## NEONATOLOGY TODAY Peer Reviewed Research, News and Information in Neonatal and Perinatal Medicine

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## Dive, Survive or Thrive: A Prescription for Post-Traumatic Thriving

#### Randall Bell, PhD

Randall Bell is a sociologist and economist with Landmark Research Group, LLC. He specializes in disaster recovery projects worldwide. Dr. Bell completed his graduate studies at UCLA and his doctoral studies at Fielding Graduate University. He is the author of "Post-Traumatic Thriving: The Art, Science, & Stories of Resilience."

#### Abstract:

Medical problems and procedures, along with a host of other issues, can be traumatizing. The fallout for post-traumatic effects can linger for decades. In any traumatic episode, the body switches off the parasympathetic (rest and digest) nervous system while turning on the sympathetic (fight-flight-freeze) system. In this mode, the body pumps high levels of adrenaline through the bloodstream. This is a basic survival instinct based on the need to escape the trauma and get to safety.

Trauma causes a well-researched chain reaction. It shifts the brain activity from the outer "human brain" to the inner "reptilian brain" that governs instincts. This can result in a blurred and distorted mental state, so when the trauma ends, many patients remain stuck in the sympathetic nervous state. It is somewhat like a car at full throttle while parked in neutral.

The human body is not designed to have a continual flow of high adrenaline levels flowing through the bloodstream. Yet, this is precisely what unresolved trauma does. This state of perpetual trauma hurts, so many self-medicate with any of the many harmful activities designed to dull the pain. Of course, self-medication only deadens the hurt but does nothing for the underlying unresolved trauma.

Health care professionals have their specialties, yet all should be versed in the fundamental steps patients can take to flip the parasympathetic nervous system back on. Two of the most effective techniques are "grounding" and "sitting in the fire." They are simple practices, can cost nothing, and get right to the heart of healing the unresolved trauma. When included in the overall prescription, both physical and emotional healing can occur.

"It had been nearly 50 years since the heart surgeons at Loma Linda University had opened up my skinny chest to perform open-heart surgery to correct a congenital defect, coarctation of the aorta. The surgery had been a complete success, right down to the fact that the surgeons never had to use any stents or synthetic materials."

#### A Trip to the Doctor

There I was, all wired up by my cardiologist and ready to take a treadmill stress test. Her office had a commanding view overlooking the calm Pacific Ocean. I had just walked five miles that morning and felt great. Now, I just stood there looking at the ocean, all set to go.

It had been nearly 50 years since the heart surgeons at Loma Linda University had opened up my skinny chest to perform openheart surgery to correct a congenital defect, coarctation of the aorta. The surgery had been a complete success, right down to the fact that the surgeons never had to use any stents or synthetic materials.

Since the operation, and up until now, I had enjoyed near-perfect health. My cardiologist plugged in the wires, and then a look of shock came over her face. She said, "Something is wrong." She pulled the jack out, looked at it, and plugged it back in. She then said, "Something is very wrong. Your standing pulse is 150 beats per minute." The look on her face told me that this was not good.

That moment changed everything.

While my outstanding childhood heart surgeons had corrected my physical heart problems, I had unresolved post-trauma issues related to my heart conditions. I had electrocardiograms all the time as a child, and I recall being wired up like a Christmas tree on countless occasions. As a child, my cardiologist was a woman, as was my current cardiologist as an adult. I did not recognize it, but this similar situation had triggered me. While on the outside, I looked fine, my racing heart was a clear sign that my childhood trauma had never been resolved.

It appeared to both my cardiologist and me that I was suffering from PTSD. Yet, I had been entirely unaware of it. After all, decades before the doctors told me that everything was fixed and I was good to go, and wanting to forget the whole incident, I rarely spoke about my childhood heart problems. I wanted to be a tough kid, and I stuffed those distant memories down deep.

When this all happened, I was working on my next project, a book to be called "Post-Traumatic Thriving." I knew that 66% to 85% of the population had experienced at least one trauma by college age. What I did not realize, until that day, was that I was one of them.

I had to go home and re-edit the entire book from the language of "you" to "us." I could no longer be a preacher; I was now in the same boat as the reader. I had to rewrite most of the book, as I had to accept that I was not just researching trauma recovery; I was living it.

With my childhood trauma, I had done everything exactly wrong. I did what many do in the aftermath of their trauma. Specifically, I did not talk about it. Why would I? While the hospital, doctors, nurses, and volunteers were terrific, and they all took excellent care of me, the whole ordeal was tough. As a young boy, it made me cry, and I believed that boys should never cry. I tried, unsuccessfully, to just forget it ever happened.

"While on the outside, I looked fine, my racing heart was a clear sign that my childhood trauma had never been resolved."

#### **Toughen Up Buttercup:**

For years, I have been a volunteer in prisons, jails, and homeless shelters. I am always surprised how often childhood trauma comes up. Child abuse is a huge problem. It is responsible for 50% of depression, 66% of alcoholism, 75% of suicide, intravenous drug use, and domestic violence. If childhood traumas were processed correctly, workplace productivity would go up, and incarceration would go down dramatically. It is clear that if we want a better world, the starting place is to address unresolved trauma.

The "judgment center" of the brain, the cerebral cortex, develops from birth to about age 21 to 26. Damage to the cerebral cortex by trauma or abuse can impact the ability to focus and make sound judgments in adulthood. In my volunteer work in San Quentin Prison, most of the inmates suffered from covert or overt child abuse or were involved in underage drinking or drug abuse. Overt abuse is raw, physical assault, while covert abuse is mental and twists our emotions, but both cause harm.

*"Unresolved trauma, particularly childhood trauma, is easily the most massive problem facing humankind."* 

Unresolved trauma, particularly childhood trauma, is easily the most massive problem facing humankind. Homelessness, alcoholism, drug addiction, violent crime, anger addiction, teenage pregnancy, extreme politics and religion, depression, disease, and suicide are often secondary symptoms of the underlying issue of unresolved trauma.

Emotional pain hurts. We want the pain to stop, so we stuff it. Depression and anxiety can lead to a host of issues. We usually wind up with feelings of irritability or being unsafe, not trusting others, hypervigilance, engaging in overly controlling or obsessive behaviors, taking extreme risks, having difficulty concentrating, feeling unlikable or unlovable, disordered eating, and utter hopelessness or despair.

Self-medication occurs when we attempt to suppress or withdraw from an uncomfortable reality or trauma. We try to leave it behind and escape to a place of pleasure, mystery, and even indulgence. This is understandable because life is tough, trauma hurts, and we want the suffering to stop. Many people self-medicate because they don't have access to mental health care, so simply saying "get help" is not always useful advice. We may experience a level of pain so strong that no amount of healthy behavior can soothe us. Our "healthy" outlets themselves became triggers because they enabled us to endure the pain longer. Higher doses of prescribed medications come with their side effects.

The things we once judged, we use. The problems seem overwhelming, so some of us turn to alcohol. The problem is that alcohol creates even more depression. We may be too anxious to eat, but when we use marijuana, food suddenly tastes good again. It can also help us sleep and stave off nightmares. Like many who had unresolved traumas, I self-medicated.

Of course, self-medication can take many forms, but my personal choice was workaholism. It would be easy to say, "Well, I'm a workaholic, but at least I'm not an alcoholic." But I knew better. That would be self-righteous and hypocritical. The reality is that my choice was just as damaging as any other. It all hinders the healing, and it all causes harm.

In the aftermath of my childhood trauma, I tried to be tough and bury my feelings, which was not working out too well. Now, like anyone facing their traumas and their choices for self-medication, I began my quest to find authentic answers.

"Trauma creates three choices. We can 'dive' and remain stuck in the trauma indefinitely. Some work hard to overcome their traumas and 'survive.' Still, others use the emotional fuel from their traumas to do something of value and 'thrive.'"

Trauma creates three choices. We can "dive" and remain stuck in the trauma indefinitely. Some work hard to overcome their traumas and "survive." Still, others use the emotional fuel from their traumas to do something of value and "thrive." Ultimately, I found that all post-traumatic thrivers find solutions in two simple practices, "sitting in the fire" and "grounding."

#### Grounding:

One day I was on a small plane that made an obscure connection from Phoenix to South Dakota. As I sat down in my airline seat, I heard a voice say, "Hey, are you Randall Bell?" I looked up and said, "Yeah. Sean?" Sean and I had been colleagues about 15 years before, and we had not seen each other since. But there he was, seated right next to me.

It was exciting to see Sean. He is a dynamic, intelligent, thoughtful guy who has a gift for creativity. Of course, we caught up on what we had both been up to.

Then Sean looked at me and said, "You know, Randall, you will not believe it, but I have been to prison." This came as a surprise, and I replied, "Wow. So, tell me about it!" Sean then told me about

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how he joined a board of directors for the Insight Prison Project, a non-profit group that reaches out to both victims and offenders and helps them heal from their trauma. I listened intently as Sean told me about going into San Quentin prison and the mind-blowing stories of life transformations.

Sean could see on my face how interested I was, and he said, "Hey, if you want to go to prison too, I can get you in!" The whole thing seemed fascinating, so I said, "Jesus taught that we should visit those in prison, and I have never done that, so I am in." I promptly submitted my paperwork and was approved by the San Quentin Warden to go inside.

Just getting inside a prison is an ordeal. First, I had to fill out a lengthy application and submit it to the warden. I found it ironic that I had to pass a criminal background check to get into prison. When I was first scheduled to go, our trip was abruptly postponed because there had been an escape attempt, and the prison went into lockdown.

After several more weeks, the day finally came when I was allowed inside. I met Sean in downtown San Francisco, and we drove over the Golden Gate Bridge to the prison. I was told not to wear anything blue or red, as those were gang colors. This left me few options, so I wore khaki trousers and a white polo shirt. I could not bring in a cell phone or any personal belongings except for my driver's license and one car key. We went to the guard office, where my ID was checked against prison records. Then we walked down a very long, concrete walkway towards the prison itself.

There another guard checked my ID a second time, searched me, and put an invisible stamp on my wrist that could only be viewed under ultraviolet light. Then I was escorted into a steel cage where the door was locked behind me, and for a third time, a guard checked my ID. When we passed this barrier, the other side's steel door was unlocked, and we went into a small holding area where we finally swung open an old, massive iron door.

Suddenly, we stood in the prison courtyard. As we walked across the concrete, I looked to my left and saw a large building that housed California's death row. We veered to the right and into a small room with cinderblock walls and plastic chairs. Then in came the inmates, all dressed in blue pants and smocks. They smiled and seemed happy to see us, and being new; I introduced myself. They all went out of their way to make me feel at ease. The chairs were arranged in a circle, and I took a seat. I had no idea what to expect.

After we received a brief welcome, we were asked to close our eyes. We went through a "grounding" exercise that others call "meditation" to avoid any perceived conflicts related to religion. I cannot explain the feeling when I realized that I was meditating for the first time while sitting between two men convicted of murder. Yet, these men were so docile and kind.

I never heard much about meditation over my entire life, nor did I have any real interest in it. That all changed that morning. I did not know it was coming. I was already uncomfortable just being there, but the experience felt surreal.

The process was simple, more of a focused-breathing exercise. All

we did was sit comfortably in our chairs, close our eyes, take a few deep breaths, wiggle our toes, feel our knees, feel the pressure of the chair underneath us, wiggle our fingers, relax the muscles in our face, listen to our breathing, take several deep breaths, and open our eyes again. This is one of the most common and basic forms of "grounding," simply becoming aware of internal sensations, such as our breathing, any aches or pains, or a racing heart.

When I first began volunteering at San Quentin Prison, I was startled to learn how much the inmates practiced and enjoyed meditation as they worked to transform their lives. For virtually every prisoner I met, it was a daily practice. It is something a person can do anywhere, it costs nothing, and it offers considerable benefits. I liked it so much that occasionally I found myself repeating it when I got home.

A couple of months later, I was visiting with my cardiologist, who told me about a Harvard neuroscientist, Dr. Sarah W. Lazar, who learned about meditation by accident. Dr. Lazar had injured herself while training for the Boston Marathon. Her physical therapist told her to do stretching exercises, so Dr. Lazar took up yoga.

Dr. Lazar told reporter Melanie Curtin, "The yoga teacher made all sorts of claims that yoga would increase your compassion and open your heart, and I would think, 'Yeah, yeah, yeah, I'm here to stretch.' But I started noticing that I was calmer. I was better able to handle more difficult situations. I was more compassionate and open-hearted and able to see things from others' points of view."

Her curiosity peaked from this experience; Dr. Lazar researched the scientific literature on meditation and found evidence that the practice reduces a host of problems, such as anxiety, depression, and stress. It also improves the overall quality of life. Intrigued by both her own experience and the academic literature, Dr. Lazar began doing neuroscience research at Harvard Medical Center using brain scans.

"Meditation has a host of verifiable benefits. These include cognitive thinking skills, mental health, workplace performance, relationships, and overall well-being."

Dr. Lazar compared people who had meditated for years with others who did not meditate at all. The study showed that those who meditated had increased gray brain matter in several regions of their brains, including the areas responsible for decision-making, auditory senses, and memory. In a stunning discovery, the neurological team found that 50-year-old people who meditated had the same amount of gray matter as those who were 25.

In another study, Dr. Lazar put people who had never meditated into an eight-week program. In only two months, the brain scans showed a measurable thickening in several brain regions responsible for learning, memory, emotions, and empathy. Their brains also revealed shrinking of the areas associated with stress, anxiety, fear, and aggression. Now, from both my experience as a prison volunteer and Dr. Lazar's studies, I was now convinced that "grounding" or meditation is a powerful remedy. I now have a six-inch-thick binder containing scientific studies published on the topic of meditation. Hundreds of university studies from schools such as Harvard, Stanford, Brown, Yale, UCLA, and Vanderbilt provide verifiable and reproducible studies demonstrating its effectiveness.

"Grounding" switches off the sympathetic nervous system and turns on the parasympathetic. Meditation has a host of verifiable benefits. These include cognitive thinking skills, mental health, workplace performance, relationships, and overall well-being. It also measurably reduces chronic pain, mind-wandering, fearful memories, PTSD, and symptoms related to childhood adversity.

Meditation and mindfulness also improve character and ethical behavior. Mindfulness, or the mind-body connection, simply means being present in the moment or changing our focus of awareness on the present. We are not thinking about the regrets of the past or the anxiety over tomorrow, but our minds are in the here and now. This means that we do not dwell on times outside of our current control but rather maintain a clear focus on what is happening and suspend concerns on whatever has happened or might happen. We take life one day at a time. In a mindful state, we function in sync intellectually, spiritually, and emotionally. Furthermore, it means that we are aware of our physical state—our body and our breathing. We are motivated to deliberately pause before reacting to situations in terms of what we say, think, feel, or do.

We can reflect upon how much control we have over a situation and all the possible choices and outcomes. We can note the difference between acting out or simply walking away. From this evaluation, we can see how to respond better going forward. We can use the experience to generate growth that otherwise might not have been.

While the effects are powerful, meditation is deceptively simple. We mainly focus on our breathing. Some include mantras to their reflection, such as thinking of the word "so" while inhaling and "hum" while exhaling. Some use audio-guided meditations or create visualizations to expel unwanted energy or to focus on an abstract concept, such as compassion. Blank-mind meditation is another form where we dismiss all thoughts from our minds. Some sit, some stand, some walk, and some perform yoga poses or exercise forms as in tai chi or qigong.

"Grounding' or meditation lays the cornerstone for transformation. While simple, it resets our brain waves, letting the calming effects ripple out to fill our entire day. It offsets what eastern civilizations call 'monkey mind' or what westerners call 'anxiety.""

Generally, it takes 5 to 30 minutes a day to see results, but some suggest it only takes six deep breaths to get the benefits of "grounding." It may be better to have a shorter session in the morning and another in the evening, rather than one long one. It is best not to meditate right after exercising and be sitting rather than lying down. Several apps can help develop this habit. The most significant benefits come when we meditate daily, even for a few minutes. By eliminating distractions and being mindful of "now," we connect with our inner voice. If a distracting sound or thought comes to mind, we don't judge it but gently observe and bring our minds back to our breathing.

"Grounding" or meditation lays the cornerstone for transformation. While simple, it resets our brain waves, letting the calming effects ripple out to fill our entire day. It offsets what eastern civilizations call "monkey mind" or what westerners call "anxiety."

Some equate meditation with religion. As faith is a personal journey, prayer looks different to different people. However, prayer and "grounding" are two different things. "Grounding" is focusedbreathing and an effort to listen to our inner voice, while prayer is not focused on breathing but instead communicating with God or a higher power. How this is combined or not combined is a personal choice.

My cardiologist explained more about how brain waves work and prescribed 10 minutes of meditation a day, every day. I just sit comfortably, close my eyes, and focus on my breathing. It is easy, and my blood pressure dropped considerably.

Almost without exception, everyone I know who heals from trauma has a ritual of some kind, often in the early morning. They meditate, but they may also pray, stretch, read something inspirational, have a good coffee, or plan out their day. However, this is done; deep breathing exercises are at the core.

"When we sit in the fire, the raw words often burn with emotion. During these moments, we can be tempted to mask the hurt with humor, sarcasm, or some other distraction, but we must sit in the fire. We must talk about that ugly stuff."

As demonstrated from the cells in San Quentin Prison to the great halls of Harvard Medical School, "grounding" or meditation is shown to physically and emotionally heal broken hearts.

#### Sitting in the Fire:

With my childhood trauma, I had made the classic mistake of not talking about my heart defect or my surgery.

Society and perfectionist cultures tend to downplay the difficult experiences in life. Internal pressure builds up when we "suck it up," "sweep it under the rug," or dodge the real conversations. Not only does this prevent healing, the pressure builds up like a volcano.

I also learned about "sitting in the fire" in San Quinton Prison. This means that we are honest and have difficult conversations about what is real. We candidly discuss the details of the trauma without



sugar-coating or glossing over anything. Opening up to these vulnerable conversations allows us to relieve the pressure.

The crimes committed by the men in San Quentin are horrific. As terrible as they are, their back-story as children is often worse. When we sit in the fire, the raw words often burn with emotion. During these moments, we can be tempted to mask the hurt with humor, sarcasm, or some other distraction, but we must sit in the fire. We must talk about that ugly stuff.

The ultimate goal is to have a conversation with a trusted person or group where we can express what really happened. It is remarkably healing to sit in the fire, and there are basically three options:

The ideal way to have a dialogue and process trauma is with a trained therapist. A competent therapist will allow us to express the full extent of the trauma without judgment and keep the conversations confidential.

"A somewhat similar thing happened with me as a patient when I was told that my surgery was a success and just sent home. It is great when a war is over and wonderful to know that surgery was a success, but there is more."

Access to therapists is limited within prisons, so they have found other ways and have turned to group therapy. We can find a trusted family member, friend, or group; however, there are two essential criteria. First, the person or group must simply listen without interrupting or being judgmental. Second, they must be trustworthy and keep our conversations strictly confidential. If these conditions are not met, this could lead to being re-traumatized.

In prison, everyone must keep the information confidential, as a leak could result in death on the prison yard or denial for parole. The process works, and for those who graduate from the program and are paroled, the recidivism rate is remarkably low.

Third, until we find a therapist or a trusted person or group, we can journal our experiences. We write about life before our trauma, the trauma itself, and what has happened since. We can maintain the journal and continue to write about the experiences as additional thoughts come to mind. Writing things down organizes our thoughts and emotions and relieves the pressure.

"Sitting in the fire" is essential. We will never heal from a trauma that we bottle up inside. While doing this, there is anything but calm. My heart races as I hear the stories. Once we are finished, there is inevitably a profound calm and immeasurable relief.

#### A New Prescription:

A soldier is trained to go into combat, and when the war is over, they are just sent home and expected to move on as if nothing had happened. A somewhat similar thing happened with me as a patient when I was told that my surgery was a success and just sent home. It is great when a war is over and wonderful to know that surgery was a success, but there is more.

Yes, my doctors and all the hospital staff had done a brilliant job repairing my physically damaged heart; however, what was missing was that I had undergone a traumatic childhood experience that would stick with me for decades. I am not alone. Millions undergo traumatic experiences, so these principles, coming from the health professionals that we trust, are enormously helpful for complete healing.

It is useful to know that, with simple practices, we can turn parasympathetic and sympathetic nervous systems, on or off. For example, we can quickly flip on our sympathetic nervous system by merely watching horror movies. But the opposite is also true.

"Grounding" is medically proven to switch the body's nervous system from "stress" to "calm." These deep breathing exercises are simply taking in long, deep breaths and exhaling slowly - such as meditation or yoga exercises. Laughter, watching funny videos, telling jokes, or comedy clubs are also outstanding for flipping on the "calm" switch. Biorhythms are important, as they tell us when we are hungry, angry, lonely, or tired. Taking action flips on the parasympathetic switch. "Sitting in the fire" ultimately brings similar relief and calming results.

Trauma is complex, and many potential remedies are left for a broader discussion; however, health care professionals should know the fundamentals and integrate them into their lives and practices.

My cardiologist modeled this philosophy of total healing. She prescribed medications for my heart condition, but she did more. Like many doctors, she gave me a written prescription that included a diet and exercise regimen. Specifically, I was to cut out all added salt, processed sugar, and run at least 10 minutes a day.

"As healthcare professionals awaken to more research and realities surrounding unresolved trauma, they can care better for themselves and their patients. Of course, some patients should be referred to licensed trauma counselors; however, at a minimum, health care professionals should be aware that physical remedies are only a part of the overall healing process."

But she did not stop there. She told me to start "grounding" exercises twice a day and recommended – rather strongly – that I take a meditation class. She also took the unprecedented step of providing a safe place for me to talk about my experiences as a child who underwent open-heart surgery. She even helped me process my PTSD by letting me stop by her office and step onto the treadmill to overcome the triggering effect it had on me. In other words, she "sat in the fire" with me.

Today, I am no longer triggered by my childhood trauma. The results are measurable, and my heart rate while standing on a treadmill has gone from 150 to about 75. I have successfully processed my trauma. I achieved this mainly by "sitting in the fire" and "grounding" exercises. Now when thoughts and discussions come up about my childhood trauma, they pass harmlessly through my mind without triggering my sympathetic nervous system. That is the goal of resolving our traumas.

Furthermore, as a result of my cardiologist's efforts to treat both my physical heart and post-trauma issues, my blood pressure has dropped dramatically, my energy is higher than ever, and I can now run five to ten miles, which I could never do before. At an age when people let things go, I got going.

As healthcare professionals awaken to more research and realities surrounding unresolved trauma, they can care better for themselves and their patients. Of course, some patients should be referred to licensed trauma counselors; however, at a minimum, health care professionals should be aware that physical remedies are only a part of the overall healing process.

Along with the necessary medical procedures, surgery, physical therapy, and prescription drug regimens, physicians may take a holistic approach, just as my cardiologist did. Specifically, with what is now known about resolving trauma, physicians should add two essential elements to their prescriptions, (1) deep breathing "grounding" exercises, which are proven to switch on the para-sympathetic nervous system, and (2) "sitting in the fire" and not allowing those traumas to stay bottled up.

With these two practices, we not only deliberately switch on the parasympathetic nervous system, but we also help heal the body, mind, and soul.

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Disclosures: Dr. Bell is the author of "Post-Traumatic Thriving: The Art, Science, & Stories of Resilience."

NT



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8

Brilliant! Dr. Bell bridges the journey from grief to growth. This is classic wisdom on healing from our heartbreaks and ultimately enjoying a fulfilling life.

- Christine Theard, M.D.

# Post-Traumatic Thriving

The Art, Science, & Stories of Resilience



Randall Bell, Ph.D.



## **VIRTUAL 37TH ANNUAL CONFERENCE ADVANCES IN THERAPEUTICS AND TECHNOLOGY: CRITICAL CARE OF** NEONATES, CHILDREN. **AND ADULTS**



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## MiOra Means "My light"

Özlem Rafaela Equils, MD, FAAP

#### About MiOra

MiOra, pronounced as Me-Ora, means "my light." MiOra (miora. org) is a national 501(c)3 based in Los Angeles. MiOra was founded in 2016 by Dr. Ozlem Rafaela Equils, who is a pediatric infectious diseases physician. MiOra Board is composed of Michael Deitch (American Heart Association), Karin Kricorian (Disney), Alex Chen, MD (Health Net), Christopher da Costa, MD (FDA), Willie Watts-Troutman, RN, and Brian Harris, CPA.

MiOra's mission is to improve the diversity in STEM and healthcare fields while improving public health. MiOra does this by providing no-barrier, certificate public health internship opportunities to passionate high school and college students, and graduate students. MiOra is all-inclusive and accepts passionate students who are not working towards a college degree but looking for a certificate apprenticeship program.

The students learn about important public health issues and solutions. They then implement health education programs within their own communities and improve community health.

"The students who are interested in data and research learn about data collection. MiOra partners with UCLA Masters of Applied Statistics program and the USC School of Pharmacy Moving Targets LA program. MiOra students learn how to collect data on their programs' impact, analyze their data, and develop posters and papers. The students who are interested in policy change are involved in developing policy recommendations."

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volved in developing policy recommendations.

MiOra provides paid internships. This support allows the students to focus on their internship and gain real-world experience. Experiential internship strengthens their resume for advanced training (medicine, pharmacy, epidemiology, data management, etc.), helps them gain confidence, and increases their employability.

MiOra partners with academic, government, non-profit, and forprofit industries to improve community health. MiOra interns are exposed to a broad network of experts and mentors.

The interns who are interested in developing their leadership skills have the opportunity to supervise junior interns and develop novel programs. If you are interested in being involved as an intern, mentor or if you would like to support MiOra, please email <u>admin@miora.org</u>.

Disclosure Statement: The author has no relevant conflicts of interest to declare.

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NEONATOLOGY TODAY is interested in publishing manuscripts from Neonatologists, Fellows, NNPs and those involved in caring for neonates on case studies, research results, hospital news, meeting announcements, and other pertinent topics.

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What to do when you or a loved one is infected.

#### **HYGIENE TIPS**



**BATHROOM** 

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Miora

Sep 17, 2019 - 😚

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chelle Seu 🖾, Daniel Lopez, Michaela Nave v Rodriguez, Elsie Ureta & Ozlem Equils

mmunity Mental Health Journal 1201 | Cito this article



## Ways to Manage Covid 19 @ Home

## Household

## Sick



## Maneras de manajer COVID-19 en casa

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## We've had a great year of Neonatology Grand Rounds webinars!

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#### NEO: The Conference for Neonatology | February 15–19, 2021

While you're planning for 2021, don't forget to save the date for NEO: The Conference for Neonatology! We're going virtual this February to bring critical topics that influence the practice of neonatal medicine presented by leading experts in the field.

**Register now!** 

Peer Reviewed

## Section on Neonatal-Perinatal Medicine Update – Raising our Voices

Lily J. Lou, MD, FAAP

#### Dear All,

I am primarily writing to you today about advocacy-the importance of using our expertise and trusted voices to improve healthcare for newborns and their families by speaking up about the laws and policies that govern their care. Although most all of us have demanding full-time jobs, I believe it is also our obligation, part of our professionalism, to go one step further and use our hard-earned knowledge and insight to advocate on behalf of our patients and families and for our profession. While we can tremendously impact the well-being of one baby at a time through our clinical care in the NICU, we can influence health legislation in ways that improve the plight of many babies at once, helping our lawmakers understand sound health policy. The SONPM includes advocacy as one of its strategic domains and prioritizes an approach that streamlines such activity by providing tools, training, and resources to make it easy for neonatologists to take on this role.

Here are links (same session, on different platforms) to a hotoff-the-press podcast that features James Baumberger (AAP Sr. Director of Federal Government Affairs) and Pat Johnson (Dir of Federal Government Affairs), along with SONPM members John Zupancic, Shetal Shah, Ashley Lucke and myself—talking about what neonatologists should pay attention to as we prepare for a new administration and a new Congress this month.

- <u>https://soundcloud.com/totrep/cross-section-jan-2021</u>
- <u>https://podcasts.apple.com/us/podcast/cross-section-aap-neonatal-perinatal/id1299474910#episodeGuid=tag%3Asoundcloud%2C2010%3Atracks%2F958399306</u>

Like any skill, legislative advocacy can feel foreign and awkward at first. With practice and with time to understand the process, identify the holders of influence, learn about resources, and develop trusted relationships, it becomes comfortable and increasingly effective. Not taking advantage of our immense credibility as pediatricians would be a huge missed opportunity. Our legislators are trying to understand competing interests that range from farm subsidies to trade agreements to energy to highway maintenance. They work hard to prioritize their attention and US dollars by listening to their constituents; if we are not there talking about what our patients need, they are listening to someone else talk about other interests vying for the same finite funds.

The AAP has enormous resources to help us deliver effective messages to our representatives, backed up by data, and coordinated for maximal effect. The main Advocacy website <a href="https://services.aap.org/en/advocacy/">https://services.aap.org/en/advocacy/</a> has links to a myriad of useful tools, including an updated 2020 Blueprint for Children (a comprehensive legislative agenda, regardless of who is in office) and Transition Plan for the incoming Biden-Harris administration. There are COVID-19 advocacy resources and information to help with taking a stand on health care access for children, vaccines, tobacco & vaping, and other topical issues. The Advocacy

Action Center highlights high priority issues in play and facilitates communicating with your specific Members of Congress with a single click. AAP members can sign up for a mailing list that provides action alerts and regular child health advocacy updates. AAP sponsors Days of Action, focusing calls and letters on top issues for children on specific days to concentrate the attention of Members of Congress. A Subspecialty Day of Action was held in October of 2019. Two AAP member Committees—on Federal Government Affairs (COFGA) and State Government Affairs (COSGA) guide the work and provide opportunities to serve the Academy on a national level. The inspiring annual Legislative Conference has been re-named the Advocacy conference.

So how is this relevant to neonatologists? Can't other pediatricians do this?

First, there are issues more important to our patients and to us than to non-neonatologists. Some examples include the Newborn Screening Saves Lives Act, coverage for genomic testing, Medicaid and CHIP (often the payment source for 75% of NICU patients) and state coverage for donor milk for premies. Other pediatric issues also impact us in the NICU: the Subspecialty Loan Repayment program, treatment for substance use during pregnancy & support for families at risk for foster care, COVID relief for Medicare but not Medicaid, extending maternal Medicaid coverage up to 12 months after delivery, the VACCINES Act, paid parental leave, funding for the NIH and the CDC that supports our research and care activities. Second, many pediatricians are active advocates, but no-one carries the weight of a doctor who cares for newborns when talking about newborns and their care firsthand.

"The SONPM has just formalized its Advocacy Committee charter and determined the composition of its leadership council. There is an opportunity for one more neonatologist to join the group as an at-large member please contact me if you would like more information."

The SONPM has just formalized its Advocacy Committee charter and determined the composition of its leadership council. There is an opportunity for one more neonatologist to join the group as an at-large member—*please contact me if you would like more information.* You will also find this posted on the AAP Volunteer Network list as a national opportunity. Shetal Shah, the committee co-chair, has taken the 150 recommendations in the Transition Plan and pulled out the neonatology-specific issues. Look for this list on the Advocacy web page.

The AAP Federal Government Affairs office has developed neonatology specific materials to support our advocacy work. This committee is working on a priority list and plan for Section advocacy. We are developing a listserv for members interested in receiving legislative alerts relevant to neonatology. A toolkit for state coverage of donor milk coverage is available (thanks again, Shetal). The section remains committed to supporting the development of advocacy skills for neonatologists. Again, we plan to provide scholarships to the Advocacy Conference—which will take place virtually (including virtual meetings with members of congress) on April 11-13<sup>th</sup>, 2021. We hope to host additional advocacy workshops at our national meetings. We offer these tools to make it more effortless for our members to efficiently and effectively engage in meaningful advocacy. We are the best citizens if we use our gifts for maximum benefit; our unique knowledge and perspectives should be voiced in the service of our patients and our communities. We can and will make a difference.

"The section remains committed to supporting the development of advocacy skills for neonatologists. Again, we plan to provide scholarships to the Advocacy Conference—which will take place virtually (including virtual meetings with members of congress) on April 11-13th, 2021."

One of the most powerful things you can do in advocacy is to share a story. In closing, I'll share this video (5:51 long) from The Food Bank of Alaska that beautifully makes the case that we should support their cause. We still do, so I'd say it works.

https://www.youtube.com/watch?v=S8nARtygkys

Take care and stay well,

Lily

Disclosure: There are no reported conflicts.

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#### **OPIOIDS** and NAS

When reporting on mothers, babies, and substance use LANGUAGE MATTERS



#### I am not an addict.

I was exposed to substances in utero. I am not addicted. Addiction is a set of behaviors associated with having a Substance Use Disorder (SUD).



#### I was exposed to opioids.

While I was in the womb my mother and I shared a blood supply. I was exposed to the medications and substances she used. I may have become physiologically dependent on some of those substances.



#### NAS is a temporary and treatable condition.

There are evidence-based pharmacological and non-pharmacological treatments for Neonatal Abstinence Syndrome.



#### My mother may have a SUD.

She might be receiving Medication-Assisted Treatment (MAT). My NAS may be a side effect of her appropriate medical care. It is not evidence of abuse or mistreatment.

## My potential is limitless.



I am so much more than my NAS diagnosis. My drug exposure will not determine my long-term outcomes. But how you treat me will. When you invest in my family's health and wellbeing by supporting Medicaid and Early Childhood Education you can expect that I will do as well as any of my peers!

Learn more about Neonatal Abstinence Syndrome at www.nationalperinatal.org



## SHARED DECISION-MAKING PROTECTS **MOTHERS + INFANTS DURING COVID-19**

**KEEPING** MOTHERS + INFANTS TOGETHER



Means balancing...



#### EVIDENCE

We encourage families and clinicians to remain diligent in learning up-to-date evidence.

#### PARTNERSHIP

SHARED DECISION-MAKING

What is the best for this unique dyad?

S EEK PARTICIPATION ELP EXPLORE OPTIONS A SSESS PREFERENCES R EACH A DECISION E VALUATE THE DECISION





#### TRAUMA-INFORMED

Both parents and providers are confronting significant...

GRIEF

FEAR

UNCERTAINTY

#### LONGITUDINAL DATA

We need to understand more about outcomes for mothers and infants exposed to COVID-19, with special attention to:

- MENTAL HEALTH
- POSTPARTUM CARE DELIVERY



NEW DATA EMERGE DAILY.

NANN AND NPA ENCOURAGE PERINATAL CARE PROVIDERS TO ENGAGE IN CANDID CONVERSATIONS WITH PREGNANT PARENTS PRIOR TO DELIVERY REGARDING RISKS, BENEFITS, LIMITATIONS, AND REALISTIC EXPECTATIONS

Partnering for patient-centered care when it matters most





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## PROTECT YOUR FAMILY FROM RESPIRATORY VIRUSES

pertussis

flu coronavirus



## WASH YOUR HANDS

RSV

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Sneeze and cough into your elbow.

USE AN ALCOHOL-BASED HAND SANITIZER.

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Avoid crowds. Protect vulnerable babies and children.



NICU-NET

NICU-NET is a private and moderated forum for neonatology professionals. Membership is available to physicians, nurses, and other caregivers in neonatal and perinatal medicine. Conference announcements and other news of interest to members may be posted here. Please do not post messages with identifiable patient information of any kind. Vendor posts and messages of a commercial nature will be deleted.

To post to the list, send email to

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Message archives from the U. of Washington NICU-NET (1994-2003) and Yahoo Groups NICU-NET (2003-2019) are available on Google Drive. You can download them using this link: <u>https://drive.google.</u> <u>com/drive/folders/1MoPTrDjzmGbsZlK</u> <u>qY9MczihApWaFbREK?usp=sharing</u>

To contact the list owners, use the following email address:

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*Thirteen-year-old Emily Rose Shane was tragically murdered on April 3, 2010 on Pacific Coast Highway in Malibu, CA. Our foundation exists to honor her memory.* 

In Loving Memory

August 9, 1996 - April 3, 2010



Each year, the Emily Shane Foundation SEA(Successful Educational Achievement) Program provides academic and mentoring support to over 100 disadvantaged middle school students who risk failure and have no other recourse. We have served over 700 children across Los Angeles since our inception in the spring of 2012. Due to the COVID-19 outbreak, our work is in jeopardy, and the need for our work is greatly increased. The media has highlighted the dire impact online learning has caused for the very population we serve; those less fortunate. **We need your help now more than ever to ensure another child is not left behind.** 

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The average cost for the program to provide a mentor/ tutor for one child is listed below.



1 session	\$15
1 week	\$30
1 month	\$120
1 semester	\$540
1 year	\$1,080
Middle School	\$3,240

he Emily Shane Foundation is a 501(c)3 nonprofit charity, Tax id # 27-3789582. Our flagship SEA (Successful Educational Achievement) rogram is a unique educational initiative that provides essential mentoring/tutoring to disadvantaged middle school children across Los Angeles and Ventura counties. All proceeds directly fund the SEA Program, making a difference in the lives of the students we serve.

## Data types and different ways to store data in R

#### Fu-Sheng Chou, MD, PhD

#### Data, Information, and Knowledge:

In the realm of information sciences, there is a well-established information pyramid as illustrated in Figure 1. (1) Data sits at the bottom, is in a large quantity; interpretation of data brings information that the human mind can process and use to form knowledge. Here is a brief example:

Data are quantified observations that by themselves show no meaning -

"10" in the statement of ten apneas in the past 24 hrs,

Information is the interpretation of a multitude of data -

Ten apneas in the past 24 hrs with feeding intolerance, and

**Knowledge** is a plausible interpretation of information gathered based on established facts or knowledge -

New-onset frequent apnea episodes with feeding intolerance may be a sign of systemic infection.

"In medical school, we learned about medical knowledge. In residency, we learned to apply the medical knowledge to practical patient care, and in fellowship, through scholarly activity, we started to get deep into data and information."

In medical school, we learned about medical knowledge. In residency, we learned to apply the medical knowledge to practical patient care, and in fellowship, through scholarly activity, we started to get deep into data and information. Modern medicine is built upon this information pyramid (Figure). Now, with artificial intelligence, the circles are going to roll even faster.

Data science is a field that deals with data, which is the element in the pyramid with which we have the least contact. A data scientist would say, 80% of data science work is cleaning up the data. This is how terrible we, as amateurs, are when we hand over a table to our analytics colleagues and friends.

Hadley Wickham, the author of *R* for Data Science and many books, the creator of the *tidyverse* package and many others, and the chief scientist at RStudio, introduced the concept of **tidy data**, which he defined as "a consistent way to organize your data in R," in the introduction of Chapter 12 in *R* for Data Science. (2) A famous line by Dr. Wickham, in a reflection to a famous quote by the Russian writer Leo Tolstoy, states:

Tidy datasets are all alike, but every messy dataset is messy in

#### its own way.

There are various types of data (e.g., number, character, datatime, etc.), and each programming language deals with data types slightly differently. Luckily, to me at least, it is quite intuitive when it comes to data type recognition and management in R. Getting the data type right is the first step towards successful projects and a bright future with R.

"Getting the data type right is the first step towards successful projects and a bright future with R."

**Tidy data** is not just about data type; instead, its spirit lies in the word "organize." Organizing data requires grouping them into containers (the invisible ones). A data table is a container; a vector is also a container. There are various types of containers built-in R. Choosing the right one to store your data is important.

So, I think, before we start building our first webApp for the neonatal abstinence score, we should first introduce data types and containers. Let's get started!

Working with data types in R

Basic data types:

- **Numeric**: This is the data type for continuous variables, for example, urine output.
- **Integer**: Integer can be thought of as a subtype of numeric, but more importantly, use it on variables that do not allow fractions, e.g., neonatal abstinence score, length of hospital stay, N-PASS scores.
- Logical: The Yes' and the Noes. This is the data type for comparisons.
- **Character**: This is the data type for text.
- **Factor**: Factors are a special data type that is useful for categorical variables. The beauty of the factor data type is the ability to re-level the variables. Please see below.

#### Data type conversion:

In R, you can convert data types by using a group of functions that start with "as.": as.xxxx(). For example:

- > a = 1.2
- > as.numeric(a)
  - [1] 1.2



> as.character(a)

[1] "1.2"

> as.factor(a)

[1] 1.2

- Levels: 1.2
- as.integer(a)

[1] 1

To check the data type, use a group of functions that start with "is.": is.xxxxx(). For example:

> a = as.factor(1.2)

> a

[1] 1.2

Levels: 1.2

> is.factor(a)

[1] TRUE

> is.numeric(a)

[1] FALSE

Now, try and type as.numeric(a), and see what happens:

> as.numeric(a)

[1] 1

Why do we get the result of numeric 1 back? It is because 1.2 is the first level of the factor (well, there is only 1 level), so, when you convert a factor into a numeric data type, R converts the "level" of the factor, not the "content" of the factor. See more examples below when I show you multi-level factors stored in a container.

"Try and convert data types back and forth. Come up with simulated data content that your research projects will have. Convert data types back and forth. If you run into errors, Google the error messages. Alternatively, you can email me."

Try and convert data types back and forth. Come up with simulated data content that your research projects will have. Convert data types back and forth. If you run into errors, Google the error messages. Alternatively, you can email me.

#### Containers for data storage

In the above example, when we typed > a = 1 earlier, a is the container or an *object*, and 1 is the content that was placed in the container a. There are different types of containers:

Vector: store content of the same data type. For example:

```
b <- c(1, 3.2, 5.7)</li>
b
```

[1] 1.0 3.2 5.7

>

>

In this example, container b stores three pieces of data of the same type (numeric). Pay attention to the "[1]" before the content in the result: this is a numeric indicator of the **position** of the data inside the vector. Now try this:

c <- c(1:25)										
С										
[1]	1	2	3	4	5	6	7	8	9	10
[11]	11	12	13	14	15	16	17	18	19	20
[21]	21	22	23	24	25					

First of all, the colon sign gives a range of the numbers between the two numbers that flank the sign. Secondly, you can now appreciate better that the numbers in the square brackets provide the **position** of the data in the vector.

By the way, the sign "<-," yeah, exactly, a "smaller" sign followed by a hyphen to make it look like a left-pointed arrow, is the sign that R recognizes as putting the stuff on the right side to the left side, which is usually a container. Compare this syntax to a linear equation: y = 2 + 3x, where x = 1. In R, you will code as:

> x <- 3

> y <- 2 + 3 \* x # this step stores the result in y, a container

> y # this step calls the container y

[1] 11

- List: I have mixed feelings about lists. There are pros and cons. For the pros, lists are easy to use. You treat it like a plastic bag, into which you throw everything. Imagine that you just went to the grocery store. You bought a box of eggs, two bottles of milk, and a stack of cheese. You put them all into a giant bag. Whereas the box, the bottle, and the plastic wrap for the stack of cheese are all vectors (because inside these containers you have content of the same type), the bag is a **list**, which allows you to store all kinds of data, even if they are in different types. Now try this:
  - > my\_list <- list(2, "neonatology", c(3.4, 5:8))</pre>
  - > my\_list
    - [[1]]
    - [1] 2
    - [[2]]

[1] "neonatology"

[[3]]

[1] 3.4 5.0 6.0 7.0 8.0

> class(my\_list)

[1] "list"

Now you get it, right? You have a container called *my\_list*, which stores three objects: the first one is numeric data 2, the second one is a character data "neonatology," the third is a vector with five numbers. When you check the container type with the function class(), you get a return saying that *my\_list* is indeed a list. I use class() to check the type of container I am working with.

