

Yale CANCER CENTER *answers*

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Welcome to Yale Cancer Center Answers with your hosts doctors Francine Foss, Anees Chagpar and Steven Gore. Dr. Foss is a Professor of Medicine in the Section of Medical Oncology at the Yale Cancer Center. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital and Dr. Gore is Director of Hematological Malignancies at Smilow. Yale Cancer Center Answers features weekly conversations about the research diagnosis and treatment of cancer and if you would like to join the conversation, you could submit questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. This week you will hear a conversation about pediatric neuro-oncology with Dr. Asher Marks. Dr. Marks is Assistant Professor of Pediatrics in Hematology/Oncology and Director of Pediatric Neuro-oncology at Yale School of Medicine. Here is Dr. Steven Gore.

Gore So pediatric neuro-oncology, this is a brain tumor right? I think as a parent that is the scariest, most awful thing we worry about.

Marks It is, absolutely. When I first meet with a family and I have to give this terrible diagnosis, I make it clear that this is probably the worst thing that they are ever going to go through and often I am giving them the worst news anyone will ever hear. The one silver lining, if you can call it that, is that the success rates in treating brain tumors are better than most people think for pediatrics and we are getting better every day. It really depends on the tumor. It depends on the location, and something that we focus on now is trying to diminish long-term side effects of both the tumor and treatment while we continue to improve our overall success rates.

Gore I am definitely very eager to get to the positive silver linings, but before we get there, why don't we start with what age are kids at risk for brain tumors?

Marks It really runs the gamut in terms of age at risk, from infants all the way up to teenagers depending on the tumor that we are talking about. With pediatric brain tumors when we look at them at a molecular level, we know that they differ from adult tumors and when that switch in the underlying biology occurs, I do not think we are all that sure, it is probably somewhere in the 20s or 30s, but the types of tumors can range from actually babies that are born with tumors all the way up into late adolescence.

Gore What would I see as a parent if my kid were developing a brain tumor?

Marks It is a great question and it is one that we get often. Unfortunately, the signs you often start seeing are those that happen very commonly in every day scenarios, so before I get into it, I do not want anyone to freak out, to be scared, because I am going to say some things that you will think back and say, gee I see that every week, should I be getting an MRI, should I be bringing my child to the pediatrician. The things that are obviously very concerning and emergencies are things like seizures, terrible headaches that are not going away for hours on end, changes in what we call the focal neurologic findings, so one arm is weak, one leg is weak, there is a change in vision, things like that, so those are kind of obvious and those are situations where parents are rushing their kids to the ER. The situations that I warned about when I started are things like headaches, things like

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slow changes in vision, and these symptoms have their own uniqueness with a brain tumor, so for example, if we saw a child with headaches mostly in the morning when they first wake up, if we see there is headache associated with vomiting in the morning, then we get a little bit more concerned. More than likely it is not a brain tumor, but that is when we kind of start raising our antenna. I have to say I feel for these primary care pediatricians because they are dealing with symptoms like this all the time and it is sometimes tough to say, when am I going to pull the trigger, when am I going to get that scan and you can have primary care pediatricians who will go their entire career and see very few if any brain tumors, so that can kind of give you a sense as to how rare these are despite the fact that many of the presenting symptoms are quite common.

Gore I would assume in contrast, eye strain and headaches and, I cannot see the board mommy, those happen almost every day, right?

Marks Absolutely, yeah.

Gore Just so you know, when my kids were young, there were any number of symptoms that my wife was concerned about that they were becoming autistic, or to her, schizophrenic.

Marks Sure, sure.

Gore Gratefully, my kids are healthy adults, and they never had any major problems, but we had to talk her down, just to hang out the dirty laundry, but that is why they pay me the big bucks on the radio. So, it sounds like most of the diagnoses will be made by primary care physicians or some will come through the ED, emergency department, if a kid presents with new seizures, most of us would take them to the emergency room.

Marks I would say that most of the new diagnoses come through the ER. We have had diagnoses come from ophthalmologists where they do their eye exam and they see findings consistent with a brain tumor during that period of time. We also occasionally see children presenting from the primary care doctor who sent them for an MRI and all of a sudden these MRI results come back quite alarming and then we immediately get a phone call and usually at that point send the kids to the ED and work them up from there.

Gore So the kids will get admitted to the hospital usually?

Marks On first diagnosis, unless it looks like something that has been there a long time and there are absolutely no symptoms, in a situation what we call kind of cheekily, an incidentaloma,

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something that sounds incidental, then yeah, we often do admit from the beginning just to get everything in order whether it is necessary or not to get things in order to make sure that the ball gets rolling and that the kids are safe.

Gore My guess is that the parents are to fond of this incidentaloma.

Marks We are not too fond of incidentaloma. It is a situation where we see it and we can ignore it and we follow it with serial MRIs.

Gore: But you do not think it is really anything serious at that point.

Marks We do not know how much of the population is walking around with these ditzels that we would see if we scanned everybody in the world.

Gore So they are not really tumors, they are just something.

Marks A lesion if you will.

Gore I know in most cancers to make a diagnosis one has to actually get a piece of tissue and do a biopsy, is that the case with brain tumors as well?

Marks For the most part, it is, unfortunately.

Gore You are going to drill into my kid's head?

Marks I am not.

Gore Good, I still like you then.

Marks Dr. Michael DiLuna is a phenomenal pediatric brain surgeon here at Yale. He does all of are pediatric cases.

Gore He is not running for President. That is another DiLuna.

Marks That is another, yeah.

Marks So there are a few situations where we can look at the tumor and we can say, given the clinical situation, the patient's history and exactly what this looks like on scan, we know what it is and we do not really have to go in.

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Gore Really?

Marks It is unusual. I would say a few incidences or perhaps with patients with an underlying syndrome called neurofibromatosis, we know that they often get low-grade gliomas and they have a very characteristic look on scan.

Gore That is the elephant man disease, right?

Marks I do not know, I never examined the elephant man.

Gore I think he had neurofibromatosis.

Marks Yeah, with neurofibromatosis, we can often kind of pick those out. The other ones are very bad tumors called DIPGs, diffuse infiltrating pontine gliomas, and these have a very distinct look on MRI. Anything out of this realm, we often need a biopsy. Fortunately, because Dr. DiLuna is so good and we have advanced so much in brain surgery techniques, we can often get in and out without much neurologic deficit, get our diagnosis and make a plan from there.

Gore So you are not trying to resect the whole tumor or remove the tumor?

Marks Not always, we like to get as much as we can. That being said, there are tumors that are exquisitely sensitive to chemotherapy and radiation, and if we get into the sense that that is what it is and we know that an aggressive resection is going to result in loss of morbidity, we sometimes try to get in and out and then go back for a second surgery if necessary.

Gore How do you deal with the kids if they are not infants? This must be the very most terrifying thing ever, I think it is terrifying to me as an adult, I just cannot imagine being a 5-year-old or a 7-year-old or 13-year-old and going for brain surgery.

Marks Absolutely, and I have to give a hand to my ancillary services for that. We work very closely with social work who is excellent with the parents, good with the kids, but even more so in relating with the kids, we have got a department called Child Life and these are very well trained, experienced practitioners who are used to working with children in these situations, and they are used to dealing with children's stress and anxiety and then working around that, working through it and being able to educate them. And I think when a person goes into a situation, knowing as much as they can, that helps relieve the stress and relieve that anxiety. The unknown is always the scariest.

Gore Oh, yeah.

Marks So Child Life plays a very important role in getting our patients through emotionally intact.

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Gore I understand that this is off topic, but I understand that one of the pediatric oncology social workers won a compassionate practitioner award recently for Smilow?

Marks Yes, Maricel, she is phenomenal.

Gore Yeah, I read the nominations and it was a very moving ceremony where she got that award as compassionate caregiver.

Marks We were incredibly proud of her. She is amazing. She consistently goes above and beyond and fortunately we have got many people in our department that do that.

Gore I have the utmost respect for you guys and neuro-oncology, to me, it is a cut above. Okay so we have gotten the kid to the OR without having to chain him down or we did chain him down, he has had a surgery, he has gotten through that hopefully well, he or she, now what happens?

Marks Now is the hard part. There is a lot of waiting afterwards and like I said, the unknown is always the scariest, and we try to give as much information to parents as we can prior to the biopsy in terms of what they can expect afterwards, but the reality is we often do not know if this is a benign tumor or a malignant tumor. We do not know if we are going to have be talking about radiation or chemotherapy or further surgery and so after surgery oftentimes, parents have to wait several days until we get that final pathology and that is often where I kind of enter the picture and I try to introduce myself as a member of the brain tumor team because to be honest not all of these are cancers. And I think that word holds a lot of weight when parents in this situation are delicate and in a very fragile emotional state.

Gore So you have not even met them yet?

Marks Sometimes I have, it depends on the situation. It depends on how long the patient was there prior to surgery. There are times when Dr. DiLuna has to come in at 2 a.m. for emergency surgery and I do not see them until 7 or 8 in the morning, so sometimes I will have to come in after surgery, sometimes I go in before, but usually when I go in before it is to say hi, I will be around, but I do not have much to say now.

Gore Do you wear a clown nose or anything cool like that?

Marks No.

Gore I want my pediatrician to wear a clown nose and wig.

Marks It is funny, people don't like to meet me and I cannot blame them.

Gore Yeah.

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Marks And sometimes they say, hopefully we will never have to see you again.

Gore I get it. So they get the pathology and what happens then?

Marks Once we have the pathology, I can usually give the parents an initial sense of what treatment is going to look like. Most patients are presented at our oncology tumor board where we discuss with radiation oncology, radiology, neurosurgery and other oncologists as to what we think is best from a team approach. Many cases that are more complicated, I will even present at a collaborative Brain Tumor Board that I participate in along the East Coast with other institutes such as Children's National Medical Center, Walter Reed, King's Daughters in North Carolina, so we will go through a process of analyzing the kids very closely and coming out with a plan.

Gore This is a fascinating topic and we will take it up after the medical minute which we are now going to take a short break for. Please stay tuned to learn more information about adolescent oncology and in particular, pediatric neuro-oncology with Dr. Asher Marks.

*Medical
Minute*

Genetic testing can be useful for people with certain types of cancer that seem to run in their families. Genetic counseling is a process that includes collecting a detailed personal and family history, a risk assessment and a discussion of genetic testing options. Only about 5 to 10% of all cancers are inherited and genetic testing is not recommended for everyone. Resources for genetic counseling and testing are available at federally designated comprehensive cancer centers such Yale Cancer Center and at Smilow Cancer Hospital at Yale-New Haven. The Yale Cancer Center Cancer Genetic Counseling Program is a new frontier in the fight against cancer. The program provides genetic counseling and testing to people at increased risk for hereditary cancer and helps them to make informed medical decisions based on their own personal risk assessment. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. More information is available at yalecancercenter.org.

Gore Welcome back to Yale Cancer Center Answers. This is Dr. Steven Gore and I am joined tonight by our guest, Dr. Asher Marks. We were discussing adolescent oncology and pediatric neuro-oncology. Asher, before the break, you were telling me that for really complicated cases, you participate in a tumor board that is across the East Coast.

Marks Yes.

Gore How does that work? It cannot be face to face right?

Marks It is the magic of teleconferencing, absolutely. I trained in Washington and when I left, I installed some software on my laptop that let me talk to them whenever I felt the need. We can consult on cases together and every institute kind of involved in this tumor board has a camera and we meet every two weeks.

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Gore Wow and how long do you meet for?

Marks As long as necessary, anywhere from half an hour to one hour.

Gore That has got to be powerful because I cannot imagine that even at the biggest centers there are many of you.

Marks Absolutely.

Gore And it can seem very lonely making decisions I would think for a kid.

Marks You have nailed it right on the head, these are very rare tumors and there are experts scattered throughout the country and most institutes do not need more than one, so this is a great way for us to bounce ideas off each other and really keep up to date as to who is doing what and it is a very valuable tool.

Gore Is therapy really tailored to the individual or is it pretty much, this kind of brain cancer is treated this way and that kind of brain cancer is treated that way?

Marks We are getting there. Right now, it is more of a situation of whether this brain cancer is treated that way and that is treated another way, but what we are discovering is that the names that we have for these cancers come from what we call the histologic diagnosis, kind of looking at the cells.

Gore How they look.

Marks Yeah, and fortunately as technology progresses, we can actually look at what the proteins on the cells look like or what the DNA in the cells look like. So that is where the personalization is coming in from. A great example of where that is headed is actually in a new trial that we will be opening soon in collaboration with St. Jude, where we are looking at medulloblastoma, they are the most common ones.

Gore Medulloblastomas.

Marks Medullo yes. It is the most common malignant brain tumor in childhood and it used to be this one group, the question used to be, radiate now, radiate later, give this chemo, give that chemo. About five years ago, some collaborative groups, much of it led by Mike Taylor in Toronto, have actually discovered that these tumors are actually more like four different types of tumors.

Gore You are kidding.

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Marks With very unique molecular characteristics and prognostic implications, so this upcoming trial is going to be looking at molecular markers on these tumors and tailoring to four different therapies. The hope is that as time goes on we get more used to targeted therapies and we will be tailoring even more.

Gore And how many centers will participate in that trial? This is, as you said already a rare tumor and then you are dividing it into four subtypes, right.

Marks Exactly, you got it, so the more we learn about these tumors, the more subtypes, the harder it is to actually study them, so this particular study, I do not think they have all of their institutes pledged on yet. But I can tell you that one of the greatest advances we have seen in pediatric cancer treatment is through the Children's Oncology Group which is through the NIH, through the NCI, these are all national organizations, and what it has allowed us to do for the past several decades is collaborate and share our data and due to this collaboration, we have been able to increase cure rates tremendously. We have discovered that practicing in a silo and studying in a silo just does not work. We can never get the numbers we need to make progress.

Gore We know adult oncologists do not play in the sandbox as well as you pedi oncologists do.

Marks Yes, and how can I put this politically, children do better than adults, I do not know if it is because of what we do or because of what the kids do.

Gore Probably a little of both.

Marks Yes, but they do pretty well.

Gore That is great and so you said that some of these tumors are very chemotherapy sensitive, so will most kids be getting chemotherapy for the brain tumors?

Marks Most kids, for the most part, yes, I would say the majority of the kids will be getting chemotherapy for the brain tumors. The exception to that would be these very benign looking low grade tumors in which case we can often get away with just resection and careful monitoring. If there is progress, we will have to go to a more kind of low-dose chemotherapy to keep them in check.

Gor And is radiation part of the treatment as well for some patients?

Marks Absolutely, radiation is something that we consider very closely. It is something that we do not do willingly. Radiation has its own unique side effects, especially in younger children. We know that we can see IQ drops, we can see cognitive deficits down the road, we can see increased risks for secondary cancer, increased risk for endocrine disorders, and so we use it when we need to and that is often in more malignant tumors or tumors that are growing out of control.

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Gore But some kids will get only chemotherapy.

Marks Absolutely.

Gore Doesn't that affect the growing brain, developing brain?

Marks That is a great question and I think that there is some more recent data that suggests it does but not nearly as much as radiation and age absolutely plays a role in it, so we do not like to give these therapies unless we absolutely have to.

Gore My adult patients all talk about chemo brain.

Marks Chemo brain, yes.

Gore We do not really understand much of that, I mean apparently it is a real thing.

Marks Absolutely, yeah.

Gore On the other hand, I would imagine the kids are more plastic and they can probably take a joke a lot better than adults. Not that chemo is a joke, I do not mean that.

Marks Absolutely, no they bounce back, the pediatric brain is much more plastic than the adult brain and so we are certain to see, looking at brain development, that perhaps these kids are forming new interneuron connections after some are broken.

Gore As the kids are being treated, are they in misery most of the time? I am always struck at the hospital when I see the little kids wheeling around in their little cute little things that they have got, their little bald heads and everything, but they all seem pretty happy, I mean am I just seeing a subset of unusually well-adjusted kids?

Marks No, I always tell the parents during the first meeting about the use of chemotherapy, I saw, have you ever know anyone on chemotherapy, and their answer is usually yes, and that person often who is not doing well was nauseous and was skinny, cachectic, miserable, and I often follow it up with, well I want you to know kids tend to do much better and their bodies are like I said, they bounce back and I think mentally kids a lot of times they lack the anxiety that adults have.

Gore They do not know any better.

Marks They do not know any better. And so people always say, how do you deal with kids with cancer and I often have to say, I think I would have a tougher time with adults. The kids have just this elasticity that makes them truly inspiring.

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Gore Wow, so you wanted to give us some better than we expect news about these terrible diagnoses. How well are we doing?

Marks It depends on how you want to break down the tumors. If we are looking at brain tumors overall, I think we are probably about 60 to 70% cure rate.

Gore Wow.

Marks So we are getting there. With that being said, I think we are continuing to struggle with long-term effects of the tumors and treatment itself and so that is where we are putting substantial energy. We are trying to reduce the doses of radiation as much as possible without changing cure rates. We are trying to get more targeted therapies and we are improving our surgical techniques.

Gore I am sure that even if there is some cognitive loss, if quality of life is good I think probably the kids and the parents are more than grateful.

Marks Absolutely. Our overall goal is survival with quality of life that is acceptable to the parents and I think we achieve that most of the time.

Gore I guess that the other part of your job has to do with adolescents and cancer.

Marks Yeah.

Gore Is that also just brain cancer?

Marks No it is not. There is a significant number of patients in there with brain cancer, if you look at cancers overall in kids about 25% are brain cancers, so we have got that group, but I also help as Medical Director of the Adolescent and Young Adult Clinic in the Children's Hospital, so we see patients aged around 13 to lower 20s and we are extremely lucky that in this clinic we have a psychiatrist and psychologist there every week.

Gore How about a policeman?

Marks We have the social workers for that. You know it is interesting, adolescence, they are not adults, they are not kids, they often feel that they are kind of the lost patients. They do not belong either place. They do not want to walk in the clinic and see a clown.

Gore Sure.

Marks They want their own space.

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Gore Right.

Marks And so we are working right now to provide that for them. Right now we have the services in place. We have the programmatic issues starting to get ironed out. Hopefully, we will soon begin building actually an adolescent kind of inpatient center, an area for the adolescents to kind of hang out when they have to be inpatient, so they feel like it is their space.

Gore Lots of MTV and videogames.

Marks Oh yeah, you got it. We are actually working with an organization called Teen Cancer America, which is kind of the brainchild of Roger Daltrey from the WHO.

Gore Wow.

Marks He implemented this program in England and given its influence there, he has actually made this part of legislation that hospitals need to provide special services for adolescents with cancer. I do not think we are quite that far here in the States, but he is certainly making us aware of the issues and we are certainly working with them to achieve that.

Gore Did he have any particular personal connection with adolescent cancer?

Marks I think he has always been an advocate for teenagers and I think he has seen the dark side of cancer and from what I understand his personal position has actually kind of moved him in this direction and introduced him to this issue.

Gore Interesting. You mentioned Roger Daltrey, and I think about 'Tommy' and you just think about that whole sort of mythic sort of lost child, adolescent.

Marks Yeah, exactly.

Gore Not being heard or he cannot see.

Marks Exactly.

Gore So in some ways it is very, I do not know, poetic, but maybe I making too much out of it.

Marks No, I think it is a bit poetic, I really do.

Gore So is this a busy clinic?

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- Marks We are getting busier. You look at the big issues in adolescents, particularly adolescent teens and there is a psychosocial aspect of a feeling that they do not belong, the inability to relate to their peers, I mean, your peers are dealing with who has got the hottest phone and you are dealing with a tumor. So it is hard to relate to your peers, and we try to introduce them to each other, try to get their social networks going again, and try to make sure that they get the support that they need from ancillary services. So it is becoming busier. Our psychiatrist and psychologist are starting to expand a little bit to the inpatient unit and see as many kids as they can on Thursdays. We are getting there, we are in the process of hiring more staff to help these kids through the medical system and help them get all the resources that they need.
- Gore And do most of the kids come from Connecticut?
- Marks Right now, they do. I would say that most of them are from Connecticut.
- Gore I know that our cancer center is certainly reaching out to some of the neighboring states as we develop certain specialized services and this would seem like a real draw or maybe other places like in New York are also very up to speed about this, I do not know.
- Marks I think we are a bit ahead of the curve on this. I came from a very big center and politics is difficult and I think it is difficult to get these resources as quickly as you need them and it is a very big deal for us to have psychology and psychiatry in that clinic every day where we can say, I think this kid is really struggling, I think he would benefit from some of these services.
- Gore So you have been here about a year and a half.
- Marks A year and a half, correct.
- Gore And what drew you here to New Haven?
- Marks I was extremely impressed with The Children's Hospital as well as Smilow Cancer Hospital. I think that Yale is in a very unique position where we have got experts in many different fields working side by side. I did much of my training at a very large Children's Hospital and I think we were a bit isolated, we did not have the researchers right there, we did not have the adult docs right there, and I think a lot gets done here in the hallways where you can stop someone and say, let me run this idea by you or, what would it take to bring this idea to fruition, translational research and so I think it is a very exciting time here in terms of advancing both patient care and research.

Dr. Asher Marks is Assistant Professor of Pediatrics and Hematology/Oncology and Director of Pediatric Neuro-Oncology at Yale School of Medicine. We invite you to share your questions and comments, you can send them to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YC. As an additional resource, archived programs are available in both audio and written format at yalecancercenter.org. I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another edition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas.