Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.

Welcome to Yale Cancer Answers with Doctor Anees Chagpar. 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’s a conversation about gynecologic cancers with Doctor Elena Ratner. Dr Ratner is a professor of obstetrics, gynecology and reproductive sciences at the Yale School of Medicine, where Doctor Chagpar is a professor of surgical oncology.

So, Elena, maybe we can start off by you telling us a little bit about yourself and what it is you do.

Sure, I take care of women with ovarian cancer, uterine cancer, cervical cancer, and vaginal cancer. My passion is early cancer detection and even more so cancer prevention, which is really the future and I would argue, the present, of cancer treatments. I have a lab that deals with drug development and new novel targeted therapies for ovarian cancer.

The treatment of ovarian cancer nowadays is so different from what
it used to be in the older days. We now truly believe in targeted personalized care and that is very much what I do and how my practice runs and that is what my lab does as well. I also have a great interest and again, a passion for survivorship and taking care of women who are fighting cancers or have fought cancers, and are survivors. I am a cofounder and a director of a sexuality and menopause program for Smilow where we take care of women who are going through hormonal changes to aid them in their quality of life and survivorship. Wow, that's a lot. So let's dig into a few of those things. To start with, you mentioned a variety of cancers, cervical cancers, vaginal cancers, uterine cancers, ovarian cancers. It seems like there are so many cancers associated with the female gynecologic and reproductive system. And yet they're all a little bit different. So can you talk a little bit about the epidemiology of all of these cancers,
how often do they occur and a little bit more about how we can, as you say in terms of prevention and early detection, how we can either prevent or detect these cancers early. It seems that they all might be a little bit different in terms of how easy that is to do, some might be more of the silent cancers and some might be things for which we have ready screening tests. That’s a wonderful question. So you are so right, gynecologic cancers are diverse. Last month actually marked gynecologic cancer month. And yes, we are always going to be aware that gynecologic cancers there are so many different cancers that are part of it. So let’s take it 1 by 1. So cervical cancer that is the cancer that is more commonly associated with the HPV virus, this is the kind of cancer where Pap smears play a very important preventative role. The good thing about cervical cancer
0:04:00.174 –> 0:04:02.915 is that usually it is pretty slow
0:04:02.915 –> 0:04:05.896 growing and as long as you keep having
0:04:05.896 –> 0:04:08.436 pap smears routinely per protocol,
0:04:08.44 –> 0:04:10.648 usually we’re able to catch a
0:04:10.648 –> 0:04:12.565 great majority of these cancers
0:04:12.565 –> 0:04:14.415 in the pre cancer stage.
0:04:14.42 –> 0:04:16.805 The HPV vaccine very much
0:04:16.805 –> 0:04:19.19 changed the entire nature of
0:04:19.19 –> 0:04:22.035 cervical cancer and cervical cancer became
0:04:22.035 –> 0:04:25.65 much less common and luckily we see
0:04:25.65 –> 0:04:28.507 very little of it in this generation
0:04:28.507 –> 0:04:32 of women who were vaccinated for the
0:04:32.094 –> 0:04:35.088 HPV virus with the vaccine.
0:04:35.09 –> 0:04:38.219 This HPV vaccine really is one
0:04:38.219 –> 0:04:41.9 of the few incredibly successful
0:04:41.9 –> 0:04:47.675 examples of cancer prevention in this cancer.
0:04:47.68 –> 0:04:50.455 Uterine cancer is the most
0:04:50.455 –> 0:04:52.12 common gynecologic cancer.
0:04:53.341 –> 0:04:55.783 Here in the states we have
0:04:55.783 –> 0:04:58.279 an epidemic of obesity.
0:04:58.28 –> 0:05:00.398 Obesity unfortunately increases
0:05:00.398 –> 0:05:05.34 women’s risk of having endometrial
0:05:05.442 –> 0:05:08.306 cancer very significantly because
0:05:08.306 –> 0:05:12.602 estrogen is produced by this adipose
0:05:12.706 –> 0:05:16.58 tissue when we have extra obesity.
0:05:16.58 –> 0:05:19.142 So that contributes.
0:05:19.142 –> 0:05:20.85 Diabetes contributes.
0:05:21.263 –> 0:05:24.154 But the good news with endometrial cancer
0:05:24.154 –> 0:05:27.249 is that usually women have symptoms.
0:05:27.25 –> 0:05:29.548 And that is actually the most
0:05:29.548 –> 0:05:31.08 important thing about endometrial
cancer, is that women are always aware that once they reach menopause, if they start having bleeding again, that is not normal. And even though most women who do bleed after menopause actually do not have cancer, some do. And the good news about endometrial cancer is it’s very curable and usually detected very early as long as women know that kind of bleeding is abnormal and usually all you would need is just a biopsy and that would catch again usually either an early cancer or pre cancer. The most challenging cancer within the gynecologic cancers remains ovarian cancer. You know we call ovarian cancer the cancer, that whispers because it is very difficult to find these cancers early. My passion is early detection, prevention. So I actually do not believe that ovarian cancer whispers. I believe that it is not whispering, it is speaking and we’re just not listening to it. So early detection and prevention of ovarian cancer relies in huge part to advocacy and awareness and
not only teaching women about signs and symptoms of ovarian cancer, but making sure that women get the care they deserve.

