

Support for Yale Cancer Answers comes from AstraZeneca, proud partner in personalized medicine developing tailored treatments for cancer patients. Learn more information at 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, in honor of Melanoma Awareness Month, it is a conversation about melanoma with Dr. Dale Han. Dr. Han is an Assistant Professor of Surgical Oncology at the Yale School of Medicine, and Dr. Gore is a Professor of Internal Medicine and Hematology at Yale and Director of Hematologic Malignancies at Smilow Cancer Hospital.

Gore I do not know who makes up these months, because I think you need a special calendar depending on what you are looking at. It seems like every month has something, right?

Han Absolutely and now it is almost every day for something new.

Gore Exactly. But melanoma, I would think that maybe the summer months should be melanoma months. Melanoma is a skin cancer, right?

Han Absolutely. Melanoma is one of the forms of skin cancer, and although it represents less than 5% of all skin cancers, it is actually the third most common. It is associated with about 80% of all skin cancer-related deaths. So, it is a very serious form of skin cancer.

Gore And it is my understanding, and correct me if I am wrong, that many melanomas, if not most, in terms of risk of causation, have to do with exposure to ultraviolet light from sunlight and so on right?

Han Well, that is a risk factor that most people associate with melanoma, but actually there are multiple risk factors and the most common are the ones that most patients are exposed to the most, certainly ultraviolet radiation exposure, but there are also other risk factors including a person's phenotype, meaning who they are, their skin type, are they red haired, blonde haired, blue eyed, so forth. Genetic mutations such as germline mutations that may make you more prone to developing melanomas and so forth, so there are certain other factors, but certainly these play a lesser role compared to ultraviolet light radiation exposure.

Gore Gotcha. So, we are trying to make our audience aware of melanoma, so I think all of the red-headed, blue eyed types are already getting nervous. How would I know that I have a germline mutation? I do not even know what that is.

Han A germline mutation is essentially a mutation that is passed on to you and one that you can pass on to your children. Less than 5%, or probably closer to about 2-3%, of all melanomas are associated or can be brought about by a germline mutation. Certainly, a vast minority of patients have melanomas that are associated with these. But when you see your physician, one thing you

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should do is relate any family history of cancers. Certainly, patterns of cancer cluster together, especially if you have had multiple first-degree relatives who have had melanomas and certain other types of cancers may raise the red flag and maybe we should check and see if there is a germline mutation.

Gore So, you might be aware that there is a lot of cancer and particularly that there are several people who have had melanoma in your family, is that right? And just mention that to your doctor.

Han Absolutely. But even with multiple people having melanomas in your family, that does not necessarily mean that you are harboring a mutation that makes you prone to developing melanoma.

Gore Maybe I will go to the beach without any sunscreen and get fried all the time, right?

Han Exactly. It is more like that you all have the same exposures to ultraviolet radiation exposure.

Gore Let's say I am a sunbather, which I am not, but I might have been at some point in my life. Han You look rather tanned.

Gore You think? That is the ethnic background I think, but be that as it may, I do use sunscreen now, but I did not back then and I have had more than my share of burns, but skin cancer, everybody knows people who have had skin cancer, so they get it lasered off or they get it frozen off, why should anybody be that concerned about it?

Han Well, there are a couple things to consider for melanoma. The first is that the incidence in melanoma has been dramatically increasing. Melanoma has been increasing about 1-4% per year and between 1950 and about 2001, the incidence of melanoma in the United States has increased over 600%, and now your lifetime risk in the United States of developing melanoma is approximately 3%.

Gore 3%?

Han And about 90,000 new cases of invasive disease are expected in 2018 with about 87,000 additional cases of melanoma in situ. So, we are talking about big numbers.

Gore Wait a minute. That does sound like a lot, but you are losing me a little bit on this in situ thing and invasive thing. Can you explain to me what that means?

Han So, cancer develops along a spectrum and in situ disease is essentially proliferation of abnormal cells that have not broken through a barrier called the basement membrane and have not invaded into deeper tissues and the dermis.

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Gore So, they are kind of at the top layer of the skin still?

Han Exactly, and technically, this disease in situ has no invasive components that are seen as opposed to a diagnosis of melanoma where a pathologist on a biopsy or on a surgical specimen will see melanoma cells that have broken through the base membrane, have invaded down into the dermis and there is a depth or thickness that is associated with it.

Gore I see. So, I guess people would like to have their melanoma detected when it is in that early in situ phase.

