

## Healthline with Yale Cancer Center

*Hosts*

Edward Chu, MD Chief of Medical Oncology

Kenneth Miller, MD Director of Supportive Care

WTIC Newstalk 1080

### The Detection and Treatment of Ovarian Cancer

#### Guest Expert:

**Thomas Rutherford, MD**

*Associate Professor of Gynecologic  
Oncology*

*Yale School of Medicine*



*Healthline with Yale Cancer Center is a weekly broadcast on WTIC Newstalk 1080  
Sunday Mornings at 8:30*

*Listen live online at [www.wtic.com](http://www.wtic.com) or*

*Listen to archived podcasts at [www.yalecancercenter.org](http://www.yalecancercenter.org)*

*This is Healthline. A joint venture of WTIC NewsTalk 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 most up-to-date information on cancer care every Sunday morning at 8:30 a.m. here on the station WTIC NewsTalk 1080. Our Healthline program features some of the nations 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. We would like to give you help by sharing information. We would also, again very important, share with you our hope, because cancer is a disease which is treatable and curable. We will answer your questions and give you the latest information on cancer. And if you would like to submit a question about cancer to Healthline please email us at [Healthline@Yale.edu](mailto:Healthline@Yale.edu) or you can call and I would ask you to write down this number, 888-234-4-YCC. And, we will try to answer your questions on the air today or in the future broadcasts.

Chu Today our program focuses on the advances in the detection and treatment of ovarian cancer and our special guest is Dr. Tom Rutherford, Associate Professor of Gynecologic Oncology and a leading expert in the detection and treatment of ovarian cancer here at the Yale Cancer Center. Tom, thanks so much for being with us today on Healthline.

Rutherford Thank you.

Miller Tom, I would like to start with a brief overview. Basically, what is ovarian cancer and how common is it?

Rutherford Ovarian cancer is not a very common tumor and, basically we need to look at what age group the cancers occur in. In the younger age group, these are ladies in their teens, 20s, and early 30s, they develop a type of ovarian cancer called a [germ cell tumor](#). These tumors are seen in young women

and they are entirely different than what we think about as an ovarian cancer. When we think about an ovarian cancer, we think about the [Gilda Radner Ovarian Cancer](#), which is an [epithelial type of tumor](#). These generally occur in women of 45 years of age and older. They are tumors that are unfortunately detected later. The ovarian epithelial tumors, the Gilda Radner Ovarian Cancer, these tumors are broken down into two types, one being the epithelial, like what we think about with Gilda Radner, and the second one being what is called a borderline type of ovarian cancer. This is still an ovarian cancer but it is treated differently than the way we treat epithelial tumors are treated.

Chu Tom, for the most common form of ovarian cancer, which I gather is the epithelial type, the Gilda Radner type, what are the main risk factors?

Rutherford The bottom line is that we do not really know what causes ovarian cancer. We do know, however, that there appears to be a genetic link through the [BRCA 1](#) and [BRCA 2](#) genes. We know that these tumors occur in families, meaning people who have family histories of ovarian, breast, colon, prostate, and pancreatic cancer are at higher risk. These tumors occur as a genetic subset in families and a lot of times we don't know why they occur. They can be carried both through male and through female lines. If mom had it or grandmom has had an ovarian cancer and I am the son and don't have any daughters and I have a son and pass it on and my female grandchildren could then have ovarian cancer. It can pass on right through the male.

Miller Thank you for answering that. But, I want to go back over this again, because I think it is fascinating and very important information, because there is a myth that many women believe and that there is not a risk of developing ovarian cancer if there is no family history or that there is not a risk if it is not on your mother's side of the family. So, can you go back?

Rutherford Yes, that is correct. Most ovarian cancers we know today are what are called sporadic ovarian cancers. That means they occur and we don't know why or if there is any previous history. A good number of patients have no previous history of ovarian cancer in their family. They may have a large history of a breast cancer, they may have a large history of colon cancer, but some of these people have absolutely no history at all of cancer at all. The risk of ovarian cancer is 1 in 70 in the general population and if you compare that to breast cancer which is 1 in 8 you can see that it is much less common and that is why it is often much harder to detect.

Chu And if women do have mutations in the BRCA 1 or BRCA 2 gene, how much does that increase their risk of developing ovarian cancer?

