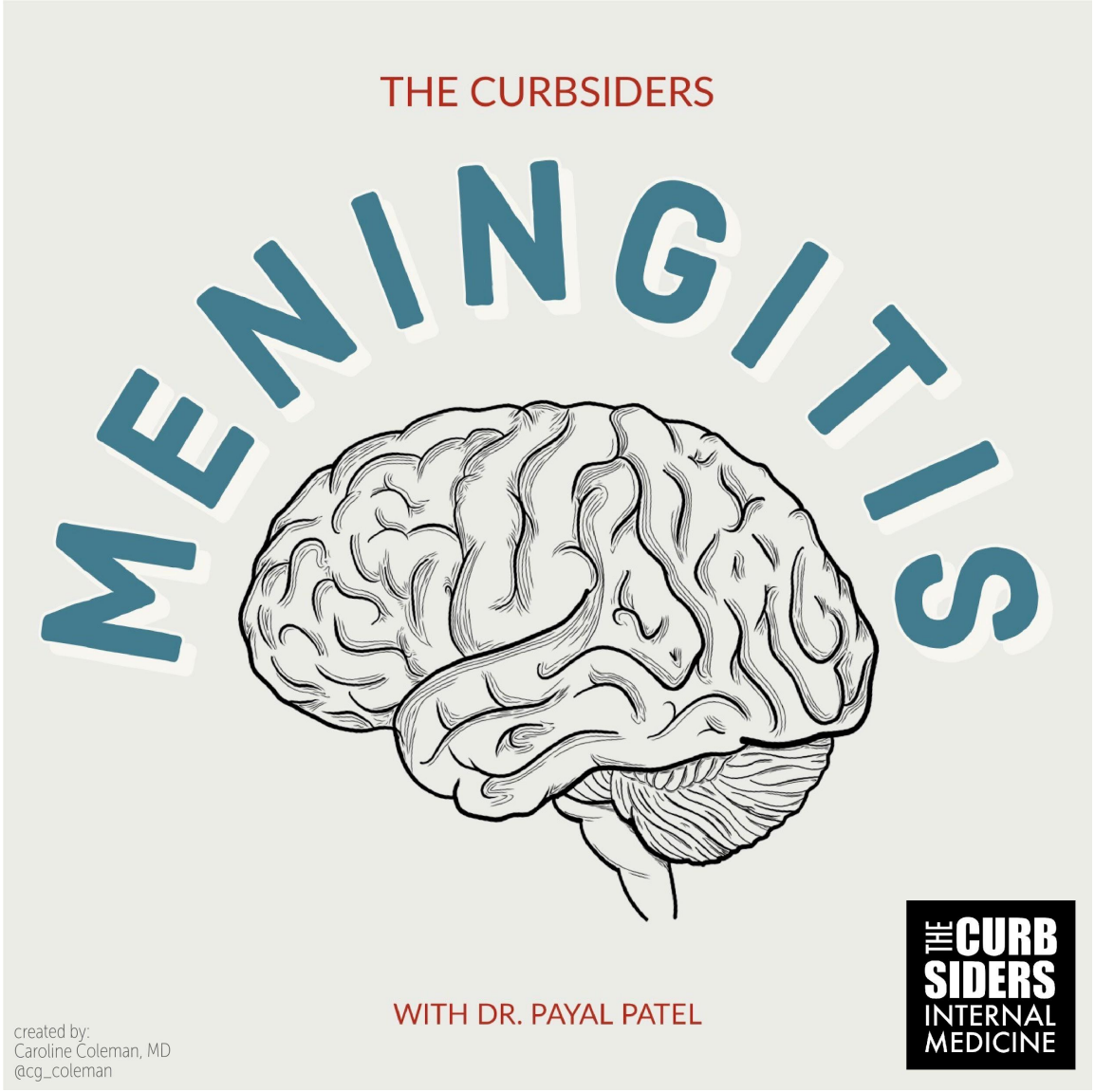
#346 Meningitis



[The Curbsiders Podcast theme]

Matthew: Welcome back to The Curbsiders. I'm Dr. Matthew Watto, feeling a little out of sorts because Paul Williams is not here tonight. But I do have a fantastic cohost, who I will introduce in a second. On tonight's show, we're going to talk about meningitis with a great guest, Dr. Payal Patel. And now, here with me, returning cohost, producer, extraordinaire, I guess, music producer extraordinaire and famous Kelly Clarkson fan is the great doctor Monee “got money” Amin. Monee, thanks for coming back and how have you been?

Monee: I've been fantastic. Thanks for asking and how have you been?

Matthew: I've been great. After your last appearance on the show, a lot of people wanted to hear your mash-up. So, I'll probably have to put it in the show notes again, too, and I hopefully, they don't take it down off YouTube. But really happy to have you back. Before you tell the audience about our guest and what we talk about on the show a little bit of a teaser, can you tell them what is it that we do on The Curbsiders?

Monee: Sure. We are the internal medicine podcast. We use expert interviews to bring you clinical pearls and practice-changing knowledge. We have a great conversation tonight with our guest, Dr. Payal Patel. She is an infectious disease doctor at The University of Michigan and Ann Arbor VA Healthcare System. She completed fellowship in Infectious Diseases at Beth Israel Deaconess Medical Center and Harvard Medical School. She also completed a master's in public health from the Harvard School of Public Health.

She is passionate about antimicrobial stewardship, and teaches and mentors medical students, residents, and fellows. She consults for the CDC on Global Antimicrobial Stewardship and has worked on building Antimicrobial Stewardship programs in India, Italy, and Japan. And this was really cool, she is currently a voting member of the Presidential Advisory Council on combating antibiotic resistance. So, Dr. Payal Patel teaches us some great stuff tonight. The first and most important is, if you're thinking LP, you should LP. And then she really breaks down how to triage, how to go through diagnostics and treatment for patients that have meningitis. So, it's great conversation.

