Welcome to Yale Cancer Center Answers with your hosts doctors Anees Chagpar, Susan Higgins and Steven Gore. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. Dr. Higgins is Professor of Therapeutic Radiology and of Obstetrics, Gynecology and Reproductive Sciences and Dr. Gore is Director of Hematological Malignancies at Smilow and an expert in Myelodysplastic Syndromes. 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. Tonight you will hear a conversation about head and neck cancer with Dr. Hari Deshpande. Dr. Deshpande is Assistant Professor of Medicine in the Section of Medical Oncology at Yale School of Medicine. Here is Dr. Anees Chagpar.

Chagpar Unlike breast cancer, colon cancer or lung cancer where there is a defined organ that is involved with these malignancies, head and neck cancer is a rather large area. What exactly do we mean when we are talking about head and neck cancers?

Deshpande We mean cancers of what we call the upper aerodigestive tract and that is everything from the front of the mouth, the lips all the way down to the larynx and the upper esophagus, so in other words, we are not talking about the brain, the eyes, and generally not cancers of the skin, although in our clinics for head and neck cancer, we do see people with very aggressive skin cancers that occur on the face and also cancers of the thyroid.

Chagpar So these cancers of the upper aerodigestive tract are not things that a lot of people know about or talk about at least. Tell us more about how common they are and how they present?

Deshpande They are actually not uncommon, we see about 50,000 new cases of these cancers every year in this country. They present with symptoms, however, that all of us get. We are always complaining, in the winter especially, of a hoarse voice or sore throat and sometimes a lump or lymph node in the neck and these are the most common ways they present. There are a little more sinister ways they present, if you are coughing up blood that could be a sign of a malignancy, but generally if you have a hoarse voice or sore throat or especially a lump in the neck that does not go away by the time you would expect it to, usually after a couple of weeks, it is worth getting checked to see whether there is something else going on.

Chagpar And when you say checked, what does that mean? Is that a blood test, is that an x-ray, is that somebody saying, open your mouth and say ah? How exactly are people checked for these cancers?

Deshpande Initially it is a visit to your primary care physician and they will probably say, open your mouth and say ah, that is the best way to look at what we call the oral cavity, so that is everything in the mouth back to the start of the tonsils. Unfortunately, you cannot see much

further back than that and so the ENT surgeons or the ear, nose, and throat surgeons have devices that can look further back, either a special mirror that they will push to the back of the mouth or a fiberoptic 3:47 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%200830%20YCC%20Answers%20%20Dr%20Deshpande_231404 3 laryngoscope which is a very small flexible telescope with a camera at the end that can see all the way down into the larynx, into the upper esophagus and see whether there are any malignancies there.

Chagpar So if you see one of these, how do you make the diagnosis? Can you actually take a biopsy through these little scopes? Deshpande Yes you can, and obviously if the cancer is in the front of the mouth, then the ENT surgeon can see it right there in the office, they can easily take a biopsy just by looking at it. These laryngoscopes are able to do biopsies as well, so they can very quickly make a diagnosis after the specimen is being sent out to the pathologist.

Chagpar How bad are these cancers? Let's suppose you had a sore throat or a cough and it did not go away, you went and saw your primary care doctor who referred you to the ENT specialist who did the fiberoptic laryngoscope and saw something and biopsied it and now you are sitting in their office and they say, guess what, you have head and neck cancer, should you be very scared, is the prognosis terrible, what is that like?

Deshpande Just like with most of the cancers that we see, the prognosis depends on the stage and we come up with the stage based on how big the cancer is, whether or not any lymph nodes are involved and whether or not it spread to other parts of the body. The staging of head and neck cancer is a little bit complicated. For most cancers, when you hear stage IV, it means it has spread all over the body. For head and neck cancer, it is slightly different. We have a stage IVA, stage IVB and a stage IVC and IVA, even though it sounds like a very aggressive stage, it is kind of in the middle of the head and neck staging and we still treat those cancers for cure. I would tell people if they first hear that they have a cancer of the head and neck and by cancer I mean something called a squamous cell cancer, that is what the pathologist looks at under the microscope and the appearance is called a squamous cell cancer, those cancers can have very, very good survival rates even in stage III and IVA disease.

