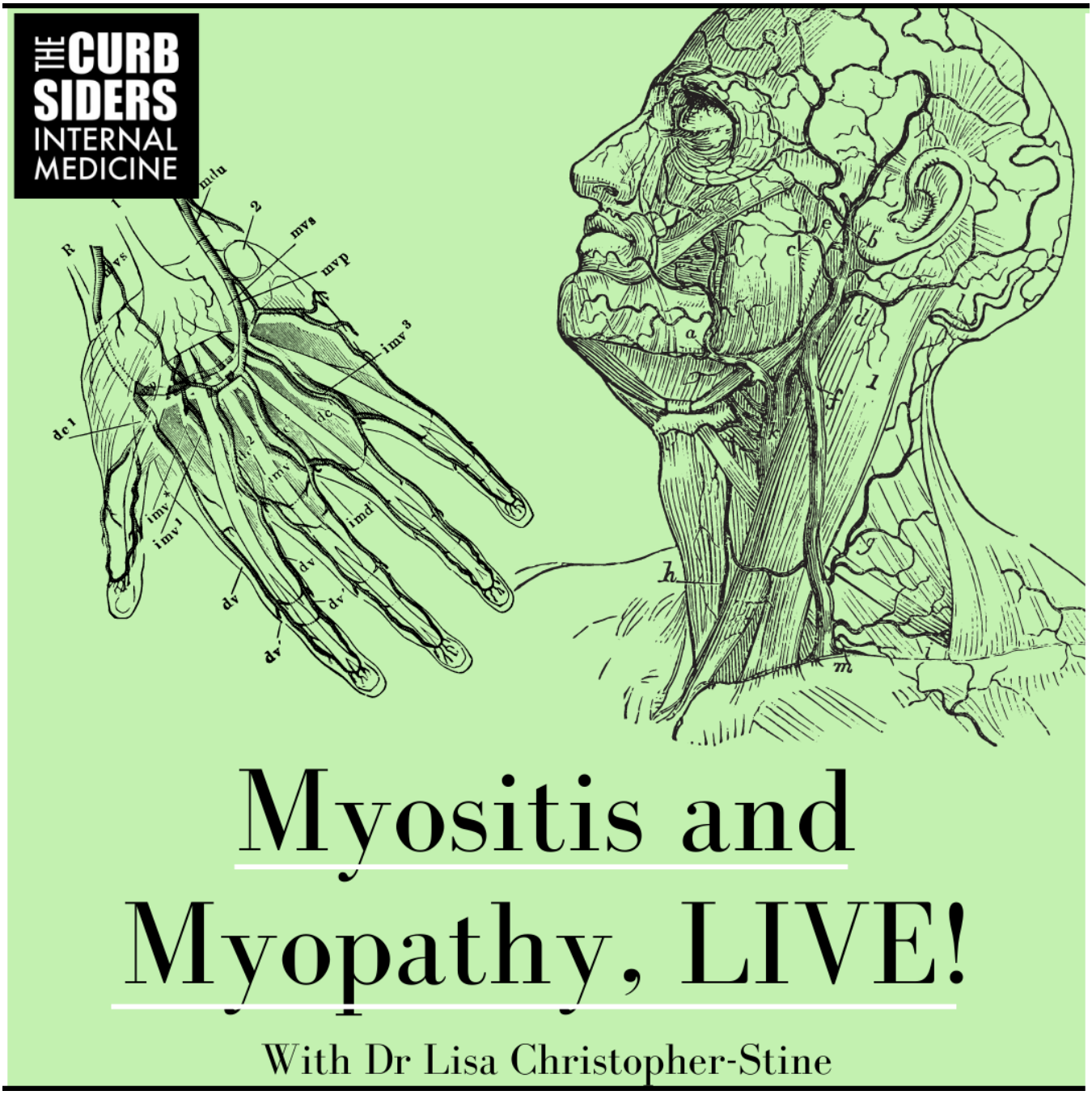
#348 Myositis and Myopathy, LIVE!



[Curbsiders theme]

[Disclaimer]

Matt: Welcome back to the Curbsiders. I'm Dr. Matthew Otto here with my great friend, Dr. Paul Nelson Williams. And, Paul, as always, this feels totally natural.

Paul: Completely natural. It's like the first time every time.

Matt: [chuckles] Yeah. For the audience, people are going to be hearing this at home, we have an audience in front of us, which always feels weird. Today, we're going to be talking about myositis with the great Dr. Lisa Christopher-Stine, who we will introduce in a moment. But, Paul, I need to clear the air about something.

Paul: Yeah, lay it on me.

Matt: We have been doing the podcast for seven years, as we've said in our intro here. Every time we do a podcast, featuring somebody from Johns Hopkins, apparently we tend to leave the S off of John. And we get these emails from listeners. Actually, there's been news articles written-- not about our show doing this, but just [Paul chuckles] Hopkins alumnus writing about how it really irks them. I believe they call it the "unforgivable offense" which I can link to in the show notes for those of you who follow the show after the fact. But Paul with that, would you tell people what is it that we do on the Curbsiders, because I think people are probably bewildered right now?

Paul: Sure. No, yeah, and now that we're apologizing for--[crosstalk]

Matt: We're bleeding listeners.

Paul: Johnny Hobbes, we're talking about Steve Osler. We are The Internal Medicine Podcast. We use expert interviews to bring you clinical pearls and practice changing knowledge. And as you mentioned, we have the great Dr. Lisa Christopher-Stine here to talk to us about the myopathies and myositis.

Matt: Yeah, for the people in the room here, our learning objectives today were to really, like we wanted to understand how might you recognize myositis? As an internist, what is the workup that we should be doing that makes sense to do? Where's our lane in this? And then finally as primary care, what do we need to do to give high value primary care to people that have myositis that are seeing Dr. Christopher-Stine and how can we partner to give them good care. With that, Paul, would you read our guest bio, and then let's get on with the interview?

Paul: Sure, because there is nothing less nerve wracking [chuckles] than reading to a large group of people in a cathedral-like room. We are thrilled to be joined by Lisa Christopher-Stine, MD, MPH. She is an associate professor of medicine and neurology and the co-founder and director of the Johns Hopkins Myositis Center. She joined the faculty of the Division of Rheumatology at the Johns Hopkins

University in 2003. In addition, she serves as the cochair of the institutional review board at the Johns Hopkins University Bayview campus.

Matt: Doing great.

Paul: Thank you. I'm trying. She is also one of 24 core faculty members to teach in the Johns Hopkins Medical School/Colleges Advisory Program which provides clinical skills instruction in the first year of medical school, and continued career advising throughout all four years in the medical school. As a clinician scientist, she is the principal investigator of the Johns Hopkins Myositis Registry, currently numbering over 3000 patients recruited worldwide, developed by her and her colleagues. She has an interest in patient reported outcomes and has been the cochair of an international efforts through the outcome measures in rheumatology organization. And without further ado, may I present Dr. Lisa Christopher-Stine.

Matt: You know, Paul, I remembered I just wanted to interrupt you--

Paul: You just ruined the applause, buddy.

