

Yale CANCER
CENTER

answers

WNPR Connecticut Public Radio



Hosts

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Prevention and Early Detection of Melanoma

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Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Francine Foss, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and he is an internationally recognized expert on colorectal cancer. Dr. Foss is a Professor of Medical Oncology and Dermatology and she is an expert in the treatment of lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This evening Ed and Francine welcome Dr. David Leffell. Dr. Leffell is the Deputy Dean for Clinical Affairs at Yale School of Medicine, the David Paige Smith Professor of Dermatologic Surgery, and author of the book "Total Skin."

Chu David, in past shows, we have discussed the two most common types of skin cancers, namely basal cell and squamous cell cancer, but this evening we are going to focus our discussion on the third type of skin cancer called melanoma. Perhaps we could start off by defining what is melanoma?

Leffell Melanoma is a cancer of the pigment cells of the skin. Basal cell cancer and squamous cell cancer arise in the epidermis, or the top layer of the skin. Melanoma, however, arises from the bottom of cells of the top layer of the skin, the epidermis, and these are pigment cells that are designed to respond to ultraviolet radiation from the sun, and when they respond to the sun, they lead to the tanning reaction.

Foss David, how common is melanoma?

Leffell Melanoma is quite common and unfortunately its incidence appears to be increasing. I think that there will be about 70,000 new cases diagnosed this year and approximately 8000 people will die from melanoma.

Foss Is the increased incidence of melanoma related at all to the changes in the ozone layer, and to what degree does global warming and all the other things happening in the environment influence the incidence of melanoma?

Leffell It's not really clear. It's important to note that not all melanomas are due to ultraviolet radiation from the sun. It's a difficult thing to figure out, but it's estimated that only about 60% of melanomas are in some way related to sun exposure. Melanoma can definitely occur where the sun doesn't shine and we will talk a little later about the proper steps with respect to full body skin examination to diagnose melanoma at its earliest treatable stage. We think that lifestyle, probably more than changes in the ozone, have a greater impact on those melanomas that are in some way related to ultraviolet radiation, not just from the sun, but from these tanning parlors as well.

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Chu Is there any age in which you tend to see a higher incidence of melanoma, and also, is there any particular predilection, males versus females etc.?

Leffell That's a great question because recently there was a report that demonstrated that the incidence of melanoma in young women in their 20s and 30s was increasing and at a greater incidence rate than for individuals, males and females, in other age groups. Typically, melanoma is more common in men over 50 and its increasing incidence in younger women is concerning.

Chu Is the increasing incidence in younger women perhaps due to the fact that a lot of these individuals are going to tanning salons and trying to have that 'wonderful tan'?

Leffell We don't really know, but it's certainly a possibility. Back in the early 90s, the incidence for younger women had leveled off and then it started taking off again and it is difficult to necessarily take a behavior or social behavior pattern and try to link it definitively to a change in the incidence of any particular cancer, especially when we are dealing with a relatively short period. But the reality is that we know that ultraviolet radiation causes mutations in the skin, we know that it plays an important role in causing basal cell cancer and squamous cell cancer that I mentioned at the outset, and we know that it does play a role in certain melanomas.

Foss David, could you talk a little bit about potential genetic connections with melanoma, does it run in families for instance?

Leffell There are forms of melanoma that are familial and there are genes that are associated with it, but in the scheme of things, they actually represent the minority of cases. So, individuals that have a family history of melanoma are at increased risk for developing the disease and need to be monitored especially closely. There have also been studies recently that have looked at the gene that controls for red hair and light pigmentation, and a variety of complex interpretations suggest that that gene may result in biological events that increase the risk of developing melanoma. We have always known that red hair and blonde hair are independent risk factors for developing skin cancer and now there seems to perhaps be a genetic link.

Chu What about say darker colored skin, like African Americans or Hispanics, is that the same level of risk or perhaps because of their darker skin color, there is a reduced risk for developing melanoma?

Leffell There is probably a reduced risk for developing the most common types of melanoma, which

5:33 mp3 file <http://www.valecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

are superficial spreading melanoma and nodular melanoma, but people with darker skin actually can be afflicted by a different type of melanoma and its a mouthful so I will try to get it out correctly, acral lentiginous melanoma, or ALM, and this is a form of melanoma that develops on hands and feet and in the nails, and can be especially concerning.

