00:00.000 –> 00:14.400 Support for Yale Cancer Center Answers comes from AstraZeneca, a global science-led biopharmaceutical business committed to bringing to market innovative oncology medicines that address unmet needs for people living with cancer. More at astrazeneca-us.com.

00:14.400 –> 00:53.900 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 understanding your pathology report with Dr. Angelique Levi. Dr. Levi is an Associate Professor and the Director of Outreach in the Department of Pathology at the Yale University School of Medicine. Dr. Gore is a Professor of Internal Medicine and Hematology at Yale and Director of Hematologic Malignancies at Smilow Cancer Hospital. 00:53.900 –> 01:06.100

Gore Pathology, wow! I think a lot of our listening audience, they think pathology and they think Quincy, the Morgue.

01:06.100 –> 01:06.600

Levi That's so funny, you say that. That was my nickname in medical school.

01:06.600 –> 01:06.700

Gore Quincy?

01:06.700 –> 01:07.700

Levi Yes.

01:07.700 –> 01:09.400

Gore You don't look anything like Jack Klugman?

01:09.400 –> 01:12.900

Levi No, but in anatomy, I guess, you know, that is what my partners called me.

01:12.900 –> 01:14.100

Gore Oh! Were you really into the anatomy thing?

01:14.100 –> 01:18.200

Levi I guess I was, it stuck all 4 years.

01:18.200 –> 01:20.500

Gore And did you know you were headed towards a career in pathology?

01:20.500 –> 02:18.600

Levi No. Definitely not. I would say I was open to everything. I wanted to do something, so I thought involving children, so for sure, I thought I would be in pediatrics. I really loved my rotation on the wards in OB/GYN, happy families,

delivering babies, doing surgery, and it was not until I did an elective through a summer program at my medical school where I did some research and was exposed to the visual aspect of pathology and I am a very visual learner and very curious in it, always seemed to answer those questions of why? And so, that was intriguing to me. And going through clinical rotations, the lifestyle of every other night call for those specialties that were most appealing to me probably would not have fit my, you know, my persona, so that didn't work out.

02:18.600 –> 02:24.800

Gore I guess, but I guess that dates you to before all these rules about nobody takes call on that.

02:24.800 –> 02:24.900

Levi Absolutely.

02:24.900 –> 02:28.300

Gore You know, I wouldn't have guess that looking at you for our listening audience.

02:28.300 –> 02:31.700

Levi Every second and third night call is definitely in the mix at that time.

02:31.700 –> 02:39.100

Gore Well, yeah, I lived through that myself. So, what do pathologists do if they are not in the morgue, which apparently you are not mostly?

02:39.100 –> 03:10.200

Levi So, the vast majority of pathologists community based and otherwise diagnose disease. So, we are responsible for writing reports on tissue that comes to the lab and that tissue can come to the lab by a surgical procedure or a biopsy or even a fine-needle aspiration. And so, much of what we do is behind the microscope and compiling reports for those treating physicians whether they are oncologists, general surgeons or dermatologists.

03:10.200 –> 03:20.600

Gore Does everything that gets removed by a doctor or other kind of practitioner or in the hospital, does everything has to be reviewed by a pathologist?

03:20.600 –> 03:44.100

Levi So, there are PAs that work in the lab and they will assist pathologists, but only with pathology oversight. So, there may be gross descriptions which are part of a report, also the macroscopic description that would be initially reviewed by perhaps the PA, only under the supervision of a lab directed by a pathologist.

03:44.100 –> 03:56.400

Gore Sure, but like let's say, I go to a dermatologist and she removes something that she is certain is not going to be a malignant or anything to worry about, does she oblige to send it for review or is that her judgment?

03:56.400 –> 03:57.300

Levi No, that's her judgment.

03:57.300 –> 04:02.000

Gore I see. So, not everything that gets removed has to be pathologically reviewed? 04:02.000 –> 04:12.100

Levi If it is sent to a pathology, a pathologist will review it and submit report. If it not, if the treating or clinical person decides not to send it, that we would not see it.

04:12.100 –> 04:45.200

Gore So, it is the judgment of the person who is taking out the tissue. Okay, gotcha. And, you know, I know how important it is and how hard it is sometimes to differentiate what is often like the biggest concern for patients, not always, but is this cancer or not right? A lot of biopsies or tumor removals or mass removals, that is kind of a focus, obviously not exclusively and it seems to me that I remember that is not always so easy to do?

