Support for Yale Cancer Answers is provided by AstraZeneca, working to pioneer targeted lung cancer treatments and advanced knowledge of diagnostic testing. More information at astrazeneca-us.com

Welcome to Yale Cancer Answers with doctors Howard Hochster, 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 Dr. Hochster is joined by Dr. Jonathan Leventhal for a conversation about sun safety and skin cancer. Dr. Leventhal is an instructor in the Department of Dermatology and Director of the Yale Onco-Dermatology Clinic. Dr. Hochster is Professor of Medicine and Medical Oncology and Associate Director for Clinical Sciences at Yale Cancer Center.

Hochster Can you start out by telling us a little bit about your background and how you came to the field of dermatology?

Leventhal I went to NYU for medical school, and it was in medical school that I first became interested in the field of dermatology as a whole during patient rotations, seeing the profound impact that skin disease had on a patient's life not just physically but also emotionally. I did my training here at Yale in dermatology, and it was during my residency training where I interacted with lots of cancer patients at Smilow and worked with mentors that treated such patients and that is when I really became interested in caring for cancer patients who developed adverse events on their skin due to treatment.

Hochster Dermatology is an area of demand today for people who are medical students and want to go into practice, but you have taken the hard road of being in a cancer center and dealing with skin cancer. Can you give us any insight into that?

Leventhal My interest has always been in medical dermatology primarily. And nothing brings me greater joy than being able to help our cancer patients stay on their potentially life-saving treatments, and improving their quality of life. I think my experience as a resident here at Yale opened my eyes to that, and I never turned back.

Hochster Let's turn to skin cancer. How do you classify skin cancer?

Leventhal Skin cancer, as you know, is the most common type of cancer in the United States, 1 in 5 Americans may develop skin cancer during their lifetime. So, it is really important that people are aware of how common it is and the different types. There are 3 main types of skin cancer – basal cell skin cancers are the most common, followed by squamous cell skin cancers and then there is melanoma. And even though melanoma is only about 1% of skin cancers, it is the deadliest form, and unfortunately the incident rates of melanoma have been tripling over the past 3 decades. So, it is very important that the people are aware of the significant burden that melanoma can have on their lives if they are to be diagnosed with it.

3:25 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal $313023\ 5\ v1.mp3$

Hochster Let's talk about the non-melanoma skin cancers now – basal and squamous. What causes these and what should patients be looking for?

Leventhal Primarily the cause for basal cell and squamous cell skin cancers is UV or ultraviolent radiation and radiation damage on the skin. The UV causes mutations in our DNA that then leads to the development of cancer. And what the patients should be looking out for with basal cells and squamous cells are new lesions on their skin that seem to be irritating or non-healing or scab over, something that they have not had before. Basal cells generally are on sun exposed areas, particularly the face and often patients will describe it to me as it is kind of like a pimple that just does not quite heal, it persists, and that seems to be one of the most common complaints. Squamous cell skin cancers can present from sort of pink scaly lesions on the skin to a more painful warty growth.

Hochster And so, it is sun exposure for both of these, correct?

Leventhal Yeah.

Hochster And these skin cancers are fairly common, but they are also commonly treated just with surgical excision?

Leventhal Right. And the treatment of these skin cancers is generally by surgical treatment, and the type of surgical treatment depends on the type of skin cancer. For instance, squamous cell skin cancers are generally excised more completely and cut out. Where some thin basal cells on the body can actually be treated by methods called electrodessication and curettage, for which a dermatologist will scrape and burn off the lesions. In general, the majority of skin cancers are treated surgically.

Hochster Burning can also mean freezing?

Leventhal Freezing with liquid nitrogen. That is more of a treatment for the precancerous spots, but it is really the curettage. Now with that said, there actually are a few nonsurgical methods to treat skin cancer and those include creams, and we usually save those for more of the indolent type of skin cancers like thin basal cells or very thin squamous cell in situs, and those can be treated by creams such as imiquimod or fluorouracil cream.

Hochster You said it is UV irradiation. Is that like regularly being out in the sun to get tanned?

Leventhal Correct.

Hochster And does sun tan lotion protect you?

 $5:\!54$ into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal 313023 5 v1.mp3

Leventhal Absolutely. There are 2 main types of UV radiation that can facilitate a skin cancer. That is UVA and UVB. So, sunscreen and sun protective behavior can absolutely reduce your chance of getting skin cancer.