The cons for a list container type, as you probably noticed, is that the content in the list is segregated into various compartments. The numbers inside double square brackets are the relative position of the content in each compartment. How do we call the content inside each compartment and copy the content into another container?

> the	new_list <- my_list[3] 3rd compartment inside <i>new_list</i>	#	place
>	new_list		
	[[3]]		
	[1] 3.4 5.0 6.0 7.0 8.0		
> list	class(new_list) is still a list	#	new_
	[1] "list"		
> the	another_new_list <- my_list[[3]] content of the 3rd compartment # inside another_new_list	#	place
	[1] 3.4 5.0 6.0 7.0 8.0		
> er_l	class(another_new_list) new_list is a numeric vector	#a	noth-

[1] "numeric"

I hope you get the idea from this example. You use **single square brackets** to move the entire compartment into a new container; the new container is still a *list*. Or, you use **double square brackets** to move the content inside the compartment into a new container; the new container, which is a *vector*, will assume the type that R will try to coerce all the content into.

Now try this:

- > everything <- unlist(my\_list)</pre>
- > everything

[1] "2" "neonatology" "5" "6" [6] "7" "8"

In this example, you use the function unlist() to break apart the compartments and put everything in a giant container named *everything*. R will coerce everything into one data type, as the container *everything* is a vector (if you do not specify a container type, the default in R is a vector type).

A final word on the list is that, just like vectors and lists have names, the compartments inside the list can be named and called upon by their names. Try this: list(HR = c(120, 145, 140), RR = c(24, 35, 34), FiO2 = c(0.21, 0.22, 0.33)). We will talk more about it later.

• **Dataframe**: This is basically a two-dimensional table. To create a dataframe, do the following:

> df <- data.frame(HR = c(120, 145, 140), RR = c(24, 35, 34), FiO2 = c(0.21, 0.22, 0.33))

HR RRFiO2 1 120 24 0.21 2 145 35 0.22 3 140 34 0.33

> df

A data frame has row numbers (they are actually stored as the *character* type), which you can change to row names by using the rownames() function. Each column may have a column name, which can be changed using the colnames() function.

To call content stored in a data frame, memorize this rule: **container[row, column]**.

- To call the second row: df[2,]
- To call the second column: df[,2] or df[, "RR"]
- To call row 2 column 3: df[2,3]

A dataframe can store any type of data, but data in each **column** needs to be of the same data type. Think of this as having your research subjects in rows and the variables in columns:

	HR	RR	FiO2
Subject 1			
Subject 2			
Subject 3			

#### Summary:

"3.4"

In this post, we introduced common data types and data containers. These are the foundations of data collection and organization.

Try to create different types of containers on your R console and compare them to your data on the Excel spreadsheets.

"In this post, we introduced common data types and data containers. These are the foundations of data collection and organization. Try to create different types of containers on your R console and compare them to your data on the Excel spreadsheets."

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As we indicated last month, we look forward to a number of new features as well.

- 1. An online submission portal: Submitting a manuscript online will be easier than before. Rather than submitting by email, we will have a devoted online submission portal that will have the ability to handle any size manuscript and any number of graphics and other support files. We will have an online tracking system that will make it easier to track manuscripts in terms of where they are in the review process.
- Reviewers will be able to review the manuscript online. This portal will shorten the time from receipt of review to getting feedback to the submitting authors.
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- 4. A new section called news and views will enable the submission of commentary on publications from other journals or news sources. We anticipate that this will be available as soon as the site completes the beta phase
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#### PARTNERSHIP

SHARED DECISION-MAKING

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> S EEK PARTICIPATION ELP EXPLORE OPTIONS A SSESS PREFERENCES R EACH A DECISION E VALUATE THE DECISION





- Both parents and providers are confronting
- significant...

  - FEAR
    - GRIEF

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# A Life's Journey

Iranian village to a university professor in the United States of America in this memoir. As a boy, his unruly behavior was sedated by scholastic challenges as a remedy. At age twelve, he left home for junior high school in a provincial capital. At first, a lack of selfesteem led him to stumble, but he soon found the courage to tackle his subjects with vigor. He became more curious about the world around him and began to yearn for a new life despite his financial limitations. Against all odds, he became one of the top students in Iran and earned a scholarship to study medicine in Europe. Even though he was culturally and socially naïve by European standards, an Italian family in Rome helped him thrive. The author never shied away from the challenges of learning Italian, and the generosity of Italy and its people became part and parcel of his formative years. By the time he left for the United States of America, he knew he could accomplish whatever he imagined.

## Houchang D. Modanlou

Paperback USD 24.99 **Peer Reviewed** 

#### **Fellow Column:** Late-Onset GBS Lower Extremity Cellulitis in **Premature Neonate with a GBS Négative Mother** with Alternative Modes of Transmission: A Case Report

Bansari Patel, OSM, Lakshan Fonseka, OSM, Nasser Hashem, OSM, Kersti Bellardi, OSM, Mitchell Goldstein, MD

#### Abstract

Purpose: To report a case of cellulitis-causing late-onset Group B streptococcus (GBS) GBS in a neonate with a previously negative antenatal tested mother. This report aims to discuss the various transmission modes potentially causing this case of cellulitis, such as contaminated breast milk.

Case Description: A preterm neonate, born via cesarean section (C-section) at 29 weeks gestation to a G1P0 mother with a negative GBS rectovaginal antenatal swab test, subsequently developed late-onset cellulitis in the lower extremity due to GBS 19 days later.

Methods: This is a retrospective case report followed by clinical observation, blood cultures, imaging, and antibiotic interventions.

Results: A neonate with left lower extremity cellulitis was found to be GBS positive from a previously negative antenatal GBSnegative mother.

Discussion: As GBS is a common pathogen of neonatal sepsis and less commonly cellulitis, testing rectovaginal fluids once may not be enough to prevent neonates and preterm infants from protecting against transmission. As there have been rare cases of GBS-contaminated breast milk, culturing and testing of breast milk should also be considered, especially in preterm infants.

"As there have been rare cases of GBScontaminated breast milk, culturing and testing of breast milk should also be considered, especially in preterm infants."

#### Introduction:

Group B streptococcus (GBS) has been considered a long-standing and common etiology of early-onset neonatal sepsis and meningitis but also has been known to cause cellulitis less frequently. (1) When present, the cellulitis most commonly manifests as inflammation and induration on the face and submandibular area of the infant. We report an interesting case of a premature 29week gestational age neonate that developed left lower extremity cellulitis 19 days after birth and ten days after beginning expressed breast milk (EBM) feedings. As GBS may cause premature birth despite negative antenatal testing in the mother, GBS may be implicated in the late-onset infection in this case. (2) As the previous testing of rectovaginal fluids was GBS-negative in the mother, this screening potentially points to some unreliability of testing rectovaginal fluids to prevent late-onset GBS infections in neonates and will have to be explored further. As there have also been previous rare cases of GBS-contaminated breast milk reported in the literature, breast milk culture may be a reasonable additional option to aid in the prevention of horizontal transmission of GBS infections in neonates, especially in high-risk preterm infants. (3)

"We report an interesting case of a premature 29-week gestational age neonate that developed left lower extremity cellulitis 19 days after birth and ten days after beginning expressed breast milk (EBM) feedings."

#### Case Summary:

The neonate is a preterm infant born at 29 weeks gestational age to an 18-year-old G1P0 Hispanic woman with a blood type of O negative. The mother has a medical history of chlamydia infection a few months prior and a history of marijuana use, with the last urine drug screen negative. Due to a non-reassuring fetal status and fetal decelerations, a cesarean section was performed. The mother received two doses of betamethasone and magnesium sulfate before delivery. The infant initially required respiratory support with PPV, FiO2 of 100% that was gradually decreased to 30%. The baby was placed on RAM cannula with a CPAP of +6 prior to transport to the NICU. APGAR scores were 2, 5, and 9 at 1. 5, and 10 minutes.

On admission, the male infant's temperature was 36.7, heart rate 152, respiratory rate 38, blood pressure 56/32, and mean O<sub>2</sub> saturation of 96%. At 29 weeks gestational age, the birth weight was 1240 g (26-50th percentile), head circumference of 27 cm (26-50<sup>th</sup> percentile), and length 40 cm (76-90<sup>th</sup> percentile). Upon physical exam, there was mild nasal flaring with moderate intercostal retractions present. Breath sounds were clear but equally decreased bilaterally. The neonate responded to tactile stimulation, though tone and activity were decreased. The skin was pink and perfused, with no rashes, lesions, or vesicles noted. The infant was made NPO and started on TPN with initial glucose of 64. The baby was given caffeine citrate, placed on PPV, and noninvasive mechanical ventilation with FiO<sub>2</sub> 28%, PIP 24 cm H<sub>2</sub>O, PEEP 6 cm H<sub>2</sub>O, at a rate of 25 breaths per minute. Initial chest



x-ray showed lungs well expanded with haziness bilaterally, consistent with RDS. Sepsis workup, including CBC, CRP, and blood culture, was performed, but IV antibiotics were not started on admission. Initial lab results were within normal limits with values of WBC 10.6 cells x  $10^9$ /L, Hgb 15.1 g/dL, Platelets 198 x  $10^9$ /L, with a normal differential (1% band forms). Blood culture was negative. There were no known maternal risk factors for infection.

Seven days post-admission, the infant began having multiple frequent spells of bradycardia and desaturation with feeding intolerance. CBC and CRP screening were obtained, and IV antibiotics of ampicillin and gentamicin were started. IV vancomycin was added when the left leg was noticed to have an 8 cm erythematous, nondemarcated swelling ten days after EBM feedings were started. WBC was elevated at 28.5 cells x 10<sup>9</sup>/L with a CRP of 17.8 mg/dL, and blood cultures were positive for Group B streptococcus. X-ray of the left leg showed no sign of osteomyelitis. Lumbar puncture was negative for meningitis. WBC and CRP trended down, and left leg cellulitis resolved a week later. Vancomycin was discontinued the following day; IV ampicillin and gentamicin were continued for the entire course of 21 days.

"Although essential to prenatal care, the standard rectovaginal swab for GBS does not reveal all details necessary to eliminate suspected sepsis in the neonate."

#### Discussion:

Although essential to prenatal care, the standard rectovaginal swab for GBS does not reveal all details necessary to eliminate suspected sepsis in the neonate. As seen in previous studies, GBS colonization in the pregnant woman can be intermittent, persistent, or transient, with 51% of women clearing the bacteria during their pregnancy and 19% having had the organism at some point in the pregnancy. (4,5) In fact, studies show that if a woman is tested negative antenatally, up to 9% can test positive if swabbed again postpartum. (4) Due to the lack of persistent positive results, a one-time antenatal rectovaginal swab does not empirically eliminate the possibility of a future GBS infection. The prevention of GBS infections becomes even more difficult in preterm babies due to the increased risk of infection, especially with a prolonged rupture of membranes. (2) In fact, maternal GBS colonization itself can directly cause preterm birth before infecting the neonate, whether upon birth or late-onset. (2) As a result, GBS has become a complex and capricious organism to monitor in the mother and neonate.

We present a case of late-onset GBS infection born to a mother with a negative antenatal swab for GBS. The patient's initially normal WBC and afebrile status did not warrant antibiotic use, yet ten days following EBM administration, the WBC and CRP were significantly elevated. The subsequent blood cultures positive for GBS, accompanied by left lower extremity cellulitis, created an unusual presentation, as only 4% of late-onset GBS infections share this characteristic. (1) This aligns with a review of 32 cases of GBS cellulitis-adenitis, in which 91% of patients showed bacteremia as the most common manifestation of GBS infection. (5) In addition, late-onset infections tend to occur within the time frame of 4 to 5 weeks of life, whereas this case presented as cellulitis 19 days after birth and ten days after adding EBM to the patient's diet. (6) These details warrant an investigation into the source of GBS.

The pathophysiology of late-onset GBS remains unclear. One potential source stems from household contacts, including parents, siblings, and other caregivers that may be colonized by GBS. Alternatively, the infection may be hospital-acquired. An essential yet overlooked consideration is the contamination of the mother's breastmilk. EBM is GBS positive in 0.8 to 3.5% of mothers. (3) EBM may test positive despite a negative rectovaginal swab, highlighting its potential as an underlying culprit of lateonset GBS. As EBM is given frequently to the patient, there is also a 35% recurrence rate. (7) However, the origin of GBS in EBM is ambiguous. It may originate from preexisting colonization of the newborn's throat that is then passed to the mother's mammary gland, converting a previously GBS-free mammary gland to a potential source of recurrent infections. On the other hand, the origin may be the mammary gland itself, transmitting the infection to the newborn through EBM feeds. (3,7) Future research is necessary to differentiate between these possibilities and likely include testing EBM before the first feed.

Thus, it may be warranted to introduce breastmilk culture as the standard of care to better control rates of late-onset GBS infections, especially in at-risk premature infants. A study aiming to identify GBS infection sources with 160 mother-baby pairs discovered colonization of GBS in neonates after leaving the hospital, even with exposure to intrapartum antibiotics and with GBS-negative mothers upon hospital discharge. (8) Although some studies claim culturing breast milk is costly and purposeless due to EBM's multibacterial contamination, the process may still be beneficial in preterm babies who are already more susceptible to infection. (9) The existence of GBS in breast milk should not be a contraindication to breastfeeding. An alternative option may be antibiotic prophylaxis while breastfeeding GBS-positive EBM. (9) Breast milk does have a wide variety of nutritional and immunologic benefits for the baby. However, it can be a source of life-threatening GBS bacteremia, meningitis, or other local infections for the preterm neonate. Culturing EBM and accounting for its GBS status can be a critical piece of information for the immunodeficient neonate and prevent systemic infections.

"Culturing EBM and accounting for its GBS status can be a critical piece of information for the immunodeficient neonate and prevent systemic infections."

#### Conclusion:

A late-onset GBS infection manifesting as cellulitis in a premature

neonate, born to a mother considered GBS-negative per rectovaginal swab as presented in this case report, provides the opportunity to discuss possible etiologies and solutions to prevent late-onset infections in the future. The literature has shown that the standard of care with a one-time rectovaginal swab for GBS during pregnancy has exhibited inconsistencies, including false negatives, leading to premature birth and subsequence neonatal sepsis. This unique case of late-onset GBS in a patient at less than three weeks of life and who began receiving breastmilk ten days before initial signs of infection suggests that breastmilk, a commonly overlooked source of infection, warrants further investigation. Breastmilk benefits are numerous and well-established, but investigating breastmilk through culturing to ensure its safety before adding it to a premature neonate's diet is often argued against in communities promoting breastfeeding. However, this simple step could be added to care standards to promote early antibiotic prophylaxis and detect potential threats to an already immunocompromised patient. Culturing breast milk should empower patients' mothers, families, and providers to know that all steps are being taken to ensure their premature babies' safety and prevent or lessen the burden of late-onset infection while benefiting from a breastmilk diet.

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#### NT





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## The Important Role of Building Provider-Patient Trust in Improving Maternal and Infant Health Outcomes

Barb Himes, IBCLC



#### Saving babies. Supporting families.

First Candle's efforts to support families during their most difficult times and provide new answers to help other families avoid the tragedy of the loss of their baby are without parallel.

"We are learning more and more about the fatal effects of racial disparities in U.S. maternal and infant health – the mortality rate of Black mothers in the United States is three to four times higher (42.8 for every 100,000 live births) (1) than their white counterparts – and twice to three times as many Black babies die before their first birthday than do white babies."

We are learning more and more about the fatal effects of racial disparities in U.S. maternal and infant health – the mortality rate of Black mothers in the United States is three to four times higher (42.8 for every 100,000 live births) (1) than their white counter-

To every NICU nurse who has cared for these precious babies we say..... "Thank you." parts – and twice to three times as many Black babies die before their first birthday than do white babies.

The reasons include disparities in access to quality health care, but they also include racial bias on the part of health care providers, (2) resulting in dismissiveness, false assumptions, and failure to build trust. As we have previously reported, Black women in the U.S. can experience "an inescapable atmosphere of societal and systemic racism [that] can create a kind of toxic physiological stress, resulting in conditions — including hypertension and pre-eclampsia — that leads directly to higher rates of infant and maternal death." (3)

The issue of trust leads to the critical flip side: Black newborns have a greater chance of surviving childbirth if their physicians are Black doctors, according to a 2019 study (4). Its authors note that the disparity is likely the effect of structural racism, a "social construct that has gotten under the skin." (5)

The evidence suggests racial concordance between health care providers and patients can lead to relationships freer from stress, fears, and maternal concerns about being dismissed, resulting in relationships of greater trust between the provider and patient.

But there is a problem: According to the Association of American Medical Colleges, only five percent of American doctors identify as Black. Dr. Valerie Montgomery Rice, dean of the Morehouse School of Medicine, a historically Black medical school, believes that healthier outcomes depend in part on:

- A patient's trust in a doctor
- A positive doctor-patient relationship
- An understanding of the patient's environment

She notes this can occur "through a cultural lens. If you can relate to something about that person's story or have some indication of what their experience has been, then the recommendations you make as a provider are going to make a difference."

In light of this need, Morehouse and CommonSpirit Health have recently announced plans to increase the U.S. Black physician population by launching five Morehouse regional medical school campuses in underserved communities that also have Common-Spirit facilities and by recruiting students from provider-deprived

Did you know that premature and low birth weight babies have a 4x greater risk for SIDS?

At First Candle we're educating parents, grandparents and caregivers about safer sleep to make sure all babies reach their first birthday. Learn more at firstcandle.org communities. The curriculum will include cultural competency in patient care. (6)

This is a heartening and overdue step that needs to be built upon, but it is also important to face the reality that the current majority of health care providers is likely not to be Black. This, however, does not mean building greater provider-patient trust cannot be achieved and that it should not be strongly pursued. There are steps that can and should be taken.

At First Candle, our Straight Talk for Infant Safe Sleep training program actively explores unconscious bias and works with care providers to improve communication with patients, to better understand their real-world obstacles and objections to adopting safe sleep guidelines and breastfeeding, which can significantly reduce the rates of infant mortality. The awareness raised with Straight Talk participants and the learnings from these sessions can positively affect the providers' work to reduce sleep-related infant mortality and influence overall approaches to patient-centered care.

"The aim is for providers to develop and demonstrate an ability to listen, learn, and engage in respectful dialogue with families. Providers must engage themselves as they look for ways to engage their patients."

The aim is for providers to develop and demonstrate an ability to listen, learn, and engage in respectful dialogue with families. Providers must engage themselves as they look for ways to engage their patients. How do I feel about my patient and her pregnancy journey, before, during, and after? What beliefs and experiences do I bring to this relationship of care?

It is important to reach patients "where they are", where they live and feel.

- Assume good intent
- Be open
- Consider another perspective
- Word choice is important
- Listen, pause, reflect

This includes looking at your own assumptions, which could range from gender (doctors are males, nurses are females) to racial and socioeconomic stereotyping. The intent should be to respect your patient's and her family's wishes and needs, remembering that each family is unique and that bias exists.

Another area of sensitive engagement may include **Adverse Child Experiences (ACE)**. Our childhood experiences have a significant lifelong impact on our health and the quality of our lives. ACE has been linked to risky behavior, psychological issues, serious illness, and even death. Some ACEs are childhood abuse, neglect, and household challenges. Being aware of potential ACEs can help the provider to consider home visiting programs, parenting training, domestic violence prevention, mental illness and substance abuse treatment, quality childcare availability, and community support for parents.

The provider-patient relationship is an opportunity to practice **active listening** to understand what patients are truly saying.

- Consciously work to build trust and establish rapport.
- Ask specific questions, which can also be reflective in nature: What do you think about this? How do you feel about this?
- Include verbal affirmations in your conversations (I understand; I see).
- Show interest and concern.

This evaluation extends to the physical environment: Is the waiting room and its staff welcoming and inclusive? In a meeting, is the provider looming over the patient, or are they on equal footing? If it is a telehealth video session, is the provider lit and positioned to be visually approachable and conversational? Is the patient's partner invited to participate actively?

"The practitioner's medical knowledge and experience is the foundation for sustaining maternal and infant health, and his or her interpersonal understanding and true desire to foster a trusting relationship can further that knowledge, to result in improved health outcomes for mothers and babies of all ethnicities, gender identifications, and circumstances. "

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#### **About First Candle**

First Candle, based in New Canaan, CT, is a 501c (3) committed to eliminating Sudden Infant Death Syndrome and other sleeprelated infant deaths while providing bereavement support for families who have suffered a loss. Sudden unexpected infant death (SUID), which includes SIDS and accidental suffocation and strangulation in bed (ASSB), remains the leading cause of death for babies one month to one year of age, resulting in 3,600 infant deaths nationwide per year.

Disclosure: The author is the Executive Director and Chief Executive Officer of First Candle, Inc., a Connecticut not for profit 501c3 corporation.

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nurse who has cared for these precious babies we say..... Thank you."

Did you know that premature and low birth weight babies have a 4x greater risk for SIDS?

At First Candle we're educating parents, grandparents and caregivers about safer sleep to make sure all babies reach their first birthday. Learn more at firstcandle.org

The National Urea Cycle Disorders Foundation



The NUCDF is a non-profit organization dedicated to the identification, treatment and cure of urea cycle disorders. NUCDF is a nationally-recognized resource of information and education for families and healthcare professionals.

www.nucdf.org | Phone:

## Time is precious, just like your patients.



## The 34<sup>th</sup> Annual Gravens Conference on the Environment of Care for High Risk Newborns Virtual Event: March 3, 4, 10, and 17<sup>th</sup>, 2021 On-demand: March 24 – September 30, 2021

Save the Date: March 3, 4, 10, and 17, 2021 Call for Abstracts: Due Weds, Oct 28, 2020

The 34<sup>th</sup>Annual Gravens Conference

on the Environment of Care for High Risk Newborns

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Sheraton Sand Key Clearwater Beach, Florida March 3-5, 2021

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Visit: <u>www.TheGravensConference.com</u> Questions? email nrose@usf.edu

## The Survey says RSV



What you need to know about RSV RSV stands Respiratory Syncytial Virus



rus

#### WHEN IS RSV SEASON?

Typically RSV season runs from November - March. But it can begin as early as July in Florida and end as late as April in the West.

Protect babies and families this RSV season Educate. Advocate. Integrate.



Consult the CDC's RSV Census Regional Trends to learn more www.cdc.goutsuitesearchila-suiveillance.to







#### **Educate Yourself**

Did you know that more than half of the babies admitted to NICUs were not born prematurely? See our fact sheets.



Post on Social Media See examples at nicuawareness.org and nationalperinatal.org/NICU Awareness



#### Recognize NICU Staff

Let them know the difference they are making in our babies' lives. Write a note, send an email, or deliver a gift to show them that you appreciate them.



## Share Your Story

Most people have never heard of a NICU before. Let others know about the extraordinary care that NICUs provide.



#### Join Our Community

Get involved. Become a member of our organizations and share your talents.

#### This project is a collaboration between



www.nicuawareness.org www.nationalperinatal.org/NICU\_Awareness

## **Raising Global Awareness of RSV**

Global awareness about respiratory syncytial virus (RSV) is lacking. RSV is a relatively unknown virus that causes respiratory tract infections. It is currently the second leading cause of death – after malaria – during infancy in low- and middle-income countries.

The RSV Research Group from professor Louis Bont, pediatric infectious disease specialist in the University Medical Centre Utrecht, the Netherlands, has recently launched an RSV Mortality Awareness Campaign during the 5<sup>th</sup> RSV Vaccines for the World Conference in Accra, Ghana.

They have produced a personal video entitled "Why we should all know about RSV" about Simone van Wyck, a mother who lost her son due to RSV. The video is available at <u>www.rsvgold.com/awareness</u> and can also be watched using the QR code on this page. Please share the video with your colleagues, family, and friends to help raise awareness about this global health problem.





Peer Reviewed

## "The Iowa Way" Have We Got This All Wrong?

Rob Graham, R.R.T./N.R.C.P.

I dedicate this column to the late Dr. Andrew (Andy) Shennan, the founder of the perinatal program at Women's College Hospital (now at Sunnybrook Health Sciences Centre). To my teacher, my mentor and the man I owe my career as it is to, thank you. You have earned your place where there are no hospitals and no NICUs, where all the babies do is laugh and giggle and sleep.

*"I recently had the pleasure of watching a webinar from Iowa Children's Hospital presented by Dr. Jonathan Klein focusing on their management of the sub-24 week gestation infant. To say the least, I was gobsmacked. This unit reports chronic lung disease rates of 11% in this population."* 

I recently had the pleasure of watching a webinar from Iowa Children's Hospital presented by Dr. Jonathan Klein focusing on their management of the sub-24 week gestation infant. To say the least, I was gobsmacked. This unit reports chronic lung disease rates of 11% in this population.

How can this be? The unit I practice in has of yet had little success with those infants of 22 weeks gestation and a chronic lung disease rate of 50% in the 23-week gestation strata. Our chronic lung disease rates in higher gestational age groups are considerably better, giving an overall rate of approximately 9%. This number is impressive in itself, given the number of micro-premature infants we treat, but the lowa data is humbling.

What are we doing wrong? When it comes to premature infants, we know that all are not created equal, and the degree of pulmonary maturity dictates our approach to ventilation. Since resuscitation has only recently been offered to those infants of less than 23 weeks gestation and discouraged until recently at 23, we have limited experience and data in this group. Our approach to their ventilation to date has been the same as those of 24-25 weeks gestation. Perhaps this is the first mistake we are making. For decades we have been advocating an "open lung" approach to ventilation, aiming for full recruitment. Even here, there is disagreement as to what that is. In conventional ventilation, ten ribs of lung inflation is considered "hyperinflated"; however, this should not be considered hyperinflation when ventilating with a high-frequency mode. Sheer forces with high-frequency ventilation are considerably less than those imposed by conventional ventilation. (This assumes the chest film is relatively clear and not hazy, indicating under-recruitment or gas trapping. Simply counting ribs is an inadequate measure of proper recruitment.)

What about the 22-23 week gestation lung? We have been using the same targets in this population as the rest of our patients, aiming for ten ribs of inflation in high-frequency modes. We know that the lung is not as developed at this age as the "older" infant. There are fewer alveolar ducts to recruit, and the conducting airways are fragile. Alveolar duct formation and later alveolar development do not happen all at once. Instead, they develop more like flowers on a plant that appear in stages. The terminal bronchioles and alveolar ducts are capable of some gas exchange. The challenge here is to provide enough minute volume to support gas exchange without damaging the lung structure and inhibit the alveolar duct and subsequent alveolar development. This process is a challenge as a mountain of evidence shows that mechanical ventilation interferes with pulmonary development (this may not be as severe with high-frequency jet ventilation) (1) as does oxidative stress, two factors that are unavoidable at this gestational age.

"We know that the lung is not as developed at this age as the "older" infant. There are fewer alveolar ducts to recruit, and the conducting airways are fragile. Alveolar duct formation and later alveolar development do not happen all at once."

Iowa reports using PEEP as low as  $5 \text{ cmH}_2\text{O}$  in 22-23 week gestation patients, a number most of us would consider too low. But is it? Could it be that this relatively low level of PEEP is enough to maintain airway patency in these patients without creating microtears and resulting air leak? Are we asking for more inflation than the lungs can provide? Could we be creating chronic lung disease in the pursuit of lung-protective ventilation? This practice is the

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standout difference between ventilation of these infants in Iowa with their management in the NICU I practice in. The difference in pulmonary outcomes is difficult to dismiss.

There is more. We have all been conditioned to consider ventilation with an endotracheal tube to be bad and, as a result, aim to extubate even the smallest babies at the earliest opportunity. I have stated before the relative success with early extubations depends in no small part on the level of expertise when invasively ventilating as well as the use of adequate CPAP levels post-extubation to maintain recruitment. As a result, it is not uncommon to extubate the extremely premature infant after a week or so of ventilation. Perhaps this, too, is a mistake.

#### "As a result, it is not uncommon to extubate the extremely premature infant after a week or so of ventilation. Perhaps this, too, is a mistake."

lowa does not practice early extubations when treating these infants; they are not left to struggle on CPAP in high FiO<sub>2</sub>, something that in and of itself may be more harmful than gentle, lung-protective ventilation. The role of oxidative stress in pulmonary development is well known, producing smooth muscle hypertrophy, reactive airways disease, and altering alveolar development. (2) Interestingly, the main interface for non-invasive support in lowa is the good old fashioned nasal pharyngeal tube (NPT), a standard endotracheal tube cut at approximately 4 cm with a standard 15 mm connector attached to a ventilator circuit. (In my experience, there are fewer issues with nasal bridge or septal breakdown with the NPT).

As a long-time proponent of high-frequency ventilation and highfrequency jet ventilation in particular, it made sense to me that lowa also utilizes high-frequency jet ventilation as their primary form of invasive ventilation. It has been suggested that high-frequency jet ventilation allows for somewhat normal apoptosis and pulmonary development. A study by Dr. Dick Bland and Dr. Kurt Albertine showing this was presented at the Snowbird conference in 1999; however, that study was never published. (3)

"Third generation oscillators with volume targeted options are to date unavailable in the United States. It remains to be seen whether or not volume targeted oscillation would result in similarly better outcomes when compared to high-frequency jet ventilation."

Third generation oscillators with volume targeted options are to date unavailable in the United States. It remains to be seen

whether or not volume targeted oscillation would result in similarly better outcomes when compared to high-frequency jet ventilation. I suspect there is some benefit here, but the tiny radius of the 22-23 week gestation infant greatly attenuates the oscillatory waveform—physics favour high-frequency jet ventilation in these infants, in my opinion.

It is difficult to extract a single practice from a unit with successful outcomes and apply them alone in another setting. Ventilation is no exception; there are so many local variations, even within the scope of a study that replicating results can prove difficult. With high frequency ventilation, even the user may affect the outcome. The "gentle resuscitation" approach from Cologne, Germany comes to mind, as does Dr. Roberta Ballard's study on inhaled nitric oxide to prevent chronic lung disease; the whole is indeed greater than the sum of the parts.

"Ventilation is no exception; there are so many local variations, even within the scope of a study that replicating results can prove difficult. With high frequency ventilation, even the user may affect the outcome."

Several other lowa practices stand out. Not using humidity is one. Instead, their approach uses high total fluid intakes to counter insensible losses and aims for more rapid skin keratinization. This approach seems to reduce the incidence of sepsis. This makes sense because very humid environments are breeding grounds for pathogens, and sepsis is one of the biggest contributors to mortality and poor outcomes. (3)

In this column, I have stated before that one's NICU ventilation toolbox is incomplete without the availability of high-frequency jet ventilation. I believe "the lowa way" gives credence to this view.

Perhaps when dealing with 22-23 weeks gestation, it's the lowa way or the highway! It is, after all, difficult to argue with success.

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Disclosures: The author receives compensation from Bunnell Inc for teaching and training users of the LifePulse HFJV in Canada. He is not involved in sales or marketing of the device nor does he receive more than per diem compensation. Also, while the author practices within Sunnybrook H.S.C. this paper should not be construed as Sunnybrook policy per se. This article contains elements considered "off label" as well as maneuvers, which may sometimes be very effective but come with inherent risks. As with any therapy, the riskbenefit ratio must be carefully considered before they are initiated.

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#### The PREGNANT MOM'S Guide To Staying SAFE DURING COVID-19





*Thirteen-year-old Emily Rose Shane was tragically murdered on April 3, 2010 on Pacific Coast Highway in Malibu, CA. Our foundation exists to honor her memory.* 

In Loving Memory

August 9, 1996 - April 3, 2010



Each year, the Emily Shane Foundation SEA(Successful Educational Achievement) Program provides academic and mentoring support to over 100 disadvantaged middle school students who risk failure and have no other recourse. We have served over 700 children across Los Angeles since our inception in the spring of 2012. Due to the COVID-19 outbreak, our work is in jeopardy, and the need for our work is greatly increased. The media has highlighted the dire impact online learning has caused for the very population we serve; those less fortunate. **We need your help now more than ever to ensure another child is not left behind.** 

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1 session	\$15
1 week	\$30
1 month	\$120
1 semester	\$540
1 year	\$1,080
Middle School	\$3,240

The Emily Shane Foundation is a 501(c)3 nonprofit charity, Tax id # 27-3789582. Our flagship SEA (Successful Educational Achievement) Program is a unique educational initiative that provides essential mentoring/tutoring to disadvantaged middle school children across Los Angeles and Ventura counties. All proceeds directly fund the SEA Program, making a difference in the lives of the students we serve.



## National Perinatal Association Annual Conference 2020 – Multidisciplinary Care in the 4th Trimester

Viveka Prakash-Zawisza, MD, Jerry Ballas, MD, MPH

The National Perinatal Association (NPA) is an interdisciplinary organization that strives to be a leading voice for perinatal care in the United States. Our diverse membership is comprised of healthcare providers, parents & caregivers, educators, and service providers, all driven by their desire to give voice to and support babies and families at risk across the country.

Members of the NPA write a regular peer-reviewed column in Neonatology Today.



Educate. Advocate. Integrate.

"This year the chosen theme focused on the 4th Trimester and the various areas of vulnerability for parents and infants during this time, as well as the resources available for support."

As a national group of perinatal advocates, providers, and parents, the National Perinatal Association strives to select a theme for its annual conference that reflects cur-

Readers can also follow NEONATOLOGY TODAY via our Twitter Feed @NEOTODAY rent trends and best practices that most impact the perinatal community. This year the chosen theme focused on the  $4^{th}$  Trimester and the various areas of vulnerability for parents and infants during this time, as well as the resources available for support.

The 4<sup>th</sup> Trimester is defined as the period of time following birth up to 12 weeks postpartum. This time period is so named as it reflects the particular features of the early postpartum weeks as being a continuation of the pregnancy in many ways. Human babies are born without the ability to move independently or feed themselves, making them entirely reliant on a caregiver to meet their basic needs. As such, in many ways, they are still in a fetal state despite being outside the uterus. In parallel, the new mother is physically healing from childbirth, figuring out how to breastfeed, and learning all about her new baby's cues. It is a time of intense critical bonding for both infant and parent, an establishing of psychological, emotional, and physical connection and attachment. Given how special and fleeting this time is, the need to protect a mother's ability to stay with her newborn without interruption and to receive whatever support necessary in case of physical or mental health needs is paramount. Therefore, this year's conference topics were related to strengthening state and federal parental leave policies, health equity, perinatal mood and anxiety disorders, substance use disorders, and special considerations for NICU parents. The undeniable impact of the Covid-19 pandemic on the perinatal landscape was also woven throughout the conference.

#### A meeting like no other:

While this may seem like a typical superlative, an organization may use to boost its conference profile, this year's NPA conference was literally like no other annual meeting held in its 40-year history. While necessary in light of the Covid-19 pandemic, the pivot to a virtual platform was uncharted territory for NPA. Aside from the technological and logistical hurdles we had to overcome, there was the genuine concern of capturing the same interest and anticipation most speakers, attendees, and sponsors reserve for in-person events of this kind. As spring turned to summer, and it became increasingly apparent that our postponed meeting would become a virtual meeting, our Conference Committee internally adopted the mantra "We Got This," took a collective breath, and then made the announcement to all our speakers, presenters, sponsors, and attendees.

"As spring turned to summer, and it became increasingly apparent that our postponed meeting would become a virtual meeting, our Conference Committee internally adopted the mantra "We Got This," took a collective breath, and then made the announcement to all our speakers, presenters, sponsors, and attendees."

To our surprise at the time, the announcement barely made any waves. Speakers stayed committed, sponsors stuck with us, poster presenters pivoted to video format, and attendance increased as the conference approached. What would become abundantly clear, especially now looking back on such an amazing turn of events, is that the passion and expertise of our presenters, the growing interest in the 4<sup>th</sup> Trimester, and the feeling of fellowship NPA meetings are known for would overcome the barriers put in place by Covid-19.

#### Day One: Caring for the Family Unit:

There could not have been a better way to start such an impactful meeting than having Jenné Johns and Shanté Nixon team up to discuss their unique perspectives on starting their families. From Jenné's intense NICU experience and ongoing mission to educate others to Shanté's journey



## NPA 2020 Conference: Day One

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 Disrupt breastfeeding Adversely impact maternal mental health

- ble the workload fo
- oital staff
- obably not prevent in



## NPA 2020 Conference: Day Two

The PARTNER Model

CNM, FACNM, FAAN December 3, 2020

POSTPARTUM PAUSE: **IDENTIFYING GAPS IN** PREPAREDNESS FOR PARENTING

to motherhood through adoption, the ambitious goal of defining the full spectrum of perinatal care and the 4th Trimester was perfectly set. Blythe Thomas from 1,000 Days then followed up by piecing together many aspects of Jenné and Shanté's stories to drive home the importance of substantive family medical leave policies and provide updates and resources to help advocate for change at the legislative level. We then heard from Rebecca Feldman, CNM, about the power of collaborative, perinatal group programs aimed at optimizing mental health treatment and reducing barriers to care in the 4<sup>th</sup> Trimester. Finally, Jerry Ballas provided an overview, a current snapshot of the effects of Covid-19 on perinatal care, and some of the innovations that have emerged from the pandemic, including a resurgence in telehealth and traumainformed care. In addition to these live sessions, pre-recorded breakout sessions were available to attendees. Diana Rodin and Sharon Silow-Carroll presented effective strategies for improving postpartum visit attendance among Medicaid participants. At the same time, Regina Troxell shared her unique perspective on navigating the 4<sup>th</sup> Trimester as a Child Neurology trainee and the shortcomings of current medical education regarding providing compassionate family medical leave.

#### Day Two: Medical Care:

The second day started with an amazing review of the latest and most effective approaches to caring for opioid-exposed newborns by Susan Hwang, MD, PhD. A living legend then followed her in the field of midwifery, Dr. Ginger Breedlove, CNM, PhD, who gave one of the most thought-provoking and eye-opening talks identifying gaps in preparedness for parenting by weaving together stories, experiences, research, and observations from her own vast clinical experience, as well as her personal experiences as a mother and grandmother. She was followed by none other than Sue Hall, neonatologist and a cornerstone of NPA, who not only gave a stirring presentation focused on trauma-informed care in the setting of giving birth amid Covid-19, she did so at the last minute when a speaker was unable to present. Finally, Noelle Ciara, DSW, LCSW, expertly tied together many of the themes for the day as she described a novel, attachment-based practice model she helped develop and now manages that supports providers working with mothers and infants impacted by opioid use disorders. The second day's breakout sessions provided insight into



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specific resources being developed by different working groups within NPA. Dr. Vincent Smith discussed NPA's ongoing initiative to develop comprehensive, evidence-based discharge and transition resources for NICU families, while a trio of NICU psychologists, Drs. Shelly Steinwurtzel, Allison Dempsey, and Sage Saxton provided updates on the myriad of projects spearheaded by NPA's Maternal Mental Health Group and the National Network of NICU Psychologists.

#### Day Three: Mental Health:

The meeting culminated with five incredible presentations that looked at mental health in the 4th Trimester from five unique perspectives. Dr. Neill Epperson began the day with a deep, analytical journey into the genetic, neuronal, and biologic impact of maternal childhood adversity on pregnancy, fetal, and infant outcomes. Dr. Naomi Bar-Yam then took attendees to the other end of the analytical spectrum by providing epidemiologic and biomedical data on unexpected pregnancy outcomes to provide greater context when defining the 4<sup>th</sup> Trimester at a societal level. Dr. Mandy Allison then presented specific strategies for confronting disparities in the 4<sup>th</sup> Trimester and confronting socioeconomic gaps through nurse-family partnerships to improve the health and wellbeing of families in her region. We then heard from yet another living legend, Dr. Marilyn Sanders, who emphasized the deep-rooted themes of our conference by describing the importance of the first one hundred days of newborn life and how even in a setting as potentially chaotic as the NICU, there were proven strategies to promote safety, security, and connectedness between parents and their newborn. And finally, NPA's own Sage Saxton brought together our entire conference with a thorough, powerful, and empathetic talk on diagnosing and treating postpartum depression, anxiety, and mood disorders. Rounding out the final day were two informative breakout sessions. The first was from Celeste

St. John-Larkin, MD and Jennifer Paul, PhD, discussing perinatal mood disorders from the lens of infant mental health, and the second was by Laurel Wilson, IBCLC, who provided an updated, contemporary view of cannabis use and its potential implication during the perinatal period.

#### Looking ahead to brighter days:

Our 2020 conference was a testament to NPA's mission to serve as a national leader in promoting evidence-based advances in perinatal and postpartum care and elevating the voices of the most vulnerable parents and families so that all newborns and their parents are given the dignity and protection they deserve during the 4<sup>th</sup> Trimester. The New Year brings with it the promise of a widespread Covid vaccine, amplification of solutions to health inequity and racial disparities, several state and federal bills supporting mothers and infants in the postpartum period, and further understanding of perinatal mental health and substance use disorders. With great hope, determination, and a newfound respect for the ability to convene in the absence of a physical convention, we are already planning for our 2021 conference that is scheduled to take place December 1<sup>st</sup>-3rd. Whether it will be in-person in Denver, completely virtual, or a hybrid convention, we are confident it will provide the quality, passion, and multidisciplinary appeal that has become the hallmark of the National Perinatal Association.

Disclosure: The National Perinatal Association <u>www.nationalperina-</u> <u>tal.org</u> is a 501c3 organization that provides education and advocacy around issues affecting the health of mothers, babies, and families.

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## Postpartum Revolution





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For more information, contact the meeting planner at nrose@usf.edu



50

## SHARED DECISION-MAKING **PROTECTS MOTHERS + INFANTS**

**DURING COVID-19** 

## **KEEPING MOTHERS + INFANTS TOGETHER**

Means balancing the risks of...

- HORIZONTAL INFECTION
- SEPARATION AND TRAUMA



## **EVIDENCE**

We encourage families and clinicians to remain diligent in learning up-to-date evidence.

## PARTNERSHIP

What is the best for this unique dyad?

SHARFD **DECISION-MAKING** 

S EEK PARTICIPATION **H** ELP EXPLORE OPTIONS A SSESS PREFERENCES **R** EACH A DECISION **F** VALUATE THE DECISION





## **TRAUMA-INFORMED**

Both parents and providers are confronting significant...

