

Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale New Haven. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This week, Drs. Foss and Chagpar welcome Dr. Wendell Yarbrough. Dr. Yarbrough is Section Chief of Otolaryngology and Director of the Head and Neck Program at Smilow Cancer Hospital. Here is Francine Foss.

Foss Let us start off by having you tell us a little bit about yourself, how long you have been here at Smilow Cancer Hospital and where you came from?

Yarbrough I am brand new to Smilow, I have been here about two months and I am really excited to be here with the people that are at Smilow, both on the clinic side and on the research side.

Chagpar Tell us a little bit about otolaryngology, or head and neck cancers. What do you do on a daily basis?

Yarbrough I am one of those people that like to do lots of things, so it is hard to say on a daily basis, but I do take care of patients on a daily basis. I am a head and neck cancer surgeon, and head and neck cancers are cancers of the mouth, throat, voice box, and also the sinuses, nose and ears, salivary glands and thyroid, and so I take care of those patients on the surgical side. The great thing about being in an academic institution is that there is a great team that also helps take care of those patients and I think team based care is really one of the keys for providing the best care for patients with these complex cancers. The other side of my life is research and that is another exciting thing about an academic institution like Yale, there is a lot of innovation going on and we do a lot of research on head and neck cancer, and salivary cancers, to try to find new treatment methods and weaknesses of the cancer that can be exploited.

Foss Can you talk a little bit about the field of otolaryngology? You are specifically a cancer surgeon, but do all otolaryngologists specialize in cancers of the head and neck?

Yarbrough Otolaryngology is a diverse field. One section of otolaryngology is

head and neck cancer surgery and those are the doctors who take care of head and neck cancers. There are other sections in otolaryngology that take care for ear disease, sinus disease, tonsillar infections and voice disturbances, but the one big area is taking care of cancers of the head and neck.

Chagpar Tell us a little bit more about this multidisciplinary team, what does it look like for patients with head and neck cancers?

3:18 into mp3 file <http://yalecancercenter.org/podcasts/2012%201104%20YCC%20Answers%20-%20Dr%20Yarbourgh%20copy.mp3> Yarborough Head and neck cancer is a cancer of the upper air digestive tract, which means basically the tongue, the throat, the voice box, and those cancers affect speech and swallowing, and they can also be outwardly apparent with lumps or bumps on the face or neck so these cancers are ones that are in areas of high complexity, and a lot of different functions that are taken for granted by most patients start being affected by these tumors or by the treatment and I think because of that it is particularly important to have a team of doctors and supportive care personnel to help these patients through the treatment. Lots of times during the treatment, patients may have trouble with swallowing and lose weight even before the treatment starts, and they may also have trouble communicating, and the group of doctors that help to take care that are hematologists, oncologists which provide chemotherapy, and radiation oncologists on the treatment side along with head and neck surgeons, but the larger team really includes speech and language pathologists and supportive care personnel such as physical therapists and occupational therapists.

Foss Do patients get evaluated by this whole team before you start to actually do the surgery?

Yarborough Yeah, that is a great question. In fact, some patients are not treated surgically at all and that is one thing we are trying to determine better, which patients are going to be best treated with surgery and which patients are going to be best treated non-surgically? For this reason it is important to have the entire team evaluate patients before the treatment decision is made and we have weekly tumor board conferences where all the doctors gather together and make recommendations as to which treatment would be best for the patient. On the research side, we are trying to determine markers and tools that will help us make those decisions better for each individual patient.

Chagpar Let's shift gears a little bit to talk about the research. Tell us a little bit about what you see as the new advances in researching your particular

area and where you see the field going?

Yarbrough I think for patients it is a particularly exciting time if they are afflicted with cancers of any type, but particularly those related to the head and neck. For years, salivary cancers and thyroid cancers have been treated similarly. So, a patient comes in with a diagnosis of one of these tumors and we cannot at this point really say that the tumor should be treated in a particular way, so what we end up doing is treating most patients in a similar fashion based on the size of the tumor, the location of the tumor, and the type of tumor within that area, but what we are moving towards, and there are a couple of areas of progress in the recent past, is being able to locate some molecular characteristics of the tumor such as gene mutations, amplifications or over expression of certain molecules and then based on that, offer treatment to a particular patient. One of the best examples of that right now is there is a virus that is associated with tonsillar cancer and tongue based cancer called the human papillomavirus, and if patients have that virus it is one good indication for us that surgery may not be necessary. So we try to treat the majority of those patients without surgery.