Matthew: Yeah, a lot of very specific and actionable pearls on the episode. I found it very helpful. And Monee, before we get on to it, did you have a pun?

Monee: I think I did and we're going back to my roots of music. So, unlike Def Leppard, tonight, we are bringing on the headache, not the heartache.

[laughter]

Matthew: A reminder that this in most episodes are available for free CME through VCU Health at *curbsiders.vcuhealth.org.* Well, Payal, we've been talking for a little while here and the audience we got to bring them in at some point. So, tell them a little bit about yourself and tell them about some hobby or interest you have outside of medicine. Of course, they've heard your full bio, but tell them-- they want to know you personally.

Payal: Yeah, definitely. So, I grew up in Houston, Texas. I would say, I am a Tex-Mex aficionado.

Matthew: [chuckles]

Payal: During the pandemic, I have made every type of salsa that exists. And I am a salsa expert as well as an infectious disease doc as you [crosstalk].

Matthew: So impressive.

[laughter]

Matthew: For the audience, the reason that Monee and Payal are friends happens to do with food and I believe, what was the pizza topping Monee?

Monee: This is going to be controversial for people but jalapeno, pineapple.

Matthew: [laughs]

Monee: [crosstalk]

Payal: Yes.

Monee: Pineapple, spicy and sweet. Delicious.

Payal: Exactly. We are pro jalapeno pineapple people.

Matthew: I am not going to judge anything. Monee, I'll let you take it where you want to from here with the line of questioning.

Monee: [laughs] Along the lines of things that you like Tex-Mex being one of them, do you recommend anything you've seen like TV or movie of late that brings you the kind of way that Tex-Mex does?

Payal: [laughs] Actually yeah, it's actually a book and now a show. I remember my last flight before the pandemic. I'd gotten on the flight and I picked up a book called *The Flight Attendant*. The book was excellent. It was really great and I really loved it. And then months later, I had no idea they were turning it into a show and the show itself has really taken the book to another level. So, if you're someone who likes reading and seeing that put onscreen, I have really enjoyed *The Flight Attendant*, the book as well as the series.

Monee: It is so [crosstalk]

Matthew: That is a good recommendation.

Monee: I talk about it with everybody that will listen. It is so good.

Payal: That's awesome.

Matthew: [laughs] By the way, Monee, I have to mention this, because yesterday, I was driving in my local area and I saw that Kelly Clarkson now has some daytime talk show. So, I was thinking that I would have to bring this up with you. [laughs]

Monee: Matt, the show has been on the air for 3 Seasons now and you're just now learning it.

Matthew: [laughs]

Monee: I am very sad for you. The highlight of the show is-- [crosstalk]

Matthew: Well, I guess, the billboard advertising is working. [laughs]

Monee: Yeah, she's about to take over Ellen's timeslot since it's going off the air. Literally, they're putting her show on the timeslot. So, that's probably why. Just for people to know, she sings a cover of a song at the start of every episode and that's what makes it unique and fantastic. The end. Okay.

Matthew: All right. Well, maybe we'll get a separate pick of the week from you, but I have one more question for Payal before. Payal, do you have any favorite advice or feedback that you received? It could be recently, it could be any time during your career? Just some favorite advice that comes to mind.

Payal: Yeah, my piece of advice is actually related to the topic that we are going to be talking about today, meningitis. And it's something that an ID attending told me when I was a resident and I now pass on to my teams and that is, if you're even considering an LP, there's a little voice inside of you wondering if you need to do an LP on a patient. The answer is probably yes and the reason is, if the LP is positive, that's actually very helpful and it might direct your therapy. But also, if it's negative, it's actually also helpful because usually the patient who is getting an LP is on multiple antibiotics, sometimes multiple antivirals. And so, the positive or negative LP can both be very helpful. So, at the end of the day, if you're thinking about getting an LP, you should get the LP.

Matthew: Yeah, and I love de-prescribing. So, I'd be happy for negative LP if I got the de-prescribe. Before we read you a case, Monee, I just wanted to give you a chance to-- Did you have a pick of the week that you wanted to share with the audience because your previous picks of the week have been such tremendous hits?

Monee: Okay, yeah, [crosstalk] so, I'm sorry to disappoint the fans, but this one is not Kelly Clarkson related.

Matthew: [laughs]

Monee: Anyway. But it does involve a pop queen. One of my favorite podcasts called Switched on Pop. It's definitely been helping me through these darker news days that we've been having. They recently did a four-part series called Listening 2 Britney and it's not your standard free Britney content. They break down that four landmark songs in her career, and talk through the evolution of how her sound changed, and how producers changed, the way they produced her voice from a lot of character and personality in her first album, and then you get to that last album, and that came out around her first demise, if you will. It's just really interesting, and fun, and they're super nerdy about it, and I love it. So, Switched on Pop, Listening to Britney, highly recommend.

Matthew: Another great recommendation by Monee. I'm actually curious about this one because from what you were telling me off air a little bit, it sounds very interesting. But it's time for a case from Kashlak. So, let's hear about, I believe it's Miss Hudson here.

Monee: Yeah, Miss Hudson, somebody very similar to someone I saw when I was on procedure service a few weeks ago. She's 41, she has a history of hypertension, and her friend brings her in with a couple hours of fever, neck stiffness, and altered mental status. When she gets to you, she's febrile, tachycardic, but normotensive. And her exam is notable that she's a little drowsy, but she is alert-oriented and she has a positive Brudzinski sign. And her labs are notable for an elevated white blood cell count and a creatinine of 1.5 with a baseline of 1. So, I think at this point are there any things on the case that you want to know, like, history and physical wise that are helping you make your differential for Miss Hudson?

