

Yale CANCER CENTER *answers*

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Hosts

Anees Chagpar MD
Associate Professor of
Surgical Oncology

Francine Foss MD
Professor of Hematology

Steven Gore MD
Director of
Hematological
Malignancies

Endocrine Oncology

Guest Expert:
Glenda Callender, MD

*Assistant Professor of Surgery in Endocrine
Surgery, Yale School of Medicine*

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Welcome to Yale Cancer Center Answers with your hosts doctors Francine Foss, Anees Chagpar and Steven Gore. Dr. Foss is a Professor of Medicine in the Section of Medical Oncology at the Yale Cancer Center. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital and Dr. Gore is Director of Hematological Malignancies at Smilow. Yale Cancer Center Answers features weekly conversations about the research diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. This week you will hear a conversation about endocrine oncology with Dr. Glenda Callender. Dr. Callender is Assistant Professor of Surgery in Endocrine Surgery at Yale School of Medicine. Here is Dr. Steven Gore.

- Gore I do not think people really think of endocrine organs as cancer, like diabetes we think of, what do you do?
- Callender I am an endocrine surgeon, so I operate on the three main endocrine organs, at least they are the three main organs if you are an endocrine surgeon, the thyroid, the parathyroid and the adrenal glands. There are lots of different types of disorders that can affect the endocrine organs and some of them are certainly cancers, but there are other things that can happen to the endocrine organs as well.
- Gore What would typically be the kind of surgery someone would need for these endocrine organs?
- Callender When we talk about the thyroid, very often we are operating out of a concern for cancer or because there is a definite cancer in the thyroid, but sometimes, the thyroid can make too much thyroid hormone or there are other specific reasons why the thyroid would need to come out. When it comes to the parathyroid glands, cancer is actually very, very rare, although it can happen, but typically we are operating for a disorder called hyperparathyroidism.
- Gore That is a lot of syllables.
- Callender It certainly is. It is actually quite complex too, but it basically just means that one or more of these little tiny parathyroid glands have started to grow too large and it causes the patient's calcium to be too high, so it is really not a concern for cancer as much as a problem related to the function of the glands.
- Gore It is not a good thing for calcium to be too high?
- Callender No, actually, the calcium level is very important for the body. Pretty much all of your body's functions are controlled based off of calcium levels and so when the calcium levels are too high, all sorts of things can happen, patients can feel really bad for one, they can develop kidney stones, pancreatitis, ulcers and also they can develop very severe osteoporosis and bone fractures. And we do not think people really want any of those things and it can be prevented or reversed if it is caused by the parathyroid glands by a successful parathyroid surgery.

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- Gore Interesting, so I assume that among those three organs, thyroid problems would be the most common, is that right?
- Callender Yes, by far the most common. Parathyroid problems are also pretty common, primary hyperparathyroidism is actually found in up to 2% of women who are postmenopausal, so it is actually fairly common. Adrenal problems are the least common problems that we see. Sometimes, it is just a growth that somebody has been discovered to have in their adrenal glands and sometimes the growth can produce hormones and cause all sorts of different kinds of problems, but adrenal problems are a lot rarer than thyroid or parathyroid problems.
- Gore Fascinating, so you are operating on these organs whose main job is to produce hormones and hormones are pretty potent substances as I recall, so it seems like you must need a certain amount of expertise to be able to manage the medical complications, or do you always work with a medical endocrinologist when you are operating?
- Callender We very commonly work closely with our endocrinology colleagues. You are right. Certainly, unlike other organs that do have specific functions, but you can take them out and they are just less difficult to manage, I would say, the endocrine organs really do have to be very carefully managed medically because the hormones that they produce either have to be given back in the form of a pill or there is some form of management that we have to do, but yes, our endocrinology colleagues are absolutely critical to us being able to do our jobs. That is one of the things about an endocrine surgeon, part of training to be an endocrine surgeon includes becoming familiar with the medical management of these disorders either before or after the organ has been removed.
- Gore I know many people may be familiar with overactive thyroid gland because classically people sometimes have bulging eyes or racing heart beats, is that the usual things that people are symptomatic with when their thyroid gland is overactive?
- Callender What you are referring to is Graves' disease which is actually an antibody that your body makes to the thyroid and it makes the thyroid produce too much thyroid hormone which sort of revs the body up too much and that antibody also reacts with some tissue behind the eye which causes the eyes to bulge forward. Graves' disease is the most common type of overactive thyroid problem, but there are others. Typically though patients are found because they develop symptoms and they go to the doctor and somebody checks. Occasionally, somebody might go in for something else and have some thyroid test checked and be found to have hyperthyroidism or an overactive thyroid but that is less common.
- Gore And hyperthyroidism is not always managed surgically right, there is a lot of medical managements for that?