Hochster Should we wear those hats with the ear flaps?

Leventhal Correct, yes. Ideally broad brim hats.

Hochster It is not enough that I just put the SPF-30 on my ears?

Leventhal So, putting SPF-30 on your ears is a great start and as well as reapplying it, but ideally, if possible, wear a broad brimmed hat or avoid the sun and seek shade, that would be preferable. But yes, if you cannot, then SPF-30 sunscreen and reapplying it often is very important in preventing UV damage and ultimately reducing a chance of skin cancer.

Hochster The sunblock with these SPF formulations, does that protect against both UVA and UVB?

Leventhal Correct. And so, it is important when you purchase a sunblock that you find one that is called broad spectrum, meaning that it blocks both UVA as well as UVB. And many people do not realize that UVA rays can actually penetrate the car window. So, even when you are in your car, you can have UV damage on your skin.

Hochster Just the sun in general, anytime you are out there. So, what about people who like to go and get sunburned, you know lay out and tanning, that is not good behavior?

Leventhal Unfortunately, it is very common. I see this all the time as a dermatologist, people love being outdoors and getting a sun tan or get sunburn or at tanning beds. We know now, that sunburns and tanning beds both increase your risk of developing skin cancer, including melanoma, which is potentially lethal, and so there has been a lot of push towards preventing tanning, especially in younger individuals.

Hochster I want to come back to that in a minute, we are on the shoreline here. I see people who are fishermen, people who work on the shoreline, who have a lot of sun damage on their skin. You see a lot of actinic damage, sunspots and things like that, over years and years of exposure. What do these people need to do for their skin health?

Leventhal That is a great question. It used to be thought that only sunburns and sun damage from when you were younger mattered, but now we know that it is really cumulative sunburns throughout life that increase the risk of skin cancer, and so, no matter how much sun damage you have had previously, they can always start practicing sun protective behavior and avoiding getting burned, wearing a hat, sunglasses, applying a broad-spectrum sunscreen that is SPF-30 or above, reapplying it every few hours, especially after swimming or sweating and they even sell UV protective clothing, you can purchase it at stores or online, and I recommend that to all of my patients.

8:49 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal 313023 5 v1.mp3

Hochster So, those of our shoreline listeners who love to sit out at the beach, wherever there is a lot of reflected light, you do not have to be just lying out to get the UV damage, but if you go outside and you are going to be in the sun, if you are working out in a boat or whatever, even at this stage, you should put on the sunblock?

Leventhal Correct.

Hochster That is interesting. And what are the laws now about the tanning beds and all that? I mean, people here at Yale have led some of the research that shows that tanning beds can actually lead to early skin cancer.

Leventhal Right. And there was actually a big study from Minnesota recently that suggested that young women who tanned indoors were 6 times more likely to develop melanoma than those who did not. And so, a lot of this is driven by State legislation, but many states have already set laws to prevent individuals less than 18 years of age from tanning, which I think is a great start.

Hochster But no matter what your age is, when you get into the tanning booth, that is going to increase your risk of skin cancer, including all the types that we have talked about – basal, squamous and especially melanoma which is the most serious form of skin cancer.

Leventhal Absolutely.

Hochster A tan is kind of a healthy look, but if you go through UV light to get it, it is probably not a healthy practice.

Leventhal Right. There is actually no such thing as a healthy tan. Anytime patients have a tan, that means that their skin has been UV damaged. And it is not just so much that the UV damage will cause mutations that lead to skin cancer, but UV can break down collagen and elastin in your skin and can lead to wrinkles and having unhealthy-appearing skin. And so, for all these reasons, it is important to prevent UV damage to your skin.

Hochster Are there some other risk factors like skin types and things like that, that predispose people?

Leventhal Absolutely. For instance, for melanoma, the cause is likely a combination of environmental and inherited genetic risk factors. So, for the risk factors that we cannot control, the type of skin and ability to burn matters a lot.

11:20 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal_313023_5_v1.mp3

Leventhal So, patients who are very fair skinned with light hair and light eyes and lots of freckles have increased potential to burn and are at increased risk for developing melanoma. Patients who have over 100 moles or over 5 atypical

moles have also largely increased risk of developing melanoma. And so, these are risk factors that we cannot control, but it is important to know about because for people who have these risk factors, they should be screened for skin cancers by a dermatologist.