Foss There have been conflicting reports in the medical literature and in the press about exposure to sunlight and balancing the risk of melanoma with the need for vitamin D, can you give us a little bit of guidance about how much sun exposure is enough sun exposure?

Leffell Sure, the amount of sun exposure that results in production of vitamin D in the skin, and that's really what you are referring to it, and it turns out that ultraviolet light will convert cholesterol molecules in your skin to forms of pre-vitamin D, and vitamin D actually is not a vitamin as we understand it, its more correctly a hormone and it is an important hormone, and ultraviolet radiation in our environment can be used to stimulate normal vitamin D production in the skin with as little as 15 minutes twice a week of exposure, say at lunch time when the sun is high. The real question is, and there has been a lot in the media about this, whether one has to go out of their way to get extra sun exposure to get vitamin D. One of the issues that is driving this is the recognition now that vitamin D plays a role in certain cancers, perhaps in other diseases, such as diseases of aging, and there is a legitimate question about what normal vitamin D levels should be. The general feeling though is that the risk of developing melanoma and other skin cancers probably far outweighs the risk of not developing enough what we call endogenous vitamin D, because it is so easily provided with vitamin supplementation.

Foss So, you are generally recommending the use of sunscreens for everybody.

Leffell The use of sunscreen with a sun protection factor of 30 and ultraviolet A blocking is recommended for everyone, especially those who are at risk for developing skin cancer.

Chu All of us have these moles on various parts of our skin. When does one need to begin to worry that this mole might in fact be a melanoma?

Leffell You are right, the average adult has about forty moles, and moles are a normal part of the skin and they represent benign, noncancerous collections of pigment cells. There is an entity that is referred to as an atypical mole. These are moles that have, if you will, gone sour and they can be related to the development of melanoma. In some cases they can be a red flag and they tell you to get in to see the doctor, while that particular growth may not be a melanoma, it certainly gets your attention and the attention of your physician. The question

8:42 into mp3 file <http://www.valecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

about how often to be examined really relates to the risk factors. Standard recommendations are that after the age of 50 you should have an annual full body skin examination, but certainly if you have a family history of melanoma, if you have any of the independent risk factors such as light hair or red hair that I mentioned before, blue, gray, or green eyes, a single blistering sunburn in childhood, that is before the age of 18, all of these are factors that put you at increased risk for melanoma, and you should have a complete skin examination as soon as you are aware of the fact that you fall into those risks groups.

Foss I would like to get back to something you mentioned earlier, which is the incidence of melanoma in non-sun exposed areas; how frequent is this? I am sure this is certainly something that people miss because often times we only focus on our arms and our legs. Can you tell us a little bit about that and what we can do to screen for that?

Leffell That's an extremely important question because while we talk about the sun and protection against ultraviolet radiation, which is extremely important, somehow in that message another important point does get lost, and that is that not all melanomas occur on sun exposed areas. It's essential that you have a full body skin examination by someone who is trained in doing skin exams and that they look through the scalp all the way to the bottoms of the feet, and that includes looking between the toes. Many other dermatologist and I have diagnosed melanomas between the toes, certainly in the scalp, and it can be a challenge for individuals with full heads of hair, something I can't really sympathize with, but you have to very carefully go through the scalp with a comb or blow dryer on low and really make sure that you have examined every inch of the scalp. The genital area is important to examine as well. We have certainly seen melanomas in that location and I think that its very common for patients to come in and we say, okay, you are here for your full body skin exam, we will give you a gown, please change into it. They will say, "No, no, no, just look at my face, I am sure I don't have anything else." Then we ask the patient whether they are familiar with what they have on their back and very quickly they recognize the importance of having a full body skin exam, but you know, your question is important for another reason in that there is a sense that the majority of melanomas are actually first identified by the patient or by the spouse or partner. I can't tell you the number of times that a melanoma patient is sitting in front of me, usually a male with their girlfriend or wife sitting in the corner shaking her fingers saying, I told him to come in six months ago or whatever. In general, the doctor will do a full skin exam as much for educating you about what to look for as to find worrisome lesions. Worrisome lesions don't develop on a schedule and patients have a sixth sense of when

11:49 into mp3 file <http://www.yalecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

something is not right. They may not know the biological explanation for what they see, but they to say, “Doctor, I just do not like it.” And if the patient says that, it gets biopsied even if I think that it looks normal.

Chu David, there is a thing called the ABCs or I guess, ABCDs of worrisome lesions, can you take us through that.