- FEAR
- GRIEF
- UNCERTAINTY

## LONGITUDINAL DATA

We need to understand more about outcomes for mothers and infants exposed to COVID-19, with special attention to:

MENTAL HEALTH
POSTPARTUM CARE DELIVERY



NEW DATA EMERGE DAILY. NANN AND NPA ENCOURAGE PERINATAL CARE PROVIDERS TO ENGAGE IN CANDID CONVERSATIONS WITH PREGNANT PARENTS PRIOR TO DELIVERY REGARDING RISKS, BENEFITS, LIMITATIONS, AND REALISTIC EXPECTATIONS.

#### Partnering for patient-centered care when it matters most.



Association of



nationalperinatal.org nann.org

# **NICU** Awareness



#### Educate. Advocate. Integrate.

## **Did You Know?**

Most NICU babies have special needs that last longer than their NICU stay. Many will have special health and developmental needs that last a lifetime. But support is available.

Learn about the programs in your community. Seek out other families like yours. Then ask for help. Working together we can create a community where our children will grow and thrive.

#### Special Health Needs

Babies who have had a NICU stay are more likely to need specialized care after they go home. **Timely follow-up care is important.** 

NICU babies have a higher risk for re-hospitalization. So every medical appointment is important. Especially during cold and flu season when these babies are especially vulnerable to respiratory infections.

#### Who Can Help

- pediatricians
- neonatal therapists
- pulmonologists
- neurologists
- gastroenterologists
- cardiologists
- nutritionists
- CSHCN Programs for Children with Special Health Care Needs

#### Special Developmental Needs

## Any NICU stay can interrupt a baby's growth and development.

Needing specialized medical care often means that they are separated from their parents and from normal nurturing.

While most NICU graduates will meet all their milestones in the expected developmental progression, It is typical for them to be delayed. This is especially true for preterm infants who are still "catching up" and should be understood to be developing at their "adjusted age."

#### Who Can Help

- IBCLCs and lactation consultants
- Early Childhood Interventionists
- developmental pediatricians
- occupational therapists (OTs)
- physical therapists (PTs)
- speech therapists (SLPs)
- WIC Special Supplemental Nutrition Program for Women, Infants, and Children
- social workers and case managers

#### **Special Educational Needs**

Every child has their own unique developmental needs and **every student has their own unique and special educational needs**.

Take advantage of the services and support that can meet your child where that are and help them reach their future educational goals.

Call your local school district to request a free educational evaluation. Learn about all the available programs and support.

#### Who Can Help

- Preschool Program for Children with Disabilities (PPCD)
- Special Education programs under the Individuals with Disabilities Education Act (IDEA)
- educational psychologists
- speech therapists (SLPs)
- occupational therapists (OTs)
- reading specialists



## Medical Legal Forum: A Timely Scenario (Fall 1985)

#### Gilbert Martin, MD

The phone's ringing could not even fully wake me as my mouth was as dry, and my senses dull.

"Gene, it's me."

"Wha, who . . . . eecch . . . I just couldn't clear my throat. Suddenly my gut tightened as a sense of fear brought me to a more alert level.

"Gene, wake up; it's Gerri."

"What time is it? What's the matter? Are you okay?" The words ran out of my mouth as I was now fully awake. "Gene, something is wrong with the baby. Dr. Iretolin just came to see me. She has periods where she just stops breathing. I'm so...so..."

"Hold on, honey; I'm getting dressed. I'll be there in twenty minutes."

"The only problem with the whole procedure had been all the necessary paperwork, as clerks, nurses, doctors, and aides of all sort made us sign form after form about understanding side effects from medications, anesthesia, and all the possible things that could go wrong. This "informed consent" process was standard procedure, so the doctor said, but to me, it was a waste of time and a pain."

As I washed my face and dressed, I thought about what Gerri had said. She had given birth to a seemingly healthy 8-pound baby only nine hours earlier. Her labor and delivery were easy, and the baby seemed fine. The only problem with the whole procedure had been all the necessary paperwork, as clerks, nurses, doctors, and aides of all sort made us sign form after form about understanding side effects from medications, anesthesia, and all the possible

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things that could go wrong. This "informed consent" process was standard procedure, so the doctor said, but to me, it was a waste of time and a pain.

I finished dressing, grabbed my car keys, and left the house. Intervalley Hospital was only ten minutes away, but the ride seemed endless even though there was little traffic. I had to use the Emergency entrance and ran through the crowded hall to the staircase leading up to the maternity floor. The stairwell was brightly lit, and there were signs at each level.



"Use the handrails;" "Proceed cautiously," "Slower walkers keep to the right," and "We are not responsible for accidents" were only a few of the signs I passed as I bounded up the stairs. Maternity was on the third floor. Opening the stairwell door and ignoring the "look both ways" warning, I ran to Gerri's room. The small light behind her outlined her hair, giving it an eerie appearance.

"Gene," she said, reaching for me, "I'm so glad you're here."

"It will be all right, honey," I said, holding her close. "Now tell me again, what is so wrong?"

"The doctor says that Kari has periods where she stops breathing. They're trying to find out why. You'd better speak to him yourself. I think he is in the special ...the special care nursery."

"I'll go there right away. Do you feel strong enough to go? Perhaps you'd better stay here and rest."

"I want to go with you, but ... Gene, I'm so....."

"Shh, shh ... let me hold you a second. Easy now. It will be fine ... I promise."

As I left Gerri, I felt bewildered, drained, and now afraid. I asked

the nurse for directions to the special care nursery, and she used the intercom to ask Dr. Iretolin to come out.

I waited only a few moments and the door opened as a short, youngish looking man in a yellow hospital gown walked out.

"Mr. West?"

I nodded.

"I'm Dr. Iretolin. Believe me, I'm sorry to bring you out at such a late hour but I think it's important to talk to you about Kari." The doctor was obviously tired, but he had a gentle, understanding air bout him.

"Sit down with me a moment," he continued, guiding me to a chair in the anteroom. "Let me explain the situation to you."

"I don't understand this at all, doctor. Kari was fine a few hours ago. What, just what can be so terribly wrong now?"

"Kari seemed fine at birth and several hours afterward. However, for some reason, she has had periods where she just stops breathing. A certain number of these breathing lapses, called apnea, may be normal, but her pauses are becoming more frequent, and they are beginning to affect the rest of her system. We have to find out why these are occurring."

"What, what do you think she has? What can we do? Will you do something quickly?"

"Yes, yes, yes," he continued, "But Kari may have one or a combination of many problems. She may have sepsis, or infection as you would call it. She might have low blood sugar or even something wrong with her heart. But in order to find out the reason, she needs to have some blood tests, a spinal tap, some x-rays, and possibly she may even have to be placed on a respirator in order to help her to breathe."

"Okay, okay, whatever you want. Only please hurry up and let's get started. I want everything done as soon as possible."

"Yes, Mr. West, I understand your concern. But before we start testing or begin treatment, you must understand all the procedures and the risks involved and must sign a consent form for each and every procedure or medication."

"What, again?" I asked, even more bewildered.

"I'm afraid so," continued Dr. Iretolin. "I'm sure the OB staff told you about the "ICACMPSE" process."

"The what?" I asked.

"The Informed Consent Act Concerning Medications, Procedures, and Side Effects. This was passed by Congress in 1987 to try to curtail malpractice suits, which often developed years later, I'm sorry, but it's the law."

"Fine, fine. Tell me what to do or where to sign."

"I'm afraid it's not as simple as that, for you must first understand the material, take a short exam testing your knowledge, and then sign the form. Follow me to the "Informed Consent Room."



Stupefied, I followed him down a short corridor to a gray door. We went inside, and in front of me was a long, narrow room with cubicles, each containing a videotape setup. Despite the late hour, the room was filled. Each cubicle had its own heading.

"Let's start here, Mr. West," said Dr. Iretolin. I sat down on a chair as he turned on the video. In a moment, the subject appeared. "The Spinal Tap Procedure" was printed on the screen. In the next half an hour, I sat through this tape and was subjected to a miniseries on antibiotics, apnea, and something called mechanical ventilation. My head was swimming.

"Now, can I see Kari? I asked.

"Of course," said Dr. Iretolin, "follow me. First, you must put on this gown...here, let me help you. Now wash your hands carefully for the full three required minutes."

After finishing, I followed the doctor into the nursery. The room was a beehive of activity with beeping alarms and foreign sounds I had never heard.

"Kari is over here, Mr. West."

I walked slowly to the incubator. Kari looked big compared with some of the other babies I had noticed, but she seemed pale under the bright lights. I shielded my eyes and looked at the baby.

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I heard Dr. Iretolin say to one of the nurses, "We must remember to dim the nursery lights. I understand that there is some evidence that a well-lighted nursery may lead to an increased incidence of retrolental fibroplasia. The lawyers will have a feast on that issue."

"What is retrolen...well anyway," I turned and asked Dr. Iretolin, "Can you start treatment yet?"

"As soon as you sign all of the consent and freedom from liability forms. I have them right here.?

"The doctor produced a sheath of material, and I methodically signed them all, not really caring. What the heck, I said to myself. These are only forms anyway. I finished quickly and gave the material to Dr. Iretolin.

"Thank you, Mr. West," he said, smiling. "Now, we can begin. Why



don't you go downstairs and have a cup of coffee? I'll call you when we're done."

For the first time, I felt totally drained. A cup of coffee might do me some good. I decided to forego the stairs and take the elevator instead. The door opened, and there was an elevator operator seated at a small stool in the front. The musical sounds of Ella Fitzgerald singing "A Foggy Day" came from a small tape recorder in the corner.

"First floor, please," I said as I walked inside.

Good morning, sir" was the answer. "Before we go down, however, I must tell you that there is a one in 7656 chance that we might experience a power failure in this elevator, and you must sign a consent form before we proceed."

"I must sign what??" I sputtered.

"It's all part of the legislation," he continued. "We cannot take a chance on your not understanding the risks involved in riding this elevator."

I looked up, took the offered pen, and signed.

"A foggy day in London town."

Had me low and had me down...."

THE PERINATE.

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#### **Disclaimer:**

This column does not give specific legal advice, but rather is intended to provide general information on medicolegal issues. As always, it is important to recognize that laws vary state-to-state and legal decisions are dependent on the particular facts at hand. It is important to consult a qualified attorney for legal issues affecting your practice.



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## New Nutrition Standards Should Shape Americans' Food and Beverage Choices

Michelle Winokur, DrPH, and the AfPA Governmental Affairs Team, Alliance for Patient Access (AfPA)

The Alliance for Patient Access (allianceforpatientaccess.org), founded in 2006, is a national network of physicians dedicated to ensuring patient access to approved therapies and appropriate clinical care. AfPA accomplishes this mission by recruiting, training and mobilizing policy-minded physicians to be effective advocates for patient access. AfPA is organized as a non-profit 501(c)(4) corporation and headed by an independent board of directors. Its physician leadership is supported by policy advocacy management and public affairs consultants. In 2012, AfPA established the Institute for Patient Access (IfPA), a related 501(c) (3) non-profit corporation. In keeping with its mission to promote a better understanding of the benefits of the physician-patient relationship in the provision of quality healthcare, IfPA sponsors policy research and educational programming.



How many serving of seafood should expectant mothers consume per week? How many fruits and vegetables should children have each day? When should babies start on solids?

Many parents, and even some health care providers, many not be certain. But consulting the new *Dietary Guidelines for Americans* will provide the answers. (1)

The *Dietary Guidelines* are updated jointly by the U.S. Departments of Agriculture and Health and Human Services every five years. The agencies released the newest edition in late December. Under the call to action "Make Every Bite Count," the new *Dietary Guidelines* provide a framework for healthy eating at each stage of life.

The latest version of the *Dietary Guidelines* includes, for the first time, information about nutrition for infants and toddlers. Evidence has shown birth through age 2 is a pivotal time of growth and development. "It also is key for establishing healthy dietary patterns that may influence the trajectory of eating behaviors and health throughout the life course," according to the document.

Key recommendations for infants and toddlers include:

 Feeding an exclusively human milk diet for the first six months of life. The *Dietary Guidelines* suggest sourcing pasteurized donor human milk from a reliable source, such as an accredited bank, if mother's milk isn't available. Feeding infants iron-fortified formula is the acceptable alternative to human milk.

- Provide infants with supplemental vitamin D soon after birth.
- Introduce nutrient-dense complementary foods around 6 months of age. Potentially allergenic foods, such as peanuts, egg, cow milk products and wheat, should be introduced along with other complementary foods.
- Avoid foods and beverages with added sugars, and limit foods and beverages higher in sodium.
- Encourage eating foods from all food groups. Foods rich in omega 3s, iron, zinc, and vitamin D, such as seafood, are important for introducing nutrients crucial for development.

The new *Dietary Guidelines* also offer expanded guidance for pregnant and breastfeeding women. Consumption charts of various foods show these groups of women, on average, eat less than the recommended amounts of vegetables, whole grains and seafood. Two to three servings, totaling 8-12 ounces, of seafood choices lower in methylmercury per week has been shown to provide nutritional value to mothers and to benefit their babies, including babies' brain development.

"Consumption charts of various foods show these groups of women, on average, eat less than the recommended amounts of vegetables, whole grains and seafood."

Finally, the *Dietary Guidelines* offers three principles for everyone to consider when making food and beverage selections:

1. Meet nutritional needs primarily from nutrient-dense foods and beverages.





What's the difference between the Dietary Guidelines Advisory Committee Report & the Dietary Guidelines for Americans?

## COMMITTEE REPORT VS DIETARY GUIDELINES



An overview of the latest available science on a variety of nutrition topics



The Dietary Guidelines Advisory Committee a balanced group of nutrition science experts WHAT IS IT?

WHO WRITES IT?



Recommendations on what the average American should eat and drink to promote health and prevent chronic disease



U.S. Department of Agriculture (USDA) and U.S. Department of Health and Human Services (HHS)



U.S. Department of Agriculture (USDA) and U.S. Department of Health and Human Services (HHS)

WHO IS THE AUDIENCE?



Nutrition policymakers and health professionals



Informs USDA and HHS as they develop the Dietary Guidelines for Americans HOW IS IT USED?



Used as the basis for federal nutrition policy; adapted by medical professionals to meet specific needs; developed into nutrition resources for the general public; and much more



## THE DIETARY GUIDELINES FOR AMERICANS CAN HELP YOU EAT HEALTHY TO BE HEALTHY

The *Dietary Guidelines for Americans* provide science-based advice to help everyone—no matter their age, race, socioeconomic, or health status—achieve better health by making every bite count.



For more information about the *Dietary Guidelines*, visit DietaryGuidelines.gov.

- 2. Choose a variety of options from each food group: vegetables, fruits, grains, dairy and protein foods.
- 3. Pay attention to portion size.

Following these principles can help Americans of every age make healthy dietary choices. "A fundamental premise of the 2020-2025 *Dietary Guidelines* is that just about everyone, no matter their health status, can benefit from shifting food and beverage choices to better support healthy dietary patterns," notes its executive summary.

The *Dietary Guidelines* are the product of an extensive review of the most current research and medical knowledge on a variety of specific nutrition topics. The final version also incorporates public comments along with input from other federal agencies.

To learn more, visit the <u>Dietary Guidelines for Americans website</u>, which includes the recommendations in English and Spanish, as well as other consumer-friendly resources. (1)

#### **References:**

U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020. Available at <u>DietaryGuidelines.gov</u> and <u>https://www. dietaryguidelines.gov/resources/downloadable-graphics</u>

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### The 2021 iCAN Advocacy and Research Summit

Amy Ohmer



International Children's Advisory Network

"Founded in 2014 by Dr. Charlie Thompson, iCAN, a registered 501(c)3, has grown to represent children ages 8-18 on four continents in over 29 (including one virtual) chapters. This unprecedented growth results from the strong partnerships between the American Academy of Pediatrics, Georgia Tech, other academic institutions, and a large number of hospitals and other committed stakeholders."

#### Greetings from iCAN -

Welcoming a new year brings forth planning our favorite annual event - the 2021 iCAN Advocacy and Research Summit. Each year, iCAN focuses on this exciting week-long event as a way to bring our youth members from 29 chapters and 4 continents together to share their expertise from around the world. At iCAN, one of our strategic goals of creating advising opportunities for children living with rare, complicated, and chronic conditions is



realized through creating cross-collaboration between our kids, industry partners, and community leaders. During the Summit, youth members of iCAN make a difference throughout all facets of pediatric healthcare and clinical research through sessions with industry. The youth members often present original research and chapter updates through a poster presentation, as well as spend time during the week creating innovative new research solutions. With a roster filled with medical, research, and community speakers, the youth learn about updates in pediatric clinical research, scientific advancements, and a better understanding of how to share their own stories to improve care.

"Now in our 7th year, the Summit will be held in Lyon, France, from July 12-16, 2021. Through a partnership with iCAN's local chapter, KIDS France, activities will be held at the University of Lyon. Youth Members will be invited to share in a hospital tour, meet local physicians, and be immersed in French culture."

Now in our 7th year, the Summit will be held in Lyon, France, from July 12-16, 2021. Through a partnership with iCAN's local chapter, KIDS France, activities will be held at the University of Lyon. Youth Members will be invited to share in a hospital tour, meet local physicians, and be immersed in French culture. For our industry and community partners, the time spent with youth members provides a wealth of learning and understanding for projects including protocol design, new medicines, device development, and more. Our youth members have enjoyed lifelong friendships and industry connections, with many continuing to college to study in the fields of research, science, engineering, and medicine. Registration will open in March for all attendees, and sponsorship/engagement opportunities are currently open by submitting an email to info@icanresearch.org. All are invited to attend this family-friendly event, and more information, including updated highlights as our fun planning continues, may be found on the iCAN website at www.icanresearch.org/summit. We hope to see you there!

Want to know more about iCAN? Visit <u>www.iCANResearch.</u> org and sign up for our monthly newsletters, join or start a KIDS chapter, or request information on engaging better and supporting our youth members.

#iCANMakeADifference #2021iCANSummit #iCAN

The author has no conflicts of interests to disclose.

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#### **OPIOIDS and NAS**

When reporting on mothers, babies, and substance use LANGUAGE MATTERS



#### I am not an addict.

I was exposed to substances in utero. I am not addicted. Addiction is a set of behaviors associated with having a Substance Use Disorder (SUD).

#### I was exposed to opioids.

While I was in the womb my mother and I shared a blood supply. I was exposed to the medications and substances she used. I may have become physiologically dependent on some of those substances.



## NAS is a temporary and treatable condition.

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#### My mother may have a SUD.

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Learn more about Neonatal Abstinence Syndrome at www.nationalperinatal.org



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## PROTECT YOUR FAMILY FROM RESPIRATORY VIRUSES

flu

coronavirus





#### WASH YOUR HANDS

often with soap and warm water.

GET VACCINATED

for flu and pertussis. Ask about protective injections for RSV.





SOA

#### COVER COUGHS AND SNEEZES.

Sneeze and cough into your elbow.

USE AN ALCOHOL-BASED HAND SANITIZER.



#### STAY AWAY FROM SICK PEOPLE

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# High Altitude Climbing, High Reliability, COVID-19, and the Power of Observation

Daved van Stralen, MD, FAAP, Thomas A. Mercer, RAdm, USN

#### Abstact:

Attempts to climb Mount Everest failed for thirty years until a mountain climbing physiologist joined the efforts. This story demonstrates the value of context, inductive processes, and pragmatism to generate local knowledge and solutions in austere, hazardous environments. In these environments, imperfect information and inaccurate models can kill. This story, viewed from the climbers' experience rather than scientists or leaders, underscores the vitality of engaged individuals overcoming physical, social, and mental adversity to "gain altitude." At the individual level, what high altitude climbers learned can support the neonatologist's efforts for the neonate to "gain life."

Three times men had climbed to more than 28,000 feet, unaided by oxygen apparatus, and failed to reach the summit. Eric Shipton (1952) (1)

"In 1953, Sir Edmund Hillary and Tenzing Norgay achieved Mount Everest's summit, at 29,032 feet, the highest point on Earth. Not only did this feat change high altitude climbing practices, but it also led to advances in science that culminated in two scientific and medical expeditions: the Himalayan Scientific and Mountaineering Expedition of 1960-61 (2) (the "Silver Hut" Expedition from the wood hut painted in silver (3)) and the American Medical Research Expedition to Mount Everest 1981 (4). "

#### Introduction:

In 1953, Sir Edmund Hillary and Tenzing Norgay achieved Mount Everest's summit, at 29,032 feet, the highest point on Earth. Not only did this feat change high altitude climbing practices, but it also led to advances in science that culminated in two scientific and medical expeditions: the Himalayan Scientific and Mountaineering Expedition of 1960-61 (2) (the "Silver Hut" Expedition from the wood hut painted in silver (3)) and the American Medical Research Expedition to Mount Everest 1981 (4). Thirty-five years after Hillary and Norgay's success, adventure travel was beginning to bring to the summit those without mountaineering experience, culminating in the highly publicized 1996 Mount Everest disaster when eight climbers died in a single blizzard (5, 6).

During the previous 30 years, from 1921-52, mountain climbers from eleven expeditions to Everest failed to climb higher than about 27,000 feet (7-11). The highest altitude climbers had reached was 1,000 feet from the peak: an altitude that seemed the limit of human endurance with climbers.

George Mallory: Lassitude is common, [what] was unduly exhausting [was]...anything that might be considered abnormal, such as cutting steps, [d]iminution of desire to reach the summit (12).

Bill Tilman: Lethargy and loss of judgment...becoming callous and fatalistic. A climber on the upper part of Everest is like a sick man climbing in a dream (8).

In 1953, climbers from the British Mount Everest expedition reached the summit.

My initial feelings were of relief-relief that there were no more steps to cut-no more ridges to traverse, and no more humps to tantalize us with hopes of success. I looked at Tenzing..., there was no disguising his infectious grin of pure delight...It was 11:30 a.m...I turned off the oxygen and removed my set...I now produced [the camera] and got Tenzing to pose on top for me, waving his ax on which was a string of flags – British, Nepalese, United Nations, and Indian.

Sir Edmund Hillary (13)

The year before the successful climb, the British Joint Himalayan Committee had sent a 1952 British preparatory expedition to Cho Oyu, a 26,800-foot mountain lying 20 miles west of Everest. Included in the climbing team was a physiologist who was also an experienced climber. The expedition leader had suggested that the expedition "carry out experiments in the use of oxygen apparatus; to study physiological problems of high altitude climbing, such as acclimatization and deterioration, diet and liquid consumption; and to test clothing and equipment" (14).

One year after the physiologist, Gifford Pugh, joined the effort, Sir Edmund Hillary and Tenzing Norgay reached Everest's summit, smiled, removed their oxygen set, and took photos. From Eric Shipton's list of studies (above) (14), we know high altitude climb-

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ers were cognizant of the problems impeding success and were familiar with human performance science in low oxygen environments.

"There is an allure in taking this story as a battle over oxygen at high altitude or comparing hypoxic lung function between high altitude mountain climbers and the premature neonate."

There is an allure in taking this story as a battle over oxygen at high altitude or comparing hypoxic lung function between high altitude mountain climbers and the premature neonate. Such constrained, decontextualized views generally come from an authority group and limit one's perspective. When they become the dominant view, they limit meaning and interpretation. Instead, we use the Everest climbers' story to demonstrate observation and engagement as domains of expertise to achieve high reliability. Everest climbers' expertise produced articulate, accurate observations of the problems they encountered and characterized the need for better science (7, 8, 12, 15). Scientists' expertise produced a better understanding of environmental hypoxia and engineered technology for oxygen administration that could be readily adapted from military aviation (16-18).

This is not about querying climbers for their needs, teaching science to climbers, or teaching climbing to scientists. If that were the case, the parties involved would have solved the problem far sooner. Nevertheless, just as a gap exists between theory and practice (19) or discrete concepts and continuous perception (20), a discontinuity, a separation, exists between the protected, wellcontrolled laboratory study and the dangerous, volatile high altitude environment.

This is a story of engaging multiple problems embedded in a variety of domains within an unforgiving environment. Knowledge must be in hand rather than called upon when needed. It is in this sense that we draw together high altitude climbing and neonatology. "Predicting what would happen to the first human beings to climb that high [27,000 feet] was therefore literally a matter of life or death – here, inaccurate models could kill" (18). We can say the same for the smallest premature baby; inaccurate models could kill.

#### High Altitude Climbing and Neonatology as Liminal Spaces

One crosses a vague threshold when entering the high-altitude environment. As for any extreme environment or experience, you cannot quite tell when things are about to change or have changed. The familiar structured environment with recognizable internal logic is lost. The individual rapidly transitions to an unstructured environment with unrecognized internal logics that disorient, confuse the senses, create isolation, and maybe existential fear. Perception and sensemaking also transition as familiar objects gain additional meanings that create ambiguity and paradox. Affective judgment becomes more critical to sensitize one for detecting subtle or nuanced threats and hazards and the salience of early heralds of failure. A new identity is gained with acceptance into a new community (21). Without losing our sense of proportion, the mind works similarly whether you enter the liminal space on your first day on the job, your first resuscitation as an intensive care nurse, fellow, or attending as well as during a live-or-die situation (personal communications from colleagues and experiences of the authors).

This threshold marks liminality (liminal = threshold), an anthropology term referring to the crossing of a threshold in life. In anthropology, "liminal" refers to rites that signify status changes, such as from childhood to adulthood. COVID-19 has formed an expanded liminal space where the threat of COVID-19 has a more significant effect on operations and society from maladaptive stress responses and fear reactions than through death alone. COVID-19 has generated an ecology of fear (22). Before COVID-19, the NICU safely sheltered babies; now, the NICU space itself may bring harm. High altitude and the NICU are liminal spaces.

"This threshold marks liminality (liminal = threshold), an anthropology term referring to the crossing of a threshold in life. In anthropology, "liminal" refers to rites that signify status changes, such as from childhood to adulthood. "

Inaccurate, possibly deadly models created with missing knowledge or lack of experience at altitude interfered with acceptance of the use of oxygen apparatus by climbers. Similarly, inaccurate models for COVID-19, despite constant refinement and improvement, interfere with prevention and management acceptance. In these situations, observation is all we have.

However, observation within the liminal space may be for familiarity and homeostasis security or for the discordant event to identify threats and support safety. Mountaineering and HRO make a big deal about the difference between the familiar and the novel. Our brains rapidly identify patterns fundamental for intelligence, language, imagination, invention (23). Through pattern recognition and engagement, we use the familiar to learn by doing (24). A person may find or fit rules and concepts into the observed patterns, gaining a false sense of security (22, 24). Our brains rapidly identify threats through the amygdala, triggering reflexive vigilance and action (25). When neuromodulated, the elicited stress-fear-threat cascade's adaptive functions drive effective action while maladaptive responses create significant damage (26).

Perceptions also divide between cortical hemispheres, differentiating the novel (right hemisphere) from the familiar (left hemisphere) unrelated to handedness. With age, the functions meld to produce wisdom.

The right hemisphere identifies novelty for rapid, diffuse responses to the unexpected and to support avoidance. It can maintain high levels of arousal, supporting the negative, intense effect necessary for high-risk engagement. Assessing multiple objects and their context, noticing small differences between stimuli, and parallel processing all support global analysis in the liminal space (27). Right hemisphere behaviors include predator responses (27) and social interactions (28) that drive avoidance, fear responses, predator escape, and aggressive responses (27). There is also a bias toward social interactions and attendant bonding and affiliation, including facial recognition and reading facial expressions, gaze directions, and intonation (28).

"Familiarity is how an organism approaches food and conspecific social interactions. Social emotions, awareness of other beings, and a generally positive affect drive social connection (28)."

The left hemisphere identifies the familiar and is more developed for cognition. Familiarity is how an organism approaches food and conspecific social interactions. Social emotions, awareness of other beings, and a generally positive affect drive social connection (28). Focused attention supports considered responses to decide between alternatives and generate sequential actions (27).

Our brain and behaviors have prepared us to function in the liminal space if we can maintain neuromodulation (29). People may not recognize when they enter a liminal space since some spaces are contingently liminal. For example, a routine winter climb changes to a liminal space as a storm arrives or parental visitation of their baby, interrupted by abrupt pulmonary hypertension, becomes a liminal space. The problem is not the abrupt change as much as long episodes of routine operations that generate complacency in the team and expectations from the sojourner. We risk losing acknowledgment of the subtle routines that are necessary to maintain high reliability. For example, in high altitude climbing, the abrupt decrease in air pressure from an unexpected storm, the equivalent to a rapid increase in altitude, disrupted a group of adventure teams on Everest in 1996. Eight climbers died.

#### **Liminal Spaces and Inductive Processes**

The liminal space environment would create the ecology of fear (22) but for the absence of a threat recognizable by the sojourner. Consequently, sojourners may operate oblivious to dangers, interfere with operations, or, more seriously, use their expectations to drive operations. The rarity of a severe life threat can be hard to explain to outsiders, as we see with the social and political acceptance of the COVID-19 threat. On Everest in 1996, some sojourners expected to reach the summit, an accomplishment they had purchased, and some leaders had created a mystique of omniscience, an eminent capability that created passive fellow guides. Such leader myth-making stifles communication of disconfirming information and stifles concerns about ascending during a storm (5).

The environment is the enemy in a liminal space. Organizations operating in the liminal space that rely on strong leaders, of whatever style or philosophy, run the danger of failure from abrupt changes (5, 30, 31). The liminal space is not an environment where monitoring, sensemaking, or attention can help us. When the problem is embedded in a hostile environment, observation and engagement are the functions we rely upon as we explicate. In the liminal space, constant observation and reciprocal feedback, generating and testing information, all rely on inductive processes.

Leonhard Euler (32) describes the problem this creates:

We can place our highest hopes in observations; they will lead us continually to new properties, which we shall endeavor to prove afterward. The kind of knowledge which is supported only by observations and is not yet proved must be carefully distinguished from the truth; it is gained by induction as we usually say...Indeed, we should use such a discovery as an opportunity to investigate more than exactly the properties discovered and to prove or disprove them; in both cases, we may learn something useful.

George Pólya (32) described observation as "an accurate watching and noting of phenomena as they occur in nature with regard to cause and effect or mutual relations." But observation can identify facts that do not align with our minds and knowledge, for example, when climbers considered the use of oxygen at high altitudes, discussed below. We adapt our minds to newly observed facts by using *inductive processes*. That is, we should revise our beliefs if our observations generate a compelling reason to change (32). The experiences of high altitude climbers created observed facts that challenged knowledge. Neonatology is no different. Like high altitude climbing, neonatology relies heavily on observation and inductive processes to adapt to newly emerging facts.

"Neonatology is no different. Like high altitude climbing, neonatology relies heavily on observation and inductive processes to adapt to newly emerging facts."

We have only observation to adapt our knowledge to emerging facts. This observation drives inquiry, described by John Dewey as "always a behavioral response of a reflective organism to its environing conditions....inquiry belongs to 'action or behavior,' which takes place in the world, not just within the mind or within consciousness...Inquiry...is what Dewey termed an 'outdoor fact'" (33).

In the disorientation of the liminal space, knowledge, and facts suffer. To engage the liminal space, we reduce complexity by actions guided by reciprocal feedback from the environment, a method also used by a special group in SOCOM (US Special Operations Command, personal communication). The individual can then immediately initiate inquiry while concomitantly reducing volatility and threats. The standard method of initially investigating or differentiating complexity, chaos, and uncertainty needlessly expends time, allowing it to worsen.

We build from perception to observation, which then drives inquiry and experience. From experience, we give meaning to our actions and the information we generate. Coincidently, this parallels the philosophy of pragmatism. In the liminal space, we do not have certainty, particularly for antecedent events, impairs our ability to act from what happened earlier. This experience also interferes with scientific logic and the Cartesian approach to reach truth (34) or bring about a resolution. Instead, we use the possible consequences of our actions to guide inquiry, likely the most difficult tenet of pragmatism to appreciate (34).

Perception, not recognition, generates observation. John Dewey diminishes recognition as the 'use of matter as a means.' Perception carries our past experience into the present to enrich its content, forming observations (35). Observation is then in service to an outcome, achieving 'practical consequences,' and not to a process (36). Observation as pragmatism moves us forward, whether to gain altitude on a mountain or gain life in the NICU.

"Perception may seem dependent on definitions, but definitions come up short in the turmoil of the liminal space. Descriptions of how something is used, an action performed, or a situation experienced all carry meaning. "

Perception may seem dependent on definitions, but definitions come up short in the turmoil of the liminal space. Descriptions of how something is used, an action performed, or a situation experienced all carry meaning. Too quickly, labeling things becomes an unconscious act (35) with nothing learned when we analyze definitions (Charles Sanders Peirce in (36)). Instead, the *conscious* act of experience as a "cooperation of internal needs and external materials" converts 'cause and effect' into 'means and end,' transforming simple interactions into more complex participation (35). This conversion is an observation as cause and effect, used in the inductive processes described by Pólya (32).

The liminal space generates extreme experiences and identifies discrepancies between the individual's appraised meaning and more global meaning. Reappraisal integrates the events, causes, and implications of the experience, reducing existential stress (37). Inquiry as *interaction and participation* is to operate in the liminal space as a meaningful experience rather than sensations or "brain events" (35, 38). Life-threatening situations are unique, and the pragmatic leader induces a sense of shared experience, tying into the ideals of optimism, hope, and resilience (30, 39). Reappraisal, as a regulatory strategy, contributes to this resilience (40).

Pragmatism is to resolve disruption. Experience brings resolution. When we complete an experience, we give it meaning (41).

#### The Problems of High Altitude

When we view Everest's problem as low atmospheric oxygen pressure and climbers' intransigence to accept carrying the oxygen apparatus, we reduce the problem to the "use of oxygen." While bringing clarity to the failure of the British Mount Everest expeditions, it misleadingly creates distinctions between theoretical and practical challenges, sporting and scientific conduct, research and operations goals, and the influences of laboratory studies and field operations (18).

Such reductionist, de-contextual approaches move the discussion away from situations where nuanced local forces strongly influence action. Once out of the immediate environment, we can readily believe we would not have had such judgment. Discussion of Everest climbers allows for admiration of the climbers while modestly diminishing them for their resistance to oxygen. Evaluating decisions made by healthcare professionals and parents operating in a challenging environment comes under similar scrutiny. This differentiation is the practical distinction between the normative and pragmatic stances (24).

Instead, we will present the distinct problems described by the climbers with the science that was then available: acclimatization, oxygen, appetite and thirst, fatigue, and temper. Engagement of a situation focuses one's attention, decision-making, and efforts on subtle though critical elements. For example, retrograde intubation is a method to intubate the trachea by passing a guidewire percutaneously from the cricoid membrane then out the nose or mouth. Many review articles introduced this procedure to emergency medicine. One author (DvS) had initiated the development of a resuscitation manikin for this procedure (42), leading to a discussion with numerous emergency physicians. Several had attempted the technique, experiencing the endotracheal tube passing over the guidewire and consistently entering the esophagus. The review articles had omitted holding the guidewire taut while guiding the endotracheal tube, a maneuver vital for success (43). The high altitude climbers' observations and descriptions came from the intimate engagement of mundane yet life-threatening situations. Their concern was how to gain altitude. For various reasons, their concerns and the vital information they generated did not reach those who need it, or the information was lost.

At high altitude came "great exhaustion, from which it is not possible wholly to recover without a prolonged rest at a very much lower altitude" (10). Is that the most serious obstacle on Mount Everest? It depends on whether it is top-down from the expedition organizers and leaders or bottom-up from expedition climbers. It depends on whether it is from outside of the events, a fixed-point to assure progressive forward motion, or within, moving with the flux of events while striving to endure. Eric Shipton described it as a more serious obstacle than "the altitude, the severe cold, and the wind." The value placed on seriousness may differ between a spectator and an insider. The high-reliability theory makes a big deal of these differences. The series describing HRO for *Neonatology Today* is an effort for synthesis. When this is not synthesized, science and theory move in a different direction from practice and operations.

#### Acclimatization

Eric Shipton described climbing the last 4,000 feet to the top of Everest in a single day drained the climbers; they were too exhausted to continue. The British attempts to climb Mount Everest in 1922 and 1924 failed after the climbers "had gone too high too soon." In 1933 they again "under-rated the resources of our opponent" (1). Climbers knew they could gain altitude through acclimatization. For example, Charles Howard-Bury found he had more energy after six months living in Tibet, then applied that experience to climbing above 18,000 feet (15). They also found that slow acclimatization resulted in the capacity to eat more normal food (44), essential for maintaining vitality.

Extended acclimatization, though, comes with costs and risks. Food and fuel necessary for prolonged stays must be transported, but climbers also found physical deterioration. While sufficient food was available, the lack of appetite during acclimatization caused decreased food intake, a possible cause of the rapid physical deterioration during acclimatization (10).

Acclimation helped Everest climbers reach. 27,000 feet, now they needed to find a way to climb higher. While the alpine climbing community had known that oxygen could augment or replace acclimatization, it was a visit to Oxford in 1921 regarding stoves that brought scientists closer to the climbing community (17, 18). Georges Dreyer's oxygen tests for aviation using a low-pressure chamber became a source of information for mountain climbers (17, 18). John Haldane had conducted studies of acclimatization on Pikes Peak in 1911 (16). The effects of acclimatization become apparent after 2-3 days. A more sensitive response to  $CO_2$  results in respiratory alkalosis and a subsequent increase in breathing.  $CO_2$  levels reached 2/3 normal levels after two weeks. Hemoglobin also increases over several weeks (16).

Fatigue is an early effect of acute hypoxemia when newly arrived in villages at 7,000 feet, an experience one author (DvS) uses to teach lung dynamics. Visitors to Mammoth Lakes, California, state the cause of their fatigue is lack of sleep, excitement, or too much / too little food. However, a few breaths of "pressure breathing," forced exhale against pursed lips, resolves the fatigue, demonstrating its pulmonary nature. This method also treats high altitude pulmonary edema at 20,000 feet (personal experience, DvS).

"The effects of acclimatization become apparent after 2-3 days. A more sensitive response to  $CO_2$  results in respiratory alkalosis and a subsequent increase in breathing.  $CO_2$  levels reached 2/3 normal levels after two weeks."

Scientists had predicted that acclimatization would be impossible above 20,000 feet (7). Experience seems to bear this out. At heights greater than 18,000 feet, a prolonged stay "permanently lowers the vitality" (15), with physical lethargy progressively more intense, leaving climbers gasping and panting at rest (10). The body "simultaneously loses both weight and strength" (12), and at about 21,000 feet, muscle wasting becomes consequential (10) and may offset the benefit of acclimatization (8). Nevertheless, Everest climbers did acclimatize at 21,000 feet and even higher (7). "Why [scientists made their prediction]...will always remain a mystery to me; but possibly they were misled by the fact that so many climbing expeditions in the past failed somewhere in the region of 23,000 feet above sea-level," Charles Granville Bruce (7). Everest climbers searched for the balance between acclimatization and deterioration (10, 12).

We could too readily discount the acclimatization controversy as a product of armchair science at a distance from the mountains, the result of crude measurements and unrefined hypotheses, or we could reject experience as spurious or superstition. A review of the causes of Mount Everest deaths above 8,000 meters (26,247 feet) over 85 years questioned whether adequate acclimatization is possible at that altitude (45). Before rejecting the degree of the climbers' experience, we may better be served by understanding the practical reasons for such beliefs, the context of operations, and their interactions.

Eric Shipton described the amount of time spent in sleeping bags. When the sun disappeared around 4:00 p.m., it became too cold to sit outside. They commonly remained in their sleeping bags until 9:00 a.m. in good weather. Bad weather would keep them in their tents for much longer (10). Within seven days of bed rest during bed rest studies, the thigh muscle decreases by 3%, small but significant. After 20 days, maximal torque decreases in the ankle (9%) and knee (16%) extensors, quadriceps muscle decreases by 10%, and lower limb power, force, and velocity decrease by 19.8–43.6%. By four weeks, fatigability increases, and exercise capacity decreases (46). This has no relation to the use of oxygen.

Without knowing the science, the Everest climbers reported the limitations and risks of acclimatization as a general physical deterioration and loss of muscle mass, similar to what is measured in bedrest studies. Elsewhere they describe increased fatigability with time in higher altitudes. This ability to use observation produced from engagement had initiated learning by doing and advanced climbing, albeit slowly. Responding to the impossibility of acclimatization above 20,000 feet, the climbers considered science as informational rather than dictatorial. They acted within local circumstances, typical of the pragmatic stance.

"A science that does not accurately describe the situation or allow for variation risks irrelevance. This is less a property of science than the mistranslation of analysis, deductive processes, and reliance on deterministic inferences."

A science that does not accurately describe the situation or allow for variation risks irrelevance. This is less a property of science than the mistranslation of analysis, deductive processes, and reliance on deterministic inferences. Climbers come from a pragmatic stance of synthesis, inductive processes, and affective inferences (24). While the use of science from a fixed-point frame of reference does not translate well to high altitude climbing, science from within the flux and flow of events and the consequent doubt and unpredictability does.

#### Oxygen

The use of oxygen as a means to gain altitude shifted to its use for some beneficial effect. The Everest climbers were familiar with the research on high altitude aviation and oxygen. Working in a chamber pressurized to 25,000 feet was helped by 1 liter per minute oxygen flow (47). Hugh Ruttledge (48) thought the use of oxygen might replace acclimatization and provide strength for difficult stretches to climb higher.

Oxygen was not a matter of particular importance to expedition leaders (7, 12), who believed it provided no effect for some climb-
ers while it helped others (12). For those it helped, some thought the benefit was from inadequate acclimatization (12) or illness (8). George Mallory believed oxygen might have restorative value, thus leaving its use to one's personal opinion (7). Even with this skepticism, Mallory used oxygen, including his last climb to his death. When Bill Tilman used oxygen, he felt "sprightly" and climbed more easily to 25,000 feet but without increased speed (8). At 25,000 feet, for George Finch, oxygen made carrying a strenuous load feel a brief walk (7).

"The belief developed that oxygen helped with exertion, and climbing became less difficult, but the climber could have reached higher altitudes without oxygen (7)."

The belief developed that oxygen helped with exertion, and climbing became less difficult, but the climber could have reached higher altitudes without oxygen (7). Some of the difficulty came from the 35-pound weight of the oxygen apparatus, which counterbalanced any advantages (7, 8). However, around 23,000 feet, its restorative function brought some advantage though it still seemed possible to climb Everest without the oxygen (7). Some considered oxygen unethical or unsportsmanlike, but most of these discussions were in Britain and not commonly discussed on the mountain. Oxygen would be considered ethical if the lack of oxygen alone prevented reaching the summit (8).

Noel Odell described a peculiar benefit of acclimatization overuse of oxygen - the speed of descent unencumbered by the oxygen apparatus. In fairness to the use of oxygen, speed came from glissading, an indulgence the apparatus interfered with (12). One glissades by sliding down the snow on one's feet, supported by the ice axe, and an accepted descent method for Everest climbers.

These discussions of oxygen's benefits and drawbacks come from the normative stance, a fixed point way from engagement in the flux of events (24). This is similar to healthcare discussions of new therapies or new diseases such as COVID-19, discussions made at a distance from the patient and caregivers immediately involved with care.

"What would make the person right?" generates useful information for learning and improving programs. It moves our thinking into the flux of events; what is it that I do not see that would make them do it - unnoticed causations, missing information, corrupted communication, and other influences that are washed out when we evaluate from a distance.

Within the flux of events, decisions for using oxygen were based on the incomplete flow of information between scientist and climber, instability on a steep slope, the sense of suffocation from the mask, or sudden loss of oxygen flow, causing sudden unconsciousness.

The discontinuity between contextual practice and decontextualized theory from science that Pugh would later productively engage (19) is well-described by Tilman (8):

It is an engaging but fatal characteristic of scientists that once presented with a material problem of this kind [oxygen at high altitude]. They set about the solution with a single-minded devotion that excludes any other considerations whatsoever, be they ethical, humane, or merely of common sense.

Scientists had warned that climbers could probably not reach any great height without oxygen (7). They added the warning that to stop using oxygen probably would cause death (7), inadvertently creating a reason not to use oxygen: if climbers are at altitude without oxygen and become disconnected, they may suddenly collapse (Francis Younghusband (7)). In effect, not using oxygen appeared safer. One solution offered was protection from collapse by acclimatization at 21,000 feet or only use oxygen above 27,000 feet (12). Without close communication, climbers found practical solutions based on the environment with little involvement of science.

Yet, climbers made excursions to 24,000 feet and remained conscious without oxygen. For the climbers, this was evidence supporting the greater probability they could reach the summit without the oxygen apparatus's additional weight (Howard Somervell (7)). The use of aviation as a model did not apply to climbers; airmen may have value in the pressure chamber, and oxygen for them is essential, but in mountain climbing, they have survived without oxygen (15). The pragmatic stance of the climbers is apparent in Shipton's query: "No one has yet produced a satisfactory answer to the objections by actual demonstration, and the debate continues" (10).

"This difference between scientists and climbers lies in the domains they learn cognitive, affective, or psychomotor (49). Scientists tend to learn in the cognitive learning domain of facts, concepts, models, and theories. The cognitive domain more readily translates into objective measures for progress toward competence in the subject or discipline."

This difference between scientists and climbers lies in the domains they learn - cognitive, affective, or psychomotor (49). Scientists tend to learn in the cognitive learning domain of facts, concepts, models, and theories. The cognitive domain more readily translates into objective measures for progress toward competence in the subject or discipline. The cognitive domain provides our common verbal knowledge, knowledge organization, and cognitive strategies. The affective learning domain (50), in contrast, focuses on "how this will help" and provides the context necessary to give meaning to information. This approach increases the motivation to learn and to understand better the knowledge that was gained. Motivation describes responsiveness to phenomena, valuing knowledge, and the worth of an object or idea.



"I think the most obvious lesson to be learnt is that the only trials and experiments of any value at all are those carried out by mountaineers themselves at heights of over 23,000 feet." He also stated, "[S]cience and mountaineering should be kept distinct," Bill Tilman (8).

Some climbers would not wear the 35-pound oxygen apparatus because of the weight (15). Finch believed the advantages counterbalance the disadvantages of the weight, particularly above the foot of the North Col slopes because full recovery from fatigue is no longer possible at 23,000 feet (7). Weight requires energy to carry, but the climber conserves energy with rhythmic movement, balance, and precise placing of the feet (10). Weight shifting from the oxygen apparatus could cause instability on a steep slope (7, 8, 10).

"Today, human factors studies would have helped the problem with face masks and the sense of suffocation (7, 8). Because oxygenation and sensation are independent entities, the climber may remove the mask to relieve the sense of suffocation yet not recognize hypoxemia."

Today, human factors studies would have helped the problem with face masks and the sense of suffocation (7, 8). Because oxygenation and sensation are independent entities, the climber may remove the mask to relieve the sense of suffocation yet not recognize hypoxemia. One climber reported: "I noticed then that our faces were all a curious blue colour in the morning, due to what is called, I believe, cyanosis of the blood. I cannot say what the effect will be if oxygen is taken to aid the human effort." (15). Suffocation is arguably the most fearsome way to die.

The most serious threat from oxygen use, because it is beyond the climber's control, was the sudden loss of oxygen flow. The Mount Everest Committee was warned about this problem with oxygen – if oxygen ran out at 27,000 feet, the climber might immediately collapse (7). Finch, a physical chemist and oxygen proponent, warned that interrupted flow would cause sudden unconsciousness (7). Somervell (7) and Shipton (10) wrote of their concerns that oxygen might run out at attitude producing sudden collapse of the climber. Causes for interrupted flow include breakdown or accident with the apparatus (7, 10), problems with face mask, an oxygen supply that lasts only 8 hours (7, 10).

Information supporting sudden collapse came from aviation tests in pressure chambers (10, 17, 18). Everest climbers were also familiar with several incidents of death from ballooning at 27,000 to 30,000 feet (51). In 1862 a meteorologist and his assistant reached 26,000 feet and had become paralyzed, unable to release the gas valve. The assistant finally reached the valve with his mouth, and they descended, but not after reaching 30,000 feet. The second incident in 1875 led to the deaths of two passengers, the scientist survived. That balloon also reached 30,000 feet.

They knew the stories, but the stories belonged to the scientists,

not the climbers. The empirical experience of the climbers differed from the empirical studies of the scientists. Mount Everest climbers had acclimatized without oxygen, attained the same altitudes as the balloonists, and could still climb without oxygen (12). Somervell (7) described an accident with the oxygen apparatus. The climber did not become immediately unconscious; the apparatus was then disconnected and repaired. The scientists had warned they could not reach such heights without oxygen, but the climber had and stayed conscious despite the sudden loss of consciousness.

But it was the insidious nature of the "want of oxygen" (51) that remained:

Body and mind become feebler little by little, gradually and insensibly. There is no suffering. On the contrary, one feels an inward joy (16).

The subject does not recognize a loss of consciousness and hotly denies it. To convince the subject, the subject will write while the experiment is conducted (10).

From climbing:

The intelligence is gradually numbed as the oxygen supply diminishes, and the body comes nearer to exhaustion (7).

These descriptions of the "want of oxygen" gain richness from personal engagement and the climbers' pragmatic stance. The "want of oxygen" problem had become more accurate: fatigue embedding into a dangerous high altitude environment. This dilemma differs from a singular situation: the continual drive to act, the rhythmic forward movement step after step, exhaustion comes painlessly. Scientists with single-minded devotion worked to solve problems, then offered facts from their labs. The Everest climbers worked to gain altitude, a continuous process, while science worked to make models, a process with a conclusion.

The human body responds to the low partial pressure of oxygen with hyperventilation (16), which appears to defend alveolar PO<sub>2</sub> at about 35 mmHg (4). Alveolar CO<sub>2</sub> levels decrease from 22 mmHg at 29,000 feet to 14 mmHg at 25,700 feet (52). At 8,000 meters (about 26,000 feet), this hyperventilation level produces alveolar PCO<sub>2</sub> of 8.0 mmHg and arterial blood pH between 7.7 and 7.8 (4). The only gas measurements from an Everest expedition before 1950 were on the 1933 expedition. Measurements at 23,000 feet and a barometric pressure of 339 mmHg showed an alveolar CO<sub>2</sub> concentration of 19.3 mmHg (53).

Notwithstanding medical professionals' belief that hypoxemia causes feelings of suffocation, descriptions by those who have experienced hypoxemia are of insidious onset related to decreasing awareness associated with comfort (including the authors' personal experience). This relationship is essential information when we discuss limitation or withdrawal of support when ethically indicated. Also, chronic hyperventilation with  $CO_2$  levels of 19.3 mmHg at 23,000 feet and 8.0 mmHg at 26,000 feet lend support to the experience in long-term mechanical ventilation when the voluntary respiratory effort of patients creates respiratory alkalosis, though to a lesser degree, with an average pH of 7.46 and average  $CO_2$  26 mmHg (range 23.1-28.8) (54). These well-documented experiences in extreme environments inform our ability to provide compassionate care to our patients and families.



### Diet

Appetite is consistently decreased at high altitudes (7, 8, 12, 15). At 22,000 to 23,000 feet, after a week or so, hunger is absent. It is impossible to eat enough, even with tempting foods (8). This is consequential with loss of weight at altitude (8). Thirst is not felt above 24,000 feet (8).

"Whether breast or bottle-fed, the infant will tire out and, despite feeding by breast or bottle, does not finish the feeding. Heart failure, inadequate oral intake, and increasing dehydration reach the degree that heart failure is buried in hypovolemiadehydration."

It may confound some that one can be dehydrated without thirst. When dehydration causes hypovolemia, the initial blood flow decrease is to the stomach, which causes an ileus and loss of appetite. Heart failure in infants also causes an ileus. Whether breast or bottle-fed, the infant will tire out and, despite feeding by breast or bottle, does not finish the feeding. Heart failure, inadequate oral intake, and increasing dehydration reach the degree that heart failure is buried in hypovolemia-dehydration. The mother reports her infant is feeding but, unless specifically asked, does not report her infant finished the feeding. The quickest way to demonstrate this is to look at the reverse; your thirst quenches before the water is absorbed.

### Fatigue and temper

Climbers feel lazy. There is always needed effort to concentrate thoughts (15); lassitude is common, there is lack of determination (7); diminution of mental operations, will power, the strength of purpose, desire to reach the summit (12); and lethargy and loss of judgment, becoming callous and fatalistic (8). Full recovery from fatigue is no longer possible at 23,000 feet (7).

Intense cold and heat loss reduce available energy (15) and sapped their desire and ability to climb (8).

Climbers have peevishness and irritability at a level of 22,000 feet (7).

Poor sleep is common, which "lowers the vitality enormously" (15).

### Ethics and kindness

Climbing in an austere, hostile environment, relying solely on each other for rescue, creates an accepted ethical bond. This bond, by necessity, exceeds the drive to gain altitude and reach the summit. "And of all the principles by which we hold the first is that of mutual help," George H. Leigh-Mallory (15). If any climber or porter was sick or abnormally exhausted, he must be escorted to a lower altitude at the first opportunity. It is taken for granted that such an evacuation may interfere with the expedition.

In all, it may be said that one factor beyond all others is

required for success...The climbers must have above all things if they are to win through, good fortune, and the greatest good fortune of all mountaineers, some constant spirit of kindness in Mount Everest itself.

### George H. Leigh-Mallory

In 1985, while approaching Kyajo Ri peak (20,295 feet), a French climbing team encountered a European climber and his Sherpa guide. One was delirious and the other unconscious. The French team could not move an unconscious body from an altitude near 19,000 feet, but they did have hydrocortisone, at the time a suspected treatment for altitude illnesses. They injected the medication in the thigh of the unconscious climber, who awoke well enough that the French team could evacuate both climbers to Thame in the Solu Khumbu District. That is where they approached one of the authors (DvS) for permission to climb the author's permitted mountain, Mount Pharchomo (20,581ft). At the time, a permit restricted access for a four-day period when only the permitted climbers could be on the mountain. They presented their plight as a matter of fact situation as if they had encountered someone limping, despite the missed climb, delays, and costs. The ethics of high altitude climbing is one of kindness in the Himal.

(When in the US and recounting the story of the hydrocortisone, American physicians quickly pointed out to the author that no research supported the use of hydrocortisone for high altitude illness, especially high altitude cerebral edema.)

It is a testament to the attitudes necessary for climbing and the climbers' drive to continue pressing their accomplishments despite the mental and psychological strain. Engagement as pragmatism and inductive processes, also found in military and public safety operations, undoubtedly contributed to their high-stress capacity and performance.

The Everest climbers placed their hopes in observation and reciprocal feedback from the environment. Actions supported their knowledge while discovering what worked and what did not, forming a continuous cycle that generates information and knowledge. Each step created a "different" situation. The "sensed" situation, or the situation they used for management, will not exist for later review. Only the "monitored" situation will; that is the situation they could describe to others, use for documentation, and learn. The two situations are not identical. The mountain drives reality. Climbers change models with each step and each storm. Scientists developed models for use on the mountain. Prediction with inaccurate models and communication with imperfect descriptions will kill (18).

Like the climber's goal to gain altitude, the neonatologist's goal is to gain life. High altitude climbers must explore different routes to reach the summit, and even known routes may not be available depending on snow and weather. This process is valid for the care of a specific baby, for resuscitations, and discipline. Unlike other specialties, neonatology does not have an endpoint; gaining life means entering an altitude never before attained, which becomes the basis for the next increase. Climbing does not have an endpoint; each step is a different step, and every mountain is a different mountain.

### **Engagement Advances Climbing:**

The liminal space is not only a physical space; it is a social space

(21). An individual with high altitude climbing and medicine or physiology expertise can fall into a social liminal space. Griffith Pugh and George Finch were mountaineers and scientists. Not fully respected by high altitude climbers for their science and not accepted into the social club of gentlemen who also climb.

"Like the climber's goal to gain altitude, the neonatologist's goal is to gain life. High altitude climbers must explore different routes to reach the summit, and even known routes may not be available depending on snow and weather. This process is valid for the care of a specific baby, for resuscitations, and discipline. "

### George Finch

The Making of a Mountaineer by George Finch (55) was a mountaineering classic when published in 1924, inspiring generations of mountaineers (17). Finch had advocated for the use of oxygen, including at rest after his experience spending two unplanned nights at 25,500 feet (56). Hunt recognized his advocacy for oxygen heavily influenced its use on the successful 1953 Everest expedition(11). The equipment used was similar to that developed by Finch for the 1922 expedition (17). He believed that above 23,000 feet, the physical deterioration from poor sleep and appetite outweighed the benefit of acclimatization (56). He also was a strong advocate for better food, including pre-packed rations (56). As a scientist with engineering skills, he participated in equipment design and advised the Everest Committee on oxygen (17). John Hunt lauded Finch for showing how the physiological problems might be solved (17).

Despite setting an altitude record of 27,320 feet on the 1922 Everest expedition, Finch was excluded from the 1924 expedition (56). Until he set that record, he had been denied membership to the Alpine Club (56). He had been denied the opportunity to participate in several Mount Everest expeditions because of his personality (17).

An elitist system dominated British alpine climbing. Finch did not fit in because of his reputation for being outspoken and an unconventional Australian. He had made guideless ascents, which many members of the Alpine Club opposed. Odd by today's standards, but "scientist" was not a respectable occupation for a gentleman (17). Personal interactions and social standards excluded an individual who could engage in high altitude climbing with science and ensure the accuracy of the high altitude climbing models.

### Gifford Pugh

Gifford Pugh served an internship at Lambeth Hospital, London. He competed in downhill, slalom, and cross-country ski races during his university studies, being selected for the 1936 Olympic cross-country team. An injury prevented his participation. He had experience climbing regularly in Europe. During WWII, he joined the Ski and Mountaineering School at the Cedars of Lebanon, training mountain troops and Special Operations Executive (SOE) in survival techniques. In Lebanon, he studied research on fatigue and conducted his studies evaluating soldiers for mountain warfare. This included developing soldiers' physical capacity, the equipment they used, and their diet (56, 57).

Michael Ward, a physician and mountain climber, had conceived of climbing Everest from the south and became involved with the Everest expeditions. His pursuit of physiology as the primary impediment led him to Gifford Pugh (57). Their discussions developed the need for high flow rates of supplementary oxygen, a large daily fluid intake, and adequate protective clothing and boots (11, 56, 57).

Pugh's plan included oxygen, including descent and sleep, for climbers and Sherpa above 23,000 feet. Acclimatization for four weeks. Water at 3-4 liters per day. A European diet for the climber with special meals for climbers going to high altitude. Better hygiene, including food hygiene. They would not sleep in local houses. [The heat is considered to be contained in the smoke; therefore, they do not build chimneys in their homes. DvS] Better clothing used a thermal insulation system ("Clo values"), sleeping bags that pull over the head, and RAF masks adapted for climbing (56).

Pugh brought Everest the expertise of the high altitude climber and expertise in science, marrying the two through synthesis and similar inductive processes. His was not a hybrid approach or a back-and-forth activity. Pugh engaged the discontinuity between *contextual* practice and *decontextualized* theory (19), the separation between *continuous* perceptions and static, *discrete* concepts (20), and the separated concepts of sensemaking (58) and enactment (59, 60).

### Hidden voices and the dominant account

Once a dominant account develops, voices become hidden, and knowledge is lost. For example, a dominant account developed for the 1996 Mount Everest disaster (6) about teamwork, decisionmaking, how to offset individuals' natural shortcomings, and selfdiscipline among the topics, making the story amenable to business leadership. With the dominant account, we lose the effect of the liminal experience (21) and the liminal space (5). The dominant account reduces problems within the liminal space to science versus practice, which creates inaccurate models - models that can kill (18). This is not from history and not from an event too large for us. After the action, interviews of fire and EMS responders to a terrorist shooting initially reflected the dominant account. Because we ensured each interview team had one member with extensive experience in live-or-die situations, the interviewee would rapidly begin an accurate description of their experience. Information had changed (61). We chose the climber's hidden voices in extreme environments - high altitude, cold, isolated - to investigate the 30year failure to climb Mount Everest successfully. Then the abrupt success.

First-person accounts of the 1996 Everest disaster have created a large number of "lessons learned" articles for business leadership. This body of literature, each article was written by a single individual involved but without perspectives from other participants, has become the dominant account of the disaster. Michael Elmes and Bob Frame (6) interviewed those with hidden voices, other climbers and Sherpa porters. The dominant account becomes a mistranslation of a liminal event, reduced and simplified to fit a normative view framed from a spectator's fixed point. Context and meaning, critical for engagement, is lost. The dominant group sets the discourse, defines categories and classifications, sets limits of what can be spoken about and what cannot, and who can speak with legitimacy. The dominant account is the privilege of being listened to (6).

The dominant account excludes contextual elements such as physiological factors, the weather, and the business nature of adventure climbing. Consider the strenuous exercise, minimal sleep, poor nutrition, and dehydration in the participants, constraining rational and effective decision-making and team formation. Published discussions and 'lessons learned' do not reflect the physiological and mental demands in the high altitude environment described and quoted in this article. The armchair climber and disaster expert can think now and give sage advice. The dominant account too readily becomes disaster voyeurism.

The Sherpas are hidden voices in the 1996 disaster, as they are in the Everest saga (57). A bottleneck occurred halfway up the mountain attributed to the two lead Sherpas' failure, referencing one as a 'showboat' and a 'gold- brick.' Some of this comes from clients' perceptions, sojourners having little contact with a Sherpa and ignorant of Sherpa culture. The dominant account became one of the Sherpas lacking discipline and succumbing to self-centered interests.

"Success in this environment comes from the hidden voices, the neonatologist, physician, nurse, respiratory care, dietitian, ward clerk, family, and more. Build the expertise to which you will later defer. Nevertheless, listen to the hidden voices."

### **Conclusion:**

The successful climb of Mount Everest in 1953 followed the incorporation of several individuals, Gifford Pugh and Michael Ward, with the necessary expertise to engage the science and the environment. Engagement builds on perception and inquiry, which generates Shannon information (Shannon information is the information generated when uncertainty is converted to certainty.) Knowledge from both observations and "information of experience" must be continuously proven accurate by continued engagement and inductive processes. Pragmatism, always moving ahead by monitoring for consequences of our actions, is a necessity for austere or hazardous situations. Resolution of our experience produces the meaning of what we accomplished.

Whether a liminal space, high altitudes, or the ecology of fear, we enter with engagement and inquiry to generate information. Through inductive processes, we penetrate the unknown, using pragmatism for direction and guidance. This dynamic, which reduces complexity using reciprocal feedback, is shared between mountain climbers entering high altitudes to gain altitude and neonatologists engaging hazardous physiology to gain life. This richness is not found in the dominant account. It lies with the hidden voices.

Success in this environment comes from the hidden voices, the neonatologist, physician, nurse, respiratory care, dietitian, ward clerk, family, and more. Build the expertise to which you will later defer. Nevertheless, listen to the hidden voices.

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# How Will the COVID-19 Vaccine Reach Developing Countries?

Suzanne Driscoll, M.Ed, MBA

"Distribution to various locations in the U.S. has already begun, and plans are being formed in each state as to who will receive the vaccine first. However, the concern is that high-income countries will hoard supplies for their own populations causing delays in distribution to poorer countries."

Hope is in the air as the world eagerly awaits the approval of new COVID-19 vaccines. After nine long months of quarantines, economic fallout, and over <u>1.45 million deaths</u>,(1) several pharmaceutical companies are expecting approval of their vaccines by the U.S. Food and Drug Administration (FDA) (2) within the next few weeks. Distribution to various locations in the U.S. has already begun, and plans are being formed in each state as to who will receive the vaccine first. However, the concern is that high-income countries will hoard supplies for their own populations causing delays in distribution to poorer countries.

Latin America has experienced a third of the world's deaths from the coronavirus, and Africa has now <u>passed two million cases</u>. (3) Quarantines and business shutdowns have hit poor countries especially hard, where people live on the margins even in prosperous times. It is believed that many COVID-19 infections and related deaths in Africa are likely being <u>overlooked</u> (3) as testing rates in the continent are among the lowest in the world, and many deaths of all types go unrecorded.

### **Coalitions Lead the Way:**

The <u>COVID-19 Vaccines Global Access</u> (COVAX) Facility (4) was launched by The <u>World Health Organization</u> (WHO) (5), <u>Gavi</u>, (6) and the Coalition for Epidemic Preparedness (<u>CEPI</u>).(7) Their main purpose is to ensure equitable access to COVID-19 vaccines to end the pandemic's acute phase worldwide by the end of 2021. The goal of their Access to COVID-19 Tools (<u>ACT Ac-</u>



celerator) (8) plan is to accelerate the development, production and distribution of COVID-19 tests, treatments, and vaccines. The plan states that once a vaccine is shown to be safe and effective and authorized for use, "all countries will receive doses in proportion to their population size, albeit initially in reduced quantities. This will enable every country to start by immunizing the highest priority populations."

In the second phase, vaccines would continue to be deployed to all countries so that additional populations can be covered according to national priorities.

Specifically, the allocation of vaccines will occur in the following way:

- 1. An initial proportional allocation of doses to countries until all countries reach enough quantities to cover 20% of their population.
- 2. A follow-up phase to expand coverage to other populations. If severe supply constraints persist, a weighted allocation approach would be adopted, taking into account a country's COVID threat and vulnerability. This would be decided based on how fast the virus is spreading and how vulnerable a country's health system is in regard to the availability of beds in hospitals.

COVAX is taking the lead to recruit countries to join their effort to buy and fairly distribute COVID-19 vaccines around the globe. In September 2020, they announced that countries representing two-thirds of the world's population have agreed to the plan. However, the U.S. and China are noticeably absent from the list.

Critics have argued that countries most in need should get the vaccine first, but it is believed that the proposed allocation method was the best way to get agreement from all parties. The 92 lower-income countries that have joined COVAX will have vaccine doses purchased for them. Wealthier countries will pay for their own supplies. Thus far, only <u>\$700 million</u> (9) has been raised to pay for the vaccine in lower-income countries, short of the \$2 billion thought needed by the end of the year.

Whether they support the COVAX plan or not, wealthier countries such as Great Britain, the United States, France, and Germany have already negotiated deals with pharmaceutical companies directly, meaning that the vast majority of the world's vaccine supply for next year is already reserved.

### **Bill Gates Plays an Active Role:**

Retired Microsoft founder Bill Gates helped launch and bankroll Gavi and CEPI and is one of the World Health Organization's largest donors. His \$50 billion <u>Bill & Melinda Gates Foundation</u> (10) is working actively to procure coronavirus vaccines for more than 150 countries.

For over two decades, Gates and his team have been funding re-



search and distribution for a variety of vaccines such as polio and tuberculosis, and they also work to eradicate malaria and reduce HIV infections. The foundation is able to draw on connections and infrastructure they have built over the years to help guide the effort.

When many western pharmaceutical companies stopped making other types of vaccines that were unprofitable, Gates stepped in with providing subsidies, advance commitments, and volume guarantees.

"We know how to work with governments, we know how to work with pharma, we've thought about this scenario," said Gates in a recent <u>interview</u>. (11) "We need—at least in terms of expertise and relationships—to play a very, very key role here."

Gates has not had much luck in obtaining funding from the U.S. for the global vaccine effort, as well as for therapeutics and diagnostics. He asked the Trump administration and both parties of Congress for \$8 billion, but so far, no commitments have been made.

"The COVID-19 vaccine will reach developing countries eventually. The question remains as to how soon they will receive it and how many more people will die waiting for that to happen."

### Increasing the Supply:

One proposed solution to increase the supply of vaccines is to compel the vaccine makers, who have benefited greatly from government funding, to share their technology and data with other countries. Several such as South Africa, Kenya, Mozambique, and India are advocating through the <u>World Trade Organization</u> (12) that the enforcement of coronavirus-related intellectual property rights regarding vaccines is suspended. Many pharmaceutical companies are opposed to the idea.

The COVID-19 vaccine will reach developing countries eventually. The question remains as to how soon they will receive it and how many more people will die waiting for that to happen.

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# Interpreting Umbilical Cord Blood Gases: Cord Occlusion with Terminal Fetal Bradycardia: Part II

Jeffrey Pomerance, MD, MPH

### Case 11: Umbilical Cord Occlusion with Terminal Fetal Bradycardia, Severe

From this point forward in these installments, all base deficits are extracellular fluid base deficits, and for consistency, all have been calculated using the equations supplied by CSLI (Clinical Laboratories Standard Institute). If your hospital already uses the CSLI equations, no adjustment is necessary.

 $BD(ecf) = -(HCO3^{-} - 24.8 + 16.2 \times (pH - 7.4))$  $Log(HCO3^{-}) = pH + Log(PcO_{2}) - 7.608$  $HCO3^{-} = 10^{(Log (HCO3-))}$ 

Much earlier in my life, I could have handled these equations. Today I would not even try. However, my computer spits out the results without a moment of hesitation. If you choose to, you can use your computer in the same way.

The mother was a 39-year-old, gravida 2, para 1, aborta 0, with an intrauterine pregnancy at 38 0/7 weeks' gestation. Membranes ruptured spontaneously with egress of clear fluid. There were mild uterine contractions. On external monitor, the FHR was approximately 140 bpm with moderate variability. Pitocin was begun because of failure to progress. Deeper and more prolonged variable decelerations ensued and Pitocin was discontinued. Terbutaline was administered with initially good recovery. Shortly thereafter, the FHR suddenly fell into the 60s and an emergency cesarean delivery was performed. At delivery, the male infant weighing 2951 g had a single tight loop of umbilical cord encircling his neck. The cord was clamped, cut and removed from around the neck. Resuscitation included suctioning, stimulation, and very brief bagmask positive pressure ventilation with 100% oxygen. Apgar scores were 3 and 9 at one and five minutes, respectively.

Cord blood gas results were as follows:

	Umbilical Vein	Umbilical Artery
рН	7.20	6.96
Pco, (mmHg)	54	104
(kPa)	7.20	13.87
Po, (mmHg)	35	35
(kPa)	4.67	4.67
BD (mmol/L)	7	9

At 20 minutes of age, an arterial blood gas in room air was:

	Infant's ABG
рН	7.27

Pco (mmHg)	56
2 (kPa)	7.47
Po, (mmHg)	81
² (kPa)	10.80
BD (mmol/L)	1

A central hematocrit was 58%; when repeated one hour later, it was 50%.

"The umbilical venous blood sample demonstrates a mild respiratory acidosis. The base deficit of seven is in the normal range. The umbilical arterial blood sample, on the other hand, is quite abnormal. The pH is severely depressed on the basis of a severe respiratory acidosis and a mild metabolic acidosis."

### Interpretation

The umbilical venous blood sample demonstrates a mild respiratory acidosis. The base deficit of seven is in the normal range. The umbilical arterial blood sample, on the other hand, is quite abnormal. The pH is severely depressed on the basis of a severe respiratory acidosis and a mild metabolic acidosis. The  $Po_2$  of 35 is high, suggesting contamination with an air bubble. Some blood gas analyzers no longer report results if they detect air bubbles. This is further supported by the fact that the  $Po_2$  in the arterial sample is not lower than the  $Po_2$  in the venous sample, thus breaking one of the "rules" of the relationship between these two sample sites. However, it is very clear from the large differences between the venous and arterial sample was contaminated with an air bubble, as I think it was, the "true"  $PCo_2$  would have been even higher and the "true" pH even lower.

The differences between the pH and Pco<sub>2</sub> values are very wide indeed. This finding supports the diagnosis of umbilical cord occlusion with terminal fetal bradycardia. The widened pH and Pco<sub>2</sub> differences are the result of partial restoration of umbilical arterial blood flow over a significant period of time. The umbilical venous pH is almost normal while the umbilical arterial pH is very low. Extreme differences between venous and arterial cord blood pH that are associated with variable decelerations and cord compression are not a new discovery; this observation dates back to at least 1977. (1) Umbilical venoarterial Pco<sub>2</sub> differences of greater than 25 mmHg in infants with an umbilical artery pH of less than 7.00 are associated with an increased incidence of neonatal seizures, hypoxic-ischemic encephalopathy, cardiopulmonary dysfunction, renal dysfunction, and abnormal development at discharge. (2) Infants with evidence of cord compression and terminal bradycardia will become significantly hypovolemic (3) and anemic (4) With the umbilical vein occluded and restored umbilical artery blood flow, an excess of blood accumulates in the placenta, unavailable to the fetus. Following delivery, as the fetus either spontaneously reconstitutes a normal blood volume or the newborn is given volume expansion, the hematocrit will fall. In the infant described above, the central hematocrit fell from 58% to 50% over the first 80 minutes of life; complete equilibration may take longer. This suggests a loss of approximately 14% of the fetal blood volume into the placenta (50/58 = 0.86). This is not unexpected, as cord compression has been observed to result in an increase in villous blood volume, sometimes by more than 50%. (5)

The follow-up ABG at 20 minutes of age, taken directly from the infant, has normalized. This is a little surprising as many infants will have a worsened base deficit when retested shortly after delivery. However, considering that this infant was quite vigorous by five minutes of age, and had only a moderate metabolic acidosis in the umbilical artery sample, quick recovery may well have occurred. An infant with normal cardiopulmonary function can quick-ly metabolize lactic acid to bicarbonate.

Mercer et al (6) have suggested the possibility that milking of the umbilical cord before clamping may be an effective way to remedy fetal/neonatal hypovolemia, especially if resuscitation can be accomplished at the perineum. Their suggestion was specifically aimed at therapy for newborns following shoulder dystocia with vaginal delivery (see Case 17 in an upcoming installment), but the concept seems applicable to other newborns with significant hypovolemia from all causes. Hosono et al (7) have investigated milking the umbilical cord in premature infants. Hemoglobin was higher in the milked group by 2.4 g/dL. This procedure might well obscure the interpretation of the cord gas results; however, optimizing care of the newborn is everyone's first priority.

"Studies in this area are warranted. Improved communication between the obstetric and neonatal teams would be essential as a history of a vulnerable cord followed by a prolonged terminal bradycardia should raise suspicion of significant fetal/neonatal hypovolemia."

Although this particular infant was probably not depressed enough to require such therapy, other infants might be (see Cases 13-16 and 18 in future installments). Studies in this area are warranted. Improved communication between the obstetric and neonatal teams would be essential as a history of a vulnerable cord followed by a prolonged terminal bradycardia should raise suspicion of significant fetal/neonatal hypovolemia.

**Key Points** 

- When umbilical cord occlusion with restoration of umbilical artery blood flow is prolonged, differences between umbilical venous and arterial blood gas values may be extreme.
- Cord occlusion with termination of both venous and arterial

blood flow, but with temporary partial restoration of umbilical arterial blood flow (as typically occurs with cord occlusion and terminal fetal bradycardia), results in a net transfer of blood into the placenta. The greater the umbilical venoarterial pH difference, the more time in which umbilical artery blood flow continued in the absence of umbilical venous return. Also, the more likely the resultant fetal hypovolemia and subsequent neonatal anemia will be critical.

### Case 12: True Knot in Cord

The mother was a 30-year-old, gravida 2, para 0, aborta 1 with an intrauterine pregnancy at 39 6/7 weeks' gestation. The pregnancy had been uneventful. Fetal activity was reported as normal and unchanged. The initial FHR was 140-150 bpm and had occasional accelerations. As labor progressed, variable decelerations appeared and became increasingly severe over time. Baseline beat-to-beat variability, originally moderate (normal), diminished and became absent. Seventeen hours after admission, a severe fetal bradycardia precipitated an emergency cesarean delivery under general anesthesia. At delivery, a tight true knot in the umbilical cord was found. Apgar scores were 1, 3 and 5 at one, five and 10 minutes, respectively. The infant was floppy and unresponsive. Resuscitation included positive pressure ventilation and intubation. Birth weight was 3370 g. The placenta weighed 624 g and revealed no histiologic abnormalities.

Cord blood gas results were as follows:

	Umbilical Vein	Umbilical Artery
рН	7.31	6.85
Pco, (mmHg)	44	116
(kPa)	5.87	15.47
Po, (mmHg)	33	15
(kPa)	4.40	2.00
BD (mmol/L)	4	13

A CBG blood gas at age 45 minutes was as follows:

	CBG
рН	7.00
Pco, (mmHg)	67
<sup>*</sup> (kPa)	8.93
Po, (mmHg)	45
(kPa)	6.00
BD (mmol/L)	15

Bicarbonate and normal saline were administered IV. The infant remained floppy and non-responsive at 32 minutes of age. A WBC count and differential were as follows: 26.0K/mm<sup>3</sup> with 10% bands and 36% neutrophils. The hematocrit and platelet counts were 50% and 148K, respectively. Ampicillin and cefotaxime were started and discontinued after four days when the blood culture was reported as negative. A CT of the head at age two days was normal and no seizures were noted at any time during the six days of hospitalization. Kidney and liver function tests results were normal.

### Interpretation



The umbilical venous blood sample is normal. The umbilical arte-

" The most likely pathophysiology is as follows: Initially, in terminal cord occlusion, both the umbilical vein and the umbilical arteries are occluded. Usually, however, the blood flow in the umbilical arteries is restored temporarily due to increasing fetal blood pressure."

rial blood sample is very abnormal. The pH is severely depressed on the basis of a combined severe respiratory acidosis and a moderate metabolic acidosis. Every clinician should be aware of the type of base deficit reported at their hospital. Extracellular fluid base deficit should be encouraged. The umbilical pH, Pco, and base deficit venoarterial differences are very wide. The follow-up blood gas demonstrates a much improved Pco, and a marginally higher base deficit. Most commonly, newborns who have markedly depressed one-minute Apgar scores, have some degree of acid washout (increased base deficit) on their first follow-up blood gas. However, by age 45 minutes the base deficit already may have improved from what it was earlier. It should be noted that in the face of poor perfusion, a CBG may be misleading. The inaccuracy tends to make the base deficit appear worse.

There is nothing that distinguishes this set of cord gases from others with cord compression and terminal fetal bradycardia already presented. What is noteworthy is the cause of the abnormalities in blood gas values, namely the true knot in the cord. True knots in the umbilical cord have long been known as an occasional cause of stillbirth, but seldom seem to cause a problem during labor and delivery. (8) Although the placenta was said to have shown no histological abnormalities, one would expect to see a dilated umbilical vein on the placental side of the knot. Perhaps the knot in the cord was untied in the delivery room.

"A true knot has little impetus to tighten during labor and delivery unless the cord is anatomically critically short or made functionally short by being wrapped around a fetal body part."

Although the diagnosis seems straightforward, it is always possible that an unidentified occult cord prolapse caused the cord occlusion rather than the true knot in the cord. A true knot has little impetus to tighten during labor and delivery unless the cord is anatomically critically short or made functionally short by being wrapped around a fetal body part.

**Key Point** 

Although rare, a true knot in the umbilical cord may result in

the classical cord blood gas findings associated with cord occlusion and terminal bradycardia, namely widened differences between umbilical venous and arterial pH, Pco, and base deficit.

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Disclosure: The author has no disclosures.

### NT





# Survey Says: RSV





### NATIONAL SURVEY,

Specialty Health Gare Providers say:

They treat RSV as a priority, often" or "always" evaluating their patients

RSV is the "most serious and dangerous" Illness for children under four

Barriers to access and denials from insurance companies limit patients' ability to get preventive **R5V** treatment



Only 18% know "a lot" about RSV

Uternsolves "very well" prepared to prevent RSV

### RSV EDUCATION & AWARENESS CAN HELP After parents learned more about RSV, they were:



### **OPIOIDS and NAS** When reporting on mothers, babies, and substance use LANGUAGE MATTERS



### I am not an addict.

I was exposed to substances in utero. I am not addicted. Addiction is a set of behaviors associated with having a Substance Use Disorder (SUD).

### I was exposed to opioids.

While I was in the womb my mother and I shared a blood supply. I was exposed to the medications and substances she used. I may have become physiologically dependent on some of those substances.



### NAS is a temporary and treatable condition.

There are evidence-based pharmacological and non-pharmacological treatments for Neonatal Abstinence Syndrome.



### My mother may have a SUD.

She might be receiving Medication-Assisted Treatment (MAT). My NAS may be a side effect of her appropriate medical care. It is not evidence of abuse or mistreatment.

### My potential is limitless.

I am so much more than my NAS diagnosis. My drug exposure will not determine my long-term outcomes. But how you treat me will. When you

invest in my family's health and wellbeing by supporting Medicaid and Early Childhood Education you can expect that I will do as well as any of my peers!

Learn more about Neonatal Abstinence Syndrome at www.nationalperinatal.org



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### Abstracts from the California Association of Neonatologists Cool Topics in Neonatology 26<sup>th</sup> Annual Conference

John Cleary, MD



# Cool Topics in Neonatology

### **26th Annual Conference**

Friday, Saturday & Sunday March 6 - 8, 2020 Coronado Island Marriott Resort Coronado, California



The Poster Abstracts Table of Contents from the 26<sup>th</sup> Annual Conference are presented below:

Abstract # 2

Abstract # 3

Relationship of NICU Stress and Cortisol Variability with Very Low Birth Weight Infant Behavioral Outcomes at 2 and 4 Years

NEC PREVENTION CARE BUNDLE LED TO SUSTAINED LOW INCI-DENCE OF NECROTISING EN-TEROCOLITIS IN VERY LOW BIRTH WEIGHT INFANTS: 10-YEAR QUAL-ITY IMPROVEMENT PROJECT

Correlation between Total Serum Bilirubin and Transcutaneous bilirubin levels in extremely preterm infants less than 30 weeks gestation.

Barriers to optimal breast milk provision in the Neonatal Intensive Care Unit (NICU)

Decreasing the number of unnecessary X-ray retakes in a Tertiary Level Neonatal Intensive Care Unit (NICU).

Standardized Algorithm for Non-Invasive Pressure Based Weaning Strategy for Infants Less Than 32weeks and/or 1500gm: Lung Protective Strategies

A Case Series of Neonatal Aspergillosis: An Emerging Fungal Infection in the Extremely Low Gestational Age Neonates Neurodevelopmental Follow-up Program: Quality Improvement

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Abstract # 12	Use of Point-of-Care Ultrasound to Serially Assess Umbilical Venous Catheter Tip Location	Abstract # 27	Direct Umbilical Vein Injection of Epi- nephrine with Cut Umbilical Cord Milk- ing
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Abstract # 38	Functional differences among B. in- fantis strains in infant probiotic prod- ucts	Abstract # 54	Improving oral colostrum administra- tion within first hour of life in Neonatal Intensive Care Unit infants
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California Association of Neonatologists (CAN) and AAP District IX Section on Neonatal-Perinatal Medicine

# Cool Topics in Neonatology

27th Annual Conference A Virtual Educational Conference

Friday, Saturday & Sunday March 5 - 7, 2021









Abstract Title: Growth outcomes and biochemical differences in preterm infants less than 1250 grams at birth fed human milk with human milk-based fortifier versus bovine milk-based fortifier

Name: Millie Chang, MD

PGY-5

**Co-Authors:** Lorayne Barton, MD; Ting-Yi Lin, MD; Rangasamy Ramanathan, MD; Rowena Cayabyab, MD

Organization: LAC-USC

Abstract Overview: TITLE: Growth outcomes and biochemical differences in preterm infants less than 1250 grams at birth fed human milk with human milk-based fortifier versus bovine milkbased fortifier. Authors: Millie Chang, Lorayne Barton, Ting-Yi Lin, Rangasamy Ramanathan, Rowena Cayabyab Background: Exclusive human milk (EHM) feeding has been shown to improve feeding tolerance, decreased rate of necrotizing enterocolitis, late onset sepsis, retinopathy of prematurity, bronchopulmonary dysplasia and length of hospital stay in very low birth weight infants. However, there is insufficient evidence on growth outcomes and nutrition indices in preterm infants fed EHM. Purpose of Study: Comparison of growth outcomes and laboratory values in preterm infants less than 1250 grams at birth fed human milk with human milk-based fortifier (EHM) versus bovine milk-based fortifier (HMF). Methods Used: Retrospective data collection on preterm infants less than 1250g at birth admitted to NICU from January 2016 to November 2019 who were fed with human milk with human milk-based fortifier (EHM-26cal/oz, protein: 0.025g/ml) or bovine milk-based fortifier (HMF-24cal/oz, protein: 0.025g/ml). Demographics, clinical outcomes, anthropometric measurements (at birth, achievement of full feeds and at discharge); and laboratory values (achievement of full feeds and tolerated feeds for 3 consecutive days and off parenteral nutrition) were collected. Data was compared using chi square test or Wilcoxon rank sum test as appropriate. Infants with congenital anomalies/genetic syndromes were excluded. Summary of Results: Seventy four preterm infants were included in the study. Birth anthropometrics were similar in both groups. Preterm infants fed EHM were of significantly lower gestational age (GA) at birth and achieved full feeds at an earlier postmenstrual age (PMA). However, the time to full enteral feeding was not significantly different between the type of fortification of human milk. Infants fed EHM had similar PMA at discharge, higher discharge weight and weight percentiles; discharge head circumference and length compared to infants fed human milk fortified with bovine based HMF. Extrauterine growth restriction (EUGR) was significantly lower in preterm infants fed EHM. Serum albumin and BUN levels were significantly higher in preterm infants fed EHM at achievement of full feeds (Table 1). Clinical outcomes were not significantly different between the two groups. Conclusions: Preterm infants fed EHM with higher caloric density had improved nutritional indices after achieving full enteral feeding resulting in fewer infants with EUGR. Despite lower GA in infants fed EHM, PMA at discharge was not significantly different from infants fed human milk with bovine milk based HMF.