Rutherford If you have a mutational defect, BRCA 1 or 2, the risk can be up to 85% based upon an age of 85. So, if the whole population lives to 85, there is a very high risk of developing ovarian cancer.

- Chu And, if a woman should have, for instance, a prior history of breast cancer and also has the mutation, either BRCA 1 or BRCA 2, does that then place that woman at increased risk for developing ovarian cancer?
- Rutherford Actually it does. In a BRCA 2 positive patient, the risk does increase significantly for a [fallopian tube](#) cancer, which is consistent with an ovarian cancer. The fallopian tubes and the ovaries are very close, coming off of the uterus, and many times they are indistinguishable from one another until the surgery is performed and the tumor mass is reviewed by pathology and they pinpoint where it started.
- Miller Tom, who should be screened for ovarian cancer?
- Rutherford There is definitely a high-risk population that needs to be looked at, and the Ashkenazi Jewish population is known to have an increase in mutations and an increase in ovarian cancers. People with family histories of ovarian, breast, colon, prostate, and pancreatic cancers, should be screened. A patient who has colon cancer or breast cancer is at higher risk for an ovarian cancer. But the real answer is probably the entire population. Through routine gynecological examination that should be performed. As a part of the examination, a routine pelvic exam is done and that should be done on a yearly basis.
- Chu Tom, if there is a very strong family history of ovarian cancer, are there any genetic tests that can be done, and what do we have here available at the Yale Cancer Center?
- Rutherford The [CA125](#) test is a blood test that is done.
- Chu Maybe you can tell us a little bit more about what CA125 means and stands for?
- Rutherford The CA125 is a serum blood test. It is used to monitor or follow response in women with ovarian cancer. It is one of the more common tests that everybody thinks about, when they think about ovarian cancer, like the PSA test in prostate cancers. The problem with the CA125 is that patients who have early stage, stage I and II ovarian cancer, most of the time, or 40% to 50% of the time, do not have an elevated CA125. Unfortunately, patients who come in with advanced cancer, which is stage III or IV, often do have elevations in the CA125. As a result, we are using it not so much for screening, but to determine whether the treatment we are providing is beneficial. Now, at Yale we have come up with a new blood test. This test is looking at blood markers or proteins in the blood that may be elevated if a patient has ovarian cancer. We currently have this test out. It has been marketed to LabCorp who is in the process of making the test available on a national level. Currently we are evaluating patients. We take a blood test, we run the test, and we see if there is an elevation in these blood markers. Based on the results, it gives us some indication if there is evidence of a tumor.

- Chu            Would your prediction be that as we look into the future we will be able to use a blood test like this to be able to detect ovarian cancer earlier and will that have an impact on the cure rate?
- Rutherford    I believe in time, we are going to be able to detect these tumors much earlier than we can currently. The test is currently looking at patients who do have cancer and patients who are in a screening program that we have here at Yale. We have been able to determine that a patient has recurrent disease prior to the disease being picked up by routine CA125, physical exams, CAT scans or any evidence of symptoms from the disease. We are also able to determine when a patient has an elevation and by using an ultrasound found out that she had a very small nodule on an ovary which, at first I did not think to be malignant, and then it turned out that, yes, she did have an early ovarian cancer all the time that the CA125 was normal. The other problem with the CA125 I want to tell you about is the problem of the false positive elevation. The CA125 can be elevated due to menses, pregnancy, endometriosis, diabetes or anything that causes irritation of the abdominal cavity such as diverticular disease in the older age. That is actually one of the big problems with that serum test. The new test that we are developing does not have false positive elevations.
- Chu            Tom, maybe let us just take a step back and go back to the basics for our listening audience. What are some of the symptoms that are typically associated with ovarian cancer?
- Rutherford    The problem with ovarian cancer, it is a disease that whispers. You go out to dinner, you had a spaghetti dinner, and have a little bit of acid from the dinner and it goes away the next morning. Two weeks later you have some fish and it just didn't quite sit right. And then you have a little bit of abdominal pain but you were lifting something. And this goes on for month after month, after month. Ultimately, people who are having changes in their bowel or their bladder function, people having persistent recurrent abdominal pain, people who have abdominal bloating need to have a pelvic evaluation, because if you look at the people with ovarian cancer many times patients are found to have had symptoms for 6-9 months prior to being diagnosed. But it is a disease that whispers.
- Miller        We would like to remind you to please email your questions to us at [Healthline@Yale.edu](mailto:Healthline@Yale.edu). You can also call us. We are going to take a short break for a Medical Minute. And please stay tuned to learn more information about the detection and treatment of ovarian cancer with Dr. Tom Rutherford from the Yale Cancer center.