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Callender Correct, yes, for Graves' disease specifically there are actually some medications that can be used temporarily and radioactive iodine is sometimes an option and surgery is sometimes an option, so it really depends on the actual picture of a particular patient.

Gore How would I know if I needed thyroid surgery then, I mean, in general, obviously I do not go around saying, I wonder if there] is something wrong with my thyroid today.

Callender The most common reason why somebody would need thyroid surgery is if there is a lump in their thyroid or a nodule and many of them are found these days because patients are going in for all sorts of other types of studies and somebody says, well you know the carotid arteries look fine, but there is something over here in the thyroid, but if you are wondering if you have something wrong with your thyroid, really the best thing to do is just at your next visit with your primary care physician, ask them to do an exam of your thyroid, just feel it with their fingers.

Gore Really with your fingers?

Callender Yes, if there is a substantial amount.

Gore No scan needed?

Callender Well, if they feel something with their fingers, then they would proceed to get an ultrasound and then maybe a biopsy, but if you did an ultrasound on every single person out there, we would find thyroid nodules in almost half and in fact by the time women are postmenopausal, let us say over age 50 or so, more than half have thyroid nodules, so you have to almost be careful with what you find, because if you go and do an ultrasound on everybody, then all sorts of people are going to need to have more ultrasounds and biopsies and all of a sudden all sorts of thyroids are coming out and maybe it was a small nodule that would have never caused any problems anyway. So if it is something that is going to cause you problems it should be able to be found on a physical exam by your primary care physician.

Gore So I go and see my doctor for my annual physical, let's say, and not because I am worried about my thyroid because I never worry about my thyroid since I am not a postmenopausal woman for better or for worse, I would be postmenopausal if I were a woman but I am not, anyway, so I am not worried about my thyroid, my wife probably should be, sorry about that, anyway when I go to see my internist and he examines me and finds a lump, now should I be terrified? When I hear lump and nodule that usually strikes terror into me.

Callender No, a nodule is a growth and growths can be benign or growths can be malignant.

Gore Isn't a benign growth when the doctor wants to make you feel good?

Callender It actually has to with whether or not the growths can spread to other parts of the body. So if it is
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benign, it does not have any risk of spreading, but sometimes it still needs to be removed surgically, but many times it does not, but if it is a cancer, of course, it usually needs to come out. You should not be terrified though if somebody finds a nodule on your thyroid because the vast majority of nodules, let us say more than 95% are benign. So, yes if a nodule is found, it may need to be evaluated with a biopsy or something using a fine needle, but in the vast majority of cases when all is said and done, it can probably just be observed.

Gore Do I have to go to a surgeon to get this biopsy done?

Callender No, typically the endocrinologist or a radiologist will do the biopsy. They would typically inject a tiny amount of numbing medicine and then use a very fine needle to pass the tip into the nodule. They use ultrasound so that they can see the tip going in. Then, they suck out some cells from the nodule, score them on a slide and send them off to the pathologist for the pathologist to look at under the microscope.