### Abstract # 3

Abstract Title: NEC PREVENTION CARE BUNDLE LED TO SUSTAINED LOW INCIDENCE OF NECROTISING ENTERO-COLITIS IN VERY LOW BIRTH WEIGHT INFANTS: 10-YEAR QUALITY IMPROVEMENT PROJECT

Name: Maria Fe Villosis, MD

Neonatologist, NICU Director-KFH PC

**Co-Authors:** Ma. Teresa C. Ambat, MD., Kambiz K. Rezaie, MD., Karine Barseghyan, MD

Organization: Kaiser Permanente

Abstract Overview: BACKGROUND: Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergencies in preterm newborns and remains a serious complication associated with significant morbidity and mortality in this population. Over the past two decades, multicenter groups have reported reductions in the incidence of NEC among preterm infants. Although highly variable, an average rate exceeding 5% was reported by the majority. This coincided with reports of modifications in practice using continuous quality improvement (CQI) initiatives aimed specifically at reducing NEC risk or reducing risk of mortality and many morbidities associated with extreme prematurity. OBJEC-TIVE: To evaluate the result of NEC prevention CQI on the incidence of NEC among very low birth weight (VLBW) infants admitted to Kaiser Foundation Hospital Panorama City (KFH-PC) NICU from 2009-2018 METHODS: A cohort of 439 VLBW infants admitted to KFH-PC NICU from 2009-2018 was included in this retrospective study utilizing VON database. RESULTS: NEC incidence at KFH-PC NICU decreased from baseline of 6.7% in 2009 to an average incidence of 1.5% with a range of 0-4.9% during the years 2010-2018. The VON observed: expected ratio in the most recent epoch (2016-2018) was 0.5 (5th and 95th confidence limits 0.2 and 0.9, respectively). At KFH-PC NICU, the average rate of discharge on breastmilk was 91% during the study period. The practice modifications we implemented focusing on feeding strategies included: standardized feeding protocol, exclusive human milk diet, human milk-based fortifiers, and recent addition of probiotics. Infection prevention, controlling use of antibiotics and antacids were also integral to our bundle of care. CONCLUSION: Practice modifications based on evidence from clinical trials targeting reduction in NEC which were executed through CQI initiatives at KFH-PC NICU led to sustained reduction in its NEC rate lower than most reports in recent publications.

### Abstract # 4

### Abstract Title: Correlation between Total Serum Bilirubin and Transcutaneous bilirubin levels in extremely preterm infants less than 30 weeks gestation.

### Name: Meera Sankar, MD

**Clinical Associate Professor** 

**Co-Authors:** 1.Meera Sankar MD, Neonatology/Pediatrics, Stanford University, Stanford, CA 2.Dilip Bhatt MD, Neonatology/Pediatrics, Neonatology/Pediatrics, Kaiser Permanente, Fontana, CA 3.Anup Katheria MD, Neonatal Research Institute, Sharp Mary Birch Hospital, San Diego, CA, 4.Priscilla Joe, MD Neonatology, UCSF Benioff Children's Hospital Oakland, Oakland, CA, 5.Maria Cortes, NNP, Neonatology, Santa Clara Valley Medical Center, San Jose, CA, 6.Virna Paje MD, Neonatology/Pediatrics, Kaiser Permanente, Fontana CA 7.Manoj Biniwale MD & 8.Ram Ramanathan MD Division of Neonatal Medicine, Keck School of medicine of USC, LAC+USC Medical Center, Los Angeles, CA

### Organization: Stanford University

Abstract Overview: Title: Correlation between Total Serum Bilirubin and Transcutaneous bilirubin levels in extremely preterm infants less than 30 weeks gestation Background: Measurement of Transcutaneous bilirubin (TCB) level is a safe, noninvasive, cost effective and widely used method for screening term and late preterm infants with hyperbilirubinemia. Limited data exists regarding the validity of TCB use in extremely preterm (EP) infants. Objective: The primary objective was to evaluate the correlation and agreement between total serum bilirubin (TSB) and TCB levels in EP infants. Design/Methods: This was a prospective multicenter study conducted at tertiary and regional NICUs in California. EP infants between 23.0-29.6 weeks of gestation admitted to the NICU without congenital anomalies were included. TCB measurements were performed within 30-60 minutes of TSB measurements during the first 3 weeks of life. Trained NICU staff measured TCB levels by using Drager Jaundice meter (JM-103) or the BiliChek transcutaneous bilirubinometer. Neonates with TSB readings in the phototherapy range received phototherapy as per the standard protocol. We examined the difference between TCB and TSB values, gestational age, maternal race, ethnicity and neonatal morbidities. Descriptive statistics were generated for entire group using IBM SPSS statistical software version 26. Correlation between TSB and TCB levels was assessed with Pearson's correlation analyses. Bland-Altman analysis was used to show the differences against the mean of the two methods. Results: 299 paired TCB and TSB measurements (58 infants) were analyzed. Median gestational age was 27.2 weeks (IQR 25.5-28.3) and postnatal age ranged from 1 to 18 days of life. TSB values ranged from 0.41 to 14.7 where as TCB values ranged from 0 to 15.5. Mean difference between TCB and TSB was 0.37

(SD +/-2.56). Pearson bivariate correlation testing revealed moderate level of correlation between TCB and TSB with a coefficient of 0.625 (p<0.001). Proportionate bias was noted in infants with higher bilirubin values. Bland Altman analysis of log transformed data (Figure 1) showed a good agreement at 95 percent limits with mean of 0.0074 (SD 0.267). Regression equation predicted TSB= 2.68+0.42(TCB) with r squared of 0.39 suggesting weak to moderate correlation (Figure 2). Conclusions: TCB levels correlated moderately with TSB levels in this ethnically diverse population of EP babies in California NICUs. TCB may be a useful screening tool for monitoring jaundice in EP newborns. Larger studies are needed to validate these findings.

### Abstract # 5

# Abstract Title: Barriers to optimal breast milk provision in the Neonatal Intensive Care Unit (NICU)

Name: Meera Sankar, MD

**Clinical Associate Professor** 

**Co-Authors:** 1. Meera N. Sankar MD, Neonatology/Pediatrics, Stanford University, CA, 2. Ya'el E Weiner, Stanford University, CA 3. Peiyi Kan, Stanford University, CA 4. Sharon Rea, BA, IBCLC, Stanford University, CA 5. Henry Lee MD, Neonatology/ Pediatrics, Stanford University, CA

Organization: Stanford University

Abstract Overview: TITLE: Barriers to optimal breast milk provision in the Neonatal Intensive Care Unit (NICU) AUTHORS: Meera N. Sankar MD\*, Ya'el Weiner, Peiyi Kan, Sharon Rea & Henry Lee MD Neonatology/Department of Pediatrics, Stanford University, Stanford, CA, United States. INTRODUCTION: In the high risk NICU setting, breast milk use is associated with decreased morbidity and improved neurodevelopmental outcomes. This retrospective study aimed to identify patient and systems barriers to optimal breast milk use in infants admitted to a regional NICU in California. METHODS: 699 babies born at 23-41 weeks of gestation with no congenital anomalies admitted to the NICU within 3 days of birth from 9/2015 to 6/2018 were included. We examined: maternal factors and demographics; neonatal data, need for resuscitation and morbidity; length of stay; frequency of lactation support in first week, during NICU stay, and at discharge; age at first lactation consult; and breastfeeding in the NICU. Bivariate analysis and logistic regression were used to examine patient and lactation consultant service factors associated with breast milk use at discharge. RESULTS: Breast milk use at discharge for all infants was 89.7%: for extremely preterm (EP) 80.3%, moderate preterm 94.2%, late preterm (LP) 86.3%, and term 92.3%. Low birth weight, morbidities, length of stay, public insurance and lack of lactation support at discharge (OR 0.19 [0.09-0.38]) were associated with significantly no breast milk use at discharge (Table



1). In EP infants, need for resuscitation, morbidities, black race, singleton births, lack of lactation support during NICU stay and at discharge along with lack of breastfeeding in the NICU decreased breast milk use (Table 2). In term infants, sepsis, home on gavage feeds, lack of lactation support at discharge, and lack of breastfeeding in the NICU significantly decreased breast milk use (Table 3). In LP infants, inborn, C-section, older maternal age, frequency of lactation support in first week (OR 1.77[1.15-2.74]), and during NICU stay (OR 1.32[1.03-1.68]) increased breast milk use. Older age at first lactation consult (OR 0.88[0.78-1.00]), lack of lactation support at discharge, and lack of breastfeeding in the NICU (OR 0.17[0.04- 0.66]) decreased breast milk use (Table 4). LP infants benefitted from lactation support from admission through discharge. Black race and lack of lactation support at discharge were associated with decreased breast milk use in EP infants. CONCLUSION(S): Compared to term infants, LP and EP infants had lower rates of breast milk use at discharge, particularly with decreased use of lactation services. Lactation support should be targeted to increase breast milk use in these high-risk populations.

### Abstract # 7

Abstract Title: Decreasing the number of unnecessary Xray retakes in a Tertiary Level Neonatal Intensive Care Unit (NICU).

Name: Sheila Kalyanam, MD

Neonatology Fellow

Co-Authors: Guadalupe Padilla, MD Virender Rehan, MD

Organization: Harbor- UCLA Medical Center

Abstract Overview: Background: Depending on the diagnosis, birth weight, gestational age (GA), and length of stay of an infant admitted to a NICU, it is often necessary to perform a large number of radiographic examinations. In our NICU it was perceived that an excessive number of repeat X-ray examination were performed due to improper positioning or foreign objects obstructing the view of the intended field. Due to the potential harmful effects of radiation exposure, particularly on the developing organs, it is necessary to keep neonatal X-ray examinations to a minimum. Objective: Our goal was to decrease the number of X-ray retakes by 50% by applying the PDSA (Plan-Do-Study-Act) model, education on proper positioning, and a "two-person hold" approach. Design/ Methods: We initially performed a telephonic survey of 20 regional NICUs and queried their practice of positioning babies during X-ray examinations; 19/20 units had a policy of two persons, i.e., a registered nurse (RN) and a respiratory therapist (RT), holding the infant during X-ray examination. Using the PDSA model, baseline data was collected from Aug-Dec 2018 which included GA, type of X-ray, presence of a central line/ ETT, or positioning aid. We documented the numbers and reasons for retaking the images. An educational video was created to demonstrate holding the infant in the correct position. All NICU RNs and RTs completed this education module. Staff champions were identified to provide ongoing hands-on support. Post intervention data was obtained from Aug-Dec 2019. Setting/Patients: Patients admitted to the NICU at Harbor- UCLA Medical Center Results: The preintervention retake rate was 56% (35/62), which, post intervention, decreased to 17% (18/105) (Image. 1). Image. 2 displays post-intervention decreases in retakes in specific sub-categories identified for most retakes. Conclusion: Education and assistance from RN and RT champions decreased the rate of unnecessary retakes from 56% to 17% exceeding our primary goal. Limitations: Many challenges and opportunities have been identified, e.g., un-reliable data collection if it is not collected immediately and is relied upon re-call, false perception that extremely low birth weight infants do not move much during X-ray examination and therefore, do not require two-person hold, etc., which will be the focus of our next PDSA cycle.

### Abstract # 8

Abstract Title: Standardized Algorithm for Non-Invasive Pressure Based Weaning Strategy for Infants Less Than 32weeks and/or 1500gm: Lung Protective Strategies

Name: James Fritzell Jr, MD

Clinical Director Small Baby Program Miller Children's Hospital

Co-Authors: Irma Reyburn RRT Ching Tay, MS

Organization: Mednax

Abstract Overview: Background: The concept of less invasive forms of respiratory support in premature infant populations is well established in its role in reducing lung injury and the co-morbidities associated with chronic lung disease (CLD) and bronchopulmonary dysplasia (BPD). A reproducible evi-dence based approach to weaning or removing this form of support for the continued uninhibited respiratory and neurodevelopmental progression has not been established in this population. In our 95 bed level III unit, we have adopted an algorithmic reproducible pathway based on estab-lished evidence based practices to remove infants from less invasive pressure based respiratory support to minimize and protect their ongoing development. Objective: Create an weaning algorithm strategy for less invasive pressure based respiratory support in infants < 32 weeks and <1500gm. Educate staff (respiratory therapist and nursing staff of Small Baby Program) to the clinical pathway established in the algorithm. Demonstrate application and retention of algorithm based practice. Methods: An algorithm, based upon evidence based literature, was created for infants less than 32 weeks gestation and/or less than 1500gm that required pressure based less invasive respira-tory support



(CPAP/HFNC) and are now at 21% FiO2 requirements. Education sessions, visual bedside algorithm charts and PDSA cycle timetable were established for the support care teams (nursing, respiratory therapists and physician). Ongoing data collection for clinical outcome measures (BPD, home oxygen requirements and in-hospital days) were collected for all eligible infants. Results: Bedside auditing demonstrated 100% compliance in bedside visual education tools, >95% appropriate level of respiratory less invasive support as per algorithm delineation and early demonstration of reduction in un-necessary oxygen exposure. Conclusion: The standardization and reproducibility of a pressure based weaning algorithm in a level III NICU is possible through education and ongoing clinical visual cues and super-user mon-itoring/auditing for eligible premature infants. This quality intervention can provide a standardiza-tion in respiratory support to maximize consistency in care and reduce unintended complications of over or under exposure to inappropriate respiratory support. We believe that this standardiza-tion in respiratory care will lead to a reduction in BPD rates, decrease home oxygen require-ments and shorten overall in-hospital days.

### Abstract # 9

Abstract Title: A Case Series of Neonatal Aspergillosis: An Emerging Fungal Infection in the Extremely Low Gestational Age Neonates

Name: Alexandra Iacob, MD

**Neonatology Fellow** 

**Co-Authors:** Cherry Uy, MD, University of California Irvine Neonatal/Perinatal Division Chief and Professor of Pediatrics Fayez Bany-Mohammed, MD, University of California Irvine Professor of Pediatrics Antoine Soliman, MD, Miller Women's and Children's Long Beach Neonatal Intensive Care Unit Medical Director Muhammad Aslam, MD, University of California Irvine Professor of Pediatrics

Organization: University of California Irvine

Abstract Overview: Title: A Case Series of Neonatal Aspergillosis: An Emerging Fungal Infection in the Extremely Low Gestational Age Neonates Authors: Alexandra Iacob, MD1,2\*, Cherry Uy, MD1, Fayez Bany-Mohammed, MD1, Antoine Soliman, MD2, Muhammad Aslam, MD1 1 University of California – Irvine, Department of Pediatrics, Orange, CA 2 Miller Children's & Women's Hospital, Long Beach, CA Introduction: Aspergillosis is a fungal infection that can manifest through pulmonary, abdominal, cerebral, cutaneous or endovascular symptoms. Primary cutaneous aspergillosis is emerging as a new infection predominantly in the extremely low gestational age neonates (ELGAN), likely due to very thin epidermal layer and immaturity of the immune system. Very few case reports detail the presentation and management of these infants. The objective of this study was to assess the presentation, management, and overall outcomes of neonatal aspergillosis in a series of ELGANs. Methods: Data from neonates with confirmed aspergillosis in the last 6 years at two affiliated academic institutions was retrospectively collected. Chart notes and laboratory values were reviewed to assess mode of presentation, images of lesions, choice of antifungal medication, duration of treatment, and overall outcome of each patient. Results: The series included 7 patients (4 males) with mean birth gestational age of 23w5d and mean birth weight of 570 grams. The mean age at the first presenting symptom was 9±4 days of life. All 7 infants manifested with a skin lesion on the back. All cases were confirmed primary cutaneous aspergillosis as only the skin scrapping culture was positive with negative blood and urine cultures. All infants were managed with liposomal amphotericin B, the standard first line antifungal. Micafungin was added as dual therapy for three infants due to ongoing new lesions presenting while on liposomal amphotericin B. Six of 7 patients have completed treatment, as evidenced through resolution of the skin lesions. The mean duration of therapy was 47±9 days. All 6 infants survived and were discharged from the hospital. The seventh patient is under active treatment. Conclusion: High index of suspicion and early recognition is critical for neonatal aspergillosis in ELGANs. All cases in the series were limited to primary cutaneous aspergillosis without evidence of invasive aspergillosis. Prolonged course of liposomal amphotericin B was well tolerated and associated with overall good outcome.

### Abstract # 10

# Abstract Title: A MULTIDISCIPLINARY APPROACH TO NICU ANTIBIOTIC STEWARDSHIP

Name: Harjinder Singh, A4638333

Neonatologist

**Co-Authors:** Harjinder Singh MD – Neonatologist Pankaj Mistry MD – Neonatologist Shahid Kamran MD - Neonatologist, Medical director Susan Wilkinson. RN , NICU Quality Supervisor Sheri Landazuri, BSN,RN ( Clinical IV NICU )

Organization: Pomona Valley Hospital Medical Center

**Abstract Overview:** TITLE: Multidisciplinary Antibiotic Stewardship reduced the NICU Antibiotic Use Rate (AUR) Authors: Harjinder Singh MD\*, Susan Wilkinson RN BACKGROUND: Broad spectrum antimicrobial use in the NICU has been associated with emergence of multi-drug resistant gram negative bacilli and development of invasive candidiasis. Prolonged use of empiric antibiotics for early onset sepsis(EOS) in ELBW infants has been associated with increased risk of mortality, NEC and late onset sepsis. After observing a modest decrease in AUR from 22%-19.99% in 2018 related to increased awareness , in January 2019 we ini-



tiated a multidisciplinary NICU antibiotic stewardship. SMART AIM: To reduce the AUR in NICU from 22% to 17% by January 2020 DRIVERS OF CHANGE: Addressed variations in physician practices by standardizing approach to management of suspected sepsis in NICU. Guidelines were developed for management of EOS in infants less than 35 weeks, greater than 35 weeks and the late onset sepsis in NICU SETTING: 53 bed Level 3B Community NICU METHODS: We assembled a Multidisciplinary Antibiotic Stewardship Team (Nov 2018) that included Neonatologists, Pharmacists, NICU Quality Supervisor, Infection Prevention Nurse, Clinical IV RN NICU and Medical Directors of NICU and the hospital Infection Control. The team defined member roles and responsibilities, reviewed current literature, benchmarked community NICUs practices, developed standardized guidelines for sepsis management(March 2019), implemented daily antibiotic rounds(April 2019) and educated staff and pharmacists. MEASUREMENTS: AUR data was collected monthly using the electronic medical record. Hospital readmission rate was monitored as a balancing measure to detect possible under treatment. **RESULTS:** Interventions were implemented as indicated above and the AUR declined over a 12 month period from 19.99% at the beginning of the stewardship program to 13.52% by January 2020. Compliance with the established guidelines exceeded 95% DISCUSSION: Gradual but significant reduction in AUR was observed when evidence based standardized approach was adopted for management of suspected sepsis in a large NICU. AUR for ampicillin and gentamicin also demonstrated similar decline. Ongoing challenges include improving compliance with established guidelines and avoiding administration of unintended doses of antibiotics. FUTURE STEPS: Incorporate elements of stewardship program into standard NICU practice, dissemination of stewardship practices to include night shift staff and expansion of the stewardship program to all well newborns at our facility Acknowledgement: Antibiotic Stewardship Team and NICU Staff Members

### Abstract # 11

Abstract Title: Outcomes of neonates with severe hypoxicischemic encephalopathy receiving cooled blood hypothermia.

Name: Eiji Hirakawa, MD

Neonatologist

**Co-Authors:** Itaru Hayasaka, MD, PhD. neonatologist Satoshi Ibara, MD, PhD. neonatologist

Organization: Nagasaki Harbor Medical Center, Nagasaki, JA-PAN

Abstract Overview: Introduction Therapeutic hypothermia (TH) has improved outcome in Hypoxic Ischemic Encephalopathy

(HIE), however ,especially in severe HIE group, their outcomes are not enough. In terms of head MRI image, 48% neonates who received TH has some abnormal signal 1). Therefore, deep brain hypothermia, long term hypothermia, Xe, Epo and stem cell transfusion have been studied as an adjunctive therapy. None of them are a promising therapy for improving outcomes in severe encephalopathy. Hypothermia on ECMO have been reported at 2003 2). Neonatal ECMO study of temperature have reported no difference between hypothermia and normal temperature group who received ECMO 3). However, hypothermia on ECMO in the high-risk population with moderate or severe HIE have been reported as safe and efficacious at 2019 4). Our team has introduced cooled blood hypothermia on ECMO for severe encephalopathy since 2014. We report the outcome of cooled blood hypothermia in neonates. Methods HIE patients have been divided two groups, surface cooling and blood cooling, according to severity at admission. On blood cooling group, ECMO have been introduced for cooling within 6 hours. ECMO pump works at 10 ml/kg/min, and blood temperature is set at 33.5 degree. Cooling protocol is same in both group, 33.5 degree for 72 hours. Fentanyl is used as sedative drug. Respiratory support on ECMO is used for the patients who developed PPHN as needed. Results 38 HIE patients have been admitted from Jan,1 2014 to May, 31 2018. 29 of them have been treated on surface cooling, 8 cases have received cooled blood hypothermia. One case has dropped off followup program. Background in cooled blood hypothermia are birth weight is 2908±423g, Gestational Age is 38±2.1week, Cord blood; pH 6.87±0.15, CO2 94.7±27.1mmHg, BE -18.6±-6.7mmol/L, Apgar Score; 1 min 1.1±1.2, 5min 2±2.2, 10min 1.4±2.2. In terms of head MRI at discharge, 3 of them have abnormal signal at basal ganglion. Developmental score at 1.5 years old is normal in four patients, one is in border line. Conclusion We introduced cooled blood hypothermia for severe encephalopathy who supposed to have poor prognosis. 57% (4/7) of them are normal development at 1.5 years old. Cooled blood hypothermia for severe HIE might be effective.

### Abstract # 12

Abstract Title: Use of Point-of-Care Ultrasound to Serially Assess Umbilical Venous Catheter Tip Location

Name: Caroline Noh, MD

Fellow

**Co-Authors:** Pai VV, Vallandingham S, Manipon C, Dasani R, Houghteling PD, Balasundaram M, Davis AS, Bhombal S

Organization: Stanford University

Abstract Overview: TITLE Use of Point-of-Care Ultrasound to Serially Assess Umbilical Venous Catheter Tip Location AU-THORS Noh CY\*, Pai VV, Vallandingham S, Manipon C, Dasani

R, Houghteling PD, Balasundaram M, Davis AS, Bhombal S. BACKGROUND Umbilical catheter placement is a routine neonatal procedure, and radiographs are often used to confirm tip location. Recent studies have shown that ultrasound can readily identify umbilical venous catheters (UVC) tip location with greater accuracy than radiographs and that ultrasound-guided UVC placement is a faster method to place catheters requiring fewer manipulations and radiographs. Studies have demonstrated the propensity of UVCs to migrate over time, and inappropriately positioned catheters can pose significant risk. The impact of using ultrasound to survey UVC tip location over time is unknown. OBJECTIVE To evaluate the use of point-of-care ultrasound (POCUS) for UVC placement and surveillance, and its impact on patient manage-DESIGN/METHODS At a large academic neonatal inment. tensive care unit (NICU), POCUS was utilized at the time of UVC placement as able, and surveillance POCUS of UVCs was performed 2-3 times a week as guality improvement endeavor. PO-CUS scans were used as an adjunct and did not replace radiographs obtained as part of standard care. If the tip was identified to be in unfavorable position, the primary physician was notified, and a confirmatory radiograph was obtained at their discretion. Patient demographic data, ultrasound findings, interpretation, and subsequent clinical interventions were documented in a standardized database. RESULTS A total of 179 scans were performed to evaluate UVC tip location on 97 patients from January through December 2019. Among 15 scans performed at the time of placement, 4 UVCs (27%) were adjusted prior to obtaining confirmatory radiographs, which then confirmed optimal placement. Out of 164 scans performed after placement, 35 scans (21%) identified UVCs to be in an unfavorable position, which prompted manipulation or removal of 28 UVCs (80%). The average time spent to identify UVC tip location by POCUS was 6.1 minutes. CONCLU-SION Utilizing POCUS to survey UVC tip location can be done quickly, without radiation, and can identify unfavorably positioned catheters with potential to improve the management and safety of patients with UVCs.

### Abstract # 14

Abstract Title: The Relationship between Gestational Age, Fetal Sex, and Immunologic Age: Deep Profiling of the Newborn Immune System using CyTOF

Name: Laura Peterson, MD

**Clinical Fellow** 

**Co-Authors:** Xiaoyuan Han, PhD; Kazuo Ando, MD, PhD; Amy Tsai, BS; Edward Ganio, PhD; Natalie Stanley, PhD; Nima Aghaeepour, PhD; Brice Gaduilliere, MD, PhD

**Organization:** Stanford University, Department of Pediatrics, Division of Neonatology

Abstract Overview: Background Dysregulated immunity lies at the heart of the most severe morbidities of prematurity: sepsis, bronchopulmonary dysplasia, retinopathy of prematurity, and periventricular leukomalacia. For unknown reasons, male infants are at increased risk. A comprehensive understanding of the newborn immune system may shed light on the pathophysiology underlying these important diseases. High-dimensional mass cytometry (CyTOF) is a novel technology that allows for the characterization of dozens of immune cell types and their signaling behaviors, providing the opportunity to create an unprecedentedly detailed map of the newborn immune system. Methods Cord blood was collected at delivery. Samples were stimulated with immunologically active compounds, including lipopolysaccharide (LPS), interferon alpha (IFN $\alpha$ ), and interleukins (IL) 2, 4, and 6. The samples were stained with antibodies to 24 phenotypic markers and 15 phosphorylated (i.e. activated) signaling proteins and run on Cy-TOF. Analysis was performed using multivariate machine learning (CITRUS) and traditional univariate statistics. Results Eighteen cord blood samples have been analyzed, including from nine term babies (GA  $\geq$  37 weeks), four GA <34 weeks (preterm group), and five GA 34-36/6 weeks (late preterm group). There were no demographic differences between groups. Differences were seen in rates of preeclampsia, c-section delivery, and antenatal steroids (Table 1). Analysis revealed numerous immune system-wide differences. As an example, there was a linear relationship between increasing GA and NFkB signaling in T cells, as evidenced by increased levels of IkB, an NFkB inhibitor, at earlier GA (Fig 1A-C). NFkB is required for T cell activation, which is the basis for adaptive immunity. Another example is the relationship between increasing GA and response of STAT-6 to IL in innate immune cells (Fig 1D-F). STAT-6 is a mediator of the anti-inflammatory cytokine IL-4. Male fetuses had decreased numbers of all subsets of T cells and increased numbers of innate inflammatory cells, including Dendritic Cells (DCs) and Natural Killer (NK) cells (Fig 2). A larger sample size is anticipated prior to abstract presentation. Conclusions This study is the first to use CyTOF to comprehensively map the cellular composition and signaling behavior of the newborn immune system. Results suggest that premature newborns suffer from a combination of an impaired adaptive immune system and a dysregulated innate immune system that has diminished response to counter-regulatory cytokines such as IL-4. The increased vulnerability of males to morbidities of prematurity could be partially explained by decreased numbers of T cells and increased numbers of dysregulated innate immune cells.

### Abstract # 15

Abstract Title: Critical congenital heart disease screening modification to decrease the gap in diagnosis: QI project

Name: Priya Jegatheesan, MD

NICU Director

**Co-Authors:** Angela Huang, RNC, Weifen Den, NNP, SudhaRani Narasimhan, MD, IBCLC, YT Lan, MD, Dongli Song, MD, PhD, Balaji Govindaswami, MBBS, MPH



### Organization: Santa Clara Valley medical center

Abstract Overview: Background: Oxygen saturation screen in newborns decreases mortality by early diagnosis of critical congenital heart disease (CCHD), however misses upto 25% of CCHDs, especially those with left ventricular outflow tract obstructions. To decrease the gap in the sensitivity of CCHD screening we modified our screen to include perfusion index (PI). Objective: To implement a modified CCHD screen universally in order to increase the sensitivity of identifying CCHD. Method: The CCHD screening criteria was revised to include the 2 new criteria: PI <0.7 and saturation <95% to repeat the screen. Modified criteria were implemented in December 2018 in well baby nursery and in April 2019 in NICU following nursing and provider education and electronic health record update. Failed CCHD cases were reviewed during weekly clinical meetings. Electronic reports were obtained monthly. Failed and repeated screens were reviewed and summarized in SPS control charts. Baseline data was collected from January to November 2018. Results: Of 5,105 newborns screened, 8 (0.2%) failed the screen which included 2 CCHD cases during the baseline period, 1 pulmonary hypertension (PPHN) that required respiratory support, 5 mild PPHN or transitional circulation not requiring treatment. The number infants who required repeat screening increased from baseline 0.5% to 1.6%, while failed screen remained the same at 0.2%. Conclusion: Broadening CCHD screening criteria increased number of repeat screens but not failed screens. Large number of screens are needed to evaluate the sensitivity of the modified CCHD screening in asymptomatic newborns.

### Abstract # 16

### Abstract Title: Neonatal Resuscitation in the Emergency Room: Testing Knowledge and Confidence of Residents

Name: Shannon Liu, MD

Neonatal Perinatal Medicine Fellow

**Co-Authors:** Shannon Liu, MD\*, Loren Yaeger, DO, Evan Sander, MD, Priya Shastry, DO, Nicole Flores-Fenlon, MD, Aarti Jain, MD, Yvette Liza Kearl, MD, Rangasamy Ramanthan, MD, Fiona Wertheimer, DO, Manoj Biniwale, MD

Organization: LAC+USC Medical Center

**Abstract Overview:** Emergency Medicine (EM) residency training is a diverse discipline, encompassing many facets of adult and pediatric medicine. Currently, neonatal resuscitation program (NRP) training is not a required ACGME milestone. As neonatal cardiopulmonary compromise in the emergency department is rare, it is difficult for EM residents to learn and master the necessary skills to stabilize critically ill infants. Little is known about EM residents' knowledge and confidence in these skills. We conducted a survey of EM residents from a four-year academic residency program assessing their confidence in implementing NRP guidelines. We also tested their knowledge of conducting neonatal resuscitation with a quiz on NRP guidelines. A 5-point Likert scale was used on confidence questions. A total of 48 (65%) residents represented all postgraduate years participated (Figure 1). Perceived importance of NRP skills scored highly, with majority of participants expecting to resuscitate newborn infants in their future career (95.6%) and eager for structured training (97.9%) within their existing curriculum. Residents reported discomfort leading a neonatal resuscitation and were not confident in their knowledge of aspects of NRP such as targeted saturations, initiating positive pressure ventilation and intubation (Figure 2). The mean score on the quiz was 16 out of 29 (mean 55%, SD 4.4; range 0-89%). Figure 3 shows guiz guestions in which majority of residents were not able to identify the correct response (marked with asterisk). Although two thirds of residents reported prior NRP training, there was no difference in mean quiz scores among participants with prior training (p=0.19). Residents with prior training did have increased self-reported confidence in their knowledge of the indications for intubation (p=0.005), and chest compressions (p=0.005). Prior NRP training was associated with knowledge of the correct depth of chest compressions (p=0.03) but did not correlate with coordination of ventilation with chest compressions (p=0.52). EM residents desire structured training in neonatal resuscitation. They report discomfort in leading a resuscitation but moderate confidence with skills required to resuscitate a newborn; however, when tested on content they scored poorly. Prior training did help with building some confidence but did not improve the content knowledge. A structured simulation curriculum specifically geared towards EM residents to learn NRP skills needs to be implemented.

### Abstract # 17

Abstract Title: Factors Affecting Infants of Unexpected Deliveries Presenting to the Emergency Department

Name: Shannon Liu, MD

Neonatal Perinatal Medicine Fellow

**Co-Authors:** Shannon Liu, MD\*, Loren Yaeger, DO, Evan Sander, MD, Priya Shastry, DO, Nicole Flores-Fenlon, MD, Maria Martes Gomez, DO, Bret Nolan, MD, Rangasamy Ramanthan, MD, Fiona Wertheimer, DO, Manoj Biniwale, MD

Organization: LAC+USC Medical Center

Abstract Overview: Perinatal mortality is high in unexpected de-

liveries. The objective was to analyze unplanned out of hospital deliveries and threatened deliveries presenting to a single center Emergency Department (ED) and compare maternal and infant characteristics. This is a retrospective chart review of pregnant women who were admitted to the Labor and Delivery Unit from the ED between June 2015 and December 2019 at LAC+USC Medical Center. Electronic records of women who delivered infants or presented with threatened deliveries to the ED and went into labor within 24 hours of admission were included. Those with an intrauterine fetal demise were excluded. A total of 107 live births met inclusion criteria. The median maternal age was 28 years (IQR20-36 yrs), and median gravida 3 and parity 1. Infants born before hospital arrival comprised 45% of the population. Only 8% of women presented after trauma or motor vehicle accident, while the remaining were in labor. Illicit substance use was confirmed in 45% of mothers and 20% had a psychiatric diagnosis. Limited prenatal care was seen in 58% of women. None of these factors were statistically significant for delivery before ED arrival. Maternal drug use at any point during pregnancy was significantly higher in infants delivering before ED arrival (p=0.02). Substance use was noted to be higher in women receiving limited prenatal care (p=0.018). Median infant gestational age was 38 weeks (IQR 34-42wks) with mean birth weight of 2787g (SD 720g). Significantly more infants born before hospital arrival were classified as small for gestation age (p=0.04) and had first measured temperature less than 36.5 degrees Celsius (p=0.004). Advanced resuscitation, including positive pressure ventilation, intubation or chest compressions was required in 35% of infants and 44% required NICU admission. Infants of substance abusing mothers were more likely to require advanced resuscitation (p=0.008). Mortality rate for all neonates was 7.5%. Infants who died had a lower mean maternal age of 23 years (p=0.029) and lower mean gestation age of 31 weeks (p=0.046). Our results highlight the significant mortality associated with unexpected deliveries presenting to the ED with increased morbidities in the infants requiring resuscitation and higher NICU admission rates. Substance use and limited prenatal care appear to be significant factors to before hospital delivery. Special care should be given at maintaining temperature in infants born before hospital arrival.

### Abstract # 18

Abstract Title: Analysis of Non-Human Proteins/Peptides in Human Breast Milk by Mass Spectrometry

Name: Shiyu Bai-Tong, MD

Fellow

**Co-Authors:** Kathleen Luskin MD, Sandra Leibel MD, Majid Ghassemian PhD, Jessica Kitsen BS, Diba Motazavi BS, Kerri Bertrand MPH, Tina Chambers PhD, MPH, Sydney Leibel MD, MPH, Bob Geng MD

**Organization:** UCSD Medical Center and Rady Children's Hospital, Division of Neonatology

Abstract Overview: Background: Human breast milk is shown to decrease the risk of atopic diseases in full term babies. But its allergenic effects on preterm babies and the etiology of its protective effect have not been established. We aim to perform a broad analysis of non-human proteins and peptides in human breast milk using mass spectrometry. Methods: Four breast milk samples were obtained from Mommy's Milk, a human milk research biorepository in San Diego for mass spectrometry analysis. Two samples were from preterm infant's mothers and two were from term infants' mothers. Mothers filled out food and environmental exposure surveys when donating their breast milk. We utilized the University of Nebraska Allergen Protein Database and The Universal Protein Resource (UniProt) protein sequence database to identify a total of 2211 protein/peptide sequences. Results: Each sample had between 806 and 1007 proteins/peptides, with 37 to 44 non-human proteins/sample encompassing 26 plant and animal species. Bovine proteins/peptides were the most numerous; seven unique Bos taurus proteins/peptides were found in all samples. Cat, dog, mosquito, salmon, and crab were detected in all four samples. All maternal donors ingested fish, shellfish and tree nuts. Aeroallergen proteins/peptides, including dust mite and mold were identified in all samples. Two almond proteins were detected in three samples. Two samples contained latex and chicken. One sample contained several unique proteins/ peptides, including carrot, two molds (including Penicillium citrinum) and American house dust mite-like protein. Conclusions: These findings represent the first breast milk mass spectrometry analysis with identification of known allergenic proteins from food and the environment. The correlation between the exposure of allergenic protein in human milk and the development of atopic disease is unclear. This raises the question of whether breast milk can serve to induce sensitization or tolerance in infants. We are currently conducting a prospective study aiming to analyze allergenic peptides in preterm infants' milk feeding and their risk of atopic disease later on in life.

### Abstract # 19

Abstract Title: Delayed cord clamping for 2-3 minutes further reduces RBC transfusion in very preterm infants

Name: Priya Jegatheesan, MD NICU Director

**Co-Authors:** Dongli Song, MD, PhD, Priya Jegatheesan, MD, Angela Huang, RNC, SudhaRani Narasimhan, MD, Matthew Nudelman, MD, Claudia Flores, Sonya Misra, MD, Christina Anderson, MD, James Byrne, MD, Balaji Govindaswami, MBBS, MPH

Organization: Santa Clara Valley Medical Center



Abstract Overview: Background: Delayed cord clamping (DCC) increases blood transfusion from placenta to the newborn at birth. DCC >30-60 seconds reduces risk of transfusion, morbidity, and mortality in preterm infants. We increased the duration of DCC from 1 minute to 2 minutes in 2016 and 3 minutes in 2018 in order to further decrease the risk of red blood cell (RBC) transfusion. Objective: To evaluate the risk of RBC transfusion in preterm infants < 33 weeks of gestation after increasing the duration of DCC to at least 2-3 minutes. Methods: DCC for 30 seconds was included in the standardized delivery room management bundle for preterm infants in 2008. DCC duration was increased to 1 minute in March 2011, 2 minutes in July 2016 and 3 minutes in January 2018. Use of erythropoietin for prevention of anemia was standardized in 2016. Demographics, delivery room and neonatal interventions, early (<72 hours) transfusion and any transfusion during NICU stay were obtained from the prospectively maintained NICU database. Transfusion data were summarized as SPC control charts. Demographics and outcomes were compared between Infants who received at least 60 seconds: 1-minute DCC from January 2014-June 2016 and those who received at least 120 seconds: 2-3 minutes DCC from July 2016-December 2019. Results: During the study period, 192 preterm infants were born and 75% received the intended duration of DCC. The half-yearly control charts show the trend to lower rate of early and any RBC transfusion (Figure 1, 2). There was no difference in neonatal demographics between the DCC groups (Table1). There was an increase in use of erythropoietin in the 2-3minutes DCC group. There was a significant reduction in any RBC transfusion from 17% in 1-minute DCC group to 8% in 2-3minutes DCC group. This reduction remained significant even after adjusting for the increase in erythropoietin use. There was no difference in hematocrit values. There is no difference in death, but there is a significant increase survival without major morbidities from 77% to 88% in the 2-3minutes DCC group even after adjusting for GA. Conclusion: Extending the duration of DCC to 2-3 minutes further reduces RBC transfusion in very preterm infants and improves their survival without major morbidities.

### Abstract # 21 Abstract # 20 Abstract Title: Improving Postoperative Management Scores Abstract Title: Decreasing Length of Stay in Very Low Birth Weight (VLBW) Infants (POMS) Name: Irfan Ahmad, MD Name: Irfan Ahmad, MD **Professor of Clinical Pediatrics Professor of Clinical Pediatrics** Co-Authors: Melissa Powell MSN, CRNP, NNP-BC, Michel Co-Authors: Kristine Golder, Karen Mitchel, Diana Hurtado, Sar-Mikhael MD, Megan Norton RN, BSN, Joe Kim, MD and Mustafa ah Lauridson, Su Freck, Kushal Bhakta and Jack Sills Kabeer MD Organization: CHOC Children's Hospital and UCI Organization: CHOC Children's Hospital and UCI Abstract Overview: Background: Preterm infants born weighing

Abstract Overview: Background: Anesthesia and surgery place

significant stress on neonatal physiology. Lack of timely recognition and management may contribute to adverse outcomes. Aim: Increase the percentage of infants returning from operating room (OR) with all POMS within target range from baseline median of 33.3% to 85% by December 2018 and sustain this improvement for 12 months (December 2019). Interventions: We enrolled in CHNC STEPP IN Next STEPPs project in April 2017. Baseline data were collected from March to June 2017. Credit was given if all four measurements were within target range (temperature 36.1-38 C, pH 7.2-7.5, pCO2 31-75mm Hg, glucose 46-200mg/dl). Multi-disciplinary team and key driver diagram helped organize efforts and interventions were tested in multiple PDSA cycles beginning in July 2017. The first PDSA cycle (P1) focused on structured perioperative handoffs (POH). Intraoperative IV fluids guideline (IFG) was implemented in P2. Focus of P3 was real time POMS feedback to anesthesiologists. IFG was modified in P4 focus was to sustain gains in P5 and 6. Results: P1 interventions resulted in median shift to 57% with decreased post-op hypothermia and acidosis contributing to gains. This gain was sustained during P2 with decreased postop hyperglycemia. Median shifted to 77.8%, following P3 interventions. Gains were stabilized and sustained during P4-6. Lessons Learned: Addressing four physiologic variables simultaneously was challenging. Understanding the importance of postop stability was key in aligning multiple disciplines in NICU and OR. POH tool provided structured multidisciplinary communication. Multi-center collaboration on glucose management resulted in modified intraoperative IFG, leading to improved glucose control. Barriers to change included struggle with audit sheets completions and returns. Educating nurses, seeking help from unit secretary and process mapping led to improvement. While our median has not reached our goal of 85%, we have reached goal values in last 2 months. Next steps: Continue emphasizing importance of perioperative physiologic stability during PHO. Refine newly developed perioperative improvement bundle in a variety of surgical conditions in infants with different levels of maturity with appropriate guideline modifications. Our next focus will include optimizing postoperative pain control in infants.

less than 1500g have prolonged length of stay (LOS) in the NICU

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which places significant social and economic stress on families and healthcare system. Aim: Decrease mean LOS for inborn VLBW infants from postmenstrual age (PMA) of 40 to 37 weeks from July 2018 to June of 2019 and then sustain this till June Interventions: This project was part of Intermediate Im-2020. provement Science Series (I2S2) course (Cincinnati Children's Hospital). Multidisciplinary team addressed key drivers of change, which were tested in multiple incremental small change Plan-Do-Study-Act cycles (PDSA). New guidelines were developed for feeding advancement, nippling progression, management of apnea/bradycardia (A/B) and parent discharge education. Reminders were placed for timely completion of prescriptions and screening tests. Weekly multidisciplinary discharge rounds were initiated. Results: Baseline mean PMA at discharge (DC)was determined from previous 6 months. Cyclic implementation of improvement processes resulted in shift in DC PMA mean from 40 to 37.6 weeks and narrowing of control limits (decreased vari-Lessons Learned: Improvements in several processes ability). were achieved resulting in DC of VLBW infants at a lower PMA. Simultaneous work from three improvement teams (with focus on single drivers of change) improved efficiency but created difficulties with coordination of meeting times and some complaints of "QI fatigue" amongst staff. Participation of hospital chief operating officer in meetings helped maintain enthusiasm. Faster advancement in feeds led to decrease in time to full feeds without changing NEC incidence (balancing measure). Nippling advancement guideline decreased variability in practice and a A/B guideline led to improved charting and less DC delays. Parents were able to complete all DC teachings a day prior to discharge using the Parents DC education sheet. Parent representation was instrumental in providing key perspectives. Achieving full nipple feeds and getting off nasal cannula remain important barriers to early discharge. Next steps: Continue to refine nippling progression guideline and reach consensus when to discharge some infants on nasal cannula or partial gavage feeds.