There’s a lot of literature that women with ovarian cancer usually feel symptoms for a good six months to a year to even two years sometimes before the cancer is actually diagnosed. And there’s literature that women go from one provider to another provider before they are finally appropriately diagnosed. So it is very, very important for women to know that, especially around the time of menopause, especially a little bit later than menopause, if they start developing things like weight gain or their clothes not fitting well or some bowel symptoms or bladder symptoms, early satiety, eating a little and not being able to eat more, getting up at night and especially if these symptoms come kind of all at once, that is something that they need to be seen by their provider. There’s a lot of literature that there’s many different things that cause these symptoms that are not cancer.
And a lot of them are hormonal. But the difference between the women who experience these symptoms hormonally is that those symptoms come and go. The women who subsequently develop ovarian cancer, these symptoms usually happen every single day for two weeks. So it is very important for women to always be aware and listen to their bodies and when they listen to their bodies and present to their providers, for providers to be educated and to understand this kind of constellation of symptoms. That would require further workup. Prevention is key. You know, early detection is challenging. Prevention is so, so important because we know that many of these cancers are actually genetic and have certain genetic mutation that predispose women to these cancers. So that is why it is so important to know your family history and what genes you carry and do that kind of risk reduction from that knowledge. And then the last kind of group of gynecologic cancers that you had mentioned earlier were vaginal cancers and cancers of...
kind of the external genitalia. 
Those are often cancers that we don’t hear a lot about. 
Can you tell us a little bit more about those? 
Yeah, you’re exactly correct. Those cancers are much more rare. They are also commonly HPV driven and a lot of them also involve the cervix. But with more commonly either cancer of the vulva or pre cancer of the vulva. And again, luckily a lot of these are caught in the precancerous stage. And as long as women again are aware of their anatomy and aware if they have some ulcers or bleeding or some nodules on the outside of their body that doesn’t feel normal or feels new, that they should be seen by their provider and that lesion should be biopsied. Again, luckily, those are usually seen or felt, and usually they can be cured or even better, caught in the precancerous stages. So, you know, it sounds like really you need to be very concerned about getting an HPV vaccine if you can. If you meet guidelines for that, number 2, making sure that you get a a PAP smear on a regular basis and that you’re really paying attention to to symptoms.
Can you talk to us a little bit more about the HPV vaccine and who is eligible for it?

It seems to me that historically it has only been for young girls. And now the criteria have expanded for women who may not have had it before up to a certain age limit.

Can you talk more about that?

Yeah, absolutely.

