$00:00.000 \rightarrow 00:10.900$ Support for Yale Cancer Center Answers comes from AstraZeneca, a biopharmaceutical business that is pushing the boundaries of science to deliver new cancer medicines. More information at astrazeneca-us.com $00:10.900 \rightarrow 00:41.300$ Welcome to Yale Cancer Answers with doctors Anees Chapgar 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, it is a conversation about skin cancer with Dr. David Leffell. Dr. Leffell is the David P. Smith Professor of Dermatology and Professor of Surgery, and Dr. Chagpar is a Professor of Surgery at the Yale School of Medicine. $00:41.300 \rightarrow 00:52.300$

Chagpar So, David, maybe we can start off by kind of setting the scene of how common skin cancer is, what causes it and what we can do about it?

 $00:52.300 \dashrightarrow 01:07.000$

Leffell Well, generally speaking, skin cancer is the most common cancer among humans. We typically think about basal cell cancer, which is the most common cancer in humans, squamous cell cancer and melanoma.

 $01:07.000 \dashrightarrow 01:17.900$

Chagpar And so, how frequent is that? I mean how many people in the US every year are diagnosed with these cancers? Is this something that everybody should really be concerned about?

 $01:17.900 \longrightarrow 01:40.800$

Leffell Well, it is certainly something that people should be concerned about. We do not have as good data for basal cell cancer and squamous cell cancer as we do for melanoma because melanoma is tracked in tumor registries and there are about 90,000 new cases a year of melanoma. But based on other sources of data, there are at least a million cases of basal cell cancer a year in the United States.

 $01:40.800 \dashrightarrow 02:12.300$

Chagpar You know, some people, you mentioned that basal cell and squamous cell cancers of the skin are not tracked in tumor registries, many people often do not even think of them as cancers, they tend to be fairly well treated and do not cause a whole lot of trouble. Should people really be thinking about basal cell and squamous cell cancers of the skin like a cancer? I mean, is this something that they need to seek medical attention for or is it something that is incidentally noted and pretty much just a bump in the road of life?

 $02{:}12.300 \dashrightarrow 02{:}43.300$

Leffell Well, it is true that when it comes to health, we all have enough to be paranoid about. The reality is that basal cell cancer is a cancer. It causes local destruction of tissue and because it occurs mainly on the face, it can be very problematic. Squamous cell cancer of the skin in particular is usually diagnosed at a stage where it is easily treated, but unlike basal cell cancers, squamous cell cancer of the skin can not only metastasize, but people can die from it.

 $02:43.300 \rightarrow 02:59.700$

Chagpar Hmm... So, that is good information to know. So, before we start talking a lot about melanoma, I thought maybe we could learn a little bit more about what to look for in terms of basal cell and squamous cell cancers of the skin.

 $02:59.700 \dashrightarrow 04:55.200$

Leffell Well, probably in my experience and this is independent from the types of things that you read about on health websites, the singlemost prominent feature that people come in with, with respect to basal cell cancer is a sore that healed up, went away and then came back. From my perspective, that is probably a cardinal indication of a basal cell cancer and it is tricky because basal cell cancer is so slow growing that it can heal up and then people decide they do not have a problem. However, it is continuing to grow and there are many different types of basal cell cancers, just like there are many different types of Chevrolet or Toyotas. There are basal cell cancers that can infiltrate deeply into the skin and when they are near areas such as the eye, it can be very problematic. And then, there are basal cell cancers that are called superficial and they really can find themselves to the epidermis, which is the top layer of the skin and viewers can imagine a sheet of paper if they want to understand just how thin the epidermis is. Superficial basal cell cancer is less concerning of course than infiltrative or other forms of basal cell cancer. Now, squamous cell cancer typically shows itself as a rough, raised area. People often think that they have a wart or they have some sort of other benign growth. More advanced squamous cell cancer of the skin can bleed just as basal cell cancer can bleed, and occasionally there will be other symptoms that people will attribute to it, but most often it is a spouse or partner that identifies the lesion and says you should have that checked out.

 $04:55.200 \rightarrow 05:11.700$

Chagpar So, should people, you know, if you, you mentioned that basal cell cancers generally occur on the face and they generally look like a sore that may have healed up and comes back and squamous cell cancers can occur anywhere on the skin, generally sun-exposed areas, is that right?

