



*Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center. Dr. Miller is a medical oncologist and he specializes in pain and palliative care, and also serves as the Director of the Connecticut Challenge Survivorship Clinic. If you would like to join the discussion you can contact the doctors directly. The address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and the phone number is 1-888-234-4YCC. This evening Ken Miller welcomes Dr. Hari Deshpande to talk about head and neck cancers. Dr. Deshpande is Assistant Professor of Medical Oncology and co-Director of the Head and Neck Cancer Program at Yale Cancer Center.*

Miller We're going to talk tonight about head and neck cancer which is a topic that I think a lot of people do not know very much about. What does it mean? What types of cancer develop in the head and neck?

Deshpande Head and neck cancers are cancers that are in the mouth, all the way down to the lungs. We do not include cancer of the brain, even though obviously, the brain is part of the head. Head and neck cancers tend to be what we call squamous cell cancers; 90% of the time they are that type of cancer cell. They are cancers of the lining of the mouth, the throat and the larynx. They tend to be cancers that grow in that area before spreading to other areas, which they do at a very late stage.

Miller When people hear that a neighbor, friend or cousin has cancer, they usually hear that they have breast cancer, lung cancer or colon cancer. How are those different? Are those squamous cell cancers or is that a different type?

Deshpande That usually is a different type. Those are something called an adenocarcinoma, and they tend to behave slightly differently in that sometimes lung cancers and colon cancers may not be detected until they have already spread to different areas, whereas with head and neck cancers, because they effect your speech and swallowing, tend to present quite early on. Therefore, they are picked up usually in earlier stages.

Miller It sounds like it is a different type of cell arising at a different place and with a different biology to it.

Deshpande That is correct, yes.

Miller What are the symptoms that would bring a patient to come to see you, or an ear, nose and throat doctor?

Deshpande Usually they see the ear, nose and throat doctor after they see their primary doctor. Usually it is

**2:51 into mp3 file [http://yalecancercenter.org/podcast/Answers\\_Jun-01-08.mp3](http://yalecancercenter.org/podcast/Answers_Jun-01-08.mp3)**

symptoms such as sore throat or a hoarse voice that has not gotten better despite antibiotics. In general, if you or someone you know has risk factors for head and neck cancer and their symptoms do not improve after a couple of weeks or a month, they need to see their ENT doctor to have more investigations done.

Miller What are those risk factors?

Deshpande These days they are mainly cigarette smoking and alcohol. It seems that the combination of the two is important. As opposed to lung cancer where cigarette smoking is by far the main cause, in head and neck cancer we tend to see it more in people who both smoke and drink alcohol heavily.

Miller For a social drinker or someone who drinks lets say a glass of wine now or then, is that person at risk?

Deshpande Not as far as we know, they have to smoke cigarettes heavily as well and there are other risk factors which seem to be somewhat less important, things like family history, which accounts for a very, very small percentage of the disease, and a virus called the human papilloma virus or HPV. That seems to be increasing in incidence, whether that it is because fewer people are smoking or whether it really is increasing in incidence, we really do not know at this time.

Miller We talked about cervical cancer being associated with HPV or human papilloma virus, is that the same type of virus?

Deshpande Yes, it seems to be the same type of virus but we do not know why some people will develop head and neck cancer. Even though we find human papilloma virus in many people, only some of those will go on to develop head and neck cancer, but it does appear to be the same type of virus.

Miller It is really fascinating to me and makes me hopeful too that perhaps some of the vaccines that would work to prevent cervical could prevent head and neck. Is there any data on that yet?

Deshpande There is a little bit of data, not very much. At last year's annual meeting of the American Society of Clinical Oncology, there were a couple of abstracts and other experiments presented on human papilloma virus and vaccines, but so far there have not been huge studies like those done with cervical cancer that showed a very, very good benefit. My own feeling is that probably we wont see a benefit because most of head and neck cancers are still from cigarette smoking and alcohol, and it is just a small minority that are from human papilloma viruses. In order to see a benefit, we would have to treat many, many people with HPV associated cancer before you see a difference.