Payal: Yeah, definitely. I think this is a really key part of the history and this patient is really lucky because a friend brought them in. One thing that I would say, I've learned from seeing some of these patients in the past and I think it's really important to think about right at this moment when you're admitting this person seeing them for the first time is trying to determine, if meningitis is on your differential. If this could be meningitis or could this be meningoencephalitis. There are some really key things on exam that the patient may not be able to tell you, but their family member or someone that they live with may be able to tell you. And that really drive your concern one way or the other. I would be asking the friend, "Okay, you know her well. Do you feel her personality is different today than maybe like how she usually is?"

And another really concerning thing would be if they said, "This person has been sleeping for two days," remember, you are like, decreased level of consciousness. That's what we learn in med school, that's what the test question is. But in reality, what do you see is, someone who's like, "Man, I've just been sleeping or my partner has been sleeping for three days" and then they also have these symptoms. That becomes really concerning for an encephalic picture along with meningitis. So, that would be kind of the ding, ding, ding things that I would be asking her friend.

Matthew: Yeah, those things always scare me. I always pray that the answer is no sleepiness, no change of personality. In general, this whole topic scares me. That's why I thought it was a good idea for a show. [chuckles]

Payal: Yes, it is. It is really scary and I think it's been around for so long, but I think that there is a lot of takeaways and hopefully, we'll hit some of them today. But the first one that I think a lot of people forget about is, again just trying to determine meningitis versus meningoencephalitis. That's when the brain is involved and that's when you start seeing some of these personality changes, decreased level of consciousness, perhaps coma, if it's getting too late.

Matthew: Yeah. Because with bacterial meningitis, altered mental status can be part of it. Are you calling that something different than like-- is that bacterial meningoencephalitis or you separate that out a little bit?

Payal: Yeah. I know, it's hard. I do that they'll say like irritation. Irritation is part of it and then usually the altered mental status might be a little bit of confusion. But with the florid encephalitis, people might be doing things that are almost thought to be psychotic. Just completely out of character for that person and then paired with intense sleeping. Those should scare someone into really widening that differential and rushing that workup for things that could cause encephalitis as well.

Matthew: Great. That's really helpful. What's next, Monee?

Monee: Now that meningitis and encephalitis have entered my mind this causes immediate mental hyperinflation, because there are so many things that are running through my mind. I need to start antibiotics probably, do I LP, do I not LP, do I get a CT? And then

after all those things, do I send the entire kitchen sink off or do I not? So, let's just start back with antibiotics, and then the LP part, and then we can go from there?

Payal: Yeah, love it. Okay, I totally agree. I think order of things and timing of things with meningitis could be tricky and hard for to remember what to do first. I would say, at the end of the day, the most important thing is, if it's bacterial meningitis, of course, you've got to get antibiotics into that patient. Remember your favorite ID doctor on your shoulder saying, "Did you get blood cultures before you got those antibiotics?" The reason that these blood cultures are particularly important in meningitis is that about 50% of people may have a bacteremia with their bacterial meningitis. And so, that means that you could get that culture yield really quickly. It could alter your duration of therapy. I would say very, very key early on, if you can get the blood cultures before you start antibiotics, that would be really helpful. And getting antibiotics started is really helpful. So, that is really key.

Now, thinking about the LP, the LP timing is important. And CT, I think we've all learned in our lives like, “You’ve got to get a CT before LP.” But there's been studies that show that we probably do way too many CTs and that they delay getting the LP doing all of the other really important stuff. The IDSA, the Infectious Disease Society of America and some other guidelines say is that if there is some concern for like mass effect, if they have some risk factors which include things like immune-compromised for having something that could potentially, you absolutely need to get a CT. You can find those on up-to-date or the IDSA guidelines. Those few things would make you get a CT. But most people who are presenting including this patient that we have in front of us, you don't have to delay the LP to get that CT. So, that's really important to remember.

Then the other thing to remember is, again, I said that getting those blood cultures and antibiotics, that's really important. Because I know, I remember myself being in that role being like, “Oh, my gosh, I have to get an LP, I have to get an INR, I've just [laughs] How long is this going to take?” That's why I don't want most people to-- I would say most ID doctors would say, “You don't want to delay the antibiotics to figure out the logistics of the LP.” It does have to happen. But the LP is important to happen soon, because, again antibiotics can change your yield of what you're going to be seeing on the LP. It pains me when I get consulted on the fifth day this person is being empirically treated for bacterial meningitis and they still haven't gotten an LP and I'm like, “Every hour, I see this culture result being less helpful.” So, that's how I think about all of those first things that need to be ordered.

Matthew: Yeah, and we'll probably have to-- When we talk about treatment later, we might have to squeeze you on like, “What do you do when the LP was delayed and they were on antibiotics, and you're chasing your tail a little bit?” But of course, that in real life that happens more often than I wish it would. So, it sounds like right now, you're saying blood cultures, those should be easier to get when you get the initial labs, and then antibiotics should be started soon. If there's going to be a delay, the LP should probably come as soon as possible.

Payal: Yeah.

Matthew: Maybe it comes after the antibiotics, but hopefully not by too much. The CT, we're probably over CT-ing people and really immunocompromised or people were really suspicious for mass effect. Those are the people that really need it.

Payal: Yeah, you might be able to even see on physical exam or maybe your ER colleagues have helped out and told you, “This person has papilledema.” You're doing your exam and you see a focal deficit, a focal neuro deficit. That's weird. That's abnormal. Again, raising my concern for something like encephalitis, something going on in the brain that on your physical exam could alter your pretest probability. If you see something like that, I think then it totally makes sense to get a CT.

Matthew: Yeah. Great.

Monee: Okay, so, Payal, I've done the LP and I was panicked through the entire thing, but I got it. I got the fluid and I'm always curious about your expert opinion about, do I send every single test I can order? Because there's a lot of them. I feel I don't always know if sending West Nile on every patient is a good plan.