Gore And the pathologist, first of all, can they always tell if it is cancerous or not based on the biopsy?

Callender No they cannot, unfortunately. The thyroid is a very complicated organ from that perspective because unfortunately some of the features of thyroid cancer look just like the features of thyroid inflammation, and so, in certain times, the pathologist can say, this is definitely benign and other times the pathologist can say, this is clearly cancer, but many times, the biopsy will actually fall into a gray area somewhere in between and in some cases, it is okay just to watch because the risk of cancer is low, but sometimes the risk of cancer is higher and then the whole nodule has to come out and so that is the type of patient who would end up needing surgery.

Gore Now I seem to remember from medical school, which was quite a long time ago, that sometimes it was recommended that if they were not sure if a nodule might be malignant or not, I could be remembering this incorrectly, but to give thyroid hormone to suppress the growth. Is that something that is still done, sort of as a test?

Callender That is not really done as much anymore.

Gore See, I am showing my age.

Callender Well, that is okay, your age and your concerns over being a postmenopausal man.

Gore There you go.

Callender You have got lots of issues today.

Gore Exactly.

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- Callender What we found over time was that giving thyroid hormone to try to suppress thyroid nodules and make them shrink did not really work too well and so nowadays that is not really done as often.
- Gore Got it. So you do the scan, you do the biopsy and then you decide if this is something that can be watched or if we need to have the growth taken out and then is that something where you can excise just the little nodule or are you taking a piece of the thyroid or the whole thyroid, what is usually involved?
- Callender Typically if the whole nodule needs to be removed, the part of the thyroid in which the nodule is lying has to be removed as well. For example, if it is a small growth that is on the right side of the thyroid, usually that would mean that the entire right lobe of the thyroid or the right half of the thyroid would have to come out. It is unusual to be able to take out just the nodule because the thyroid is a very bloody organ and typically we need to take the whole blood supply and then remove that side in order to make surgery safe.
- Gore And does that usually cure the patient then if it is cancerous?
- Callender Well if it is cancer, very often we will recommend removing the entire thyroid as well as some lymph nodes. Removing only half of the thyroid is typically done for nodules that we think have a reasonable chance of being benign, but yes, in the case of thyroid cancer often removing the thyroid with the appropriate lymph nodes will be a cure. Thyroid cancer has a very good prognosis compared with other types of cancers, at least the most common forms of thyroid cancer do, and so many patients undergo surgery and potentially radioactive iodine afterward and are cured over the course of their lives.
- Gore Then why are you giving the radioactivity?
- Callender The thyroid is an amazing organ because thyroid cells and thyroid cancer cells are actually the only cells in the body that take up iodine, so let us say that we are doing a thyroidectomy, that means removing the thyroid for thyroid cancer, and we take out some lymph nodes and the pathologist evaluates everything under the microscope and the pathologist finds that the thyroid cancer is, however big it is, but let us say there has been some spread to the lymph nodes that were removed, well that tells us that the thyroid cancer has started to spread outside of the thyroid and so it could have spread farther away than that, maybe to the lungs or the liver or the bones, so giving the radioactive iodine allows the whole body to receive a treatment for thyroid cancer.
- Gore That is fascinating and we will definitely want to talk more about this and other endocrine cancers after the break, but right now, we need to take a short break for a medical minute. Please stay tuned to learn more information about endocrine cancer from Dr. Glenda Callender.

Medical

Minute Breast cancer is the most common cancer in women and in Connecticut alone approximately 3000
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women will be diagnosed with breast cancer in 2014 and nearly 200,000 nationwide, but there is new hope. With earlier detection, noninvasive treatments and novel therapies, there are more options for patients to fight breast cancer than ever before. Women should schedule a baseline 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, Yale Cancer Center and at Smilow Cancer Hospital at Yale-New Haven to make innovative new treatments available to patients. Digital breast tomosynthesis, or 3D mammography, is transforming breast screening by significantly reducing unnecessary procedures while picking up more cancers and eliminating some of the fear and anxiety many women experience. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. More information is available at yalecancercenter.org.