#### *Medical Minute*

*This is a Medical Minute brought to you as a public service by the Yale Cancer Center. Cancer patients become cancer survivors the first day they are diagnosed. There are over 10 million cancer survivors in the US and the numbers keep growing. However, there are long-term side effects of cancer including heart problems, osteoporosis, fertility issues, impaired growth and an increased risk of second cancers. Ending cancer treatment can be both exciting and scary. Most people are relieved to be finished with the demands of treatment. But, many also feel concerned*

*about whether the cancer will come back and what they can do to prevent a relapse. Cancer survivors require long term specialized care and support. For more information long on to [www.YaleCancerCenter.org](http://www.YaleCancerCenter.org).*

Miller Welcome back to Healthline. This is Dr. Ken Miller and I am in the WTIC Studios with my co-host Dr. Ed Chu and our guest Dr. Tom Rutherford, who is an expert from the Division of Gynecologic Oncology at the Yale Cancer Center.

Chu Tom, we were just talking about the symptoms associated with ovarian cancer and you were really emphasizing the point that ovarian cancer is a whispering disease. It does not really present with typical symptoms. How does ovarian cancer get diagnosed?

Rutherford Many times what happens is a patient is seen first by their primary care physician and they are treated for the flu or a GI bug, then that persists and they are sent to a GI physician who often does the colonoscopy or the upper GI series. The symptoms continue and then they get a CAT scan. So, it is an accidental diagnosis. Because many times these masses are much smaller than a pregnancy. So, you don't see a big mass or the abdomen becoming enlarged. Many times, however, as the patient is going through the long process of diagnosis, all of a sudden she has a massive accumulation of fluid in the abdomen called [ascites](#) and the massive bloating that occurs that is what tips off an advanced ovarian cancer.

Miller Tom, it has been exciting to hear about some of the new screening techniques that are available and are becoming available and especially about the work that is being done at Yale in terms of screening. But for women who are diagnosed with early stage ovarian cancer, what is the treatment?

Rutherford The treatment for an ovarian cancer is basically surgical excision and staging of the disease, which means what we want to do is take out the primary tumor. If she is in child bearing years yet, you want to do the surgery if it is limited to that ovary; you also want to look at the lymph nodes along the major vessels in the abdomen and the pelvis. There is a fat pad that hangs off the stomach called the omentum, our tumors often go there, so we would sample that area as well. And again, if pregnancy is a thing that we need to think about, and there is no other disease, we would do what is called a conservative surgery, meaning we leave the other ovary if it looks normal and the uterus. If the lady is not thinking about future fertility, we would do a complete [hysterectomy](#) and remove the uterus, cervix, tubes, and ovaries, as well as the lymph nodes and the omentum.

Chu So, Tom once the surgery has been performed, is there any role for giving [adjuvant chemotherapy](#) afterwards?

Rutherford If a patient has tumor confined to the one ovary, if that tumor is what is called a well-differentiated tumor, she may not need to have chemotherapy. But if the tumor is stuck in the pelvis, meaning it

is a little more than stage I or if there is more disease or if it is a high-grade disease, an adjuvant chemotherapy would be appropriate for that patient.

Chu Earlier this year there was a great deal of buzz that was coming out of a recent study showing that intraperitoneal chemotherapy seemed to confer advantage to woman following surgery. Perhaps you could elaborate on that for our listening audience.

Rutherford The intraperitoneal chemotherapy study was performed in patients with advanced disease. So, it was not an early disease trial. If you look at survival on the patients with stage 1 to 2, we actually do very well, because we are able to resect the disease in total. And our survival probably, in our hand, is better than 85%..

Miller Tom, we are going to take a break in a minute, but I did want to share with you an email that we received. It is from Ann who lives in Branford. She says,

*I am 36 years old, I have been under treatment for infertility for 3 years. At what point should I become concerned with the possibility that the fertility drugs could cause ovarian cancer?*

Rutherford There has been some documentation and literature that fertility drugs may increase your incidence of cancer. The rate of risk would be minimal at best. So, what we would need to do is to follow her closely on routine examinations twice a year. But the real question is, does the drug cause an increase in cancer risk or is it the primary infertility that is really the cause? The answer is, we don't know.