### Abstract # 22

Abstract Title: Simulating Success through Multidisciplinary Team Training Exercises

Name: Irfan Ahmad, MD

**Professor of Clinical Pediatrics** 

**Co-Authors:** Nandini Arul MD, Christina Clay RN, Maria Thrasher RT, Justin Cain SS

Organization: CHOC Children's Hospital and UCI

**Abstract Overview:** Background: Simulation training has been shown to improve team performance. Latent safety threats (LST) are identified improvement goals that impact delivery of optimal care to the patient. Simulations help identify these LST and help

reinforce positive team behaviors. Aim: Simulation training has been shown to improve team performance. Latent safety threats (LST) are identified improvement goals that impact delivery of optimal care to the patient. Simulations help identify these LST and help reinforce positive team behaviors. Setting: Level IV NICU within a freestanding Children's hospital with Pediatric Residency and Neonatal Fellowship Programs. 104 Bed NICU with surgical NICU, Small Baby Unit, Neuro NICU and Cardiac NICU. Methods: We joined California Perinatal Quality Care Collaborative (CPQCC) Simulating Success quality improvement project in March of 2018. Team members received simulation instructor training at Center for Advanced Pediatric & Perinatal Education (CAPE). Video recorded simulations and debriefings were started in July 2018 with first 10 serving as baseline. An improvement bundle was implemented in January 2019 with modifications during multiple PDSA cycles. Results: A total of 22 simulation exercises were done InSitu in labor and delivery, NICU and in a simulation lab. After implementation of the change bundle, LSTs decreased and there was a shift in the median to 2 LST per simulation. On further categorizing the LST's we found 58.7% of them were technical and 36.2% were behavioral issues. We focused our learning objectives in improving those weaknesses during subsequent simulation exercises. We were able to find solutions for some of the system errors identified. Discussion: Through these exercises, all respiratory therapists, 46% of nurses and 73% of physicians attended ≥1 simulation session. Barriers included finding suitable storage space for equipment and time commitment from facilitators. These were in-situ simulations which are inherently challenging. These issues were discussed during team meetings with CPQCC faculty/other centers and solutions were implemented. The hospital was able to provide a simulation lab and a dedicated sim specialist which made subsequent simulations more efficient. Significant improvements have been made in team performance as evidenced by decline in median LSTs getting us closer to our goal of 1 LST per simulation. Next steps: Achieve all staff participation of  $\geq 1$  simulation per year. Enhance simulation training to include procedural skills like chest tube placements/paracentesis. Implement a solution based tracking of system errors identified.

### Abstract # 23

Abstract Title: Symptomatic Treatment Approach Versus Nonintervention for Patent Ductus Arteriosus in Very Low Birth Weight Infants

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#### Name: \* Ma Teresa Ambat, MD

Neonatologist

**Co-Authors:** Maria Fe Villosis MD, Karine Barseghyan MD, Kevin Rezaie MD (all are Neonatologists)

Organization: Kaiser Foundation Hospital - Panorama City

Abstract Overview: Background: Reports on clinical experience with less aggressive strategies for patent ductus arteriosus (PDA) management are continuing to emerge and suggest that a more permissive approach does not result in worse outcomes. Some studies have reported that nonintervention that allows spontaneous PDA closure did not increase the risk of mortality, bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC). A more recent publication also showed that it was not associated with increased risk of long-term neurodevelopmental impairment. Currently, wide variation in practice continues to exist and the effect of active treatment compared with nonintervention remains unclear. Objective: To evaluate and compare outcomes of two management approaches for PDA in very low birth weight infants (VLBWI) admitted to Kaiser Foundation Hospital-Panorama City (KFH-PC) NICU Design/Methods: This is a single-center, retrospective study of VLBWI admitted to KFH-PC NICU. Outcomes of symptomatic treatment used in period I (January 2010-June 2015) were compared with nonintervention or conservative treatment approach used in period II (July 2015-September 2018). Results: We retrospectively analyzed data from the medical charts in 315 VLBWI (184 in period I, 131 in period II). In period I, there were 77 VLBWI who had PDA of which 67 (87%) were treated with indomethacin, 2 (2.5%) had both indomethacin treatment and PDA ligation and 10 (13%) had spontaneous closure prior to discharge. In period II, there were 69 VLBWI who had PDA of which 3 (4.3%) were treated with indomethacin and 3 (4.3%) had PDA ligation without prior indomethacin treatment. Those who had PDA ligation in period II were transferred to another facility where they had PDA ligation following the facility's treatment protocol for PDA. In period II, spontaneous closure was observed prior to discharge in 51 (74%) and after discharge in 7 (10%) VLBWI. Late onset sepsis, IVH and death prior to hospital discharge did not differ significantly between the 2 time periods. In period II, BPD was significantly lower (p=.003) as well as the time to reach full feeds (p<.001). Trends for oxygen use at discharge, NEC and ROP were also lower in period II but not statistically significant. Conclusion(s): In this study, we found that conservative approach compared to symptomatic treatment resulted in high spontaneous closure of PDA without increasing the risks of death and major morbidities in VLBWI.

### Abstract # 25

Abstract Title: Impact of a Parent Video Viewing Program in the Neonatal Intensive Care Unit

#### Name: Jennifer Weber, MD

Neonatal-Perinatal Medicine Fellow

**Co-Authors:** Jennifer Weber, MD\* Hadley Sauers-Ford, MPH, CCRP Kristin Sohn, MD Ashley Hanhauser James Marcin, MD Daniel Tancredi, PhD Kristin Hoffman, MD

Organization: University of California, Davis

Abstract Overview: Introduction: The NICU is a unique healthcare setting, where given the complexities of caring for a critically ill baby, the parent population is at high risk for emotional distress and disrupted parental bonding. To address this, many NICUs have begun using bedside video cameras to facilitate virtual visits by parents and other family members. We examined parents' selfreported perceptions regarding the NICU experience in relation to these video visits. Responses from families that voluntarily utilized the video cameras for virtual visits were compared to those from families that did not use the cameras. Methods: Using a prospective study design, families were enrolled following informed consent and were asked to complete a series of two surveys, one at time of enrollment and the second at time of discharge from the NICU. Responses from families that voluntarily utilized the video cameras for virtual visits were compared to those from families that did not use the cameras. In addition to parent surveys, additional data were collected on each subject, including demographics, breastmilk feedings at discharge, and use of video visits. One hundred respondents who completed both surveys were included for analysis. Student's T-test was used to compare subjects using the video cameras to those who did not use video visits for each survey response variable. Results: 30% of parents (N = 30) utilized video visits. Characteristics such as gestational age (GA) and breastmilk feedings at enrollment were similar between groups. Length of stay was significantly extended in the video visits group (Table 1). Families who used video visits experienced a more sustained intention to breastfeed or pump breastmilk compared to nonusers with a mean over time difference between groups of -0.95 points (95% CI: -1.76, -0.14). The percentage of babies receiving breastmilk at discharge was likewise higher in the video visits group (83% vs. 66%, p = 0.03). Additionally, there was a trend toward improved parental involvement in the babies' care in the video visit group (Tables 2-3). Conclusion: The extension of technology to allow parents to view their babies remotely may be one way of mitigating some of the stressors related to NICU hospitalization. Participation by parents in video viewing of their infant in the NICU was associated with sustained intention to breastfeed over the duration of the NICU stay and a trend toward improved self-perception of involvement in care. These findings justify further study of video viewing in this high-risk population.

### Abstract # 26

Abstract Title: Implementation of Eat, Sleep, Console as Pri-

Name: Charles Egesdal, MD

Resident (PGY-3)

**Co-Authors:** Charles Egesdal\*, MD Priscilla Joe, MD Joanne Kuller, RN, CNS Bette Flushman, MA Kathryn Ponder, MD

Organization: UCSF Benioff Children's Hospital Oakland

Abstract Overview: Title: Implementation of Eat, Sleep, Console as primary treatment for Neonatal Abstrinence Syndrome in a level IV NICU Authors: Charles Egesdal\*, MD, Priscilla Joe, MD, Joanne Kuller RN, CNS, Bette Flushman MA, Kathryn Pon-Background: The incidence of NAS has increased nader MD tionwide with the opioid epidemic across our country. Traditionally, treatment has focused on the use of pharmacologic opiate agents which are associated with long hospital stays and prolonged drug exposures. The ESC model has shown that interventions focused on non-pharmacologic therapies for infants with NAS can dramatically reduce hospital length of stay (LOS), morphine exposure, and costs. The approach focuses on the use of physiologic determinants to dictate the need for interventions as opposed to symptoms of withdrawal. This approach is not regularly implemented in neonatal ICUs. Objective: The aim of our project was to implement the ESC approach for infants admitted with NAS to our level IV NICU, and improve outcomes defined as a reduction of average LOS by at least 50% and a reduction in morphine exposure by 50%. Design/Methods: ESC nursing training was provided. NAS babies were assessed for their ability to feed, sleep for > than 1 hour, and be consoled within 10 minutes. Infants abilities to accomplish these physiologic outcomes guided pharmacologic and non-pharmacologic interventions with non-pharmacologic interventions being prioritized. Medical records for NAS babies admitted to our NICU in 2019 were reviewed and compared to our NICU baseline retrospective data from 2015-2018. Infants who were premature (<33w GA), on iNO, or on HFOV were excluded. Results: A total of 12 infants were enrolled in our study from January to August of 2019. A total of 29 infants were used for comparison using our retrospective data. The mean length of stay at our institution for babies admitted with a primary diagnosis of NAS decreased from 29.8 days to 10.3 days, a reduction of 65%, with a p value of 0.002. Our mean morphine exposure days, defined as a 24 hour period during which an infant received morphine, decreased from a mean of 24.2 days to 0.42 days, a reduction of 98%. Volunteer hours were recorded with an average of 27.7 hours per infant of volunteer cuddling. 91.67% (11/12) of our infants were placed in foster care following discharge. Conclusion(s): Our project displays that the ESC approach is an effective option even for patients admitted to a high acuity level IV NICU without a mother present to provide care. With the use of ESC in addition to adjunctive approaches such as volunteer cuddlers, we were able to significantly decrease the length of stay and morphine exposure of patients in our unit admitted with NAS. Abstract # 27

# Abstract Title: Direct Umbilical Vein Injection of Epinephrine with Cut Umbilical Cord Milking

Name: Peggy Chen, MD

Clinical Fellow

**Co-Authors:** Peggy Chen, MD\*; Payam Vali, MD; Amy Lesneski, BS; Morgan Hardie, BS; Ziad Alhassen, MD; Houssam Joudi; Deepika Sankaran, MD; Satyan Lakshminrusimha, MD

Organization: University of California, Davis

Abstract Overview: Background: Acute perinatal asphyxia remains a significant cause of morbidity and mortality. Early return of spontaneous circulation (ROSC) in asphyxial arrest is associated with better outcomes. In severe bradycardia/asystole, NRP recommends administering epinephrine (EPI) by a low umbilical venous catheter (UVC). Umbilical access with a low UVC is timeconsuming and requires advanced skills and specialized equipment. Direct umbilical vein (UV) injection offers the potential for quick administration of IV EPI with milking of the cut umbilical cord to flush EPI into the circulation (Figure 1). Objective: To show feasibility and effectiveness of direct injection of EPI into the UV followed by cord milking as a guick method of IV EPI adminis-Methods: Ten near-term fetal lambs were exteriorized. tration. intubated, and instrumented. The umbilical cord was occluded to induce asphyxia, then tied and cut at the placental end to leave a long 15-20 cm segment. After 5 minutes (min) of asystole, resuscitation following current NRP guidelines was initiated. Upon initiation of chest compressions, preparation to administer EPI began. IV EPI of 0.03 mg/kg/dose was administered into the UV at the base of the umbilicus with a syringe attached to a 23G needle, followed by 3 quick successive cord milkings to flush EPI. If ROSC was not achieved, a UVC was placed and UVC EPI was given and repeated every 3 min until ROSC with a max of 4 doses or 15 min of CPR. Plasma samples were collected to analyze pharmacokinetics. Results: The average weight of the lambs was 3.65



± 0.71 kg. The male:female ratio was 6:4. 90% of lambs achieved ROSC; 70% following direct UV EPI injection alone. Average time of UV EPI administration was 2.28 ± 2.13 min and average time to ROSC was 5.82 ± 2.81 min. Plasma EPI assay concentration for two lambs showed an average concentration of 562 ± 471 ng/ mL, similar to historical values following UVC injection of 0.03 mg/ kg EPI (450 ± 190 ng/ml, Vali et al. JAHA 2017). Conclusion: In an asphyxia cardiac arrest lamb model, direct UV EPI administration followed by cord milking is quick and efficacious with a good success rate of ROSC. Preliminary data suggest adequate epinephrine plasma concentration following direct UV EPI administration. Experiments are underway to compare success and time to ROSC between direct UV and UVC EPI administration. Further evaluation of direct UV EPI followed by cord milking may have high relevance in resource-limited settings.

### Abstract # 28

# Abstract Title: Piezo1 in the Biomechanical Stretch of the Small Bowel Muscularis

Name: Geoanna Bautista, MD

Fellow

**Co-Authors:** Yingjie Du BS, Nicolle Martin, Nam Phuong Nguyen, Mutian Hua BS, Elmira Tokhtaeva PhD, RS Solorzano-Vargas, Michael S. Lewis MD, Ximin He PhD, Matthias Stelzner MD, James Dunn MD, PhD, Martin G. Martin MD

Organization: University of California, Los Angeles

Abstract Overview: Introduction: Biomechanical stretching of the small bowel has clinical and therapeutic implications for pediatric and neonatal patients with small bowel obstruction (SBO) and intestinal failure. Little is understood of the mechanism by which biomechanical stretching results in the thickening of the muscularis and expansion of crypts and intestinal stem cells (ISC) of the epithelium. Piezo1 is a stretch-induced ion channel involved in the modulation of trophic effects in mechanosensitive tissues and is expressed in the gut. Methods: In vivo and in vitro methods were used to determine whether Piezo1 in smooth muscle cells (SMC) is necessary in mediating stretch-induced intestinal growth. Using the Piezo1/Myh11-ERT2/Cre-LoxP system, we generated a mouse model with a tamoxifen (Tam) inducible-Piezo1 knockout (Piezo1 $\Delta$ SMC) in the SMC of small bowel muscularis (SBM). In vivo, mice received Tam and had distal SBO surgery to induce biaxial stretch. In vitro, SBM was isolated from mouse pups and plated on 2D monolayers on a soft tissue scaffold composed of a thermo-responsive hydrogel to induce ~50% stretch by cooling from 37°C to 33°C. Confocal microscopy was used to record SBM contraction/Ca2+flux using a GCaMP indicator. The rhythmicity, frequency and magnitude were quantified with MATLAB. Results: In vivo: Mortality rates were similar between control (Piezo1WT) and Piezo1ASMC. Obstructed Piezo1WT and Piezo1ASMC mice had a significant increase in crypt size and SBM compared to non-obstructed mice. Although, there was significant attenuation in crypt elongation in Piezo1 $\Delta$ SMC mice compared to Piezo1WT. There were no statistical differences between both groups in obstructed SBM width. In vitro: At 37°C, Piezo1WT SBM cells have spontaneous and rhythmic contractions associated with Ca2+flux. At 33°C, Piezo1WT cells seeded on hydrogels doubled in frequency of contractility/Ca2+flux, compared to Piezo1WT cells seeded on plastic, which had decreased contractility/Ca2+flux. When Yoda1, a Piezo1 agonist was added to Piezo1WT cells on plastic at 33°C, contractility/Ca2+flux resumed. In contrast, Piezo1∆SMC cells displayed decreased frequency and disorganized pattern of contractions/Ca2+flux, which diminished further on stretching at 33°C. When treated with Piezo1 shRNA, Piezo1WT cells had decreased contractions/Ca2+influx. Conclusion: Our data suggests that Piezo1 in the SMC of the SBM partly mediates crypt expansion associated with SBO, and is required for the maintenance of regular, rhythmic SBM contractions/Ca2+flux with and without biomechanical stretch.

### Abstract # 29

### Abstract Title: Implementation of a Bedside Point-of-Care Ultrasound Program in a Large Academic Neonatal Intensive Care Unit

Name: Caroline Noh, MD

Fellow

**Co-Authors:** Pai VV\*, Dasani R, Noh CY, Vallandingham S, Manipon C, Houghteling PD, Balasundaram M, Davis AS, and Bhombal S.

Organization: Stanford University

Abstract Overview: TITLE Implementation of a Bedside Pointof-Care Ultrasound Program in a Large Academic Neonatal Intensive Care Unit BACKGROUND In the adult and pediatric critical care population, bedside clinician performed ultrasound has been shown to provide rapid diagnostic capability, affect patient management and improve procedural accuracy. For neonatal providers, training in ultrasound and the use of ultrasound for diagnosis and management is increasing, but overall the use of ultrasound in the Neonatal Intensive Care Unit (NICU) is still uncommon compared to other critical care fields. OBJECTIVE To describe the process of implementing a Point-of-Care Ultrasound (POCUS) program in a large academic NICU and evaluate the role of ultrasound in neonatal care during early adaption of this program. DESIGN/METHODS Two faculty, 1 fellow and 2 neonatal nurse practitioners (NNP) attended a regional 2-day immersive course in POCUS in November 2018 and subsequently began performing regular scans in their NICU. For all fellows, attendings and

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nurse practitioners in the NICU, a 2-day POCUS course was organized by the core team in June 2019 to expand the number of NICU providers with knowledge of ultrasound basics and skills in POCUS. Team meetings occurred monthly and included internal quality assurance review. Additional multidisciplinary QI sessions were held with radiology. Joint conferences, teaching, and bedside scanning sessions were held monthly in conjunction with pediatric critical care faculty and fellows. The NICU POCUS team established guidelines for performing POCUS in the NICU, created an image bank and procedure log, with the goal of eventually achieving individual credentialing. **RESULTS** In addition to the core team of 5 providers initially trained in POCUS, an additional 22 providers attended a local 2-day POCUS course in June 2019. A total of 233 POCUS scans were performed on 123 patients from 12/2018 to 12/2019 by 7 fellows, 4 attendings, and 5 NNPs or neonatal hospitalists in 6 diagnostic and procedural applications: central line (PICC/UVC), bladder, lung, cardiac assessment, lumbar puncture/spinal fluid assessment and vascular access (Table 1). Utilization of bedside clinician performed ultrasound resulted in 20.2% (47/233) cases of diagnostic or error prevention (Table 2). CONCLUSION Implementation of a bedside POCUS program is labor intensive and benefits from a team approach in a large academic NICU. Bedside clinician performed ultrasound findings can provide valuable information in the NICU and impact clinical management.

### Abstract # 30

# Abstract Title: Fetal Central Nervous System Anomalies- How to Prognosticate

Name: Monika Bawa, M.S, M.Ch

Additional Professor

**Co-Authors:** Nilesh tank- Senior Resident Ravi P Kanojia- Professor Ram Samujh- Professor

**Organization:** Postgraduate Institute of Medical Education and Research

**Abstract Overview:** Aim: To assess the prevalence and outcome of antenatally diagnosed central nervous system malformations (CNS). Method: Prospective study conducted on antenatal mothers who were diagnosed with fetal central nervous system anomalies (brain and spine) on ultrasound over a period of two years. Detailed data was recorded in terms of gestational age at diagnosis, comorbidity, TORCH infection, triple screening, ultrasound, associated anomalies.Outcome was analyzed as need for MTP, fetal and neonatal demise, need of surgery and overall outcome. Results: Out of 521 antenatally detected congenital malformations, 163 patients (31.28%) had CNS malformation with isolated choroid plexus cyst (CPC) being the commonest (39.26%). Average size of CPC was 7.8mm (3-15mm) and it disappeared in all. Isolated corpus callosum agenesis (CCA) was seen in 6.74%, prominent cisterna magna (PCM) in 7.36 %, CPC with ventriculomegaly in 4.9%. Isolated ventriculomegaly was found in 44 patients (26.99%), while 11 patients had ventriculomegaly with associated malformations. 16 patients with >15mm ventricular size had a poor outcome postnatally. 12.88% had isolated NTD. MTP was advised in 9.81% and 3.06% died after birth. 11% patients underwent surgery. Conclusion: Isolated CPC, isolated ventriculomegaly of < 15 mm, isolated CCA, isolated PCM carry a good prognosis hence the parents should be counselled positively.

### Abstract # 32

# Abstract Title: Neonatal Normothermia in the Golden Hour, Kaiser Southern California Region

Name: Sandra Short-Bartlett, MD

Partner Neonatologist, Kaiser Orange County

**Co-Authors:** Mandhir Gupta, MD (NICU Director, Kaiser Downey), David Braun, MD (Regional Neonatology Quality Initiatives, Past Regional Physician in Charge for Neonatology, (1999-2019), Marielle Nguyen, MD (NICU Director, Kaiser Orange County, Regional Physician in Charge for Neonatology 2019-), Dilip Bhatt, MD (Partner Emeritus, Past NICU Director, Kaiser Fontana), Nirupa Beckham, MD (Partner Neonatologist Kaiser Fontana/Ontario) and the Kaiser Southern California Regional Neonatal Normothermia Practice Improvement Committee

Organization: SCPMG

Abstract Overview: Introduction: Numerous studies have demonstrated that neonatal outcomes are improved if normothermia is maintained. In 2016 VON's Roger Soll clarified the care gap: "Despite decreases, nearly 4 in 10 babies are cold..." At Kaiser Southern California, we had improved our <32 weeks or <=1500g NICU admission temperatures from 72% normothermic in 2012-14 to just 77% in 2016. While we overall had better results than the VON VLBW average, our Fontana facility regularly attained over a 90% normothermia rate. In 2017 we established perfor-

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mance goals, and we undertook an even more ambitious Quality Improvement project to achieve the Fontana benchmark throughout our Region. Methods: Each center formed a multidisciplinary Normothermia team lead by OB/NICU Physician, Nursing and Respiratory Therapy champions. Local teams worked on their own quarterly PDSA cycles - utilizing checklists, audit tools, EHR/ CPQCC data, and provider/staff feedback. We conducted periodic Regional teleconferences and posted regularly on a Microsoft teams site - a format for ongoing discussion, emphasizing our AIM Statement, Key Driver Diagram, literature/education, successful and unsuccessful strategies, buy in, team roles, optimization of new and existing equipment, documentation, results, and plans for future improvement. We focused on several Key Drivers: keeping patients warm in the delivery room with a bundle of techniques, careful temperature monitoring, and maintaining a stable temperature during transport to the NICU. Results: Neonatal Normothermia improved from 77% to 92% over the two year study period. 93% of our centers were at or above our 90% Normothermia goal for 2nd Quarter 2019. Only 0.3% of the babies were admitted in the moderate hypothermia range. 5.3% of babies were hyperthermic early in the project, but this dropped to 3.6% which was below our baseline 2016 rate of 3.8%, but above our goal of <3%. Conclusions: We observed drastic improvement in our small baby NICU admission temperatures over the duration of the project. We had challenges with hyperthermia, which improved over time. Our future goals will be to sustain or surpass our success, to improve uniformity of data collection, documentation, and checklists, and to determine which interventions are most important and cost effective.

## Abstract # 33

Abstract Title: Impact of a Small Baby Program on Infants of Periviable Births



Name: Ting-Yi Lin, MD

Neonatologist

**Co-Authors:** Ching Ching Tay, MS, CNS, RNC-NIC; James Fritzell, MD; Antoine Soliman, MD.

**Organization:** MemorialCare Miller Children's & Women's Hospital

Abstract Overview: Background Survival of extremely low birth weight (ELBW) infants has improved significantly in the last decade. Clinical programs instituted in many neonatal intensive care units (NICU) targeted at the ELBW population have demonstrated their value by improving outcomes and survival without major morbidities. Yet, little is known if such clinical programs, usually implemented through a quality improvement approach, have any impact on the outcomes of extremely low gestational age neonates (ELGAN) between 22 to 24 completed weeks. Method The aim of our project is to improve survival and reduce major morbidities of ELGAN between 22 and 24 completed gestational weeks. In the first phase of our project, we sought to understand the current outcomes for ELGAN after 1 year of implementing a small baby program in our level III NICU. The Small Baby Program at Miller Children's & Women's Hospital Long Beach began in late 2016. The program brought a significant culture change in our approach to care of very preterm infants using age-specific guidelines and checklists. Development and adherence to established guidelines and checklists are overseen by a multidisciplinary leadership team, who is also responsible for monitoring process and outcome measures. Some of the key practices introduced focused on care during the golden hour such as delayed cord clamping, thermoregulation, early parenteral nutrition, and timely surfactant administration. Results All infants delivered between 22 and 24 gestational weeks at our facility were included in the data analysis. Infants delivered at outside centers or with known congenital anomalies were excluded. Between 2018 and 2019, there was a total of 27 inborn periviable infants; 22 weeks (n=1), 23 weeks (n=8) and 24 weeks (n=18). Overall survival rate was 78%; 100% at 22 weeks, 75% at 23 weeks, and 78% at 24 weeks. Of the infants who were discharged home, 13% had no major morbidity, 17% had 1 major morbidity, 25% had 2 major morbidities, and 17% had 3 or more major morbidities. Conclusion This preliminary assessment suggests that survival rate of periviable infants at our institution is comparable to recently published multi-national data. More encouragingly, a third of survived infants were discharged home with only one or no major morbidity. Consequently, we have determined that our Small Baby Program has the potential to further increase survival of these periviable infants with excellent outcomes. The program steering team will focus next on tailoring care to this specific population through additional guidelines and checklists.

#### Abstract # 34

Name: Katherine Chung, MD

Neonatologist

**Co-Authors:** Katherine Chung MD\*, Lori Brown MD, Barbara Donnelly MD, Theresa Lueck MD, Adrienne Macdonald MD, and Jeanne (Jing) Li MA.

Organization: Cottage Santa Barbara Hospital

Abstract Overview: BACKGROUND: Existing protocol at our institution was to automatically initiate antibiotics for babies born to mothers with maternal chorioamnionitis, resulting in NICU admissions and antibiotic usage for asymptomatic infants. Furthermore, CBCs and CRP levels were frequently drawn in the newborn nursery, despite having questionable utility in predicting early onset sepsis (EOS). We sought to improve our neonatal sepsis screening practice by aiming for a 20% reduction in unnecessary NICU admissions, lab draws, and antibiotic use, without missing a case of EOS. METHODS: The Plan Do Study Act method of quality improvement was used for this project. Pre-intervention baseline data was collected for the 6 month time period February-July 2018. Post-intervention data was collected for the time period February-July 2019. The following measures were analyzed: antibiotic usage out of total live births, antibiotic usage out of inborn NICU admissions (greater than or equal to 35 weeks), asymptomatic NICU admissions, nursery patients with CBC or blood culture drawn, positive blood cultures, and readmissions for EOS. IN-TERVENTIONS: We instituted universal EOS screening on all newborns >= 35 weeks gestational age using the Kaiser Sepsis Calculator. We worked to build the sepsis calculator into the hospital's electronic medical record system and provided education to the nursing staff and physicians. We updated hospital policies to reflect sepsis calculator implementation, and developed an algorithm for nursing workflow. **RESULTS** Since implementation of the EOS calculator, antibiotic usage out of total live births dropped from 3.31% (32/967) to 2.41% (24/997) over the course of 6 months, a 27% drop from baseline (p=0.29). During the same time period, antibiotic usage for infants >=35wks gestation in the NICU dropped from 42.67% (32/75) to 26.97% (24/89), representing a drop of 37% (p=0.052). There was a significant drop in laboratory draws from 15.22% (142/933) to 8.35% (81/970), a percentage decrease of 45% (p<0.001). There were 7 asymptomatic NICU admissions for antibiotic administration due to maternal risk factors during the baseline period; this number dropped to 0 after calculator implementation and was sustained over the six month period. There were 0 positive blood cultures in both the baseline year and after calculator implementation, and there were 0 re-admissions for missed early onset sepsis. CONCLUSIONS Implementation of a sepsis risk calculator has produced a reduction in antibiotic usage, asymptomatic NICU admissions, and laboratory draws. Long term data must be analyzed to demonstrate sustained improvement and statistical significance.

Abstract # 35

Abstract Title: Impact of probiotic Bifidobacterium longum subsp. infantis EVC001 on patient outcomes in neonatal intensive care units

Name: Marielle Nguyen, MD

Regional Physician in Charge, Neonatology

**Co-Authors:** M Nguyen, MD; Heaven Holdbrooks, RN; Prasanthi K Mishra, MD; Maria A Abrantes, MD; Carrie McGuckin, RN; Cindi Hein, RD; Steven A Frese, PhD

**Organization:** Kaiser Permanente Southern California-Orange County

Abstract Overview: Introduction: Dysbiosis in the gut microbiome affects the health of preterm neonates and increases the risk for diminished growth and infection. Probiotics have been considered to correct this in preterm infants, but there are a variety of organism, strain combinations, and differing levels of quality which complicate interpretation of meta-analyses. The objective of this pilot study was to evaluate the use of a single strain probiotic containing activated Bifidobacterium longum subsp. infantis EVC001 (EVC001) in medium chain triglyceride oil, compared to the previous protocol using L. reuteri DSM17938, in neonatal intensive care units. We hypothesized that the known ability of EVC001 to utilize human milk oligosaccharides, colonize the infant gut, and resolve dysbiosis would be associated with improved clinical Methods: Deidentified medical health records were outcomes. collected from patients born in NICUs within a single health care system in California. Two time periods were examined; the period where L. reuteri DSM17938 was used and patient data from the first year of EVC001 use. Total nutrition (TPN hours), length of stay, antibiotic use, and infection (incidences of late onset sepsis, NEC, intestinal perforation, and urinary tract infections) were compared. Data were analyzed by Wilcoxon rank sum test with continuity correction. Results: Data from 141 individuals was collected in this pilot study. Only 90 infants remained in these hospitals for the duration of their NICU stay. In this population, infants fed EVC001 had a shorter duration of stay (by 5 days, 95%) CI: 61-84 days vs. 64-90 days) and fewer hours on total parenteral nutrition (by 105 hours, 95% CI: 218-299 hours vs. 292-435 hours), in an otherwise similar population in terms of gestational age (95% CI: 27-29 weeks). Other monitored outcomes were not significantly different between the groups given the small sample size, but directional trends to lower rates of NEC and infections were observed as well. Conclusion: This pilot analysis of patient outcomes shows promising trends toward a medically relevant decrease in the duration of stay and TPN usage in a preterm population fed EVC001 (an estimated savings of \$23,800 per patient, relative to DSM17938). Future analysis using additional hospitals matched for feeding protocols, with a larger sample set, as well

as prior to any probiotic use will provide additional insight into the impact EVC001 has on preterm infants.

### Abstract # 36

Abstract Title: Elimination of hypothermia (<36.5C) in Extremely Low Birth Weight (ELBW) Infants for Last Six Years (2014-2019). Best in all California NICUs. Experience of Single Level III NICU

Name: Dilip Bhatt, MD

Neonatologist

**Co-Authors:** Nirupa Reddy, MD, NICU Hospitalist Reinaldo Ruiz, MD, Obstetrician Darla Bustos, RN, NICU Toria Peacock, RN, OB Roman-Angelo Dizon RCP Sunjeeve Weerasinghe, NNP Rangasamy Ramanathan, MD

Organization: Kaiser Hospital, Fontana

**Abstract Overview:** Background: Perinatal care practices, including initial stabilization and resuscitation of newborn infants have improved dramatically over the past 5 decades. Yet thermal management around the time of birth continues to be a major problem with many newborns admitted with hypothermia. Objective: Our Hospital Perinatal Quality Improvement Committee developed a quality improvement bundle to decrease hypothermia in all preterm babies. Staff education including nurses of L&D and NICU, Obstetricians, Neonatologists, NNP, and Respiratory Care



Practitioners is critical. Stabalize the temperature in normothermia range (36.5-37.5C) in DR/OR prior to transport to NICU. Take axillary temperature in DR/OR q5 minutes. No umbilical vessel catheterization in DR/OR except for resuscitation. No surfactant administration in the DR/OR. Axillary temperature of infant was taken within minutes of NICU admission. This is a prospective study from 2014-December 31, 2019. Results: We studied 200 consecutive cases. Nine out of 200 were <500 grams, 25/200 were <24 weeks gestational age, 5/200 (2.5%) among ELBW infants had hypothermia. Hyperthermia (>37.5C) was 6.5% 13/200. Overall normothermia (36.5C-37.5C) rate for this 200 ELBW was 90% (18/200). Overall mortality in ELBW was 14.5% (29/200). We tried to keep the OR and DR temperature 74F. Conclusion: Our NICU has eliminated hypothermia (<36.5C) for last six consecutive years in more than 90% of ELBW. There was not a single case of moderate hypothermia (32-36C) in last six years. Our NICU has the best result in all NICUs of California to eliminate hypothermia in ELBW infants.

#### Abstract # 37

# Abstract Title: Zooming Into the Future of Neonatal Transport with Telemedicine and TeamSTEPPS

Name: Casandra Boylan, BSN, RN, RNC-NIC

**Clinical Nurse** 

**Co-Authors:** Casandra Boylan, BSN, RN, RNC-NIC\*; Albert O. Antonio, DO

**Organization:** Miller Children's and Women's Hospital Long Beach

Abstract Overview: Background: Telemedicine is becoming an important component of the modern health care system as a multipurpose intervention. As a consultation tool, telemedicine provides timely access to subspecialty care that result from provider shortages. As high reliability organizations, regional and tertiary hospitals who extend their neonatal services to birthing centers and level I/II nurseries rely on patient-centered, outcome-optimizing high fidelity communication systems. TeamSTEPPS is an evidencebased teamwork system developed to improve patient safety and reduce medical error, built upon a framework to enhance team performance centered on 4 principles: Communication, Leading Teams, Situation Monitoring, and Mutual Support. Methods: This is quality improvement project collaboration between the NICU and Neonatal transport team. Our aim in this initial phase since implementing telemedicine is to understand outcomes of patients consulted through this technology. The neonatal/pediatric critical care transport team transports +190 neonatal patients per year with 35 patients referred by telemedicine. Mechanisms include TeamSTEPPS concepts consisting of: SBAR, Closed-loop communication, Mutual support, Handoff, Brief, Debrief, and Utilization of checklists. In-house staff, outside facility feedback along with transport case reviews reflecting a need for enhancing team performance and communication during telemedicine consults were the main drivers of change. Results: A six month chart review revealed that not all telemedicine consults resulted in NICU admission, reducing maternal-infant separation. Change in Transport Risk Index of Physiologic Stability (TRIPS) score favored improved patient outcomes. Time to dispatch after telemedicine consults was reduced compared to transports without telemedicine. Discussion: Currently there are no TeamSTEPPS applications in practice during neonatal telemedicine consultation to ensure that our service performs as a high reliability organization. Ongoing review of feedback from the referring facility and accuracy in TRIPS score documentation would be helpful to ameliorate inter and intra-facility practice variance through several PDSA cycles. This understanding would help drive high fidelity simulation and didactic sessions to target interventions and improve patient outcomes.

#### Abstract # 38

Abstract Title: Functional differences among B. infantis strains in infant probiotic products

Name: Rebbeca Duar, PhD

Sr. Microbiology Scientist

**Co-Authors:** Giorgio Casaburi, PhD, Sr. Bioinformatics Scientist; Lindsey N.C Scofield, Research Assistant; Ryan D. Mitchell Sr. Research Associate; Camila Ortega, PhD, Scientist, Analytical Chemistry; Steven A. Frese, PhD, Director Microbiology and Bioinformatics.

Organization: Evolve Biosystems, Inc,

Abstract Overview: Background: Human milk oligosaccharides (HMO) in breastmilk influence the composition of the intestinal microbiome by serving as growth substrates to select strains of bifidobacteria. Over 200 individual HMO structures have been identified. However, lacto-N-tetraose (LNT), lacto-N-neotetraose (LNnT), and 2'-Fucosyllactose (2'FL) in FUT2+ mothers, are disproportionally abundant. The biological role for their abundance in the context of colonization of Bifidobacterium longum infantis in the infant gut has not been determined Objective: B. infantis EVC001 durably and stably colonizes the gut when fed to breastfed infants. In this study, we use a trait-matching approach to determine if the ability of B. infantis EVC001 to utilize these highly abundant HMO plays a role in the colonization success of this strain. Further, we explore the ecological consequences of the inability to ability to access these HMO. Methods: The genomes of EVC001, and 11 other strains of B. infantis isolated from infant probiotics were sequenced and compared to the type strain ATCCC 15697. Genomes were examined for the presence HMO-

utilization genes and the ability to grow on LNT, LNnT, 2'FL and free HMO from breast milk. Colonization dynamics of B. infantis EVC001 and a strain exhibiting an impaired HMO-utilization profile were determined by quantitative PCR using bacterial DNA extracted from stools samples of a breastfed infants supplemented with equivalent amounts of each strain. Results: Strains fell into two distinct groups. B. infantis EVC001 and strains in group I conserved all HMO-utilization genes. Whereas strains in group II lacked three genes located in the H5 cluster and involved in the active transport of HMO. Growth data and glycoprofiling after HMO fermentation revealed that the absence of these genes impairs the ability to utilize LNT and LNnT as well as pooled HMO, but not 2'FL. Further, competition experiments between EVC001 and a strain in group II revealed that EVC001 reaches higher numbers, demonstrating that to access these HMO has an associated fitness advantage when it comes to colonization of the breastfed infant gut. Conclusions: This work provides evidence of the genetic and functional adaptation of B. infantis to the breastfed infant gut, supporting the notion that human milk and B. infantis have a co-evolutionary relationship. Results also show that genotype and HMO-utilization profiles are highly predictive of colonization success and should be considered when selecting strains for use in probiotic applications for infants.

#### Abstract # 39

Abstract Title: Artificial intelligence reveals key biomarkers of necrotizing enterocolitis in the preterm infant gut microbiome

Name: Giorgio Casaburi, PhD

Sr. Bioinformatics Scientist

**Co-Authors:** G. Casaburi, PhD, S. Kazi BS, R. Duar, PhD, B. Ling, PhD, S. Frese, PhD, K. Sylvester, MD

**Organization:** Evolve BioSystems

Abstract Overview: Artificial intelligence reveals key biomarkers of necrotizing enterocolitis in the preterm infant gut microbiome. G. Casaburi\*, PhD1, S. Kazi BS1, R. Duar, PhD1, B. Ling, PhD2, S. Frese, PhD1,2, K. Sylvester, MD3, 1. Evolve Biosystems, Inc, Davis, CA, United States. 2. Department of Surgery, Stanford University, Stanford, California, United States of America 3. Department of Food Science and Technology, University of Nebraska, Lincoln, NE, United States. Introduction: Necrotizing enterocolitis (NEC) is an intestinal disease that primarily affects premature infants, causing an inflammatory process that can lead to intestinal tissue damage and death. NEC is a leading cause of overall infant mortality in the United States, affecting 0.1% of newborns per year in North America while reaching treatment costs of up to \$200,000 per patient. Although outcomes related to prematurity illness have remarkably improved, the mortality rate for NEC has remained constant at up to 50% or more depending on severity. Objective: The major limitation in NEC prevention dwells in the inability to predict which subset of premature infants is at risk for developing NEC. Recently, gut dysbiosis has emerged as a major trigger in NEC, particularly supported by the fact that NEC cannot be produced in germ-free animals. Here, we present a new, non-invasive approach that combines functional and taxonomical data from infant gut microbiomes to develop an algorithm capable to predict metagenomics biomarkers of NEC among a preterm infant population. Methods: A total of 1,712 raw publicly available shotgun metagenomic datasets were collected, (NEC=253; and healthy preterms=1,459). Taxonomic and functional analyses were carried out and dataset was divided based on corrected gestational age (cGA). Several machine learning models were tested to identify functional core biomarkers able to distinguish NEC from healthy preterm microbiomes. Results: The 29-32 weeks cGA population reported a significant level of prediction accuracy among models (up to 99.8%). Intersection of models led to the identification of top proteins and super pathways, which were then coupled with taxonomic classification to establish a collection of biomarkers able to discriminate NEC from healthy preterms. The most discriminatory bacterial species was Enterobacter cloacae. In vitro assay confirmed biomarkers role potentially responsible for NEC onset. Conclusions: This is the first computer model capable to identify causative NEC biomarkers from microbial signatures. Future efforts to minimize the frequency and severity of NEC should focus on reducing exposure to risk factors, including bacterial biomarkers by using safe and stable interventions such as systemic microbial gut modulation.

#### Abstract # 40

### Abstract Title: Maternal Antenatal Marijuana Use Lowers the **Biologic Potential of Umbilical Cord Mesenchymal Stem Cells**

Name: Adnan Ismail, MD

Fellow Physician

Co-Authors: Adnan Ismail MD1\*; Yona Nicolau MD1; Cherry Uy MD1; Fayez Bany-Mohammed1; Muhammad Aslam MD1 1. Pediatrics-Neonatology, UC Irvine School of Medicine, Orange, CA, United States

Organization: UC Irvine Medical Center

Abstract Overview: Background: Human umbilical cord derived mesenchymal stem cells (MSCs) have been extensively studied with therapeutic efficacy in several injury models. Our work has shown therapeutic efficacy of MSCs and their secreted factors in experimental neonatal chronic lung disease and pulmonary hypertension models. Maternal antenatal drugs and disease states can affect the efficacy of MSCs. At present, very limited data are available on maternal marijuana use during pregnancy affecting the MSC biologic potential. Objective: We hypothesized that human umbilical cord Wharton's jelly MSCs harvested from marijuana exposed cords will lack biologic potential compared with nonexposed cords. Our aims were: 1. To generate human umbilical cord MSCs from marijuana exposed and non-exposed cords. 2. To determine in vitro properties and secreted factors between the two groups. Design/Methods: Human umbilical cord Wharton's jelly MSCs from marijuana exposed and non-exposed umbilical cords were isolated and cultured according to our modified protocols. Marijuana exposure was considered positive if mothers have smoked marijuana within the prior two weeks before delivery with a positive urine drug test. In vitro growth, differentiation, and secreted factors were analyzed utilizing duplication time, Western immunoblot, and proteomics analysis. Results: MSCs were harvested from 3 pooled marijuana exposed cords with 3 nonexposed cords as control. Marijuana exposed MSCs had much shorter duplication and differentiation time compared to nonexposed MSCs. Interestingly, although the marijuana exposed MSCs grew faster, they had lower concentration of cardiopulmonary protective secreted factors compared to non-exposed MSCs. Conclusion(s): Marijuana exposure during pregnancy leads to a reduction in biologic potential of human umbilical cord MSCs. Further in vitro and in vivo studies are underway to determine the extent of this relationship.

