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## **What's New in the Treatment of Head and Neck Cancers**

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*Support for Yale Cancer Answers comes from AstraZeneca, committed to researching innovative treatments to address unmet needs in head and neck cancer. Learn more at [astrazeneca-us.com](http://astrazeneca-us.com).*

*Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about head and neck cancers with Dr. Rahmatullah Rahmati. Dr. Rahmati is an Assistant Professor of Surgery at Yale School of Medicine and Dr. Chagpar is an Associate Professor of Surgery at Yale and the Assistant Director for Global Oncology at Yale Comprehensive Cancer Center.*

Chagpar      There are a lot of things in the head and neck right? There are eyes and nose and ears and throat and tonsils and skin and teeth, but when we talk about head and neck cancers, what specifically are we talking about?

Rahmati      I would like to talk about head and neck cancers that involve what we call the upper aerodigestive tract. That is basically your mouth, your throat, and your voice box.

Chagpar      And how common are those? Most of us think about cancer and we know the big ones; we know breast cancer and lung cancer and colon cancer. Very few people talk about voice box cancer. How common are these head and neck cancers?

Rahmati      Fortunately, not that common. There is about 60-65,000 new cases of head and neck cancer in the United States annually. It is a much bigger problem globally, about 500,000 cases, but again, in the United States about 60,000 new cases.

Chagpar      And what causes it?

Rahmati      Various risk factors; the most common risk factors are tobacco use, alcohol use and in the last few decades HPV related head and neck cancers; in particular HPV-related cancers involving the tonsils and the base of tongue.

Chagpar      Many of us when we think about HPV, we think about cervical cancer, we think of it as a sexually transmitted disease. How is it that HPV causes oropharyngeal cancers? Is that from sexual contact or is that a systemic spread, how is it that HPV causes tonsil cancer?

Rahmati      Exactly as you just mentioned, it is a sexually transmitted infection and the mode of transmission as it pertains to head and neck cancers is similar. It involves oral sex basically as the main mode of transmission.

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- Chagpar When we think about HPV-related cancers, we often talk on the show about the HPV vaccine, so is that effective in head and neck cancers, is it the same strains as you would get in cervical cancer?
- Rahmati It is in fact. There are what are called high-risk types of HPV, in particular type 16 and type 18, which are associated with cervical cancers and other cancers in the sort of genital area, and similarly in oropharyngeal carcinomas, 70% of them in the United States that are HPV related are mostly related to HPV 16 and 18.
- Chagpar In order to prevent head and neck cancers, just like cervical cancer and anal cancers, vaccination is recommended?
- Rahmati Absolutely. In fact, the Centers for Disease Control advises vaccinating boys and girls starting from the age of 9 and individuals can be vaccinated up to the age of 26.
- Chagpar What if people have not been vaccinated, let us say they still have not been exposed to HPV, is there an opportunity to get vaccinated beyond the age of 26 or is that a hard cutoff by the CDC?
- Rahmati It is not a hard cutoff. It is mainly a recommendation. Certainly, if an individual were to have never engaged in any sort of sexual contact or activity, then absolutely, it would be very reasonable for that individual to undergo vaccination. Another thing that could be considered is to be tested to see if they have antibodies in their blood system against those HPV surface markers. And if they were negative, then in that individual, theoretically vaccination would be of benefit.
- Chagpar Good to know. So, are those the only ways to really prevent head and neck cancers, do not smoke, do not drink, and get vaccinated?
- Rahmati Those are the big risk factors, absolutely. Obviously, if there is a strong family history of cancer or any other sort of genetic predisposition and it is kind of difficult to change those circumstances, but again, tobacco, alcohol and HPV are the main risk factors for head and neck cancer.
- Chagpar The other thing that you mentioned which ties into risk factors is the fact that this is particularly common in certain parts of the world outside of the United States. And certain cultures that come from various parts of the world may have habits that predispose them to head and neck cancers, can you talk a little bit about that?
- Rahmati In particular regions of the world, like Asia and certain countries within Asia, there is a tendency to use something called beetle nut. Beetle nut is actually 2 different things.

It is the leaf of the beetle tree, which is used to wrap the areca nut, which is the fruit of the areca plant and it is basically mixed in with other things including nicotine and individuals place it within their mouth. And the use of beetle nut increases the risk of oral cavity cancers. So, cancers involving the tongue, the inner cheeks of the mouth, the floor of mouth are more related to the use of beetle nut. And then, in other parts of the world, in particular South East Asia, esopharyngeal carcinoma is of a higher incidence. Individuals there can have dietary influences that affect the incidence of nasopharyngeal carcinoma, just to explain what nasopharyngeal carcinoma is, it is cancer located in basically the back of the nose. And so, certain foods that are cured with salt, if it is high in the diet, they can potentially predispose to nasopharyngeal carcinoma, and also the Epstein-Barr virus is associated with nasopharyngeal carcinoma. So, those two predispose individuals to that type of cancer.