 $05:11.700 \dashrightarrow 05:56.800$

Leffell That's right. In fact, in both cases, we actually understand how the cancers are caused and we know what the agent is that causes a cancer, and that agent is ultraviolet radiation from the sun. Work that we have done on the patched gene helped us identify the way in which ultraviolet radiation mutates an important gene that can lead to basal cell cancer. Similarly, there is another gene called the p53 gene that can be mutated by the sun and that can

lead to both precancers called actinic keratosis, which in turn can develop into squamous cell cancer.

 $05:56.800 \rightarrow 06:33.900$

Chagpar And so when you think about, you know, basal cell cancers being the sores that heal up on the face, squamous cell cancers being raised, rough patches that can be anywhere on the skin, I mean, should all of those lesions mandate a visit to a dermatologist? I mean that would be for every pimple, every thing that looks like it might be a little bit of a psoriasis or a raised lesion, or is this something that people just kind of can watch for a bit, I mean or should all of these really mandate getting somebody to look at them?

 $06{:}33{.}900 \dashrightarrow 07{:}35{.}300$

Leffell Well, typically we recommend a full body skin exam once a year for people that are at risk for skin cancer and that includes people with fair skin, light-colored eyes, light-colored hairs -- they are the ones that are most at risk because they are most susceptible to damage from ultraviolet radiation from the sun. You are right, you cannot worry about every little thing that comes up, but I have also been struck over the years that people have a sixth sense. Sooner or later, whether it is a sore that keeps coming back or whether it is the rough area that changes in some way, people generally know their bodies. They may deny that the lesion is a problem and they may not want to go to the doctor, that would actually be a normal response, but I think people often should trust themselves and if they think something is wrong, it probably is.

 $07:35.300 \longrightarrow 08:06.800$

Chagpar Yeah. Good advise for sure. Now, one of the questions I have is, we have heard a lot on this show about people who are fair-skinned, light eyes, light hair, red hair being more susceptible to sunlight and more predisposed to getting skin cancers, does that mean that people who are, you know, darker skinned, Asian people, African-American people, really are less at risk? Should those individuals worry about skin cancer at all?

 $08:06.800 \dashrightarrow 08:50.400$

Leffell Well, it is true that they are less at risk, but they are not at no-risk, they do not have a free pass. We routinely see basal cell cancer and squamous cell cancer in individuals with darker skin or who tan regularly. And of course, basal cell cancer and squamous cell cancer can occur in anyone, so I think that going with the odds, it is less likely but in our program at Yale, we routinely see people with skin cancer who are not stereotypical type of individual we would expect.

$08{:}50.400 \dashrightarrow 09{:}08.300$

Chagpar Yeah. And I just wanted to clarify one point. You mentioned people who tan, so people who tan as opposed to people who were born with a darker

skin color, those people in general would be at high risk simply because of the increased risk of UV radiation right?

 $09:08.300 \rightarrow 09:34.700$

Leffell That's right. And we talk about different skin types. The first skin type, skin type 1 are individuals who in the sun burn. The second type are people who burn but then tan. And the third type are the people that go out in the sun and because they are more darkly pigmented, tan and do not burn. All three types can develop skin cancer.

 $09:34.700 \dashrightarrow 09:55.100$

Chagpar Well, you know, we have talked a little bit about basal cell cancer, squamous cell cancer, certainly anybody who has any of these areas that are of concern, listen to your body and go and get that checked out. But I think when we talk about skin cancers, a lot of us put a lot more of the focus on melanoma, because melanoma is more deadly, is that right?

09:55.100 --> 10:29.300

Leffell Well, certainly melanoma in general is more deadly. It is important to remember though that when melanoma is diagnosed at its earlier stage, the cure rate is in the 90s, perhaps 95% or greater. And that makes a case for a full body skin exams and making sure that you know your body, you know your moles and if you see anything changing, that you get it checked out because the danger of melanoma relates directly to its depth, and its depth most often relates to how long it has been there.

 $10:29.300 \dashrightarrow 10:58.100$

Chagpar So, let's talk a little bit about how to recognize a melanoma. Certainly, for people who are darker skinned, who can still get melanoma but may not be, you know, getting screened once a year like their fair-skinned counterparts, but for anybody, even in between doctor's visits, if you see something, you should say something; so what are the things that we should be looking for when we see something that mandates going and getting it checked out?

