

Support comes from AstraZeneca, a global science led biopharmaceutical business committed to bringing to market innovative oncology medicines that address high unmet needs. More information at astrazeneca-us.com. Welcome to Yale Cancer Answers with Drs. Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers is our way of providing you with the most up-to-date 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 the treatment of head and neck cancers with Dr. Barbara Burtness. Dr. Burtness is a Professor of Medical Oncology at Yale School of Medicine and Dr. Chagpar is an Associate Professor in the Department of Surgery at Yale School of Medicine and the Assistant Director for Global Oncology at Yale Comprehensive Cancer Center.

Chagpar So Barbara, you know, I think we hear a lot about cancer in the media these days, but often times we hear about breast cancer, lung cancer, colorectal cancer, tell us a little bit more about head and neck cancers.

Burtness So head and neck cancers are cancers that arise in the linings of the mouth and nose and the throat and the voice box or that arise in salivary glands or the sinuses or thyroid cancer, but the big majority of these cancers are cancers that start in the back of the throat, on the tongue, or in the voice box. In the past, almost all of these cancers were caused by exposure to tobacco and alcohol, but in recent years, we have seen a really dramatic uptick in the different kind of head and neck cancer which is head and neck cancer in the tonsil or the base of the tongue or the back of the throat which is caused human papilloma virus. Human papilloma virus is the same virus that has been associated with cervix cancer in women for many years. It is a kind of human virus, it is very prevalent, there are 200 different types of human papilloma virus, and there a handful of these types that are strongly associated with causing cancer. Luckily, we have a vaccine and if people get treated with the vaccine, if they get vaccinated, when they are between the age of about 11 and 26, the evidence is very good that they will be protected from getting cancer or genital warts from human papilloma virus and it is an important vaccine both for girls and boys, but we have many people in the United States who have been exposed to this virus before the vaccine was available and we are still concerned about the possibility that these people could become patients by developing head and neck cancer in the back of the throat.

Chagpar So first key message I guess is that this vaccine is both for boys and for girls because it is not just a cervical cancer vaccine, it also protects you from head and neck cancers and both boys and girls have oral pharynxes and tonsils and back of the throats, and so both boys and girls need to be vaccinated, but you mentioned that they should be vaccinated sometime between the ages of 9 and 26, what happens if you are 30 years old, you have never been vaccinated, and you are listening to this radio program and you are thinking to yourself - "I don't want to get head and neck cancers." What should they do, should they still get vaccinated or is it too late?

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Burtness That scenario, that we probably will be learning more about as we study people who have been vaccinated. The current recommendation is to consider taking the vaccination up until the age of 26. People who are concerned should discuss it with their physicians and stay tuned because as we develop more vaccines and more booster strategies, there may be a time in the future where we actually measure whether or not you are immune to the virus before we make a different recommendation about vaccination for older adults, but at the moment, the recommendation is up to age 26.

Chagpar And when you mentioned the other thing which is that while HPV causes some head and neck cancers, other head and neck cancers are caused by smoking and by alcohol. So tell us more about that and what are the recommendations in terms of, is there an appropriate "safe limit" of alcohol that people can consume without being concerned about head and neck cancer?

Burtness Alcohol and head and neck cancer is probably predominantly a cofactor. So, when we see patients who had a lot of alcohol exposure and who have head and neck cancers of nonvirally associated kind. It is usually associated with tobacco exposure. So if I have 1 message for people who are listening today is that if you are smoking, you should try to quit smoking and there are a lot of benefits to quitting smoking, it improves your cardiac health, it lowers your risk of many kinds of cancers, many cases improves quality of life, it saves money and there are a lot of reasons to think about giving up smoking. And the belief is that if you have been a smoker, you may continue to have an increased risk of head and neck cancer relative to people who were never smokers, but you will reduce your risk compared to if you continue to smoke.

Chagpar So, I am sure that people are listening to this program and thinking I know I really ought to quit smoking, people keep telling me I ought to quit smoking, but quitting smoking is really hard. So what are some steps that people can take in order to help them to quit smoking, I mean because it is not so easy?

Burtness That is right, it is hard. On the other hand, over half of everybody in the United States who was ever a smoker has successfully quit smoking.

Chagpar So there is hope.

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Burtness So there is, people focus on the fact that many people have been able to do it, they will realize that they can do it too. There are a lot of strategies to help people quit smoking. We have a very strong smoking cessation program here at Smilow and we work hard to get our patients to think about meeting with tobacco cessation counselors. I think that it helps people to focus on what are the upsides of quitting smoking, so it is probably somewhat easy to think

about the downsides like how much you are going to thinking about having that next cigarette, but if you realize that within the first couple of days of quitting smoking, you reduce your risk of a heart attack. If you focus on how much better your quality of life is likely to be the avoidance of emphysema, the avoidance of cancer, many times there might be people in your life who have been begging you to quit smoking and this will make them happy. Those are all things that can be helpful as well there are a lot of medical strategies now, so we have nicotine replacement, it comes in a variety of forms, there are medications that can moderate the symptoms of withdrawal, so I would really encourage people to look into joining a program or getting some counseling to set a quit date, think about the ways in which quitting smoking could be helpful.

Chagpar Alright, especially with the New Year, it is a great time to make that as a resolution. So talk to your doctor if you smoke. Now, what kind of people get head and neck cancer. Is it predominantly in one particular racial group or a particular age group or is this a nondiscriminating kind of cancer that affects everybody?

Burtness So the average age of people who get head and neck cancer is in their low 60s, but we do see people with head and neck cancer even in their 20s and we see people with head and neck cancer in their 80s, so the very fact of not being in your 60s does not mean that if you have a nonhealing sore on your tongue that you should not go get it checked out, younger people do get head and neck cancer. People of all ethnicities and in all parts of the world get head and neck cancer. There are some differences. Human papilloma virus related cancers seems to be more common in the United States, in Northern Europe than it is in other parts of the world and as I have been saying, heavy exposure to tobacco and alcohol is associated with head and neck cancers and so not true that is a form of discrimination, but people who have been using a lot of tobacco and alcohol are at a higher risk.

Chagpar Yeah, you know, I just got back from Bhutan doing some global oncology work there, I guess the other thing for people from certain parts of the world is chewing betel nut, which is often mixed with tobacco. Do you see that a lot in Asian people in the US or is that really not something that has been brought over by immigrants from other parts of the world?

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Burtness We do see a fair bit of that, particularly in people from south Asia, it is associated with a condition that is called submucosal fibrosis, so there is a lot of scarring inside the mouth, inside the lips and the cheeks and underneath the tongue, that can precede the development of these kinds of head and neck cancers and there is also a precancerous condition, we also see this in people with cigarette smoking, tobacco exposure called leukoplakia where there are these little white plaques that form on the inside of the mouth and sometimes when we biopsy these, we can see that they seem to be precancerous and regular

dental care can be helpful because dentists are very good at identifying these areas of white plaque and suggesting when a biopsy should be done. You know, I guess we just asked everybody who is listening and who smokes cigarettes to think about quitting cigarettes, but if you are listening and you chew betel nut, I think that you should think about quitting that too, because it has a strong association with the cancers inside the oral cavity. Interestingly, there is a lot of great research into head and cancer that comes out of cancer hospitals in India and they also have a lot of the kind of head and neck cancers that we do that is associated with cigarettes smoking. It is not all betel nut in that part of the world.

Chagpar What about e-cigarettes, are e-cigarettes safe in terms of head and neck cancer or they to be avoided as well?

Burtness I think that is something that we are still learning about. There are concerns about e-cigarettes in terms of are they a good strategy for longterm quitting compared to other kinds of nicotine replacement, but the evidence to date seems to be that they are not as carcinogenic, so I think that the jury is still out but probably between e-cigarettes and a pack of cigarettes.

Chagpar Yeah, avoid the pack of cigarettes, ok. So we have talked a little about risk factors and prevention in terms of vaccination. How do people recognize head and neck cancer? I mean you mentioned these little white spots, kind of hard to see that in the inside of your mouth or nonhealing ulcer. Other warning signs that people should be paying attention to and really going, getting them checked out without thinking that it is just, you know a sore for sure. Burtness So the sort of 7 cardinal signs of cancer that people have seen on posters and sort of holed here but it would be an area that was not healing, something that was swollen or painful, but was not normal and so if we would just kind of go from top to bottom in the area of the head and neck, people who present with cancers in the back of the nose, those are called nasopharynx cancers, they will often give a history of that they have had bleeding or discharge or obstruction in their nose for several years before the diagnosis was made. So chronic sinusitis should be evaluated by an ENT surgeon, there should be a careful evaluation if you have evidence that one of your sinuses is obstructed chronically. Then it turns out that earaches are not really common and normal for grown adults, so an adult who has the kind of earache that in a child, you would say I will give him a course of amoxicillin and the child would be better, in an adult that should be taken seriously and there should be a full evaluation of the area of the head and neck. I mentioned nonhealing wounds on the tongue, so tongue cancer with a mass or an ulcer that persists over the course of months is certainly concerning.

00:13:25 into MP3: https://ysm-websites-live-prod.azureedge.net/cancer/2018-YCA-0204-Podcast-Burtness_326519_5_v1.mp3 Burtness New-onset hoarseness can sometimes be a sign that there is something wrong with the larynx or the voice box and so somebody who has developed hoarseness and it does not go away over the course of a couple of weeks, they should think about getting evaluated, and then the last thing is if there is a swelling in lymph node in the

neck that does not get better, sometimes you get those when you have a cold or something, but if it is not better, not going down and not improving within a couple of weeks after you are over the cold that is also something that should be evaluated.

Chagpar Excellent. Well, we are going to take a short break for a medical minute and when we come back, we are going to learn more about head and neck cancer, how to recognize it and how to treat it. Medical Minute Support comes from AstraZeneca, committed to researching innovative treatments to address unmet needs in head and neck cancer. Learn more at astrazeneca-us.com. The American Cancer Society estimates that there will be over 1500 people will be diagnosed with colorectal cancer in Connecticut this year. 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 to 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. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital. More information is available at YaleCancerCenter.org. You are listening to WNPR, Connecticut's Public Media Source for news and ideas.

Chagpar This is Dr. Anees Chagpar and my guest, Dr. Barbara Burtneess joins me tonight to talk about treatment of head and neck cancers. Now before the break, we talked a little bit about prevention, a key message, make sure that both boys and girls are vaccinated against HPV by the age of 26 to really protect yourself against virally associated head and neck cancers and key message #2 in terms of prevention was to avoid tobacco, whether it is pack of cigarettes or betel nut mixed with tobacco, all of those things increase your risk of head and neck cancer. Now Barbara, before the break you were telling us about signs and symptoms, sores that do not heal, hoarseness that is new, earaches that are in grownups that really should not be expected. Let's suppose you have one of those symptoms and you go to your doctor and your doctor proceeds through a number of tests and presumably a biopsy to diagnose head and neck cancer. Tell us more about the prognosis, is that a death sentence and how is it treated?

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Burtneess Well the first thing to say is that many kinds of head and neck cancers are highly curable and that is one of the reasons that we think prompt detection and appropriate workup and high quality care make a big difference. So you said the person goes to their doctor and they get a battery of tests and a biopsy, I do have to say that very often we hear a story that the person went to their doctor and they got antibiotics first because the natural assumption when you have a sore throat or you have a swelling in your neck is that you have strep throat or something like that. So not that it is wrong to take antibiotics, but it is wrong to assume that because you took antibiotics, you know, everything is going to