Matt: Oh, I'm sorry.

Paul: And this is where-- uproarious applause but they are never going to [unintelligible [00:03:43]

[applause]

Matt: I apologize.

Paul: There we go, that's appropriate. Now, you can chastise me.

Matt: Maybe another applause break after this, Paul, because this is where we normally in the show, I just probably wanted to say, know on the show, I have a little bit of a reputation for weird picks of the week, I've recommended a jump rope, I've recommended a pull up bar. More recently, Paul, I've been playing video games, as you know, and actually took quite some acclaim. I've actually won an award.

Paul: Do what you got to do, man.

[laughter]

Matt: Actually, it was atrophy, Paul. Atrophy because this is the show about myositis.

Paul: Don't you do this. You don’t have to indulge in this.

Matt: Audience, if you want to applaud that, applause break? No? Okay.

[chuckles]

Matt: Dr. Christopher-Stine, before we get started, is it okay if we call you Lisa because this is meant to be just like an informal, very casual conversation between colleagues? Can we call you Lisa?

Lisa: Absolutely.

Matt: Okay. Lisa, can you give the audience a one liner about yourself and maybe throw in a hobby or interest outside of medicine? Maybe you want to talk about axe throwing, not to set you up, but please?

Lisa: Sure. Good morning, everybody. As you heard, I'm Lisa Christopher-Stine. I'm an adult rheumatologist. I also have a joint appointment in the Department of Neurology. I came here to Hopkins in 2001 to do a two to three-year fellowship. And 21 years later, I grow where I'm planted. I found a great family at Hopkins, is an extended family for me. You heard in the intro, I was the cofounder of the Johns Hopkins Myositis Center. I was explaining prior to starting that we commemorated the 15th anniversary of that Center last night by all of us going axe throwing, which I highly recommend, and I suggest that the Wellness Committee take this on. It was a fantastic bonding.

Matt: I think Paul and I are going to hit it up on the way home today.

Lisa: [chuckles] Highly recommended. I live in Baltimore City. I've been married to my husband of almost 24 years, whom I met at a summer campus as counselor.

Matt: Oh, wow.

Lisa: So, we've been a million years together. I have two boys who are 16 and 12, and a cat for almost 20 years. And other than the cat, everybody's taller than me in my house.

[laughter]

Lisa: And I really enjoy, I think, for about myself what I love is stepping out of my comfort zone doing something new and this definitely qualifies. [chuckles]

Matt: Podcasting in front of a live audience? Yeah, it's not for everyone, but you're doing great.

Lisa: We'll see. Yeah, for sure. I think you said hobby or interest. My two favorite hobbies are travel, especially internationally and entertaining. Both of those were awesome since 2020. So, I think now for the pivot for me has been outdoor entertaining. Love to have people at our home. We have 100 and almost 20-year-old home, have wraparound porch, and really appreciate it being outdoors with people I love. So, that's definitely my forte.

Paul: Excellent. Our typical follow up question is any recent book, movie show, any piece of culture that you've enjoyed lately that you think other people would benefit from or also enjoy?

Lisa: Yeah, I think one of the most important books, which is a quick read is Jillian Horton's *We Are All Perfectly Fine*, it's a memoir. It's her personal memoir. She's a Canadian physician. She's involved in student education and in clinical practice, and mid-career realized, for lack of a better word, some burnout, she was really feeling fatigued. Goes to a retreat, and the book is funny, it's heartbreaking, it's just a great read, and I think it's great for any doctor, but I think it's really good for even outside of general medical practice, I can't recommend it enough quick read and a very important one.

Matt: Well, maybe one last question before we get on to the interview. There're a lot of young people here in the audience, and also in our listening audience. What is some career advice that you want people hearing this to take with them that you found valuable? It doesn't have to be the best you've ever heard. Just like some advice.

Lisa: It's a great question. There's so much advice I think you hear throughout your career. I actually think probably one of the most memorable things I heard was actually not by the speaker, but by someone attending a conference. So, I often go to how to say no to things, how to be more efficient, and many of those. It was someone who stood up who said, one of her mentors told her, "If you don't like the sound of a project that's due in four to six months from now, today, it's not going to be any better in four to six months from now," which sounds obvious, but I really catalog that. And it helps me make sure that my priorities are set.

Matt: Paul, this reminds me of the past guest told us, she always says, "Thank you so much. I'm honored to be considered for this. Let me think about it and talk it over with my inner circle." And then that will really decrease the number of times you say yes to something that like six months from now you're like, "Why did past me say yes to this?"

Paul: 100%. It's a great trick by the person offering like six months from now, because that just seems so abstract. I can tell you, but I'm sure I won't be doing anything at that time. That sounds great. And it's just so easy to say yes to something like that. That's a great advice.

Matt: But, Paul, we talked about Kashlak last night at dinner. Kashlak, actually not a real place. Sorry, people who tried to apply to it on [unintelligible [00:08:55] But, Paul, I believe we have a case from Kashlak.

Paul: We do, stellar transition, seven years, we're doing great.

Matt: Thank you.

Paul: We're going to talk to you about Chris. Chris is a 52-year-old male. He has a history of high blood pressure. He's on lisinopril and hydrochlorothiazide. He has hypercholesterolemia with an LDL of 195 at baseline, a 100 on treatment. He's on high dose of atorvastatin. He's seen in your office for routine follow up for high blood pressure and just for context is at primary care office right now. Over the past six months, Chris has been having low energy, gradual difficulty climbing stairs, his kids make fun of him for having trouble getting out of deep chairs. It just takes him a long time to get up. So based on what Chris is telling us so far, so obviously, we're going a talk on myopathy and myositis but in the

primary care office as this might trigger the thought about this. Are there anything else in the history that you would want to know or where should we start with Chris?

Lisa: Sure. I think we'll take his symptoms at baseline, and the fact that it's been going on for six months. We'll talk about all the things, I guess, myopathy, but if you're thinking about the inflammatory myopathy is myositis, it's generally a subacute process. Six months would not be unusual. I thought it was interesting you said that his kids pointed this out to him. I find it amazing the amount of denial that people will have in telling themselves they're getting older. Newsflash 52, Lisa is not old. But people will say, "Oh, I thought I was just getting a little older, a little stiffer." So that is of importance to me.

I also want to mention the atorvastatin, so surely something that is myopathic, direct myotoxin or we can talk a little about this, but atorvastatin can also be associated with an autoimmune version of statin myopathy. So, all of those things are-- I'm thinking about them. And I don't hear any pain or stiffness, I mostly hear weakness. And then you mentioned deep chair. So, most people can get off a higher seated chair, where they get into trouble with myopathy is lower chairs, so a low couch, toilet seats. I don't hear anything about upper body yet. So, I'd be curious more about that and we'll talk more about that. So deep seated chairs, subacute, and then the fatigue. Trying to dissemble, people say they're weak, this guy sounds like he's both weak and fatigued. Separating asthenia, this fatiguing feel versus true weakness, very important.