Chu In follow up to that question and a bit of a twist, is there any evidence to suggest that estrogen supplementation might increase the risk for developing ovarian cancer?

Rutherford Actually no, in fact patients who are on birth control pills will decrease their risk of ovarian cancer significantly. The other thing that decreases the risk of ovarian cancer is a [tubal ligation](#) prior to the age of 35. The interesting thing with tubal ligation is that it also decreases your risk of developing breast cancer.

Miller This is fascinating information. We are going to take a break in a minute for a Survivor's Story. We would like to remind you to please email your questions to us at [Healthline@Yale.edu](mailto:Healthline@Yale.edu). Again, we are going to take a short break and then we will be back with Dr. Tom Rutherford to learn more about ovarian cancer.

#### *Survivor's Story*

*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 the corner in the battle against cancer. There are*

*over 10 million cancer survivors now living in the US. They are the true heroes in the war against cancer. Here is the story of a hero from Gilford.*

*My name is Kathy, I am a cancer survivor, and I am the mother of 3 girls. I was diagnosed with breast cancer at age 40. I had had my baseline mammogram at 36. But with no family history of breast cancer, I was told to return when I was 40 for another mammogram. I got the diagnosis that no one prepares you for, cancer. But I was lucky, I was referred to the Yale Cancer Center where I met Dr. Lannin and I underwent a double mastectomy in the summer of 2004. I still take tamoxifen daily but have been cancer free ever since. If there is one message that I want to convey to all women, it is to get a regular mammogram. I am a perfect example of how early detection is part of the cure.*

*This Survivor's 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 Studios with my co-host Dr. Ed Chu and our guest Dr. Tom Rutherford who is an expert in the detection and treatment of ovarian cancer at the Yale Cancer Center. Tom, I wanted to start out by asking about woman who has more advanced ovarian cancer and the treatment available to them. We were talking a couple of minutes ago about how some women have surgery and then have chemotherapy. For women with advanced ovarian cancer, do you ever do it the other way around?

Rutherford Yes, we do. It is called [neoadjuvant chemotherapy](#). If we have a patient that we do not deem to be surgically resectable due to the volume of disease usually up around the gallbladder fossa or into what is called the mesentery, which is support tissue of the bowel, we would treat that patient with chemotherapy. Once, we have the disease shrunk down then we would take them to the OR to surgically perform the original surgical staging that we do routinely for an ovarian cancer. After which, we would put them back on chemotherapy. This is actually a treatment modality that was originated at Yale by Dr. Peter Schwartz. It has actually led to the treatment of many other advanced cancers such as colon and breast cancer, using the same modality.

Chu Tom, I know that you played a very leading role in developing new clinical trials for the treatment of patients with advanced metastatic ovarian cancer. Please discuss our listeners what is going on in your clinical investigations program.

Rutherford Currently, we have a drug called phenoxodiol. We started with phenoxodiol in the laboratory using cells lines that had been treated with phenoxodiol to see the effect that it has. And, what we found is that it causes cell lines to die. And the question was why? If you have a normal cell, it should undergo what is called apoptosis at the end of its life. A cancer cell has lost the ability to do apoptosis, which is programmed cell death; all cells need to do this. And the reason that the cancer cell becomes problematic is loses the ability to die. What we found is that this drug phenoxodiol will reverse one of the blockers to apoptosis allowing the cell to go on and die. The

other thing we found is that, if you take that blocker off that pathway and then treat the patient with chemotherapy you need much less chemotherapy to effect the same response as using chemotherapy alone. So, phenoxodiol seems to be a biologic modifier of a pathway to let a cell go on and die.

Chu And, I think what is really fascinating about this drug phenoxodiol, which apparently comes from a plant in Australia, is that it is able to reverse the development of drug resistance and restores chemo-sensitivity. As a pharmacologist, I think this is just fantastic.

Rutherford That is absolutely correct. We have a trial that we just completed looking at patients who are either platinum, meaning cisplatinum or carboplatinum or [Taxol](#) or Taxotere, resistant. We put them back on phenoxodiol and retreated the patients with the drug that they were resistant to and affected a response in about 40% of the patients, a pretty good response rate. We currently are looking at how to give the drug phenoxodiol. As with any new product, you are never sure, should you give it using an IV or should I give it orally? So, we have another trial looking at patients who have been previously treated and have recurrent ovarian cancer and we are placing them on oral phenoxodiol along with a drug called Taxotere, which is a cousin to Taxol.