Hochster And what is the recommendation for that, for dermatologic skin cancer screening?

Leventhal That is an interesting question because we do not really have great guidelines by the United States Preventative Task Force, but what is generally recommended by the American Cancer Society and the American Academy of Dermatology is that patients who are at increased risk of developing skin cancer or those who have had a skin cancer should be screened by a dermatologist at least yearly. Now, for patients who have had melanoma or other types of skin cancer develop more frequently, I recommend screening them at least 2-3 times yearly to try to pick up skin cancers earlier on before they can potentially spread.

Hochster And what do you as a dermatologist do when you do a skin cancer screening?

Leventhal I perform a total body skin examination from head to toe and that includes looking through the hair in the scalp, looking through all the crevices including the private parts, and I look for lesions that are not normal, and things that could be basal cell, squamous cell or a melanoma. And then when I find one, I will perform a skin biopsy, which is a very simple procedure to sample the lesion and then a pathologist will look at it under the microscope and come up with a diagnosis.

Hochester So, the main thing is that you have to inspect the whole skin, everywhere?

Leventhal Correct.

Hochester Do you use your eyeballs and a little magnifier kind of thing?

Leventhal We use our eyeballs and I also use a device called dermatoscope, which many dermatologists use. And this provides magnification to the lesion and helps better inspect the properties of these skin lesions, and some studies suggest that by using a dermatoscope, this may increase the sensitivity in diagnosing a skin cancer.

Hochester We are going to take a short break for a medical minute. Please stay tuned to learn more information about sun safety, melanoma and cancer treatment with cutaneous side effects with Dr. Jonathan Leventhal.

13:56 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal_313023_5_v1.mp3

Medical Minute Support for Yale Cancer Answers is provided by AstraZeneca, a science-led biopharmaceutical company dedicated to elevating conversations

about biomarker testing to improve outcomes for advanced cancer patients. Learn more at astrazeneca-us.com. There are over 13 million cancer survivors in the US and over 100,000 here in Connecticut. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life changing experience. Following treatment, the return to normal activities and relationships may be difficult and cancer survivors may face other long-term side effects of cancer, including heart problems, osteoporosis, fertility issues and an increased risk of second cancers. Resources for cancer survivors are available at federally designated comprehensive cancer centers such as the one at Yale Cancer Center and at Smilow Cancer Hospital to keep cancer survivors well and focused on healthy living. More information is available at YaleCancer-Center.org. You are listening to WNPR, Connecticut's public media source for news and ideas.

Hochster Welcome back to Yale Cancer Answers. This is Dr. Howard Hochster and I am joined tonight by my guest Dr. Jonathan Leventhal, and we are discussing sun safety and skin cancer. Jonathan, in the first part of this segment, we talked a little bit about the exposure risk factors for skin cancer. We did not talk much about melanoma. You mentioned that melanoma is more serious. Can you tell us a little bit about what melanoma looks like and what people should be concerned about and why melanoma is such a problem?

Leventhal First of all, melanoma is a malignant tumor of the melanocytes. These are the cells in our body that produce pigment and protect us from UV damage. So, melanoma can present in a variety of ways, but in particular, patients will often describe it appearing like a mole that seems to be changing or different or new. Melanoma is usually a pigmented lesion that is asymmetrical, has irregular borders, the colors may not be perfectly uniform and most importantly, it is a changing lesion on your skin. And rarely, melanoma can present as an amelanotic lesion, meaning it lacks pigment, it would appear pink or red in color. And melanoma has become a big problem because of not only just the increasing incidence but also because of the potentially lethal nature of it. And melanoma is a type of skin cancer that often affects individuals in the prime of their life in their 40s, 50s and 60s, not just elderly individuals who have accumulated lots of sun exposure over their life.

Hochster So, for the treatment of melanoma, what is the general approach?

Leventhal Once the diagnosis is made, the type of treatment depends on predominantly the depth of the melanoma in your skin. And that leads to a staging mechanism. And so, for melanomas that are not very deep in the skin, the ones that have a better prognosis, the treatment is surgical excision. 17:17 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal_313023_5_v1.mp3

Leventhal For melanomas that are deeper, oftentimes what is called a sentinel lymph node biopsy will be performed by a surgeon and that is a procedure where the surgeon will sample the draining lymph node to see if the melanoma cells involve the lymph node. And that predominantly helps with the prognosis and staging of the melanoma. And unfortunately, if melanoma does spread, which it may, particularly the deeper melanomas, then referral to an oncologist is required and patients may need to be treated with different types of chemotherapy or radiation or even newer targeted therapies or immune checkpoint inhibitor therapy.

