

Welcome to Yale Cancer Center Answers with doctors Francine Foss and Lynn Wilson. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Wilson is a Professor of Therapeutic Radiology and an expert in the use of radiation to treat lung cancers and cutaneous 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 1-888-234-4YCC. This week, Francine and Lynn welcome Dr. Rossitza Lazova. Dr. Lazova is Associate Professor of Dermatology and Pathology and Director of the Yale Dermatopathology Fellowship.

Foss Could we start off by having you talk a little bit about your background and explain to our audience what dermatopathology is?

Lazova I am a dermatopathologist and a skin pathologist. When someone has a rash or a pigmented lesion or an area suspicious for cancer, oftentimes the dermatologist takes a piece of tissue to be examined under the microscope. My colleagues, dermatopathologists, and I, perform that microscopic examination. We look at the tissue under the microscope in an attempt to make a correct diagnosis so the patient is treated appropriately. We look at very thin sections of tissue that are stained with hematoxylin and eosin, blue and pink, and determine whether the patient has cancer or not and what type of rash they have. Once we determine that and make the correct diagnosis, the dermatologist can properly treat the patient. It is always very important since if we make a wrong diagnosis, the patient's management will be different. If we diagnose a lesion as cancer, and it is not, then the patient will have an unnecessary treatment, often surgery. On the other hand, if we diagnose a lesion as noncancerous, and it is cancer, the patient will be undertreated and will not get the proper treatment for their condition.

Foss As a dermatopathologist, in your training, did you ever actually do clinical dermatology? Did you ever actually see the patients with these lesions or do you just look under the microscope at the skin?

Lazova Dermatopathology training follows training in either pathology or dermatology. So, all dermatopathologists have basic training. They are both certified in the specialty of either pathology or dermatology and the dermatopathology fellowship is one year of additional training only in skin pathology. Derma in Latin means skin, hence dermatopathology is pathologic changes in the skin and we train for at least one year in skin pathology or dermatopathology, and as part of this training, we do six months of training in the opposite specialty that we trained in. For example, I have a pathology background; therefore, I did six months of training in dermatology, so I looked at patients. I studied dermatology so I am capable of recognizing skin diseases. Of course,

I am not as well trained as dermatology residents and practicing dermatologists, but I do have basic knowledge in dermatology to incorporate with my background in skin pathology.

3:50 into mp3 file http://yalecancercenter.org/podcasts/2011_1120_YCC_Answers_-_Dr_Lazova.mp3Foss One of the things that not many people in the audience probably know is that the skin is actually the largest organ in the body.

Lazova That is absolutely correct. The skin is the largest organ in the body and in my opinion, the most wonderful organ in the body because it is very easily examined. It is on the surface so we can basically see what is happening. We can detect very early any changes that appear on our skin, and therefore, we have a great chance of treating any disease at a very early stage with great success.

Lynn How did you become interested in dermatopathology?

Lazova I was a resident in pathology at the University of Rochester. I am board certified in anatomic and clinical pathology, and as part of my training, I studied cases in skin pathology with my teacher Dr. Glynis Scott. I was fascinated but by her ability to diagnose different skin diseases by looking at cells and patterns of cells, and even by a few cells she was able to make the diagnosis so I became very interested in dermatopathology because it was very difficult and yet fascinating to me. I decided to study that field and proceeded with the Fellowship in dermatopathology and I was fortunate enough to train with the best expert in dermatopathology of all time, Dr. Bernard Ackerman.

Foss Rossitza, for those of us who see a lot of patients with rash, a rash is a rash in the clinic and the only way that we really know what we are dealing with is because the dermatopathologist tells us based on the biopsy.

Lazova Yes, that is correct. I have to slightly disagree because dermatologist will tell you that different rashes are different so they are able to recognize many rashes clinically based on typical features, but in many other cases, they may mimic each other. Therefore, biopsying a lesion and examining the rash under the microscope is extremely important, and 99% of the time, we as dermatopathologists are very helpful and we can make the correct diagnosis, and therefore, the patients can be treated properly.

Foss Can you tell us what kinds of cancers you deal with?

Lazova We encounter different types of cancers, melanocytic cancers and non-melanocytic cancers. The most common cancers are squamous cell carcinoma and basal cell carcinoma. They are epithelial cancers. They arise from the epidermis, which is the outermost layer of our skin. The squamous cell carcinomas and basal cell carcinomas are related to sun exposure. Therefore, the more sun exposure one gets the greater the chance of developing those cancers. On the other hand,

7:09 into mp3 file http://yalecancercenter.org/podcasts/2011_1120_YCC_Answers_-_Dr_Lazova.mp3

melanoma is one of the deadliest cancers and also develops in the skin. Melanomas are very interesting cancers because they can be very thin and yet years later they can metastasize and they can kill a patient. It is extremely important to make an early diagnosis and try to treat the patient as early as possible for better success.

Lynn There are some more unusual types of skin cancers such as Merkel cell carcinoma and that may not necessarily be related to the sun, and I think more recently they felt there might be a viral relationship, exposure to a virus and Merkel cell carcinoma, for example. You must see all sorts of different things, the common things in basal and squamous cell carcinomas and melanomas but you must see a whole host of very rare skin diseases as well. Is that the case?

Lazova That is correct. We see a whole range of different types of cancers including Merkel cell carcinoma. Merkel cell carcinoma unfortunately is also one very bad behaving cancer that can spread to lymph nodes very early and develop into widespread metastatic disease. We find more and more that many cancers are associated with viruses and some other infectious diseases and this is fascinating.

Foss Another aspect of what you probably see are patients with other kinds of cancers like solid tumors, for instance, who can present with skin metastasis.

Lazova That is correct. Sometimes we find surprises in the skin. We find metastasis from cancers from other parts of the body that present in the skin and then we have to deal with the dilemma of is this a primary skin cancer or is it a metastatic cancer that originated in another part of the body, and fortunately, we have many techniques and tests that can help us to make the correct diagnosis. We have special stains, we call them immunohistochemical stains, which can highlight some types of cancers but are negative in other types of cancers. These are extremely helpful for us in making the correct diagnosis.

Foss Can you also comment on the use of genetic tests on skin biopsies?

Lazova Genetic tests are necessary sometimes to make the correct diagnosis. In melanocytic lesions, there are few genetic tests where genomic hybridization and FISH or Fluorescent In-Situ Hybridization are often used to determine whether a growth from melanocyte is cancerous such as melanoma or noncancerous, a benign mole. I can tell you later about my exciting research with mass spectrometry in Spitzoid lesions, which is not genetic but certainly very exciting.

Lynn You provide the physician who takes the biopsy with a lot of other information as well. You might say, this is a melanoma, but you provide the size, how much room there is between the edge of the

10:45 into mp3 file http://yalecancercenter.org/podcasts/2011_1120_YCC_Answers_-_Dr_Lazova.mp3

melanoma and the edge of the specimen margins, and lot of that information I think is very helpful to the clinician. You actually provide a lot more information than just making a specific diagnosis.

Lazova That is correct. In addition to making the diagnosis of melanoma, we provide certain characteristics of the melanoma to guide the clinician as to how to treat the patient and many of them have prognostic significance. They help the clinicians orient the patient as to what their options are for treatment what their survival probability is and so forth. For melanoma, in particular, we would measure the depth, which is the most important prognostic factor and characteristic factor for treatment. Again, in the prognosis of melanoma, the deeper the melanoma the worse the prognosis is. So, it is extremely important for the melanomas to be discovered early when they are still very superficial and treated as early as possible for better success in treatment.

Foss There are lots of different kinds of pigmented skin lesions and I am sure you see a whole spectrum of them, but are there specific risk factors for patients to develop melanoma or are there specific things that you look for in one of those pigmented biopsies?

Lazova There are risk factors for developing melanoma. One of them is the genetic risk. There are families with greater risk for developing melanomas, and it is very important for members of such families to be aware of that and perform self-examination, pay attention to their skin, pay attention to benign moles, whether they change in color, whether they start itching, bleeding, whether they increase in size and seek a doctor's attention, and also regular doctor's examinations particularly by dermatologists for screening and monitoring those lesions.

Lynn What are some of the screening options for melanoma?

Lazova One of the best screening options is self-examination, because if you wait and you go to see a doctor very late in the development of some growth on your skin it might be too late or your options are not going to be as good as if the cancer is discovered earlier. So, we have to look at our skin everywhere, even between our toes. Use a mirror to look at your back or ask your loved ones, relatives, friends to examine us, if possible, or just go to a dermatologist once a year or once every few years for pigmented lesions to be compared and tested, because a dermatologist takes pictures. They compare the size and they really follow the lesions and their development to make sure that they do not transform into cancer.

Lynn We are going to take a short break for a medical minute. Please stay tuned to learn more information about dermatopathology with Dr. Lazova.

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Medical

Minute The American Cancer Society estimates that over 1000 patients will be diagnosed with melanoma in Connecticut each year. While melanoma accounts for only about 4% of skin cancer cases it causes the most skin cancer deaths. Early detection is the key. When detected early, melanoma is easily treated and highly curable and new treatment options and surgical techniques are giving melanoma survivors more help than they have ever had before. Clinical trials are currently under way at Yale Cancer Center, Connecticut's federally

designated Comprehensive Cancer Center, to test innovative new treatments for melanoma. The Specialized Programs of Research Excellence and Skin Cancer Grant at Yale, also known as the SPORE grant, will help establish national guidelines on modifying behavior and on prevention as well as identification of new drug targets. This has been a medical minute brought to you as a public service by Yale Cancer Center. More information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Wilson Welcome back to Yale Cancer Center Answers. This is Dr. Lynn Wilson and I am joined by my co-host Dr. Francine Foss. Today, we are joined by Dr. Lazova and we are discussing dermatopathology. You just mentioned that it was critically important for people to take a look at their own skin to do self-examination, and see the dermatologist for skin examination, and relating to melanoma, tell us what the A, B, C, D distinction means?

Lazova Before that, I would like to mention that many of us have benign or noncancerous moles on our skin. These are flat or elevated areas of this skin with pink or tan color, or white brown to dark brown color. These benign moles are often present at birth or develop during childhood or early adulthood. Melanomas on the other hand, usually develop during adulthood and each person should carefully examine his or her skin periodically. If they see bumps or pigmented areas that are enlarging, that become itchy, that change in color, or start bleeding, they should seek the care of a dermatologist right away. Does one have melanoma or not and what are signs of melanoma? It is easy to remember. The rule for melanoma is the A, B, C, D, criteria. If one has a pigmented spot on the skin they can examine it for A, which stands for asymmetry. If you draw an imaginary line in the middle of the lesion one half should be the mirror image of the other. This is symmetry. If, however, one half is different than the other, the lesion is asymmetric, and it could be melanoma. B stands for border. The border or periphery of a noncancerous benign mole is smooth and regular. On the contrary, the border of melanoma is irregular, notched, and blurred. C stands for color and noncancerous moles are uniform in color. In a melanoma, there might be quite a variety of colors such as light brown, dark brown, red/black, pink, white, blue and even purplish, and finally D is for diameter, or size of the lesion. Usually noncancerous moles are small. Melanomas are usually larger than 6 mm or a quarter of an inch. Let us repeat the A, B, C, D rule for melanoma. Melanomas are A-asymmetric, B-have a border which is irregular, C- have

18:28 into mp3 file http://yalecancercenter.org/podcasts/2011_1120_YCC_Answers_-_Dr_Lazova.mp3a variety of colors in them, and D-diameter, they are larger than 6 mm or a quarter of an inch. An asymmetric lesion with irregular border, different colors in it and large in size could be melanoma so please seek

the doctor's attention immediately and preferably that of a dermatologist.

Foss Can you tell us, what are Spitz nevi and how is that related to melanoma?

Lazova As I mentioned, there are many noncancerous benign moles, Spitz nevus is a type of benign mole. It usually develops in children or young adults. They usually develop on the face or lower legs, often near the knee. Spitz nevi present as flat or slightly elevated bumps, which may have pink, tan, white, brown, or even dark brown color and they grow very fast. Again, Spitz nevi are benign moles that often develop in children. Melanomas on the other hand, as I mentioned, usually develop in adults, however, in extremely rare occasions children may have melanoma so it is extremely important to differentiate the Spitz nevus from a melanoma in children.

Wilson Does that oftentimes require a biopsy to make that distinction?

Lazova That is correct, very often it is important to biopsy a lesion to make sure it is indeed Spitz nevus and not a melanoma, and in many cases, unfortunately, it is very difficult even microscopically with all our knowledge and histopathologic criteria. It is very difficult to differentiate the Spitz nevus from a melanoma that resembles a Spitz nevus, we call them Spitzoid melanomas. We study these lesions in great depth. We show them among each other, we share the information and we examine them thoroughly and even though sometimes we send them to experts in dermatopathology that are worldwide experts, it is very difficult to predict with certainty at the behavior of those lesions. It is impossible in rare cases to say whether a lesion is a benign mole, Spitz nevus, or Spitzoid melanoma.

Wilson How does one develop a Spitz nevus, and if that is what they have, how is that treated?

Lazova We do not know why we develop moles or Spitz nevus as one type of a mole. In general, we have melanocytes in the epidermis, this is the outermost layer of our skin. These melanocytes are present in the basal layer of the epidermis, normally. They actually produce melanin, which is the pigment that gives the color of our skin. The more melanin we have, the darker our skin is. We do not know exactly what turns on the melanocytes to grow, but when they start to grow they form these benign moles or nevi and when large melanocytes start to grow they form Spitz nevi. Under the microscope the

melanocytes of Spitz nevi are very large. They are prominent in a part called nucleus and abundant cytoplasm, and this is the rest of the cell. So they are very large and they look like cancer cells, but yet these are benign moles.

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Foss Are they associated with sun like other kinds of melanoma?

Lazova They are not, this is an interesting part, they develop in children, they do not develop on sun exposed areas, although, you can say the face is sun exposed, but when they develop so early in childhood sun is definitely not associated with their development.

Wilson Do you need to do anything about them, how are they treated or do they need to be removed or can you just leave them alone?

Lazova There is controversy in that area, whenever the dermatologist encounters a lesion that is suspected to be a Spitz nevus they biopsy it most of the time. We confirm the diagnosis that it is indeed the Spitz nevus and now there is a split in the way dermatologists choose to treat that. Most dermatologists will excise the lesion regardless of the fact that we tell them it is Spitz nevus because in rare occasions, as I mentioned, under the microscope it looks like Spitz nevi, but yet later they behave badly as melanomas. They want to make sure by removing 1mm or 2mm of normal skin around the Spitz nevus that they have removed it completely and they have lowered the chance of it behaving in a bad way.

Foss Rossitza, we talked a little bit earlier about some interesting research that you are doing. Could you tell us a little about that?

Lazova Yes, I would be very happy to mention my research. As I said previously, in rare occasions it is very difficult to tell apart benign Spitz nevus from malignant Spitzoid melanoma and we all are frustrated with that and can you imagine being a parent of a child with a Spitzoid lesion and the doctor tells you I am not sure whether your child has a benign mole or has the deadliest cancer and your child may die from it. This is very frustrating for us, and it is extremely frustrating for patients, and for parents of patients. So, I decided to do something in the field and I am studying Spitz nevi and Spitzoid melanomas

by doing mass spectrometry. This is a relatively new method that has been employed more and more in the medical field for studying different areas and I studied these lesions with mass spectrometry with great results. I achieved great specificity and sensitivity. I was able to differentiate in my 100 cases Spitz nevi from Spitzoid malignant melanoma so I am hoping that this study would be very helpful to clinicians in the future.

Foss Can you tell us a little bit about this mass spectroscopy technique that you are using and whether that is something that is available to say the average dermatopathologist?

Lazova This is a very new approach, and in fact, melanocytic lesions have never been previously studied by mass spectrometry. When I say melanocytic lesions, I mean formalin-fixed paraffin-embedded tissue sections that I am studying. These are the tissue sections from biopsies. Fresh tissue has

26:11 into mp3 file http://yalecancercenter.org/podcasts/2011_1120_YCC_Answers_-_Dr_Lazova.mp3 been studied by mass spectrometry, but not the regular tissue sections that we use in our everyday practices as pathologists and dermatopathologists. So, this is the frontier of this new technique being applied to dermatopathology, and particularly, to melanocytic lesions and Spitz nevi. Therefore, it is not available to the regular practicing dermatopathologist, however, at this time they can send interesting cases to the Yale Spitzoid Neoplasm Repository that I founded three years ago and there cases can be studied by mass spectrometry, and I have already gotten cases, one from Chile, one from Switzerland, data sent to me to be studied by mass spectrometry, and people are getting more and more interested in this new technique, and I am hoping to continue working in this area and can hopefully help.

Wilson You are also the Director of the Fellowship Training Program and obviously Yale is a large academic center, and you are doing research, you are providing the clinical pathology services, but education is an important part of what you do as well? Tell us a little about that and tell us about the fellowship program?

Lazova I am very proud to be Director of the Dermatopathology Fellowship at our laboratory in the Department of Dermatology. I became Director of the Fellowship more than 10 years ago and we have one fellow a year who trains in dermatopathology and as of next year we will have two fellows who train in dermatopathology. As I mentioned, these fellows can be from either a pathology or dermatology background, and therefore, they will be trained for six months

in either pathology or dermatology to gain knowledge of the other field and they are engaged in teaching activities throughout their fellowship. They study with us at the Multi Headed Microscope. In addition to our fellows, we also train pathology and dermatology residents. We always have visiting medical students, visiting residents from throughout the country, we have visiting physicians from throughout the world. Right now, we have a physician dermatologist from Thailand. We had somebody from Turkey who just left, and it has been an incredible international participation.

Dr. Rossitza Lazova is Associate Professor of Dermatology and of Pathology and Director of the Yale Dermatopathology Fellowship. If you have questions or would like to add your comments, visit yalecancercenter.org, where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.