

Healthline with Yale Cancer Center

Hosts

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WTIC Newstalk 1080

Advances in the Treatment of Ovarian Cancer

Guest Expert:

Peter Schwartz, MD

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Healthline with Yale Cancer Center is a weekly broadcast on WTIC Newstalk 1080

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This is Healthline. A joint venture of WTIC News Talk 1080 and Yale Cancer Center. Yale Cancer Center is a resource for cancer programs throughout Connecticut developing new advances in prevention, screening, diagnosis and treatment. On Healthline, you will hear from some of the leading doctors in the country. Healthline is not intended to provide medical advice. Yale Cancer Center urges you to consult with a qualified physician in your community for diagnosis and for answers to your medical questions, and now, our co-hosts, oncologists, Ken Miller and Ed Chu.

Miller Good morning and welcome to Healthline. My name is Dr. Ken Miller, and I am the Director of the Survivorship program at the Yale Cancer Center in New Haven. I am here in the WTIC studios with my colleague and co-host, Dr. Ed Chu, who is the Chief Adult Oncologist at the Yale Cancer Center. Good morning Ed.

Chu Good morning Ken. Healthline with the Yale Cancer Center is our way of providing you with the most up-to-date information on cancer care every Sunday at 8:30 a.m. on WTIC Newstalk 1080. Our Healthline program features some of the nation's leading oncologists and cancer specialists who are in the forefront of the battle to fight cancer right here in our State of Connecticut.

Miller Each week, Ed and I will be joined by a different expert from the Yale Cancer Center. Together we will discuss the myths about cancer, the latest treatment available to people with cancer, and advances in clinical research. Our goal is to give you help and hope by answering your questions and giving you the latest information on cancer care. If you would like to submit a question to us or to our guest, you can email us at Healthline@yale.edu, or you can call 1-888-234-4YCC. Again, we will try to answer your questions on line either today or on a different program.

Chu Today our program focuses on recent treatment advances for ovarian cancer. It is my great pleasure to introduce our special guest, Dr. Peter Schwartz, the John Slade Ely Professor and Vice Chair of Obstetrics, Gynecology and Reproductive Sciences at the Yale School of Medicine. Dr. Schwartz is one of the nation's leading experts in the treatment of ovarian cancer. Peter, thanks so much for being with us today on Healthline.

Schwartz Thank you very much Ed.

Miller Peter, I want to start off asking you, how common is the diagnosis of ovarian cancer?

Schwartz In the United States, the ovaries are generally described as the fifth most common site for women to develop cancer, and ovarian cancer is the fourth most common cause of death from cancer in the United States.

Chu What is ovarian cancer, and what does it involve?