Chagpar Epstein-Barr virus? A lot of people might know that one from mono?

Rahmati Correct, same virus.

Chagpar So, if you have had a history, many people who went to college used to call mono the kissing disease, if you got mono when you were in college, does that put you at an increased risk of getting nasopharyngeal cancer later in life?

Rahmati Not really. It is quite a rare cancer and that relationship here in the United States, we just do not see.

Chagpar So, there are a number of risk factors for developing these head and neck cancers, really the nice thing about it is that many of these risk factors aside from family history which as you said you cannot do much about, you really can do something about; you can avoid alcohol, smoking, eating beetle nut if you are from that particular part of the world, you can get vaccinated and so on.

Rahmati Absolutely. Which is also why we have noticed a decrease in head and neck cancer in particular of the voice box over the decades due to reduction in tobacco use.

Chagpar After we talk about prevention, what we often talk about when we are thinking about cancers is, if you cannot prevent the disease from occurring, can you at least prevent the disease from killing you. And oftentimes, we do that with secondary prevention or screening. Is there a screening test for head and neck cancers, should people be going and getting a doctor to look inside their mouth every year or how should that work?

- Rahmati Great question. We do not have specific screening tests, but certainly if someone were smoking on a very regular basis and in combination with significant alcohol intake, it would not be a bad idea to see their primary care physician on an annual basis and have it checked. Obviously, if there were any new symptoms that the patient had that were unusual to them, in particular changes in their voice that may signify a lesion or a growth on their vocal cords, that would be a reason to seek medical attention for further investigation. Certainly, if they noticed an ulcer or pain in the mouth associated with bleeding, some irregularity that was never there before, that can be brought to their doctor's attention or they can seek evaluation by an ear, nose and throat doctor or perhaps even their dentist, or sometimes it is their dentist that notices it on examination during a routine dental visit.
- Chagpar I think one of the things is that we often neglect is to really look inside our mouths, and we think, I have a little bit of a mouth sore, my tooth hurts a bit I have a little bit of a cough so my voice may have changed because maybe I was yelling too much at the football game last night, whatever; when should these symptoms really trigger us to get things checked out? Head and neck cancers are not very common, nobody is thinking, that nosebleed might actually be a nasopharyngeal cancer, but sometimes it might be?
- Rahmati That's a great point. I think that any symptom that persists over 4 weeks is worth being evaluated so that persistent sore throat, perhaps reduced hearing, recurring nosebleeds, pain with swallowing, difficulty swallowing, changes in the voice – anything that has persisted over 4 weeks is worth having evaluated. Often patients come in because they have noticed a lump in their neck and that would signify that potentially something is lurking in there in their throat and is now metastasized or spread to a lymph node in the neck.
- Chagpar So, certainly if you have these symptoms, you go and get them checked out and the first person you would likely go to is your primary care doctor. So, what happens after that?
- Rahmati The primary care physician after performing an examination, they may refer the patient for imaging with an ultrasound or CT or MRI depending on the circumstances, but that may set the stage for further investigation with either referral to a physician like myself or for a needle biopsy perhaps if there was a mass in the neck or perhaps a biopsy inside the mouth.

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- Chagpar      What is the most common head and neck cancer that you see?
- Rahmati      The type of cancer that is called squamous cell carcinoma. Again, it can be involving the mouth, so the tongue or the area under the tongue or the back of the throat. The tonsil and base of tongue.
- Chagpar      So, somebody presents with say a bleeding ulcer in that area, they go to their primary care doctor, the doctor looks inside their mouth and lo and behold sees an ulcer, ultimately get some imaging, which shows that there is a lesion there, what usually follows next is a biopsy. How is that done, is that usually done with a needle biopsy, is that a surgical biopsy, how does that take place?
- Rahmati      Depending on the location; if it is in the mouth and is easily accessible, we can perform a biopsy right in the office with a little bit of local anesthetic. If there is a suspicious lymph node in the neck, then we can organize for an ultrasound-guided needle biopsy with the guidance of an ultrasound machine and a thin needle, a specimen would be obtained from the neck mass and that would be sent for pathology.
- Chagpar      We can get this diagnosis and it sounds like it is not too difficult to obtain, but after we take a short break for a medical minute, we will learn how we are going to treat head and neck cancers.