be okay and so if you go to your doctor and you have a sore throat, a lump in your neck, or a swelling in your neck and you take the antibiotics and things are not better at the end of 2 or 3 or 4 weeks, it is really important to go back in and get checked again. And at that point, it is quite likely that your doctor will say I need you to see an eyes, nose and throat surgeon and send you to an ENT, and that person is quite likely going to pass a scope down and look around the inside of your throat and the back of your nose and evaluate everything. If something looks abnormal, if there is a growth or a swelling, there could well be a biopsy at that point and there could well be a scan like a CAT scan or something to see how many lymph nodes are swollen, to see what areas are abnormal, and then pretty often at that point, the ears, nose, and throat surgeon will say you know I am not a cancer specialist, lets get you to somebody who is very expert in managing head and neck cancer. And head and neck cancer surgeons work very closely, hand and glove, with what we call a multidisciplinary team and that involves not only the surgeon but also radiation oncologist, a medical oncologist, a speech and swallow pathologist, who is expert at assessing what kind of differences in swallowing and speaking would you experience if you had an operation for a given tumor as opposed to you took radiation for that tumor, and so usually you find yourself evaluated by a pretty big group of people and you are like, "wow, this is a lot of people and a lot of appointments," but the point of that is to allow all those specialists to come together in what we call tumor board or multidisciplinary tumor board and go over the scans and the biopsy and the location of the tumor and then, there are a number of treatments that might be equally curative for a patient, so surgery followed by radiation or radiation given together with chemotherapy or radiation given by itself or surgery given by itself. Different patients will have different curative options and our goal is always to pick the approach that has the best chance of cure as well as the best preservation of function. So if something is in your voice box and you can be cured by taking radiation, you probably do not want to have your voice box removed. On the other hand, there are some areas where a tumor can be removed very simply and you might not even need radiation or you might need radiation but not chemotherapy, and so the goal in our decision making is always to find the sort of the most parsimonious approach to the best cure with the best functional outcome. Now one of the things that has been going on in our field is really interesting, is that it turns out that the human papilloma virus associated cancers and the tobacco associated cancers are not really behaving the same when you treat them with surgery, chemotherapy, radiation and many of the treatments that we have developed over the years and that we have proven over the years can cure people might represent just the right amount of therapy for the tobacco associated kind of cancer, and too much therapy for the human papilloma virus associated cancer.

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Burtness cont.'d So we now have different trials, when we are looking at new treatments, we separate out the HPV related cancers and the others because in

HPV, for people who have smaller tumors and who are not smokers, a lot of our questions have to do with could we cut back on treatment a little bit; whereas for the other kinds of cancers, we are still looking to add new treatments to make the cure rates higher.

Chagpar And so talk a little bit more about some of these new therapies, what kinds of things are on the horizon, what kinds of things are exciting in the field of head and neck cancer because it sounds like head and neck cancer very much like other cancers is a moving field where new and exciting things are happening that are really making this a curable disease.

Burtness Yes absolutely, so many stages of head and neck cancer are highly curable and so we do not want to leave behind the things that have cured many patients, so surgery, well-delivered radiation from a radiation-oncologist who specializes in head and neck cancer, those are still really good techniques, but for patients who have a high risk of recurrence or for patients where their cancer comes back, there are a number of really new things that we are looking at and one of those is immunotherapy, this is not unique to head and neck cancer, it has had a big impact on other kinds of cancer as well, but we recognize that some medicines that can kind of take the brakes off the immune system and help the immune system be better at recognizing that cancer cells do not belong there. Some of those treatments are active in head and neck cancer and they are active actually in both of the kinds of head and neck cancer that I have been talking about. So for people where the cancer has come back after conventional treatment, we often look to start with a combination that includes an immunotherapy drug on a clinical trial or if the person gets treated with chemotherapy and the chemo is not working well anymore, we switch over to immunotherapy. So a lot of the clinical trials that we have open in the Yale now have to do with how could we make the immunotherapy better, so instead of one immunotherapy drug, we might add a second one. For the people with HPV-related cancer, we can add a vaccine to HPV together with the immunotherapy. We have treatments that are called targeted therapy which kind of try to make the cancer cell less responsive to growth signals and there is some evidence that by combining of some of those, we can get better effects. We are interested in combining those with immunotherapy. So particularly for patients who have higher risk of recurrence or where the cancer has come back, some of these new treatments offer really a different outlook to them we had a few years ago.