- Schwartz Ovarian cancer is a disease that starts on the surface of the outside of the ovary. It can grow locally and invade the local tissues in the pelvis. It can spread around the abdominal cavity and into the [lymphatic system](#). Unlike other tumors, such as breast, colon, or lung cancer, it doesn't spread through the blood stream. So patients with ovarian cancer develop symptoms related to the pelvis and to the abdominal cavity, and the disease tends to stay in those areas throughout the patient's lifespan.
- Chu What are some of the typical symptoms that a woman might complain about?
- Schwartz A number of years ago it was thought that this was "the silent disease." That is, there weren't any symptoms associated with ovarian cancer. But starting in the year 2000, based on a survey that was done including 1,700 American and Canadian women, it's clear, ovarian cancer is associated with symptoms. They are subtle and they are easily confused with other conditions. Typically, abdominal bloating, distension, vague non-specific abdominal complaints, urinary frequency, are the symptoms that women experience. The problem is they can easily be confused with irritable bowel syndrome. About 20% of Americans have irritable bowel syndrome, but only about 25,000 women are diagnosed with ovarian cancer each year. That is a huge difference, and it's easy for the patient to ascribe the symptoms to be due to something unrelated to the reproductive tract. The ovaries themselves don't cause pain. It's easy for the doctor to ascribe the problems to be due to something other than reproductive tract.
- Chu If a woman should experience any of the symptoms that you have just described, who should they seek medical attention from?
- Schwartz Many women use obstetricians/gynecologists as primary care physicians, particularly while they are still in the reproductive age, but I think that once a woman gets into the postmenopausal era, there is a tendency to shift their care to primary care doctors, internists and family doctors. If a patient has unexplained abdominal discomfort that persists for more than two weeks, pelvic pain, pressure on the bladder causing urinary frequency, she must demand a pelvic examination to begin the evaluation for possible ovarian cancer.
- Miller Some of these symptoms are for women who have ovarian cancer that has become very, very evident. There may be a tumor there that is putting pressure on the bladder. Is there a way to screen for earlier detection?
- Schwartz The screening process is really not well developed. About 5-10% of American women will have an inherited susceptibility toward ovarian cancer. Based on family histories, a number of sites, Yale included, have set up early ovarian cancer detection programs. Ours was one of the first, if not the first, in the United States. We look for women who have first degree relatives, mothers, sisters, or, God forbid, daughters with ovarian cancer. That makes them eligible for the program. There is a National Cancer Institute program that is directed through the [Gynecologic Oncology Group](#) where we are the number two contributor to the program in terms of patient accrual. In general, if you are not in the family syndrome where there are a lot of women with breast and some with

ovarian cancer, it can be difficult to recognize whether you are at an increased risk for the disease. We did a study in Connecticut in which we looked in the seven largest hospitals over a two-year period of time. The women at highest risk were Caucasians. There were no non-Caucasian women with ovarian cancer in any of those hospitals during that time period. The second greatest risk was having a first degree relative with ovarian cancer. In that study, the risk was 18 fold higher. We now know through national studies, it's about 3 ½ fold higher than those who don't have such relatives. We also know that having children has something to do with reducing your risk for ovarian cancer. So a woman with no children in Connecticut has five times the risk of someone with five or more children. Someone with 1-2 children has twice the risk.

Miller Are there any environmental factors or dietary factors that increase the risk of ovarian cancer? Along those lines, is there anything that women can do to reduce their risk?

Schwartz To begin with, we don't recognize any particular dietary factors. There had been studies years ago looking at breast cancer patients, and whenever there are breast cancer studies, there is always a spin off for ovarian studies. One study suggested that a high lactose intake may be associated with the development of the cancer. It has never really been borne out. What we know are the factors that can reduce the incidence of ovarian cancer in the population as a whole. The major factor is reducing the number of ovulatory cycles a woman experiences in her lifetime, and that can be accomplished in a variety of ways. The first way is to have children. When you are pregnant you don't ovulate. Second, is breast feeding. People talk about the benefits to the child regarding breast feeding, but there is also a tremendous benefit to the mother. When a mother breast feeds she also doesn't ovulate so you prolong that period of ovulation. The third way to reduce risk is to use birth control pills, particularly for five or more years. Birth control pills work by telling the brain, the ovary is making plenty of hormone. It doesn't have to stimulate the ovary to release eggs. So there are hormonal ways to reduce ovulation, and they seem to reduce the risk of ovarian cancer significantly. The final way, based on some small studies and then the very large Nurses' Health Study, is to have a [tubal ligation](#). We don't understand the mechanism. I have a lot of thoughts about it if you want to hear them, but basically interrupting that passageway between the outside and the inside also reduces the risk of ovarian cancer significantly.

Chu Are there any dietary interventions, Peter, that have been shown to be effective in perhaps reducing the risk?

Schwartz Not to my knowledge. Although people have looked at reducing animal fat in their diet as one way of doing it. It's not clear if that works well for ovarian cancer.

Miller Is this a myth or this is the truth? Many women feel that when they are over age 65, they don't need a [pap smear](#) or a pelvic exam. Is that truth or a myth?

Schwartz I would put that high in the myth category. One thing that is very clear to us is that we are more successful in curing people with ovarian cancer when we find the disease early,

when it's confined to the ovary. The pelvic exam is not a terrific way of identifying ovarian cancer early, but it really saves lives and it cures people.

Having the patient go see her obstetrician/gynecologist or primary care physician for a pap smear after age 65, if she has not had abnormal pap smears in the past, probably isn't crucial. But getting there, getting that pelvic exam, being able to discuss symptoms, being encouraged to get the annual mammogram, being encouraged to get a colonoscopy, that's all part of good health care, and that's what we expect our obstetrician/gynecologists and our primary care physicians to provide as part of that annual pelvic exam.

Miller We would like to remind you to please email your questions to us at Healthline@yale.edu, or call us at 1-888-234-4YCC. We are going to take a short break for a medical minute. Please stay tuned for more information about the treatment advances in ovarian cancer with Dr. Peter Schwartz from the Yale Cancer Center.

This is a medical minute brought to you as a public service by the Yale Cancer Center. Breast Cancer is the second most common cancer in women. In Connecticut alone, approximately 3,000 women will be diagnosed with breast cancer this year. But there is new hope for these women. Earlier detection, non-invasive treatment and novel therapies provide more options for patients to fight breast cancer. In 2006 more women are learning to live with this disease than ever before. Women should schedule an annual mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection and a healthy lifestyle, breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as the Yale Cancer Center to make innovative new treatments that have not yet been approved by the Food & Drug Administration available to patients. For more information, visit their website at YaleCancerCenter.org, that's www.yalecancercenter.org

Miller Welcome back to Healthline with the Yale Cancer Center and WTIC. This is Dr. Ken Miller, and I am in the WTIC studios with my co-host, Dr. Ed Chu, and our guest, Dr. Peter Schwartz, who is an expert in the treatment of ovarian cancer.

Chu Peter, before the break we were talking a little bit about the potential role of Pap smears and screening. I am wondering if you could elaborate a bit more on the screening methods that are currently being recommended to see if women might have ovarian cancer.

Schwartz The National Cancer Institute has come across with some policy statements recommending that women only undergo ovarian cancer screening if they have a strong family history of ovarian and breast cancer. But there are only two routine tests currently available to try to identify ovarian cancer early. One is an ultrasound usually done by the endovaginal route, and the other is [CA 125](#), a blood test that measures the molecules in the bloodstream. The problem with the CA 125 test is that it can be elevated for a lot of benign gynecological conditions, and it is also elevated in conditions like liver disease and heart disease. We have had a patient with an overactive thyroid with excessive fluid,

which caused an elevated CA 125. It is not specific. It probably would work better in postmenopausal women without benign gynecological problems that are not going to interfere with the test.

Chu Peter, I understand your group here at Yale has been at the forefront of trying to develop new serum markers that might be able to detect ovarian cancer at an earlier stage. I was wondering if you could elaborate on that?

Schwartz We have a Discovery to Cure program, and it starts with basic science research. We then go into a translational research lab, and finally we apply it to the patients who are participating in our research programs. Dr. Gil Mor, an MD/PhD in our gynecological oncology laboratory, has looked at both proteins associated with inflammation in the bloodstream and proteins associated with cancer. He has been able to identify a profile of four proteins that are either excessively expressed or under expressed in the bloodstream. After a series of studies this is now going to a national trial. Labcore has a patent on it, the NCI is studying this through the National Early Detection Research Network, and we are very excited about this as possibly a marker for the early detection of ovarian cancer.

Miller It sounds like it will be a wonderful advance in detecting the disease earlier.

I want to read you an email that we received from Judy who lives in Terryville:

My doctor found this cyst on my ovary. How can I feel confident that this is not cancer, and does the cyst put me at high risk of developing ovarian cancer?