Payal: Totally. Yeah. That's a great question. The way I think about this as someone who does internal medicine and infectious disease is, okay, when you do the LP, I know it can be really difficult. But if you can get more fluid than you need, that’s really helpful from an ID perspective. Not just in meningitis, but really for many of the patients that I see, when I write a consult note and when I teach, I often say, “There's the first shelf of stuff that we're going to do like today right now” and then there's the top-shelf stuff that I'm going to keep in my back pocket and we're going to order that if we need to.

Meningitis is such a great example of that first shelf stuff that we're going to order like cell count from the CSF, protein, glucose, the culture, the basics. That stuff is so incredibly helpful and will help you determine later on if we're going to have to send stuff like molecular diagnostics, West Nile, all of that other stuff that belongs on that top shelf. I would say, if you can't get as much CSF as you can, I usually call the lab and tell them to hold some of the CSF, and then there's that third shelf where we really can't figure out, we might need to do something like universal PCR or some of that crazy stuff. So, that's how I think about it.

Monee: So, what is that first line that you send off?

Payal: Yeah, definitely. I feel you on being nervous about this. I used to write it down on a piece of paper, [laughs] so that I would always have [unintelligible [00:19:44], because I was always so scared. I was going to forget to send off the serum, because you got to send off the serum protein and all that stuff at the same time. I think the bare minimum that I want to see when I'm consulted on someone who might have suspected meningitis is the cell count and diff. Now, that is money right there. That is going to help me so

much. Cell count and diff, that's the most important thing, definitely a culture Gram stain that's both equally important. To me, it could end there, and I wouldn't be mad at you, okay?

Matthew: [laughs]

Payal: [laughs] You get the glucose and protein I'll be even happier. But those first two are really, really, really important to us, infectious disease.

Matthew: You mentioned the serum as well. So, you're comparing the serum glucose to the CSF glucose and same with the protein.

Payal: Exactly.

Matthew: And you mentioned the panel testing. From my reading, it seems like the panel testing, sometimes, it includes the Neisseria and the Strep and H Flu, and those ones seem to be very good like the PCR test. But I was reading that as you expand that panel more and more that the sensitivity specificity don't work as well. So, then you might get some results that you're like, "Oh-oh, what do I do with this?" Maybe it was just something common and you didn't even need that, and now, you have this red herring or something like that. So, that was my interpretation. I'm not sure if you see that happen, if that's a caution we should leave to the audience, or maybe the source I read.

Payal: That's right. Yeah, that's right. When I think of these advanced diagnostics and the things that we use them for, we often use these PCR panels so many times inappropriately in GI. If I was like, "Can I get rid of the PCR panel, I would get rid of completely, make it disappear, GI PCR," but when the encephalitis and the meningitis panel came out, I was thankful and I would say, many infectious disease docs are thankful because we see so many cases where we never figure out what's going on. Just like you describe, the person got antibiotics, the LP was seven days late or something. And so, adding to this huge unknown in the field of brain infections and spine infections, that was really a true, I think, a boon. While the sensitivity and specificity of those non-big three that you talked about, that's again, Strep pneumo, Neisseria, and Heamophilus, those are usually the top three and it is very good at detecting those. I think anything added to that X box is helpful. So, overall, I think it's helpful and it's nice to have in many hospitals.

Matthew: Okay. But as you said, your first-round test you gave us the bare minimum is all the classic stuff that if we were doing, most of us should know how to interpret and-- [crosstalk]

Payal: Yeah, totally.

Matthew: Or you're going to tell us more, hopefully, teach us more about how to interpret those things. Is that where we're going next with this, Monee? Do you want to go through some potential profiles for Miss Hudson before we talk about the treatment and then we'll do the treatment next?

Monee: Yeah, I think that makes sense since we are talking about the advanced diagnostics, and all that stuff, and then the bare minimum.

Matthew: Yeah.

Monee: Got the LP, sent it off, got some studies back pile. I want to go through a couple different profiles and talk through your thought process. So, let's start with a patient who's got a low glucose, high protein, and neutrophilic predominance in the white blood cell count and the fluid analysis.

Payal: If you are telling me this you called ID and you're like, "All right, I got this. Here's the glucose and the protein." I'd be like, "Stop right there. [laughs] What is the white blood cell count?" The most important thing for me and this is probably just how I think about it, but the most important thing and what I always ask students and stuff and residents is like, "What do you think is a normal white blood cell count?" The range will vary widely within a team. And really, if you were to do an LP on us, right now, we should have zero to one white blood cells. Again, I said at the beginning that getting an LP is very helpful. If you have zero to one white blood cell count that it doesn't matter. If differential doesn't really matter, none of that other stuff matters. That's pretty normal. But if it's 200, 2,000 that changes things like a bunch. So, let's say, Monee, you're telling me about this person, it's about a hundred or so white blood cells, that's definitely got my attention. Really anything above five white blood cells for me has got my attention.

You're saying it's a neutrophilic predominance. And so, most common causes of bacterial meningitis worldwide and in the US continue to be Strep pneumo, Neisseria meningitidis or also known as meningococcal meningitis and Haemophilus. Those are the three things that would be on top of my differential. You told me she's in her 40s, so again we're always thinking about the patient and what their risk factors might be. I don't think that she's immune compromised. So, thinking of that really there's typical bacteria. If the patient was much older or immunocompromised or very, very young like a little baby, then I would be thinking about Listeria or some other organisms as well.

Monee: I think that breaks it down pretty simply. And so, let's change it to a lymphocytic predominance and see what that gets us. So, high protein lymphocytic predominance, and the white blood cell count, and the fluid.