7:11 into mp3 file <http://yalecancercenter.org/podcasts/2012%201104%20YCC%20Answers%20-%20Dr%20Yarbourgh%20copy.mp3>Foss The kind of screening that you are talking about, the genetic screening of the tumors, can you explain to us how that actually happens? The patient comes into the office with a tumor, what are the steps that happen between seeing the patient and actually getting that kind of information?

Yarbrough For most standard types of tests, routine biopsies that are done for the diagnosis can be used to determine for instance the presence or absence of the virus that we were talking about. But for more innovative or unproven diagnoses, right now, biopsies are taken from the patient if they allow us to take them for research purposes and then those tumors that are taken for research purposes at the time of the resection or biopsy can be screened by new technologies that can sequence almost every gene in the human genome to look for mutations that may predict response. Once again, related to weaknesses of certain tumors, we have recently found that a subset of head and neck cancers are particularly prone to being killed with typically DNA damaging agents that are used for head and neck cancer, so these are patients where once again, we may recommend some of those treatments so that they can avoid the complications and side effects of other treatments.

Chagpar Is this kind of sequencing and profiling routine, or is this something that is done under a clinical trial?

Yarbrough There a couple of situations, the first one is a clinical trial and ideally we would like to have clinical trials, and we are moving in this direction, to have clinical trials that are based on identification of certain molecular defects. So in other words, you only get entered on the clinical trial if you have a certain molecular defect, but also just routinely sequencing patients is done on a research basis so it does not affect how they are cared for but the hope is we will find new weaknesses of the tumor that can be targeted in future patients and perhaps in future clinical trials.

Foss Wendell, there are lots of new gene pathways that have been identified that we have talked about in the context of solid tumors that there are common cancer pathways and some of those we have drugs now that target. Do you foresee that there will be common cancer pathways in head and neck cancer and what is the future with regard to using some of these targeted therapies?

Yarbrough Certainly there will be. Right now, each tumor is individual and I think people are beginning to understand that and so as we start to learn more about these tumors we are hoping we will be able to target them. Right now head and neck squamous cell cancers are typically not driven by oncogenes that have been easy to target with drugs, however, we have found some weaknesses that can be targeted and I think combinations will be available in the near future.

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Chagpar We are going to talk a little bit more about that after we come back. We are going to take a break for a medical minute. Please stay tuned to learn more information about otolaryngology and head and neck cancers with Dr. Dell Yarbrough.

Medical

Minute This year over 200,000 Americans will be diagnosed with lung cancer and in Connecticut alone there will be over 2000 new cases. More than 85% of lung cancer diagnoses are related to smoking and quitting even after decades of use can significantly reduce your risk of developing lung cancer. Each day, patients with lung cancer are surviving, thanks to increased access to advanced therapies and specialized care. New treatment options and surgical techniques are giving lung cancer survivors more hope than they have ever had before. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale, to test the innovative new treatments for lung cancer. An option for lung cancer patients in need of surgery

at Yale Cancer Center is a video-assistant thoracoscopic surgery also known as VATS procedure, which is a minimally invasive technique. This has been a medial minute. More information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined today by my co-host Dr. Francine Foss and our guest Dr. Dell Yarbrough. We are discussing otolaryngology and head and neck cancers, and right before the break Dell, you were talking a little bit about targeting therapies to cancers. Tell us a little bit more about that, particularly in the whole realm of head and neck cancers and some of the work that is going on in your laboratory.

Yarbrough One reason why I said it was an exciting time to be involved in cancer research, but also an exciting time for patients is because I have patients that call me up with tumors that either have no treatment that is a good treatment for their tumor, or they have already been treated with multiple modalities and they do not have a good option left and I think that what we are learning with targeted therapies is that even if tumors become resistant to more standard therapy, they may have a weakness that can be targeted, and our lab has been involved in trying to find some of these molecular defects that predict weakness of the tumors, and in particular, some of the non-carcinogen driven tumors sometimes have drivers that can be more easily targeted. With head and neck squamous cell carcinoma, which is driven by tobacco carcinogens and smoking primarily, oncogenic targets are not as obvious and I think for those some combinations will be needed.

Foss Can you talk about some of these orphan tumors that you were referring to?