Schwartz If you are in the reproductive age, we know that [cysts](#) are very common. So what we want to know is what this cyst looks like. Usually the doctor finds it because he or she has done an ultrasound. If the cyst looks like a simple cyst, a thin walled cyst like a balloon filled with water, that's benign. If it has multiple solid and cystic elements in the tumor, that's when we get worried about cancer. But in reproductive age women, [endometriosis](#) can give you false positives and a variety of benign ovarian cysts can give you that appearance. In postmenopausal women, cysts less than 5cm are very common. It is estimated that 20% of women who are age 60 will have ovarian cysts if you look hard enough for them. The overwhelming majority will be less than 3cm in diameter. Again if those cysts look like a balloon filled with water, that's benign.

Miller Do those pose a risk of turning into cancer?

Schwartz We have no knowledge that those simple cysts ever turn into cancer. One of the real problems with ovarian cancer is that we don't recognize a pre-cancerous phase. It's not like cervical cancer where you do a Pap smear to pick up the pre-cancerous changes, or even breast cancer where there are pre-cancerous changes. Ovary doesn't express that, or at least, we haven't recognized it.

Chu We have a very interesting email from Chris who lives in Orange. She writes:

My mother and grandmother are both ovarian cancer survivors, and I have read that women with a strong genetic link to ovarian cancer may choose to have their ovaries removed in an effort to prevent the disease. Is this recommended?

Schwartz It is recommended, but some further evaluation for Chris would be appropriate. There is a test looking for genetic mutations in the [BRCA1](#) and [BRCA2](#) gene, and Chris has a 50% chance of having inherited one of those two mutations if in her family, her mom or grandmother, have one of those mutations. As far as being followed versus prophylactic ovariectomy, this should be based on further evaluation.

Chu I think it's important to note that we have a very superb genetic counseling office led by Ellen Matloff at the Yale Cancer Center, and any woman who fits in this category should seek genetic counseling, wouldn't you say so Peter?

Schwartz As part of our own ovarian cancer section program, Chris would be qualified. Ellen would be someone we would send Chris to for the genetic counseling part of it.

Miller Again, we would like to remind you to please email us your questions at Healthline@Yale.edu. We are going to take a short break to listen to a survivor's story. Please stay tuned to learn more information about ovarian cancer with Dr. Peter Schwartz.

A few years ago the diagnosis of cancer was a death sentence for many patients. But today, thanks to advances in clinical research, we are turning a corner in the battle against cancer. There are over 10,000,000 cancer survivors now living in the United States. They are the true heroes in the war against cancer. Here is the story of a hero from Fairfield.

I visited a walk-in clinic on Christmas Eve in 1999 because I thought I had the flu. The doctor there suspected that it was something more serious, and as he examined my belly he found a mass. I was referred to Dr. Tom Rutherford, a gynecologic oncologist and researcher at Yale Cancer Center where I had surgery and received chemotherapy for Stage II ovarian cancer. Because of early detection, excellent treatment and the benefit of the latest research, I recently celebrated 6 years as a cancer survivor. Today I am a fervent believer that women should pay attention to changes in their bodies, and should not be reluctant to tell their physicians any concerns they have, even those they feel might sound trivial. Early detection is the best way to cure cancer.

This survivor story has been brought to you by Yale Cancer Center.

Miller Welcome back to Healthline. This is Dr. Ken Miller, and I am in the WTIC studio with my co-host Dr. Ed Chu, and our guest Dr. Peter Schwartz, and we are talking about some of the latest breakthroughs in the treatment of ovarian cancer.

Peter, throughout your career as a gynecologic oncologist and surgeon, what advances have you seen in terms of surgical treatment of this cancer?

Schwartz The major advance in surgical treatment of ovarian cancer has to do with the advanced stage diseases. There is no question that aggressive cytoreductive surgery, meaning making a maximum effort to take out the entire tumor, is now recognized worldwide as the initial first step in the treatment of the advanced stage ovarian cancer. That's been the biggest breakthrough, the acceptance of that kind of a surgical procedure.