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- Miller That is a good point. Cervical cancers are such a high prevalence of the virus you can have a bigger impact and see it quicker.
- Deshpande That is correct
- Miller This is a remainder so I will take the opportunity to say, please stop smoking and have your relatives stop smoking.
- Deshpande Yes, definitely.
- Miller If someone is out there and says, why bother to quit because I have that risk already, if they quit will their risk of head and neck cancer begin to drop?
- Deshpande It definitely will drop. In fact, we know that even if they develop the cancer, with head and neck cancer, it is possible to remove a lot of these cancers even if they are at a fairly advanced stage. But if they do not stop smoking, the risk of the cancer coming back is over double the risk of someone who does stop smoking. It definitely will go down whether or not they develop the cancer.
- Miller I want to focus on someone who has been treated for the cancer successfully.
- Deshpande Yeah.
- Miller If they continue to smoke, what are their risks of recurrence compared to if they were to say they are done with smoking?
- Deshpande They have two main risks. They have a risk of a recurrence of the head and neck cancer and they also have a risk of what we call a second primary cancer, which usually will occur in the lung, but it could be anywhere that smoking related cancers occur. The risk of recurrence is probably close to 10% in someone who continues to smoke. It is not insignificant and it may even be higher. It is very difficult to collect that data. Certainly, if they stop smoking, it could be as low as 3%. It is a real difference compared to if people stop smoking to if they continue to smoke.
- Miller In your practice you work with a group of people, many or most of who have been smokers and may have been drinking heavily. Can you think of a number of success stories where people have quit?
- Deshpande Most people, I am happy to say, do stop smoking. I think they hear it from so many people, whether it is the nurses, or the medical assistants or the physicians, and they are very, very

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motivated to stop. There are unfortunately a few people who do continue to smoke and I have seen some of those people develop second cancers, which is very unfortunate.

- Miller Absolutely. Let's talk a little bit about two related topics. One is, if someone has symptoms, how is the diagnosis made and secondly, after someone has been treated how do you monitor them?
- Deshpande To answer the first question, usually they do see their primary doctor and occasionally the primary doctor will see a lump on the neck of that patient and that could mean that one of the lymph nodes in the neck is affected. That is not an uncommon way that the diagnosis is made. Often at that stage the primary doctor, or a radiologist, can put a small needle in there and make the diagnosis. Usually, however, the symptoms will be a sore throat, change in the voice or a problem swallowing. Then the ENT physician will have to make the diagnosis using something called a fiberoptic laryngoscope, which is a smooth flexible telescope that goes down as far as the larynx, and they can see exactly what is going on.
- Miller A biopsy of some kind will establish the diagnosis. CAT scans, MRIs, what tools do you use?
- Deshpande CAT scans and MRIs are used usually to determine stage of the disease. We usually stage diseases in cancer in a uniform way using something called that TNM system. T stands for the size of the tumor, N stands for the lymph nodes, whether or not they are involved, and M is whether the cancer has metastasized or spread to other areas. Head and neck cancer staging is slightly different from the staging of other cancers. Most cancers are staged in 4 stages where stage 4 means the cancer has spread over the whole body. Stage 4 for head and neck cancer could mean one of three things, either it has spread to many lymph nodes in the neck, the cancer itself is very large, or it could mean that it has spread over the body. Two of those stage 4 cancer types, stage 4A and stage 4B if you like, are technically still treatable and often curable by either surgery or radiation alone.
- Miller For other types of cancer, say lung cancer or breast cancer, stage 4 would mean you probably would not operate, but with head and neck cancer even with stage 4 some of those patients can still have surgery.
- Deshpande That is correct, yes, especially stage 4A cancer patients. In fact, the whole staging system changed about 6 years ago to create this new stage 4A category to determine which patients could still be treated with an operation. I said surgery or radiation alone, I meant surgery or radiation is the primary modality with chemotherapy as an adjunct to that.
- Miller For patients who have had a head and neck cancer, they have surgery for a stage 1, 2, or 3 or perhaps even 4. In terms not so much of the treatment, but the monitoring afterwards, because again some of these patients have risk of recurrence or for a new cancer developing because of

12:27 into mp3 file [http://yalecancercenter.org/podcast/Answers\\_Jun-01-08.mp3](http://yalecancercenter.org/podcast/Answers_Jun-01-08.mp3)

smoking or alcohol, what do you recommend in terms of monitoring?

Deshpande We usually see those patients every three months and the ENT physician, usually Dr. Sasaki or Dr. Ross, will also see them as well. They will have physical exams just like anyone at their primary doctor's office and they will also have a fiberoptic laryngoscopy exam from the ENT physician. We also attempt to do CAT scans every 3 to 6 months, and that is because sometimes we can pick up small lymph nodes or small tumors either in the digestive tract, as we call it, or the lymph nodes in the neck much earlier than we can detect them by feeling the area.

Miller People are at risk of developing other cancers especially if they are still smoking. It sounds like that is your opportunity to find a new cancer, if it were to develop, earlier.

Deshpande That is correct and we usually do a scan or a chest x-ray, a CAT scan of the chest, to look for the second primary cancer.

Miller We would like to remind you that you can e-mail your questions to us and to Dr. Hari Deshpande at [canceranswers@yale.edu](mailto:canceranswers@yale.edu). We are going to take a short break for a medical minute. Please stay tuned to learn more information about head and neck cancer with Dr. Hari Deshpande from the Yale Cancer Center.