# Abstract # 41

Abstract Title: Association between blood carboxyhemoglobin level and bronchopulmonary dysplasia in extremely low birth weight infants

Name: Thea Tagliaferro, MD, MPH

Neonatology Fellow

Co-Authors: Cayabyab Rowena MD, MPH, Professor of Pediatrics Barton Lorayne MD, MPH, Associate Professor of Pediatrics Ramanathan Ramanathan MD, Professor of Pediatrics

Organization: USC, Keck School of Medicine, LAC-USC Medical Center, Division of Neonatology

Abstract Overview: Background Carboxyhemoglobin (CO-Hb) can be endogenously formed in the presence of oxidative stress and may be elevated in inflammatory lung disease. There is lack of evidence of its relationship with development of bronchopulmonary dysplasia (BPD) in extremely low birth weight infants (ELBW). Objective: To evaluate the relationship between blood CO-Hb levels in the first 14 days of life in ELBW infants and development of BPD at 36 weeks postmenstrual age (PMA). Methods: Retrospective study of 58 ELBW infants born at LAC-USC Medical Center between June 2015- and June 2019, that survived to 36 weeks PMA. CO-Hb values were collected daily from day of life (DOL) 1 to DOL 14. BPD definition per 2001 NICHD criteria

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was used. Wilcoxon Rank sum test was used to compare the differences in continuous variables. Logistic regression was used to adjust for the confounding variable GA in the association between blood CO-HB levels and BPD. Results: 53/58 ELBW infants with BPD at 36 weeks PMA had a median GA in weeks of (25 (2) vs 29 (2) in non-BPD infants (p=0.012), and median BW of (730 (220) vs. 920 (160) grams, p= 0.0003) respectively. Blood CO-Hb levels were significantly higher in BPD patients compared to non- BPD infants (Table 1). 40% of patients had severe BPD at 36 weeks PMA. However, severity of BPD was not significantly correlated with CO-Hb levels. Logistic regression analysis showed invasive mechanical ventilation to predict development of BPD but Table 1. Combined CO-Hb at different DOL not CO-Hb levels. BPD and BPD Non-BPD p CO-Hb at DOL 1 to 52.54 (0.42) 1.78 (0.58) 0.028 CO-Hb at DOL 6 to 10 2.40 (0.60) 1.81 (0.31) 1.65 (0.33) 0.006 CO-Hb at DOL 11 to 14 2.21 (0.39) 0.015 Data reported as: Median (IQR) Conclusions: BPD patients had significantly lower gestational age and birth weight at 36 weeks PMA. While CO-Hb levels within the first 14 DOL are higher in BPD patients compared to non-BPD, they did not predict later development of BPD. Fetal hemoglobin (HbF) may have falsely elevated CO-Hb values in our population. This needs to be further studied in a larger sample size correcting for HbF.

## Abstract # 42

Abstract Title: Pulmonary hemorrhage in extremely low birthweight infants: Significance of the size of left to right shunting through a valve incompetent patent foramen ovale

Name: Jaclyn Kappico, MD

Neonatal Perinatal Medicine Fellow

**Co-Authors:** Bijan Siassi, MD, Associate Professor of Pediatrics and Cardiology Mahmood Ebrahimi, RDCS Lorayne Barton, MD, MPH, Associate Professor of Pediatrics Manoj Biniwale, MD, Associate Professor of Pediatrics Rangasamy Ramanathan, Professor of Pediatrics

**Organization:** USC/LAC+USC Medical Center, Keck School of Medicine

**Abstract Overview:** Background: Pulmonary hemorrhage (PH) in extremely low birthweight (ELBW) infants is usually attributed to the presence of a large patent ductus arteriosus (PDA). However.

most neonates with a large PDA do not develop PH. Therefore, there may be other factors contributing to the development of PH. Objectives: We investigated whether there was any difference in the echocardiographic findings of ELBW infants with PH and control infants without PH. Methods: This was a retrospective cohort study of live born infants with birthweight of less than 1000gm, who lived for at least 24 hours. Clinical and echocardiographic data were analyzed for infants with PH and a control group of infants matched for gestational age (GA) and birth weight. Results: Over an eleven-year period, 214 neonates were born weighing less than 1000 grams who lived for more than 24 hours at LAC+USC Medical Center. Twenty had PH with an incidence of 9.3%. Of 20 infants with PH, four were not included in the study (3 infants had either necrotizing enterocolitis, sepsis or were post-PDA ligation and one did not have an echocardiogram). The other 16 infants with PH all had a PDA, yielding a PH incidence of 7.9% potentially related to having a PDA. Sixteen infants with PDA and similar GA and birthweight were randomly selected as controls. There was no significant difference in Apgar scores, birth weight classification, surfactant administration, ventilator days, bronchopulmonary dysplasia, length of stay, size of PDA, LA/Ao ratio, or shortening fraction between the two groups. However, there was a significant difference in the presence and the size of left to right shunt through the foramen ovale between the groups. All control infants had a L-R shunt through the PFO with average size of 2.27mm (range 1.4 to 3.4), whereas 5 of 16 infants with PH had no L-R shunt and average PFO measurement was 0.85mm (range 0 to 1.53, p-value< 0.0001). Conclusion: In addition to a large left to right shunt through the PDA, pulmonary venous congestion as a result of blocked or restricted left to right shunting through the foramen ovale may predispose ELBW infants to PH.

#### Abstract # 43

Abstract Title: Effect of temperature and brain injury on apparent diffusion coefficient changes in newborns undergoing therapeutic hypothermia

Name: Carolina Zenobi, MD

Neonatal-Perinatal Medicine Fellow

**Co-Authors:** - Tai-Wei Wu, Assistant Professor of Clinical Pediatrics, Fetal and Neonatal Institute, Division of Neonatology Children's Hospital Los Angeles, Department of Pediatrics, Keck School of Medicine, University of Southern California - Jessica L. Wisnowski, Assistant Professor of research Radiology and Pediatrics, Fetal and Neonatal Institute, Division of Neonatology Children's Hospital Los Angeles, Department of Pediatrics, Keck School of Medicine, University of Southern California - Benita

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Tamrazi, Assistant Professor of Clinical Radiology, Radiology, Children's Hospital Los Angeles - Stefan Blüml, Associate Professor of Research Radiology, Radiology, Children's Hospital Los Angeles/USC

**Organization:** USC Keck School of Medicine, LAC+USC Medical Center/Children's Hospital Los Angeles

Abstract Overview: Background: Apparent diffusion coefficient (ADC) changes are useful in detecting ischemic brain injury by the principle that cytotoxic edema restricts Brownian motion of water molecules. Other than pathology, tissue temperature may also affect the kinetic movement and diffusion of water. We hypothesize that ADC values are more restricted when regional tissue temperature is reduced, such as during therapeutic hypothermia (TH). Objective: To determine the effect of temperature on diffusion restriction or ADC values in infants without radiographic evidence of brain injury. To compare magnitude of ADC changes during and after TH in infants with and without injury. Design/Methods: MR spectroscopy measures local tissue temperatures non-invasively by quantifying chemical shift difference. In this study, we compared ADC values with brain temperatures during and after TH in infants with hypoxic-ischemic encephalopathy. We excluded data if duration between scans was >5 days to minimze the effects of injury evolution on ADC. Injury severity (normal-mild vs. moderate-severe) was scored by a pediatric neuroradiologist based on previously published methods. Corresponding ADC values and tissue temperatures in thalamus (Thal), basal ganglia (BG), parietal gray matter (GM) and white matter (WM) were compared. Paired comparison of temperatures and ADC were performed. Comparison of ADC changes between the two injury severity groups were performed. Results: Overall, data from 34 suspected HIE newborns (22 normal-mild and 12 moderate-severe) were analyzed. Mean gestational age was 38±2 weeks and birthweight 3231±641g. Mean duration between MR scans (during/after TH) was 3.7±1.1 days. In all patients, mean ADC and brain temperature significantly increased during and after TH, Table 1. In normal-mild group, whereby ADC changes due to evolution of injury is minimal, ADC increased after TH (838±86 vs. 910±84x10-6 mm2/s, p<0.0001), with ADC value increasing ~25x10-6mm2/s per degree Celsius change ( $\Delta$ ADC/ $\Delta$ Brain Temp). In moderate-severe group, there was a significant increase and more variable change in ADC (867±171 vs. 1057±240, p<0.0001), Figure 1. When comparing regions, the GM and WM had the greatest increase in ADC values for both injury groups. Notably, patients with the most severe injuries had worsening diffusion restriction (decrease in ADC) even after rewarming. Conclusion(s): Aside from brain injury, low tissue temperature may be another factor contributing to diffusion restriction in infants with HIE during TH.

#### Abstract # 46

Abstract Title: B. infantis EVC001 metabolites improve enterocyte proliferation in vitro Name: Bethany Henrick, PhD

**Director Immunology & Diagnostics** 

**Co-Authors:** Stephanie Chew, MSc; Amy M. Ehrlich, PhD; Johann S. Prambs, BSc, Bethany M. Henrick, PhD

Organization: Evolve Biosystems

Abstract Overview: Introduction: Short chain fatty acids (SCFA) are an important energy source for host cells to maintain homeostasis. Indeed, SCFAs account for 50-70% of the energy used by intestinal epithelial cells (IECs) and provides nearly 10% of our daily caloric requirements. Given previous findings that showed exclusively breastfed infants colonized with B. infantis EVC001 have significantly increased fecal SCFA concentrations compared to infants not colonized with B. infantis, we investigated the effect of fecal water (FW) from these two distinct populations on enterocyte proliferation and morphology in vitro. Methods: FW were derived from fecal samples collected from infants colonized with B. infantis EVC001 (EVC001) and infants not colonized with B. infantis (controls). FW were added to adult and premature enterocyte cell lines to assess growth, proliferation and cytotoxicity. Microscopic images were taken to observe morphological differences. Results: Intestinal epithelial cells (IECs; Caco-2 and HIEC-6 cells) exposed to EVC001 FW showed significantly increased proliferation, as shown by cell count and real-time ATP expression, compared to medium alone and control FW (P < 0.0001). Conversely, enterocytes exposed to EVC001 FW showed significantly decreased lactate dehydrogenase activity, an indicator of compromised membrane integrity, compared to controls FW (P < 0.01). Specific bacterial metabolites, lactate and acetate, at median physiological concentrations found in EVC001 infant FW significantly increased Caco-2 cell proliferation compared to medium alone (P < 0.01, P < 0.05, respectively), while control FW levels did not significantly increase proliferation. Physiological concentrations of butyrate or formate from EVC001 or controls did not increase proliferation rates of IECs. Furthermore, control FW negatively altered the morphology of enterocytes compared to cells exposed to EVC001 FW or medium alone. Conclusions: EVC001 FW and specific bacterial metabolites, lactate and acetate, significantly increased enterocyte proliferation compared to control FW and medium alone, while control FW negative affected cell growth, membrane integrity and cell morphology. These data suggest that metabolites produced by B. infantis EVC001 promote enterocyte growth and improve intestinal integrity in both adult and premature infants.

#### Abstract # 47

Abstract Title: Progress Towards Screening for Hyperammonemia in Oregon

Name: Brian Scottoline, MD PhD



**Co-Authors:** Cynthia Le Mons Executive Director National Urea Cycle Disorders Foundation Pasadena, CA 91105 Amy Yang MD Assistant Professor of Medical and Molecular Genetics Oregon Health & Science University Portland, OR 97212 Executive Director National Urea Cycle Disorder Foundation

Organization: Oregon Health & Science University

Abstract Overview: Background: Neonatal hyperammonemia (NH), with an aggregate incidence of ~1/10000 births, is frequently due to a metabolic disorder, namely a urea cycle disorder (UCD) or an organic acidemia. NH can be lethal, causing an estimated hundreds of deaths per year, and if survived, causes significant neurologic impairment. Early intervention for younger siblings born with the same genetic condition have demonstrated that intravenous calories, ammonia scavengers, dietary management, and eventual liver transplant can lead to good outcomes. NH can be difficult to diagnose in the newborn period because symptoms overlap with those for neonatal sepsis, delaying diagnosis and treatment. Some states screen for distal UCDs, but proximal UCDs, in particular ornithine transcarbamylase (OTC) deficiency, are symptomatic long before newborn screening results return. Efforts to improve NH diagnosis have thus far been unsuccessful, due to rarity and misconception that the disease is essentially lethal and without a cure. We describe the development and ongoing efforts to obtain ammonia levels for neonates less than 30 days old in Oregon who present with sepsis. Objective: To improve the diagnosis of NH in Oregon, prior to the onset of irreversible neurologic damage, multiorgan failure, and death. Methods: The key elements of this effort are 1. Formulation of a care pathway for NH detection that specifies an ammonia level with initial sepsis evaluations in neonates  $\geq$  36 weeks from dol 2 (one day old) to dol 30. The guideline includes an ammonia drawn from any source (arterial, venous, capillary) and a clinical algorithm based on ammonia level, including emergency treatment; 2. Education regarding NH and the pathway at all institutions with NICUs in Oregon, with wider efforts for adoption in well-baby, pediatrics, family medicine, and emergency medicine services across the state in process; 3. Support for institutions to adopt the practice; 4. Support for data collection at interested institutions; 5. Close collaboration with the National Urea Cycle Disorders Foundation to refine methodology and for support. Results: Of the 12 NICUs in Oregon, 9 have adopted or are in process of adopting the guideline and 4 are working on data collection involving Epic. This represents well over half of the NICU beds, and hospitals with over half of the in-hospital births in Oregon. Conclusion: It is feasible to institute a state-wide practice guideline to improve early NH diagnosis and treatment before neurologic damage, multiorgan failure, and death. We are working to collect data to track outcome.

Abstract # 48

# Abstract Title: Preterm infants fed B. infantis EVC001 Demonstrate Significant Changes to the Gut Microbiome Composition and Reduction of Intestinal Inflammation

Name: Marielle Nguyen, MD

Regional Physician in Charge

**Co-Authors:** H. Holdbrooks, P Mishra, M Abrantes, S Eskew, P Roth, J Garma, C Oca; C McGuckin, C Hein, S Chew, R Mitchell, S Kazi, G Casaburi, S Frese, and B Henrick

**Organization:** Division of Neonatology, Kaiser Permanente Southern California

Abstract Overview: Background: Gut microbiome dysbiosis negatively affects the health of premature infants and increases risk for infection and diminished growth. Additionally, microbial dysbiosis has been linked with increased enteric inflammation, which is a major driver of many adverse clinical outcomes in premature infants, including necrotizing enterocolitis. In this study, we hypothesized that gut microbiome composition has a beneficialn effect on enteric inflammation in preterm infants, similar to findings in term infants. We compared fecal samples from infants at similar corrected gestational age to evaluate the cytokine profile and gut microbiome of infants fed Bifidobacterium longum subsp. infantis EVC001 compared to those that were not fed B. infantis EVC001. Methods: Prospective fecal collection was performed at Kaiser Permanente Southern California (Anaheim and Irvine, CA). All infants in the hospital born at less than 32 weeks gestational age OR less than 1500 g received 8 x 109 CFU activated B. infantis EVC001 suspended in MCT oil daily as standard of care. Fecal samples (n = 298) were collected during routine diaper changes and were subjected to shotgun metagenomics and cytokine profiling. Results: The gut microbiome of preterm infants fed human milk was depleted in Bifidobacteriaceae, relative to term infants, but could be restored in infants fed B. infantis EVC001. Proinflammatory markers were significantly correlated with signatures of dysbiosis. Proteobacteria correlated with the pro-inflammatory cytokine IFN-y (P=0.01), and Enterobacteriaceae, specifically, correlated with IL-1b (P = 0.014) and IL-2 (P = 0.017). Peptostreptococcaceae correlated with IL-2 (P=0.0002), IL-4 (P = 0.005), and IL-8 (P = 0.002). Fecal calprotectin levels were also positively correlated with Staphylococcaceae (P = 0.005). Interestingly, antibiotic resistance genes were significantly reduced as Bifidobacterium levels increased (R = -0.60; P < 0.001), in agreement with our previous findings in term infants. Conclusion: Our findings indicate gut dysbiosis (i.e. the absence of Bifidobacterium) is associated with increased intestinal inflammation and antibiotic resistance gene carriage in preterm infants. Early addition of B. infantis EVC001 to the diet represents a novel strategy for controlling the composition of the premature infant gut microbiome, as well as preventing dysbiosis-driven enteric inflammation and the dissemination of antibiotic resistant bacteria.

## Abstract Title: Neonatal Resuscitation Education in a Community Hospital: Simulation vs Video-based?

Name: Linda Truong\*, DO

**Clinical Assistant Professor** 

**Co-Authors:** Melinda Porter, RN, CNS, NNP-BC, Christine Johnson, MD

Organization: Stanford University

Abstract Overview: Background: Simulation-based education has been shown to be a superior method of maintaining and improving neonatal resuscitation skills by healthcare providers. However, current programs can be resource intensive and financially prohibitive, particularly in community hospital settings. With electronic devices becoming commonplace, access to videobased education can be used to supplement or replace simulation-based education. Objective: To determine if simulation or video-based education results in higher retention of neonatal resuscitation knowledge among neonatal nurses (RN) and respiratory therapists (RT) in a community neonatal intensive care unit Methods: A prospective comparison of simulation vs. (NICU) video-based neonatal resuscitation education was conducted at a community level III NICU July-Aug 2019. 63 RNs and 28 RTs participated in educational sessions consisting of 2 simulations followed by video debriefing and teaching. Learners also watched internally created videos on topics ranging from equipment review to proper resuscitation technique according to the Neonatal Resuscitation Program. Learners were divided into 2 groups: the simulation group (SG), who attended the simulations first then watched the videos, and the video group (VG) who watched the videos first then attended the simulations. SG completed an inperson pre-assessment quiz (PRE) prior to their session and an electronic post-assessment quiz (POST) after their session, prior to viewing the videos. VG completed PRE electronically prior to their session, watched the videos, and then completed an in-person POST at their session. The PRE and POST were identical, internally generated, and consisted of 10 NRP based questions designed to test retention of knowledge and skills. Results: 56 learners (39 RNs+17 RTs) from SG and 35 (24 RNs+11 RTs) from VG completed PRE. 3 learners were lost to follow up: 2 from SG and 1 from VG. The improvement in average scores of all learners was statistically significant (p<0.01). In subgroup analysis, learners from both SG and VG had significantly improved scores (p<0.01), but there was no statistically significant difference between the POST scores of the 2 groups (Table 1). While those in VG had higher overall POST scores, the largest improvement in Conclusion: In conclusion, simulationscores was seen in SG. based neonatal resuscitation education showed a trend towards higher retention compared to video-based education. In community hospital settings, video-based resuscitation education may be a suitable substitute.

Abstract # 50

# Abstract Title: Effect of diuretic exposure on the growth and body composition of very preterm infants

Name: Sonya Misra, MD MPH

Attending Neonatologist

**Co-Authors:** Nudelman, Matthew, MD; Chin, Donna, RD; Uriarte, Sahar, RD; Den, Weifen, NNP; Govindaswami, Balaji, MBBS MPH; Jegatheesan, Priya, MD; Song, Dongli, MD PhD.

Organization: Sant Clara Valley Medical Center

Abstract Overview: Background: Appropriate infant growth is essential to optimize neonatal outcomes. Diuretics have been suggested to interfere with growth and their effect on body composition (BC) of infants is unknown. Objective: To evaluate the effect of diuretic exposure on the growth and BC of preterm infants born less than 33 weeks of gestation (GA). Design/Methods: We included all 285 preterm infants of <33 weeks GA born from 2014 to 2019 who survived to discharge. Standardized enteral and parenteral nutrition were followed. Individualized nutrition was provided with a focus on catch-up growth. BC was measured by air displacement plethysmography (ADP) within 1 week of discharge. Growth anthropometrics, weight, length and occipitofrontal circumference (OFC) at birth and discharge, were collected prospectively. Z-scores were obtained using growth charts (Fenton 2013/WHO). Growth velocity was calculated using the exponential model (Patel 2005). Diuretic exposure was obtained from NICU database and was grouped as <4, 4-14, and >14 days of exposure. Chronic lung disease (CLD) was defined as oxygen need <36 weeks post menstrual age. Growth measures and BC were compared between diuretic exposure groups in infants of <33 weeks and <30 weeks. Kruskal Wallis, Fisher exact test and Multivariable linear regression were performed. Results: Demographics are described in Table 1 and 2. Nineteen percent of <33 weeks and 43% of <30 weeks were exposed to diuretics, respectively. Lasix and Diamox were used for intermittent dosing and Aldactazide was used for chronic use. Infants exposed to diuretics had lower GA, birth weight, length, OFC, were older at discharge and had higher CLD. The weight and length velocity, fat % were higher and fat free mass % was lower in diuretic exposed infants (Table 1, 3). In <30 weeks GA, diuretic exposed infants were discharged later, and had more CLD but their growth measures were similar to unexposed (Table 2). There was no dose effect of diuretics. After adjusting for birth length and GA at discharge the BC measures were not significant (Table 3, 4). Conclusions: Growth measures and BC were not adversely affected by diuretics in preterm Infants who received individualized nutritional support. The growth differences between infants <33 weeks that were

exposed and non-exposed may be secondary to the unexposed older infants having a shorter NICU stay with less time for catch up growth.

### Abstract # 51

Abstract Title: The First Sixty Minutes: Implementation of Golden Hour Guidelines in a Level III NICU

Name: Radhika Narang, MD

**Director of Neonatal Transport** 

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Organization: VALLEY CHILDREN'S HEALTHCARE

Abstract Overview: Background: The unique characteristics of preterm infants put them at risk for hypothermia, hypoglycemia and respiratory distress. Best outcomes for pre-term infants are contingent on effective communication, teamwork, and clinical skills. Objective: The project started in May 2018 to implement a standardized multidisciplinary approach to the resuscitation and stabilization processes for infants born <32.6 weeks GA and/or < 1500 grams. Design: 2017 admissions to the satellite NICU were reviewed to gather baseline data. The records revealed that 79% of VLBW infants were within range for the recommended admission temperature (36.4C to 37.5C) and 60% of VLBW infants were within range for admit glucose level (>40 mg/dl). There was great variability in time to surfactant but 80% of the gualified VLBW infant received surfactant within 120 minutes of life. Patients: All infants 32.6 weeks GA and/or < 1500 grams admitted to the Valley Children's Satellite NICU at St. Agnes Medical Center SMART AIMS: By October 15, 2020, 80% of infant's meeting criteria will demonstrate: ¥ Admission temperature > 36.5°C ¥

Within 60 minutes: Initiate IV fluid & obtain an initial point of care glucose ¥ Admission glucose > 40 mg/dL ¥ Administer surfactant within 120 minutes (if indicated) Interventions: We established key drivers for advancing each objective • D e livery room(DR) checklist: Increase DR temperature, hypothermia prevention bundle • Protocols for automatic umbilical line placement and for starting fluids and obtaining labs • Guidelines to standardize surfactant administration • Sim-

ulation based training for all providers, nursing and respiratory staff Results: Total number of patients = 124 Admission Temperature >  $36.5^{\circ}C = 62\%$  Initial Glucose > 40 mg/dl = 66% IV Fluids Initiated within 60 minutes = 53% Glucose Obtained within 60 minutes = 61% Surfactant Administered within 120 min = 93%Discussion: The satellite NICU is uniquely placed within another hospital system. The influx of new nurses/RCPs training at any given time creates a significant challenge in meeting our goals. We were able to successfully standardize and improve the rate of surfactant administration. We were not able to meet our target for admission temperature and hypoglycemia. Through sequential PDSA cycles, we have identified gaps that contributed to this. Our focus includes collaboration with host facility to educate their staff to adjust DR temperature specially with the implementation of delayed cord clamping. And continue simulation based training for our staff to appropriately utilize the newly acquired temperature probes and plastic bags for resuscitation and to follow the umbilical lines protocol.

### Abstract # 52

# Abstract Title: Moms in the NICU: A Pilot to Empower Moms, Lower Health Care Barriers, and Reduce Preterm Birth

Name: Kimber Padua, CRC

**Clinical Research Coordinator** 

**Co-Authors:** Grace M. Lee, MD MPH Associate Chief Medical Officer for Practice Innovation, Stanford Children's Health Professor of Pediatrics, Stanford University School of Medicine Rebecca Robinson Administrative Director, California Perinatal Quality Care Collaborative Jeffrey B Gould, MD, MPH Professor-Med Ctr Line

Organization: CPQCC

**Abstract Overview:** Objective: Moms often spend hours and days at the bedside with their premature infants. As women care



for their infants in the Neonatal Intensive Care Unit (NICU), their own health needs often become secondary. Despite spending time in a healthcare setting, clinicians often miss an opportunity to engage moms to care for their own health. Our objective was to develop and pilot a NICU-based intervention to reduce the risk of recurrent preterm births by engaging and empowering moms to improve their own health in between and during future pregnancies by creating: a maternal birth story, including accurate information on potential factors associated with preterm birth to help manage future pregnancies, and a health plan for mom to help support actions aimed at improving her own health. Method: A toolkit for Moms in the NICU was developed by a multidisciplinary team of Maternal Fetal Medicine (MFM) physicians, Obstetricians, Neonatologists, neonatal nurses, and parents. Moms participated in a one-on-one consultation with the MFM clinician to share their birth story, clarify any concerns or issues related to their pregnancy and delivery, and discuss relevant interventions to improve their health and to reduce the risk of preterm birth during future pregnancies. Moms developed an individualized post-partum health plan and were provided with a personalized health record with suggested interventions to enable effective communication with obstetric providers during subsequent pregnancies. A 6-week follow-up phone interview was conducted to identify successes and barriers to implementing their health plan. Results: Participants reported experiencing reassurance, understanding, and in some cases, revelation and relief. Maternal Fetal Medicine providers offered a balance of compassion and medical knowledge to support moms who felt distress from their birth experience. By promoting maternal engagement and empowering moms during their one on one consultation, we were able to provide clarification from a clinical standpoint, encourage a prolonged interpregnancy interval, and support moms in their development of a postpartum health plan. Conclusion: By developing and implementing the "Moms in the NICU" program, clinicians will utilize the time that a mother spends in the NICU as an opportunity to empower them to care for their health. Topics addressed include but are not limited to: getting treatment for any acute and chronic health care issues, understanding the importance of their inter pregnancy interval, providing enhanced access to family planning that would enable optimizing future prenatal care. The 6-week follow-up will allow the identification of barriers to carrying out their postpartum health plan, and provide guidance for future interventions.

#### Abstract # 53

Abstract Title: Are prenatally opiate and/or polysubstances exposed male neonates at higher risk for Neonatal Abstinence Syndrome?

Name: Angela Huang, RN

**Quality Coordinator** 

**Co-Authors:** Priya Jegatheesan, MD Balaji Govindaswami, MD Matthew Nudelman, MD Jessica Haas, RN Dongli Song, MD Arrin Brooks Sean Loudin Jodi Pitsenbarger Cynthia Massey Taylor Maddox Todd Davies

Organization: Santa Clara Valley Medical Center

Abstract Overview: Background: A recent large statewide study using payor data has shown increased neonatal abstinence syndrome (NAS) in male neonates exposed to perinatal opiate and polysubstance use. Sex distribution variation in the hospitalized neonates may be due to biology, population sociocultural characteristics or the healthcare delivery system. Objective: To examine if prenatally opiate exposed inborn males were more likely to require pharmacological treatment for NAS, at 2 regional perinatal centers in different states, using different screening strategies. Design/Methods: Available data was collected in inborn neonates 2014-2019 in two regional perinatal centers: Center 1 (San Jose, CA) and Center 2 (Huntington, WV). Data was examined retrospectively to determine prevalence of perinatal substance exposure at birth, and frequency of NAS treatment in substance/ opiate-exposed neonate. Chi square was used to compare the percentages of males and females in the exposed neonates and NAS treated neonates. Results: 34818 consecutive livebirths between 2014 and 2019 at 2 regional perinatal centers included 19,133 in Center 1 and 15685 in Center 2 (Table 1). Prenatal substance exposure was documented in 3% and 10.5% neonates in Centers 1 and 2 and opiate exposure was 0.6% in Center 1 and 9.3% in Center 2 (2017-2019). Of the substance exposed, 22% were opiate exposed and 2% were treated for NAS in Center 1 and 80% were opiates exposed and 71% were treated for NAS in Center 2. Of the substance exposed neonates at both centers, there was no difference in male and female proportion in the opiate exposed neonates or those who were treated for NAS (Table 2). Conclusion: Centers differed significantly in perinatal substances exposure, opiate exposure, and NAS treatment. There was no difference in sex in opiate exposure or NAS treated neonates in our study. We did not observe difference in sex distribution despite regional variations in population characteristics and/or exposure to different perinatal substances and/or differences in healthcare delivery. Prospective data collection is critical to characterize both infant and discrete prenatal substance exposure.

#### Abstract # 54

Abstract Title: Improving oral colostrum administration within first hour of life in Neonatal Intensive Care Unit infants

Name: Angela Huang, RNC, MPH

Quality Coordinator

**Co-Authors:** Alga Kifle, RN, April Grady, RN, Andrea Abbas, RN, Jennifer, Donahue, RN, Uyen Nguyen, RN, Laura Berritto, RN, MHA, Sudha Narasimhan, MD, Priya Jegatheesan, MD

Organization: Santa Clara Valley Medical Center

Abstract Overview: Background Early colostrum administration provides optimum colonization and immune benefits to NICU infants. Early expression of colostrum in the first hour has been linked to improved mother's milk supply and breastfeeding. Setting AAP level 4 Regional NICU within a public hospital. Staff from NICU and Labor and delivery units, including nurses, neonatal nurse practitioners, neonatologists, and infants' families participated in this project. Aim To increase percentage of NICU infants who receive colostrum within the first hour of life from a baseline of 16% in 2017 to 50% by 2018. Design/Methods We used Plan Do Study Act rapid cycle quality improvement method. Patient demographics, delivery method, time to colostrum administration were collected retrospectively from October 2017 to February 2018 as baseline. Changes were implemented in March 2018 to July 2018, and sustainability was monitored monthly until December2019. Patients Infants born and admitted to our unit within one hour of life are included. Exclusion criteria included maternal contraindication for breastfeeding including exposure to illicit substances, or critical maternal medical conditions. Results During study period, 327 eligible infants were admitted to our center, 79 (24 %) of whom were born <33 weeks GA. The percentage of eligible infants receiving colostrum in the first hour improved from 16% to 53% (p<0.001) (Table 1). Time to first colostrum administration improved from median of 113 minutes (IQR 76, 274) to 60 minutes (IQR 36.5, 113) (p<0.001). The percentage of infants <33 weeks GA receiving colostrum in the first hour improved from 24% to 69% (p=0.001), and time to first colostrum administration improved from median of 116 minutes (IQR 76, 527) to 49 minutes (IQR 30, 76) (p=0.006) (Table 2). Vaginally born infants were more likely to receive colostrum within 1 hour than infants born via C-section (64% vs 54%, p=0.04). Conclusion We increased the percentage of infants receiving colostrum within the first hour of life through a multidisciplinary approach and have sustained our improvement. We observed lower rate of early colostrum in c/ section-born infants which highlights challenges and is an area for further improvement efforts.

# Abstract # 55

Abstract Title: Implementing transcutaneous bilirubin screening in infants >30 weeks gestation in NICU

Name: Maria Cortes, DNP, NNP-BC

Neonatal Nurse Practitioner

Co-Authors: Priya Jegatheesan MD, Dongli Song MD, PHD,

Patricia Scott DNP, NNP-BC, C-NPT, Andrea Abbas MSN, RN, Monica Stemmle MD, Balaji Govindaswami MBBS, MPH, Gloria Micotti BSN, RNC-NIC, Faviola Del Real BSN, RNC-NIC, Renelyn Tong BSN, RNC-NIC,

Organization: Santa Clara Valley Medical Center

Abstract Overview: Background: Despite studies demonstrating accurate correlation and clinical utility of transcutaneous bilirubin (TcB) screening in preterm and term infants, TcB technology is underutilized in the NICU setting. Purpose/Aim: To evaluate the effect of a TcB screening for hyperbilirubinemia on the number of serum bilirubin levels obtained per infant who were born at > 30 weeks' gestational age (GA). Methods/Interventions: This is a single-center quality improvement project conducted from January 2019 to September 2019 at Santa Clara Valley Medical Center (SCVMC), a California regional NICU. A TcB screening protocol using Philips Bilichek TcB meter was implemented in May 2019 (Figure 1) in all infants born at > 30 weeks gestation and admitted to NICU. Threshold for obtaining serum bilirubin was established as greater or within 2mg/dl of phototherapy threshold for each gestation. The protocol was disseminated via group education to providers and individualized hands on demonstration on use of TcB meter to nursing staff. GA, birth weight (BW), number of serum bilirubin, peak bilirubin, phototherapy exposure, and number of phototherapy days were compared between baseline pre-protocol (Jan-April 2019) and post-protocol period (May-September 2019) using t test, ranksum test, chi square as appropriate. Results: A total of 108 infants with median GA of 35weeks (30w-41w3d) and BW of 2346g (970-4786g) were included: 52 infants in preprotocol and 56 infants in post protocol period. TcB was obtained at least once in 98% of post-protocol study infants. Compared to pre-protocol, post-protocol period had a significant reduction in number of serum bilirubin obtained per infant (4 vs 2.4, p<0.001) and phototherapy exposure (50% vs. 21%, p=0.004) (Table 1). In the >35 weeks GA subgroup, 34% never had a serum bilirubin test done in the post-protocol in contrast to 100% in the pre-protocol period. In the 30-34 weeks GA subgroup post-protocol period had a significant reduction in phototherapy exposure (88% vs. 38%, p<0.001). There was no difference in the GA, BW, peak bilirubin, or phototherapy days between pre and post-protocol periods. Implications for Practice: This single center study shows implementation of TcB screening protocol in the NICU reduced serum bilirubin sampling. Education and implementation of TcB protocol improved clinican's adherence of phototherapy guidelines thresholds and reduced phototherapy exposure in neonates > 30 weeks GA. Sharing our experience regarding the effect of TcB screening protocols in the NICU will facilitate best practice in evaluation and management of hyperbilirubinemia in NICU.

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Abstract Title: Mapping inflammatory markers in non-invasively ventilated very low birth weight infants at risk for bronchopulmonary dysplasia: a comparison between bubble continuous positive airway pressure and nasal intermittent mandatory ventilation

Name: Anupama Chundu, MD

Neonatal-Perinatal Medicine Fellow

**Co-Authors:** Chundu, Anupama; Uy, Cherry; Bany-Mohammed, Fayez; Nicolau, Yona; Aslam, Muhammad

Organization: University of California Irvine

Abstract Overview: Background: Bronchopulmonary dysplasia (BPD) is a chronic debilitating disease of extremely premature infants leading to high morbidity and mortality. Respiratory distress syndrome requiring oxygen, mechanical ventilation, and surfactant treatment in early life leads to lung inflammation with later development of BPD. At present, very limited data exist on the protective role of non-invasive ventilation in early life lung inflammation and later development of BPD. Objective: This study analyzed the relationship between two types of non-invasive respiratory support methods that are used routinely in neonatal intensive care units: bubble continuous positive airway pressure (bCPAP) and nasal intermittent mandatory ventilation (NIMV). We enrolled a cohort of preterm infants born at < 32 weeks gestational age and/or birth weight < 1500g with randomization into bCPAP vs. NIMV groups at birth and analyzed the lung inflammation in the first week of life. Design/Methods: Babies < 32 weeks gestational age and/or birth weight < 1500g were enrolled into an institutional IRB approved study. Card randomization into bCPAP vs. NIMV groups was performed at enrollment with no cross over between groups. The nasopharyngeal aspirates were collected at the time of placement on noninvasive ventilation, at 4 days of life, and at 7 days of life. Luminex assays were performed on samples to determine lung inflammation at baseline and evolution over time between the two groups. Maternal and neonatal clinical data were collected. Results: A total of 28 babies have been enrolled into the study. At prsent, 8 babies (3 in bCPAP group and 5 in NIMV group) have data and sample analysis completed. The baseline maternal and neonatal data were similar between bCPAP and NIMV groups. The average gestational age in bCPAP group was 30.4 weeks compared with 29.5 weeks in NIMV group. Average birth weight in bCPAP group was 1327g compared to 1175g in NIMV group. Luminex assay revealed that several of the proinflammatory cytokine levels were higher in the bCPAP group compared to the NIMV group. Levels of IL-6, IL-1β, MCP-1α, IP-10, and IL-8 were similar at baseline samples, but higher in second and third samples in bCPAP group compared to NIMV group. Conclusion(s): Our study showed that bCPAP leads to more lung inflammation compared to NIMV in first week of life. Further patient enrollment and data collection is underway to reach study power.

#### Abstract # 58

# Abstract Title: Potential Role of FOX Family Transcription Factors in the Pathogenesis of Bronchopulmonary Dysplasia

Name: Avideh Rashed, MD Doctor of Medicine

**Co-Authors:** Saverio Bellusci, PhD; Cho-Ming Chao, MD PhD; Feng Gao, PhD; Rangasamy Ramanathan, MBBS MD; Parviz Minoo, PhD

**Organization:** LAC+USC Medical Center and Children's Hospital Los Angeles

Abstract Overview: Bronchopulmonary dysplasia (BPD) is a chronic lung disease most commonly seen in preterm infants as a result of long-term mechanical ventilation and oxygen exposure. The pathogenesis resulting in BPD is not completely understood. Studies using postmortem BPD lung tissue have shown that there is altered expression of a number of developmentally important genes. Our aim was to identify the genes that play a role in the pathogenesis of BPD. We generated three independent genetic models of BPD-like phenotype by disrupting the signaling pathways of TGF $\beta$ , PDGF $\alpha$ , and IGF-1 in neonatal lung in mice. The mutations to disrupt the pathways were induced in secondary crest myofibroblasts (SCMF) whose role is critical for normal alveologenesis. RNAseq analysis was performed which identified a cluster of differentially expressed genes that were common amongst the three BPD-like phenotypes. To assess the physiologic relevance of a specific subset of the identified genes, we examined their expression in a well-established hyperoxia-induced hypoalveolization mouse model. We analyzed gene expression using a total of ten mice exposed to hyperoxia compared to eight combined controls at three different points during neonatal life. mRNA expression was assessed by quantitative RT-PCR. Expression of Foxq1, Foxd1, Foxc2 were decreased in the mouse BPD lungs suggesting a role for the selected genes in the pathogenesis of BPD. We further demonstrate that Foxd1 is expressed in SCMF and ablation of SCMF during alveologenesis via Foxd1cre arrests alveolar formation leading to a BPD-like phenotype. To validate our findings in the mouse model, we show that Foxd1 is also reduced in human BPD lung tissue. Collectively, these observations support the notion that disruption of Foxd1 and FOX family transcription factors may play a major role in the pathogenesis of BPD in preterm infants.

#### Abstract # 59

Abstract Title: Improving Growth in the Very Low Birthweight Infant: A Quality Improvement Project

Name: Robin Koeppel, RN, CNS

Neonatal Clinical Nurse Specialist

**Co-Authors:** Rebecca Coleman, MD Janice Pianalto, RD Jennifer Jones, IBCLC Pam Aron-Johnson, RN

Organization: UCI Medical Center

Abstract Overview: Background: adequate nutrition is vital to the health and welfare of very low birthweight infants; unfortunately, the incidence of extra-uterine growth restriction is high in many NICU's, especially in those infants less than 1000 grams. As part of our participation in the CPQCC nutrition collaborative, we identified our incidence of infants discharged as growth restricted (discharged with weight below the 10th percentile) to be 23%. Objective: Improve nutrition in VLBW infants by reducing the number of infants discharged with a fall in z-score greater than 0.8 by 20% by March 31, 2020. Design: this is a Quality Improvement (QI) project using evidence-based interventions; no experimental practices or equipment were involved. Setting: 30-bed NICU with a high-risk perinatal delivery service, neonatal surgery, and specializing in care of the very low birth weight infants. Patients: infants <1500 grams and/or less than 32 weeks admitted and discharged from UCI are included in the QI project. Interventions: multiple interventions have been implemented including conduction twiceweekly Nutrition Time Out, modified TPN guidelines and feeding protocols. Nutritional goals were also modified, including re-gaining birthweight by day of life 10 and initiating TPN and intralipids within two hours of life. Measurement: the primary outcome is the difference between birthweight and discharge z-score. Other measurements are time to first feeding, time to initiating TPN, intralipids and first enteral feeds, days to regain birthweight. Results: for those infants 1000-1500 grams, we have reduced the number of infants discharged with fall in z-score greater than 0.8 by 20%. Limitations: results represent a QI project conducted at a single center. Conclusions: QI activities focused on nutrition can result in improved growth in VLBW infants.

## Abstract # 60

Abstract Title: Measuring Infant Body Composition with Free-Breathing MRI

Name: Daniel Cho, MD

Resident Physician

Co-Authors: Sevgi Gokce Kafali, MSc - Graduate Student Re-

searcher Shu-Fu Shih, MSc - Graduate Student Researcher Tess Armstrong, PhD - Associate Professor Shahnaz Ghahremani, MD - Associate Professor Holden H. Wu, PhD - Associate Professor Kara Calkins, MD, MS - Principal Investigator

Organization: UCLA Mattel Children's Hospital

Abstract Overview: Background: Childhood obesity is a major problem. Preterm and low birth weight infants are at risk for future metabolic syndrome. In adults and older children, increased visceral adiposity and hepatic fat, and decreased lean body mass, are associated with metabolic syndrome. We have developed a novel research tool, free-breathing magnetic resonance imaging (MRI), to quantify body composition, including visceral and subcutaneous adipose tissue and hepatic fat (using proton-density fat fraction, PDFF). However, there is a lack of research studying these body composition biomarkers in infants. Objectives/Hypothesis: The goal of this project was to expand our profile of body composition biomarkers and determine if free-breathing MRI can measure lean body mass in infants. We hypothesized that birth weight would positively correlate with lean body mass and adipos-Methods: This was a single site, prospective pilot study. Our ity. inclusion criteria included infants < 12 months of age. Exclusion criteria included contraindications to MRI and infants whose parents did not provide consent. Infants were fed, rocked to sleep, and swaddled in a vacuum immobilizer prior to placement in the MRI scanner for a 20-30 minute research study. Lean body mass indices were measured in terms of area of the paraspinal muscles in the lumbar region and area of the gluteal muscle on a selected slice using medical image analysis software (Figure 1). These measurements were correlated to birth weight, gestational age, subcutaneous and visceral adipose tissue volumes, and hepatic PDFF using Pearson coefficients (r). Results: 9 subjects (55% male) completed the study. The mean (±SD) gestational age and age at the time of the study was 36+/-4 weeks and 4+/-2 months, respectively (Table 1). Body composition profiles for each subject are also depicted in Table 1. There was a non-significant correlation between birth weight and gluteal muscles (r=0.6, p=0.07), and between gluteal muscles and subcutaneous adipose tissue (r =0.6, p=0.06). Conclusion: In this study, we successfully measured lean body mass indices in infants. We noted that lower birth weights are associated with decreased lean body mass and subcutaneous adipose tissue. Free-breathing MRI is a non-invasive tool that can be used in longitudinal studies to help uncover the early origins of obesity and associated metabolic complications in preterm and growth restricted infants.

