

Support for Yale Cancer Answers comes from AstraZeneca, dedicated to providing innovative treatment options for people living with cancer. Learn more at [astrazeneca-us.com](http://astrazeneca-us.com) Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists, who are on the forefront of the battle to fight cancer. This week it is a conversation about ocular oncology with Dr. Renelle Lim. Dr. Lim is an Assistant Professor of Ophthalmology and Visual Science at Yale School of Medicine and Director of the Ocular Oncology Program at Smilow Cancer Hospital. Dr. Chagpar is an Associate Professor of Surgery at Yale and the Assistant Director for Global Oncology at Yale Comprehensive Cancer Center.

Chagpar Dr. Lim, maybe we should start by you telling us a little about yourself and what exactly you do.

Lim I am dual fellowship trained in ocular oncology and oculoplastic surgery and very passionate about both fields. There is a lot of overlap between plastic surgery and ocular oncology and I will tell you a little bit about what they are. Ocular oncology involves cancers in and around the eye and so our patients come in and we do a full ophthalmologic examination, we look at the surface of the eye, we dilate and take a look at the retina and we really advocate that patients have yearly dilated exams because cancers in the eye can be completely asymptomatic. When they do occur, they need to be treated relatively quickly because sometimes cancers in the eye can spread to other parts of the body.

Chagpar And the other part of what you do you said is very much related?

Lim Yes, oculoplastic surgery, where we treat conditions which involve the eyelid and orbit. Oftentimes you can have neoplasms or cancers that involve the eyelid or orbit. I also do functional eyelid surgery where patients need their eyelids lifted and these procedures can help patients to see better.

Chagpar Let's do a deeper dive into the cancers that occur in the eye. The first thing you said is that many of these are asymptomatic and so people need dilated exams, is that everybody and starting at what age?

Lim We certainly recommend dilated exams, and cancers in the eye can happen in children, they can happen in adults. Let's talk about childhood intraocular cancers. So the most common intraocular childhood cancer is retinoblastoma and parents can look for strabismus or ocular misalignment or what we call a lazy eye and that can be a warning sign, also white pupillary reflex, lots of people are taking pictures all the time and if you

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look at the picture and you notice an asymmetry in the pupil where 1 pupil is white and the other one is dark or you can see a red reflex, that is a warning sign and the parents should bring the children in right away, as we know children do not really complain, they won't say, I don't see well and so these are subtle

changes that parents really should be aware of and if something like that is noticed by the parents, definitely a dilated exam is warranted.

Chagpar Sticking with the theme of children and eye cancers in children, if you have a child who does not have a lazy eye or who does not have a white pupil when you take a picture with them, then do they need dilated exams every year periodically just for screening, or are they good?

Lim Most schools will do vision testing and that serves as a screening for developmental issues with the eyes and lot of times, children may fail a school screening and then will be referred to an ophthalmologist at which point they certainly will have a dilated exam and childhood intraocular cancers are not very common, but that is 1 way that we can detect them in asymptomatic children that have absolutely no other signs.

Chagpar Let's talk a little bit more about what happens after that. A child presents with one of any number of symptoms or is picked up by a screening test at their school, they come in, they get a dilated exam, that is really just where the ophthalmologist dilates the pupils and takes a look in the back of the eye, right?

Lim That is exactly right.

Chagpar And so at that point, what exactly are you looking for in these children when you look in their eye and how is the diagnosis of retinoblastoma or any other cancer made?

Lim Through ophthalmoscopy, that is the physician actually looking into the eye and we have a direct view with any type of retinal cancer in the eye. We can assess retinal detachment and any other kinds of growths. Now, there are other ocular neoplasms or cancers that can occur even on the surface of children's eyes involving the conjunctivae, some of them are benign growths and others are less likely to be a malignant growth on the conjunctiva and the same in adults. So cancers can occur on the surface of the eye and when they do occur on the surface of the eye, they are more likely to be benign neoplasms like nevi or pigmented growths or other more malignant neoplasms like squamous cell carcinoma which can involve the cornea and conjunctiva and even adults, some adults have a tumor inside their eye and can be completely asymptomatic and don't even realize it which is again the reason that we stress having dilated exams.