So HPV vaccine, as I mentioned before, really just has been miraculous. You know, we have in the cancer industry talked about and thought about and researched vaccines for generations. This one truly made a tremendous difference.

You know from my world of clinical practice, I see cancer, cervical cancer or even cervical severe precancer so much more rarely now that this vaccine became commonplace.

And you’re exactly correct.

When this became available, it was for young girls from age 9 to 25. There was a lot of thought that we wanted to give it before girls were sexually active. Before they actually were exposed to HPV,
Now that this vaccine is actually indicated for women up to age 45. And there is some thought that even for women who have some sort of HPV strains that getting a vaccine would help them fight the other strains that they don’t yet have, especially if they have new partners and would be exposed to other strains of HPV. I wholeheartedly recommend the HPV vaccine, but not just to girls, but also to boys. Yeah, because it it sounds like it can certainly prevent a number of cancers. Talk to us a little bit more about screening. You had mentioned Pap smears, and many women know that they should be getting Pap smears but may not be familiar about things like, well, when should we start that and how often should we get pap smears? And when should they stop? And is it just a pap smear or do people do HPV testing at the same time? Can you help us to understand a few of those questions?

That’s a discussion that a lot of us have frequently. The guidelines for Pap smears have really been changing quite greatly over the years. And we understood that these...
Cancers are really HPV driven. We now understand that it’s really HPV that drives them. So right now, even more important than the Pap smear is the HPV testing. And for women who don’t have the HPV, for them, the Pap smear guidelines are much more relaxed. So that’s the key for that. And so we are going to pick up the conversation and learn a little bit more about screening and perhaps treatment right after we take a short break for a medical minute. Please stay tuned to learn more about gynecologic cancers with my guest, doctor Elena Ratner. Funding for Yale Cancer Answers comes from Smilow Cancer Hospital, where their liver cancer program brings together a dedicated group of specialists whose focus is determining the best personalized treatment plan for each patient. Learn more at smilowcancerhospital.org. The American Cancer Society estimates that more than 65,000 Americans will be diagnosed with head and neck cancer this year, making up about 4% of all cancers diagnosed when detected early, however, had a neck cancers are easily treated and highly curable.
Clinical trials are currently underway at federally designated Comprehensive cancer centers such as Yale Cancer Center and its Milo Cancer Hospital to test innovative new treatments for head and neck cancers. Yale Cancer Center was recently awarded grants from the National Institutes of Health to fund the Yale Head and neck Cancer Specialized program of Research Excellence, or SPORE, to address critical barriers to treatment of head and neck squamous cell carcinoma due to resistance to immune DNA damaging and targeted therapy.