Payal: This also gets me very excited, because now I can tell you to stop [laughs] the vanc and the ampicillin, and the ceftriaxone, and all of the things that have been started. Again, why an LP is so high yield? Because just with that cell count and that diff, we're

really able to change the differential quite a bit. If you're seeing, again let's say, it's about 20 white blood cells and a lymphocytic predominance, you don't know exactly what it is, but it would very rarely be those typical bacterial pathogens. You're already thinking it's something atypical. That differential is very wide and that now we're going to have to start reaching into that second shelf maybe to see what else is going on. But now, again, depending on that white blood cell count, risk factors, we might be thinking about viral meningitis, fungal meningitis, tick-borne, TB, like the differential could be really wide and includes aseptic meningitis as well.

Matthew: I wanted to ask about lactate as well. I know that wasn't on the shortlist and I saw you mentioned aseptic meningitis. Supposedly, lactate levels tend to be higher in that than in bacterial meningitis. That was something that I saw in a couple of other sources. Do you find that helpful clinically? I find lactates are always-- I'm a little wary of lactates.

Payal: Yeah, there has been research on some of these other inflammatory markers like lactate, procalcitonin, CRP. I usually don't ask for those. Sometimes, the team will send those and I'll help interpret them. But I like to go to my go tos. If my go tos are there, it's going to help me with the differential and those other things are not as sensitive and specific or really helpful in thinking about the differential.

Matthew: Yeah. Okay. So, nice. Maybe nice to have sometimes, but doesn't have to be there.

Payal: Yeah.

Matthew: Monee, what else are we going to put Miss Hudson through potentially with this differential? They will eventually settle on one and talk about what treatment we want to pursue.

Monee: This last one is my favorite. Normal glucose, normal protein, neutrophilic predominance. So, it's a little muddy.

Payal: Yeah.

Monee: Kind of confused, please help.

Payal: That's a tough one. Again, I would be working at cell count. Is this like a 10, is this like a 5,000? If it's a 5,000, my concern is crazy high. I'm still really concerned about a typical bacterial pathogen. But if it's low and it's like [laughs] stone-cold normal glucose, stone-cold normal protein and we see these. People don't follow the medical books. They'll have weird CSF profiles. The things that I would be thinking about are things like syphilis. Neurosyphilis is something that we see a lot. Remember that there are some of these bugs that will early on be neutrophilic and then later can become lymphocytic, and those things include TB, they can include some of the viral pathogens. It's not necessarily a reason to get a second LP, but it can sometimes muddy the results just like you said.

Matthew: Yeah, I tend to get the patient with, Monee, I'm not sure about you, but I get the patient with zero to four white blood cells and glucose and protein that makes no sense. And probably, it's because we're getting it and the person has been partially treated, and maybe we've partially sterilized or treated them. But Monee, you get that too.

Monee: Oh, all the time and I'm always super happy about it.

Matthew: [laughs]

Payal: I will say like, I think if it's florid, I also get consulted on those. You guys will consult ID on those. I think even though, as I said, each hour, each day that goes by, you haven't gotten the LP, the yield continues to go down. But if it's a florid bacterial meningitis, they're not going to have a stone-cold one white blood cell in their LP. So, yet again you can at that point pull off vanc, ceftriaxone, all of those things because that person has something going on, but it's not a typical bacterial meningitis.

Matthew: Payal, I wanted to ask in follow-up. You gave us a lower cut-off of you said. More than five white blood cells that what piques your interest. Are there higher number cut-offs that make you think, “Oh, this is definitely bacterial or this is definitely one diagnosis or another?”

Payal: Not as much. For me, it's really that lower number. If it's a lower number, my differential is wider. But really, the higher it goes it’s going to be usually a more typical bacterial pathogen. Whereas if it's a lower number, let's say, five,10,15, 20, your differential is very wide at that moment because it could be infectious, it actually could be not infectious, and you won't be able to tell just with that cell count.

Matthew: So, these panel tests we were talking about maybe they're more helpful there.

Payal: Yeah, exactly. And that's when you start thinking about fungal endemic stuff, where do you live, did that person travel, and using some of those other things to help you think about stuff, too.

Monee: I think it's come up a couple of times in passing about aseptic meningitis. I'm curious from the other parts history and the stuff what things do you use to help you discern that this might actually be more aseptic than anything else?

Payal: Yeah. Man, that's hard. I definitely see why you guys are asking about this. Very difficult. This is where you go into that second shelf, because it has to be almost a diagnosis of exclusion. You don't want to miss something else, especially in this part of your body. And so, this is around the time that we start looking at, what time of the year is it? Is it time for West Nile, has that been

reported around here, is that something we need to think about? That would be the time where you do reach into that second shelf, start sending off some of that viral stuff. Is this person immune-compromised, could they be at risk for something like a fungal meningitis? That's when you really want to start ruling out those other atypical causes.

If everything remains negative and sometimes if you're lucky enough to have that history, “Oh, by the way, I took my cousin's bacterium yesterday for an upper respiratory infection.” That's actually very helpful at that point. But I think aseptic meningitis, maybe ID doesn't get consulted on it that much. But I would say, we don't see it nearly as much as we see all of these other infectious types of encephalitis or something like cancer-causing meningitis, or some of these other non-infectious things that aren't just an aseptic meningitis, or it's a viral meningitis. Those things are much more common.

Matthew: Yeah, the differential gets broad and that's where-- I think usually we ask the question when should we consult ID? I think most hospitalists would consult ID for any patient with meningitis, meningoencephalitis, it's just too high risk.

Payal: No one would fault you at all. Yes, that is completely fine, completely fine.

Matthew: [laughs]

Monee: I would hope. Very recently, the thought crossed my mind. So, I definitely called probably sooner than I normally would have but yeah.

Matthew: To recap what we talked about with the testing, our first line, cell count with differential. That's what we're most interested in because that's really going to start to point us big time in one direction. And then the other stuff can fine tune that. The classic bacterial meningitis is low glucose, high protein, and elevated cell count, neutrophilic predominance. If there's a lymphocytic predominance, then you're telling people usually pull off some antibiotics, this is probably viral or something else.

Payal: Exactly, which is nice, because at least, they don't need five IVs going into them which is good.

[laughter]

Matthew: To free up the line.

Monee: This is such a [crosstalk] from treatment.

Payal: [laughs]

Matthew: And then you said your second line or your top shelf thing, usually you ask like save some fluid in the lab because we might order a second round of testing. That's where these panel PCR tests can be helpful, because we could do some of the more specialized and really broaden our differential, if it's a lymphocytic predominance or if it's not just a classic bacterial meningitis.

Payal: Exactly. I think that's something that I've really noticed in the different places that I've trained. I trained in San Antonio. We saw quite a bit of TB meningitis. I've never seen that outside of Texas. Then I trained in Boston and we saw a lot of Lyme. I haven't seen that as much in Michigan. We see fungal meningitis here very often. And so, I think depending on where you are that second shelf is going to be really different based on some of those endemic things that are going on around you.

Matthew: Monee, anything else with the diagnostics that you think we should talk about? I think maybe we go back to Miss Hudson and talk about what treatment we should start on her. I'll let you take it.

Monee: Yeah, I think that we've hit all the high points on diagnostics and really have a good, very thoughtful and simple way to break it down. I think it's reasonable. Now, that I've mentally hyperventilated, gotten the LP, and sent off the studies, at the same time, I'm also thinking about treatment. And so, my problem is always, “Do I start everything?” I think the answer is probably yes, but I'm kind of curious. And then, I also wonder about the antiviral piece. But we can start back with just do I start everything? And then the steroids question.

Payal: Oh, yeah, definitely. That's a great question. The steroids have been confusing I think over time. Now, this is again where the risk factors and those things really matter. Also, I think that would come up when you're thinking about it, but is this like a community-acquired meningitis or did this person just have neurosurgery two weeks ago? Very different. Those things can really change your empiric antibiotics. And then really important to remember that whatever antibiotics you're using, must get through the blood-brain barrier. And so, that's really important to remember. That's how I think about it. Did this person have a neurosurgical, something going on trauma to the head that would change the etiology of these organisms? Then that becomes where I'm more scared about things like MRSA and Pseudomonas or is this like a community acquired, which is really the more common? And that's the patient that we're talking about right now and that's when you can start narrowing your antibiotics.

Then again, are they really old, are they really young? Those are the things we remember from when we studied this, when we were in med school, it's totally okay to look this up. Totally okay to always look this up. But usually, vanc and ceftriaxone are a good choice. Not because of Staph aureus. This is big part that I think people don't remember. It's not because MRSA is causing bacterial meningitis. It's because Strep pneumo has become resistant over time. And so, there's a possibility that it could be resistant to ceftriaxone, there's a possibility that you would need vanc for it. And if you were to only do vanc, you would be missing

Gram-negatives and ceftriaxone covers many of the potential organisms. So, for that reason, vanc and ceftriaxone are good go-to and they both get through that blood-brain barrier really nicely.

Monee: Okay. You've talked about risk factors for something like Listeria, where you might add something else. So, I think it'd be helpful to, I don't know, Matt. What do you think? Because there is so many scenarios we could go through.

Matthew: Yeah, I think by age-- She's under 50. I saw 50 as the cutoff where you start to worry about Listeria, but is there anything that makes you add the ampicillin coverage to a person under 50 if they give out Listeria or any other bugs?

Payal: I think it really is immunocompromised as well.

Matthew: Okay.

Payal: Listeria is thankfully rare enough. But I will say that again, this is where these blood cultures are so important. Because often, when someone has Listeria meningitis, they will also have the bacteremia listeriosis. And so hopefully, you're going to have yield from your blood culture quickly as well-- Listeria, well, I should say, I wish it was quickly, but Listeria will take longer to grow than some of this other stuff like Strep. You want to have as much of a yield as possible. Then it's important to remember people may not remember this, Listeria, the cephalosporins don't work. That's why we use ampicillin. And so, that is why you are on five antibiotics when you're thinking about bacterial meningitis. Ampicillin is specifically for listeriosis and then vanc and ceftriaxone will really cover that wide array of other organisms.

Monee: No, that's great.

Matthew: And you mentioned, if the person-- She's coming in, we think if this is bacterial meningitis, it's community acquired as far as we know. No head trauma, no recent surgical procedure in the CNS. But if she had a recent surgical procedure or she had some head trauma or something, how would that change that initial you mentioned the three antibiotics particularly?

Payal: Yeah, that's a great question. I think as things change in all of our hospitals, we will continue to see probably more healthcare-associated meningitis. It's going to be something that we're all going to see definitely, in ID, we see this all the time. This is actually a common ID board question. Because again, you're thinking about, what are the organisms in an operating room that you're worried about? Those are MRSA and pseudomonas. What are antibiotics that will cross the blood-brain barrier that will treat MRSA and Pseudomonas, which are different than what we're thinking about in community-acquired meningitis. And so, vanc, there's your go to. Vanc is going to be covering the MRSA and crosses the blood-brain barrier.

You have a couple of options that often quiz my team. There are two cephalosporins that cover Pseudomonas and most people cannot remember cefepime, but other people can't remember ceftazidime. And so, those are two good options. And then if you were to uncover that this person actually has MSSA and that grows, perhaps in a blood culture or in the CSF, many times we use cefazolin, but nafcillin is actually probably better for CSF. So, that would be a take-home point that nafcillin is a good choice here for MSSA meningitis or brain infection. Your empiric regimen is probably going to be something like vanc, cefepime or vanc, ceftazidime. If you want to impress me, you're going to use ceftazidime because I wouldn't be like, “Oh my gosh, no one ever remembers about ceftazidime.”

Matthew: We want to impress you. So, we probably will.

Payal: [laughs

Matthew: Our listeners, they want to impress you.

Payal: [laughs]

Monee: Yeah. Any of them they end up rounding with you one day.

Payal: [laughs]

Matthew: Okay. To summarize the antibiotics first and if it's a primary, we think there's primary community-acquired, non-immunocompromised patient. At least, vanc and ceftriaxone, if they're older or immunocompromised, we might add ampicillin to that to cover Listeria.

Payal: Yeah.

Matthew: And then if they've had head trauma or especially a recent surgery and we're trying to cover hospital-acquired bugs, then that would be vanc and cefepime or if we want to impress you, ceftazidime.

Payal: [laughs] Exactly.

Matthew: And then once we find out whether this is MSSA or MRSA, we might switch to nafcillin.

Payal: Exactly. Yeah, exactly.

Matthew: Maybe this is the point for this question. We mentioned sterilizing the CSF. Maybe you don't have a good answer, maybe no one does. How long do we think it is before the antibiotics are given before the CSF becomes unreadable? Is it hours, days?

Payal: Oh, it's definitely not hours.

Matthew: Okay.

Payal: Oh, that thing's going to be florid for a while.

Matthew: [laughs]

Payal: It's definitely like days. Depending on the infection and the load, it could be longer than that. That's why the utility of repeat LPs is usually not there unless that person is doing worse. You think you never grew something, you're worried that you're missing something, that is the time that you would do a repeat LP. And so, that's one of the reasons that we don't have the exact answer to that. But I do think about it similar to-- I know many of us have treated bad SBP and you'll do a repeat para only, sometimes, only to see if it's getting better or worse. It would be similar if you did a repeat LP. If your white blood cell count is going up [laughs] that is bad. So, that's how I would think about that.

Matthew: Okay, very cool. And then I think we should talk about steroids as well because that's confusing to me.

Payal: Yes.

Matthew: And I'm also confused why some places they seem to work in some in the developed world, but not lower income countries. I'm not sure if--

Payal: Yeah.

Matthew: Can you speak to who should get the steroids and when should they get the steroids?

Payal: Definitely. Yeah, this is really an important point. It's really hard. You can't tell when someone's walking in what bug they have and that's the hard part. And so, what we know is that in high income countries, per the studies that have been done right now, and according to the most recent Cochrane Review, in high income countries steroids are helpful if they are given before or with antibiotics for Strep pneumo in adults and may prevent deafness in kids with Haemophilus. So, really, there seem to be benefits for

Strep pneumo and Haemophilus. And those are two of the most three common types of bacterial meningitis. And so, no one is going to fault you. If someone comes in with a community-acquired or this community-acquired pick and you give them steroids before or with that first dose of antibiotics, they're probably not going to be helpful if you give them afterward. Okay, that's something to remember.

And then I think it's important to remember that once hopefully, you're getting that LP, hopefully, you're getting that information, and if it's not Strep pneumo, you should stop the steroids. I think there's been a lot of muddled ways and I'm not sure that everyone gets that. I also find it strange that the studies have-- There have been nine studies done in middle or low-income countries and they haven't shown that benefit. The thought process is that maybe people present earlier, when you have easier access to care that you present much earlier in your process with meningitis and that might have something to do with it. So, that's that international perspective on steroids.

Matthew: Yeah, it was interesting. I was trying to think through, like, how would that work? The papers I read didn't really speculate. So, I figured I'd just ask you rather than look it up myself, so thank you.

[laughter]

Matthew: Monee, do you see people also throwing antivirals in the mix when someone comes in initially? I wanted to know, is that common practice or is that just happen to be where I work?

Monee: I will say that I don't see it too much where I work right now, but I remember in training, I did it a lot. When I was specifically in the ICU that was something that my attendings frequently had me do. Actually, I think we're both curious what the practice should be for this, the antiviral-- [crosstalk]

Payal: That’s a really good question. Yeah. I think I definitely have seen it everywhere. Again, this is why I get consulted at first, it's all like 20 microfields, I'm like, “Please, why?” I get it. After seeing the sequelae of HSV meningitis, encephalitis. I would say it's fine to go ahead and start it early. But you have to listen to your results once they come back. You have to be willing to change. I think another thing that can be fearsome for people is that apparently, an early HSV PCR can be negative. That again, you have your cell count there, you have your differential, so that's only one piece of your puzzle. I think if you had a lymphocytic predominance, you don't have another answer, your initial HSV, PCR is negative. That's a good reason to perhaps repeat, keep that antiviral going but that is usually not the case. As soon as you have that initial cell count a diff back, you're going to be able to make some decisions about your antivirals and your antibacterials.

Matthew: And hopefully, we'll have your help interpreting.

Payal: Yes, totally.

Monee: So, you really do hang your hat on the neutrophilic and lymphocytic predominance in terms of helping guide, stopping antibiotics.

Payal: Yeah, almost more than so many other-- So many times we're in that gray zone, where we as ideal will be like, “I don't know. This could be this or this.” But in meningitis, I find it incredibly helpful to help direct management.

Monee: Okay, great. Miss Hudson, her culture has come back, positive for pneumococcal infection. So, this is the point where, obviously, we can stop some stuff. But we can also start thinking long term. So, I always am curious, how long am I supposed to keep people on antibiotics and the steroids in this situation?

Payal: Yeah, great question. Hopefully, at this point, I'm sure you've consulted your local infectious disease team and we're going to be happy to help with the duration and all of this. This is kind of, I hate to say like an easier case, because Strep pneumo, we know what to do, we got this. You want to know if they had bacteremia or not. That could potentially change things. Some of the cases that I've seen have been horrible otitis media leading into meningitis, leading into osteomyelitis. You really want to see, “Is this just a meningitis? Is it also a meningitis and a bacteremia? Is it also an ear infection and an osteo?” So many times, there might be more than one thing going around that can really affect duration. But if this is just good old simple Strep pneumo meningitis. It's about 10 to 14 days and we will help you decide the final duration on that. The steroids, I could be wrong, but I think they're about four days. Again, they are really helpful early on to try to help decrease that inflammation and the Strep just going crazy. And so, that's when it's really important is early on.

Matthew: From what I was looking up, it looked like the longest-- There is varying durations based on the bacteria and you just have to look that up. Gram-negative infections seemed like the longest, like, a three-week duration or something like that.

Payal: Exactly. That's right. You know, Matt, antibiotic stewardship in general, we're continuing to do so many of these trials. For many years, we had just been doing the same thing. Endocarditis is six weeks. Osteomyelitis is six weeks. And so, we're beginning to have more and more information in other disease states. We haven't gotten there in meningitis yet. But things like Strep pneumo bacteremia, sometimes we have oral options. I think that potentially depending on future work could be a future target for antibiotic stewardship research to see if we could shorten some of these, if we could go to orals earlier some of those things.

Matthew: Yeah, it's been really cool to see how all the treatment durations were just pushing the envelope over the past decade that I've been on in practice here.

Monee: I was literally about to say the same exact thing, Matt.

Matthew: [laughs]

Monee: It's getting shorter and shorter.

Matthew: [laughs]

Monee: All right, Miss Hudson has completed her IV antibiotics. She's discharged, and she came back to her PCP, and she's still having some generalized neurologic issues that really impacted her ability to go back to work as an IT specialist at Chick-fil-A. So, this is the part that I want to be able to talk to my patients about which is anticipatory guidance in terms of what to expect when they're recovering from this infection.

Payal: Yeah, man, this is tough. This is for all types of meningitis. It could include things like HSV, it definitely includes typical bacterial meningitis. Almost up to 40% of people could have some cognitive dysfunction after this. I don't think that we talk about this enough or that maybe we know about this really as a field. Neurology probably knows a lot more about this. A lot of it has to do with again that acute flare, what happens in that-- when that bacteria is able to cut through and get into that space, what kind of horrible things it can cause? This is why before childhood vaccines, we saw so much deafness and neurologic complications with meningitis in children. I would say that in general, the burden of meningitis in the world, definitely in places like America has gone down so much because of vaccines. I know that you wanted to hit this high point as well. It definitely is, it's just such an amazing consequence of vaccines and childhood vaccines that we've seen meningitis go down, not just in children but in adults as well. That's really been incredible.

I also want to do a shoutout to antibiotics and antibiotic stewardship here, because mortality was 95% from bacterial meningitis before antibiotics. If we don't use our antibiotics wisely, we could get back there way sooner than we would ever want to. And so, I think while morbidity and mortality can be quite devastating for meningitis or encephalitis, we have made major headway in the prevalence of these conditions in the last few decades.

Matthew: This has been really fantastic and I think we're at a point where we can get take-home points, so, we can let you get back to your family. And thank you so much for all your time. It's been really great hanging out tonight and talking about meningitis, a very scary topic. But you're making me feel better. So, thank you.

Payal: Awesome. Good. Yeah, I totally feel you on it being scary, but I think if you what to get, you could make things better right away, which is good.

Matthew: So, take-home points are like, maybe give the audience two or three favorite take-home points that you think you'd want them to remember from this talk.

Payal: Sure. Yeah, I think I will start with just again that very first take-home point and that is that if you think you may need to get an LP, there's a little voice, if it's my voice from this podcast telling you, maybe you should get an LP, you probably should get that LP. It's going to help whether it's negative. That's going to really help change your differential. If it's positive, depending on that get those basic things, that's going to be really helpful. Then the second take-home point, I think, is when you see someone with meningitis, thinking about how to triage, what happens and when, I think blood cultures, antibiotics, LP. If they have risk factors for a CT, then get that CT. But that doesn't have to happen on every patient that you see.

Matthew: Well, this has been so fantastic. Any resources or anything in general that you'd like to plug or point the audience towards?

Payal: Yeah, definitely. I think got a shoutout to my homies, Infectious Disease Society of America.

Matthew: [laughs]

Payal: Those guidelines, they haven't been updated in a while since 2004.

Monee: 2004.

Payal: Yeah, it's been a while.

Matthew: Wow.

Payal: But I got to say, I read through them and much of what they're saying still rings true, partly because of the research and lack of research that we've had. Those durations are still there. So, I would say have those there, you don't have to remember all this on your own. There is a lot of really good resources out there and consult your ID team. We're always happy to help with this.

[music]

Matthew: This has been another episode of The Curbsiders, bringing you a little knowledge food for your brain hole.

Monee: Yummy.

Matthew: [chuckles] I was waiting for it. Get your show notes at *thecurbsiders.com* and sign up for our mailing list to get our weekly show notes in your inbox, plus twice each month, you'll get The Curbsiders Digest with great practice-changing updates on articles, guidelines, news in internal medicine. We're committed to high-value practice changing knowledge. And to do that, we need your feedback. So, please subscribe, rate, and review the show on Apple Podcasts or on Spotify. You can also email us at *thecurbsiders@gmail.com.* Reminder that this and most episodes are available through VCU Health at *curbsiders.vcuhealth.org* for CME. I wanted to give a special thanks to Dr. Monee “got money” Amin for writing and producing this episode and to our whole team. The Curbsiders is produced and edited by the team at Pod Paste, Elizabeth proto runs our social media, and Stuart Brigham composed our theme music. And with all that, Monee, until next time, I've been Dr. Matthew Frank Watto.

Monee: And I’ve been Dr. Monee “got money” Amin. Thank you and goodnight.

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