Matt: Are there follow up questions you asked to suss that out between the two?

Lisa: Yeah. I often will say, "What if you're in a movie theater, and it's a crowded movie, there's a fire, how easily is it that you just don't want to get out of that chair, it's a little hard, you're stiff, or you really can't get out of that chair? Does somebody have to help you? Have you had to use chair arms to physically push off the chair? That's definitely different than just overall fatigue. And also then separating out joints. A lot of people will say, especially in the small joints of the hands more than the hips, they'll say, "It's weak, I can't turn a jar." I'm like, "Is it weak or is it a little bit of stiffness or pain?" So, just teasing those questions out?

Matt: In primary care every day, you see the person with osteoarthritis of the knee that says, "Oh, yeah, I have trouble getting up from a chair because of the knee pain or stiffness. But this, what we're trying to give here is a flavor that's totally different for this person.

Lisa: Right, and painless. Again, you can certainly have pain with the inflammatory myopathies, which is what we actually are not taught, we're taught it's a painless weakness, but having pain in the absence of weakness, highly, highly atypical of an inflammatory myopathy, so you are generally weak without pain, maybe weak with a little pain, not pain on its own, and really making sure that there's no pain that is the responsible component of that statement.

Matt: I definitely want to talk more about the exam as well. If you start to get the sense someone like this that they might have myopathy, myositis, do you start to go through a different review of systems? Do you recommend we ask certain high yield questions that should then really, like key us in more that we're going to do a baseline workup for that?

Lisa: Yeah, sure. For here, I haven't heard yet at all about any rash. And sometimes it might not be visible on that exam. Usually, it's persistent, but sometimes the rashes that go along with inflammatory myopathies, the amount of myositis can come and go. Asking specifically about rashes, high yield rashes would be the eyelids or the MCP and PIP joints. Fatigue, they've already talked about, so this feeling of being unwell, systemic symptoms. When I'm really thinking about inflammatory processes, remember, it's not really just muscles, it's all the systems. Thinking about that in a systemic process, are they losing weight? Are there fevers? Do they have Raynaud's phenomenon? A 52-year-old man highly atypical to have new onset Raynaud's at the age of 52. Young woman in her 20s, not so much, or sometimes people come in, but have had Raynaud's for years. So that's less typical of autoimmune process.

Paul: Let me give you a little more history, and then I want to hear what your physical examination would look like for this patient. Let's say that our patient has been, he says, occasionally he chokes on food, say solids and liquids. And he attributes this to eating too fast, not something he thought so much about maybe this came out during the review of systems. He also, speaking of rashes, notes some hyperpigmentation of the neck and the upper back that is itchy for him. And then he sometimes also has burning and itching of the scalp. So, he's giving you some more inflammatory symptoms as you're talking things through. I'm wondering, first of all, if this history changes anything, and I would love to hear what your examination would look like for this particular patient.

Lisa: Now you have somebody with weakness that we don't know labs, we're not sure, we're thinking the weakness is true weakness and rash. The rash that you tell me about is not the prototypic rash or the pathognomonic rash. I'm not hearing eyelids, MCPs yet. Scalp is very important in a lot of the autoimmune diseases, but especially in dermatomyositis where scalp is often involved itchy and we miss it because it's under your hair. So, the patient often has to tell you about it, so remembering to think about that. The hyperpigmentation is of interest to me. This has been going on six months, so it's possible that some of the hyperpigmentation represents post-inflammatory rashes. I'll just make one note that depending, I don't know the skin tone of the patient. In darker skin tones, hyperpigmentation can certainly still be post-inflammatory, but we're finding that we see hyperpigmentation sometimes as the first process where it's an active rash. I think typically we're always taught about this idea of violaceous or red rashes. And I want to be clear, I really think we need to be careful about understanding the spectrum of skin tone.

Matt: A quick plug for the Skin of Color Society, which they have a great website that has very-- they have nice pictures on there trying to address this disparity in dermatology in medicine, medical images specifically. A lot of dermatologists are trying to fix this now, which is good, because I agree with you. If you look up textbooks, it's mostly lighter color skin. For this patient here, we're keying in, we think that this person has true weakness. They have some rationale. And anything else, like, on the exam-- you taught me some cool things. What is the appropriate way to test for muscle weakness? Let's say of the neck or at the hips?

Lisa: Sure. Muscle weakness is generally tested by resisting an examiner, you're trying to see whether or not the person can resist your full strength. The two muscle groups that I think we forget to examine

supine are the neck flexors and the hip flexors. The reason that is is that if you are seated, you can recruit and cheat a bit. It is not unusual for a trainee to tell me somebody is strong at the hips because they haven't put them in the supine position. And then technically speaking, hip extensors should be examined on prone. Those are the three muscle groups that really need to be examined positionally to bring out the true weakness.

Matt: So, you have them laying on the table, you put your hand on their upper thigh and try to resist against them that way?

Lisa: Yeah. When you examine any muscle group, I always think of it as a fulcrum. And so you want to be closest to the next, that the furthest joint, because you want to give yourself and you want the unfair advantage. So you want to have the lever when you're--

Matt: You're close to the knee when you're testing.

Lisa: Yeah, close to the hip.

Matt: Okay, got it.

Paul: We were talking a little bit before we started about grip strength, which apparently I've been doing wrong for the past decade.

Matt: Yeah, this was a revelation as well.,

Paul: A great chance to correct me in front of a large group.

Lisa: I want to be clear, you can definitely test grip strength, you're not doing it wrong. But one of the, I think, little pearls that I've been taught by my neurology colleagues, because distal strength can give us a wider differential things like inclusion body myositis or other neurologic processes-- really careful when we test hand strength in particular. So, forearm flexors are the most common distal group of muscles that's affected especially with IBM, inclusion body myositis. So, I teach trainees now to reach fingers for the first palmar crease. It's not really a true grip, but rather the first palmar crease and then try to pry those fingers up. And I think if you try-- people are sitting there doing it, the audience, you can't help yourself, but you have to do it. Pry your friend’s fingers. I can convince you that it seems like that should be weak. The little frail old lady of 90 can hold her finger flexors tight. So otherwise, if you grip, you can recruit your intrinsics and cheat. And we really miss subtle early forearm flexor weakness. So little pearls, just to remember first palmer crease.

Matt: Can you tell us similarly, how do you test for the neck flexor weakness? Correct me if I'm wrong, people often with myositis have weakness of the neck flexors that’s out of proportion to the neck extensors.

Lisa: Correct. So again, that's supine, you ask the patient to flex their neck up off the bed off the examiner's table.

Matt: Am I holding their forehead down in an aggressive way during this?

[laughter]

Paul: And on the throat.

Lisa: No, [chuckles] I recommend reasonable force and you can usually tell so, someone, yes, please be careful with their neck, ask if they have any neck issues and you're pushing down, and you really should be able to see them within reason, resist your strength fully. Again, impressively help people can hold their neck pretty strong.

Matt: So, you test supine for the flexors and then prone for the extensors of the neck-- at the hip.

Lisa: The neck extensors can be also done by lying flat. So, it's supine neck flexors extensors, the only real muscles that need to be done prone are the hip extensors.

Matt: Okay.

Paul: And we should, I guess, get on to diagnostics eventually. But we alluded to some of these things, but if you wouldn't mind to cataloging skin finding specifically that we should be particularly cognizant we're looking for just so that we actually have them grouped together-- [crosstalk]

Lisa: Sure. Yeah, this has a large differential. If I'm thinking about skin rashes in the myositis world, so obviously with their skin rashes in lupus in other rheumatic diseases, the prototypic ones I've told you about before are eyelids and MCPs, but we look for V-neck sign, so on the chest, the back which across the shoulders is a shawl sign. Some people also have arm erythema. We look for what's called a Holster sign where obviously hold a gun holster, and that's on the lateral hips. We look for both either flat or papular areas on extensor surfaces. In addition to the MCPs and PIPs, all the extensor surfaces, so that's ankles, knees, elbows. If it's flat, we usually call that-- it's called Gottron's sign, if it's something where you've closed your eyes, you can feel it, it's usually Gottron's papule. It can be either flat or papular tends to be as we talked about erythematous, but can also be hyperpigmented.

Matt: From my reading, the heliotrope rash around the eyes and the Gottron's papules on the hands are pathognomonic for dermatomyositis, are there other things that cause that? To me, it looks nonspecific and I might mistake it like does this person just get hit in the eyes? [Lisa laughs] Are they wearing their goggles too tight or something? I don't know.

Lisa: Yeah, I'm not sure I know a differential for heliotrope. It's usually pretty much solid. Although actually psoriasis, so in some cases, psoriatic lesions can actually appear on the upper eyelid, that tends not to ring the eyelids. When you see on the upper and lower lid margin, that's consistent with a heliotrope. Although a heliotrope can be below the lid, above the lid, both. I don't think tight goggles is on the list. As far as the knuckles or the MCPs, there's something called knuckle pads, which is

repetitive trauma. So, anything that can cause trauma on the knuckles, and that's usually again seen in isolation, wouldn't be seen with other rashes. So, that's what I'm thinking.

Matt: Okay. That's very helpful. And we had a prior show, we talked about scalp a little bit, mostly for hair loss. Is alopecia a prominent feature or is it more just the itching, burning of the scalp that they--?

Lisa: It's both, I'm glad you brought that up. In general, people can have like full loss, total hair loss in the beginning when the disease is very active. So, alopecia is something we ask about scalp rash. One thing I should mention about these rashes is that they're generally pruritic. They're often photosensitive, but not exclusively. So obviously, the V sign is often photosensitive, but most people don't necessarily have their hips exposed per se. We see these rashes in the winter. So, it's not exclusive to that. And the itch is really important. We can talk about differential, but most rashes, interestingly, the thing that gets most confused with these rashes is lupus, and lupus tends to not itch. And dermatomyositis is an incredibly pruritic rash. The scalp is probably the most itchy area for patients. And I really think you can't underestimate it. It sounds benign, but many patients really tell me that that has been the most significant part of their illness. They can't sleep, they can't function. So scalp itch, while sounding like seemingly benign, it can be pretty significant.

Matt: All right, people, so look out for the scalp itch in your patients. I know now it's going to be one of those things that is going to just like kick off in my mind when I'm talking to people.

Paul: Part of it might be [crosstalk]

Lisa: And within reason, with all of the other things.

Matt: With other things, yes.

Lisa: Certainly, scalp itches for a hundred other reasons. But, yes, in this case.

Paul: I think we just establish this as pathognomonic. I feel good.

[laughter]

Matt: I don't know about you, Paul, but in the back of my mind whenever I'm seeing anyone in primary care with any kind of pain or weakness, I'm always in my head like, "Do they have rashes? Is there inflammatory arthritis?" I'm thinking like arthralgia, arthritis, could this be a connective tissue disease? And so it's good to try to put these together. Oftentimes, it's something else, but I always try to get excited about this thing and not miss it.

Lisa: I'm glad you mentioned arthritis, that's one of the things in the beginning when we talked about associated symptoms, like Raynaud's and other things that can be autoimmune. Arthritis sometimes it's a presenting symptom. So sometimes patients really present with an inflammatory arthritis, that is often symmetric, and they get labeled as rheumatoid arthritis before any of this develops. So, a good history for an inflammatory process and the joints are very important.

Matt: Okay. Well, why don't we get on to some [crosstalk].

Paul: Should we get the exam first?

Matt: Oh, yeah. Okay, go ahead.

[laughter]

Matt: Sorry.

Paul: You always trying to jump to the diagnosis, this is a recurring theme. Let's see what Chris actually looks like, and then we can talk about maybe what we're starting to think about here. One examination, Chris has normal muscle bulk and tone. No rales on lung examination, no findings of heart failure, benign cardiac exam. We're calling it 4+/5 strength in both the shoulders and 4-/5 strength in both hips. Grip strength is normal though I may or may not have assessed it correctly. He has no plaques on his hands. He does have some mild redness of his upper eyelids, cheeks, and nose including nasolabial folds, but not his chin or forehead. So now we have the examination and now, Matt, if you want starting to diagnose the patient, you can go--[crosstalk]

Matt: Yeah. Let's interpret these physical exam findings. We've talked about a lot of it already based on this, are you more worried about this person? What diagnosis do you think is most likely right now or what's in the differential?

Lisa: It's tough, so if it were the rash alone in the absence of weakness, again on the differential, sometimes psoriasis. They often get diagnosed with eczema which at this point, I don't think that's the case, but that's the number one diagnosis first for sure and then lupus. And you mentioned in your description that it was inclusive of the nasolabial folds, another quick clinical pearl. My patients actually made shirts for me that say, "It's not lupus."

[laughter]

Lisa: Because they often get [crosstalk] lupus. And the nasolabial folds are included and not spared in dermatomyositis, and they are almost always spared in lupus. So that's a quick look see that you can save your patient from the wrong diagnosis.

Matt: I think talking about the differential diagnosis or the mimics, you just mentioned lupus, and I think that's what-- Yeah, so the mimics, what should be in our differential, as an internist seeing this person, we're thinking maybe myositis. But what else do we need to think about? And we can go from there.

Lisa: Sure. If the rash is a non-prominent component in the beginning, so when you first heard about the patient, we're not seeing the rashes as much. It's difficult when the rashes are so clear like this, you're really zoning, I think, one, two and three would be dermatomyositis. But if we step back and we think about myositis in general, the most common mimics, especially in the absence of a rash, we see

adult-onset muscular dystrophy, it's not common, but certainly it's not rare in the sense that we make the diagnosis a fair amount. This can look identical clinically, actually, interestingly when we get to the biopsy, it can be an inflammatory process. So having an index of suspicion there, for sure.