 $10:58.100 \dashrightarrow 12:04.200$

Leffell I think that any change in a mole, in size, color, shape, if it becomes itchy, any development of a new mole that has any of those features are things that should set off an alarm and should send you to the doctor to be evaluated. It is true that many people come in because we have done a great job as a society, educating people about the warning signs, it is true that people come to see the dermatologist or the internist or family practice doctor with growths that they are very frightened about because of course they have been on Google, and they have seen pictures that they think are similar to what they have; when in fact, what they have are more benign lesions, but it is not expected that listeners should be making that distinction. If you have something you are concerned about, get it checked out, and if your partner or spouse or family members has something you are concerned about, speak up.

 $12:04.200 \longrightarrow 12:53.000$

Chagpar So, great, great information. Now, if one of the things that I think listeners may have some trepidation about, nobody like to go and see their doctor, I am the first one to admit that I do not like to go and see the doctor either. And so, I think the point of, you know, seeing something and getting it checked out early listening to your body is one of the key messages that you have, but part of it might also be a fear of what the doctor is going to say when they see this. So, you can either say, it is nothing which is certainly reassuring, but if it is something, tell us about what the steps are that happen at the doctor's office that may help us in terms of making that diagnosis?

 $12:53.000 \rightarrow 15:12.500$

Leffell Well, the only way to properly make a diagnosis of skin cancer is to do a biopsy. And right away that word instills fear in a lot of people and the idea of what might be involved can also prevent people from going to see the doctor. But a biopsy is a very simple procedure. In a skin biopsy, the area is numbed up with lidocaine anesthetic and the lesion is shaved off with a scalpel or a sterile blade and a Band-Aid is put on the site. The aftercare is simple and the site typically heals up within a week or two. But it is that biopsy specimen that is sent to a qualified dermatopathologist, in other words a physician who has special training in skin pathology, looks at the specimen under the microscope and can determine not only whether it is a skin cancer or a melanoma, but what kind of melanoma it is. And that is important, you know, we are seeing more and more cases of melanoma in situ. Melanoma in situ instills a great deal of fear in people because they hear the word melanoma. In fact, melanoma in situ is what we call stage 0. It is confined to the epidermis, the top layer of the skin and because of that, it has no potential to spread in the body, yet because we understand the potential dangers of advanced melanoma, people with melanoma in situ I think get unnecessarily worried. The treatment for melanoma in situ is pretty straightforward. It is an office surgery procedure. And I think it is important to make that point because we are seeing more of it. I will mention a historical note, previously melanoma in situ was called by its Latin name lentigo maligna, and like most Latin names, they are indecipherable to the average person and in that case that was pretty good because people did not get worried. Now, that we refer to it as melanoma in situ, there is a greater degree of anxiety that is probably unnecessary.

 $15:12.500 \dashrightarrow 15:20.600$

Chagpar Right. So, people need to put more emphasis on the in situ part than on the melanoma part. In situ meaning essentially a precancer.

 $15:20.600 \rightarrow 15:28.800$

Leffell Yes. I mean it is a malignancy, it is a cancer, but it is confined to the top layer of the skin and is noninvasive.

 $15:28.800 \dashrightarrow 16:00.800$

Chagpar Noninasive. Exactly. Just like many other in situ cancers that our listeners may have heard about, whether it is a cervical carcinoma in situ or a breast cancer in situ, all of these do not really have the ability to spread, so when you can catch it at that in situ phase or stage and that is really good. Now, because it is still a malignancy, I want to get into how we treat it, but we will do that right after we take a short break for a medical minute.

16:00.800 --> 16:11.900 Medical Minute Support for Yale Cancer Answers comes from AstraZeneca, dedicated to advancing options and providing hope for people living with cancer. More information at astrazeneca-us.com. 16:11.900 --> 16:56.400 This is a medical minute about lung cancer. More than 85% of lung cancer diagnoses are related to smoking and quitting even after decades of use can significantly reduce your risk of developing lung cancer. For lung cancer patients, clinical trails are currently underway to test innovative new treatments. Advances are being made by utilizing targeted therapies and immunotherapies, the BATTLE-2 trials aims to learn if a drug or combination of drugs based on personal biomarkers can help to control non-small cell lung cancer. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio. 16:56.400 --> 17:40.800

Chagpar This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Leffell. We are talking about skin cancer awareness and surgical treatment options, and right before the break, we were talking about melanoma in situ. This kind of noninvasive melanoma where people get really anxious about melanoma, but it is really the in situ part of the word that needs to be the focus as this is something that does not spread. No Dr. Leffell, you mentioned that this can be easily treated. What exactly is the treatment for a melanoma in situ, is it just surgery to remove this lesion or do you add radiation or other therapies to that?

