

Urological management in rare neuroimmune disorders

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[00:00:05] **Dr. Benjamin Greenberg:** I have the distinct privilege of introducing a colleague and a friend, Micah Jacobs who is joining us today and agreed to be very flexible with time as we're running a little late. Micah is a as he'll tell you a pediatric urologist and a couple of fun things. So, urology and neurology has the most frequent wrong pages in the hospital. The number of times when I was a resident that I was paged in the middle of the night at 3:00 in the morning about prostates was staggering and I'd have to say neurology, neurology.

[00:00:38] Micah did his medical school at Yale, went on to do urology and your pediatric urology fellowship in Seattle. He's a native Houstonian as am I. So, he spoke the language before coming here in 2011 and has been on faculty. He's an associate professor of pediatric urology, runs the Pediatric Urology Fellowship. And most importantly to us has been a great partner for caring for all the kids we have with transverse myelitis, ADEM, all the conditions we're talking about where there is bladder dysfunction involved and he was gracious enough to give some time to us on a Saturday and talk to us about urological management of these disorders. So, I'm going to turn things over to Micah.

[00:01:26] **Dr. Micah Jacobs:** Well, really, I'm super grateful that Ben Greenberg invited me to give this talk. Interesting fact about my relationship with him is that one of the longest opportunities I got to sit and talk with him was when we were both selected for jury duty for a murder case. And thankfully like at the last minute they couldn't, they washed out our jury pool, because nobody that for whatever reason. Anyhow, so we had a nice bonding opportunity. Anyhow, thank you all for honouring your bladders at the break. That makes me happy. I am a urologist and I'm over at the university or here at the university.

[00:02:14] My one disclosure is that I am a pediatric urologist. I know you guys have been hearing from quite a few pediatric folks today it seems like, but just to say and I'll explain a little bit of this as I go on. Is that although I see primarily children, a lot of the patients that I'm seeing with some of the sort of disorders that we're talking about are patients that are adult size. And so my reference point is mostly within this category, older patients in our pediatric population. The other disclosure I'll make is that there are going to be some slides here that are surgical in nature. So, if anyone is particularly squeamish, you may want to look the other way, I guess, but nothing particularly sensitive as far as genitalia or anything like that. Given that it's a pediatric talk, I did avoid that.

[00:03:08] Anyhow, so I thought it might be useful for us to talk a little bit about bladder function. Given that this is seemingly maybe a little off topic from today. Although I think you guys understand some of this very well. But notably that when we talk about bladder function and this is sort of the way I speak to both my trainees and patients and families in clinic, is that there are sort of two parts of what the bladder has to do. It's got two jobs. So, one job is the bladder has to fill up and the other job is the bladder has to empty. You want it to do that in a particular way and there are a couple of muscle groups that are important for making that happen.

[00:03:46] So, the bladder wall is a muscle group, it happens to be called the detrusor muscle, you can just call it the bladder muscle and then there's the sphincter muscle that's kind of like the doorway at the outlet, right? So you have this big muscle, that's the bag and then the sphincter muscle at the bottom. And so when you fill, you want the bladder muscle, the detrusor muscle to be relaxed, right? And the accepting of fluid as it comes down from kidneys and you want the sphincter resistance to be high. So, tone to be high and then when you empty, you want the opposite to happen. So, you want the bladder to contract and you want the sphincter to relax.

[00:04:21] And I'm not going to get into the detail here, but suffice it to say that all those muscles in the same way that, you know, all your limb muscles work and most of the muscles in your body that's controlled by nervous control. So, that's where we end up in having a discussion with the urologist in this room. And so you get all of your kind of motor function and sensory function from signalling that comes to and from the spinal cord. Just a couple of things about children. Most of what I, when we talk about children in this population, as I had said we're talking about children that are above the age of potty training. And for that reason, their bladder function really mirrors adult bladder function, especially as you get a little bit older in this population.

[00:05:10] The really young children are the children that we're thinking of that are pre potty training age and most of our data doesn't come from that population and what I'm going to be talking about. So, in new-borns, most of the voiding or peeing that happens, happens reflexively. And it's kind of uncoordinated between that detrusor muscle and the sphincter muscle. And then what happens as kids get older and they go through potty training, there's more coordination between those two that sort of help from the brain and you get volitional kind of voiding.

[00:05:43] You say like I actually want to void now instead of it being reflexive. And so, in children versus adults, children pre potty training, the large difference, like I'm saying is that it's involuntary voiding in that very young population as opposed to adults and older children where you have voluntary initiation of voiding and then all those pathways are kind of coordinating. So, what can go wrong? So from a urologist slash kind of urologist who works with disorders that have to do a spinal cord. So, you can have either increased or decreased tone or activity in either of those two muscle systems.

[00:06:24] So, this is where it helps to think about them separately a little bit. So, most dangerously is that bottom row. So, you can have detrusor pressure that's really high. So, your detrusor muscle is really squeezing hard and the sphincter outlet pressure is really high. And so what happens, as you might imagine in that case is that the pressure in the bladder goes really high and that is not so good for kidneys that are trying to get urine down to bladder. And of course, that's sort of like the main thing, the most important thing that we're trying to protect are kidneys.

[00:06:58] In addition, that's not very good for continence either. Okay, if you can't relax your sphincter muscle. Fortunately for most of our patients with some kind of neuro immune disorder, you know, most of our patients are those with transverse myelitis, but we have many others. The detrusor activity is fairly low. And so, we end up dealing with sort of how to manage that. Causes for neurogenic bladder kind of in general.

I take care of a lot of patients with spinal dysraphism. You might know that is spina bifida in most cases or myelomeningocele and many others on this list. Today, we're mostly talking about demyelinating or neuro immune disorders like transverse myelitis. But there are plenty of other patients that we see in our clinic.

[00:07:46] And so, many of these patient populations might fall more or less into any of those groups, but that I had shown before with those arrows. But in reality any patient with any neurologic dysfunction of the bladder might have any of those different issues. Just in general, and you guys know much of this presentation of a patient with a demyelinating disorder. So, there are many symptoms that show up primarily as neurologic symptoms. But from my perspective, given that this is a urologic talk and I'm a urologist mainly we're focusing on the bottom line, which are autonomic dysfunction.

[00:08:27] And primarily today, we're talking about bladder, but there are many other forms of this. And as a urologist, there are also a number of different sexual dysfunction things that can happen as well including priapism, which is prolonged and painful erection, which can be damaging. So, regarding children, some of the differences or just things that we see is that it's primarily in kids, maybe the biggest difference between the adult populations that you see maybe a slightly different distribution of some of these disorders and one in particular is that acute flaccid myelitis and at least in our population is maybe a little more common than in the adult population, but some of the symptoms and how it presents is fairly similar to adults.

[00:09:24] So, how do we sort of work up patients when they come to our office? So, some of these studies you guys might be familiar with and I'll kind of go through each of them. So, first off, particularly in the pediatric population, we really lean heavily on ultrasound and someone who maybe has a smaller body habitus or is very young, it's a really good way to just rule out any major issue with kidneys if you have a bladder problem. It's good imaging in certain patients, there's no radiation, it's painless. So, that's also kind of nice for kids.

[00:09:57] And then things that you'll see is something called hydronephrosis, which some of you might be familiar with, which is where you have fluid build-up in the kidneys because of some of those things that I was talking about. And you can see other things like maybe some bladder wall thickening or signs of that muscle is maybe being overworked. And then of course, things like stones for someone who's not emptying their bladder well. Another piece of our kind of puzzle is something called avoiding cystourethrogram. And I'll show you that that usually in our patient population with demyelinating disorders happens in the presence of urodynamic testing, which I'll talk about next.

[00:10:34] But this is a test where you place the catheter and you fill the bladder up with some X ray dye or contrast. And then you see what the bladder looks like and if there's any back flow of urine to the kidneys. So, it can tell us some of those things, it can tell you if the bladder again looks like it's overworked or there's something bad happening with the muscle there. And it can also tell you some things about the urethra where the urine exits the bladder.

[00:11:00] And then, finally, is a whole group of tests that we sort of broadly categorize as urodynamic testing. Part of that is just seeing how the urine flows out of the bladder for someone who can urinate void, right? And something called the post void residual, which is very important for our patients. Which basically tells us that when you urinate how much is left in the bladder, because that can tell us a little bit about how efficiently you're emptying and maybe some reasons why someone is either dealing with incontinence or discomfort or other problems.

[00:11:35] And then we put all this together with a sensory lead that tells us what the sphincter muscle is doing. That's the EMG part and we fill up the bladder and measure the pressures. And then we add in a lot of times a VCUG into that, which is the fluoroscopy part. And so, what you get is a study that looks something

like this and this is really confusing if you haven't seen it before. But importantly, maybe it's probably the easiest line to look at is the top line without getting too granular on this, the top line is basically measuring the bladder pressure.

[00:12:09] And so, that actually is showing us, I don't know if I can maybe see, use the little pointer or maybe there's something here, see if I can, ah, okay. So, I don't know if you guys can see this and I apologize. It's a little bit small, but just broadly you can see that there's this whole stretch of a line that's flat right there and stays low. So, this is a fairly normal urodynamic study. That's the filling part that we were talking about. So, that's when the bladder is filling up and you like the pressure low, right? And then you get to the end of the study and this person urinates and the bladder pressure goes up.

[00:12:43] And so that's the emptying part of this study. And then this is the EMG this is the electrode that's on the bottom, that tells us what the sphincter muscle is doing. In our case, we use just a patch sticker electrode in some places unfortunately for the patient, they use needle electrodes, which doesn't sound very fun. And then you're seeing what the what happens with that muscle, what the firing looks like. And then you can see in this patient they do what they should, the muscle relaxes when they get to the part where the bladder squeezes. So, this person gets kind of an A plus, right?

[00:13:16] And then this is telling us how much volume is in the bladder as they're filling up. So, what can that help us with? So, going back to some of those things that we said could go wrong if you have someone who maybe isn't, those muscles are doing the incorrect things. You can have not the study that looks nice and flat with a good thing at the end, you can have something like this where the pressure just continuously goes up. And that's actually a dangerous bladder, because that's a bladder where essentially every drop that you're putting in during the fill, the pressure gets higher and higher and higher. And that's what we would call a poorly compliant bladder.

[00:14:01] Meaning that the bladder is not accommodating of urine as it comes down from the kidneys, which is basically the worst situation for kidney health and function, right? So, and this plays into how some of our patients show up. So, most of our patients come in direct referral from Doctor Greenberg, at least in our myelitis population. So, and they have all different kinds of symptoms. So, some patients have no symptoms and we'll get to that a little bit later, but the urinary symptoms that we see are kind of common urinary symptoms. So, somebody who has to go frequently or with a lot of urge. Incontinence is obviously a huge one.

[00:14:43] And then, most concerning is the patient who just cannot urinate. And this is the way a lot of our patients present in the hospital as they come in. With a number of other complaints that have to do with maybe extremity weakness and problems in lower extremities for instance. But then on top of that, they also can't urinate and that's obviously very distrustful for a family and the patient. And so then you can see some of these abnormalities that we would pick up on a urodynamic study or other testing.

[00:15:15] How does that play out in children? So this is a study that was done at Vanderbilt. And this is a small study of 22 children. So, but again, there was a few small children, but most of these patients actually were older over a fairly long follow up and a lot of these patients had persistent bladder dysfunction. Now, they called that basically on really any symptoms. So, it didn't necessarily mean that they couldn't urinate, but they had some symptoms at least of urgency or frequency. And what they found was that some other motor recovery didn't necessarily predict what happened with the bladder.

[00:15:54] So, you could have full recovery and you, kind of, let's say they had lower extremity, weakness or inability to ambulate, but they maybe recovered that, but the bladder still had problems in those who did have

some symptoms initially. And then interestingly and worrisomely, a quarter of their patients had upper tract changes, which basically means that they had changes of their kidneys. So, it's not just a bladder thing, it's a kidney thing. And so every time as a urologist, we talk about bladder function and bladder health, we're really talking about kidney function health on top of that.

[00:16:33] And one of those patients ended up with chronic kidney disease, meaning that they lost some kidney function due to the bladder issues. So, this is our patient population. So, we had about 80 patients that were referred to us for primarily transverse myelitis. They were seen over about 20 years and we followed them for at least most of them a few years. And about half of those patients required what's called CIC, which some of you might be familiar with, which is Clean Intermittent Catheterization. Which basically that would suggest that those patients could not empty their bladders well enough on their own.

[00:17:11] And so, they had to place a catheter intermittently during the day to get their bladder to empty, to either achieve continence or to protect their kidneys from damage. And if you look at that pot, so that's the initial. So, about half of the initial patients needed that. And then if you look at what happened to them as time went on over that period. Basically a little over half of them, maybe two thirds of those, had some sort of bladder recovery and maybe about a third of them or so required continued intermittent catheterization. And that was a follow up of about three years all these are.

[00:17:52] And I have a little bit more numbers on this later, but basically most of the patients had recovery that you could track out over a few years and you could kind of predict what might happen once they got there. Interestingly, we did have one predictive factor, which was that, when one of your neurologist does an exam on you when they kept their reflexes at the initial exam that predicted maybe a better outcome for the ability for them to urinate on their own without catheterization. And I just want to move to this right here.

[00:18:27] This basically shows us what happens with recovery of bladder function and maybe it's kind of obvious to you once I explain the graph a little bit, but essentially, if you look at when they present it, that's like the time zero. And this is describing recovery, most of our patients really knew what was going to happen to their bladder within the first two or three years. So, once we got out in our follow up to several years, basically the probability of recovery at that point didn't change very much. So it helps us a little bit to tell our patients after, you know.

[00:19:04] First of all, it helps us to reassure a lot of our patients, because a lot of our patients come in at six months to a year and they look super dejected that they are still not able to urinate well. And I've had this conversation with a number of my patients to say that may be the case. But in our population, actually, we have seen that a lot of our patients do quite well actually. Even after two years some of our patients still have some really kind of market recovery. So, and then once we do get out to that two, three year point, I think that's when we start maybe feeling a little differently. But I think a lot of the distress happens in that first year or two understandably.

[00:19:45] So, this kind of gets into some of what I was saying before. I think in order to decide how we treat patients, we have to understand what our goals are and somebody better make sure I don't go over my time. I'm sorry, I'll try not to. But first of all, as I said, we really want to make sure that kidneys are kept safe. So, in all of our patients, we need to make sure that everything that we're doing is protective of kidneys. Also very important, but secondary is social continence.

[00:20:17] And I think, again, I treat a lot of patients who are younger and sometimes this is a challenging conversation, very understandably, you know, a teenager in our office who is obviously distressed about their social continence and that's first and foremost to them, understandably in a social situation. But we also

have to think and remind them how important it is that they have a healthy life ahead of them, you know? And sometimes these two things tend to play off of each other when we're talking about treatment modalities trying to get someone really dry, but maybe at the suffering of the kidneys.

[00:20:56] So, interventions to help people. So, a lot of our patients can urinate and they just have trouble staying dry or maybe emptying well. And so, it's important for us to say that sometimes all you need to do is just kind of change your patterns. So, one thing that we do with a lot of our patients, not even this population just, you know, someone who comes in day to day with issues with wetting like at school or wherever they are just to get on a schedule, because somebody who maybe could have really good sensation in their bladder before and just kind of quote new when they had to go, right? Now, they don't necessarily have that anymore.

[00:21:32] So we say, you know what, just stop every two or three hours and just urinate then and people get watches, et cetera. Now all the kids have phones too. Oh, my daughter scares me. So, the other thing is double voiding. So some people can feel it or they know, but then they go to the bathroom and they think they're empty and they're not. And so, a lot of times we just say it's probably worth going back, you know, go through your emotions of finishing and then sit back down and try again.

[00:21:58] And then we have patients who can't, who really cannot urinate or can't stay dry. And so, we lean on things like we talked about Clean Intermittent Catheterization if they can't empty their bladder to help them empty or sometimes medications to help with bladders that are overactive and making leakage. And those are medications that are very common in general in the market. You see them all over the place, both anticholinergics. Those are things like Oxybutynin and some things that you see on the market and then beta-agonist, which is Myrbetriq, which is kind of a newer medication on the market.

[00:22:33] And then operative procedures and I'll talk, I think I'm a little short on time. So, I'll try to get through some of the operative procedures. But risk based management is really what we're talking about. We're trying to make sure that what we do helps prevent kidney injury and helps people with continence at the same time. And using our tools of your dynamic studies, et cetera, maybe we can identify where the problems are and help them. So problems typically, are at those things that we talked about. So, problems of the outlet or maybe the outlet is too wide.

[00:23:11] You don't really have a reference point for some of these things, but this is the bladder outlet right here and that's like really, really wide as opposed to this bladder outlet, which is really narrow, right? So this is a low pressure outlet that's super wide and then this is a bladder that's really bad. So, it should look kind of smooth and round. And this is all irregular looks like we call that a Christmas tree appearance. One of my trainees knew I was Jewish and used to call it a Hanukkah bush for me. So, that was really funny. So, we can help surgically those things if we need to sometimes.

[00:23:49] And then some of our patients, because maybe they use a wheelchair, have a really hard time getting intermittent catheterization access. And so, for a lot of our young patients, we can provide places for them to catheterize on their abdomen, oftentimes in the umbilicus in the belly button. This is one of our patients that we did what's called an appendicovesicostomy and I'll show you some pictures later. So, surgeries for bladder outlet are things and you may have heard of some of these bladder neck injections or slings or formal reconstruction of the bladder neck or even closures in some cases.

[00:24:22] And then you have surgeries for the bladder, which are things like injection of botulinum toxin. Which we do actually fairly frequently to see in high pressure bladders or overactive bladders that will help, especially if someone's already on catheterization. Problem with that is it needs to be redone every 6 to 12 months, right? If those of you who are using Botox for other things you might know that already. And then

auto augmentation, which most people don't do, so I won't describe very much. And then there's formal bladder augmentation, which is where you take basically you take a piece of bowel, okay. And you take that bowel and then you kind of open it up. So, this is just in the OR, right?

[00:25:04] And then you sew it together in a different orientation, so now it's like a big patch. And then you sew it on to the bladder. This probably isn't the most clear if you're not familiar with the procedure. Basically, you just make a big patch on the dome of the bladder. So, you have more room and it's stretchier. And then this is just discussing surgery to help people with their catheterization who can't catheterize from below either because you've surgically done something below to block it up or they can't reach below. And those channel types are things where we use the appendix. That's called an APV or things where you use the bowel and reconfigure that to make a tube so that you can slide a catheter in from the abdomen. And these are those pictures I was just showing.

[00:25:50] So, this is another, this is a very short segment of bowel and you can kind of cut it open and kind of do this with it if that makes any sense to open it up to make a long strip out of it and then you sew it over a catheter and you make a little channel out of it. And you can do these things through open incisions like I was just showing, but you can also sometimes do things laparoscopically. And I'm probably not going to show this whole video, but this is just like one of our, I don't know if I can show this here maybe not. Probably better for time anyways, but you can do some of those procedures just through small incisions in the abdomen, laparoscopically.

[00:26:33] Usually we use the appendix when we do that just to make a tube that connects the belly wall to the bladder. And then in some of our young children, who just need a way out, we just sew the bladder to the skin that's called a vesicostomy. This patient had a little bit of irritation around it. In adults this is a little more challenging, because it can't be bagged. But in adults, there are other incontinent mechanisms that can be used. So, there's something called an Ileal conduit or an Ileal vesicostomy, which is basically where you essentially just give a drainage pathway using a piece of bowel to the skin and those are things that you can put an appliance on.

[00:27:08] So, in the same way that people have a colostomy, you can have a so-called urostomy, which is one of these things where you divert urine into a stoma. And I'll tell you most of our young patients don't really like these. Very different than the adult population who a lot of our adult population just doesn't mind. And it's actually easier, you know, you don't have to catheterize. So, a lot of times it's just so much of this depends on who the patient is and what's right for them at that time of their life. Just one case I wanted to share with you, this is one of our patients who came in 13 years old with ascending weakness and sensory loss and ultimately ended up in urinary retention.

[00:27:55] This is the MRI hospitalized for a month and was in a wheelchair for a prolonged period of time. And but had a good bladder that held a lot of urine. So, you can see the volume was really good just as a, you're not urologist, but that's half a litre of urine is plenty to hold and the pressures were nice and safe. She just couldn't empty. So, she needed to catheterize, but the problem is she wasn't able to, a female who's using a wheelchair, it's much more difficult in some of our female populations to catheterize and some of our males as well. So, we gave her a channel and she was able to catheterize and she does very well and she's gained a ton of independence.

[00:28:36] She doesn't have full mobility of her upper extremities, but enough, so she can catheterize through a stoma on her abdomen. So, this was a good option for her. So, as urologist what can we do or what can we share with our patients? So, we know a little bit, not a ton, but so risk of remaining in CIC in the first year is about half, but it does get better after that for a lot of our patients. Preserved reflex is maybe a good indicator

of recovering some bladder function. And then long term management, after everything has stabilized really involves just good surveillance and then some combination of non-surgical and surgical interventions. I think that's probably about 30 minutes. So, any questions I'm happy to answer? Yes.

[00:29:43] **Audience Member 1:** [Inaudible]

[00:29:43] **Dr. Micah Jacobs:** Yes, I have heard and read it. And you go back, because this became a big topic of discussion about five or 10 years ago. And it definitely seemed to be true for sure in some of the older population that was using it. As far as I know, there's not a lot of data on people who have started it when they're younger. We definitely have seen this is totally anecdotal, so take it with a grain of salt. In our young population that and this is primarily coming from our spina bifida population. So, different population, but we have a lot of data or we have a lot of children who have spina bifida who are on things like Oxybutynin is very common. Which is one of those medications.

[00:30:29] And if you talk to their parents and you try them on and off of Oxybutynin, there are a lot of behavior changes. So, it's very interesting. So, clearly something is going on. I mean, this is something that affects how nerves communicate with each other, correct? So, it's not too surprising. We have actually in our spina bifida population moved a lot of them over to beta-agonist. Especially in the last five years as beta-agonists have become more prevalent and we've gotten... it was easy in our older patients who could take pills and now in our younger patients, they're making granules and things that little kids can use. We've started to move a lot of them over to beta-agonist. Yeah.

[00:31:22] **Audience Member 2:** So, we were talking about bladder continents improving two three years out from their initial onset of TM. Do you see that despite improvement in their lower extremity function? So, if there is no lower extremity function or increase in their function, do you still see improvement in their bladder function?

[00:31:49] **Dr. Micah Jacobs:** So, unfortunately, there's not a great link between those two. Again, anecdotally, I think our patients that it seems like it's less likely that they're going to have good recovery of their bladder function if they don't have good recovery of lower extremity function. But there weren't a lot of really good predictors in our group of patients that I showed you other than that deep tendon reflex.

[00:32:14] **Audience Member 2:** And like our granddaughter, what we notice is that she seems to have increased sensation when we are catheterizing. Does an increase in sensation, I mean, should we be concerned if we've not seen any improvement in her motor function?

[00:32:33] **Dr. Micah Jacobs:** So, I would be reluctant to say don't try, right? Because I think that there are lots of patients that surprise us with and so we are very bad at predicting things I think personally. So, I always tell people to kind of go through your regular emotions and still just catheterize. And then at some point you might find that someone's independently urinating and you still catheterize and once you get to the point where you're like, we put the catheter in and there's nothing there. It's like, maybe we ought to stop catheterizing, you know? Most of the time the patients tell us that, you know, like this is useless.

[00:33:10] **Audience Member 2:** [Inaudible]

[00:33:12] **Dr. Micah Jacobs:** For sure. Yeah, that's fair. Yeah, and at some point sometimes it's worth kind of revisiting and giving someone a break on things. And so, it's good to kind of keep communicating with your urologist to say like this is what we're doing. Hey, is it worth maybe coming off of this or that or trying this or that? I think I'm over. So, thank you guys.