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*This is a medical minute about colorectal cancer. When detected early, colorectal cancer is easily treated and highly curable, and as a result, it is recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Tumor gene analysis has helped improve management of colorectal cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents resulting in more patient-specific treatments. More information is available at [YaleCancerCenter.org](http://YaleCancerCenter.org). You are listening to Connecticut Public Radio.*

- Chagpar      This is Dr. Anees Chagpar, and I am joined tonight by my guest, Dr. Rahmati. We are talking about care and diagnosis of head and neck cancers. Now, head and neck cancers really are cancers that occur in the upper aerodigestive tract; your nose, your mouth, your tongue, your tonsils, part of your esophagus. It is a big range of cancers, all of which kind of occur in a zone where we often don't pay much attention. One of the important things that Dr. Rahmati reminded us right before the break was if you have persistent symptoms, nosebleeds, mouth sores, changes in your voice, persistent

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cough, lumps in your neck, things that are causing you concern that have not been there before, that are still there for about 4 weeks, you really ought to go and get it checked out and do not be nervous about that because oftentimes it is simply a matter of having a medical professional looking your mouth, see if there is something there and getting a biopsy to get a diagnosis is often an office procedure, is that right?

Rahmati Absolutely.

Chagpar So, you can get a diagnosis, but the scariest thing about getting a diagnosis, Dr. Rahmati, is that nobody likes the C word. So, let us talk a little bit about prognosis. We are going to get to treatment in a minute, but how bad is head and neck cancer?

Rahmati Head and neck cancer can be quite bad if it is more advanced in stage. Most cancers are staged from stage I to IV and just to look at it in a simplistic way, stages I and II are what we might call early and stages III and IV are more advanced cancers. So, an individual with an advanced stage cancer, again if you want to use numbers and look at it from a simplistic perspective, the prognosis is 5-year survival of 50% unfortunately. So, obviously like in any cancer, we would like to detect it early and be able to manage it early because the outcomes are far greater.

Chagpar One other question that I had lingering from what we were talking about before the break, we said we do not really have great screening, but we do have things that can prevent cancers, so reduce your risk. Smoking increases your risk, alcohol increases your risk, getting vaccinated for HPV reduces your risk, but one question I had was let us suppose you have been a smoker, it is really tough to quit smoking, Dr. Rahmati, and let us suppose you drink and you drink somewhat heavily, in those people, should they routinely go for a head and neck screening? I know that in our communities we have had head and neck screening fears. Should people be going to those and getting somebody to look in their mouth every year, every 6 months or is this something that they should really go and get checked out only if they have symptoms?

Rahmati If they are aware of a head and neck cancer screening in their community, absolutely that would be a fantastic idea for the individuals there to use that resource to get checked out.

Chagpar Because as you said, I am just thinking about that statistic you gave with late-stage cancers of 5-year 50% survival rate, means that there is also a 50% mortality, that is a flip of the coin at 5 years, boy we would really like to catch these cancers early. So, if you cannot get screened, at least when you have a symptom, go and get it checked out

early so that these cancers can be detected. Let us suppose you do that, you have a sore throat, you notice a lump in your neck, you do not even wait for 4 weeks, you wait a couple of weeks and if it is still there, it has never been there before, you go to your doctor, your doctor says good thing you came, we did this biopsy and lo and behold we found a little cancer, now what?

Rahmati So, again, we would start off after the biopsy confirming that it is squamous cell carcinoma, we would do further workup with imaging to assess the extent of the disease; is it just located inside the mouth, has it spread to the neck, is it elsewhere in the body. The patient may be referred for a PET scan which would look for abnormal uptake that you might see with cancer throughout the body, and once we have completely staged it and we have an idea of whether or not this is early versus late cancer, then we talk about treatment. Again, to simplify things, for early cancers, we can employ or use single modality therapy; for instance, just surgery alone or radiation alone. If it is more advanced in stage, then that is where we use a more team-based approach with the medical oncologist and the radiation oncologist, in which case the patient may require upfront surgery followed by radiation or chemotherapy and radiation or depending on the location of the cancer, that patient may just need chemotherapy and radiation and no surgery at all. So, at that point, we would have the patient see the other members of our, if you want to call it, cancer team and we will come up with the best plan based on that patient's cancer, the extent of their cancer, location of cancer and ultimately what is most suitable for that individual.

Chagpar And I would imagine that different cancers are treated differently. For example, we lump all of these cancers into the big bucket of head and neck cancers, but I would imagine that a cancer in your nose may be treated differently than a cancer of your tongue, which may be treated different than a cancer of your voice box, is that right?