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Yarbrough Orphan tumor, by definition, is any tumor that has less than 100,000 cases per year in the United States. By definition, even the most common type of cancer that we treat as otolaryngologists is an orphan tumor, but there are some fairly rare tumors where there are less than 10,000 cases in the United States and these includes some salivary tumors, especially if the salivary tumors are broken down into the different histologies, which means that there are different types of cancer that can occur in salivary tumors, some weird names

like scenic cell carcinoma, adenoid cystic carcinoma, and mucoepidermoid carcinoma, but each tumor tends to be driven by different pathways and different key cancer drivers. Our lab has been working on the salivary tumors to try to create tools to study them because there are not great cell lines right now for these tumors and in fact some tumors have no cell lines, so we are creating mouse models of these tumors by taking human tumors, putting them into the mice, and then we are analyzing these tumors for mutations and weakness and we treat the mice and we have a few targets that we have identified that we are moving forward to clinical trials for these hard to target tumors.

Foss Are some of these tumors also hard to treat?

Yarbrough They are very difficult to treat and some of these tumors are very slow growing and even though the initial treatment may be very successful with the tumor going away and staying away, sometimes after ten or even fifteen years the tumor will come back. So some salivary tumors, particularly adenoid cystic carcinoma, can occur and be treated very successfully with 10 year survivals in the 80% or 90% range, but the 15 and 20 year survival can drop down to the 20% and 30% range, so these tumors come back late and when they come back, lots of times there is no good treatment.

Chagpar It sounds like these are diseases that have very few cases, nationwide. Can you tell us a little bit about whether there are particular centers that specialize in these types of cancers, because one could imagine that with the expertise that you were talking about that is required with this multidisciplinary approach and tumor profiling, that there are very few centers that have the volume to be able to deliver that standard of care?

Yarbrough These tumors, be they head and neck squamous cell carcinoma, which is the most common type of tumor we see with about 50,000 cases a year, or some of the less common ones with fewer than 10,000 cases a year, because the numbers are not great and because the care can be very complex and require a lot of support during the treatment before and after, there are only a limited number of larger centers that see enough of these patients to really treat them. We view each patient as an individual and each tumor certainly is individual, but I think one of the keys is complete care of the patient, not just treating the tumor but also treating the patient and their symptoms related to the tumor before treatment, to their symptoms related to the treatment and after the treatment. For

17:47 into mp3 file <http://yalecancercenter.org/podcasts/2012%201104%20YCC%20Answers%20-%20Dr%20Yarborough%20copy.mp3> really rare types of tumors such as the ones that we see, I think academic centers where these tumors and patientd can be really well treated, and also where these tumors can be studied in large enough numbers to really learn something is important.

Foss Another question that somebody in the audience might wonder about is if a patient has one of these weird tumors, say it was resected, taken out a number of years ago, can they still have that tumor studied genetically the way you are describing, or are you only talking about fresh tumors that you are resecting now?

Yarbrough Technology is really amazing these days in that a lot of tests can be done of previously resected tumors. The deep sequencing that we were talking about, where mutations are identified in human genes and amplifications as well as fusions, can be identified from tumors that were resected years ago and we learn a lot from those types of specimens. The advantage of fresh tumors is once we have an idea or we think a tumor or group of tumors has a weakness, the fresh tumors can be used to keep the cells alive and to test those cells to see if our idea is correct or incorrect, and so we utilize both tumors that were resected years ago as well as fresh tumors to try to complete the whole research program so that we can do testing before we actually have to go to patient's and subject them to a treatment that may or may not be effective.

Chagpar With these rarer cancers, one would think that the way in which they present would not be well-known to our audience. I do breast cancer and most people know that you should get a mammogram, or if you feel a lump, you should get it checked out. What about for head and neck cancers?

Yarbrough That is a very good point and it is not just the public, it is also other physicians who really do not know much about head and neck cancer and especially some of the rare orphan type tumors that we are talking about. We do community outreach and a yearly screening where we have patients come in and get a free screening, and that is conducted at Yale, but also at other centers across the nations, it is a nationwide effort, but patients should be aware of the signs and symptoms to prevent having the tumor being treated at a stage that is too late, when the tumor is too far advanced. Like most cancers, if you can catch these cancers early when the tumor is small, the chance of cure is much higher. Some of the signs and symptoms are pretty obvious once you know what you are looking for. A lump or bump on the face or neck that does not go away, bleeding from the mouth or throat or a hoarse voice that does not improve, a sore throat or numbness on the skin of the face or of the tongue, an

ulcer within the mouth that is sore when you eat, but does not heal, all of those can be signs and symptoms of head and neck cancer. I recommend that if people have those signs and symptoms that they have it examined by their local physician or by a head and neck cancer specialist because it is so important to be treated early, the

21:36 into mp3 file <http://yalecancercenter.org/podcasts/2012%201104%20YCC%20Answers%20-%20Dr%20Yarbourgh%20copy.mp3> side effects of treatment are less, and the performance and operation of swallowing and speech are affected less, if these tumors were caught early.