More information is available at yalecancercenter.org.
HPV testing is really important and it may influence what the guidelines are for PAP tests. Can you tell us a little bit more about that? The thing with Pap smears and really how I look at all cancer treatment, prevention, testing, screening, everything has to be personalized. You know, we are now living in an era where not everybody should be treated exactly the same. Everything should be individualized, everything should be personalized. So we use these guidelines that are available. But again, I wholeheartedly feel that these are just guidelines and depending on specific presentation history, family history, concerning symptoms, think these screening tests could be done more frequently. But the guidelines are now much more relaxed. We start checking Pap smears at age 21. Regardless of when the patient first starts having intercourse. Women who are 21 to 29 can have pap smears alone every three years. HPV testing alone can be considered for women who are aged 25 to 29, but Pap smear tests are still preferred. But then the bigger
group is women aged 30 to 65, and those women have three options for testing. They can have a pap smear and an HPV test every five years. That is kind of what’s preferred. Again, HPV is really associated with these cancers or precancers, so it’s important to test. Or they can just have a pap smear by itself every three years. Or they can have HPV testing alone every five years. And again, the thinking for this is that so many of these cancers are HPV driven and HPV is actually a very common virus. A lot of women in their 20s will have positive HPV Pap smears and those actually don’t matter that much because it is super prevalent. The ones that matter are the ones that are long living. So that’s why we don’t routinely start checking HPV or worrying about HPV until after age 30, because a lot of women will get the HPV and then their body will clear it, we worry about and we watch more closely.
those HPV infections that stay after age 30 and then those we watch and we just check the Pap smears together with them. Because again, whatever this is, this is usually pretty slow growing and as long as you keep checking pap smears and HPV typing at these kind of intervals, we will catch it usually in the precancerous stage. Let’s talk a little bit more about treatments and you had mentioned that everything should be personalized and in terms of not only the screening but also treatment. So for cervical cancer, for example, if you should find a precancerous lesion, how is that treated? How do you kind of go about thinking about the management of cervical cancer. Much in the world of gynecologic cancer has become better, better and smarter and personalized and individualized and much less aggressive. Nowadays we are able to replace big aggressive, radical surgeries that we used to do in the older days, 7-10 years back, we’re now able to replace the surgeries which much less aggressive,
much more quality of life centric procedures.
So for cervical cancer or moreso for surgical precancer, there’s many procedures that are available. We do these surgeries frequently for women who are young, who still want to have kids, and we’re able to make that happen. We’re able to do procedures which are fertility sparing and get rid of the precancer. But even in the world of ovarian cancer, which is again kind of the most difficult cancer that we deal with, we used to do this big surgical debulking where patients would stay in the hospital for weeks. Now we can do the same surgeries laparoscopically or robotically where women can go home the next morning. So the paradigm of ovarian cancer and really gynecologic cancer is really changing drastically and in a wonderful way. And so tell us a little bit more about the management of these cancers. So in the older days, five years back, we used to treat all these cancers in a very similar fashion.
The women would be diagnosed with this cancer, then they would have surgery and then they would have a standard chemotherapy. Nowadays, not only are we making great advances with advocacy and awareness and having women know exactly what to look out for and make sure that they’re getting the perfect care. But then they can have really personalized robotic, still radical but very minimally invasive surgery. And after that we do not treat cancers the same. We study the cancers, we take them out, we take them to the lab, we study them for multiple mutations and then we treat specifically that woman. And because her cancer is not the same as the cancer of somebody else, we treat specifically her tumor and we’re able to do so with targeted therapies in addition frequently to standard therapy that also has great success. But we’re able to know exactly what mutations that patient has and especially what mutations her tumor has and we’re able to target them specifically.
And not only will that allow us to treat the cancers better to get better outcomes, but as important, it also allows for better quality of life. And it allows women to continue living their lives with much less toxicity and much less side effects, and that’s fabulous.

But one of the things that people often fear about ovarian cancer is that it does tend to be deadly in terms of prognosis. Can you talk to us about how the prognosis of ovarian cancer has changed over the past five years, if it has? And what that kind of looks like.

So yeah, so the prognosis is improving. Women are living longer, the proportion of women who are cured is somewhat higher, and I really think that is all because of the treatments that we have been able to come up with and develop and use during this time, you know, for example.

In this search for genomic or germline mutations, we now are able to identify a subset of patients who are very sensitive to certain targeted therapies such as immunotherapy, such as something called PARP
inhibitors and the woman who have these mutations, who benefit from these treatments do marvelously. There’s really miraculous outcomes that we have had over this period of time with this new targeted therapies specifically for women who have these mutations. The improved prognosis and the improved survival is all due to that, to the fact that we are treating these things in a better way, in a smarter way and we’re able to test better and know who are the right candidates for specific targeted therapies and I think that’s only going to get bigger and it’s only gonna get better. There’s so many trials that are happening right now looking at a whole different variety of targeted therapies. And again, it’s not for everybody. Not every target is for everybody. That is the future. That is the importance of this to understand the personal approach to what this particular tumor carries and then be able to treat it with a specific drug,
specific medicine for that specific tumor. So important in terms of really promoting clinical trial participation so that we can offer patients the latest therapies that really might be targeted to their particular tumor. One of the things that I often think about in terms of ovarian cancer is the fact that in part because of, as you say, a lack of awareness, so many of these ovarian cancers present late, they present at stage 4. With distant metastatic disease, has the prognosis of those patients also improved with these therapies?