Gore Welcome back to Yale Cancer Center Answers. This is Dr. Steven Gore and I am joined tonight by our guest, Dr. Glenda Callender, and we are discussing endocrine cancers. Glenda, before the break, you were telling me about the use of radioactive iodine in patients where you took the thyroid out for thyroid cancer because you are worried that the thyroid cancer might have spread to other organs. Couldn't you do scans of the lung to see if there was any spread and just avoid the radioactivity?

Callender Yes, you can to some degree. Thyroid cancers are a little unusual because unlike other cancers, for example, lung cancer or esophageal cancer in which you would do a scan before any type of surgery in order to find out if there were spread away from the cancer, with thyroid cancer, the most common type of scan that we use is actually a radioactive iodine scan and the problem with trying to do that scan when a patient still has the thyroid in is that all of the radioactive iodine is taken up by the thyroid and it glows really brightly. But there may be a small focus of thyroid cancer in the lung that would not shine brightly at all.

Gore Gotcha.

Callender Because of the big bright thyroid, so in thyroid cancer, we actually do that type of scan after the thyroid and lymph nodes have already been removed in order to see if there has been any kind of spread.

Gore And then you only use the radioactive iodine if you see spread?

Callender No, typically it depends on the size of the nodule, so if it is a big cancer or if there has been spread to lymph nodes and we do that because we know that in those situations the chance of there having been a few cells that spread somewhere else that we would not even be able to see on a scan, that chance is high enough that the radioactive iodine is warranted and the side effects of radioactive iodine are very low overall when

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you compare it to the type of chemotherapy that is used for other types of cancers. So in patients who have a large cancer or spread to lymph nodes, typically all of them will get a dose of radioactive iodine.

Gore I see, and you say that sometimes that actually cures the patient for good?

Callender Yes.

Gore Interesting. Now, just to clarify for our audience, I think a lot of times when people think of lymph nodes, they are thinking of lymph nodes that are taken out from the arm for people who have breast cancer, and I guess people who have had swollen glands when they have had strep throat or something, but you are talking about lymph nodes that are near the thyroid gland?

Callender Yes, these are lymph nodes in the central part of the neck in most cases, so they are actually taken out through the same small incision on the front of the neck that we use to take out the thyroid gland. In some cases, there can be spread to lymph nodes out farther on the side of the neck and so it requires a larger incision to remove those lymph nodes. Lots of people worry that taking out lymph nodes will cause them to have more infections or something like this later in life. And the truth is that we just do not see that with removing lymph nodes from the neck for thyroid cancer, and the type of swelling that people get when they have lymph nodes removed for breast cancer, let us say, or for melanoma, we do not see that very commonly in the neck either. So, really removing the lymph nodes is something that is associated with a pretty good outcome.

Gore Not a big deal.

Callender Not a big deal, yes, in most cases.

Gore Now I may be outdating myself again in terms of my medical knowledge, but when I was in medical school back in the day, I seem to remember that the parathyroid glands were these tiny little things kind of stuck in the back of the thyroid. Is that still the case?

Callender Yes, that is still the case. The parathyroid glands have not changed since you were in medical school.

Gore: I am so relieved.

Callender They are four tiny little glands, two on each side. A normal one is about the size of a grain of rice and they are a funny yellow color and yes, they are right on the back of the thyroid, an upper gland and a lower gland on each side. They are so small and they look so insignificant but they are actually really important because they control the level of calcium in the body, so little tiny glands make us jump through a lot of hoops, actually.

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Gore What do you have to do to preserve them because I guess if we just took out the thyroid, you would take them out with it?