Rahmati Correct. We do go into something called organ preservation in terms of preserving certain structures like the voice box. So, in those individuals with cancer of the larynx, there may be a discussion on preserving the larynx with chemotherapy and radiation as opposed to surgery, in which case the voice box is removed. In terms of cancers that involve the oral cavity, we have to deal with the jaw bone and in those cancers, we oftentimes use upfront surgery followed by radiation or chemoradiation to avoid the potentially toxic effects of radiation to the jaw when given at full doses. So, you are absolutely right, depending on the location, we may favor one treatment over another for various reasons relating to function and respect of certain anatomical structures.

Chagpar You gave us this statistic in terms of survival for a late-stage cancer, what does that statistic look like for early stage cancers that are treated with optimal therapy?

- Rahmati      Pretty good. It could be anywhere between 70-95%.
- Chagpar      That is pretty good. But then the other question that I have is, we start talking about surgery and chemotherapy and radiation particularly in the head and neck where there are so many vital organs that do so many things- they help us to smell and to chew and to taste and to talk and to breathe, what is the quality of life, what are the sequelae, what are the complications of cancer treatment?
- Rahmati      You bring up a really good point there, it definitely can have an impact on an individual's quality of life and this is something that I often discuss with my patients, and we all as cancer physicians make it a point to explain that our goal number one is to treat to cure, but our secondary goals are to maintain optimal function, whichever amount is possible. So, unfortunately, with combination therapies, there is certainly a likelihood of some dysfunction with regard to everything that you described- impairment in speech, difficulties with swallowing, dry mouth, changes in one's ability to smell and taste. So, it is a matter of balancing between getting an oncological cure and trying to preserve function, and it is really at this point we are doing quite well with cure and our focus is slightly shifting towards optimizing quality of life in maintaining function for the patient. Certainly, with HPV-related cancers of the throat, we are seeing that the patients are doing really well compared to those who do not have an HPV-related cancer, and there are clinical trials looking at ways of deescalating therapy, meaning reducing the severity or the intensity of therapy that we are subjecting the patients to; reducing the chemotherapy, whether or not chemotherapy is even needed, reducing radiation dose, in fact we are sort of going back towards surgery for most of these patients now. So, functional capacity, quality of life are definitely important things that we keep in mind when treating these patients, we explain to them the potential side effects of therapy and hopefully future studies will allow us to more carefully address these critical issues.
- Chagpar      Tell us a little bit more about that, both in terms of why it is that HPV-related cancers do better than non-HPV-related cancers and second, tell us more about the clinical trials and the new therapies that are coming out that might actually improve quality of life while still maintaining a good cure rate.
- Rahmati      So, your traditional risk factors of tobacco and alcohol basically create over many years of exposure to those toxins, genetic damage to the entire upper aerodigestive tract. So, you have a multitude of mutations that have occurred within potentially over the entire throat, and so therefore, they tend to have tumors that can be quite resistant and have multiple types of tumors within that anatomical subsite, and therefore, those

individuals are at higher risk of recurrences, of new primary tumors or developing multiple tumors at the same time. With regard to HPV, we are not seeing that so much. It seems to be more of an inhibition of certain mechanisms that our body has to prevent cancer, the virus creates proteins that basically bind to those sort of tumor-blocking mechanisms, and therefore, we are just seeing that the patients with these HPV-related tumors seem to do better with less therapy in fact.

Chagpar      So, the clinical trials are now looking at less therapy, better outcomes in terms of functionality, what is on the horizon?

Rahmati      There was a clinical trial looking at primary surgery for HPV-related cancers and then appropriate what we call adjuvant therapy, which is either radiation or chemotherapy and radiation after surgery, and so, that trial has been completed and we do not have the results to it, so we are awaiting the results from that to shed some light onto see the feasibility of deescalating therapy in those patients. I think the other broad frontier is the use of immunotherapy in head and neck cancer. We are seeing more of its use in recurrent cancers and metastatic cancers, and again there may be some promise there. We are certainly seeing a lot more benefit in other types of cancers in the head and neck region, in particular rare salivary gland cancers as well as melanomas where immunotherapy seems to be providing significant response to some individuals with those cancers.

*Dr. Rahmatullah Rahmati is an Assistant Professor of Surgery at the Yale School of Medicine. If you have questions, the address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and past editions of the program are available in audio and written form at [YaleCancerCenter.org](http://YaleCancerCenter.org). I am Bruce Barber, reminding you to tune in each week to learn more about the fight against cancer here on Connecticut Public Radio.*