Han Absolutely. The earlier your melanoma is diagnosed whether as melanoma in situ or as a thin lesion which is up to a millimeter thickness, prognosis improves as you get thinner and thinner and thinner.

Gore Dale, I have got a lot of moles, I have always had a lot of moles and I have never paid them much mind, how would I know to be worried about it, I cannot go checking on my moles, they just seem like normal to me.

Han There are several things that we would recommend. One is your own self-evaluation because you know your body the best. You are going to look for changes in any moles that you see or the development of new moles or what we term as nevi. And essentially you are going to look for the ABCDEs. Asymmetry, border irregularities, color changes, diameter – 6 mm is what is stated although that now is a little bit controversial, elevation or evolution of the lesion and then we oftentimes add an F which is your own feeling about the lesion – if you feel that something is wrong with it, you should definitely have it evaluated.

Gore I know that sometimes I have had a lesion that my wife had picked out to tell me that it is changed or whatever and I do not know, my inclination is to kind of to minimize it, melanoma sounds so scary, I do not want to go to the dermatologist for any little thing that just seems silly.

Han You bring up an excellent point. The second thing that I was going to mention is that it is not only your own self-evaluations but evaluations by your family members, significant others and so forth, especially for areas where you cannot particularly look. The other third layer that we advocate for is for skin surveillance with a physician.

Gore What does that mean?

Han Essentially you will go see a dermatologist or primary care physician who will do a whole skin evaluation and determine where moles and nevi are located, do any of them look irregular, any of them suspicious appearing, any that would warrant a biopsy.

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Gore Does every patient of a certain age need to have a full body skin exam done by a dermatologist?

Han No, we would certainly overwhelm the entire system if every person went in to get skin evaluations, but certainly certain patients may benefit more than others, especially those who may have a family history, those who have had significant amounts of sun exposure, particularly patients who have had multiple blistering sun burns in their youth, patients who have new lesions or lesions or lesions that appear suspicious or have changed in some way, these are patients where there will be higher yield for having a skin surveillance.

Gore How much are our primary care physicians looking at all parts of the skin and paying attention to this, do you have any feeling for that?

Han Well, you are going to put me in a difficult situation.

Gore Tell the truth as you know it. That is why you are here for.

Han I think it depends on your practice patterns and your training. I think dermatologists are trained specifically in looking for skin cancers and looking for changes in moles and nevi. I think it varies a little bit more with primary care physicians who may not have the specific training and the experience for that, but certainly I mention general practitioners because there are certain areas in the country where there are not that many dermatologists, then general practitioners and primary care physicians take on this role.

Gore I have to say that when I moved to New Haven, my internist was doing kind of a routine physical and noted that I have a lot of moles, again nobody had ever indicated it was anything unusual to me and this is why I really would like you to see a dermatologist for this full body exam, which again totally caught me off guard because I had very little concern and I have got a good friend who is a dermatologist down in Baltimore, but I am a compliant patient usually and I went to see the person to whom he had referred me and it was very reassuring, it only took her about 10 minutes to do the whole full body exam and it was quite reassuring that she felt that I had a high average number she thought there is maybe a little alarmism, she did not describe it like that, she thought it was good primary care and it was reassuring to me that nothing looked bad. That said, she thought she is going to see me in 2 years.

Han Certainly, there are no specific guidelines and it all varies by practice.

Gore Okay, so let us say that my internist who was quite on the ball sent me to this person, and if she found something that she was worried about, what would happen next?

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Han So, you are saying that your internist had found it and then referred you to a dermatologist?

Gore Well, he just decided that he was not comfortable at all with my nevi or moles and sent me to the dermatologist and she found something that she was in fact somewhat concerned about.

Han So, usually the first step at that point once a suspicious lesion is found is to biopsy it.

Gore Why cannot we just watch it for a while?

Han Well, in my mind if you already have a suspicion or the F that you feel that something is wrong, in most of those cases, we will go ahead and biopsy it because again it is better to catch a melanoma in an earlier stage or as a thinner lesion than to wait and allow it to progress.

Gore Because the biopsy sounds scary.

Han Well, it does and of course any invasive procedure will sound scary, but a biopsy is an outpatient procedure, in the office and basically involves using 1 or 2 techniques, one of which is called a shave biopsy where you basically take a scrape or sample of the tumor using a razor and essentially you just inject local anesthesia, shave off the lesion and then allow the area to heal on its own. It may take several weeks and it is very well tolerated. The other type of biopsy that is performed is something called a punch biopsy where a device that looks like a small little fancy cookie cutter is used to punch out or to remove a cylinder of tissue after we have localized the area with local anesthetic. Once that is performed, the wound is closed with 1 or 2 sutures or a couple of sutures which are to be removed later on. Again, this technique is also tolerated very well.