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Chagpar So at the time of the dilated exams, you look in the back of a child's eye and you see something and what you see is suggestive of the most common tumor, let's say, which is retinoblastoma in children. We talk a lot about different kinds of cancers and one thing that always comes out is the need for a pathologic diagnosis, so oftentimes this is a biopsy, somebody putting a needle into a tumor

and actually rendering a diagnosis that says this is XYZ cancer. Does the same occur in ophthalmology, in tumors in the back of the eye?

Lim Yes, for certain tumors we are able to biopsy them. For retinoblastoma, for instance, usually the cancer has certain features. It is usually not pigmented. It is a retinal lesion. It sometimes has calcium in it. We do other sorts of ancillary testing that can help us pinpoint the diagnosis. So not only do we look inside the eye and visualize the tumor and note the characteristics that are consistent with retinoblastoma, but we also do ultrasound where we apply an ultrasound probe to the eye and we are able to assess the acoustic features and can detect calcification in that way. We can do an OCT where we can actually detect and identify which layers of the retina are involved, which is especially important for smaller tumors.

Chagpar What is an OCT?

Lim It is ocular coherence tomography where it is a noninvasive test and it gives us information of all of the retinal layers and some tumors involve just the nerve fiber layer or the inner retina, others can involve the entire retina like retinoblastoma.

Chagpar So an OCT sounds like it is a CT scan for the eye.

Lim That is exactly right.

Chagpar And so you look in the back of the eye, you do an ultrasound, you do a fancy OCT, CT scan and you see something that looks like it is a retinoblastoma, does that synch the diagnosis of a retinoblastoma or do these kids really need a needle in their eye to make the diagnosis?

Lim We tend not to directly biopsy retinoblastomas only because it can predispose children to seeding of the tumor elsewhere and we do not want that. There are newer modalities like taking a sample of the anterior chamber fluid, we call them aqueous humor, and this has not been used very frequently, it is something that is very new in ophthalmology but for other tumors, other lesions of the retina or the choroid which is deep to the retina, we can biopsy these lesions, for instance uveal melanoma is the

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most primary intraocular tumor and we biopsy uveal melanomas all the time to synch the diagnosis. Other things like metastasis, we can have metastatic lesions from lung cancer, breast cancer, and they appear in the eye and we see that all the time.

Chagpar And when they appear in the eye, do they also appear without symptoms or do people actually have symptoms when they get a metastasis?

Lim It really depends on the location. There are vital structures that if affected patients will notice right away that something is going on, my vision is blurry,

or straight lines do not appear straight to me, they appear curvy because a lot of these lesions can present with subretinal fluid which causes some visual distortion and so sometimes they are asymptomatic, sometimes they can present symptoms of blurry vision, visual distortion, even pain, some metastatic lesions can produce pain, particularly lung cancer, it is known to be very painful in the eye.

Chagpar And so getting back to retinoblastoma, just to finish that story, now I understand that there are certain genetic predispositions to retinoblastoma in these children, is that right?

Lim That is exactly right. Sometimes retinoblastoma can occur without a family history and without a genetic predisposition, we call that a sporadic case, but other times it can be hereditary when patients have a germline mutation and so if a patient has retinoblastoma, we routinely send them for genetic testing, of course we want to obtain a thorough family history to know if it is something that is hereditary or if this is the first case in the family.

Chagpar And is a retinoblastoma gene mutation something that is screened for at birth and for those children that carry that mutation are those children automatically getting dilated exams on a regular basis, how does all that work?

Lim So, it is not routinely screened at birth unless there is a strong family history, ok. Now, if there is a strong family history of retinoblastoma and let's say a parent has a germline mutation, we do screen children very early and we look very carefully with prenatal ultrasounds to see if retinoblastoma exists and that has been detected in the past.

Chagpar What is the average age which children get retinoblastoma if they are going to get it?

Lim It really depends and again, sometimes patients present in-utero, we see patients, via ultrasound, you can localize the tumor, sometimes patients are just a few months old.

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Chagpar I really want to dive deeper into how we treat retinoblastomas and so many other ocular tumors. Not only in children but adults, because everybody who has eyes is potentially at risk for developing eye tumors. We are going to learn a lot more about ocular oncology with my guest, Dr. Renelle Lim right after we take a short break for a medical minute.

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Chagpar This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Renelle Lim. We are talking about the diagnosis and treatment of ocular cancers and right before the break, we were saying that the most common cancer that occurs in the eye in children is retinoblastoma, and this is something that for some children is genetically mediated, for other children it may be sporadic, but is often diagnosed simply by seeing an ophthalmologist who can look in the back of the eye, do some scans with an ultrasound or CT and actually make the diagnosis of retinoblastoma which brings me to the question of what happens then? You look in the back of a child's eye, you see something concerning for retinoblastoma, you do all of your fancy tests, which all confirm your suspicion, what happens then, what is the treatment like?

Lim Well the treatment depends on the size of the tumor, is it bilateral. Let's say we have a bilateral case and the treatment paradigms can differ across institutions. There is a strong push to treat patients with bilateral retinoblastoma with intravenous chemotherapy, and that is one form of treatment used in conjunction with other forms. Another form of chemotherapy is intra-arterial chemotherapy where a femoral artery is cannulated, and a small dose of chemotherapy is introduced via the ophthalmic artery and that has shown very promising results in achieving tumor regression for retinoblastoma. Other forms of treatment are freezing treatment, we call that cryotherapy or laser treatments.

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Chagpar We talk about treatments for most cancers on this show, and you can think of it as 3 big buckets, there is chemotherapy, there is radiation, and there is surgery. So are you saying that most of these are treated with chemotherapy plus or minus some local therapy whether it is cryo or something like that? How much of a role does surgery play and how much of a role does radiation play in these ocular tumors?

Lim Great questions. For the most part, chemotherapy is our first line. If a patient shows signs of recurrence, you can use plaque brachytherapy to treat selected cases and when we talk about surgery for retinoblastoma, we are essentially talking about enucleation or eye removal after patients have failed other forms of treatment or if the tumor is very large at the time of presentation and unlikely to respond to chemotherapy or other local forms of therapy or in a case that has failed all of the treatments.

Chagpar And you mentioned clearly enucleation is not a good idea particularly if somebody has a bilateral case, how often is it that patients presents with

bilateral retinoblastoma?

Lim We always say in the treatment of retinoblastoma, our number one goal is to save life, next to save the eye, so we try everything to try to save the eye and then to save vision lastly, and the likelihood of enucleation really depends on the time at which the patient presents to us. If the patient is presenting very late after the tumor has had a chance to grow significantly, then enucleation is likely.

Chagpar And the breakdown for unilateral versus bilateral retinoblastoma, what does that look like, are most retinoblastomas unilateral or most retinoblastomas are bilateral?

Lim Most are unilateral.

Chagpar Oh that is good to know. We have spent a lot of time talking about the most common eye cancer that occurs in children, retinoblastoma. Let's talk a little bit about adults, what kind of cancers of the eye do adults get?

Lim The most common primary intraocular tumor in adults is uveal melanoma.

Chagpar Tell us about uveal melanoma, what it is, how it presents, how we treat it, and what the prognosis is?

Lim Uveal melanoma can affect the choroid, the ciliary body, or the iris. It can be asymptomatic or patients can present with blurry vision, eye pain, or just having some sort of distortion and so they present let's say to their general ophthalmologist, and a mass is noted, sometimes it can be pigmented like most melanomas are and

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sometimes it can be amelanotic and if there is uncertainty about the diagnosis, a fine needle aspiration biopsy can be performed where we actually take a sample of the tumor and send it to the lab and get confirmation that this is the melanoma. Other times when the characteristics are undoubtedly melanoma, we go ahead and treat and the treatment for uveal melanoma is plaque brachytherapy where we apply disk like structures to the scleral surface right on to the eye to treat cancer.

Chagpar When we talk about melanoma, I mean most of us are a little bit familiar with skin melanoma and some of the risk factors associated with that, being out in the sun, not wearing sunscreen, going to tanning salons, etc. Are the same risk factors the case in ocular melanoma?

Lim No, actually unfortunately not much is known about the risk factors, but we do know that patients with lighter skin, lighter eyes, tend to be more affected with uveal melanoma. So we always tell patients it is not really what you did, visiting a tanning salon, or staying out in the sun that predisposes you to getting uveal melanoma, it is a mutation that occurs, sometimes it is de novo,

that means out of the blue or it can arise from a benign-appearing lesion like a nevus.

Chagpar We always see on sunglasses that there is so much UV protection, does that in any way reduce our risk of uveal melanoma and should we be looking for a certain number or certain grade on those sunglasses or does it really matter, just buy whatever is cute?

Lim You can buy whatever is cute because it is not likely going to prevent getting uveal melanoma. It has not been scientifically proven to be a direct result of the amount of the UV exposure.

Chagpar Well that is good to know. You talked about uveal melanoma which is really melanoma that occurs in the back of the eye, right?

Lim It can occur in the uvea. And three structures comprise the uvea, the iris which we can see, the colored part of the eye, the ciliary body, and then further back the choroid.

Chagpar Ok and then you had mentioned early on something called conjunctival melanoma.

Lim That is right.

Chagpar Tell us about that and why that is different or whether it is the same as uveal melanoma, just in a different part of the eye?

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Lim It is completely different. It behaves completely different. It actually behaves more like skin melanoma and it presents as a pigmented or a nonpigmented nodule on the surface of the eye. The conjunctive is a thin membrane overlying the white part of the eye, the sclera and sometimes you can have a melanoma occurring on the surface of the eye and when that happens that requires more of a surgical approach and so we excise the tumor by using the no-touch technique, we try not to manipulate or touch the tumor, we only manipulate tissues surrounding the tumor to prevent seeding of these pigmented cells across the ocular surface.

Chagpar So what you are telling me is that for these conjunctival melanomas, you are taking them out, essentially taking out part of the eye with that little bit of conjunctiva but you are not actually removing the whole eye like we talked about in retinoblastoma in some cases.

Lim That is right, so we are only removing the involved portions and the safe margin to make sure that we have it all. Interestingly there are other modalities of treatment like targeted therapies and so this is really an exciting field, targeted therapy and immunotherapies, these are a form of chemotherapy that have been shown to be very useful for cutaneous melanomas, for skin cancers,

and people are living longer with skin cancers and now we are starting to use them more for conjunctival melanoma.

Chagpar Are these therapies that you give intravenously or how does that work exactly and does it only work for conjunctival melanomas or do these also work for the uveal melanomas that we talked about before?

Lim We are very lucky here at Yale to have magnificent medical oncologists, so this is really in conjunction with medical oncology and they tend to work more for conjunctival melanoma; only about 10% of uveal melanomas will respond to immunotherapy and so again, conjunctival melanoma is more similar to cutaneous melanoma. Unfortunately, uveal melanoma does not really respond to these treatments.

Chagpar Well if conjunctival melanomas are more like skin cancers, do those sunglasses make a difference now?

Lim We advise UV protection, but it has really not been shown to decrease your risk of getting eye cancer by wearing sunglasses.

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Chagpar Now the other thing that you had touched on at the top of the show was that you wear 2 hats, you deal with cancers that occur in the eye and around the eye, but there are also cancers that occur in the orbit and in the eyelid and things like that. Tell us a little bit about what are the most common cancers there and how they are treated?

Lim We can talk about the eyelid, the most common cancers are actually UV related and so we advise UV protection whether it be sunglasses or sunscreen or wearing wide-brim hats.

Chagpar Do the hats really work?

Lim Yes, they do, to reduce the amount of exposure to ultraviolet light and so if a patient does have a basal cell carcinoma that also is surgical, that is managed surgically.

Chagpar So eyelid cancers by and large tend to be kind of like skin cancers, basal cell cancers or squamous cell cancers?

Lim Yes, they are.

Chagpar Tell us about cancers that occur in the orbit?

Lim Patients can present with what we call proptosis or bulging eye because of the mass that occurs in the orbit and the orbit is really the space around the eyeball and so if you can imagine having a tight space surrounded by bone and then you have the eye in that socket and now a mass is growing pushing on the eye, it can cause blurry vision, pain, proptosis, these are just some of the manifestations. Sometimes, patients present with double vision because they



are not really able to move their eye fully and the mass can grow so large that it is actually pushing on the muscles that surround the eye.

Chagpar So these cancers that occur in the orbit, you don't really get to see them with a direct visualization when you look into somebody's eye with an ophthalmoscope?

Lim No, for these tumors, we need CTs or MRIs to help us characterize the lesions.

Dr. Renelle Lim is an Assistant Professor of Ophthalmology and Visual Science at Yale School of Medicine and Director of the Ocular Oncology Program at Smilow Cancer Hospital. If you have questions, the address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and past editions of the program are available in audio and written form at [YaleCancerCenter.org](http://YaleCancerCenter.org). I am Bruce Barber reminding you to tune in each week to learn more about the fight against the cancer. You are on Connecticut Public Radio.