



Understanding Head and Neck Cancers

Head and neck cancers, also called head and neck squamous cell carcinomas, usually begin in the squamous cells that line the mucosal surfaces of the head and neck region. Head and neck cancers can form in the oral cavity, throat, voice box, nasal cavity, paranasal sinuses, the salivary glands and the muscles and nerves in the head and neck.

The global incidence of head and neck cancers have increased considerably over the past decade. Men have been found to be more at risk compared to women. The major risk factors include tobacco and alcohol consumption, however, HPV – the human papilloma virus has emerged as a novel risk factor for these cancers.

We are talking to Dr Patrick Ha, Professor and the Chief of Head and Neck Oncologic Surgery at UCSF, to get an in-depth understanding of head and neck cancers, the current standard of care, and differences in prognosis & treatment of HPV positive and HPV negative patients. Joining us on the panel to bring in the patient perspective is head and neck cancer warrior Sean Breininger.

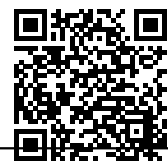
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Priya Menon: Hello and welcome to CureTalks. This is Priya Menon your host. Today on CureTalks, we are discussing Head and Neck cancers, and we have with us Dr. Patrick Ha from the University of California, San Francisco. Dr. Ha is Chief of the UCSF Division of Head and Neck Surgical Oncology whose expertise in patient care covers the full scope of Head and Neck surgery with a focus on thyroid and parathyroid surgery as well as endoscopic approaches to throat cancer surgery. Joining Dr. Ha on the panel today is a cancer survivor and advocate Sean Breininger. Welcome to CureTalks, everyone.

Dr. Patrick Ha: Thank you.

Priya Menon: Doctor, my first question on the head and neck cancer, maybe you could tell us a little bit about kind of how common it is and how it typically presents itself. I mean, my assumption is that head and neck are relatively small areas that are in some ways visible at least on the outside if not on the inside. So, it tends to present itself at typically a fairly small stage, because you would notice something before a tumor got very big. So, is that right? So, how does a typical patient present themselves?

Dr. Patrick Ha: Sure. Well, so, as you can imagine, that's a pretty broad question, but there are so many different areas of the head and neck. And interestingly, depending on where it shows up. You might have different symptoms that cancer will behave very differently and even our treatment approaches will be quite different. So overall there are about 65,000 head and neck cancers a year in the US and that covers anywhere inside the nose or throat and the salivary glands, but that's excluding the thyroid gland which has sort of its own type of behavior. But so sometimes the first thing people notice is a bump in the neck. And that might either represent a mass or it could represent a lymph node, which means it had spread from somewhere else. But from within the throat what can be challenging is that it's not always easy to see. So, things that are in the mouth you might notice that might be painful, but things deeper in the throat you may not notice. It may just feel like a tickle in the throat so it can be kind of disconcerting sometimes to try to understand what that symptom might mean if you can't see it. So, there are times like you said, when they can choose, may present early but there are oftentimes unfortunately when they can be hidden, and you



wouldn't be able to notice it until later on.

Priya Menon: Okay. So, head and neck are practically quite new for me, and I've been reading up for this show. So, what are some of the risk factors and is there any screening that is recommended for patients?

Dr. Patrick Ha: So, the biggest risk factor that we know of is smoking and as you can imagine the smoke would interface with all the different areas of the head and neck, whether it's the nose, the mouth or throat, the voice box. So, all those areas are at risk and that's a quite high incidence of head and neck cancers in the patients who are consistent smokers. Alcohol also can play a role while it's much less than that of smoking the risk if they are combined then it's even worse. So, there's something about the damage that occurs from both alcohol and smoking that increases it even higher. Lately, I'm sure we'll talk more about it. But HPV has been an increasing risk factor and that generally it is a sexually transmitted disease. So, those sexual practices can sometimes lead to an increased risk. Although it's still quite low in the grand scheme of things. But those are the predominant risk factors. And then there are some genetic disorders, and we will probably get into that but things like Fanconi anemia and there are other susceptibilities that can actually lead to an increased risk of head and neck cancers. But most of the times are required being that it's not a genetic predisposition. It's not passed down from family, different member to family member in that way. So, it's usually, some sort of change that has occurred during one's lifetime. I will say that most of the times, even though smoking and alcohol are very related to this. It isn't uncommon for it to just be sporadic meaning there's no apparent reason. And so, you can't pinpoint a true cause oftentimes.

Priya Menon: I know I'm going to reiterate, that you talked about the HPV virus. Can you talk how does these viruses reach a very high level? How do they contribute to or cause cancer formation in this particular setting? And also, maybe you could compare the prognosis as compared to HPV-related and non-HPV cancers?

Dr. Patrick Ha: Sure thing. So, I realized I forgot to answer the question about screening. So, we don't really have a great screening tool for the same, the way we do breast cancer mammography and things like that or a PSA test. But one thing that is important atleast for oral cancers, things that happen in the mouth, your dentist, and dental providers have all been trained to screen for these types of cancer. So, that is one way in which people can notice these cancers as they are smaller. When it comes to things like the voice box or tonsils or deeper inside, like I said, they're hard to see. So, there's not a great utility in screening people because it is pretty rare. So, you have to have such a large effort to try to find just a small number of folks. With respect to HPV, we didn't really know about this being a cause of head neck cancer and specifically talk about oropharynx cancer and what that means is the tonsils or the back of the tongue. So, it's very specific to that area at least in the in the US and North America, but we discovered this probably in the early 2000s when the association was noted and it seemed that there is an association with people who had this type of tonsil or tongue-based cancer, who were younger, they tended to be non-smokers. So, we're trying to understand why was this happening in this group that we thought was what should have a low incidence of this cancer and then it was discovered that the cells looked a little like they would in cervical cancer. They had a funny appearance to it and then, so they had the brilliant idea of checking for HPV, and they found it. So specifically, there are many, many different subtypes of HPV and the subtype that is most commonly associated is type 16, although there are some others that account for probably 90% of the oropharynx cancers. And the way it works is that the HPV will integrate and kind of interfere with the DNA of the cells in the tonsillectomies, interestingly it lays dormant for some time. So, it's not like a recent exposure would necessarily lead to cancer but most of the time just delayed by 30, or 40 years. So, the age group of people who get these cancers is not 20-year-olds or teenagers but it's still happening in people who are 40 and above typically. So, we don't know why that dormant period exists but somehow it is able to interfere with the cells' processes and then they turn into cancer later on. In terms of the behavioral differences as you alluded to there is a difference in the type of patient. So, meaning it can be associated with smoking. But oftentimes people who have had this cancer, they don't have the same risk factors, simply the HPV that can cause cancer in a way that may contribute to the fact that the prognosis is also much better. So, more recently we had adopted to and change our staging system to account for HPV-related oropharynx cancer because their survival was just so much different than that of patients who didn't have HPV the same type of



cancer in the oropharynx. So yeah, so the prognosis is much better. And I think what's happening now is there's been this transformation of understanding well, how do we treat it more differently. To date, we've relied on some of the same methodologies whether it's surgery or chemo and radiation, but we haven't really changed that. And so, we have to do that kind of a stepwise fashion if we're going to think about reducing or changing our treatment paradigms. So, there are a lot of clinical trials, and a lot of studies going on in centers across the country and world to see whether we could limit some of the toxicities that we imparted from our treatments and try to maintain that same success in terms of oncologic safety.

Priya Menon: Thank you, Dr. Ha. So, before we move on, I just want to get your thoughts also on the HPV vaccination.

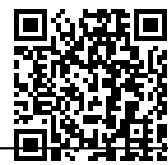
Dr. Patrick Ha: Oh, yeah.

Priya Menon: It obviously got a lot of public health attention and potential impact also in cervical cancer. What is its effect on head and neck cancers?

Dr. Patrick Ha: So, it's been sort of a slow go because when the vaccine was initially introduced, it was predominately tested in or not predominately but only tested to look for cervical cancer prevention and risk reduction. And we realized that it was the same strains of HPV that can cause cervical cancer. So, our assumption was that it would also help with head and neck cancer, but that wasn't really on the label. It also has a case that head neck cancer doesn't really get a whole lot of press. So, adding that to the label wouldn't necessarily motivate people to vaccinate more heavily or to think more about it. But that being said, more recently, the FDA did come out with the fact that the HPV vaccine would be helpful for head and neck cancer. So that is now on the label. And so, while we don't have historical data because it's going to take 30 to 40 Years once people vaccinate to understand that there's a risk reduction and there's a reduction in incidence, but we fully expect that to occur. Keep in mind that when often people who have tonsil cancer may come in and say, hey should I get the vaccine? And you might say, well, it's a little late because we don't know if there's any therapeutic benefit to it, so it's mostly preventive. So, what I counsel my patients is get your kids, grandkids and everyone around you to get vaccinated because you're sort of an indicator of what could happen and we want to prevent that, but I'm not sure that's really helping the person with cancer at hand.

Priya Menon: Sounds good. Dr. Ha, now I would get Sean into this discussion. Sean you're a cancer warrior and have had head and neck cancers. It would be great if you could share your story briefly with us.

Sean Breininger: Sure. Thank you, Priya so much for having me, and nice to see you, Dr. Ha. Yeah, so my head and neck cancer journey first started with a diagnosis of the genetic disease Fanconi anemia. I was diagnosed with the disease in June of 2011 and by that December, I was undergoing a bone marrow transplant. Fanconi anemia almost certainly led to bone marrow failure or leukemia. It is key to have a transplant before you reach those stages as the transplant becomes more difficult with either diagnosis. Even though I received a transplant, which cured the disease in the blood. I was still at high risk of getting additional cancer. So, since 2011, I've had bladder cancer, which resulted in the removal of my prostate and bladder and over 100 skin cancers, including melanoma. Those with Fanconi anemia are also seven hundred times more likely to get head-neck cancer. So, my risk of head and neck cancer was also higher because of the radiation I received during the transplant. Since 2015, I have had ten head and neck cancers, three on my gums, one on my inner cheek, two on my lips, and two on my tongue with one of those resulting in the removal of the left side of my tongue and because of metastasis removal of the left lymph nodes in my neck. I've also had two throat cancers with the second diagnosis that needed chemoradiation to treat it. I'm seen both by an ENT and an oral surgeon on a regular basis. The medium lifespan for those with Fanconi anemia is 33 and I'm currently 43 and there's not a day that goes by without me wondering when the next cancer will be diagnosed as almost certainly that will happen. But I remain hopeful that we will find even better diagnostic treatments for catching cancer in its earliest stages, as currently, that is the best way for increasing my chances of survival.



Priya Menon: Thank you. Thank you, Sean, for that. Are you currently on any treatments?

Sean Breininger: My last treatment for head and neck cancer was oral cancer I had back in August of last year that was able to be removed by surgery.

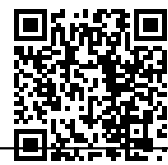
Priya Menon: Okay. I see you have quite a few questions on treatment. So, I'm going to let you ask them.

Sean Breininger: Sure. And some of these might overlap with what you've already said, Dr. Ha but I'll go. Any new trends in diagnosing patients with head and neck cancer? For example, I've had brush biopsies done, that have caught oral cancers and in the very earliest stages, but I wonder if there are others.