04:45.200 –> 05:27.500

Levi No absolutely not. But you are right, that is the focus, primary focus. We will receive a tissue and our main objective is to analyze that tissue for disease and then the disease, question is, is it cancer or isn't it cancer. If it is not, it is important to diagnose what may, what inflammatory condition it may for treatment options, but usually the burning question is as you say, is it or isn't it cancer, and that is primarily what we do, especially here at a cancer center where we come into play and you know, develop a report that is very specific to cancer.

05:27.500 –> 05:35.000

Gore So, is that not really straightforward, could we train a computer to do that, to take pictures and look at the cells and say 'oh yeah that's cancer'?

05:35.000 –> 06:26.100

Levi We are trying. Well, pathologists are trying to use the help of digital pathology and review and so not with full success and certainly not without the guidance of a human trained eye. Three are still very specific morphologic features that computers have not been able to be trained to do. Radiologists would love to also be able to do that and we are certainly developing certain algorithms in the area of digital pathology, but at the end of the day, it is a pathologist's eye and the human experience that can discern how we have

classified certain tumors and how we then go onto stage them and that then will dictate the prognosis for treatment.

06:26.100 –> 06:32.500

Gore Gotcha. So, how easy is it on average? Can you just look at a slide and say oh yeah this is cancer and no problem?

06:32.500 –> 07:14.100

Levi So, in some cases certainly, it is relatively, you know, certainly training does not take too much time, but that is for maybe for very common cases. So, I hesitate to say; yes, it could be easy in certain cases because there are like with anything else mimickers and benign mimickers of cancer, and so, it really does not come until the end of a long period of training because there is no room for error, right? So, we cannot be right 80 or 95% of the time, we really need to be right, 100% is the expectation.

07:14.100 –> 07:18.000

Gore i sure would hate to lose my prostate for a benign condition that you goofed on.

07:18.000 –> 07:56.200

Levi And that's great example of an area where it is quite complicated and the distinction between cancer and benign is very difficult, and so that is an area where second opinions have also come into play for that very reason. Folks who haven't been trained with specialty expertise in prostate pathology, you know, may not grade a certain cancer or may not recognize a certain cancer and may not do a certain test to prove or confirm cancer and so that in particular is an area that requires a great deal of skill and expertise.

07:56.200 –> 07:58.100

Gore And that is actually one of your areas of specialty right?

07:58.100 –> 08:02.900

Levi It is.

08:02.900 –> 09:05.800

Gore So, you know, our topic tonight is understanding your pathology report. You know, prostate pathology may be a good example to walk us through because I know there is all these scores and grades and Gleason, this and that and having had 2 close relatives in the past year who were to go through these process of a new diagnosis of prostate cancer, both lay people, very intelligent but watching their head swim through this, you know, really brought home to me how difficult it is and of course I guess the caveat for all of this is that patients should rely on their physicians to help them understand the pathology I guess, but you know, we have got MyChart now and eventually people are going to see their reports and I know people, you know, often come to me and

say you didn't tell me about this thing, about that thing and something that I have of course edit it up because it is not important, but it has a star next to it, so people want to know. So, what does the man with a prostate biopsy, what is he going to find on his report?

09:05.800 –> 09:45.600

Levi So, the first part of the pathology report is that each pathology specimen is a signed unique accession specimen number. So, every institution has their own system and every specimen has its own unique number. That is how we will identify that case moving forward. Then, there are patient identifiers with every pathology report and those include the name - first and last, date of birth, date of the procedure, the type of procedure, and so those are specific to that particular specimen.

09:45.600 –> 09:48.300

Gore And I guess you want to make sure it is yours.

09:48.300 –> 10:03.600

Levi Absolutely, and you want to make sure the proper laterality, the proper surgeon is receiving, which side - right versus left, the treating physicians who are also receiving the report that all of that information is accurate.

10:03.600 –> 10:05.700

Gore Does that ever get mixed up?

10:05.700 –> 10:55.500

Levi It has happened. Yes, it is. We do our very best, safety and lab oversight, so QA and QC. The next part of the report involves the actual diagnosis. And so, those pieces depending on whether cancer is present or not may look a little bit different. So, if cancer is not present, it will clearly state negative for carcinoma and all of the particular parts, and so for prostate cancer in particular, it is a set of usually 12 or 18 biopsies let's say. So, that can be up to even over 20 here. At some institutions, there is also the option of targeted biopsy, so that adds even more.

10:55.500 –> 11:02.900

Gore You mean, using some kind of visualization? Gotcha to show you where was the most likely area to find cancer?

11:02.900 –> 11:06.700

Levi Using MRI. Right. In addition to the standard 12 cores.

11:06.700 –> 11:08.600

Gore Twelve. Wow! that sounds like an ouch.

11:08.600 –> 11:21.200

Levi And so, there are many biopsies to keep track of, many sites, many sides and then if cancer is present, there is a specific synoptic report, specific to cancer.

11:21.200 –> 11:21.200

Gore What does synoptic mean?

11:21.200 –> 11:44.300

Levi So, it is almost a summary or a checklist of standardized findings that we look for in prostate cancer for example. So, it might stage the grade as you referred to the Gleason grade is what we use for grading prostate cancer. Each cancer can have its own grading system and Gleason was someone who historically developed it for prostate cancer, and we still

11:44.300 –> 11:47.700

Gore And grade, what does that mean? How intense it is or?

11:47.700 –> 11:51.400

Levi How well or poorly differentiated it is.

11:51.400 –> 11:52.500

Gore How mature the cells look?

11:52.500 –> 11:57.900

Levi How mature the cells look. So, the more mature they look, we would call it well differentiated.

11:57.900 –> 11:58.000

Gore Which is better?

11:58.000 –> 12:52.400

Levi Better. Better akin to what a benign or normal cell might look like. And poorly differentiated would be something that is not well developed. So, that would be immature and aggressive. So, Gleason is a number grading system and you know, different classification schemes use grading systems that even over time may change and the Gleason grading system has also evolved in the last few years. So, it is important when your cancer is being reviewed that it is being reviewed by someone that is current with the current grading systems and the current standardized terminology because that will dictate how the most cutting edge in current therapies may be offered.

12:52.400 –> 13:11.400

Gore You know, I know again with my relatives with their prostate cancer, there was a lot of Gleason grade and if it was this number, they were not going to worry too much, but if it was that number +1 or something like that, like 6

versus 7 or 7 versus 8, whatever it was, that was like a whole different ball of wax.

13:11.400 –> 14:04.700

Levi Exactly and so that's exactly how it is. For example, if it were a well-differentiated tumor, and as you say, it is 3+3 equals 6, 6/10, that would be something that could be watched and we have protocols called watchful waiting or active surveillance, and then if there were tumors that were called 3+4 equals 7, a score of 7/10, those may or may not be watched conservatively with some annual testing, imaging and blood work, while other Gleason scores of 4+4 equals 8 out of 10 would require some more aggressive management if the patient is well enough to do surgery versus chemoradiation for example.

14:04.700 –> 14:19.200

Gore Gotcha. Well, at least we know the pathologist needs to be able to arithmetic in the genitourinary tract, but right now we need to take a short break for a medical minute. Please stay tuned to learn more about understanding your pathology report with Dr. Angelique Levi.

14:19.200 –> 14:39.200 Medical Minute

Support for Yale Cancer Answers comes from AstraZeneca, a Global science-led biopharmaceutical business committed to bringing to market innovative oncology medicine that address unmet needs for people living cancer. More at astrazeneca-us.com. 14:39.200 –> 15:19.800 This is a medical minute about survivorship. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life-changing experience. For cancer survivors, the return to normal activities and relationship can be difficult and some survivors face long-term side effects resulting from their treatment including heart problems, osteoporosis, fertility issues, and an increased risk of second cancers. Resources are available to help keep cancer survivors well and focused on healthy living. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio. 15:9.800 –> 16:13.300

Gore Welcome back to Yale Cancer Answers. This is Dr. Steven Gore. I am joined tonight by my guest Dr. Angelique Levi. We have been discussing understanding your pathology report. Angelique, before the break you really impressed upon me, you know, the critical nature at least in your field where you have your prostate cancer, you know, on these numbering systems, I made a joke about you have to be able to add, but obviously that is nothing, the thing is actually being able to assess those cells and this is the difference between you know just watching somebody's tumor or mass or prostate and doing something potentially aggressive, so that is really impressive and I am sure the same is true of breast cancer and then the other cancer where like really making these assessments of benign versus malignant and how aggressive it is and whether I guess it invades and stuff, that's true across the broad right? These are really big decisions for patients?

16:13.300 –> 16:17.300

Levi Absolutely. Yeah.

16:17.300 –> 16:18.000

Gore There is a lot that weigh on you, does it not?

16:18.000 –> 17:10.100

Levi It is a lot pressure. And there is not room for error. And we do a great job as a physician group and set of colleagues to work together I would say. We are fortunate in academic centers to have bigger divisions and departments and folks who have subspecialty expertise, so there is always help and there is always someone to show it to. And so much so that, in institutions where I have worked currently and in the past, we do daily QA conference and so challenging cases on a daily basis are brought to a group of colleagues and we institute very kind of strict rules about cancer cases, new cancer diagnoses and patients requiring a second pathologist review or second set of eyes.

17:10.100 –> 17:10.900

Gore Always for every cancer?

17:10.900 –> 17:31.500

Levi That's our unique, in our division. So, every new cancer diagnosis will get a second pair of pathologist eyes, any challenging case is welcome to be brought to a conference that happens daily. So, it is very much inter - kind of collegial and disciplinary discipline.

17:31.500 –> 18:31.600

Gore Hmm. It is really fascinating. Right now, I am doing some consulting for a pharmaceutical company which has run some really important clinical trials and they have got an expert panel who is reviewing the assessment of how the patients responded to the treatment, and we are not reviewing the slides like you do, we are just reviewing, you know the blood counts and the pathology reports, and every case is reviewed by 2 experts and it seems like there is about 25% disagreement among these really great experts for each case and this 25% of the cases are not clear sometimes because the pathology reports are not always written in a way that we can really understand them, so somebody thinks it is, you know, not good enough and they just cannot say, but you know, just even applying the criteria that we all supposedly know very well is so complicated, so I can only imagine at your level, you are actually looking at the cells and the buck stops here, it is a big deal?

18:31.600 –> 19:37.600

Levi Absolutely. And the communication is key as you say, and we spend a lot of time as a group of physicians in our field trying to standardize how we report, specifically cancer because that has the biggest impact on treatment potential

whether it is surgery or chemotherapy, and so, we have put into place those checklist or synoptic reports and staging systems that vary kind of consistently hopefully will have us reproduce those pieces of information that come up with your stage for cancer for example. But it is not always so clear-cut and not every cancer is even definable and sometimes it is not so much that you get the answer perfectly correct as much as that you communicate that you think this needs to be removed for example or that you should remove it conservatively or with lymph nodes, and so, it may not be so critical that the answer is completely correct but that the treatment is correct.

19:37.600–> 0:19:46.5

Gore Right, it is okay to say we are not sure that this specimen is not adequate to make that distinction for example. It is important to say that I suppose?

0:19:46.5 –> 20:47.200

Levi Absolutely. So, sometimes you do not have enough specimen and you say, well in this small sample it may or may not be representative of the grade or tumor, we feel that it is worrisome enough that while we cannot make a diagnosis of malignancy, we feel the entire lesion should be removed and then we can wait until the final pathology on the entire specimen. Sometimes, it is just too complicated of a case and it may require an extra-referral and often we do ancillary tests and it is not to say that every single case is definable. Certainly, we try to categorize cases based on their markers, they might define themselves in a way, we do additional tests, sometimes molecular or stains or genetic and that will help us define a certain lineage or category that will again help with treatment options, but there is not always a perfect answer.

20:47.200 –> 21:03.500

Gore Yeah. And I think the patients do not always know this ahead of time, so they think they are getting the biopsy in the next day or two, they will just have an answer and that is really, really frustrating I find when the answer is oh! we need to do another biopsy and then the third time sometimes, that can be very frustrating for patients of course?

21:03.500 –> 21:15.400

Levi So, that lends itself also to certain procedures that might ask for an intra-operative or an intraprocedural consultation from pathology.

21:15.400 –> 21:17.200

Gore You mean during the surgery?

21:17.200 –> 22:35.400

Levi During the surgery or during an aspiration in the endoscopy suite for example and sometimes it is an issue of not having the right material and that is a sampling issue that we could also be helpful at the time of the procedure to those clinicians procuring that sample. So, in the case of cytopathology for

example, we are often called to the endoscopy suite when a fine-needle aspiration of lung or pancreas is done, those are complicated and tricky places to maneuver to try to get to lesions that might be kind of far out or located at a distance from the bronchus or in the pancreas, which is also an organ that is deep seated that is hard to get to, and in that case, pathologists will go with subspecialty expertise in cytopathology analyzing single cells instead of pieces or cores of tissues and those cells will be smeared along a slide and analyzed right there at the procedure site in the hall or in the site room with a quick stain and the adequacy again is more about are there lesional cells as opposed to what is the diagnosis or maybe how should we triage this based on what we see.

22:35.400 –> 22:39.500

Gore Just is this like are you seeing something there that is worth looking at kind of thing?

22:39.500 –> 23:16.200

Levi Absolutely. And often we can also make the call right there, but that is not the goal of the procedure. The goal of that on-site evaluation is to adequately assess a potential differential, are there lesional cells that could be malignant and if they are, maybe we should do markers for a lymphoma or maybe we should do markers for a carcinoma and maybe we should decide with this limited amount of tissue how we can best manage it so that the end result from that procedure will be a full report of what the tumor is.

23:16.200 –> 23:25.800

Gore And this cytopathology thing that I guess is one of your specialties, what people might be most familiar with I guess would be like Pap smears, that is cytopathology right?

23:25.800 –> 24:14.400

Levi Absolutely. So, that's probably the largest amount of the gynecologic side of cytopathology and that is a screening test. And that is a great example of a phenomenal screening test for cancer, and urine cytology is similar in that way, a screening test. Whereas, using cytopathology in lesional samples where you take a fine-needle aspiration of a thyroid mass or a pancreatic mass or a breast lesion, that is a bit more directed and diagnostic of a certain lesion, so there is two different kind of ways to look at cytopathology - one in a more of a screening sense and the other more of a diagnostic sense where the lesion is present.

24:14.400 –> 24:23.300

Gore So, if you are screening urine by cytopathology, are you looking for bladder cancer? What are the things might you be able to find?

24:23.300 –> 24:48.100

Levi So, bacteria and inflammation that could imply a urinary tract infection, which may be seen with some blood in the urine, you may see fragments of a renal stone along with blood and that would not be cancer, bladder cancer certainly is in the differential and sometimes even malignant cells from the kidney can go down into the urinary system into the bladder.

24:48.100 –> 24:51.900

Gore So, this would be mostly for people who have blood in the urine then, or…?

24:51.900 –> 24:52.600

Levi Right.

24:52.600 –> 25:06.400

Gore Got it. What about if somebody was found to have a mass, an apparent mass on a CAT scan of the kidney, would you, is there any role there for studying the urine or it is just better you go get the mass?

25:06.400 –> 25:22.600

Levi So, now, many lesions of the kidney if they are accessible through a needle, a fine-needle aspiration could be done of that mass. So, probably more likely a direct sampling either core biopsy or aspirate rather than a urine.

25:22.600 –> 26:04.100

Gore Gotcha. And it seems to me and again I have a skewed experience because the biopsies that I see here, bone marrow biopsies or lymph node biopsies for the most part, seems like sometimes we have to have other, you know, masses biopsied, seems like these needle aspirates or needle cores seem to be the go-to for a lot of things nowadays and sometimes it seems tricky because a lot of times it seems like we are not getting answers. Does that happen very often or is it just my skewed experience that people are doing these needle things and you still end up not being sure based on that.

26:04.100 –> 26:49.500

Levi You know, I see the other side, where I see so many aspirates where I am putting together reports, so I do not see as much of the non-diagnostic side of it, but I think the value in trying something relatively noninvasive and conservative when it may require only a few hours in an ambulatory care center rather than general anesthesia and an overnight stay makes sense even if it were not to be fulfilling the end, to at least give it a shot because there is less risk and fewer potential complications.

26:49.500 –> 27:02.000

Gore And I guess as long as the patient understands that this is what we are going to try because it is easy if we get an answer, that's great; if not, we are going to have to do something else either repeat it or just being more surgical I guess, again communication seems so important?

27:02.000 –> 27:04.300

Levi Right, setting the expectation.

27:04.300–> 27:15.200

Gore Right, which is not your job, it is the clinician's job. Do you ever feel like you are getting blamed for their failure to communicate well or their failure to understand the limitations of the test?

27:15.200 –> 27:53.200

Levi Yeah certainly. But you know that is on us as a profession as well, so we have to also set expectations for clinicians who are sending our reports to, it is more of a communication issue I think and we should be doing a better job in those cases of saying, yes the report is going to take, you know, a week, actually 2 weeks because we are doing additional testing or yes, this is a great procedure if it works but it may not work and in this percentage of time you might not get a full answer; so that is more about I think communication.

27:53.200 –> 27:58.100

Gore And do you interact with the clinicians much?

27:58.100 –> 28:49.300

Levi I do. I have somewhat of an unique role as a pathologist and carry a title of Outreach Director here for Yale Medicine, and that has kind of put a focus on having a pathology representative who is responsible to kind of communicate with clinicians and to make it easy for them and to be able to still pick up the phone or visit the office where I think now more and more that is becoming less and less of a thing or maybe more challenging to do, but it is really important to kind of keep those lines of communications open whether it is interdisciplinary weekly conference where you have an ability to do touch base or just whether you have an app with everyone's cell phone and you know how to reach out to folks because as we get busier and busier, it may be a little bit more challenging but it is even more important I think.

28:49.300 –> Dr. Angelique Levi is an Associate Professor and the Director of Outreach in the Department of Pathology at the Yale University 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 Yale-CancerCenter.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.