$17:40.800 \longrightarrow 18:48.900$

Leffell The standard of treatment for melanoma in situ is surgical excison with plastic surgery to repair the area. The majority of melanoma in situ occur on the face because that is the area that gets the majority of sun exposure. When the lesion is small, the approach is simple. You excise it with a margin and suture up the area, do some plastic surgery, so the area heals well. We deal with a fair number of relatively large lesions and in those cases, we do not want to do the plastic surgery until we are sure that it is all out. So, we will excise the melanoma in situ in the office, map it and send it off, and the patient will go home with a bandage to return a few days later once we know whether any more has to be taken. Once that process is finished, then the plastic surgery can take place. And in some cases frankly, depending on where the area is on the face, letting it heal naturally can sometimes give a better cosmetic result than plastic reconstruction.

 $18:48.900 \dashrightarrow 19:08.100$

Chagpar Hmm...So, it sounds like that is fairly straightforward. It is pretty much office based plus or minus some plastic surgery. What about other skin cancers that occur on the face? We had mentioned basal cell cancers before, is the treatment for basal cell cancers very similar to melanoma in situ?

 $19{:}08.100 \dashrightarrow 21{:}34.500$

Leffell It is actually similar but notably different in that we use a technique called Mohs' surgery, and Mohs' surgery is named after a general surgeon at University of Wisconsin who discovered the technique, invented the technique if you will, about 50 years ago and that is a method where you will remove skin cancer layer by layer and study the edges and the underneath surface while the patient is waiting. And we use that technique extensively. The skin cancer is removed and sometimes we have to go back a second time or a third time, but then follow that with plastic reconstruction in the office. The reason the Mohs' technique is so important is on the face you want to spare as much normal tissue as possible and you also want the highest cure rate because if the basal cell cancer or squamous cell cancer recurs, it becomes more problematic. And the Mohs' technique has a cure rate of 98% or more and it is an efficient approach to treating skin cancer. I did want to mention that we do not use that technique for melanoma in situ because the cells in melanoma in situ are a little trickier to read on frozen section, but there are places around the country that do that and there are ways to approach it, but for now, we rely on the permanent sections. Now, I should mention that because melanoma in situ can be a challenging lesion surgically if it is large, we can sometimes use a cream that stimulates the immune system of the skin and it is called imiguimod, brand name is Aldara, and it is a remarkable drug. It was originally developed to treat genital warts and it was discovered that it worked okay for that indication, but we found more than 20 years ago that it was very effective in treating superficial basal cell cancer like I mentioned before and can be very effective in low-grade melanoma in situ if surgery is not a possibility or if there are very faint margins left after surgery.

 $21:34.500 \dashrightarrow 21:51.400$

Chagpar So, is it ever the case that you could use this cream instead of surgery, just not necessarily that it is not surgically resectable, but if it is a small area and somebody says, you know I would rather apply a cream than have a cut on my face?

$21{:}51.400 \dashrightarrow 22{:}02.700$

Leffell Yes. There are cases where we use the cream as a primary treatment and that has to do with how active the melanoma cells are in the melanoma in situ.

22:02.700 --> 22:16.200

Chagpar And so, is it just as good as surgery or are there certain things that make you say no, you know what, you really need to have this surgically excised versus yeah this is something that is cream is just as good or maybe even better than surgery?

 $22{:}16.200 \dashrightarrow 22{:}30.900$

Leffell Surgery is definitely the gold standard. The cure rate with the cream is not anywhere near what it is with surgery, but on balance, there are circumstances where that is the treatment of choice.

 $22:30.900 \dashrightarrow 22:46.100$

Chagpar Okay. So, we use this cream and again for basal cell cancers, it sounds like just like for melanoma in situ, the modalities of treatment are really geared at local treatment?

 $22:46.100 \longrightarrow 23:49.500$

Leffell Correct. And you mentioned radiation before. Radiation really does not have a role in treating melanoma in situ. There are cases when we encounter squamous cell cancer along a nerve for example or in other circumstances where the cancer is very aggressive, where we may follow up surgical treatment with a course of radiation therapy, and probably one of the biggest innovations now literally as we speak is the approval of a drug to treat metastatic squamous cell cancer of the skin. This particular drug is a checkpoint inhibitor and you have heard that term perhaps in the context of the treatment melanoma, metastatic melanoma, but there is now a drug that will be available to treat those patients with squamous cell cancer that has spread to other parts of the body.

 $23:49.500 \rightarrow 24:07.600$

Chagpar So, that brings up a point that I wanted to make as well, which was, we talked about melanoma in situ being the kind of cancer that is not invasive, that does not have the ability to spread, and I think that you mentioned that basal cell cancers in general do not spread either, but squamous cell cancers can and do?

 $24:07.600 \dashrightarrow 24:17.100$

Leffell Yes. Basal cell cancer very rarely spreads. Squamous cell cancer definitely can, and we see cases of it routinely.

 $24:17.100 \longrightarrow 24:25.200$

Chagpar So, let us talk a little bit more about the management of the squamous cell cancers. Presumably, there are surgery involved for these as well?

 $24{:}25.200 \dashrightarrow 25{:}16.800$

Leffell Yes. The primary lesion, primary squamous cell cancer, Mohs' surgery is the treatment of choice. However, there are cases that for example may be so large that a more general surgical approach is required and we work in our program collaboratively with the head and neck surgeons, with the radiation therapists, with the plastic surgeons to take a team approach to managing more complicated cases. And I think that when we are dealing with cases where the squamous cell cancer has spread to the lymph nodes of the neck for example, our head and neck colleagues take over the care and they will do a number of things to manage that particular case, and it is usually followed up with radiation.

25:16.800 --> 25:41.200

Chagpar And so, what about systemic therapy, so giving drugs that will get into the blood stream or the lymphatic vessels to prevent spread if squamous cell carcinomas have the ability to spread and some of these as you mentioned spread to lymph nodes, how often do we follow this up or do we follow it up with chemotherapy and those kinds of agents?

 $25:41.200 \longrightarrow 26:08.700$

Leffell We do not because it is rarely indicated. And in addition, until the approval of this new drug, there really have not been any chemotherapy regimens that have been successful once squamous cell cancer of the skin has spread, they have all been very challenging. But, there is no role for adjuvant chemotherapy in routine care of squamous cell cancer of the skin.

 $26{:}08.700 \dashrightarrow 26{:}27.200$

Chagpar So, let us talk a little bit about this new immunotherapy that is coming straight off the presses, checkpoint inhibitor for squamous cell cancers. Why is it that this is now playing a role in systemic therapy whereas systemic therapy never played a role in squamous cell cancers in the past?

 $26:27.200 \dashrightarrow 27:44.100$

Leffell Well, you know, I think the evolving view is that cancer is as much a disease of the immune system as it is a disease of cells gone wild. And any of these drugs that lose the immune system or manipulate it in ways to allow the body's natural defenses to fight off the cancer are going to be successful and have proven to be successful. Whether the body develops resistance against it, you know, the immune system developed as a very complex structure through evolution for a reason and likely to see resistance and carry strategies that our old natural immune system will have when we confront the cancer with one of these immune modifiers. But, I think that the idea of using this in squamous cell cancer was actually to be expected and the clinical trial, you know, indicates a fair amount of success in a disease metastatic squamous cell of the skin where nothing really worked before.

 $27{:}44.100 \dashrightarrow 28{:}19.600$

Chagpar Right. And so, let us talk a little bit about, you know, when we think about many skin cancers that are not melanoma, melanoma in situ, basal cell cancers, many of us thought, you know, these in general are very treatable, almost curable, I think you mentioned that, you know, at least in their early stage, you know, we get pretty good cure rates. With squamous cell cancer, if it is advanced, can you tell us a little bit about what the survival rates were and are now with immunotherapy?

28:19.600 --> 28:39.600

Leffell Well, I think it is much too early to talk about that. The drug literally was approved by the FDA in the past couple of weeks. And so, it is much too early to talk about that. I think that when drugs get into broader use is when we find out how effective they are.

0:28:39.6 --> Dr. David Leffell is the David P. Smith Professor of Dermatology and Professor of Surgery at the 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 YaleCancerCenter.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.