Chagpar How do you know what stage you are at? For many cancers, at least not for stage IV but for earlier stages, it is made on the basis of pathology whether you can take the cancer out and send it to the pathologist and the pathologist tells you exactly how big it is and you sample some lymph nodes and they tell you whether those have got cancer in them or not, but in head and neck cancer, do you do that first or is this imaging and if so, do you image everybody?

Deshpande We tend to image everybody and the reason for that is unlike some of the other parts of the body, most people when they have head and neck cancer, they want to limit the amount of surgery they have. They do not want to lose their ability to swallow. They do not want to lose their voice box

or larynx and lose their ability to talk, so we typically do a PET scan and sometimes a CAT scan and an MRI to see exactly what you asked, how big the cancer is, whether or not any lymph nodes are involved, and with that information we can come up with what is known as a clinical stage. 7:26 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%200830%20YCC%20Answers%20%20Dr%20Deshpande_231404 4 What you were talking about with the surgery and looking at the lymph nodes in the pathology lab is also done in head and neck cancer for some patients and we call that the pathological stage, but we base most of our treatment decisions on the clinical stage.

Chagpar So you have all of these x-rays that tell you how big the cancer is, how many lymph nodes look like they are involved, how do you decide how to treat these cancers?

Deshpande That depends partly on where the cancer is, generally, we split the head and neck region into different subsites. The first site we call the oral cavity, and that is everything from the lips all the way back to the part of the tongue where the front and back join and just before the tonsils and for those cancers, we tend to remove them with an operation and follow it with radiation or chemo and radiation if it is a little more advanced. A little further back is the oropharynx, which is the base of the tongue and the tonsil. The cancers in the oral cavity, the anterior tongue cancers, the cheek cancers, those are very heavily related to cigarettes and alcohol. The cancers of the tonsil and invasive tongue are related to HPV, 70% or more of them are related to HPV. This is a virus, the human papilloma virus which is the same virus that causes cervical cancer and people with tonsil and base of tongue cancers tend to do very well and there is a 90% cure rate if they are HPV positive with chemo and radiation without having any surgery, so the treatments, as you could imagine, are very different depending on the site of the disease.

Chagpar Two questions, first question is, most people when they hear HPV, they think about cervical cancer and they think about it as being sexually transmitted. Is it the same thing in the oropharynx, I mean is this sexually transmitted?

Deshpande It is a sexually transmitted virus. The way it was found was people noted that ever since the 1970s the incidence of base of tongue and tonsil cancer has been going up every year and they feel that this is the change in the sexual preferences of people over the last few decades and possibly an interaction between the virus and cigarettes that may have made it less common previously and more common now, but either way, these cancers are very common in the base of tongue and tonsil area and appear to be increasing in incidence.

Chagpar The second question is this, HPV causes these cancers and so one would hypothesize that people should get an HPV vaccine so that they can reduce the incidence of these head and neck cancers, but on the other hand, people whose cancers are HPV positive tend to do really well with a 90% cure rate, so maybe it is good to get a cancer that is related to HPV, should people get vaccinated

or not?

Deshpande I think they should get vaccinated. I think the evidence for reduction in cases of cervical cancer is one of the best public health benefits that has come out with regards to medicine in recent years and one of the added benefits, we feel, will probably be a reduction in the number of 11:11 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%200830%20YCC%20Answers%20%20Dr%20Deshpande_231404 5 oropharyngeal cancers and I agree the outcomes for these HPV cancer seem to be better than the non-HPV related cancers, but even so, who wants to go through chemo and radiation. I think if we can prevent them it is much better than trying to treat them.

Chagpar How do you know whether your cancer is HPV positive or not? Is that something that is done on all biopsies when you take them out?

Deshpande Until recently, I would say that this was a test that we had to ask for in particular; however, over the past 10 years or so, any cancer that is found in the back of the tongue or the base of the tongue or the tonsils are automatically checked for HPV or a protein called P16. We call this a tumor suppressor gene that is overexpressed in patients who have HPV related cancers. In other words, if that cancer is related to that virus, then they make more of this protein which seems to affect the way that the cancers grow and also the way that they respond to treatment, so I would say it is an automatic test for the tongue, base of tongue and tonsil cancers. If you have a cancer in the front of the tongue or the larynx, it is not a test that is automatically done, we often have to ask for that in particular for that patient.

Chagpar But that is because those cancers tend not to be related to HPV, right?

Deshpande That is correct, some estimates put the instance of HPV related cancers in those other parts of the head and neck at less than 20% and we do not know if they behave better or worse, they are just not as common right now.

Chagpar Is this test done on the initial diagnostic biopsy? Because one would think that if you have a cancer at the base of the tongue or in the tonsil that is HPV positive, then maybe you forgo surgery completely because you know that these people will do well with chemo and radiation rather than having a surgery to find out the HPV status.

Deshpande That is a question that we are trying to answer in one of our clinical trials that is part of a big consortium called ECOG or Eastern Cooperative Oncology Group which has come up with a trial headed by Dr. Burtness who I work with here at Yale and Dr. Judson who is one of our surgeons, who are looking at whether or not we can cut back on the surgery as well as cutting back on the chemo and radiation for these patients.

Chagpar It certainly sounds really exciting and could have a potential huge impact for patients. We are going to learn more about that after we take a short break for a medical minute. Please stay tuned to learn more information about head and neck cancers with by guest, Dr. Hari Deshpande.

Medical Minute This year over 200,000 Americans will be diagnosed with lung cancer. 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. Clinical trials are currently underway at federally 14:27 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%200830%20YCC%20Answers%20%20Dr%20Deshpande_231 6 designated comprehensive cancer centers, such as, Yale Cancer Center and at Smilow Cancer Hospital at Yale-New Haven to test innovative new treatments for lung cancer. Advances are being made by utilizing targeted therapies and immunotherapies. The BATTLE-2 trial at Yale aims to learn if a drug or a combination of drugs based on personal biomarkers can help to control non-small cell lung cancer. 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. You are listening to WNPR, Connecticut's Public Media Source for news and ideas.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Hari Deshpande. We are talking about head and neck cancers. Hari, right before the break we were talking a little bit about an exciting clinical trial that is ongoing that is trying to see whether we can cut back on some of the side effects of surgery, particularly in such a vital area as the head and neck where people are using vital organs to swallow, to speak and so on. Tell me more about other clinical trials that are going on in this area?

Deshpande We have clinical trials now for different stages of the disease, so if people have very early stage disease where we imagine that we are only going to need an operation, they have a small cancer that if it is taken out, it is probably going to be cured. We are looking now to see whether or not we can use some of the information from the biopsy beforehand and the specimen that they get from the operation at the end to make decisions on what best treatments we can give to people with more advanced disease. We call these window trials, so people get a biopsy initially. If they find that they have a cancer in the floor of the mouth or the anterior part of the tongue that can be relatively easily removed, then we will offer those patients 7 days of chemotherapy with an agent that one of my colleagues Dr. Yarbrough has found in his labs that produce really good changes in test tubes in cancer cells to suggest it might be very useful for treating those kinds of cancers. This particular chemo is called 5-azacytidine. It has been around for a while. We treat people with certain blood cancers and myelodysplastic syndromes with it and in the lab, it seems to work in favor of treating head and neck cancer cells as well, so what these patients would have to do if they agree to go on the study is get 7 days of this treatment and after that, on the 8th day, they get their operation and then we look at it in the pathology lab. Hopefully, it will help them but it will also help patients who have more advanced disease if it turns out that this is a good treatment.

Chagpar What are the side effects of this drug? I mean one can imagine

that if patients would not normally get this drug that they may be worried about the side effects of treatment. Deshpande That is true and there are side effects as with any chemotherapy. Luckily, with this one they tend to be much less frequent but they have similar side effects that probably you have all heard of, nausea, sometimes vomiting, it can cause tiredness and sometimes it can cause low blood counts, so we follow these people once a week just to check their blood to make sure they are not reacting unfavorably to their chemotherapy but we only give the treatment once and they do not get it again, so luckily any of the long term side effects that we might see with some chemotherapies when they are given over and over again, we do not see on this particular trial. 18:27 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%200830%20YCC%20Answers%20%20Dr%20Deshpande_231404
7 Chagpar Because they only get it for 7 days.

