women who got ovarian cancer pretty much at a any age or breast cancer before menopause. In the older days, again a few years back before Myriad had the Supreme Court hearing and they lost the patent for the

testing, it used to be really, really expensive. So we needed to have these very strict guidelines as to who can be tested because of insurance being able to approve it. That is no longer the case. Myriad is now just one of the companies who provides this test. We are now a little bit free in terms of ordering this test because it is much more affordable and many companies are able to do it, but I usually say seeing a genetic counselor has a lot of benefit, you do not need to necessarily get tested for genes, but they will help you understand your pedigree, they will help you understand what cancers run in the family and if you are at an increased risk for one cancer or another. I find genetic counseling an imperative part of this and if you have any concerns at all about your family history or that you might be at higher risk, I would urge you to start with them.

Gore And so, even among Ashkenazi Jewish women, not everybody should be screened for BRCA?

Ratner There is debate and there are some editorials that have been written that maybe everybody should; but the guideline right now is no – that of course not everybody should and we really should look at our family history, but yes, it is more prevalent, it is more common in Jewish Ashkenazi population, so it would not be unreasonable.

Gore I have to say my 23 and me, which I did, screened me for BRCA 1 and 2, I mean this is something that popped out and obviously it is not a medical test, but it was kind of interesting and I don't know if they do that for everybody or if they do that because I genetically identify. Interestingly, off the topic, but I did find that I am a carrier of an Ashkenazi associated deafness chain, and we have 2 friends in Baltimore, Ashkenazi Jews, and 2 out of their 3 children are deaf and there is no deafness in their family, so you never know, it is kind of interesting.

Ratner And we are actually learning so much now from 23 and Me or from Ancestry, you will be amazed how many women I am actually now manage or see who have a BRCA gene diagnosed in one of those.

Gore Is that the case, no kidding?

Ratner Yeah, all the time.

Gore Isn't it so interesting, people are doing this for mostly social reasons and for a long time they were not allowed to disclose their medical information, the FDA prohibited that for a while.

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- Ratner Right, but now women are learning not just about their ethnicity, but exactly as you said about the genetic mutations that they could have.
- Gore What is your feeling about that? I am just kind of curious because they are not getting genetic counseling there and you get this thing in an e-mail and it says by the way...
- Ratner I would freak out. I am again a very huge believer that knowledge is power. And now I just wish that 23 and Me and these companies would actually put in a next line saying this is what you have, this is what you should be doing, you should get screened, you should see a genetic counselor, and if you are like most people in Connecticut they are finding their way to appropriate genetic counselors or GYN oncologists or breast oncologists with this information.
- Gore That's really interesting. I had not actually expected that, but like I say it happened to me in this way, I don't know what I would have done that with that information when we were having kids, although I suppose I might have had my wife screened.
- Ratner And this is just the beginning, we are just at the infancy of this information. We know so much more now than we knew 6 months ago, and I think this is only going to be growing bigger and I think it is a wonderful thing.

Dr. Elena Ratner is an Associate Professor of Obstetrics, Gynecology and Reproductive Sciences at Yale School of Medicine and Co-Chief in the Section of Gynecologic Oncology. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer here on Connecticut Public Radio.