#### Medical Minute

*The American Cancer Society estimates that in 2008 there will be over 62,000 new cases of melanoma in this country and about 2400 patients are diagnosed annually here in Connecticut alone. Melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths but when detected early, melanoma is easily treated and highly curable. Clinical trials are currently underway and federally designated comprehensive cancer centers such as the Yale Cancer Center to test innovative new treatments for melanoma. Patients enrolled in these trials are given access to newly available medicine, which have not yet been approved by the Food and Drug Administration. This has been a medical minute. You will find more information at [www.yalecancercenter.org](http://www.yalecancercenter.org). You are listening to the WMPR health from Connecticut public radio.*

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller, and I am here with Hari Deshpande who is an expert in the treatment of head and neck cancer at the Yale Cancer Center. Hari, one of the terms that we use a lot is multidisciplinary care. What does that mean for patients who come with a cancer of the head and neck?

Deshpande What it means is that many different physicians are going to see that patient and come up with a plan based on the general consensus of all those physicians. That is very important in all cancers, but especially head and neck cancer where surgeons, radiation oncologists and medical oncologists

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have to work closely together to come up with a good plan. Like many other cancers we have what is known as a tumor board meeting where we all meet and discuss patients, but what is unique about the head and neck cancer team is at our multidisciplinary tumor board, we have the patient's come into the room itself. It may be a little daunting for some patients, but they appreciate knowing that all the physicians are seeing them at once and coming up with a plan. We get to see the films and sometimes even see a video of the laryngoscopy, which is very important.

Miller So, the patients are there for this discussion?

Deshpande That is right.

Miller That is unique.

Deshpande Yes.

Miller Do they get to hear the discussion?

Deshpande They hear part of the discussion. We can ask them questions. We have 1 hour to see six or seven patients so we tend to have part of the discussion behind closed doors and part of it in front of the patient. At the end of the tumor board meeting one of us, say Dr. Sasaki or myself, will go out to them and explain what the findings of the meeting were.

Miller It sounds like a truly wonderful approach. Let me throw out a scenario where the whole team might be involved. It used to be that if a patient had cancer of the voice box or the larynx, they would lose their voice. Now there is a lot of talk about organ preservation, larynx preservation. Treating a patient with a cancer of the larynx, how might the whole team be involved with that?

Deshpande That is a very good example because any one of three different approaches can be used. If the cancer is very small sometimes they can use what's known as preservation surgery; in other words, using a laser or different surgical techniques. They can remove the cancer without removing the larynx. They can also use radiation therapy alone if it is very, very small. If it is bigger, then they tend to use a combination of radiation and chemotherapy and still hopefully preserve the larynx. The patients will not need a tracheostomy, which is the hole in the neck, and they will be able to still talk. Now, obviously, in some people these approaches do not work and they will end up needing the larynx to be removed, but even in those patients we have an excellent speech and swallow department within the ENT department. They can often have people trained in different ways of speaking, one of which is to use a vibrating device that is put against the neck that allows them to make sounds and some people are able to talk very well using that.

**18:30 into mp3 file [http://yalecancercenter.org/podcast/Answers\\_Jun-01-08.mp3](http://yalecancercenter.org/podcast/Answers_Jun-01-08.mp3)**

- Miller One of the new advances happening in cancer in general is targeted therapies. What targeted therapies do you have in head and neck cancer that are new or helpful?
- Deshpande We have one in particular which is called Erbitux, or cetuximab. Head and neck cancers, as I mentioned earlier, are usually something called a squamous cell cancer. Those cancers tend to have on the surface a lot of proteins which we term receptors, and they will attract various things in the blood, one of which is called an EGFR, or epidermal growth factor receptor. It attracts various proteins, one of which is the epidermal growth factor, and what we know about these cancers is that those receptors are very prevalent on the surface of the cancer cell, but not so present on other cells in the body. So, if you can target those particular receptors, then, in theory, you can treat those cancers. It is not quite as easy as that because they present on other cells, especially in the skin. What we found is that the side effects tend to be a little different with these treatments rather than traditional chemotherapy.
- Miller How do you use this medicine Erbitux, do you use it by itself, or do you use it with chemotherapy or radiation?
- Deshpande We tend to use it mainly with radiation. It seems to be what we call a potent radiosensitizer. In other words, if patients get radiation alone versus radiation with Erbitux, they tend to do much better in terms of survival and actually treating the cancer, if Erbitux is added to the radiation. The nice thing is that they do not seem to get the side effects that they would get if we added chemotherapy to the radiation.
- Miller We talked about surgery having a very prominent role in the treatment of head and neck cancers. How would you make the decision of whether to use chemotherapy either preoperatively or postoperatively, for a patient who has come in to the tumor board?
- Deshpande That is an excellent question. These days head and neck cancer, as well as other cancers, are beginning to incorporate chemotherapy much earlier in the treatment. With head and neck cancer, we tend to use chemotherapy up front only if we are going to use radiation afterwards. That is mainly because if you give someone chemotherapy for head and neck cancer, the surgeon then finds it very difficult to see where the margins are. We can often make the cancers get much smaller, but the surgeon does not know where to finish cutting. So, we do not tend to use it before an operation but we do use it before radiotherapy.
- Miller Very interesting. What are some clinical trials that you are involved with and excited about here at the Yale Cancer Center?

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- Deshpande We have one clinical trial using a combination of two different chemotherapies, one of which was developed at Yale called mitomycin C along with a pill called capecitabine in combination with radiation. That trial should be coming to a close soon, but we also have a lot of trials in a different type of head and neck cancer, thyroid cancer, which I have not talked about.
- Miller You are truly an expert when it comes to thyroid cancer. Tell us about that in terms of some of the new developments.
- Deshpande Thyroid cancer is really a disease by itself if you consider head and neck cancer as a whole. It does not behave like a squamous cell cancer. It is very rare to start, and it tends to have a much better prognosis. You will often hear people say that if you are going to get a cancer, thyroid cancer is the one to get. In the past they usually treated with operations and something called radioiodine. But there are many different types of thyroid cancer. There are at least four different categories that we tend to put thyroid cancers in and they tend to be treated in very different ways. For instance, the papillary and follicular thyroid cancers are treated with surgery and radioiodine preparation. Medullary cancers come from a different cell type and they tend to be treated with surgery and traditionally radiotherapy. Then there is a terrible disease called anaplastic thyroid cancer which until recently had not been able to be treated with any kind of treatment.
- Miller Let me ask you about anaplastic, because I know that is the area you have a lot of expertise, what are you working on?
- Deshpande We have a clinical trial at Yale using a new agent called CA4P, or combretastatin, which is a new class of medicine called a vascular disrupting agent. There have been a lot of trials on different ways of attacking cancers. One of the ways is to try and attack the blood supply of the cancer, and we know that agents, which are called vascular endothelial growth factor agents, or antibodies, are very effective in colon cancer and breast cancer, but this new agent actually seems to stop the blood from getting through those new blood vessels. It will cause congestion in that blood vessel. Interestingly, it was originally found from the bark of an African willow tree and it was used in the spears of the Zulu tribes. If we use it in too high quantities it is not a good thing because they used it as a poison, obviously. We have found a way of using it properly.
- Miller What a novel wonderful thing to take something that was first poison, and use it against cancer.
- Deshpande It is just amazing how it was found, I can't take any credit for that.
- Miller For patients who are treated with this drug, and I am going to ask you to say the name again, what kind of results are you seeing?

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Deshpande The name is combretastatin, and I am hopeful the company will come up with a better name in the future. It is brand new. In this particular trial, there are two patients in the country that have been treated and one of those was at Yale and we're screening another patient now. So far we have amazingly seen a stabilization of the disease. Now this is a disease that usually runs rampant within a few weeks or months. Even stable disease is a good response.

Miller For patients we would love to be able to get rid of the cancer, but also to be able to live with cancer as a chronic disease.

Deshpande That's correct.

Miller In terms of other therapies for thyroid cancer, it sounds like it is a multidisciplinary approach,

Deshpande The thyroid group here at Yale, headed by Dr. Udelsman and Dr. Sosa, who are thyroid surgeons, is very active. As I mentioned, I often do not see those patients because they do so well with surgery alone or surgery plus radioiodine. But for those unfortunate patients in which the disease has spread widely or they have anaplastic cancer, then we do have a meeting once a week with the surgeons, the nurses and the research assistants, and once again it is a whole team that comes up with an approach for that particular person.

Miller It is very exciting that there are new drugs available. Those patients with thyroid cancer, do they also come to this multidisciplinary tumor board?

Deshpande They do not come to that tumor board. They are treated in the endocrine although they are seen through the endocrine tumor board, which is a different area at Yale. In some institutions the head and neck cancer tumor board will include thyroid cancer. Here, because we are a referral center, we have enough people to see in a separate tumor board.

Miller It is very exciting and very interesting. I want to thank you for joining us on Yale Cancer Center Answers.

Deshpande Thank you very much.

Miller For myself and our staff at the Yale Cancer Center, we want to wish all of you a safe and healthy week.

*If you have questions, comments, or would like to subscribe to our podcast, you can go to [yalecancercenter.org](http://yalecancercenter.org) where you will also find transcripts of past broadcasts in written form. Next week, you will learn about drug development and clinical trials.*