Dr. Patrick Ha: Yes, I'm coming down, I think again, there are different subsites, where different things, and testing modalities may be relevant. I think for oral cancer lot of it ends up being visual. So, we do end up in sounds like you're being seen regularly by several teams to look around for white patches that don't belong or persist. That's something that people at home can do, they can open up the mouth, look around, and take a flashlight. It can be kind of scary because you're not always used to look at your own mouth. So, you'll need the help of experts, but if you notice a patch or something that hurts, or an ulcer then certainly can bring that to someone's attention and a biopsy can be performed. I think, in terms of novel areas of exploration for diagnosis, putting oral cancer, a lot of it is looked at either staining agent. So, sometimes I don't know if your practitioner uses but they can use like iodine-based solutions or dilute and blue or dyes that basically help kind of coat the area and then point to areas of concern. So, those are kind of old-fashioned in a way these solutions have been around for hundreds of years. And now the question is, are there newer sort of molecular type agents that we could use to help identify cancers. Imaging is a little bit hard because with scans there's only a certain limit of the resolution that you can have in your eyes are better than what the scans are going to show particularly because it usually starts on the surface. So, scans will show deeper things, but they kind of are limited to things that are lying on the surface or flat. So mostly, I think the trend on oral cancer is going to be towards looking at different agents, we can paint or coat, or different lights or dyes, different laser wavelengths so that we can use to help our eyes notice the areas of concern. When it gets to HPV, that is a bit different because now we have a totally different marker, that shouldn't belong. And so one new thing that's come up is using blood tests so we can actually test and see little fragments of the HPV DNA circulating around the bloodstream and it's not good for screening because again it's pretty rare. And there may be instances where people have some exposure but doesn't mean there's cancer. But then the presence of a mass or cancer, we can use that in the surveillance phase. So, it's even treated, but we can use that blood test to say, okay, that HPV level should be 0 now, and if it starts to keep up, then we know that there's something going on. So, there are certainly different circulating markers that can exist, and there are some companies who are doing customized markers. So, for example, if your cancer had a certain fingerprint or signature of its DNA, they would test that at the start and then they would look in the bloodstream to see if they can see those same markers as well. So again, it's still kind of an early phase but you can imagine that you might have a day when rather than getting scans or even exams like you do the blood test and then only when that turn positive or showed something of concern, only then need to look further, but that would allow us to look find things early.

Sean Breininger: Sure, and with diagnosing, are there any new treatments for head and neck cancer that has emerged over the past couple of years?

Dr. Patrick Ha: So, there's different classes. So, I'd say on the surgical side we are definitely doing a lot of endoscopic type of approaches. And I'm sure you've heard of the surgical robot and that endoscopic tool allows us to work around corners with high visualization and the instruments are kind of everything smaller. So that with that, miniaturization we can actually get to places just through the mouth that we wouldn't have before. I'd say that the radiation side, they're different radiation modalities. So, you might have heard of proton therapy, which is a different way of delivering the radiation energy that hopefully will lead to fewer side effects. Proton centers are still kind of emerging, so it's not like they're in every town but we'll see what happens. And whether that technology sort of sticks for head and neck cancers. On the medical oncology side, I think the biggest thing that has changed is immunotherapy and that has happened for maybe the past



five years or so where our understanding that there's an immune component to how these cancers arise or progress, and that we can actually unlock your own immune system to go fight cancer has been really intriguing. Because, as you might imagine with chemotherapy, for example, we give the drug and cancer responds, but then, once you stop the drug or cancer get smart and kind of develops resistance then that drug is no longer useful. For immunotherapy, the concept is that if your immune system can go attack it, it can recognize and attack cancer, then it's like you trained your own body to do what it needs to do. So, you can almost release and stop giving the treatment and you might still have durable effects. So, we've had patients on this, where the tumors can seemingly magically disappear, but it also can stay that way. Because it's not just that when you stop the drug that there's not a lingering effect. In fact, you train the body to kind of do what it needs to do. So that is a huge area of investigation of different combinations, different types of drugs and also understanding, when to give it, do we only give it at the end, we give it at the beginning or middle, and how do we combine that with our current treatments?

Sean Breininger: Also, we hear a lot about CRISPR gene editing in the news. Do you think that will become a treatment option for head and neck cancers?

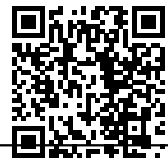
Dr. Patrick Ha: It depends on the subset of cancer. So, for example, and even for Fanconi anemia since what you have, there are still many variants of it. So, it could be that for something like that, where it's truly a genetic disorder, the idea or the concept that we could replace and fix that gene. And then get those cells to kind of behave appropriately that would be amazing. So yeah, there could be some possibility of that down the road. I mean there are obviously a lot of technologies that would need to be developed to make that reality. The issue is that for most of the other head-neck cancers, it's not a simple switch. It's not just one gene that leads to one problem and then that leads to cancer. It's usually a combination and a mix of all sorts of different types of genes. So, although we said for the blood test, that it would be kind of crazy to try to understand what the tumor is, and then find it in the bloodstream and be able to use that as a marker and we're starting actually to do that now. So, you could envision a time when there was like a series of different gene-editing tools that you could use for different variants of genes and then apply a custom level of that to different patients depending on what their errors were. So, it's possible. I don't want to say it's not possible, but it's not let's say the first thing that they're going to try, you know there are certain disorders that have just one hook and then you can change it and then it might lead to the desired result. But the head and neck cancers in general, tend to be a little more complicated.

Sean Breininger: With all these diagnoses my wife, Allison has been by my side as my primary caregiver. Do you have any words of advice for caregivers of patients with head and neck cancer?

Dr. Patrick Ha: Oh sure. Yeah. I mean the moment we meet someone from their initial diagnosis. I tell them to look it's going to be a long road, we're going to end up on the good side of it and we're going to do everything we can, but that none of it is easy. So, none of the therapies that we've talked about briefly, whether it's surgery, radiation, chemo, they all have different side effects. They all have different processes as they unfold, and we know that we're taking a toll on the patients, and we are causing a lot of harm with the hope of trying to bring back some normalcy to your life. But the caregivers often get forgotten, so I think I love it when I see patients together with their spouses or caregivers, friends, and family, and I know that covid is impacted some of that, but hopefully, we're getting back to where we can see people in person and together. But I do spend time to talk with them and just check in to make sure they're doing okay. We have a lot of support networks. So, I think that for these support groups that we often participate in and host, we encourage everyone to come, families and loved ones are often on the line. Now, again now it's mostly Zoom like this, but it allows everyone to participate in sort of understand that while you're the one going through all these treatments unfortunately that they're also shouldering quite a bit of burden. So, it is important not to forget that it's a team effort.

Sean Breininger: As a doctor, what hopeful messages do you have for us head and neck cancer survivors?

Dr. Patrick Ha: Well, I think that first off, the diagnosis can be scary. So, I think oftentimes I hope we provide is that we know what's going on. And I think that initial visit, it just by the nature of the fact that this is fairly



rare that you don't often have many friends who have gone through this or people you know that you can talk to and say what to expect. So, having that visit to understand the landscape of what needs to be done, how am I going to do? Just understand the plan basically is sort of the first step in the whole process. But I think that the hope is that everyone understands that everything we do is for a purpose. So, the harm that we cause is for the good that we hope to get at the end like we hope to reap those benefits. I think what's also wonderful, especially I'm spoiled working here at UCSF is that it's a team, so I don't ever view the surgeon is the one who's going to go in and take everything out because oftentimes we don't. As you've alluded to there are some cancers that you had surgically managed but there are some that are not, that we will go hey, this is a better case for radiation or chemo. And so, working within that team is also, I think very comforting to the providers, but also to the patient's so that you all understand that there's like a hundred different heads, thinking about your cancer and how to best treat it and then how to manage those side effects. And so, I think understanding that when you meet the following specialist and you meet the dental oncologist, you meet the social worker, the nursing, all these folks who are taking part in your care, you understand that you're being thought of not just as a disease, as cancer but more so that there's a comprehensive look into cancer that you have. So, I think all those things provide hope, and then not to mention the fact that we're still innovating, we're trying to collect tissues and do research in the lab and trying to make a difference. I think in a way that we do with our hands but also then with our minds, once we start thinking about disease more deeply and how to try novel therapeutics and introduce that to patients.

Sean Breininger: I think those are mine. Yep.

Priya Menon: Thank you, Sean. Those are great questions. Dr. Ha I'm just going to take a little step back and go back. I know you spoke a lot about the treatments on Sean's questions. Like I just want to know, just elaborate a little bit on that. So, imagine somebody who's just been given a diagnosis, right. What would be the general approach in terms of what's common and what's different based on specific situations I think for head and neck cancer preservation of function plays a very important part, like swallowing, nutrition, voice, etc.? And I know you've talked about a whole team who actually manages this. So, a little bit on that would be helpful.

Dr. Patrick Ha: Yeah, sure. So, we are sort of alluding to it, but depending on the sub-site, we may or may not favor surgery over non-surgical approaches. So, it's often the case. And there's sometimes where split down the middle, where we could do this, we could do that. It just sort of depends. So, a lot of what we do in the office is explaining the nuances of the differences, you'll often meet all the folks taking care of you and who have some opinion about what's maybe the best treatment plan for you. And then we coordinate with something called a tumor board. And I believe that most places do something similar to this, but we all meet in a room. Well, now it's on Zoom. But we meet and we talk about people. We discuss their disease, we look at the Radiology, we confirm the pathology, and those nuances can often make a difference in our thinking of what's the best treatment plan. Sometimes you have to make tough decisions on maybe the best cure would be removing the voice box, but then that person would be left altered and maybe not able to work or do the things that they enjoy doing. So maybe in those situations would even accept the slightly less optimal, cure regimen, but an attempt to try to preserve their function. So, these are pretty difficult conversations to have, they're difficult to understand, because how do you explain what it's like to have a laryngectomy, how do you explain what the voice would sound like afterward. And this is where I think patient advocates like yourself, Sean are so important. So, we have many patients for example, on laryngectomy. So, we said, look I'll talk with any patient who comes through, I know what they're going through. They can see what I'm like and help them understand, at least, I think that's so important. As we can only approach it so much medically, when we tend to talk, I guess I think about cancer and all the technicalities of what I'm about to do. But sometimes it's easier to show what it's going to be like just by meeting someone who had it done. So yeah, there are so many different aspects to it. And so that's why we've created such a big team here, but it really is through communicating not just with the patients and families, but with each other, the care team as we think about like, what is happening right now, what are we trying to optimize, how we achieve the best chance of cure, but also preserve their function and their sense of self.

Priya Menon: Thank you, Dr. Ha. One last question before we wrap up for today. If you have to pick one



research, that's particularly exciting for you right now, which one? What would it be?

Dr. Patrick Ha: Well, so I'm kind of a higher side, so a lot of my research focuses on salivary cancer. But obviously, I'm a hand in so many different areas of research. I'll broadly say that the field of clinical trials is something that is extremely exciting, and I've got to see that more and more here at UCSF. But the thought of taking novel therapeutics and bringing them into the clinic is, extremely exciting. And so, this can happen at all levels, whether it's with surgery, whether it's of radiation or chemotherapy or immunotherapy. But seeing the effects of things that we normally would not have tried and saying something dramatic, which we've seen for some of these trials where we're not sure what's going to happen, but we design it in a safe way. But then the effects can be quite profound and astonishing. So, for every one of those, you think, well think how much effort and finances and commitment to the on the patient side to undergo, these kinds of newer things has led to this result and then you start thinking more globally well, how can we now take this and make it more standard? Just that process can be pretty cumbersome. It makes it all worth it when you see these results in front of you. And then you also get filled with hope, you're saying, Sean like what do you say right? When we keep doing the same thing, we know what results we're going to get in the percentages that we can change now, but the real question is, what can we do in the future? So, from the lab side trying to create and understand, what the problems are, how to fix it and then bringing that to patients is the thing that I find really exciting. And every day we're seeing that here. So, it really motivates us to do even better.

Priya Menon: Yeah, thank you very much. Dr. Ha. Sean, I know you've gone through a lot, and you have survived. Do you have any message for the audience?

Sean Breininger: Yeah, I think my biggest message is to get screened early as soon as you feel or see something suspicious, even if you don't have a history of head and neck cancer in your family. One of my tongue cancers was basically it was a mild dysplasia and within the next six weeks with being monitored closely got metastasized and was a stage III squamous cell carcinoma that metastasized to the lymph nodes. So, these cancers can move quickly. And I just hope that when people feel something or see something that's just not quite right that they really take that seriously.

Priya Menon: Thank you, Sean. Thanks. Thank you, Dr. Ha for educating us on the head and neck cancers, and Sean for your story and those great questions, thanks. And we also thank UCSF Helen Diller Family Comprehensive Cancer Center. This talk will be available on curetalks.com. So, thank you everyone, and have a great day.

Thank you.