Miller I am going to ask you a question that I think women think about when they are diagnosed. Is this a curable disease when it's advanced?

Schwartz Across the board, it is a curable disease, but our success rate is highest, of course, when it is confined to the ovary. Unfortunately, about 70% of women don't have ovarian cancer recognized until it has advanced into the upper abdomen and they are subsequently diagnosed with Stage III or Stage IV disease. In that group of women, the standard treatment is aggressive cytoreductive surgery. That is the cancer surgery I just talked about, followed by intense chemotherapy. And about 20% of the women will be cured, but many women now will live much longer because the other major breakthrough has been the introduction of effective chemotherapy. We started with the platinum agents back in 1979, and most recently the introduction of the Taxanes has really increased the time period that woman will live, even with advanced disease that is not going to be cured.

Chu Earlier this year there was a great deal of attention in the media about a report coming from the Gynecology/ Oncology group showing that the use of interperitoneal chemotherapy added greatly to intravenous chemotherapy. Perhaps you could explain to our listening audience what that means.

Schwartz Giving the chemotherapy into the abdominal cavity, the peritoneal cavity, is the approach that the GOG (Gynecologic Oncology Group) used. In the third of three trials they have reported positive results. The concept really is two-fold. First, ovarian cancer doesn't spread through the blood stream, so you attack it in the region rather than attack the whole body. The second is that you can give much higher doses of chemotherapy into the abdominal cavity without causing as many side effects and disruption of the quality of life as when you give similar doses intravenously.

The GOG, in their initial trial, used agents that we don't currently use today as standard therapy, so people disregard the first trial. In the second trial, they had given a lot of intense intravenous chemotherapy first, and then gave the intraperitoneal, so we kind of disregarded that one. But in the most recent trial, they used very intense intraperitoneal chemotherapy along with intravenous [cisplatin](#), and they compared it to cisplatin and [Taxol](#), the two standard drugs given intravenously. They found that the women who had optimum cytoreduction, women who went through that big operation we talked about, they had virtually no tumor left behind and did significantly better than those who did not get the interperitoneal chemo.

Chu So based on that study, are you using this approach in patients who you see here at Yale New Haven?

Schwartz Nothing is as simple as it would seem even in *The New England Journal of Medicine*. It turns out that a previous [Gynecologic Oncology Group](#) study using the standard agents we use at Yale-New Haven intravenously, cisplatin and Taxol, gives an even better survival than the interperitoneal treatment regimen that was used in the most recent *New England Journal of Medicine* article.

I believe we still have to learn the best way to use IP therapy.

Miller I want to ask you about the drug [Avastin](#). We have talked on this program about the use of Avastin in breast cancer and in colon cancer. It's a very exciting drug. Is that being used in ovarian cancer, how does it work, and is that something you think is going to add to our armamentarium?

Schwartz With ovarian cancer, we now have a protocol first line from the Gynecologic Oncology Group that does use Avastin. It is used in women when we can't get all of the cancer out. So that represents a small but definite group of women. Avastin is an anti-vascular endothelial growth factor (AEGF), and it seems to play a role in ovarian cancer. There is a bit of a hedge however, and that is that 3 of 66 women who were treated in the early GOG study with Avastin developed spontaneous bowel perforations. We don't know why this happened, but we do know that all 3 had resections of the sigmoid colon, and so just as with the IP chemotherapy, one has to be careful in how you select it. It is now being recommended not to be used with the first cycle of this regimen, but be introduced once everything is healed up with the 2nd cycle. But it still is a research drug in the world of ovarian cancer. We still have to define its role.

Chu What are some of the really exciting clinical trials that your group is trying to develop at the Yale Cancer Center?