Hochster So, basically the risk factors for the melanoma, for determining the treatment, the higher risk ones are the ones that are thicker or penetrate deeper into the skin?

Leventhal Correct.

Hochester And people always have surgery to that primary melanoma, but you are saying if it is deep, then we tend to take out some of the lymph nodes in the area that the skin goes to see if it has already spread a bit to the lymph nodes. And we would generally do a CAT scan and so forth to make sure it has not spread anywhere else in the body, but we know that even thin melanomas have this propensity to spread and then it is a very serious kind of cancer.

Leventhal Yes. Unfortunately, the deeper melanomas that are stage IV have a very poor survival.

Hochster The things that we have been working on in our melanoma group here at Yale Cancer Center and Smilow Cancer Hospital is new immunotherapies for melanoma and some of those are quite effective and they are even being used now in prevention for high-risk individuals. But for people who are listening out there, I guess the main thing is to have your skin looked at, and if you have a pigmented lesion that looks like it is changing, you need to see the doctor.

Leventhal For anyone who has a new or changing lesion on their skin or a lesion on their skin that seems to be symptomatic, meaning it can be itchy, it can bleed or it can scab over, you should certainly see a dermatologist.

Hochster And you are the director for oncodermatology at the Smilow Cancer Hospital. That is an impressive title. What is exactly oncodermatology?

Leventhal Oncodermatology is a growing field in dermatology that is dedicated to treating cancer patients who develop conditions of the skin, hair or nails that are related to their treatments primarily.

Hochster For example?

20:07 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal $313023\ 5\ v1.mp3$

Leventhal For example, any cancer treatment can result in skin toxicity or adverse events. Traditional chemotherapies which have been around for years can result in hair loss as we know, but could also result in skin rashes and painful nail infections and nail swelling. And the newer targeted chemotherapies, which

have been fantastic and have sort of changed the game of treating cancer patients' have a very high probability of resulting in skin toxicity. For instance, a lot of the newer targeted agents cause acne, really severe acne oftentimes and painful lesions on patients' palms and soles with nail infections, and I see a lot of patients for this as well. A lot of the targeted treatments can also result in hair changes, and not just hair loss but also hair change in quality, color and not just on the scalp but also on the eyelashes and the eyebrows and that can be very symptomatic for patients. And the new immune therapies, the checkpoint inhibitors can also result in itchy or painful skin rashes as well, and I see a lot of that in my clinic. And radiation therapy can result in burns or eczema-like reactions in the skin and also stem cell transplantation, which is used a lot to treat hematologic patients with leukemias or lymphomas can result in skin rashes and a condition called graft-versus-host disease as well. So, really, the bottom-line any cancer treatment can result in a skin adverse event and my goal as an oncodermatologist is to improve patients' quality of lives, treat their skin conditions and allow them to stay on their potentially lifesaving treatments.

Hochster And we are very appreciative of your help in that area, as someone who give these drugs and causes skin toxicity, again we think you are doing a real service for our patients and we have to be thankful that we have a kind of hospital where we have this level of expertise. So, again, chemotherapy, even old-type chemotherapy can cause some skin problems, the newer targeted drugs tend to cause a lot of rashes, some of the antibody-type treatments can cause acne-like rashes and hair growth, I have been treating people's eyelashes, because it can get to be uncomfortable if you get big thick eyelashes that you cannot blink very well. And now with the immuno-oncology drugs, the new immune checkpoint inhibitors, there are different kinds of rashes, but you see that a lot in melanoma patients, I think they are the ones who are getting the most of these drugs or initially started, have been getting the longest, so you are seeing them for melanoma and for the skin problems.

Leventhal Absolutely. And now, these checkpoint inhibitors are used and have been approved in many cancers including non-small cell lung cancer. I see it in a lot of genitourinary cancers, and patients are presenting with many different types of rashes from these checkpoint inhibitor therapies.

Hochster But I guess I want to make the point that not everybody gets the skin rashes.

23:36 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal_313023_5_v1.mp3

Leventhal Of course, and that is a very important point that the majority of people, and even those who get the skin rash are able to stay on their treatment, and in general, the rashes can be well controlled with a number of treatments that we have for them, and so they tend to be very well tolerated.