Miller If these drugs are effective in reversing the resistance to this terrific chemotherapy drug and the treatment of the ovarian cancer, might they eventually be helpful when used earlier for women who are first diagnosed with ovarian cancer?

Rutherford The thought would be yes, but we obviously do not have the trial to prove that yet. Phenoxodiol is currently going to a national clinical trial. It is a phase 3 trial and it is being piloted through the NCI. There are going to be about 12 or 15 sites involved and I would expect that this trial will begin sometime this fall. So, at Yale, we have been able to take this drug from the laboratory all the way through to a phase 3 clinical trial in approximately 4 years of time.

Chu Which is really fantastic because in terms of classic drug development, the whole process may take up to 8-10 years. It looks like you have really been able to accelerate the process. I think the other very interesting aspect of phenoxodiol is that, in addition to being very effective in ovarian cancer, it looks like there is also pretty promising activity in other cancers as well. Is that right?

Rutherford That is correct. It seems to show some activity that it can reactivate the apoptotic pathways.

Miller Tom, one of the programs that I have heard about at Yale but don't know much about is the Discovery to Cure Program. What is that?

Rutherford Discovery to Cure is a program for the early detection and screening of ovarian cancer. And what we are trying to do is to detect the cancer before it becomes an advanced stage, which obviously is difficult. Using a Pap smear, we know if we screen for cervical cancer, if we find it earlier, we

cure it. What we are looking at are the blood tests that we have developed. We also have several experimental blood markers that we are looking at or blood proteins we are looking at that seem to have major impact too. So, I think the test is actually going to expand and hopefully become even more sensitive. Currently, the sensitivity and specificity is 95%, which is very good. When you think about it, a Pap smear is 66%. We have hopes that we will be able to detect ovarian cancer at an early stage. And, so far we have been able to determine that some women have been picked up with an early ovarian cancer using this test.

Chu If someone in our listening audience or their family or friends wants to participate in a clinical trial or in a screening trial, how would they get in contact with you or the Yale Cancer Center in terms of participation?

Rutherford We have two ways, you can call our office directly in GYN Oncology at (203)-785-4176 or you can go to the [YaleCancerCenter.org](http://YaleCancerCenter.org) website.

Miller Tom, in terms of other clinical research that is being done at the Yale Cancer Center and in GYN Oncology, are there any other clinical trials that you would like to tell us about?

Rutherford We are member of the [Society of Gynecologic Oncology](#) group. Currently, we have about 16 open trials running. These trials are not only looking at different chemotherapy modalities and new drug therapies, we are also looking at modalities to improve or decrease the toxicity of the drugs. Some of the trials we are looking at are from China to decrease nausea with chemotherapy. We have trials looking at, does chemotherapy or surgery affect the thought processes? We have trials looking at, does chemotherapy affect the bone density in patients? Because obviously once I cure you, I want you to have your normal bone density. We have other trials looking at, can I predict what the cancer cell will respond to such that if give you a drug I know that that cancer will respond that drug. And, we have two trials available, one being with Precision Therapeutics looking at the sensitivities of tumors to different therapies, and the second thing we are doing is looking at a compound called 9088. I know that if a tumor has this protein, it will be resistant to taxane therapy.

Miller If you have questions for Dr. Tom Rutherford or for Healthline, I encourage you to go to our website [YaleCancerCenter.org](http://YaleCancerCenter.org) for more information about cancer and the resources available for you. Before we sign off, Tom in your opinion, what are the key points that you would like to share with the listening audience about the detection and treatment of ovarian cancer?

Rutherford I think any patient that is having persistent gastrointestinal discomfort and upset needs to be evaluated by a GYN physician and if determined that she does have a GYN cancer she should be seen by a GYN oncologist.

Miller I would like to thank Dr. Tom Rutherford for joining us for Healthline for this very, very interesting session.

Chu I too also would like to thank Tom for a very, very informative session for our listening audience. And remember tune into WTIC NewsTalk 1080 every Sunday morning at 8:30 a.m. for Healthline with Yale Cancer Center. Our next program will focus on Cancer Prevention and our special guest will be Dr. Susan Mayne, Director of the Cancer Prevention and Control Program at the Yale Cancer Center. 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.