Schwartz Through the Discovery for the Cure Program, Dr. Gil Mor was able to identify a planisoflavinoid from Australia that is called phenoxodiol. It has some wonderful properties including being able to reverse the resistance of cancer cells to carboplatin, a very common drug that we use as part of ovarian cancer management. We took that drug from the laboratory into a Phase I trial, a trial where we just looked to see what doses were tolerated, and we were able to find some responses with patients with recurrent ovarian cancer. We then did a Phase II trial where it appears that many of the women have had responses to the phenoxodiol and now the FDA is in the process of approving an international study using phenoxodiol. Twenty five centers in the United States will participate in that trial, plus a number of Centers abroad.

Miller How can a woman access this kind of cutting-edge research in clinical study?

Schwartz They can call our gynecologic oncology clinic at 203-785-4176. That's where we see our patients. They will be directed to the right parties.

Chu Or, if you are computer savvy, you can go onto the www.yalecancercenter.org website.

Miller Let me ask about targeted therapies. That is the sort of word we are using in oncology now. Are there any other therapies that you think are going to be very important ones in the future?

Schwartz Obviously, this is a field that is beginning to open up. At the last GOG meeting I attended, there were over 150 targeted therapy agents now being evaluated by pharmaceutical companies; 50 are being incorporated into ovarian cancer trials. The biggest problem about molecularly targeted therapy is that used alone it doesn't seem to be very effective in solid tumors like ovarian cancers. So when used in single agent trials to date, there hasn't been a dramatic response. The best responses appear to be a combination of conventional cytotoxic chemotherapy, the standard chemo we have used, in conjunction with molecularly targeted therapy. There we are seeing much more activity.

Miller We have an email from Tina who lives in Middletown and she says:

I am a 5 year survivor of very early stage ovarian cancer and I am curious to know if I am at greater risk of developing other types of gynecologic cancer, like cervical cancer?

Schwartz That's an interesting question. We generally see two populations of women. One group tends to get the glandular cancers which includes ovary, uterine cancer, breast and colorectal cancer. The second group gets the squamous cell cancers, those are the lung, cervix, vulva, vagina, esophagus, the sorts of cancer often associated with cigarette smoking. I think her risks are for a the glandular type cancers. If she is a young woman with an early stage disease, she may have had fertility saved. We always worry about the other ovary. We are concerned about the uterus in terms of pelvic reproductive cancers.

Chu As this is Colorectal Cancer Awareness Month, I would also just emphasize to Tina, especially if she is over the age of 50, that she also is at increased risk for developing colon cancer. So if she hasn't gone out to get her colonoscopy screening, she should do that as well.

Miller That is good advice, and Peter, I think what you were saying earlier is important, that we should all remember that other types of screening are important as well. I think gynecologists have been wonderful throughout the years in reminding patients of this.

If you have questions for Dr. Peter Schwartz, I encourage you to email us at Healthline@yale.edu. Visit our website: www.YaleCancerCenter.org for more information about cancer and resources available to you.

Before we sign off for today's program, what are the key messages that women listening to this program and their families should remember and think about in terms of ovarian cancer.

Schwartz In terms of ovarian cancer, one must remember that there are symptoms. They are vague but they are unexplained, persistent, abdominal discomfort, pressure on the bladder causing urinary frequency, and sometimes some change in bowel habits. If that is something that persists for more than two weeks, seek help. That's really important. And demand a pelvic exam as part of your evaluation.

Chu Again, for those who are interested in learning more information on ovarian cancer, visit our website: www.YaleCancerCenter.org or call 203-785-4176.

Miller I would like to thank Dr. Peter Schwartz for joining us today at Healthline.

Chu This was a terrific session again. Thank you. And remember, tune in to WTIC Newstalk 1080 every Sunday morning at 8:30 for Healthline with the Yale Cancer Center. Our next program will focus on the role of the immune system to treat cancer, and our special guest will be Dr. Richard Edelson, Director of the Yale Cancer Center, an internationally known expert in the field of cancer immunology and cancer immunotherapy. Until then, this is Dr. Ed Chu

Miller and Dr. Ken Miller

Chu from the Yale Cancer Center wishing you a safe and healthy week.