Callender Yes, until the parathyroid glands were discovered and until surgeons figured out how to preserve them, people died after thyroid surgery because their parathyroid glands would be removed or the blood supply would be cut off and patient's calciums could become dangerously low and they could die. Today, of course, knowing where the parathyroid glands are and what they do, we just have to be very careful. One thing I love about thyroid and parathyroid surgery is how delicate it is and what you have to do is just carefully dissect these little tiny glands off of the thyroid and preserve their tiny delicate blood supplies, so it is a challenge, but it is a fun challenge.

Gore You leave them in the neck?

Callender Yes, we typically leave them right where they are with their blood supply on. They are really incredible little glands though because if in the event that we accidentally cut off the blood supply to one, which occasionally happens, you can be as delicate as you can be but sometimes there is nothing you can do or sometimes we have to remove them because if we did not, we would not be able to get out all of the lymph nodes, but in those circumstances, we can actually mince that little gland up into tiny pieces and pop it back into a muscle right there in the neck and it can grow a new blood supply and do its job, so all is not lost, but we do try to be as delicate as we possibly can with those tiny glands.

Gore It is fascinating. Is there anything new going on in the management of thyroid cancer?

Callender There are some new things going on. Here at Yale, we actually have a new study that just started a couple of months ago where we are looking at patients who have very small thyroid cancers, less than 1 cm which is just about a little under half an inch. In patients who have such small thyroid cancers, we do not really know what the right thing to do for them is. Traditionally, we would take out the whole thyroid as well as some lymph nodes, but in some patients, we wonder if maybe that is too much. We actually know from autopsy studies, so studies in which patients died of something completely other than anything to do with their thyroid, we know that if you look at the thyroid very carefully under the microscope, maybe up to a third of all people on earth are walking around with a very small thyroid cancer sitting in there and we know that in most patients these cancers never do anything. They just sit there for the rest of their lives, so is it overkill to take out the whole thyroid? Most patients tolerate taking out the thyroid very well but some people just do not feel great after their thyroid has been removed, so other institutions have looked at maybe taking out just half of the thyroid, and there is an institution in Japan that has actually been just observing these small thyroid cancers with ultrasounds over many years and they find that most of them just sit and really do not do too much. Now in our country, we do not like to just observe cancer. We like the idea of treating a cancer, so taking out just one-half of the thyroid might be a good option, but we thought, is there something we could do that is even less invasive than that and that is why we started this trial. We are actually looking at injecting the thyroid cancers with

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alcohol in order to ablate them, basically in order to kill off the thyroid cancer cells and we are going to compare a group of patients who undergo that treatment with patients who undergo standard surgery. We are not expecting to see any difference in terms of their survival from cancer, because little tiny thyroid cancers like that have such an excellent prognosis, but we are expecting to maybe see some differences in terms of how people feel after they undergo the alcohol injection versus after they have undergone the whole thyroid surgery.

Gore You expect they will feel better if they have only had the alcohol?

Callender Yes, we would expect them to feel better if they have only had the alcohol. After thyroid surgery, people typically will feel not quite themselves for a week or so and then there is an issue of a scar that has to heal. The neck is a very forgiving place. The scars on the neck usually heal up beautifully and in most cases are not very noticeable at all within six months to a year after surgery, but patients do have to be on thyroid hormones for the rest of their lives and even though we have gotten good as a medical community at managing thyroid hormone and making people feel normal again, there are some patients who just do not feel normal even though they are on the right dose of thyroid hormone and we know that patients like that, if they never had had their thyroid removed would probably have felt fine, so that is where we are thinking we will see a difference between patients who have their thyroid removed surgically for a small thyroid cancer versus having the alcohol injection for the thyroid cancer.

Gore How is this actually done? You just go right into the nodule and squirt it in?

Callender Yes, it is very similar to the fine needle aspiration biopsy that we talked about before. The radiologist, and in our case it is an interventional radiologist, will use an ultrasound to show where that tiny nodule is and then we will just take a little needle and the way that you do a biopsy, put the tip of that needle right into the nodule and inject the alcohol and with the ultrasound, we will be able to see where the alcohol is going and how much needs to be injected, does the tip of the needle need to be repositioned, etc., but it is basically very similar to the procedure for a biopsy.

Gore And is it painful when the alcohol goes in? That sounds like that might be painful?

Callender It actually is painful. It is more painful than a biopsy, so that is one of the downsides of that procedure but the pain is typically very short lived. The thyroid capsule is tender, and so when you inject alcohol on it, it is sore and people could typically expect to feel some pain right during the injection and then maybe some mild minor pain for a couple of days.

Gore That is really interesting. It sounds like you are trying to put yourself out of business.

Callender Perhaps, but it is all about doing the right thing for patients and we really do think that we are perhaps over treating patients by doing so much surgery for small thyroid cancers, but in fact, you are right, I mean many of the patients we operate on these days are being operated on for small

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thyroid cancers to a large degree identified because patients went in for something else, another imaging study and then they saw something in the thyroid that was unrelated, got an ultrasound, there was some little tiny thing, it got biopsied and boom; now we are dealing with a thyroid cancer. Certainly for patients who have larger nodules, patients where we are concerned this could be slightly more aggressive, we need to be aggressive, but if it is something that we think patients do not really need to go through, really aggressive therapy, then we would like to know the answer.

Gore Tell me about the adrenal gland, which is one of the real fascinating glands that I think people do not think a lot about. They are somewhere stuck on top of the kidneys as I recall?

Callender That is right. There are actually two adrenal glands or I should say most patients have two. They are on top of the kidneys and they make a lot of different types of hormones. Again for the adrenal glands, almost always we are operating because there is a growth in one of them and some growths do not produce extra hormones. We remove them because we are concerned as we have said you know a growth can be benign or a growth can be a cancer. When we are concerned that a growth could be a cancer, we take it out, but some growths even though they are small and we are not really concerned at all that they are cancer can actually make too much of a particular type of hormone and then the patient can develop characteristics or medical problems that are related to too much of this particular hormone and then we have to take the adrenal gland out for that reason.

Gore And can you live without an adrenal gland reasonably well?

Callender Yes, usually you can because you have one on the other side. The body is amazing in terms of all of the redundancy that it has. Sometimes, we have to manage patients very carefully after one adrenal gland has been taken out while we wait for the other one to sort of take over the function but yes, most patients can live just fine with one adrenal gland.

Gore And I remember there are two parts of the adrenal, the part that sort of seems to regulate more of the metabolism and the other part makes sort of epinephrine and blood pressure things, is that right? You take out the whole thing?

Callender Yes, usually we take out the whole thing. There are some specific instances in which we try to take out one part or the other or nodules growing in one part or the other, but typically, we take out the whole thing. The adrenal gland is just fascinating, the nodules that grow out in the outer layer which is called the cortex, typically do make hormones that regulate the salt and water balance in your body, maybe regulate your stress hormones, regulate some sex hormones and then the inner part which is called the medulla makes hormones like epinephrine, norepinephrine and when tumors or growths form in that part of the adrenal gland, it actually can make your body all of a sudden react or respond as if you are running away from a bear or a lion, although you might be just sitting at your desk minding your own business, so the types of hormone overproduction that can happen because of

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growths in the adrenal gland are really fascinating and really problematic for patients.

Gore And it sounds like it is pretty tricky surgery?

Callender The adrenal glands are very small. They do not look like they would be tricky, but the problem is they are located really deep in the body and they are around a whole bunch of other things that are quite critical, so adrenal surgery can be somewhat complex.

Dr. Glenda Callender is Assistant Professor of Surgery in Endocrine Surgery at Yale School of Medicine. We invite you to share your questions and comments, you can send them to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. As an additional resource, archived programs are available in both audio and written format at yalecancercenter.org. I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another addition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas