

Speaker 1:

Welcome to Optimal neuro|spine Podcast, a podcast about optimizing our brain and spine in health and disease. Each episode, leading neuroscientists, neurosurgeons, educators, patients, spine care, and quality improvement experts discuss their research, experience, emerging science, surgical advances, and insights about how to optimize neurological and spine care. Now here's your host, Dr. Max Boakye.

Dr. Max Boakye:

Welcome to the Optimal neuro|spine Podcast. This is the first episode of the year 2022. I hope all of you are having a happy new year. We have great schedule for you this year. We launched a show last year, had a terrific time speaking to a number of experts in a variety of different areas, and this year, we start our first full calendar year. My guest today is Dr. Andrea Behrman, who is a professor of neurological surgery at the University of Louisville. Dr. Behrman is a physical therapist and researcher specializing in pediatric neuro rehabilitation, and is currently the director of the University of Louisville's Kosair Charities Center for Pediatric NeuroRecovery at the Frazier Rehabilitation Institute. She's co-director of the Reeve Foundation NeuroRecovery Network. She oversees both a clinical program as well as a research program targeting recovery for children and adolescence swift spinal cord injuries ages 1 to 17 years.

Dr. Max Boakye:

The clinical program focuses on evidence and recovery based physical and occupational therapies that have been fast tracked in translation from science to clinical practice. Her research program develops and investigates new strategies to advance recovery for children with pediatric onset spinal cord injury, and primarily uses activity-based neuroplasticity and an understanding of the role of the spinal cord in controlling movement. Her research has been extremely successful. Her work has been funded by the NIH Department of Defense VA in the past, as well as the Craig Nielsen Foundation. Also, in the past, she's had funding from the Helmsley Charitable Trust, Foundation for Physical Therapy and the Florida Brain and Spinal Cord Injury Research Trust.

Dr. Max Boakye:

So my real pleasure to speak to her today about pediatric spinal cord injury. This is a area that is of interest because the majority of spinal cord injury you hear about is usually adults spinal cord injury. So it's really unique to have an expert who is doing really extraordinary research in pediatric spinal cord injury. Dr. Behrman is also my colleague here at the University of Louisville. Dr. Behrman, welcome.

Dr. Andrea Behrman:

Thanks. Thanks for the introduction and for inviting me to be part of your podcast. I appreciate it.

Dr. Max Boakye:

Did I miss anything in your training and background?

Dr. Andrea Behrman:

You know what? I think we should add the Kentucky Spinal Cord Injury Research Board. I was just funded by them in the last year or so. Because we're part of that community, it'd be nice to recognize them.

Dr. Max Boakye:

So that's right. That was a multimillion dollar grant, is that correct?

Dr. Andrea Behrman:

Because it's from the Kentucky local state spinal cord injury trust fund, those grants are typically three years and 300,000 or two years, 200,000. So we receive back to back grants, which is pretty unique, and the grants dovetail on one another, and they're pediatric grants. So I'm very excited about that. It's the first time I've received a grant from them.

Dr. Max Boakye:

Excellent. Tell me a little bit more about your lab and what your research focuses on.

Dr. Andrea Behrman:

So our lab works with children. I'm going to try and think the youngest we've had research is probably three years of age, up to 18. And we're using, as you mentioned, the principles of activity dependent plasticity, as well as a real understanding of the intrinsic biology of motor control to develop and apply new interventions. And the interventions are targeting to activate the neuromuscular system below the injury in children. And our aim is to enhance their physical capacity, their health and quality of life. I will tell you as a physical therapist, I probably predominantly focus on the physical realm. So being able to move your limbs, your legs, trunk control, the respiratory system. But I really appreciate collaborating with colleagues that are investigating other physiological systems as well.

Dr. Andrea Behrman:

So the lab is really based a lot on interventions. We have developed measurement instruments as well. Those are trying to, again, look at your neuromuscular capacity and not using compensation. And something unique to our lab has been to develop equipment that supports our intent providing these interventions. So sometimes the pediatric market and the equipment isn't tailored to this. So a lot of equipment is an end unto itself, not a means to an end. And so we needed to develop equipment that supports this mission, and that helps children progress and change their capacity across time.

Dr. Max Boakye:

An example of an equipment would be like a treadmill, or?

Dr. Andrea Behrman:

Right. So the first piece we did was a treadmill and that was in partnership with another engineer, Tommy Russell, here at the university. That was externally funded, and we developed a pediatric treadmill and harness system. And as many treadmill manufacturers, when we first talked to them about helping us, they weren't really interested. They just said, "Use the adult treadmill." Well, I'll just give you one example, a two-foot wide treadmill with a two-year old or a 10-month old or 15-month old in the middle of the treadmill, it's really hard to access those legs. There's a lot between the therapist and the child's legs. So even reducing that from two feet to 14 inches was important. And then there's a lot of other elements that help support the therapist, as well as the child. The same thing with the harness. We want to make a harness that all the way down to a 15-month old and would allow for progression of trunk control. So these are novel to the equipment industry, if you will, relative to pediatric spinal cord injury.

Dr. Max Boakye:

So when you are studying these kids, are you looking at their physiology and neuroplasticity and using that to guide interventions?

Dr. Andrea Behrman:

So I would say that we are trying to develop an intervention and we're assessing its impact looking at things like EMG. So what's their muscle responses activating a system that we thought couldn't be turned on below the lesion. We're looking at the movement, we measure forces. So the position a child is with their posture. Are they more stable? Are they more wobbly, so to speak? Can they control themselves if they're externally perturbed? What does that look like? We have respiratory measures that we may assess also. So those are a little bit more of experimental outcomes, as well as sometimes clinical measures that would tell you has their trunk control changed or improved.

Dr. Max Boakye:

In a nutshell, tell me why your research is important. I mean, what is the niche that you're feeling and how many researchers are doing this type of work.

Dr. Andrea Behrman:

From a pediatric standpoint, it is very hard for me to tell you there's another researcher in the world doing this, and there is another that is approaching this problem. So our advantage is we have a clinical arm and a research arm, as you described. And the clinic for years has been driven by our understanding that spinal cord injury was permanent, spinal cord was just a conduit, just carried signals, and there was little you could do after an injury to improve the outcomes for a child. So research really looked at outcomes from that vantage point, from function, independence, other things like that. This really came to be because of the work that has been done in adults previously. So uncannily, I had a study of adults and had an opportunity to enroll a child in that study, and it was kind of serendipity that it happened, and that child was not ambulatory, but by the end of the study was walking. He had been non-ambulatory for 16 months.

Dr. Andrea Behrman:

When that happened, I was like, "Whoa, this is amazing." And I'd really done only research in adults with spinal cord injury up to that point. So some other aspects of that study made me think, I need to switch to pediatrics. There's nobody doing work in children, and it's not easy work. It's made easier by those who are doing work in adults. And then we try and use some of those principles that they're unraveling and seek ways to test and use them also in children. So how do we differ? We are focused on what you would say is recovery from an injury, not building compensation strategies or braces or teaching you new ways to do things. We're trying to access the nervous system to use those biological principles that may be redundant or available for you to actually recover a capacity.

Dr. Max Boakye:

That's fascinating because you are also the core director of the Christopher Reeve NeuroRecovery Network, and I believe that's mostly adults. And so this program that you have is an innovative neuro rehabilitation for kids with spinal cord injury. And it looks like there hasn't been much focus in the spinal cord injury world on this area, it looks like.

Dr. Andrea Behrman:

I would agree. I think a gentleman or a physician who is working with providing stimulation to the diaphragm is one of the closest to us in trying to stimulate something and have it be active, not have it atrophy with the goal of removing that stimulation in the diaphragm taking over. So that's a physician who's doing that type of work. It is novel. We started the NeuroRecovery Network with adults, some teenagers, and now we do have a site in New York, Pittsburgh, London, and a developing site in Australia that are actually following the principles we're providing in the clinic and having very good results. So it is blossoming slowly.

Dr. Max Boakye:

That's fascinating. You did briefly touch on how and why you decided to focus your research in this area. It sounds like you didn't grow up thinking, oh, I'm going to at work. I'm going to be a pediatric spinal cord injury, a neuroscientist. It's something you started in the adult world, and now you've evolved. Do you still do adults or now all of your research is in kids?

Dr. Andrea Behrman:

All of my research is in children and adolescences. I do consult with Dr. Harkema for part of their adult neuro recovery program and lend some assistance and guidance to that program. But I'm totally focused on children now.

Dr. Max Boakye:

What is the epidemiology of pediatric spinal cord injury? What are the typical causes? Is it different from adults?

Dr. Andrea Behrman:

It's interesting. It's about 50% motor vehicle accidents is what's reported in children. If you go to the literature and adults, you're going to see more things also like falls. Falls has become a huge aspect in adults, but not as much in children. You can account for that with the aging population for adults. But we've never had 50% of motor vehicle accidents in children here. We get children not only acutely, but also quite chronically. So there are a lot of non-trauma type causes everything from a tumor, abscess, hematoma, spinal stroke. Probably the most recent cause of spinal cord injury in children is something we knew about in the '50s and '60s, which is a polio like virus. It's called acute flacid myelitis. It's really been with us maybe the last six, eight years. Only about 600 cases in the United States, but it has a presentation of affecting the anterior horn cell. So it's predominantly a lower motor neuron injury.

Dr. Andrea Behrman:

You can have a mixed injury. So when you have some sort of inflammation at the site, it can affect the spinal cord proper. In one child, you can have an upper motor neuron lesion, as well as a lower motor neuron lesion. These can be quite severe all the way from having a child without neck control, respiratory capacity, to involve all four limbs, to just involving one limb.

Dr. Max Boakye:

What is the life of a kid with pediatric spinal cord injury like?

Dr. Andrea Behrman:

I think answering that question also depends upon when you are injured. A lot of people think, oh, the child, they must be very depressed. If you're injured early in life, children, what they want to do is play. And they will readily adapt and find a way to play. I think it's the parents who are traumatized, if you will, by what's happened to their child at whatever age, because they had tremendous expectations and visions and hopes for their child, and those are radically changed by what's happened to them. And the parent very quickly understands the impact, not just physically, but on other systems, bowel, bladder, sex. I mean, but life is just not what it was 24 hours ago.

Dr. Andrea Behrman:

So I'm going to tell you that it's interesting, I think children adapt. I think the hardest time in their life is when they're injured as an adolescent. That's at the time you were trying to become independent, doing things on your own, and all of a sudden, you're dashed almost into infancy again, because many of the things you could do for yourself, you can't do anymore, or you're learning how to do it a different way. Just when you were trying to understand your own body image, it's all changed. You were running down a basketball court yesterday, and now you're sitting in a wheelchair or in a hospital bed. I think those teen years are very tough psychologically on children. And then how they cope with a transition into adulthood is key for those individuals.

Dr. Andrea Behrman:

So I'm going to tell you it's very different for a family. I think that's the thing to think about when you're injured as a child, the impact on the whole family, the life of a family, as well as the child. And there's a lot of risk physically about being injured as a child, but they tend to adapt much more readily than the family and the adults.

Dr. Max Boakye:

I imagine it's a little bit harder on the family psychologically, but also on the child. For example, they have to stray cath of bladder function, the bowel. Let's say an adult may have the use of their hands. If their hands are not injured, they can be trained to do some of these things, but for a child, the family may have to take care of that for a number of years, right? So that puts a lot more dependence and more is required from the family point of view, right?

Dr. Andrea Behrman:

Absolutely, Max. Again, you think in a way as a child develops and grows and develops independence, the role of the parent changes. The parent starts out as a major caregiver in infancy and as a toddler, right? Helping them dress, brush their teeth, hygiene, whatever it is. So depending upon the age when your child's injured, the parent becomes a caregiver again, and has to take care of these things, and children can learn them. And between five, six, and seven years, some of these things are taught for a child. And certainly by 10 and 11, you expect they dress themselves, do some of the self-care things from hygiene or even cathing themselves. Having someone at school to cath a child becomes important. Some of these children go to school with a nurse so that a nurse is even monitoring them for autonomic dysreflexia.

Dr. Andrea Behrman:

You can't expect a school teacher, whether a class of 20 to 30 students, to be monitoring that. So some children even have a nurse that goes to school with them to monitor for that, assist with cathing, or other positioning needs throughout the day. So life is very different. Access to playgrounds differ for

children, access for the school differs. I mean, can they get into the school? Can they get onto a playground? Parents are often seeking different ways for their child to participate. But you mentioned some of the physiological things, Max, everything from having to cath, having some sort of bowel program, those are pretty similar to adults in a way, as far as some of the daily aspects of life of a child with a spinal cord injury.

Dr. Max Boakye:

Do they have an autonomic blood pressure cardiovascular instability like adults do?

Dr. Andrea Behrman:

So it's interesting when you look at some of the what's similar and what's different in children. They do have autonomic dysreflexia, but you can talk to an adult and have them be aware of what's happening, right? You can say, "These are the things you need to be aware of if you develop a headache." So you can talk to an adult. With a child, they can be young and not know what's happening to them. So you actually have to teach others to watch. And then we'll try and work with parents because things are a little bit different. Sometimes a child's ears just turn pink or red, and that's the response. Goosebumps is another one. The flushing of the neck is probably similar to what you see in an adult, but not all these things are the exact same. A child having a headache, they don't even know how to express what's happening.

Dr. Andrea Behrman:

So being aware or knowing that that's possible, or if a child's experienced it before, and being able to share that information again with a nurse or somebody else who's monitoring it and then checking their blood pressure at those periods. They have that. They don't have orthostatic hypotension, unless you're injured as a teenager. So I think that really has more to do with the volume of blood circulation. When we stand them up, when you're starting to be 14, 15, 16, you might show signs of orthostatic hypertension, but we haven't seen it in a 2-year-old 5, 6, 7, any of these children. So that's a little bit different.

Dr. Max Boakye:

What about urinary tract infections?

Dr. Andrea Behrman:

I don't know if there's a higher rate in children. They certainly have UTIs, and I'm not sure in the adult population. Parents are so frustrated by, "Hey, I have to wait 48 hours for a test to come back to tell us what antibiotic we ought to be using, and hey, been using the wrong one for 48 hours." And so that delay is challenging for them and for the child. I don't know that the incidence is greater in children. Again, as you describe, the parents are a caregiver, a nurse, as someone is doing the cathing for them. Two things that are different in children are the development of scoliosis. So that rarely happens in an adult. Their spine's well developed, they've grown fully teenagers, but the younger you are at the age of injury, more likely you are to develop scoliosis.

Dr. Andrea Behrman:

So 100% of children injured under age five will develop scoliosis. And the closer you are to age one or infancy, you're going to develop it. What's that mean? Simply you develop a curve greater than 10

degrees, but you're more likely to develop more severe curves because you have a combination of growth and then lack of trunk control or ability to sit up, right? And so children are at great risk for scoliosis, and then they're at risk for having surgery. Surgery's not a great solution to scoliosis. Just because you fix a spine or put rods in, it doesn't mean, hey, we've solved that, that takes care of it. Children often end up less functional, fall over easier, they lose some trunk control, there's infections. They have to redo the surgery or if there's growth or use growth rod. So it's not a great solution.

Dr. Andrea Behrman:

They're also at risk under age five for hip dysplasia. So their hip joints haven't formed as they would have appropriately through weightbearing and activity. And so the femur is likely to slip out of the hip socket because it hasn't been formed, kind of like a half moon there. And without the muscles well activated, it can dislocate.

Dr. Max Boakye:

That is interesting. So let's say a kid comes to the emergency room with spinal cord injury, how are they generally currently treated? I assume after stabilization, they go to, is it a pediatric rehabilitation center or an adult rehabilitation center?

Dr. Andrea Behrman:

They will go to a pediatric inpatient unit first. I mean, they're in an acute care hospital and then they'll go to an inpatient pediatric facility. They're probably not there very long comparable to adults right now. A lot of the work is being done is to teach the family how to take care of a child, and then get them perhaps what equipment they need, and then they're sent home. But I want to reiterate, Max, that there's a lot of children that that's not how spinal cord injury comes about. So they have cancer or a tumor and they're treated primarily for that tumor, they're in some sort of cancer institute. And this is what parents have said. They leave the cancer facility with good news, "Your child doesn't have any cancer. Oh, by the way, your child trials paralyzed though." And that second step, they're not often directed to the next phase. And many places say, "Hey, just go to your local pediatric clinic, you'll be fine."

Dr. Andrea Behrman:

And I think the fact that we see 50 or 60 kids across time or in a year through various mechanisms, make us much more of an expert than someone who sees a child with spinal bifida, and maybe this is the first child they've seen with spinal cord injury ever. And so a parent feels lost at that stage. And so there are many children that are injured in, what I'm going to say, novel ways, or they went to the hospital because there was an infection. And so they're being treated for that or an abscess. And by the way, there's been pressure on the spinal cord, we've removed that, done surgery, and now you have a paralyzed child. They don't always go to a rehab program. They may be sent right home, even looking at the age of the child. Children rehab, inpatient rehab is really much more so made for adults than long term care for children. They might be there two weeks or so, but their aim is to get them home.

Dr. Max Boakye:

That's interesting. And somebody needs to be monitoring whether they're developing scoliosis and all of that. As you mentioned, it's a complication depending on their age. Is polypharmacy a problem in kids as it is in adults?

Dr. Andrea Behrman:

So I'm going to address what my knowledge knows best, Max. And that I look at two drugs that are often prescribed for children and that's either Baclofen or Botox. And Botox being an injection, and Baclofen, whether it's oral or a spinal pump. Those two are often seen as mechanisms to decrease spasticity. I don't know of other medications that are used a lot in children. And if so, they're typically there might have been Gabapentin or something pain related, but they do get those removed fairly quickly. Baclofen and Botox, I think are often introduced quite early. And it is just a historical perception and assumption that spasticity is a negative thing for function or independence, and we can eliminate that.

Dr. Max Boakye:

So looking back, how long have you been working in this field, this type of research?

Dr. Andrea Behrman:

This type of research since about 1997.

Dr. Max Boakye:

Oh wow. That's almost three decades. Looking back over the last three decades of your work, what would you say has been your most important accomplishment in this research? I came across one of your recent papers in Nature Communications, I think, published in 2021. Maybe you might want to talk a little bit about that, but kind of in your opinion, what you would see as your most important contributions to date.

Dr. Andrea Behrman:

Okay. I'm going to go in chronological order. And so we'll end with the Nature Communications, if that's all right.

Dr. Max Boakye:

Yes.

Dr. Andrea Behrman:

Early on, probably the first was a case study and I think it's published in 2008 likely, and that was the child who was part of another adult study, who could not walk after 16 months of injury, and ended up being in a study where we were using locomotor training, activity-based training. The child was training every day on a treadmill. I think at that point it was 45 sessions. He hadn't walked again in 16 months. He couldn't stand on his own. His trunk was involved. He did show what we would call some potential residual brain influence below the lesion. Meaning, if I asked him to straighten his leg, or like he was going to kick a ball, he couldn't do it right away. He couldn't do it like you and I would, like very fractionated movement. But with some intention, his entire leg moved into extension at the hip, the knee, and the ankle.

Dr. Andrea Behrman:

It wasn't rapid, it was very slow, and you almost would've said, "Gosh, was that related to when I asked you to move five minutes ago?" So that's the degree of movement capacity he had. So I was very early on in translating this from adults to children. I was learning about how to engage a child. It's very different having... This child was four, four-and-a-half at that time, having a child on the treadmill for an

hour and then working with them half hour afterwards. You can't just tell them, "Do this, do that." Everything has to have a game or play incorporated into it. So the fact that that child at session, I think it was around 23, that he took a step relative to the cue that we were giving him. But ultimately, the child learned to volitionally walk. On his, own initiate steps, used a walker.

Dr. Andrea Behrman:

His walking is not as refined as yours in mind, Max. So a lot of his steps were like a lot of flexion in then extension, mass flexion, mass extension. He kept improving till he was 12 years of age, but that first study gave me tremendous hope about what was possible with children. Also, about that study was that all six children in that study developed trunk control. And we had no idea that that was going to change. So no intent to study it. That wasn't part of the hypothesis, and suddenly I'm going, "Wow, that may be more significant than a child walking." It was at that stage that I thought, I'm going to shift from adults to pediatrics. So that was a very important study.

Dr. Andrea Behrman:

I came here to the University of Louisville where I could develop a clinic and have more of population-based research, if you will. I mean, not so large a population as with the adults, but we collected a clinical cohort across time. That's a paper by Laura Argetsinger, and that was on the responsiveness, an instrument called the SATCo, the Segmental Assessment of Trunk Control to changes in children's trunk control across time with locomotor training. So everything to date has been that a child's trunk isn't going to get any better, I mean, that ability to sit upright. Well, we show that on a scale of 20 at very clinical scale, that the average change is six points on that scale. And it turns out to be incredibly meaningful to the child and parent. So what that means is, as a parent said, "I can sit my child in a grocery cart now and push her around and not have two carts, where I'm pushing a child in a cart and I'm pushing my grocery cart at the same time, because she can sit up now. I can rest her on my hip as I walk because she doesn't fall out of my arms."

Dr. Andrea Behrman:

There's many aspects to the child's being able to use arms to play. They can pick up toys without falling over. And I think this may, in the long run, have an impact on the development of scoliosis as well. I had high hopes, Max, that we were going to have more and more children develop the ability to walk after what we found in a early study, where three out of six children walked, it was a pilot study. We haven't had that same ratio, like even at 50%. I'm going to say it's lower than 10% will walk after an injury. So that has led us down a path where we're looking at combination therapies. That leads us to the Nature Communications article.

Dr. Andrea Behrman:

It's the first article to address the safety and feasibility of using transcutaneous spinal stimulation in children. As you well know, the work here by Dr. Harkema, yourself, and others has been using predominantly epidural stimulation. [Erie Garris Saminko 00:30:56] has been using transcutaneous spinal stimulation in adults, and he has introduced that to adolescents and children with CP. So in an effort to boost our outcomes, to improve them, we wanted to look at using surface or transcutaneous spinal stimulation as an adjunct or in combination with our locomotor training to enhance our comes. So the first thing we wanted to do is see if we can even apply it in children. And what does the safety and feasibility mean? It means that first off, that a child tolerates it, it's not painful that they come back the next day, they don't cry, or they're not upset that we can actually do it and that it does no harm.

Dr. Andrea Behrman:

So an electro, when you place it on and provide stimulation, sometimes when you take it off, it's pink or red under the skin. We didn't want pink or redness, we didn't want burning, we didn't want any kind of secondary effects that would be harmful. And so we wanted to address that. And so we did, and it's a small population of eight children, but they were aged 3 to 14, and they had numerous opportunities where we're using the stimulation to give us feedback and for us to monitor them. The key points of the study is it was safe, it was feasible, and there was some proof of principle that we could apply it and change a child's immediate trunk posture. It doesn't mean they had trunk control immediately, but we could change their trunk posture. So, that gave us kind of the go ahead to use this in other ways. And we have three funded studies right now that we're looking at, upper extremity function, trunk control, and stepping in children that are non-ambulatory, using the transcutaneous spinal stimulation.

Dr. Max Boakye:

Fascinating. What is it like working with kids with spinal cord injury? What gives you the most satisfaction? I mean, emotionally, do you have to like give them candy to participate in the research programs? Are they determined, resilient? What is their mental motivational levels like?

Dr. Andrea Behrman:

So most of the time, it's the same as what we do in the clinic. Kids are motivated to play. And so as long as we have things that are of interest to them, exciting to them, grab their curiosity, they're willing to do things. But in research, sometimes there are things that we have to go through, like putting electrodes on your skin, putting motion sensors on you. I mean, we have to prepare you. Now, what we've done is made it, so we do that in about 30 to 35 minutes, and I really, we strive to make that as quick as possible and as effective and efficient as possible. The research itself can run another hour and 15, 20 minutes. I always limit the time we have with the child to two hours because after that, we're going to lose them.

Dr. Andrea Behrman:

So that's one of the challenges itself. Trying to find the right size electrodes that are going to fit on children is another thing, and having small stature in children. And so how do you measure things in a smaller scale or having, again, like electrodes that dress smaller muscles and go across larger muscle groups. I mean, they're just things like that. But working with children, it actually has been, we have to come up with strategies, like having a chart in front of them, if they can read. And we're saying, "We're going to do five things today. Here we go, one, two, three, four, five." We check them off as we go, we play a game in between. So we stop being focused and we throw all around the room a minute. We change it up so they can then focus for a period of time.

Dr. Andrea Behrman:

Likely the greatest challenge we've had is most recently doing this stimulation and stepping study, because we're asking the children to intentionally do something that is very challenging. So I'm asking the actually to try and move their legs. We don't always ask a child to intentionally do something, and I've even had a child turn and say, "Why are you asking me to do that? You know I can't move them." She's been paralyzed for five years. She's well aware that they don't move. That's a nine-year-old. And we've been through a reform consent process with the parent, the child, everybody knows why we're doing this, but it is challenging for... And even they're saying, "What do you want me to think about? I don't exactly know what that is." So even in this process, and this is a pilot study, I'm saying, "Think

about kicking a ball, think about cycling your legs, swimming." But it's been five years since the child moved. What is the focus of that intent that they're telling their legs?

Dr. Andrea Behrman:

And I've talked to the adult team, they'll say the same thing. It's not unique to children. The adults ask, "What do you want me to think about?" So that's probably the greatest challenge we've had. Max, as working with a child, when we have to get them focused, a lot of the time we can have them disconnect to what we're doing. They don't have to be as engaged in this particular study. We have them engage with us, and then we want them to be disengaged, like I don't want their focus on their legs. That's incredibly easy with them to do that. It's when we have them focus on something that is very challenging, and they even perceive that they're unable to do it.

Dr. Max Boakye:

What is the earliest after injury that you take a child into your research program?

Dr. Andrea Behrman:

The earliest after injury would be after they've been discharged from acute care... Well, let me put it this way, it depends upon the study question, right? So a lot of the time, we ask questions for children in what you would say is a chronic stage. That's certainly debated whether that's six months after an injury or a year after injury. And why do we do that? Is because every reviewer of every paper and every grant says, "How are you going to differentiate between what someone would call natural recovery and your intervention?" Or in the case of children, an argument that's presented to us often is, "Oh, well, that's just development." It's hard for me to understand that children develop out of a spinal cord injury. I've never seen that, but that argument is presented to us a lot.

Dr. Andrea Behrman:

So if you're trying to differentiate something, you often select a child that is in the chronic stage, so I'd say a year out, to participate in research, because at that time, they're not expected to improve, historically, they don't improve. That said, some of the interventions that we're providing in those cases, once we indicate that they're valuable and make a difference and effective, we would instigate those early in a child's recovery before they were in the chronic stage.

Dr. Max Boakye:

What is the future of treatment of pediatrics spinal cord injury? Do you see these methods that you're developing to be widely disseminated, let's say, in 10 years? Or what's the timeframe you think for that?

Dr. Andrea Behrman:

Oh, Max. The interventions that we have to date are not widely disseminated already. It is a challenge for anybody, for the translation of science into practice. And for years, the expectation, and I would say for adults as well, has been that, and the approach has been much more of an orthopedic approach. So Again, trying to prevent scoliosis while we're going to do surgery, trying to help hand function, we're going to do tendon transplants. So much of the work has involved some sort of surgical intervention as opposed to a neural or activity-based intervention, where you're actually trying to engage the nervous system below the lesion. That's a big paradigm shift. And I think we're still there when it comes to the interventions we have today. Trying to look at combining interventions is what our next step is really

from a research standpoint would again be a challenge because you have a different expectation and a different intent than what is predominantly presented in the clinic today.

Dr. Andrea Behrman:

I would also think we need specialized centers where children go. You can't see a child once a year and develop an expertise in trying to deliver this type of therapy. You can think of that. The same is epidural stimulation. You're going to have to go to a specialized center to do that, at least for a good long time before that's offered at a local facility. So I am hopeful because there are sites that are already implementing some of these interventions, but change takes time, and it's also not only what's presented in physical therapy schools, what's presented in medical schools, nursing. I mean, there's all different aspects of this that would change what is provided in typical education and the expectations and textbooks, things like that.

Dr. Max Boakye:

Let's say, for the parents with a kid with spinal cord injury, what is a take home message or points you'd like them to know? And also for physicians that are taking care of such patients.

Dr. Andrea Behrman:

So number one, I'd say there's hope, and that's good for... Parents often tell us they feel they were denied hope, that they were told their child has a spinal cord injury and that's that. And there's no other intervention or therapy that will help change the outcome. A mother just today was telling me that of all the things I've talked about, working arm and arm between the clinic and research, accelerating research findings to clinical practice, building a community where parents can talk with one another, she goes, "Andrea, the thing that matters most and has mattered most to us as parents is that you provide hope, and that hope is real, hope is scientifically-based, and it's not taken away from us. And we're not thinking that you're actually going to cure them and they're going to get up and run. We know that, but there's hope for our child to be quote "better."

Dr. Andrea Behrman:

So I think I'd like to give that to the parents. To physician, we did a presentation a while back and showed a child that was injured. I think it was to neurology residents, and we showed a child who was injured at age three months, a C5 injury. We didn't see that child till she was three years of age. She had incredible recovery as far as trunk control, respiratory capacity. She had been on mechanical ventilation multiple times before and now she wasn't. She'd moved from a power chair to a manual chair. And when I stopped the talk and I asked them for questions, they had none. And I said, "Well, let me ask you a question. Is there anything surprising that you saw today?" And they said, "Yes, we never would've predicted that that would happen. How did you predict that?" And I said, "I can't predict it now." "How did you know how to treat her?" And I said, "I would treat every child with a spinal cord injury."

Dr. Andrea Behrman:

I don't think you can discriminate yet between those or that you would say are responders and non-responders. What you need to do is refer them to a clinic that is doing activity-based restorative therapies, and let us be the experts, and let us continue to figure out if there are responders and non-responders. If I have a non-responder, I'm going to try and figure out another solution. It's just that we don't have the answer today. It doesn't mean that they'll never respond, it just means today we don't. So I would want to encourage physicians. They also wanted to know what level or age or things like that

would predict, and I said, "I don't think you can do that because each one of you would have not referred this particular child to us based on those criteria." And so I think we to be a little more flexible and give children the opportunity to improve.

Dr. Max Boakye:

That is amazing. A couple of more questions for you, Andrea, One is obviously this is your unique scientist doing amazing work. How are you training the next generation of cloning yourself for more people like you? And the second question is my magic wand question. If I give you a magic wand, how would you use it?

Dr. Andrea Behrman:

Okay. So how are we cloning? So a couple ways. When it comes to research, we do have graduate students, postdocs, anybody interested, look us up at www.victoryoverparalysis.org, and there are ways to get in touch with us. I would like to see more graduate students, more postdocs. You don't have to be a physical therapist or an occupational therapist. We've had people with physiology backgrounds, with exercise physiology, physiology, anatomy backgrounds come to us. And I really appreciate those who have a very strong neuroscience background, who've looked at mechanisms as key, or even we've had someone that came from an animal model background and then crossed over to the human side of research. So I'm thrilled to have those, have them go on to other faculty positions.

Dr. Andrea Behrman:

So we had Goutam Singh that worked with us on the first Nature Communications paper. He's just gone to a position at Spalding University here. Anastasia Keller is doing a second postdoc with Adam Ferguson in California. When she's looking at large databases, one of the great things there is we're combining with Adam to develop a pediatric large database. And so we're collaborating with Adam and having Anastasia, having a foot in both labs, has been able to connect those two together. I have a graduate student who's now at the University of Florida or a former at student doing research with David Fuller and others, respiratory capacity and implants for the diaphragm as well and adults with spinal cord injury. So keeping these individuals training with us and sending them back into the academics. Darren Atkinson is at university of St. Augustine in Austin, Texas. He's a predominantly teaching physical therapist there.

Dr. Andrea Behrman:

So if I look at it to training the next generation of researchers, that key is key. I think another aspect is we're actually training the next generation of therapists. So our therapist here working with us in the clinic also work with us in research. And so by working with us in research, they're preparing the path to fast track science into practice. And so they're helping at times to say, "How am I going? How are we going to be able to do this in the clinic? Let's start thinking about that, even though we're in a study. How are we going to train people? What will this look like in the clinic?" So the other thing is they bring ideas to us as far as research of the things that frustrate them or ideas they may have.

Dr. Andrea Behrman:

So we're training that generation. We hold biweekly calls with the pediatric sites across the U.S. and the world to standardize what we do. And so we keep training up clinicians using that instrument to empower and enable others to provide this therapy, or as we translate therapies into practice to be able to do that with children. That was your first question. Your second was-

Dr. Max Boakye:

The second, magic wand, yes.

Dr. Andrea Behrman:

Okay. What would I do if I was given a magic wand? So probably a couple things, but one of the first comes to mind is you may be well aware of St. Jude's Hospital for children with cancer.

Dr. Max Boakye:

Yes.

Dr. Andrea Behrman:

And how they're able to with funding, no parent ever pays for anything, lodging, travel, healthcare, bills. They are worry-free when they bring their child there. I think that would be a dream because there's so many children across the United States who can't access care. Medicaid doesn't easily allow you to cross state lines for care. So many families have a child in a state where there's no specialized care for their child. I'd love to be able to offer that or have that capacity where families could come and be much more readily receive services than they are at this point. And to be able to provide the immediate care right now, I think being able to have children across the United States and even the world access care readily without those barriers.

Dr. Andrea Behrman:

The second I would say is how we develop strategies to turn on the nervous system below the lesion and capitalize on plasticity beyond the clinic. So I'm really going at this from two angles. One, come to the clinic and let us help you, two, I'm saying, what can be provided or used in the home that families can still turn on the nervous system of a child easily in the home? They can't become a therapist, they can't do things to treat their child or do all these things, but is there a way, a more simple way, an efficient way that we can help them turn on the nervous system in the home environment? That's my use of the magic wand today. Thank you.

Dr. Max Boakye:

That's amazing. That's fantastic. And I hope all the billionaire philanthropist are there listening. Andrea, I want to thank you. You are a unique scientist doing amazing work, and I really want to thank you for starting 2022 on this high note. Really looking forward and wishing the audience a happy new year, a year of great accomplishments and great blessings. I want to thank Dr. Behrman for coming on and sharing a little bit about the world of pediatric spinal cord injury. All the information on the Nature Communications paper would be posted at our website, and also links to how you can reach Andrea if you want to refer a patient, a kid with spinal cord injury. Andrea, thank you very much.

Dr. Andrea Behrman:

Thank you so much for this opportunity. Happy new year.

Dr. Max Boakye:

Happy new year.

Speaker 1:

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