Simple things like endocrinopathies, I would lie to you if I told you I haven't missed hypothyroidism. So, hypo or hyperthyroidism, just making sure that that's not concomitant there. When we look at myopathy, we think about neurodegenerative or neurologic processes. So, inclusion body myositis, which is one of the inflammatory myopathies, but one that we talked about and why that grip/finger flexor weakness is so important. And then motor neuron disease. So, not unfortunately and infrequently, ALS is a mimic of this actually, you can even see mildly elevated muscle enzymes, so careful exams there, and we'll get to the exam but it's very important to do a full exam, a clinical neurologic exam. We talked about endocrinopathies. Infection in the sky I don't think so it's been a subacute process, but post viral, we would think about those kinds of things.

And then finally, I guess, myasthenia. So, not uncommon. For some patients with myasthenia can present with pure weakness, where we're not seeing the fatigability [unintelligible [00:27:27] fatigued, but when we talk about fatigability versus fatigue, really trying to tease that out. And sometimes they actually go hand in hand where we see myasthenia in combination with an inflammatory myopathy.

Matt: We went through the differential here, which is a broad differential. Personally, it sounds like I might need neurology, maybe dermatology, multiple different consultants to help me weigh in, certainly rheumatology. But Chris is on a statin, we told you, he's in that high-risk category, his LDL was greater than 190. He's taking atorvastatin. He's done some reading on the internet. And he says, "Doc, I'm worried. Should I just stop my statin now because I think maybe that's causing my weakness?" In general, how do you talk to patients about statin or when primary care doctors ask you what's your opinion of statins, what do you think?

Lisa: I spend a lot of time thinking about statins and the toxicity thereof. I think, in general, they're very good drugs. I see some cardiologist in the audience, [chuckles] and I promise you're not going to take away your statin. So, for this guy, because he's on a myotoxic agent, we first tried to take all of those off, at least initially. While patients with inflammatory myopathies, can in general actually take statin safely. I always remove them in the beginning. I love to talk about atorvastatin, I'll take a moment any of the statins but atorvastatin in particular is an offender in two ways because it's often given at high dose. So, high intensity statins off the bat versus ramp up. I can't tell you for sure if high dose versus low dose necessarily causes more toxicity, but truly there're two forms of statin myopathy that are in my head.

For this guy, he's got a rash and so it's a little atypical for the autoimmune version, but there's direct myotoxicity from statins, which you're all familiar with much more common. That can be anything from myalgia to rhabdomyolysis. And then years ago, my colleagues and I described autoimmune statin myopathy. And that is a more insidious process where if which is very interesting, is the patient generally on a statin on average for about 30 to 36 months, it's almost three years in. It really breaks the rules in your head and we're thinking about how could the statin be playing a role? That's easily teased out by some labs that are quick, usually by the rheumatologist or the neurologist.

Paul: I wanted to talk about labs for a second. I'm just trying to think if this patient presented to my office, how fatigue being one of the banes of primary care, someone comes in saying they're tired. Well, we're all tired. I don't know, what is it that you want for me? I'm trying to think about what my workup would look like. And if I gave myself a little bit of credit, so I think I would probably do a CBC, I would probably do a CMP because everyone gets one just by walking through the door, because they're on a statin, I would probably throw in the CK, and then the TSH for the hypothyroidism. Let's pretend for a second, I was astute enough to actually find a rash and then I talked myself into lupus. So, I just drew an ANA in this 52-year-old gentleman. Does that make sense? Is there anything else that you would add to that? Or I guess a better question to ask you is, what's your logic workup makes sense for Chris here?

Lisa: I think you've really mentioned most of the important--. I'll walk you through, first of all, I appreciate your brutal honesty. It's so true. Isn't everybody tired? So, the TSH, great. Again, also, because hypothyroidism can be concomitant with these processes, we can see Hashimoto's and other autoimmune thyroiditis, it's so important there, and it also can be the driver of the process. So thyroid is very important.

CBC, interestingly, we almost learned nothing from CBC except that we expect a normal hemoglobin hematocrit, which is atypical. Almost every one of our diseases and rheumatic diseases have an anemia of chronic disease. I cannot explain this to you, but when we see an anemia, we generally don't see a hemolytic anemia. We do not see anemia of chronic disease. When I see an anemia, I'm wondering about blood loss and iron deficiency, and then I'm going down the cancer route, which we'll talk about.

Matt: Oh, wow. I did not pick that up in my pre-reading. So, that's a great tip.

Lisa: I think it's not really appreciated. It seems atypical with all this information why that's the case. So, in general, it's not you can't have it, but it's really the exception, not the rule. And then platelets can help us. So obviously, they're sometimes elevated with an inflammatory process, you can see thrombocytosis in the beginning. CMP, probably the most notable thing that we see elevated are the poorly named liver function tests. So, transaminases that go up. And I think just as a pearl for somebody on atorvastatin who's being monitored, they're monitored for their liver function, but they're not monitored for their CK. And so, if I can just publicly announce please don't do two liver biopsies before you check a CK, [Paul and Matt laugh] which it's not really hyperbole. I've seen it. So, it's very important. So, I love that you included the CK. Some people might say an aldolase. Most primary care physicians probably don't check an aldolase. I'll mention the aldolase because it is also another muscle enzyme. Sometimes it's elevated in isolation. The aldolase can go up because of muscle origin. It can also go up because of the fasciitis that is part of dermatomyositis. Again, another little pearl, sometimes I'm trying to tease out what that aldolase is all about.

You mentioned an ANA. I love that you talked about it. This is the bane of my existence as a rheumatology fellow who is trying to debunk-- [crosstalk]

Matt: We share your pain in primary care. I mean, I don't know that anyone loves ANAs.

Lisa: Yeah, for sure. I guess, it's again another pearl and really what was remarkable is, I have had trainees call and say the ANA is negative. Can this be myositis? Turns out, yes. For dermatomyositis, most of the dermatomyositis cases are actually ANA positive. There is at least one subtype and we won't get into the thick of autoantibodies. But we're getting so specific now that there are myositis-specific antibodies, which we wouldn't ask you all necessarily to send a myositis panel. Although I know a lot of my internal medicine colleagues are getting facile with this here. An ANA is generally positive in dermatomyositis, but can be negative in at least one subset. And then most of the other autoimmune myopathies, the myositis antibodies are actually cytoplasmic. So, we'll see a normal ANA.

The thing I didn't hear you mention, I don't think I remember is an ESR and a CRP. Again, I can't tell you why, just like the anemia, for the most part, somebody in the absence of lung disease, we do actually see for whatever reason, we'll talk about the other organs. But in lung disease, we see sed rate and CRP go up, obviously, for severe joint disease, yes. Isolated muscle disease and skin tends not to raise your sed rate or CRP. So, once again, you don't have to think you've missed the diagnosis because the sed rate is four.

Matt: Normally when we talked about-- we did a prior show on lupus and one of the big labs there were urinalysis and CBC. I didn't really see it. I don't have it on the list here. And maybe now's a good time for Paul to tell people the labs, but I think we didn't have it. So, urinalysis not as much--

Lisa: We just don't generally see renal disease with the myopathies.

Matt: Okay.