Foss You mentioned that smoking is clearly a risk for some of these kinds of head and neck cancers, are there other risk factors that patients should be aware of?

Yarbrough The risk factors for squamous cell carcinoma, which is the most common type of tumor we see, really are tobacco use and chewing tobacco as well. Drinking alcohol, particularly in combination with tobacco, multiplies that risk and then the other major risk for squamous cell cancer is the human papillomavirus, which is sexually transmitted and so fortunately, there is a vaccine now that is available for the human papillomavirus that can prevent infection by the virus and the same virus types that cause uterine and cervical cancer, which the vaccine was originally created for, are the virus types that also cause head and neck or tonsillar and throat cancer. So protection against those virus types should decrease throat cancer incidence in the future.

Chagpar I may have missed it, but I thought that you mentioned that there are some of these cancers that are not mediated or induced by carcinogens, so if they were not induced by smoking or drinking or HPV, what causes them?

Yarbrough You are exactly right, and some of those tumors are, for example, salivary tumors which are tumors of the spit glands that can occur inside your mouth as well as in the major spit glands that are on the face and under the jaw line. Some thyroid cancers also have no known etiology such as smoking, drinking and those types of things. We just call those bad-luck tumors. I am not sure if it's bad luck, or maybe we are just not smart enough right now to figure out why people get those, but those types of tumors in many ways may be more susceptible to targeted therapies, which means therapies that hit one particular mutated protein or over expressed protein and with work that we have done in the research lab, it appears that that is the case for some salivary tumors that tend to be driven by one or a few mutant or over expressed proteins.

Foss We talked a little bit about some treatment options, you mentioned chemo, radiation and surgery. Patients are oftentimes left with deficits after that. Can you talk a little bit about the quality of life for a patient with head and neck cancer during the treatment and then what happens after the treatment?

Yarbrough The treatment for head and neck cancer can vary, surgical, non-surgical with radiation and chemotherapy, but you are exactly right, there can be deficits in swallowing and communication and even cosmetic defects associated with the treatment. Our goal is to restore treatment as much as possible while curing the cancer. Some people end up with resections of the tongue or scarring

25:15 into mp3 file <http://yalecancercenter.org/podcasts/2012%201104%20YCC%20Answers%20-%20Dr%20Yarborough%20copy.mp3> related to nonsurgical therapy that makes swallowing very difficult and some people have life long changes in their diet that are necessary, and the rare patient ends up not able to eat by mouth at all, but requiring a G-tube. I would say that with modern reconstruction techniques that is pretty rare these days, and of course our goal is to have every patient be able to eat by mouth to maintain their weight and maintain their health, however, the majority of patients that have certain large tumors in particular I would say, end up with changes in their diet and they may need only soft food for instance or sometimes only liquid food. Speech is another major thing that can be affected and we have speech therapists and swallow therapists that help to guide these people during treatment and after treatment to have their speech and swallowing be as good as it can be.

Chagpar We talked a little bit about diagnosing and treating these cancers and the effects that might have, but tell us about outcomes, do these patients do well in the long term? What is the natural history with treatment?

Yarbrough It actually can vary quite a bit and part of the reason for that is that each tumor is really individual and we do not understand the differences between tumors and why some are more aggressive and some are less aggressive. Some spread to lymph nodes in the neck very early on, some do not, and that spread to lymph nodes does correlate with how well people do after treatment and what the risk is of the tumor coming back, but head and neck cancer in general is not the worst type of cancer to get. You hear of some tumors where the chance for cure may be very low like 5% or 10%. There are also tumors that do very well and with those types of tumors your chance for cure may be 90% or 80%. Head

and neck cancer is kind of a middle ground. For people who have advanced head and neck cancers, the overall long term cure rate is about 50%. With smaller tumors, of course people do better, and with HPV associated tumors, people tend to do better with those tumors because they are more susceptible. For some of the salivary tumors, the survival for ten years can be quite good, but the chance of the tumor recurring after that time is also quite high, perhaps as high as 50% or 60 %. So I think that the key to the types of tumors that we deal with is that there is a big variation and what we are working to determine is why some people have such good outcomes, while some people have poor outcomes and for those with poor outcomes how can we make the treatment better?

Dr. Wendell Yarbrough is Section Chief of Otolaryngology and Director of the Head and Neck Program at Smilow Cancer Hospital. If you have questions or would like to add your comments, visit yalecancercenter.org, where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.