Gore Gotcha. So, there is no place here for freezing and/or doing anything like that?

Han You bring up an incredibly important point in that if there is any melanocytic, meaning any type of mole or nevi that looks suspicious or has the potential in your mind of in any way being a melanoma, these lesions should be biopsied and not treated otherwise with freezing or any other technique without getting a biopsy to determine what the pathology is.

Gore I am going to want to find out exactly why that might be because freezing sounds a lot better than cutting, but right now we are going to take a short break for a medical minute. Please stay tuned to learn more information about skin safety and melanoma treatment with Dr. Dale Han.

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astrazeneca-us.com. This is a medical minute about survivorship. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life-changing experience. For cancer survivors, the return to normal activities and relationships can be difficult, and some survivors face long-term side effects resulting from their treatment including heart problems, osteoporosis, fertility issues and an increased risk of second cancers. Resources are available to help keep cancer survivors well and focused on healthy living. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

Gore Welcome back to Yale Cancer Answers. This is Dr. Steven Gore and I am joined tonight by my guest, Dr. Dale Han. We have been discussing melanoma, the very serious form of skin cancer. Dale, before the break you were talking about how anything that somebody might be considering a risk for being a melanoma must absolutely be biopsied rather than frozen off, can you explain why?

Han The reason we biopsy these lesions is to determine is it actually a melanoma, or is it a benign lesion that we can just watch and follow? Let's say we froze a lesion, you will never know if that lesion is actually a melanoma.

Gore Well, why does it matter if we got rid of it?

Han Well, the problem is that, let us say, you have frozen it, there is a fairly low chance that you have actually treated that lesion adequately and there is a very high risk that it will come back.

Gore Even if it is a teeny-weeny little thing?

Han Absolutely.

Gore So, the biopsy tells you that it is bad news, it is melanoma, but let us say it is one of these superficial, I think you called it, in situ types?

Han Correct. In situ is a very, very early form of melanoma and it is very treatable. And once you treat that lesion, you can be cured of that in situ disease. The problem is that once you have had one melanoma, you are at risk for additional skin cancers and about a 5% risk down the road for a new melanoma developing.

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Gore But the treatment there is just the surgery?

Han We classify treatments of cancers in general for as treatments of the primary tumor, which in this case would be the area on the skin and cutaneous melanoma is the most common form of melanoma. There are other subtypes of melanoma such as melanoma that occurs in your eyes, on mucosal surface, but in this case, that is treatment of the area of the skin that had a lesion and then we also

consider treatment of the lymph nodes if the lesion is appropriate for that and consideration for other sites down the road.

Gore Okay, so what if it is not one of these in situ things but it has invaded into this next layer of the skin that you call the dermis, what happens then?

Han There are a couple things that we need to determine from the biopsy results, one – is it melanoma and two – what is the thickness, meaning how deep is that melanoma going into the underlying tissues. We term a thin melanoma as up to 1 mm thickness.

Gore It is like nothing?

Han I would not call it nothing, but it is something that has a much better prognosis and the good thing is that about 60-70% of all newly diagnosed cases are thin melanomas, so that is a good factor. We term an intermediate thickness between 1-4 mm thickness and thick melanoma is greater than 4 mm. So, this is to give everyone a perspective how deep these melanomas form.

Gore And 4 mm is like a pencil point really, right? This is a small thing.

Han Yes, and as you mentioned, as you get deeper and deeper and deeper, the prognosis changes. Now, if this was a thin lesion, we would treat the primary with what we call wide local excision.

Gore And then go back and re-operate?

Han Exactly. So, the biopsy is done and then you have to do a formal excision with a wide local excision, which entails not only that site with the melanoma but also in large what appears to be normal skin around the melanoma, and this is in order to ensure we get everything out #1 and two to make sure that any microscopic deposits outside of that primary lesion are also removed so that we reduce, significantly reduce, the chance of that melanoma coming back.

Gore Is wide like 8 mm or is wide like 5 cm?

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Han We have national guidelines and there have been multiple clinical trials that defined the additional margins that we utilize in doing a wide local excision. So, this will vary anywhere between 1-2 cm beyond the primary site depending on the thickness of the lesion.