Deshpande That is correct.

Chagpar Do they get it 7 days consecutively?

Deshpande In this particular trial, they do, and that is the drawback to the way this particular treatment is given. It has been given intravenously daily for 7 days.

Chagpar Hari, in breast cancer when we give people chemotherapy upfront as we do with many locally advanced cancers, one of the advantages is that sometimes we can get what is called a pathologic complete response where we as surgeons when we go in to take out the cancer find that you as a medical oncologist have already wiped out the cancer and we know that those patients will have an outstanding prognosis. Is it the same in head and neck cancer and could that be a reason why patients should consider having this trial treatment where potentially this chemotherapy can tell them that their cancer responds very well and potentially their prognosis is very good?

Deshpande I think that is something that we might aim to do in the future but the idea of this particular trial is only to get the 7 days of treatment to see what the effects are on the tumor in the lab under the microscope in the molecular level, so it is what we call a window trial. We are not really looking to see in this particular trial if we can eradicate all the cancer. Having said that, we do the preoperative treatment for head and neck cancer all the time using chemotherapy and radiation but unlike with breast cancer we often do not do an operation at the end, especially if we do not see any sign of disease, so we try and avoid an operation altogether with chemo and radiation and just like with breast cancer, there are some patients who will be completely cured of their disease using that approach of either radiation alone or chemo and radiation together.

Chagpar How do you know that you have eradicated the disease with chemoradiation if you cannot have a pathologist tell you that you have eradicated the disease?

Deshpande That is a good question and it is a question my patients ask all the time, how do we know if it worked? And what we typically do is after the end of radiation or the last day of radiation, we will count 12 weeks from that point and then do a PET scan. The PET scan is a radiology test that involves x-rays and also nuclear medicine dye that will show up where cancers are fairly accurately in people with head and neck squamous cell cancers, so if that PET scan is very positive before they take the treatment, then 12 weeks after the radiation has become all clear then that is a very good prognostic sign that the cancer is not going to come back. I agree it is not the same as removing it and showing it under the microscope, but I would say it is next best thing.

Chagpar I tell all my patients that there are only two people who can tell you anything for sure, God and the pathologist and while PET scans are very good, they may not be God, at least not for breast 21:45 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%200830%20YCC%20Answers%20%20Dr%20Deshpande_231404 8 cancer but maybe for head and neck. Tell me more about other studies that are ongoing in head and neck cancer? Deshpande We have some very exciting studies that my colleague, Dr. Barbara Burtness has brought to Yale. She is the head of the medical oncology head and neck team and she is looking, among other things, at immunotherapy and this is something that has a long history at Yale. Basically, we feel that some cancers can actually turn off your immune system and allow themselves to grow, to progress, and to metastasize and if you can turn back on the immune system then maybe you can treat those cancers. We know from here at Yale and elsewhere that these are good for cancers such as melanoma and nonsmall cell lung cancer and it looks like for squamous cell head and neck cancers, these medications, the same ones that are being used for melanoma and lung cancer, might also be very useful in metastatic head and neck cancer, so we do have a couple of trials using these immune therapies and we also have the trials as we mentioned just before the break where we are trying to get rid of some of that treatment, do less surgery, less chemo and less radiation for the patients who we expect to do well, these HPV positive cancers.