Paul: All right, let's go with the labs. So, the CMP comes back, the AST is 110, the ALT is 65, the alk phos is 150. The CKs is up a little bit of 480, the aldolase is also elevated. The CBC is normal, as are the creatinine, the potassium, ESR, the CRP, the TSH, and the ANA. Those all come back A-OK. Does that change anything for you at all? Are you fairly consistent with what you were expecting?

Lisa: Fairly consistent. Although, again if the ANA indeed is correct, which again there are some lab inconsistencies, sometimes we repeat those things. So, assuming that the ANA in fact is within normal limits and I was thinking about certain subtypes of dermatomyositis, but everything else I think really is consistent with what we just talked about.

Matt: I think, Paul, at this point, you would be probably sending this person to a rheumatologist.

Paul: That would have happened like three visits ago.

Matt: Three visits ago. Okay.

[laughter]

Paul: [crosstalk]

Matt: Yeah, well, because I always enjoy hearing, like, I think part of the best thing that's come out of the show is when guests give us like a script, like what does it sound like when you talk to this person about something, Paul? I don't know. I don't speak well, how about you?

[chuckles]

Paul: I'm all right.

Matt: Lisa, can you tell us, what does it sound like, you're seeing Chris in the office, you have these labs back, you have the history, the exam that we've talked about so far. What would you talk to him about? What do you think he has? What does this mean for him? He probably wants to know, "Do I have cancer? Am I going to die early?" Those kinds of things. But what might this sound like if we were just listening in the room?

Lisa: I think I would start out by saying that the disease looks most consistent with dermatomyositis. And if we break up the parts of those words, that's dermato, which is skin, myo muscle and itis inflammation. The disease is rare, so about one in 100,000 people unluckily so, you didn't do anything to deserve or get this disease. This is something that we believe probably has some genetic component, but it's not a genetic disease. So, patients want to know are their family members going to get it, are the children going to get it. The answer is probably no. There is an increased predisposition to autoimmunity and family. So, they may have told me one of their relatives has rheumatoid arthritis or lupus, or their children might have a slightly increased risk for autoimmune diseases in general, but in general, not a familial disease, which I think is important and helps people with their anxiety about it.

Matt: It's such a good point. Paul, you always make the point, everyone thinks they have cancer. But I think when someone gets a big diagnosis like this, they worry about family members as well.

Lisa: For sure. And then we'll talk about what I alluded to is the systemic nature of the disease. Even though we talk about skin and muscle, there is a host of other important things to think about. Two of the major features of the disease are lung disease, and that's interstitial lung disease. And then I tell them that cancer is associated with dermatomyositis. We're getting pretty good at precision and figuring out some of the antibody testing that will do this more specific, will in fact help us delineate who might be more likely to have cancer, but we're in the beginning, we really do screen everyone. So, cancer and lung disease are important.

Heart disease, so cardiomyopathy, myocarditis is rare, but important to remember. And that's with a really good diagnostician. I think at the bedside, we really pick that up so we don't necessarily interrogate the heart unless we see signs of an elevated JVP, we hear an S3, something that suggests that there's clinical heart failure or a tachycardia that's unexplained for sure. So that's a start.

Matt: Unexplained tachycardia gives me tachycardia.

Lisa: [laughs]

Matt: Yeah, I do not like that.

Lisa: And then I think that also just understanding what an autoimmune disease is. Autoimmune essentially is obviously telling them that for whatever reason their immune system has tagged their own muscles and skin as foreign and we will do further investigation. So, the first thing we're going to do is try to make sure we understand the diagnosis. If you would have talked to me years ago, I'd say that you have a muscle biopsy, but because the skin is such a good window to understanding autoimmunity, well, not specific, we would biopsy the skin. And that's done by a small three or four millimeter or circular punch biopsy done by usually dermatology, or sometimes some of our rheumatologists do it, we're looking for an interface dermatitis, so they'll undergo a skin biopsy.

And then the noninvasive way, the best noninvasive way to see muscle is with an MRI. It's a non-contrasted MRI of the thighs. We choose the thighs because the thighs are most often involved. It tends to be a symmetrical process. And it's one of the only muscles you can actually see symmetry. And at the same time, if you're trying to look at someone's arms, you have to do two images. So, for efficiency is sending somebody through-- Again, no Gad, it's a T1 and STIR or T2. So, you're essentially looking for a T1 image for architecture of the muscle, making sure there's atrophy, which we shouldn't see this early on, and looking for edema in the muscle. Edema in the muscle is not always inflammation. But it's certainly in this case, highly consistent with that. So, explaining that. If you want me to go, I don't know if we want to do this now, talk about meds and what their life looks like.

Matt: I think maybe the workup, so I had tried to put together a list and you went through the organ. So, you said muscle, MRI, you said lungs. So, we might think about PFTs or high-res CT if we have a suspicion for ILD--

Lisa: Almost always. I usually do baseline PFT and a high res. A CT scan of the-- We often in what we do once is chest, abdomen, and pelvis because you can both look for ILD as well as solid tumors. So, we actually do CT. There's some controversy as to how much we screen and what we screen with. It's a little controversy. I think we'll have a better answer soon.

Matt: People are here for your expert opinion. So, you could tell them to do a chest, abdomen, and pelvis if that’s what you'd like to do.

Lisa: I'll tell them that, once. Don't keep doing that every year but once is good.

Matt: Once is good. It's front loaded. The cancer diagnosis is front loaded, the first five years or so it kind of--[crosstalk]

Lisa: And really the first one year. For sure five years is what the literature will tell you. The first year, one year prior and one year after, if you look very carefully at the time of diagnosis, that time period is the most critical for cancer. Three years seems to be the cut point where we get a little bit less anxious. But the idea to continue a scanning, we don't do that. And then addition to chest, abdomen, pelvis, this

is a male, so a prostate exam, somewhat controversial, but I do in a gentleman of this age will be a PSA, a good prostate exam should be done and colonoscopy. And if it were a woman would add on mammography.

Matt: Yeah, Paul, I think do we give this person some choking, right? They were having some swallowing difficulty.

Paul: [crosstalk] Yeah.

Lisa: So, in that case, because of the dysphagia, which is not uncommon. It's really generally not GI, but more speech and swallow that we would probably refer to, what we would refer to for sending esophagram and trying to understand, it's almost always upper pharyngeal weakness rather than lower GI, are cousins to these diseases that overlap like scleroderma and such tend to affect the entire GI tract at times. This one really sticks mostly at the esophageal level. So, most of the time, in very rare cases, we can have gut involvement. But that's again, very exceptional.

Matt: I think maybe now to recap a little bit what we talked about because we gave a big list. For the audience, in person, they have a slide that has a list of the tests we might consider, but we said for the muscles, MRI, particularly thigh muscles might be a spot we look. I think EMG/nerve conduction study that I've seen some sources say that we didn't really get to that.

Lisa: Yeah, well, as a rheumatologist, I should, as for my neurology colleagues mention EMG/nerve conduction. Technically speaking that used to be in the diagnostics, it still is, it's in the diagnostic criteria. It depends on your-- So, I would say as a human being, if this patient says, "Do I need that to be diagnosed? Would you do that?" I think the answer is probably no.

Matt: This is more of that expert opinion that we would love to have.

Lisa: So, I think really when the rash is so clear cut, and if you're trying to decipher because dermatomyositis can be hypomyopathic or amyopathic. In those cases, when I'm not entirely sure and want to see if there really is a muscle component, CK actually, this is very confusing, but in dermatomyositis the CK can be rock solid, normal, very confusing. Those cases, EMG/nerve conduction is invaluable. The other reason to do EMG/nerve conduction for sure, if the case isn't this-- this is pretty fairly clear when you're in that myopathy differential is to help delineate with other neuromuscular diseases for sure, like ALS. You're looking for denervation.

Matt: The list, so we're looking at the muscles, the lungs with PFTs with a lung diffusion capacity, high-res CT, maybe a swallowing eval by speech and swallow, skin biopsy. And then some of the myositis-specific stuff that we'll need you to interpret. And that's definitely outside the scope is a biopsy talking about like the histopathology and the myositis-specific antibodies, the myositis-associated antibodies. I don't think we can give a list of those. But can you tell us how do the myositis-specific antibodies in the biopsy, how are you using them in your practice to-- you mentioned we're going to get to treatment next, how do you use those to figure things out?

Lisa: Yeah, sure. Without specifics, so these are so specific that they do not exist in the general population, unlike an ANA. So, it really tells me, "Yep, I've got the diagnosis." You can definitely have dermatomyositis without one of these antibodies, maybe up to like 15% to 20% of the time. They're helping me categorize and help stratify risk stratification. Some of them are more associated with lung disease. Some of them are more associated with cancer. Some of them are more associated with overlaps in other diseases like scleroderma, for example. So, I use them to help hone in.

There's one antibody I do want to mention, which is Anti-HMGCR. You might remember-- I remember in my hazy memory that that is the pharmacologic target of statins, an anti-HMGCR antibody in the right clinical context. This looks atypical for an autoimmune statin myopathy, but not impossible. Sometimes there are some rashes that can occur in that. So getting an Anti-HMGCR antibody is a quick way for me to say, "Okay, there's no autoimmune component-- likely, it's very sensitive and specific. It's widely available. There is no autoimmune component to using the statin, so that's helpful as we go on to talk about what we're going to do with this guy. Could we put the statin back? If that HMGCR antibodies positive, no how, no way, we go talking about PCSK inhibitors and all other ways that are safer. If we do have that as an antibody, the statin is absolutely contraindicated, so it's important potentially here.

Matt: Now, Paul, you had memorized all the auto antibodies ahead of time, were you going to recite them now?

Paul: Well, I mean-- No.

[laughter]

Paul: I think we're coming up little bit up against it, I would actually like to hear how we can be helpful in the primary care setting for this patient. Let's talk a little bit more about Chris. He started on glucocorticoids and methotrexate, the steroids have been tapered gradually over six months. He's now on a maintenance dose of prednisone 5 milligrams. And he comes to serve his primary care office for general counseling. So, the question is, Chris may have for us is, he has muscle inflammation, can he exercise? Should he exercise? What does that look like for him, and is it helpful?

Lisa: Yeah, sure. I think exercise is not only not contraindicated, but absolutely is helpful. So that's another question patients ask all the time, and we used to just 20 years ago probably say, "Sit down, don't move from your couch, you're going to hurt your muscles." In fact, it's exactly the opposite. And people say how much exercise is enough or too much, you'll know.

Paul: [laughs]

Lisa: Patient titrates that for themselves. So obviously, if you've gone axe throwing the next day, it doesn't feel so great, then you don't do that. Lifting weights, however, so heavier weights, I don't recommend. I recommend more reps, less weight. The reason that we bulk muscle is you tear and repair it, and so it's the repair mechanisms are likely injured. So, this idea of lifting heavy weights, I suggest against, more cardio and isometric exercises against yourself.

Matt: I think that's good news for patients with myositis that they can still move their body and help themselves that way. We talked about Chris. Let's say, he does not have the autoimmune statin myopathy. So, we would put him back on like, once we've done our diagnostic or myositis-specific antibodies, we're telling him he can exercise, don't go too vigorous especially with the heavyweights, and he can restart his statin. What do we need to do as primary care? One thing to prompt you, we had an episode air today, at least if you're here in real time, and we talked about ACP last week, they were saying, "Anyone on 2.5 milligrams of prednisone or more for three months should really be screened with a baseline DEXA and if they're moderate risk or more, you might put them on bisphosphonate to protect their bones. And it sounds like someone with dermatomyositis is certainly going to meet that. Are you using a lot of bone-preserving therapy and what else in primary care can we do to make sure that our patients are getting the best primary care?

Lisa: It's huge. One other thing before we go to bone health is I'm thinking that I like you also remind the patient that I do is particularly dermatomyositis is that the sun because of the photosensitivity of it to remind patients to use. We're talking about high level 7,500 SPF. Once that really is anything over 50, it's really helpful, but it really is. Wide brim hats if you're a woman or anybody can wear a wide brim hat, I guess.

[laughter]

Matt: Paul, I can't help but think of *Island of Dr. Moreau*.

Lisa: Just protect your face.

Matt: Marlon Brando.

[laughter]

Paul: Quick sidenote, and this is just for you people here, this is not for anyone who's listening at home, because you're actually looking at the top of my head and you see things are getting thinner here. I can't remember I told the story on the podcast before 30 seconds. I went to see a dermatologist and she said my favorite thing that's ever been told to me in the doctor's office is, "Have you ever considered incorporating a hat into your wardrobe?"

[laughter]

Paul: So, anyway, sidenote, speaking of a wide-brimmed hat is something I think about often. Thanks to this dermatologist, God bless her who is wonderful and [unintelligible [00:48:13] on her. Anyway, sorry to interrupt. Carry on.

Lisa: No, it's all good. Hats are our friend in dermatomyositis, any hat, anything with a brim because if we're here in the sun, you want to be careful to protect your face for sure which we didn't talk about. Bone health, so important. And really not only screening, but following up and making sure for bone protection. Absolutely true. So, our internal medicine colleagues are very helpful at reminding us to

make sure that we follow DEXAs. I think there's some degree-- some rheumatologists are very involved in doing their own bone health screening, but sometimes that really does come into your wheelhouse as internist for sure.

Matt: Yeah, I mean, especially if someone's may be traveling to see you at a highly specialized center, it might fall more on the primary care. I could see that happening for something like a myositis. And what about vaccinations? The timing of vaccinations, you probably think about this a lot for your job, how do you counsel patients about that? What should we think about before we're getting people started on treatment?

Lisa: If COVID has taught me anything, it's taught me that, boy, we really are probably underestimating how poorly protected patients are who are on immunosuppressants. So, we've work here that has shown certain immunosuppressants making you even more susceptible for sure of not having protective antibodies. I will tell you that I have smart phrases and sets to remind me of vaccination schedules that I can hardly keep in my head, but Pneumovax and other vaccines that I really think are more at front of really top of mind now in the COVID era. So, vaccines are hugely important and for sure, for our internal medicine colleagues.

Matt: Paul, I almost wonder if at some point, we're going to be checking titers on folks who are immunosuppressed to see and if we'll learn how to interpret titers right now, I know we don't really.

Paul: Yeah.

Matt: We're like, "If it's positive, okay, yeah, there's something happening." We don't know how much that's going to going to help. Well, what do you think, Paul? Do we have time for audience questions, is that where we should go next with this?

Paul: I think that's right.

Matt: Okay. So, if anyone from the audience would like to ask a question, we would be happy to entertain those. If not, we're also happy to end early and I don't think anyone's ever complained about a couple extra minutes in their day.

Audience: [unintelligible [00:50:28]

Lisa: I'll repeat it. So, the question is, "I wouldn't expect to see atrophy, would that change my differential?" There's a caveat that some of the inflammatory myopathies do have a quick pace. But there's really only one or two that would worry me. I would think more about a dystrophy if I see a lot of atrophy early on. Either a dystrophy or another neuromuscular process. That's actually when I'm calling my neurology friend saying, "I think this is more in your wheelhouse." So early atrophy is pretty unusual, inclusion body myositis, we can see atrophy but at six months, the interesting thing is that the inclusion body myositis by the time they come to our purview, they'll say they've been noticing things for six months. But if you really push them to like, "Oh, yeah, I fell two years ago." So, making sure their timeline is also correct. So, we do see atrophy potentially with poorly treated or delayed treatment in

any of the myopathy. So, for sure, it's possible, but in a six-month time period that definitely keeps me thinking about dystrophies and another mimics.

Matt: This reminds me of just one point that I wanted to bring up that was revelatory to me and preparation is that I always remember as a student, I'm old enough that it was dermatomyositis and polymyositis. And when we made the point about the myositis-specific antibodies in the biopsies, now we're understanding that polymyositis really probably a bunch of different things that now we're super specialized and it was so humbling to see like how many different phenotypes and antibodies and biopsy types that have made that into multiple things. I don't know how much more you want to say about that.

Lisa: I think that's another podcast. But I will say that keeps me employed for sure.

Matt: That's like a rheumatology podcast, I can imagine like a whole series on myositis specific--[crosstalk]

Lisa: Yeah, I think it just makes us think like the word polymyositis. Really very quickly, just very quick. In my head I always think you should think about a few things, which is the anti-synthetase syndrome, which in a very quick that is like remember in your hazy memory that Jo-1 associated or the antibodies that are cousins to Jo-1. That is a syndromic process, so there you're looking for roughening of the hands called mechanics hands, lung disease, arthritis, myositis, fever, that's a systemic process, that's in our wheelhouse. And it depends if you're a lumper or a splitter, I think you should split that off, because I think it's important to think about that. Muscular dystrophy, we already talked about. Inclusion body myositis, and then any of the overlaps, so it's important because it's not just semantics. If scleroderma is linked to there, often we don't see sclerodactyly and overt scleroderma, we see telangiectasias, maybe a little Raynaud's. So, they still have all the systemic complications. In my head just a quick checkbox. As I said before muscular dystrophy, adult-onset muscular dystrophy absolutely mimic of these things or occasionally motor neuron disease.

Audience: A question from the chat is, are there particular types of cancer that are more associated?

Lisa: Yeah, so ovarian cancer is overrepresented in dermatomyositis for ways we really don't understand and this is not a cancer you see in the general population as often. So, we, for sure in women often do a transvaginal ultrasound, really have to be carefully looking for that early. Often, I say that it's the dermatomyositis that brought the cancer to the forefront. Other than that, it tends to be those that are common in the population. So, more lung, breast, colon, prostate, but for sure. And then in younger people, maybe some more hematologic malignancies, but ovarian cancer is highly overrepresented. And so that's another-- glad you mentioned it. I do want to take one minute to make sure that I addressed the atorvastatin issue.

You had mentioned, should we restart it? The answer is you should restart it. But I have learned from my cardiology colleagues that I just don't go full force restarting it because in rare instances, for whatever reason that myotoxin is enough to exacerbate weakness in a rare subset of the population.

So start slow and low. Always start every other day. So, I do a Monday, Wednesday, Friday for at least a month, checking a CK carefully monthly, and then gradually increase that.

Matt: So, like 10, 20, 40, something like that?

Lisa: Right. So, not only increasing the dose, but increasing the timing. So, trying a Monday, Wednesday, Friday at first and seeing whether or not-- Interestingly, some people have excellent cholesterol reduction, even with a Monday, Wednesday, Friday dose. So just making sure we don't overdose them. I want to make sure that I make that a point.

Matt: Wonderful.

Audience: Great. So, I think we'll take one last question from the audience. [unintelligible [00:54:55]

Matt: So, the question is why proximal versus distal and is there any understanding about that?

Lisa: Oh, gosh, no, you can come do a full fellowship to try to understand that why proximal versus distal? We really don't know. And interestingly, even in the proximal muscles, if you look carefully, if you actually look at an MRI, it's such a symmetric process that you could lay one thigh over on another. It's almost like a perfect mirror image. I find it absolutely amazing that the rectus femoris is often affected in the exact same way. Whereas some of the adductors can be spared. So not only do we not understand proximal versus distal, we don't even understand within proximal, the targeted muscles, inclusion body myositis is fascinating in this way, and that the quadriceps are affected. So, the knee extensors are almost exclusively affected all the time. Yet knee flexors remain strong until nearly the day people die of something else with IBM. So, really interesting question. I don't know. It helps us from a differential standpoint, clinically, but pathologically I have no idea why.

[Curbsiders theme]

Matt: Should we should we sign off officially, people have 30 seconds for us to sign off? Okay.

Paul: I mean, I hate for you to miss this magic. So, sit tight for this. All right, this has been another episode of the Curbsiders, bringing you a little knowledge food for your brain hole.

Matt: Yummy.

Paul: Great. I hope that's humiliating.

[laughter]

Paul: Get your show notes at the *curbsiders.com*, and while you're there, sign for our mailing list to get our weekly show notes in your inbox. Plus, twice each month, you get our new Curbsiders digest, which recaps our latest practice changing articles, guidelines, and news in internal medicine.

Matt: And we're committed to high value practice changing knowledge. And to do that, we want your feedback, so please subscribe, rate and review the show on Apple Podcasts or now on Spotify. You can also contact us at *thecurbsiders@gmail.com*. And a special thanks to Dr. Christopher-Stine, Dr. Gail Berkenblit for inviting us, and to my cohost Dr. Paul Nelson Williams and to our whole team at the Curbsiders. Lot of people make the show happen. Pod Paste does editing and production for the show. Elizabeth Proto runs our social media. Stuart Brigham composed our theme music. And, Paul, with all that until next time, I've been Dr. Matthew Frank Watto.

Paul: Strong work. I remain Dr. Paul Nelson Williams. Thank you and goodbye.

[Curbsiders theme ends]

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