Leffell The A stands for asymmetry. If you imagine the lesion that you are looking at and fold it over in half, if the two halves don’t match, then it’s asymmetric. B is for border. If there is an irregular, notched, or scallop border, that’s a problem. If there is abnormality in color, for example if you see red, black, brown and white, or any combination of those that’s an indication that the body’s immune system may be having it out with the melanoma cells and the redness is actually a sign of inflammation. Sometimes the white is a sign that the battle is over and the body has successfully destroyed those abnormal cells, but in other areas of the lesion it’s clear that the melanoma is still there. Diameter is the other factor and we talk about any lesion that is greater than a pencil eraser, or 7 millimeters, but you know all of these guidelines came up many years ago and they are generally very gross. One of the most important criteria that I alluded to before, is whether the patient is concerned about the lesion, to me that says a lot.

Foss We have to take a break right now. I would like to talk a little bit more about the biopsy and the procedure for treating patients with melanoma when we come back.

*Medical
Minute*

There are over 10 million cancer survivors in the US and the numbers keep growing. Completing cancer treatment is very exciting, but cancer and its treatment can be a life changing experience. After treatment, the return to normal activities and relationships can be difficult and cancer survivors may face other long-term side effects including heart problems, osteoporosis, fertility issues, and an increased risk of second cancers. Resources for cancer survivors are available at federally designated comprehensive cancer center such as Yale Cancer Center to keep cancer survivors well and focused on healthy living. This has been a medical minute and you will find more information at yalecancercenter.org. You are listening to the WNPR Health Forum from Connecticut Public Radio.

Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am joined by my co-host Dr. Ed Chu and Dr. David Leffell, the David Paige Smith Professor of Dermatologic Surgery at Yale School of Medicine. We are today talking about early stage

14:27 into mp3 file <http://www.yalecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

melanoma. So David, could we open this section by having you describe to us how the diagnosis of melanoma is made?

Leffell The diagnosis of melanoma is made by a skin biopsy. First, as we talked about in the first segment, the patient or the doctor is concerned about a lesion and the only way to know what that lesion or growth is, is to take a sample of it and study it under the microscope, and this is a very straight forward office procedure. First, the area is numbed with local anesthesia, lidocaine, similar to what the dentist might use, and then the specimen of skin is removed. If it is very tiny, the whole growth may be removed by what is called a saucerization biopsy, or if it's larger then can easily be removed in its entirety, one might take a sample of the melanoma itself. This biopsy is very important for a few reasons. First, it tells you whether or not we are dealing with a melanoma as opposed to a benign growth or just an atypical or abnormal mole. Secondly, it gives you information about various aspects of the melanoma under the microscope, perhaps the most important of which is how thick the melanoma is. This is important because the thickness of the melanoma is the single most important factor that determines the prognosis. In other words, how well you are going to do. The melanoma diagnosis that we have been talking about today is extremely important because the vast majority of melanomas are diagnosed at the earliest highly treatable stage, probably more than 90%, and when we hear about melanoma and the seriousness of the condition, it really relates to those cases that are more advanced that may have been thicker at the time of diagnosis. But melanoma that's up to 1 mm in thickness at the time of diagnosis is easily treated simply by going back and having an office based surgical procedure that removes the melanoma and a margin of tissue around it.

Chu Who would be the person to do this biopsy? Would it be a general dermatologist or would it be someone like yourself who specializes in dermatologic surgical procedures?

Leffell Skin biopsies, including skin biopsies for melanoma, are routinely done by dermatologists, by plastic surgeons, and certainly by general surgeons, anyone who is trained in the proper techniques and is comfortable in terms of making the clinical diagnosis, so they know what kind of biopsy to do and should be very comfortable performing a melanoma biopsy. The question after that is, once you have the diagnosis the type of referral you should have for proper management of the melanoma.

Foss Can you tell us a little bit about what you do with a patient who has a very early stage melanoma, and in contrast, what you would do with the patient who has one of the deeper, more advanced melanomas.

17:30 into mp3 file <http://www.valecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

Leffell As I mentioned, the most important factor is the depth of the lesion. There are other factors as well that help you determine whether it is a high-risk lesion or a low-risk lesion. If it's a very low-risk lesion, that includes an assessment of where on the body the growth is occurring and simple removal with 1 cm margins, for example, a third of an inch or more, is sufficient to result in the maximal cure rate. However, increasingly when we were dealing with higher risk lesions, even within the category less than a millimeter, we may consider doing a sentinel lymph node biopsy, and that's a procedure where one identifies what lymph nodes that particular area drains to, and in a operating room the sentinel lymph node, or the gatekeeper lymph node, is sampled to determine whether melanoma has spread there or not. When you do that procedure and you find that that lymph node is negative for cancer, that provides great prognostic information, it doesn't necessarily have an impact on how well the patient is going to do, but it certainly helps guide an assessment of what other therapies might have to be provided. With more advanced melanomas, the sentinel lymph node biopsy becomes almost routine, and with extremely advanced melanomas, in other words in melanomas where it has already spread to the lymph nodes, there is obviously no need to do a sentinel lymph node biopsy, and these are complex issues. There is a huge amount of data emerging about the value of the sentinel lymph node biopsy and Yale Cancer Center surgeons Dr. Stephan Ariyan and Dr. Deepak Narayan are very skilled in performing this procedure and managing the surgical aspects of advanced melanoma.

Chu David, if the sentinel lymph node biopsy comes out negative, does that mean then that there is no risk for the melanoma having spread to the regional lymph nodes?

Leffell No, it doesn't, and there are large population studies that are looking at the significance of a negative sentinel lymph node. There is even a procedure where, unsatisfied with looking at the cells under the microscope, we actually look at fragments of the DNA to see if we can find fragments of DNA of the melanoma. It is an evolving area and I think one of the reasons it's so important for research to go in this area is because as we mentioned at the outset, melanoma affects a lot of young people and we don't really know where this trend is going to go, and importantly, if it is diagnosed early, it is virtually curable. So the opportunity to do self skin exams, full body skin exams, and to be appropriately suspicious of lesions that you develop can be life saving.

Foss David, is there anything easy like a simple blood test or a molecular test that can be done on the blood that would help us to know which melanoma patients have distant disease? Has that been developed yet?

20:42 into mp3 file <http://www.valecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

- Leffell That has not been developed and is certainly not in general use.
- Foss That gets me to my next point, which is that Yale Cancer Center actually has received a skin SPORE from the NCI, the National Cancer Institute, and is doing a lot of research related to skin diseases. Can you tell us a little bit about what they are doing with respect to melanoma?
- Leffell That's right, the SPORE covers a study on basal cell cancer in young people that I am directly involved with, but in the area of melanoma, there is a variety of efforts looking at tumor markers and means of identifying antigens or other proteins in the blood that will help not only identify whether melanoma is present systemically in the system, but also provide an opportunity for tracking progress.
- Chu For the patients with early stage melanoma, and as you say, the vast majority really are potentially curable once the skin lesion has been removed, is there any other treatment that needs to be done once that melanoma lesion has been removed by the surgeon?
- Leffell Generally no, for early-stage melanoma. There are cases where you are at the interface between low risk and medium risk and there are questions about the use of interferon, but even the use of interferon itself has really not held out consistently in the literature, and it highlights the point that treatment of early melanoma is relatively easy and the only limitation to treating early melanoma is making the diagnosis.
- Foss How often do patients who have already had a melanoma develop a recurrence or a different melanoma?
- Leffell The chance of developing a second primary melanoma, in other words, another melanoma different than the one that was originally diagnosed, is probably about 6%. Therefore, it's very important for those patients to be monitored. The risk of developing a recurrent melanoma, in other words the chances of the melanoma that was treated coming back, really varies with the type of melanoma and how it was treated.
- Chu How frequently should these individuals be followed up by their dermatologist to make sure that there is no recurrence of the melanoma?
- Leffell A person that has a single melanoma identified should be followed, and the protocols vary but are routine in the Cutaneous Oncology Unit at Yale, that a person should be followed every four months for the first year, and then you can go back to twice a year after that. But as Francine implied before, these patients are at increased risk for developing second

23:23 into mp3 file <http://www.yalecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

melanomas so careful monitoring of them is extremely important, and some of these patients have lesions that look very innocuous and then turn out to be melanoma. You really have to get to know your patient's skin just as the patient needs to get to know his or her own skin.

Foss Is there any role for CAT scans or PET scanning as you follow these patients who have already had a melanoma?

Leffell Not for early stage melanoma.

Chu What are your general recommendations for sun exposure and the use of sunscreen once the melanoma has been removed?