Chagpar Talk more about immunotherapy, I mean it is as you say one of these hot topics and the buzz word that is often used, certainly it is a clear clinical advance amongst many cancers, but is it really nontoxic, is it kind of like you are just boosting your immune system or does it have toxicities in and of itself that people should be aware of?

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Burtness So the first thing to say, it is much less toxic when it is given by itself

than our historical treatments, so it does not have the same kinds of side effects with risk of infection and you know, burn inside the throat and so forth that chemotherapy and radiation did. So it is easy, as you suggest to start thinking it really it does not have the toxicities that we are used to, it is a free ride and the answer is no, it is not, it does have its own side effects and lot of times, those side effects actually have to do with the very thing that we are trying to make happen. We are trying to make the immune system be more alert and friskier and what can sometimes happen is that the immune system can start recognizing normal tissues, as something that it wants to attack and so we believe that if we give a single immunotherapy drug to a person with head and neck cancer, there is about 17% chance that they will get those kind of immune-related side effects and the things that we see most commonly are diarrhea or shortness of breath and cough, luckily that almost always responds to treatment with something that will tamp the immune system down again, so we usually use steroids, and the other thing that is really interesting is once you have that immune reaction and you have gotten those immune related side effects, even though we are tamping down your immune system again with the steroids, it appears as if the effect against the cancer can often hold in those patients. So when we look at new combinations when we try to say well we know that this is one target in immune system that could make it turn on again and this is another target that could cooperate with that. One other things that we are looking for are combinations where we increase the effectiveness without really increasing the side effect profile and so there are some new strategies with the combination with a medicine called epacadostat, which is kind of boosts the main immunotherapy target that we have in head and neck cancer and it looks as if that combination nearly doubles the response rate without much difference in the side effects and so we have a big trial going with that combination now, I mentioned the HPV vaccine. We are also attempting for people of higher risk disease to get immunotherapy in a graded in with the first like treatment with the chemotherapy and the radiation because it is a different side effects profile, it looks so for as if that is something that is going pretty smoothly.

Chagpar So it is interesting when you mention the combination of immunotherapy and the vaccine because I had a few questions about that; the first is, I thought the vaccine was something that you could only give until the age of 26, but clearly patients with head and neck cancers tend to be older and then the second question is we think about vaccines, we think that the way that they work is you get exposed to an antigen and your immune system comes in and it goes and fights the antigen, so how that does work with immunotherapy - are they synergistic?

Burtress Different vaccine is the first thing to say, so there are preventive vaccines as we talked about before the break, and then there are therapeutic vaccines and in this particular vaccine, we are actually targeting a bacterial toxin to something that is made by the HPV virus and that is meant to lead the virally infected cancer cells to die and shed their antigens and provide a target for the immune system, so it is really a different mechanism than like your standard

measles vaccine or something like that.

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Chagpar Very interesting and so the other thing that you had mentioned a while ago is we kind of shift from talking about immunotherapies and kind of a medical treatment, now at least in breast cancer, you need to get radiation everyday and so you may be in a community where there is not, a particular radiation-oncologist who has specific expertise in head and neck, how important is that you travel to get that expertise or is the radiation schedules in head and neck cancer not on a daily basis?

Burtness Our radiation schedules are on a daily basis and we understand that this is a challenge for patients. The data seem to be pretty strong though they come both from collections of patients who are treated on research protocols as well as very large national databases, you know about the cancer database which represents over a quarter million patients treated with cancer around the country and so, if you look at these large databases and their number of publications that have come to the same conclusion, getting treated for head and neck cancer by radiation therapy doctor who does a large number of head and neck cases a year is associated with a substantial improvement and outcome.

Dr. Barbara Burtness is a Professor of Medical Oncology at Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at Yale-CancerCenter.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against can