Chagpar So immunotherapy is one of these really hot buzz words these days and the whole concept of revving up your immune system to fight cancers, I think is something that many people think as a good idea, does it have less toxicity than standard chemotherapy? Deshpande I would say it has different toxicity. People do not tend to lose their hair, they do not tend to get the nausea or vomiting but they can get some very strange side effects. If you allow their immune system to attack parts of the body that would not normally be attacked, typically these are the lungs, they can get something called pneumonitis or inflammation of the lungs and basically they can get inflammation of any part of the body. If it is just a mild rash, we do not worry about it too much but if someone has difficulty breathing, we have to stop the treatment and give them steroids to try and allow the body to recover. Chagpar It is interesting when we think about immunotherapies and we think about immune systems, many of us think about vaccines because that is how a vaccine works. It primes your immune system,

so that the next time it sees that antigen in that cell, your body says, aha! that is something to attack and I wonder if, particularly for cancers that are virally mediated, whether immunotherapies are particularly effective.

Deshpande I think that is a very good question. There are some of my colleagues who are much more versed in immunology that may be able to answer that question better. I would say that some of the best responses that we have seen have been in these virally related cancers and possibly it is because of the fact that the immune system is being primed in some way. 25:02 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%200830%20YCC%20Answers%20%20Dr%20Deshpande_231404 9 Chagpar Do you think that in people who have been previously vaccinated with HPV vaccine, if they then get a head and neck cancer, presumably it would be an HPV negative cancer, that immunotherapies would work better?

Deshpande I am not sure, that is a very good question, I do not know if we have enough information to look at it yet, but as more and more people are vaccinated I think those are sorts of questions that we will be able to answer better. Chagpar Are the vaccines just for girls, HPV vaccines, or have the guidelines changed with regards to that? Deshpande They have now changed, you are correct. It used to be for girls and young women between the ages of 9 and 26 but now it is for girls and boys of the same age range and the hope is that if you vaccinate girls, boys, young men, and young women, then you will get all of the population that could then cause, especially cervical cancers, but also these head and cancers, to occur. It is felt that if you vaccinate people over the age of 26, the efficacy goes down significantly and that is why it is not recommended for older people. Chagpar So that means that all other people who are our age range are out of luck?

Deshpande Well, I would say that they are less likely to respond to the vaccine, yes.

Chagpar So what can we do aside from vaccines to prevent ourselves from getting head and neck cancers?

Deshpande I think the main thing, even with seeing more of these virally related cancers, is definitely not to smoke cigarettes, that is by far the #1 cause of head and neck cancers even with the rise in HPV cancers. The interaction between alcohol and cigarettes is that alcohol by itself does not appear to cause these squamous cell cancers although it can cause other cancers in other parts of the body but when you combine alcohol and cigarettes, it does increase your risk of getting this squamous cell head and neck cancer, so definitely do not smoke and drink would be my #1 recommendation.

Chagpar So if you are a current smoker, if you quit smoking, are you still at risk for some period or do you start to get some risk reduction day #1?

Deshpande You pretty much will get risk reduction very, very quickly. I think day #1 might be a little too soon, but it does continue to go down and it continues to go down over 10 or 20 years, so definitely stop smok-

ing but continue to stop smoking for a long period of time and your risk will keep going down. We have a smoking cessation group at Yale which is very popular and I have had a lot of patients who are very positive about it but even if you cannot get into that group, there are quit lines that you can call and hopefully a lot of your colleagues and family would be encouraging for you to stop smoking because most of time, especially if they are nonsmokers, they will want you not to smoke as well. 28:32 into mp3 file https://az777946.vo.msecnd.net/cancer/2015%200830%20YCC%20Answers%20%20Dr%20Deshpande_231404
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Chagpar And when we think about prognosis, you mentioned that the HPV positive cancers are the ones that have good prognosis and the ones that are not HPV related tend to have a worst prognosis and those are the ones that are caused by smoking and alcohol. Is that right?

Deshpande That is absolutely correct.

Chagpar How bad is the prognosis? Suppose you do smoke and you do drink and you have an HPV negative cancer, you mentioned that the prognosis with HPV positive cancers was over 90%, what is it for HPV negative cancers?

Deshpande For the patients with stage III and IVA disease, these are people who get the aggressive chemo and radiation. HPV positive cancers have 90% prognosis. It is 50% or less for the equivalent stage of HPV negative cancers, so it is a big difference, probably even a different disease.

Dr. Hari Deshpande is Assistant Professor of Medicine in the Section of Medical Oncology 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 and 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 edition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas.