Social Isolation is a Biological Risk Factor in Recovery after Maternal Birth Injury

Speaker 1: This program contains graphic images and discussion of medical procedures. Viewer discretion is advised.

[Music]

Lindsey Burnett: Hi, I'm Lindsey Burnett. I'm an assistant professor here at UC San Diego and a physician-scientist. My talk is entitled Social Isolation as a Biological Risk Factor and Recovery After Birth Injury.

Grateful to Mariana for not having to introduce pelvic floor disorders. They're pretty horrible. One in four women suffer from them. These are things like urinary incontinence, fecal incontinence, and pelvic organ prolapse. She also has the same slide that I do, showing that many women consider these worse than death, and also showed a picture of them for us too.

These are these muscles that are in the pelvic floor that support our organs of the pelvis, and we can look at their muscles, both in cross-sectional area, which he showed earlier. You can see pictures with the laminin staining in green showing big muscle fibers is good, and small muscle fibers is bad. She also alluded to the fact that vaginal delivery is a sentinel event for these pelvic floor muscles. As you can see on this picture on the lower right, they undergo stress and strain exceeding 300% of their resting length, and so horrible things can happen to them. Yet at the same time, there are some women that have pelvic floor disorders after this birth experience, and there are other women that don't.

The focus of my lab is really on the things during pregnancy and postpartum. Exposures in pregnancy and postpartum that influence how these muscles adapt during pregnancy to withstand strains, and how they recover from injury after delivery. With a focus really on medications, there was a poster on ibuprofen for my lab, diet, things like dietary choline and how its role in lower urinary tract symptoms. Exercise. We have an ongoing pilot study for those interested. Then I'm going to focus particularly today on social interaction.

We use a similar model to what Mariana described. These are actually pictures from her lab and rat because she has alluded to it's bigger. But we study it in a mouse model, and these are sections showing uninjured tissue compared to simulated birth injury tissue showing smaller muscle fiber cross-sectional area.

I really wanted to think about social interaction for a very clinical reason. I run the Pelvic Health After Birth program here at UC San Diego. I personally take care of many of the women, almost all of the women that have had third, fourth-degree, and instrumented deliveries in our patient population. One of the things that was really striking about caring for this patient population was this really strong relationship between patients' perception of how traumatic their birth was, and their physiologic recovery.

We use fecal incontinence here as a surrogate marker of physiologic recovery because these tears often involve the anal sphincter. Fecal incontinence signifies that sphincter hasn't completely healed. We found much higher scores of worse perception of their birth trauma in women that are experiencing fecal incontinence, even after that trauma had already occurred, compared to those that didn't.

It made me think about what is the role between emotional health and physiological health. We came up with this hypothesis of, so there's moms, they have either trauma or no trauma during their delivery, and a certain subset of them will have severe physical injuries during their delivery, and women that have emotional support maybe have improved recovery, and women that have poor emotional support may have impaired pelvic floor muscle and anal sphincter recovery. I wanted to think about modeling that in an animal model.

Linking back to Kristen's talk, I thought about this mouse model of social support and empathy, and we designed a series of experiments where we had animals with and without birth injury, so normal birth versus birth-injured, and with and without a socially supportive partner. We've looked at pelvic floor muscle histology along the continuum. I'll show you slides, particularly from day 60, and we also looked at the metabolomic composition of serum to think about small molecules that are mechanistically involved in this process.

Lo and behold, so in birth-injured animals compared to uninjured animals, unsurprisingly, there's very, very small muscle fiber cross-sectional area, and the bystanders here are the comparative group because they're uninjured. But then with social support, there's actually improved pelvic floor muscle regeneration and improved muscle fiber cross-sectional area.

Then we started to mechanistically think about how or why this might happen. You'll see four groups here. The normal birth are in green and blue with and without social support, and the birth injury are in the pink and purple with or without social support. You can see that they segregate very clearly by metabolimic profiles. There are specific metabolites that seem to be very critical to this process, things like 4-Hydroxybenzaldehyde, which has known wound healing properties, antioxidant neuroprotective effects, and has been involved in wound healing processes.

Then also the carnitine network, which is known to be involved in skeletal muscle regeneration. There's particular members of the quarantine network, particularly phenylpropionylcarnitine, it's enhanced in the setting of social support compared to injury. This is just showing how that is so much higher in the setting of social support, akin to a normal birth compared to birth injured isolated animals.

There's a lot of literature out there in other spaces showing that these things might have effects on other systems, but never have been linked to this social support having a direct mechanistic biologic impact. Then hepatic acid also is a microbial metabolite that comes from degradation of plant polyphenols and aromatic amino acids. Again, we're starting to link this to the microbiome and changes associated with that. This has also been linked to gut microbiome in other settings such as neurodegenerative diseases.

I'm just here to say, one of the things that I really I'm passionate about is finding clinical phenotypes, looking at the clinical phenotypes, and understanding the mechanistic biology behind them. This is just a little vignette about social interaction, but there's a lot that we're learning about medications, about diet, about exercise, and how they can influence physiology in the postpartum period and during pregnancy.

Just a shout-out to some of the most important people in my life and to all my lab group. Thanks. [Applause]

Speaker 2: I have a question.

Lindsey Burnett: Sure.

Speaker 2: But what would be the biological like social isolation like carnitine is made on the liver, right?

Lindsey Burnett: It comes from many sources, including diet.

Speaker 2: What would be in your bile, maybe it's not it might take 10 years to figure it out. And what is the biological mechanism?

Lindsey Burnett: It looks like what's happening because we're doing a separate series of microbiometabolim experiments on the experiments that Kristen described is it's probably downstream processing from brain to metabolimic signature systemically, and then alteration in the gut microbiome, and then a feedback loop to metabolomics in other areas. These are likely gut microbiome derived metabolites.

We're still kind of in the process of some of that that are altering host cell metabolism in meaningful ways and creating neurologically active pepides too in the process.

Speaker 3: Chany Kumar from the Maudsley in London did really a large international study and found that in non industrialized countries where there's a lot of social support and there's the relatives and the friends, all the mother does is, I shouldn't say all, but she just breastfeeds and the housework and the meat is all provided. So they have a much lower incidence of postpartum depression. I'm just wondering, has that been looked at with in terms of pelvic floors or the emotional support?

Lindsey Burnett: I think that's also confounded a little bit, and I don't know the epidemiologic literature maybe as well. But by parity, overall parity is probably a hugely different thing in those settings too. And so we know that vaginal parity is also a risk factor. Mariana or Mimi, do you have thoughts on all of that? So they might know the epidemiologic literature from other countries better than I do.

Speaker 4: They also have institutes like that's called the core Carry Quantum Physical Therapy. So they have social support.

Lindsey Burnett: Yeah, depending upon where you are, but family social support is another thing. I think it's also difficult to measure some of this, but the biologic impact appears to be there, and how you can get it, whether it's from community, like you're saying, from pelvic floor physical therapy interactions, from other things. Maybe there's a role for metaboolmic microbiome modification as a way as a substitute since we can't seem to provide it as adequately in this country as maybe we should.

Speaker 5: I have, just a quick questions for you. This is great as usual. I may have missed it, but did you talk about the perception of the birth trauma, and then the actual birth trauma and then the optimum or just the perception?

Lindsey Burnett: The degree of, I didn't show the Table1 stuff, but all the degree of laceration, age, BMI are all identical between these groups. They're segregated. But the PDIs their perception of birth trauma is very different, and that dictates their outcome and is the strongest predictor of fecal incontinence over anything else. Which is kind of wild. Your brain's really important, it turns out. [Laughter]

Speaker 5: Thanks. [Applause]