Gore And does that leave a bad cosmetic result?

Han Well it depends on what kind of surgeon you are.

Gore In your case?

Han It is always beautiful.

Gore So, 2 cm is pretty bad right?

Han It is. And we start utilizing that at thickness of 2 mm or greater and we can consider using it for lesions between 1 and 2 mm of thickness. So, as I tell patients, just like an auto mechanic, it is really easier to take stuff out, it is really reconstructing everything that is the challenge. So, reconstructing a wound entails multiple consideration, but there are several ways we can reconstruct a wound. The first is by what is called primary closure, in which we convert the excision into an ellipse or a football shape and then close it as a line. The thing that patients have to know about this is that although the wide local excision may only be several centimeters long, the wide local excision will be about 2-3 times that length so that we can close it as a line. The second we can close a wound is using a local flap where we transfer tissue around the excision site so that we can cover that defect.

Gore It is like a skin graft kind of thing?

Han Well no, a skin graft is actually the third way we can close a wound. We transfer skin from another area of the body and basically put it onto the defect so that skin can grow onto that defect.

Gore I see. So, it probably makes a difference if it is on the back or if it is on the butt or if it is on the face, right?

Han To a certain extent. It is more about, because everyone is different, everyone's body is different, the amount of tension that we see at each location varies, and it is more about the tension that we see at that site where we have removed the melanoma and whether we can close it, convert the lesion into a football shape and closer it together as a line, whether or not there is too much tension for that and we have to actually transfer a flap or if there is just far too much tension for all of this and then we have to utilize skin from another area of the body as a skin graft.

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Gore I was just thinking more as a patient that I would not really care if it is on my shoulder or back, but I might care more if it is right in my face in terms of what the cosmetic result is.

Han And that is one of the major factors that we consider in terms of the location, the cosmetic effect of the reconstruction and certainly we consider the extent of excision, the type of procedure that we are going to utilize and may be even help from let us say plastic surgeons to help us try to create the best cosmetic result for the reconstruction.

Gore I am sure most people do not want to put their health at risk to look better, but given the choice.

Han Absolutely. If we can incorporate both, treating the oncologic issues but also providing the best cosmetic results, certainly that is the best combination.

Gore Alright. It sounds like it is pretty easy-peasy with a surgeon like you to do this, how come we still hear about people dying of melanoma, I mean I still read about that?

Han The majority of cases, the majority of patients diagnosed with melanoma, treatment of the primary site, meaning the area of the skin that developed a melanoma, will be cured, but in certain unfortunate patients, you will see more aggressive biology, meaning that melanoma will behave in a more aggressive fashion. For instance, in about 15-20% of cases overall in patients diagnosed with melanoma, you can have spread of melanoma cells to the draining lymph nodes. Now, to explain this is that, every patch of skin your body drains, specific areas, specific nodal basins in your body. Let us say, on your arm, most melanomas will drain to the armpit or axilla if there is nodal spread. So, in a certain proportion of patients, this type of melanoma where there is spread to the lymph nodes, essentially denotes a more aggressive type of melanoma. And as I mentioned as you get thicker and thicker and thicker, you will have a higher risk for melanoma potentially getting into the blood stream and seeding or going to other sites of the body, what we call distant metastasis.

Gore And if it is in my lymph node, would I feel a lump?

Han Yes that is certainly possible and about 10% patients when you look at database, actually present with enlarged lymph nodes that are found to have melanoma, but about 80-85% of patients present with just localized disease, meaning disease that you just find on the skin if it is cutaneous melanoma. So, you correct that in some patients and in a minority of patients you can have a melanoma that develops into an enlarged node, but the majority of patients who have spread of melanoma to the lymph nodes actually have what we call microscopic spread where there are only individual melanoma cells that have gone there. And so, we have a technique called sentinel lymph node biopsy that allows us to detect whether or not the draining lymph nodes have spread of melanoma to these lymph nodes.

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Gore How do you do that?

Han It is a procedure that involves use of general anesthesia and what we utilize are tracers – one can be a radio tracer and the second can be a blue dye that we inject around the primary site, and the tracers are taken up by what are called lymphatic channels that drain fluid around cells, and those lymphatic channels then go to the draining lymph nodes. The first node that drains that entire lymphatic unit is called a sentinel node and will be the first and most likely that spread along the lymphatics. By utilizing those tracers, we can identify that sentinel node and therefore make a small incision to find that sentinel node or nodes and remove them. Once those nodes are removed, we send those sentinel nodes to the pathologist who then have the job of examining those nodes to determine if there is any melanoma in them.

Gore And, do they do that while the patient is anesthetized or do you close them up and look later?

Han In general, the guidelines do not recommend what you are discussing, called a frozen section. So, the guidelines generally do not recommend a frozen section for sentinel nodes. And the major reason is that oftentimes there are only small deposits of melanoma in the sentinel nodes. If for some reason on a frozen section there is question or ambiguity as to whether or not the cells are melanoma and then you have lost that slide on processing, you may not be able to ever determine whether or not there is melanoma in that node because of issues in processing.

Gore So, in general, this examination, this pathological examination is done certainly with the pathologist's leisure pace so they can really do a good job.

Han Absolutely. You want to make sure that each section of that node is examined thoroughly.

Gore And what happens if you find cells there, bad cells?

Han I knew you were ready to go down this pathway. This is extraordinarily controversial at this point. So, to summarize, you would have a patient who was diagnosed with a melanoma. You have treated that area with a wide local excision and done a sentinel lymph node biopsy to determine whether or not there is melanoma that has spread through lymph nodes, through a sentinel node biopsy, that sentinel node biopsy came back positive let us say you were discussing, so in the past, prior to about 2 years ago, the gold standard was to recommend what we call completion lymph node dissection. So, what is this?

Gore Sounds bad.

Han This involves removing the rest of the lymph nodes in that nodal basin. So, let us say you had one node that came back positive in your armpit, your axilla, you will then do another procedure where you will remove the rest of the lymph nodes in that armpit.

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Gore It is a lot of lymph nodes, right?

Han Potentially. And the reason why this was recommended was because about 15-20% of patients with a positive sentinel node would be found to harbor additional nodes with melanoma. So, this was primarily for what we call disease control, to get all the melanoma out in that site. The controversy was that we did not know definitively if there was a survival benefit in performing this procedure, meaning in doing a completion lymph node dissection, I would not be able to tell the patient "Oh yeah, I'm definitely going to improve your survival," we just did not know.

Gore And some of them would have problems with bad swelling?

Han Exactly. With the risk of the procedure and one of the big ones that we talk about which could be chronic is something called lymphedema, which is swelling in the extremity. So, this has been controversial. However, in the past 1-2 years, two big trials have now come out, which have thrown everything into a loop for this because both of these trials assessed positive sentinel node patients and randomized them, meaning put them either into a group where you just watch them and did not do any surgery unless they actually recurred with melanoma and then you remove those lymph nodes or randomize them or put them in a group where you did this completion lymph node dissection, and what they found was actually that there was no difference in survival between these 2 groups. So, this brings us to the question of, do we really need to perform a completion lymph node dissection? The guidelines have now changed a little bit, to say that, you should extensively discuss the risks and benefits of performing this procedure and it should be considered on a case-by-case basis.

Gore Got it. Well, we are going to need to bring you back to figure out what to do if God forbid the melanoma comes back, and we have got about a minute more for awareness, so what should people do to minimize the risk of melanoma?

Han There are multiple things that can be done, and one of the big things you have to realize is melanoma has risk factors, some risk factors that you can modify right, and they are preventable things. So, certainly, the amount of ultraviolet radiation exposure you have should be changed in multiple ways or minimized or reduced, and you can do that by using sunscreen. We recommend SPF-30 and to apply that every 3 hours, and even if it is water resistant, there is no longer waterproof, to reapply as soon as you come out of the water. You should also avoid the parts where there is the highest amounts of ultraviolet radiation exposure between 10 and 4 or 9 to 4 o'clock.

Gore Good luck with that.

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Han And use sun protective clothing, in which they have sun protection woven or incorporated into the fabric itself. Certainly, as we discussed, also do your own skin exams, family members helping with that and also going to dermatologist for full skin checks.

Gore What about tanning beds?

Han I am glad that you brought that up, because melanoma is the most common form of cancer now in patients age 25 to 29, people will ask, well that is all due probably to tanning beds and social factors, it is probably multifactorial, but certainly tanning beds are at least one factor in that. What studies have shown internationally is that in countries where tanning bed use was either restricted or prohibited at certain age groups, the incidences of melanoma decreased in those countries. So, there is legislation here in the United States looking into that and trying to either restrict or prohibit tanning bed use in certain age

groups.

Dr. Dale Han is an Assistant Professor of Surgical 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 cancer here on Connecticut Public Radio.