Leffell Patients need to be very vigilant about sun protection even if their melanoma developed in a non-sun exposed area, because that suggests to me that from a genetic point of view their body has a capability of making a melanoma. And maybe for the non-sun exposed melanoma that they had, the stimulus was not the sun, but the sun could equally act as a stimulus, a second hit almost, for someone who is predisposed. Sun protection programs include using a sunscreen with a sun protection factor of 30 with ultraviolet A block, because remember SPF just refers to ultraviolet B block, they should wear a brimmed hat, and everyone thinks that a baseball cap does the trick, but I cant tell you the number of melanomas that I have seen on the tips of the ears, so you need to wear a brimmed hat and avoid the sun, and this makes me sounds like a killjoy, but during the peak hours between 10am and 4pm when the sun is strongest. If you find a way to have your leisure activity outdoors before 10 o'clock and after 4, you will probably have an easier time getting a tee time, the marina wouldn't be as busy, and the tennis court wouldn't as busy and you will be protecting your skin.

Foss My 12-year-old tries to tell me that on cloudy days he doesn't need to wear his sunscreen, can you clarify for our listeners whether or not you need sunscreen on a cloudy day?

Leffell I am pleased to tell you on public radio that you are right and he is wrong. The ultraviolet radiation does penetrate haze and clouds and people get sunburns, they could be out at baseball practice, it is a hazy day, and they think they don't need sunscreen and they come in to see me Monday morning with a full blown pink sun-burned face.

Chu Obviously the recommendation to avoid sun exposure is particularly relevant now that we are in the summer months presently.

25:46 into mp3 file <http://www.valecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

- Foss There is one other question I wanted to ask earlier, and that is the issue of the non-pigmented melanoma. I know that it is relatively rare, but can you just tell us how often it occurs?
- Leffell Everything we have talked about from the outset, when I talked about the melanocyte, the pigment producing cell, and when it goes abnormal it becomes a cancer and the cancer is known as melanoma. All of that really relates to irregularly pigmented or dark growths, which I think many people can have in their minds eye. One of the most worrisome things for dermatologists, especially dermatologists that have been in practice for a long time, is something called amelanotic melanoma. Amelanotic melanoma is a melanoma without pigment, and if you think about it and if you look at your arm or the back of your hand or your leg, I think you will all see that you may have flesh colored growths that are not concerning and you have no way to really consider that there is something to worry about. I am not suggesting that you should start worrying about them, but amelanotic melanomas are lesions that dermatologists can often be suspicious of and the patient too. The patient, as I mentioned a couple of times, might come in and say that they don't like the appearance of it. In a red-haired, very-fair skin individual it may be reddish in appearance, it may be a little dome shaped papule, but it can have other appearances as well and I think it highlights the need for very careful examination by a dermatologist.
- Chu David, there is also this entity called ocular melanoma, is there any relationship between the development of ocular melanoma and sun exposure?
- Leffell Ocular melanoma is a type of malignancy that develops on the retina, and the relationship between that and ultraviolet radiation I don't believe is as strong as the relationship between ultraviolet radiation and cutaneous melanoma. It's a good point that you make and when people have their routine eye exam, they need to make sure that they are getting a comprehensive eye exam because that's the only way it can be diagnosed.
- Chu Is there any research ongoing to try to identify agents that might be able to help prevent the recurrence of melanoma, or is the key to try to minimize or avoid sun exposure?
- Leffell I think the one area that we didn't really have much time to talk about, but that is quite special with respect to melanoma, is its relationship with the immune system. For a variety of reasons, melanoma cells are either exquisitely sensitive to aspects of the immune system, or very clever in evading it, and it's that unique interface with the immune system that has raised the possibility on an ongoing basis of developing a melanoma vaccine. A year doesn't go by that you do not hear about a new melanoma vaccine. The fact that every year you hear

28:45 into mp3 file <http://www.valecancercenter.org/podcast/aug3009-prevention-detection-melanoma.mp3>

about a new melanoma vaccine tells you how challenging it is to develop a means to harness the bodies own immune system to fight melanoma, but we will get there.

Chu Great. David, thank you so much for being with us on the show this evening and we look forward to having you come back and talk about the different types of skin cancer.

Leffell Thank you for having me.

Chu You have been listening to Yale Cancer Center Answers and we would like to thank our special guest Dr. David Leffell for another terrific program. Please join us again next Sunday evening. Until then, I am Ed Chu from Yale Cancer Center wishing you a safe and healthy week.

If you have questions or would like to share your comments, go to yalecancercenter.org where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR Health Forum from Connecticut Public Radio.