Can you talk a little bit more about metastatic ovarian cancer? Yeah. So the great majority of ovarian cancers unfortunately present manifestation exactly as you said in stage three and stage four. So all the cancers I talked about up to now with better prognosis and targeted therapies is actually about those cancers. So yes, for women with advanced disease which is very frequently how these are diagnosed, prognosis is better, therapies are better, toxicity is better, but it is really the key to curing ovarian cancer. The key to eradicating ovarian
cancer is early detection. It is education, it is awareness, education for the providers. Because if these cancers are diagnosed in stage one and stage 2, the great majority of them are cured. So that is why in addition to drug development and in addition to everything else that we do in the lab to try to understand the therapy and resistance to chemotherapy it is so important to concentrate on early detection because that truly saves lives. I think that there’s two key messages there, right? The first one is that if you have been diagnosed with metastatic ovarian cancer, the first piece of key message that I think that you pointed out is that all is not lost to that, that things are improving and that there is still hope and the 2nd is about the concept of listening to your body and trying to find these cancers earlier, but a lot of the symptoms that you had mentioned earlier are things that are really common. So is it that people should be
0:27:12.658 -> 0:27:15.214 paying more attention to that when
0:27:15.214 -> 0:27:17.734 they’re post menopausal or can
0:27:17.734 -> 0:27:20.238 ovarian cancer occur at any age so
0:27:20.238 -> 0:27:22.489 that you know if you are feeling
0:27:22.489 -> 0:27:24.307 like you are having early satiety
0:27:24.307 -> 0:27:26.532 and that your clothes aren’t fitting
0:27:26.532 -> 0:27:28.392 right and you’re having bloating
0:27:28.45 -> 0:27:30.282 and so on and that’s been going on
0:27:30.282 -> 0:27:32.61 for a couple of weeks but you’re
0:27:32.61 -> 0:27:34.088 pre menopausal you should still
0:27:34.088 -> 0:27:36.244 get that checked out or you may
0:27:36.244 -> 0:27:38.212 be feeling like that might be like
0:27:38.212 -> 0:27:40.46 being a bit of a hypochondriac.
0:27:40.46 -> 0:27:42.294 So can you help us with that
0:27:43.15 -> 0:27:44.044 wonderful question.
0:27:44.044 -> 0:27:46.726 So I think it’s important to
0:27:46.726 -> 0:27:49.026 remember that the lifetime incidence
0:27:49.026 -> 0:27:51.446 of ovarian cancer is 1.4%,
0:27:51.446 -> 0:27:53.384 which is wonderful.
0:27:53.384 -> 0:27:56.37 So yes, a great majority of women
0:27:56.37 -> 0:27:59.489 who have these symptoms will not have cancer.
0:27:59.49 -> 0:28:02.226 They will only have hormonal changes.
0:28:03.25 -> 0:28:06.31 But women who do develop cancer,
0:28:06.31 -> 0:28:09.35 almost 100% of them say they knew it.
0:28:09.35 -> 0:28:10.358 So that’s the key.
0:28:10.358 -> 0:28:12.14 It doesn’t matter how old you are,
0:28:12.14 -> 0:28:14.174 doesn’t matter what stage of your
0:28:16.4 -> 0:28:18.496 life, you know your body better than anybody else.
0:28:18.5 -> 0:28:21.196 And don’t let anybody tell you otherwise.
0:28:21.2 -> 0:28:23.696 If you feel that something is not right,
0:28:23.7 -> 0:28:25.724 you go and you seek help
see your provider and you have a pelvic exam and you just make sure that you’re being heard.

Doctor Elena Ratner is a professor of obstetrics, gynecology and reproductive sciences at the Yale School of Medicine. 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. We hope you’ll join us next week to learn more about the fight against cancer here on Connecticut Public Radio. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.