Hochster And so, what is your approach to treating the patients who have these skin toxicities from their treatments?

Leventhal lot of this depends on the individual patient and on the type of rash and how severe the rash is and we have different grades for that. But I use a combination of topical medications, so these are creams that can either be steroid creams or antibiotic creams that tend to work very well, especially for the acne-type rashes and some of the itchier dry skin. For some of the more severe rashes, I will have to use sometimes oral antibiotics and even oral steroids by mouth to help calm down the inflammation, and rarely, we have to hold treatment to allow the skin toxicity to resolve a bit before continuing it. We also use a variety of antibacterial washes that we recommend to our patients and moisturization techniques to keep the skin nice and moisturized to prevent dryness and cracking. We have some strategies to help promote hair regrowth in the form of foams or even pills by mouth in some patients, and those are sort of the main strategies that we use to treat these skin rashes.

Hochster Some of the targeted therapies and also some of the older chemotherapy drugs effect even the palms and the soles, we call that the hand-foot syndrome, so what do you do for that?

Leventhal There is hand-foot syndrome and hand-foot skin reaction. A lot of the older chemotherapies would cause hand-foot syndrome when you have red swollen hands and feet, and for that, we will often use high potency strength topical steroids, now often one of my tricks is I will have patients apply the steroid creams, then apply a cotton glove overnight, which really helps the steroid cream penetrate better. We will often use ice packs for symptomatic relief and that is the main strategy for that. Now, the targeted therapies, the newer chemos can result in very painful calluses on the hands and feet with associated numbness and tingling and that can really impact the patient's quality of life and that is called hand-foot skin reaction. And so for that, I use a variety of creams to help soften and loosen up the painful calluses and also will use topical steroid ointments as well. I think it is very important for patients who have these painful calluses, especially on their feet, to see a podiatrist, and the podiatrist can really help pare down some of the calluses and I will counsel patients to avoid contact with hot water and try to limit the amount of friction on their hands and feet because friction is something that will increase the chance of more painful lesions on the hands and feet.

Hochster And that hand-foot skin reaction is with some of the targeted therapies today?

26:31 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/2017-YCA-0820-Podcast-Leventhal_313023_5_v1.mp3

Leventhal Yes.

Hochster So, a little prevention and some moisturizers and creams can be very helpful.

Leventhal Yes, absolutely. Hochster Okay. So, what do you see as the biggest challenge today in oncodermatology? Where can you contribute the most and

is the most difficult problem for you?

Leventhal I think a lot of it is the increasing demand of patients who will develop skin toxicities, and oncodermatology is a growing field, but a lot of other institutions do not have dermatologists who specialize in oncodermatology or who see cancer patients in a time that is appropriate for them to be seen, because a lot of these reactions come on strong and they also come on quite rapidly. And so, for me, one of the difficult challenges is being able to see all these patients getting them in on time and being able to treat them for their skin reaction for treatment.

Hochster Do you think this is an area that is going to continue to expand and there is going to be more need for more dermatologic interventions?

Leventhal Absolutely, I do think so, especially with the advent of new checkpoint therapies which will be approved for many different types of cancer, undoubtedly new skin toxicities will be discovered and it will be very important for dermatologists to work very closely with oncologists, like we do here at Smilow to help keep patients on their treatments and to treat their skin disease which can have a very profound, not just physical, but emotional impact on their well being.

Hochster As someone who gives drugs that cause skin toxicity and works on the same floor in the same clinic with you, I must say that it is a great resource to have you there and it has been a really wonderful experience for our patients to be able to see you and get the right kind of care. And so, we are really glad to have you as part of the team at Smilow and Yale Cancer Center. Just to review in our last 30 seconds about skin cancer in general -- avoid the sun, avoid UVA and B radiation, use sunblock and wear protective clothing, if you have a fair skin, blonde, red heads, freckles, you should really get frequent skin exams, and what else?

Leventhal I think you covered most of it. The bottom-line is I tell my patients to be advocates for their skin, if there is anything new, itching or changing on their skin, have it evaluated and do your best to avoid UV damage because you will not just look better but you will have healthier skin and you reduce your chance of getting skin cancer.

Dr. Jonathan Leventhal is an instructor in the Department of Dermatology and Director of the Yale Onco-Dermatology Clinic. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer. You are on WNPR, Connecticut's public media source for news and ideas.