# Abstract # 61

Abstract Title: Reducing Environment-Associated Temperature Instability During Transports to Nursery

Name: Daniel Cho, MD

**Resident Physician** 

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**Co-Authors:** Esther Kim, MD - Resident Physician Neema Pithia, MD - Resident Physician Jyotirbala Ruparel, MD - Attending Physician Jimmy Nguyen, MD - Principal Investigator

Organization: UCLA Mattel Children's Hospital

Abstract Overview: PURPOSE Newborns transferred from Labor & Delivery (L&D) to Nursery units in open cribs are at risk of hypothermia secondary to convection loss during transport, possibly leading to unnecessary sepsis evaluations and antibiotic therapies. We aimed to reduce environment-associated temperature instability via a practical low-cost intervention. METHODS We conducted a prospective observational study. Nurses conducting newborn transfers from L&D to Nursery were trained in a "double hat double blanket swaddle" protocol instead of the usual single layer clothing cover. The protocol was implemented on April 12, 2018. Data such as birth weight, gestational age, pre- and posttransfer temperatures, hospital length of stay, and sepsis workups were collected on newborns four months leading up to and four months after protocol initiation. **RESULTS** Compared to the pre-intervention cohort (n=1796), the post-intervention cohort (n=1830) showed a lower proportion of hypothermic babies upon arrival to Nursery (5.5% vs 3.8%; p=0.02) and smaller temperature variation between leaving L&D and arrival to Nursery (-0.23°F vs -0.19°F; p=0.03). Small for gestational age (SGA) term newborns showed the greatest reduction in hypothermia (5.4% vs 3.3%; p=0.005) as well as newborns with birth weights 2800-3200g (7.2% vs 3.0%; p=0.004). The post-intervention cohort overall received fewer sepsis workups (6.0% vs 6.8%; p=0.31) and trended toward fewer antibiotic courses (2% vs 2.9%; p=0.72). CON-CLUSION: A practical and relatively low cost "double hat double blanket swaddle" intervention led to a decrease in environmentassociated temperature instability during transport, especially for SGA term newborns and BW 2800-3200g.

#### Abstract # 64

**Abstract Title:** a QI initiative to establish infant driven feeding with >90% compliance in infants born at 32 weeks or less in a level III NICU

Name: Sneha Taylor, MD

Attending neonatologist

Co-Authors: Cheryl McElwain MSN, RNC-NIC

**Organization:** Children hospital of Orange county

Abstract # 65

Abstract Title: Bifidobacterium longum subspecies infantis EVC001 decreases inflammation and mortality in a murine NEC model

Name: Steven McElroy, MD

Associate Professor

**Co-Authors:** Shiloh R. Lueschow; Steven A. Frese, PhD; Bethany M. Henrick, PhD; Steven J. McElroy, MD

**Organization:** Stead Family Department of Pediatrics, University of Iowa

Abstract Overview: Purpose: Historically, Bifidobacterium longum subspecies infantis (B. infantis) has been an important component of the gut microbiome of infants. B. infantis is uniquely able to break down and utilize human milk oligosaccharides (HMOs) completely, which gives some strains a competitive advantage in the infant gut. However, HMOs are not in most formulas, thusformula fed infants do not have as many bifidobacteria in their microbiome. Parallel, Necrotizing Enterocolitis (NEC) is an intestinal disease affecting mainly preterm infants with a 30-50% mortality rate and a higher incidence in formula fed infants. Treatment strategies for NEC are limited and have not improved in the last few decades, prompting research into prevention strategies. One potential prevention strategy is probiotics, though there are wide variations in strain composition, product quality and potential mechanisms of action. Recent work with B. infantis EVC001 suggests that colonization with this organism may result in a more appropriate microbiome for preterm infants who generally have inappropriate gut colonization and inflammation, both of which are risk factors for NEC. Methods: Experimental NEC was induced in 14 day old C57BI/6 mice by Paneth cell depletion (IP injection with 75ug/gbw dithizone) followed seven hours later by induction of bacterial dysbiosis (gavage of Klebsiella pneumoniae 1x1011 CFU/kgbw). In addition, mice were gavaged twice with 100 ul B. infantis or MCT oil as a vehicle control with or without gavage of the HMO lacto-N-tetraose (LNT) at 250 ul/dose or water as a vehicle control. Sixteen hours after dithizone delivery we harvested serum to look at inflammatory cytokines, then sacrificed the mice and harvested intestinal tissue for injury scoring and the cecum for microbiome analysis. Results: Analysis of NEC model survival showed improved survival in mice with B. infantis exposure (82% compared to 70%,  $n \ge 8$ ). Additionally, mice given B. infantis EVC001 in our NEC model had significant 2-fold decrease in the inflammatory cytokine IL-6 (p = 0.046, n  $\ge$  7) to approximate sham levels compared to NEC mice not given B. infantis. Finally, there was a trending decrease in the inflammatory murine cytokine KC-GRO when mice were given B. infantis in our NEC model

compared to those not given the probiotic. Conclusion: This finding supports the beneficial properties of B. infantis EVC001 and drives further research looking into NEC-like injury prevention.

#### Abstract # 66

Abstract Title: Anti-inflammatory effects of vagus nerve stimulation in a newborn rat model of acute inflammation

Name: Bradley Cacho, MD

Fellow of Neonatology

**Co-Authors:** Jonathan Abdala, BS, Christopher G. Wilson, PhD, Vadim Gospodarev, MD, Douglas Deming, MD, Lianne Pak, MS

**Organization:** Loma Linda University Children's Hospital, Division of Neonatology

Abstract Overview: Neonatal sepsis and inflammation pose a potential source of morbidity and mortality in newborns. We have previously shown that vagus nerve stimulation (VNS) modulates pro-inflammatory cytokine expression in the central nervous system (CNS). The optimal VNS parameters to reduce inflammation are not known. In this randomized control trial, we tested the hypothesis that VNS reduces the expression of pro-inflammatory cytokines in a lipopolysaccharide (LPS) model of airway inflammation. We used intratracheal injections of LPS (0.5 mg/kg in 10 µL of saline) in neonatal Sprague Dawley rats (postnatal days 10 to 12) to induce pro-inflammatory cytokine expression. The pups were anesthetized with isoflurane, and then underwent midline incision and dissection to expose the trachea. LPS was injected into the trachea to mimic airway inflammation, and the vagus nerve was then isolated via blunt dissection. The experimental group received VNS at pre-selected frequencies (ranging logarithmically from 10 to 10000 Hz) continuously for 30 minutes directly after LPS injection. Stimulation current was titrated down as needed to account for apnea (typically about 0.5 mA). After recovery, each brainstem was processed for cryosectioning and immunohistochemistry. We stained for and measured the expression of cytokines IL-1 $\beta$ , TNF- $\alpha$ , and HMGB1 in subjects with or without VNS (the control group received LPS without VNS). We then used ImageJ software and the particle analysis plug-in to quantify the number of cells in the nucleus tractus solitarius that expressed these cytokines. Using one-way ANOVA, we showed a significant decrease (p < 0.05) in the expression of IL-1 $\beta$ , TNF- $\alpha$ , and HMGB1 in LPS-injected rats that underwent VNS compared to those who received LPS alone. IL-1β was significantly decreased at frequencies of 10, 100, 1000, and 10000 Hz, TNF-a was significantly decreased at frequencies of 10 and 1000 Hz, and HMGB1 was significantly decreased at frequencies of 1000 Hz and 10000 Hz. Cytokine expression in the LPS + VNS group was similar when compared to sham rats (no LPS injection and no VNS). Our study showed that VNS at various frequencies significantly decreased the expression of early inflammatory cytokines in LPSinjected neonatal rats. Blocking the early cytokine cascade may be associated with decreased inflammation and a concomitant reduction in associated symptoms in patients with sepsis. VNS used either alone or in conjunction with antibiotics may lead to improved outcomes in neonates suspected to have an infection.

#### Abstract # 68

# Abstract Title: It is possible! Reducing Central Line Usage and CLABSI using a Multidisciplinary Process

Name: Shaina Lodhi, MD

Neonatology Fellow (PGY-6)

**Co-Authors:** Elba Fayard, MD (Professor of Pediatrics; Division Chief, Neonatal-Perinatal Medicine)

Organization: Loma Linda University

Abstract Overview: Introduction: Central lines in the NICU are a common source for hospital-acquired infections. Central line-associated blood stream infections (CLABSIs) contribute greatly to neonatal morbidity and mortality. Attributable mortality with CLAB-SI is estimated to be 4% to 20%. CLABSI can increase length of stay by up to 7 days. The cost per infection can be up to \$69,000. Success in decreasing central line usage and CLABSI rates has been demonstrated in other units with a collaborative approach targeting line care bundles, monitoring compliance, and rigorous reporting. Hypothesis: Reducing line use is the most effective way to reduce CLABSI. Multidisciplinary approach to regulate insertion, maintenance and discontinuation of central lines will decrease CLABSI. Objective: To reduce central line usage and the CLABSI rate by 20% from 2017 to 2019. Methods: We created a NICU CLABSI taskforce, which included nurses, physicians, and administrative representatives. The taskforce: 1) Developed clear indications for the placement and continuation of central lines. 2) Updated bundle practices for insertion and maintenance of central line hubs and dressings. 3) Created a nursing team that inserted lines, changed dressings and checked line position on a regular bases. 4) Provided formal education on indications and maintenance of central lines to nurses and physicians. Nurses were required to discuss the reasons for keeping the central line with the medical team daily. Physicians were asked to document the location, duration and indication for central lines in daily progress notes. 5) Audited physicians compliance and sent weekly reminders to remove central lines if they no longer met criteria. Central line days/patient days, CLABSI events/1000 line days, Standardized Utilization Ratio (SUR; observed line days/ predicted line days) and Standardized Infection Ratio (SIR; observed infections/ predicted infections) were tracked from Jan 2017 to Sept 2019. Results: The ratio of central line to patient days was reduced by 23% and the rate of CLABSI/1000 line days was reduced by 40%



from 2017 to 2019. The table shows the ratio of central line to patient days, rate of CLABSI/1000 line days, SIR and SUR from 2017 to 2019. This reduction represents 28 less hospital days, and cost savings of up to \$276,000 in 2019. Conclusion: We were able to reduce central line usage and CLABSI rates in our NICU by using a multidisciplinary approach including educating the staff, mandating strict reporting, and updating and monitoring hub and dressing practices.

## Abstract # 69

Abstract Title: Maternal Hepatitis C viral (HCV) seroprevalence at birth in women with perinatal polysubstance and/or opiate exposure.

Name: Jessica Haas, ABA, RN, MSN

NICU Clinical Research Nurse Educator

**Co-Authors:** Haas JE1, Huang, A2, Stemmle, M 2 ; Davies, T 4,Jegatheesan, P2 ; Maddox, T4 ; Werthammer, J1,3 ; Govindas-wami, B1,2,3

**Organization:** Hoops Family Children's Hospital/ Cabell Huntington Hospital

Abstract Overview: Background: Guidance for HCV in pregnancy (hcvguidelines.org) by the American Association for the study of Liver diseases and Infectious Disease Society of America are not yet widely known and screening for HCV varies, particularly in high-risk populations. Maternal HCV may indicate high-risk behavior including prior maternal substance and/or perinatal opiate exposure. We have noted at our institution (center 2) that 55% of Neonatal abstinence syndrome (NAS) treated infants > 35 weeks gestation in 2017 were born to mothers who were HCV+ at the time of their birth. Objective: To determine maternal Hepatitis C prevalence in women delivering at 2 different regional perinatal safety-net centers at a University affiliated government hospital in San Jose, CA (Center 1) and Marshall University affiliated Children's hospital in Huntington, WV (Center 2). We examined maternal HCV in all liveborns including those prenatally exposed to polysubstances and/or opiates. Design/Methods: Data collected prospectively 2014-2019 in 2 regional perinatal centers were examined retrospectively to determine prevalence HCV seropositivity at delivery of all liveborn infant(s) including those subsequently managed with Neonatal Abstinence Syndrome (NAS). Methodological variation and incomplete/missing data are limitations at the time of this submission, but data examination is ongoing. Results: 35018 consecutive livebirths at 2 regional perinatal centers 2014-2019 (some data collection ongoing) are included ~19133 in center 1 and~15885 in Center 2. Substance exposure at birth occurred in 544 (2.8% of livebirths) inborn infants in center 1 and 1600 (10%) in Center 2.Opiate exposure occurred prenatally in 120 (0.6% of livebirths) infants in Center 1 and 698 in Center 2.Hepatitis C positive status was noted prior to or at birth in 0.5% (2014-2018) and 7.5% (2017-2019) of livebirths in Center 1 and Center 2 respectively, a fifteen fold variation in maternal seroprevalence at Substance exposed infants had 5.3% HCV seroprevalence in center 1 and a 39.8% seroprevalence in center 2. Opiate exposed infants had maternal HCV seroprevalence of 1% in Center 1(2014-2018) and 9.2% for centers 2(2017-2019). Conclusion(s): Maternal Hepatits C seroprevalence is 7-10 x higher in polysubstance exposed infants compared to all live-borns in our study population. An urgent public health crisis in chronic liver injury could be averted by standardized universal screening and early treatment approaches to HCV as recommended by hcvguidelines.org









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# **Medical News, Products & Information**

Compiled and Reviewed by Mitchell Goldstein, MD Editor in Chief

NIH study suggests using cannabis while trying to conceive may reduce pregnancy chances

The use of cannabis may affect fertility.

Monday, January 11, 2021

Women who use marijuana could have a more difficult time conceiving a child than women who do not use marijuana, suggests a study by researchers at the National Institutes of Health. Marijuana use among the women's partners — which could have influenced conception rates — was not studied. The researchers were led by Sunni L. Mumford, Ph.D., of the Epidemiology Branch in NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study appears in Human Reproduction.

The women were part of a larger group trying to conceive after one or two prior miscarriages. Women who said they used cannabis products — marijuana or hashish — in the weeks before pregnancy, or who had positive urine tests for cannabis use, were around 40% less likely to conceive per monthly cycle than women who did not use cannabis. The authors noted that although the findings suggest cannabis could affect women's fertility, they should be tempered with caution as the study observed a relatively small number of cannabis users. However, the authors say their results suggest that women trying to conceive should exercise caution with cannabis use until more definitive evidence is available.

The researchers analyzed data from a broader study of more than 1,200 women ages 18 to 40 with one or two pregnancy losses. The women participated in the study for up to six monthly cycles while attempting pregnancy and throughout pregnancy if conception occurred. After enrolling in the study, the women responded to a questionnaire asking if they had used marijuana, pot, or hashish in the past 12 months, with responses ranging from never, rarely, occasionally, sometimes, often, to daily. Each woman also provided urine samples for analysis when they first entered the study and after six months if they did not conceive or at the time of positive pregnancy test if they conceived.

A total of 62 women (5%) either had a positive urine test or re-

sponded that they had used cannabis before conception.

For each monthly cycle, women who had used cannabis while trying to conceive were 41% less likely to conceive than non-users. Similarly, a smaller proportion of cannabis users than non-users became pregnant during the study — 42% versus 66%. The authors found no differences in miscarriage rates between users and non-users who had achieved pregnancy.

The authors noted that, compared to non-users, cannabis users also had differences in reproductive hormones involved in ovulation. These differences could potentially have influenced their likelihood of conception. Specifically, users had higher levels of luteinizing hormone and a higher proportion of luteinizing hormone to follicle stimulating hormone.

The authors also noted that animal studies had found that cannabis use could alter the lining of the uterus, making it less likely an embryo to implant and establish a pregnancy. Until more information is available, the authors said, women trying to become pregnant should be aware that cannabis could potentially affect their pregnancy chances.

The paper can be found online after publication at: <u>https://aca-demic.oup.com/humrep/article-lookup/doi/10.1093/humrep/deaa355</u>

About the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD): NICHD leads research and training to understand human development, improve reproductive health, enhance the lives of children and adolescents, and optimize abilities for all. For more information, visit <u>https://www.nichd.nih.gov.</u>

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Contact <u>Meredith Daly or Robert Bock</u> 301-496-5133 **NT** 

American Academy of Pediatrics, Section on Advancement in Therapeutics and Technology

Released: Thursday 12/13/2018 12:32 PM, updated Saturday 3/16/2019 08:38, Sunday 11/17/2019 and Friday 11/20/2020

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NT

Stem cell treatment corrects skull shape and restores brain function in mouse model of childhood disorder

Scientists regenerate parts of the skull affected by craniosynostosis, a common birth defect.

Thursday, January 7, 2021

Using stem cells to regenerate parts of the skull, scientists corrected skull shape and reversed learning and memory deficits in young mice with craniosynostosis, a condition estimated to affect 1 in every 2.500 infants born in the United States. according to the Centers for Disease Control and Prevention. The only current therapy is complex surgery within the first year of life, but skull defects often return afterward. The study, supported by the National Institute of Dental and Craniofacial Research (NIDCR), could pave the way for more effective and less invasive therapies for children with craniosynostosis. The findings were published Jan. 7, 2021 in Cell. NIDCR is part of the National Institutes of Health.

"This is a pivotal study demonstrating both structural regeneration and functional restoration in an animal model of craniosynostosis, said Lillian Shum, Ph.D., director of NIDCR's Division of Extramural Research. "It holds great potential for translation to treatment of the human condition."

Healthy infants are born with sutures flexible tissue that fills the space between the skull bones — that allow the skull to expand as the brain grows rapidly in the first few years of life. In craniosynostosis, one or more sutures turn into bone too early, closing the gap between skull plates and leading to abnormal growth. The resulting increase in pressure inside the skull may cause physical changes in the brain that lead to thinking and learning problems.

"The connection between changes in the skull and the development of cognitive deficits had not been fully explored," said Yang Chai, D.D.S., Ph.D., director of the Center for Craniofacial Molecular Biology and associate dean of research at the Herman Ostrow School of Dentistry at the University of Southern California, Los Angeles, who led the study. "We wanted to know if restoring sutures could improve neurocognitive function in mice with mutations in a gene that causes craniosynostosis in both mice and humans."

That gene, called *TWIST1*, is thought to be important for suture formation during development. In humans, mutations in this gene can lead to Saethre-Chotzen syndrome, a genetic condition characterized by craniosynostosis and other skeletal abnormalities.

To see if flexible sutures could be restored in mice with craniosynostosis due to Twist1 mutations, the scientists focused on a group of stem cells normally found in healthy sutures. Previous studies by the group indicated that these stem cells called Gli1+ cells—are key to keeping skull sutures of young mice intact. The team had also found that Gli1+ cells are depleted from the sutures of mice that develop craniosynostosis due to *Twist1* mutations. Chai and his colleagues reasoned that replenishing the cells might help regenerate the flexible sutures in affected animals. To test this idea, the researchers added Gli1+ cells from healthy mice to a biodegradable gel. They deposited the mixture into grooves meant to re-create the space where skull sutures had been in mice with craniosynostosis.

Skull imaging and tissue analysis revealed that after six months, new fibrous sutures had formed in treated areas and that the new tissue remained intact even after a year. In contrast, the same grooves closed in mice that received a gel that lacked Gli1+ cells.

Closer analysis showed that Gli1+ cells in the regrown sutures had different origins: some were descended from the cells that had been implanted, while others were the animals' own, having migrated from nearby areas. The findings suggest that Gli1+ cell implantation leads to suture regeneration in part by recruiting native Gli1+ stem cells to help in the process.

Further experiments showed that untreated mice with craniosynostosis had increased pressure inside their skulls and poor performance on tests of social and spatial memory and motor learning. After treatment, these measures all returned to levels typical of healthy mice. The skull shapes of treated mice were also partially corrected.

The treatment also reversed the loss of brain volume and nerve cells in areas involved in learning and memory. According



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"We have discovered that Gli1+ stem-cellbased suture regeneration restores not only skull shape but also neurocognitive functions in a mouse model of craniosynostosis," said Chai.

The scientists note that more work remains before such an intervention can be tested in humans, including studies to determine the optimal timing of surgery and the ideal source and amount of stem cells.

"This study provides a foundation for efforts to develop a less-invasive, stem cell-based therapeutic strategy that can benefit patients who suffer from this devastating disorder," Chai said.

This research was supported by NIDCR grants <u>R01-DE026339</u>, <u>R01-DE012711</u>, <u>R01-DE022503</u>, and <u>U24-DE026914</u>.

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Institute/Center <u>National Institute of Dental and Craniofa-</u> <u>cial Research (NIDCR)</u>

Contact Catherine Evans, Ph.D. 301-594-7557

# DNA-editing method shows promise to treat mouse model of progeria

Using a recently developed DNA base-editing technique, researchers correct accelerating aging disorder.

Wednesday, January 6, 2021

Researchers have successfully used a DNA-editing technique to extend the lifespan of mice with the genetic variation associated with progeria, a rare genetic disease that causes extreme premature aging in children and can significantly shorten their life expectancy. The study was published in the journal *Nature*, and was a collaboration between the National Human Genome Research Institute (NHGRI), part

> A global initiative to stop Congenital Diaphragmatic Hernia







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of the National Institutes of Health; Broad Institute of Harvard and MIT, Boston; and the Vanderbilt University Medical Center, Nashville, Tennessee.

DNA is made up of four chemical bases — A, C, G and T. Progeria, which is also known as Hutchinson-Gilford progeria syndrome, is caused by a mutation in the nuclear lamin A (*LMNA*) gene in which one DNA base C is changed to a T. This change increases the production of the toxic protein progerin, which causes the rapid aging process.

Approximately 1 in 4 million children are diagnosed with progeria within the first two years of birth, and virtually all of these children develop health issues in childhood and adolescence that are normally associated with old age, including cardiovascular disease (heart attacks and strokes), hair loss, skeletal problems, subcutaneous fat loss and hardened skin.

For this study, researchers used a breakthrough DNA-editing technique called <u>base</u> <u>editing(link is external)</u>, which substitutes a single DNA letter for another without damaging the DNA, to study how changing this mutation might affect progeria-like symptoms in mice.

"The toll of this devastating illness on affected children and their families cannot be overstated," said Francis S. Collins, M.D., Ph.D., a senior investigator in NHGRI's Medical Genomics and Metabolic Genetics Branch, NIH director and a corresponding author on the paper. "The fact that a single specific mutation causes the disease in nearly all affected children made us realize that we might have tools to fix the root cause. These tools could only be developed thanks to long-term investments in basic genomics research."

The study follows another recent milestone for progeria research, as the <u>U.S. Food</u> and Drug Administration approved the

first treatment for progeria in November 2020, a drug called lonafarnib. The drug therapy provides some life extension, but it is not a cure. The DNA-editing method may provide an additional and even more dramatic treatment option in the future.

David Liu, Ph.D., and his lab at the Broad Institute developed the base-editing method in 2016, funded in part by NHGRI.

"CRISPR editing, while revolutionary, cannot yet make precise DNA changes in many kinds of cells," said Dr. Liu, a senior author on the paper. "The base-editing technique we've developed is like a findand-replace function in a word processor. It is extremely efficient in converting one base pair to another, which we believed would be powerful in treating a disease like progeria."

To test the effectiveness of their base-editing method, the team initially collaborated with the Progeria Research Foundation to obtain connective tissue cells from progeria patients. The team used the base editor on the *LMNA* gene within the patients' cells in a laboratory setting. The treatment fixed the mutation in 90% of the cells.

"The Progeria Research Foundation was thrilled to collaborate on this seminal study with Dr. Collins's group at the NIH and Dr. Liu's group at Broad Institute," said Leslie Gordon, M.D., Ph.D., a co-author and medical director of The Progeria Research Foundation, which partially funded the study. "These study results present an exciting new pathway for investigation into new treatments and the cure for children with progeria."

Following this success, the researchers tested the gene-editing technique by delivering a single intravenous injection of the DNA-editing mix into nearly a dozen mice with the progeria-causing mutation soon after birth. The gene editor successfully restored the normal DNA sequence of the *LMNA* gene in a significant percentage of cells in various organs, including the heart and aorta.

Many of the mice cell types still maintained the corrected DNA sequence six months after the treatment. In the aorta, the results were even better than expected, as the edited cells seemed to have replaced those that carried the progeria mutation and dropped out from early deterioration. Most dramatically, the treated mice's lifespan increased from seven months to almost 1.5 years. The average normal lifespan of the mice used in the study is two years.

"As a physician-scientist, it's incredibly exciting to think that an idea you've been working on in the laboratory might actually have therapeutic benefit," said Jonathan D. Brown, M.D., assistant professor of medicine in the Division of Cardiovascular Medicine at Vanderbilt University Medical Center. "Ultimately our goal will be to try to develop this for humans, but there are additional key questions that we need to first address in these model systems."

Funding for the study was supported in part by NHGRI, the NIH Common Fund, the National Institute of Allergy and Infectious Diseases, the National Institute of Biomedical Imaging and Engineering, the National Institute of General Medical Sciences, the National Heart, Lung and Blood Institute and the National Center for Advancing Translational Sciences.

The National Human Genome Research Institute (NHGRI) is one of the 27 institutes and centers at the NIH, an agency of the Department of Health and Human Services. The NHGRI Division of Intramural Research develops and implements technology to understand, diagnose and treat genomic and genetic diseases. Additional information about NHGRI can be found at: https://www.genome.gov.

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National Human Genome Research Institute (NHGRI)

Contact <u>Alyssa Jones</u> 301-529-7228

NT

# Large clinical trial will test combination monoclonal antibody therapy for mild/moderate COVID-19

Monoclonal antibody study may have implications for the treatment of COVID-19 symptomatology.

Tuesday, January 5, 2021

A Phase 2/3 clinical trial has begun to evaluate a combination investigational monoclonal antibody therapy for its safety and efficacy in people who have mild or moderate COVID-19. The two experimental antibodies, BRII-196 and BRII-198, target SARS-CoV-2, the virus that causes COVID-19. The trial, known as ACTIV-2, is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (AC-TIV) program is a public-private partnership to develop a coordinated research strategy for speeding development of the most promising treatments and vaccine candidates. ACTIV-2 is a master protocol designed for evaluating multiple investigational agents compared to placebo in adults with mild-to-moderate COVID-19. The trial, led by the NIAIDfunded AIDS Clinical Trials Group (ACTG) and supported by PPD (Wilmington, North Carolina), will enroll participants at sites around the world.

The ACTIV-2 study began on Aug. 4, 2020, with an evaluation of LY-CoV555, an investigational monoclonal antibody discovered by AbCellera Biologics (Vancouver, British Columbia) in collaboration with NIAID's Vaccine Research Center. LY-CoV555 was developed further and manufactured by Eli Lilly and Company (Indianapolis, Indiana), in partnership with AbCellera. On Nov. 10, 2020, LY-CoV555, also known as bamlanivimab, was granted Emergency Use Authorization by the U.S. Food and Drug

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Administration(link is external) for treating mild-to-moderate COVID-19 in adults and children over 12 years old who are at high risk for progressing to severe COVID-19 and/or hospitalization. With the initiation of the BRII-196 and BRII-198 experimental monoclonal antibodies in the ACTIV-2 study, the LY-COV555 sub-study will close to enrollment.

BRII-196 and BRII-198 are investigational, neutralizing monoclonal antibodies manufactured by Brii Biosciences (Durham, North Carolina, and Beijing). Antibodies are infection-fighting proteins naturally made by the immune system that can bind to viruses and prevent them from infecting cells. BRII-196 and BRII-198 are synthetic versions of antibodies produced naturally by humans. Data on each antibody from Phase I trials that are currently ongoing support the doses being used in the AC-TIV-2 trial.

The ACTIV-2 study design allows researchers to observe the therapeutics' efficacy in a small group of volunteers and then administer it to a larger group if the antibody appears safe and effective. The trial will initially enroll 220 participants with mild or moderate COVID-19, who are at risk for disease progression. Half of the participants (110) will receive BRII-196 and BRII-198 through intravenous infusions, while the remaining half will receive placebo infusions. Participants are assigned at random to one of the treatment groups, and the trial is blinded so neither participants nor investigators will know who is receiving the antibody therapy. Participants will attend a series of clinic or at-home visits by clinicians to track their condition and will be followed for a total of 72 weeks.

An independent Data and Safety Monitoring Board (DSMB) overseeing the trial will review the data collected at 28 days. They will monitor data to see if the therapy is safe, can reduce the duration of COVID-19 symptoms and can eliminate the presence of viral RNA in the body. If there are no serious safety concerns and the results seem promising, the trial will transition to Phase 3 to enroll approximately 622 additional outpatient volunteers, for a total of 842 trial participants. These new participants will be randomized to receive the therapeutic or a placebo.

The primary objective of the Phase 3 trial is to determine if the therapy prevents either hospitalization or death by 28 days after study entry.

The study team for ACTIV-2 is led by protocol chairs Kara W. Chew, M.D., M.S., of the University of California, Los Angeles (UCLA), and Davey Smith, M.D., MAS, of the University of California, San Diego. Eric S. Daar, M.D., of UCLA, and David Wohl, M.D., of the University of North Carolina at Chapel Hill (UNC), serve as protocol vicechairs. The ACTG network is led by chair Judith Currier, M.D. (UCLA) and vice-chair Joseph Eron, M.D., of UNC. The study of BRII-196 and BRII-198 is led by Eric S. Daar, M.D., of the Harbor-UCLA Medical Center and Teresa H. Evering, M.D., M.S., of Weill Cornell Medical Center, New York City.

For more information on this study, please visit www.riseabovecovid.org(link is external), or visit clinicaltrials.gov and search identifier NCT04518410.

NIAID conducts and supports research at NIH, throughout the United States, and worldwide — to study the causes of infectious and immune-mediated diseases, and to develop better means of preventing, diagnosing and treating these illnesses. News releases, fact sheets and other NIAID-related materials are available on the NIAID website.

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Institute/Center National Institute of Allergy and Infectious Diseases (NIAID)

Contact

NIAID News & Science Writing Branch 301-402-1663

ΝΤ

Higher red cell transfusion threshold offers no advantage for treating preterm infants

Transfusion guidelines may not provide benefit..

Wednesday, December 30, 2020

What

Very low birthweight infants often need blood transfusions to survive. A National Institutes of Health-funded study suggests that providing a higher threshold of red cells within accepted limits offers no advantage in survival or reduction in neurological impairment over a lower threshold. The research was conducted

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by Haresh Kirpalani, B.M., of the University of Pennsylvania, Philadelphia, and colleagues and was funded by the NIH's *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), National Heart, Lung, and Blood Institute, and National Center for Advancing Translational Sciences. The study appears *in The New England Journal of Medicine*.

Very preterm infants (born before 29 weeks of pregnancy) and those weighing less than 1,000 grams (slightly more than 2 pounds) are at high risk for anemia because of their early stage of development, reduced ability to produce red blood cells and need for increased blood sampling as part of their intensive medical care. Previous studies suggest that anemic infants would have a lower risk of death, cognitive delay, cerebral palsy and hearing and vision loss if they received transfusions leading to higher hemoglobin thresholds within the currently accepted range. Measuring hemoglobin, a protein produced in red blood cells, indicates the proportion of red blood cells. Hemoglobin transfusion thresholds for preterm infants vary according to weight, stage of maturity and other factors.

Of 845 infants assigned to a higher hemoglobin threshold, 50.1% died or survived with a neurodevelopmental impairment, compared to 49.8% of 847 infants assigned to a lower threshold. When the two component outcomes were evaluated separately, the two groups also had similar rates of death (16.2% vs. 15%) and of neurodevelopmental impairment (39.6% vs 40.3%). The authors conclude that a higher hemoglobin threshold increased the number of transfusions, but did not improve the chance of survival without neurodevelopmental impairment.

#### Who

Andrew Bremer, M.D., Acting Chief, NICHD Pregnancy and Perinatology Branch, is available for comment.

# Article

Kirpalani, H., et al. High or low hemoglobin transfusion thresholds for preterm infants. *New England Journal of Medicine*. 2020. About the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD): NICHD leads research and training to understand human development, improve reproductive health, enhance the lives of children and adolescents, and optimize abilities for all. For more information, visit https://www. nichd.nih.gov.

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NT

# Infant opioid withdrawal therapy varies widely by treatment site

Treatment guidance for withdrawal differs from site to site.

Tuesday, December 22, 2020

What

Medical care for newborn infants who were exposed to opioids in the womb varied widely across 30 hospitals nationwide, according to a study funded by the National Institutes of Health. The study authors say that the findings underscore the need for clinical trials to determine the most effective treatments.

The study was conducted by Leslie Young, M.D., of the University of Vermont and colleagues in the Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW) Program, part of NIH's Helping to End Addiction Long-term Initiative. It appears in the journal *Pediatrics*.

Opioid use disorder during pregnancy increased(link is external) from 1.5 to 6.5 for every 1,000 hospital deliveries from 1999 to 2014, according to the U.S. Centers for Disease Control and Prevention. Opioid use during pregnancy increases the risk for maternal death, miscarriage, poor fetal growth and preterm birth. Newborns who are exposed to opioids in the womb may also have withdrawal symptoms that require medication treatment.

ACT NOW study sites varied widely in the proportion of pregnant women who received medication-assisted treatment (from roughly 6% to 100%) and prenatal counseling (roughly 2% to about 75%). Sites also varied greatly in the proportion of newborns receiving therapy with a replacement opioid (about 7% to 100%) and therapy with a secondary medication to further ease the infants' withdrawal symptoms (roughly 1% to roughly 70%).

The study authors concluded that understanding the wide variation in treatment offered to opioid-addicted mothers and their infants is an important first step for planning future studies and treatment programs.

Funding for the study was provided by NIH's *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the Environmental influences on Child Health Outcomes (ECHO) Program in NIH's Office of the Director.

Who





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PAC/LAC 1010 N. Central Ave Glendale, CA 91202 Andrew Bremer, M.D., Acting Chief of the NICHD Pregnancy and Perinatology Branch, and

Alan Simon, M.D., Medical Officer in the ECHO IDeA States Pediatric Clinical Trials Network, are available for comment.

Article

Young, LW, et al. Site level variation in the characteristics and care of infants with neonatal opioid withdrawal. *Pediatrics.* 2020.

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About the Environmental influences on Child Health Outcomes (ECHO) Program: ECHO aims to enhance the health of children for generations to come. Research conducted through ECHO focuses on five key pediatric outcomes: pre-, peri- and postnatal outcomes; upper and lower airway health; obesity; neurodevelopment; and positive health. For more information, visit: <u>https://echochildren.org</u>.

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ΝΤ

# Pregnant women in third trimester unlikely to pass SARS-CoV-2 infection to newborns

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Babies delivered at term may be less at risk for COVID.

Tuesday, December 22, 2020

Pregnant women who are infected with SARS-CoV-2, the virus

# **Keeping Your Baby Safe**

during the COVID-19 pandemic

# How to protect your little one from germs and viruses

Even though there are some things we don't know about COVID-19 yet, there are many more things that we do know. We know that there are proven protective measures that we can take to stay healthy.

# Here's what you can do...

#### Wash Your Hands Limit Contact with Others This is the single, most important thing you can Stay home when you can. do to stop the spread of Stay 6 feet apart when out. Use soap. Change your clothes when Wash for you get home. more than 20 seconds you're doing to Use alcoholstay safe. based sanitizers **Provide Protective** Take Care of Immunity Yourself Hold baby skin-to-skin. Stay connected with your family and friends. Give them your breast milk. Sleep when you can. Drink more water and Stay current with eat healthy foods your family's mmunizations Seek mental health support Immunizations Vaccinations save lives. Protecting your baby from flu and pertussis lowers their risks for complications from coronavirus. Never Put a Mask on Your Baby Z RNII Because babies have smaller airways, a mask makes it hard for them to breathe. Masks pose a risk of strangulation and suffocation. AN A baby can't remove their mask if they're suffocating If you are positive for COVID-19 Wash with soap and water and put on fresh clothes before holding or feeding your baby. · Wear a mask to help stop the virus from spreading. · Watch out for symptoms like fever, confusion, or trouble breathing. Ask for help caring for your baby and yourself while you recover.

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# flu coronavirus

pertussis





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# GET VACCINATED

for flu and pertussis. Ask about protective injections for RSV.

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that causes COVID-19, during the third trimester are unlikely to pass the infection to their newborns, suggests a study funded by the National Institutes of Health. The study followed 127 pregnant women who were admitted to Boston hospitals during the spring of 2020. Among the 64 pregnant women who tested positive for SARS-CoV-2, no newborns tested positive for the virus. NIH support was provided by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Heart, Lung, and Blood Institute (NHLBI), and the National Institute of Allergy and Infectious Diseases (NIAID).

"This study provides some reassurance that SARS-CoV-2 infections during the third trimester are unlikely to pass through the placenta to the fetus, but more research needs to be done to confirm this finding," said Diana W. Bianchi, M.D., NICHD Director.

The study, published in the journal *JAMA Network Open*, was led by Andrea G. Edlow, M.D., M.Sc., of Massachusetts General Hospital and Harvard Medical School.

The researchers studied the occurrence of SARS-CoV-2 infection in the third trimester of pregnancy, evaluating levels of virus in respiratory, blood and placental tissue samples, the development of maternal antibodies, how well those antibodies passed through the placenta to the fetus (an indicator of potential immune protection from the mother) and examined placental tissue. The results reported are limited to women in the third trimester because data on women infected during the first and second trimesters are still being collected and evaluated.

Among those who tested positive for SARS-CoV-2 in the study, 36% (23/64) were asymptomatic, 34% (22/64) had mild disease, 11% (7/64) had moderate disease, 16% (10/64) had severe disease, and 3% (2/64) had critical disease. The study included, as comparators, 63 pregnant women who tested negative for SARS-CoV-2 and 11 reproductive-age women with COVID-19 who were not pregnant.

The team found that pregnant women who were positive for SARS-COV-2 had detectable levels of virus in respiratory fluids like saliva, nasal and throat secretions, but no virus in the blood-stream or the placenta.

The researchers did not find significant differences between levels of SARS-CoV-2 antibodies produced by pregnant and non-pregnant women. However, the study team did observe lower-thanexpected levels of protective antibodies in umbilical cord blood. In contrast, they found high levels of influenza-specific antibodies, presumably from maternal flu vaccination, in the cord blood samples of both SARS-CoV-2 positive and negative women. The researchers suggest these findings may indicate that SARS-CoV-2 antibodies do not pass through the placenta as easily as other maternal antibodies.

The researchers believe theirs is one of the first reports of lessthan-expected transfer of SARS-CoV-2 antibodies to the fetus. Low transfer of these antibodies was observed regardless of the woman's severity of COVID-19 or whether she had an underlying health condition, such as obesity, high blood pressure or diabetes. The study authors noted that it will be important to determine why these maternal antibodies are less likely to cross the placenta and whether this reduced antibody transfer renders newborns more vulnerable to SARS-CoV-2 infection, compared to other infections. The authors added that it will be important to determine how lower levels of maternal SARS-CoV-2 antibodies may affect health outcomes of preterm babies because COVID-19 may increase the risk of preterm labor.

The study also found that placentas from infected women were not different from those of uninfected women, though the risk for ischemia (reduced blood flow) in the placenta appeared higher for women with more severe COVID-19. In line with an <u>earlier report</u>, the researchers also found that while the placenta expresses major molecules used by SARS-CoV-2 to cause infection — the ACE2 receptor and the TMPRSS2 enzyme — the two molecules are rarely expressed together in the same location, which may help explain why the virus only rarely affects the placenta.

The researchers suggest their findings could help improve the care of pregnant women with COVID-19 and of their newborns, as well as provide information to assist in the development of new strategies for vaccinating pregnant women.

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# COVID-19

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#### Article

Edlow AG, *et al.* Assessment of maternal and neonatal SARS-CoV-2 viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 pandemic. *JAMA Network Open* DOI: 10.1001/jamanetworkopen.2020.30455 (2020)

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142



# Genetics Corner: Trichothiodystrophy 1 Causes Neutropenia in an Infant with Congenital ichthyosis and Brittle Hair

Robin Dawn Clark, MD and Subhadra Ramaanthan, MSc, MS

## **Clinical history:**

A 10-month old male infant was referred for genetic evaluation for trichothiodystrophy 1.

He was delivered at ~32 weeks' gestation by C-section when his 23-year old G2 P1-->2 mother developed HELLP syndrome. His prenatal course had been complicated by IUGR and decreased fetal movements. Birth weight: 1474 grams (17<sup>th</sup> %ile). Birth length: 41.9 cm (33<sup>rd</sup> %ile). Apgar scores were 9 and 9 at 1 and 5 minutes, respectively. He had taut, shiny skin on his upper and lower extremities at birth, resembling collodion, which peeled during resuscitation. He was transferred from the birth hospital to the NICU at a nearby tertiary care center because of congenital ichthyosis, left eyelid fusion, and right cryptorchidism. His CBC and differential were normal.

At 18 days of age, the results of a rapid whole genome sequencing test identified biallelic variants in *ERCC2* (or *XPD*)

c.2164C>T (p.Arg722Trp): pathogenic, paternally inherited

c.5+5G>A: a splicing variant of uncertain significance, maternally inherited

The infant was discharged on day 23 of life with a diagnosis of trichothiodystrophy-1.

At ten months of age, he was in generally good health. His mother had rescheduled his genetics clinic visit the previous month, and she had no particular concerns. She was satisfied that his "skin condition" was being managed and was not severe. He had a follow up (video) appointment with a dermatologist at six months of age. An ophthalmology evaluation revealed dry eyes but no cataracts. An otolaryngologist had seen him for recurrent impacted cerumen.

# Genetic evaluation:

The infant had been mostly at home without much contact outside his immediate family because of the coronavirus restrictions. He had a history of one prior febrile illness with symptoms of a cold lasting about two weeks; he recovered but still had a persistent cough. He babbled and cooed. He had good eye contact, a social smile, and turned to his name. His mother reported that his developmental progress was "normal," but at ten months of age, he could only maintain a seated position for a few seconds.

The family history was noncontributory. The non-consanguineous parents, mother, age 24, and father, age 25, were of Mexican ancestry. They had one other child, a healthy 4-year old boy.

On physical examination, the growth parameters were poor for a 10-month-old male. Weight <1 %ile (Z= -2.47). Length <1 %ile (Z= -3.45), BMI 16.27 kg/m<sup>2</sup>, 30 %ile (Z= -0.54). The baby was socially aware, interactive, and in no distress. He had deep-set eyes, down-slanting palpebral fissures, and bilateral epicanthal folds. There were sparse eyebrows and eyelashes (Figure 1). The

scalp hair was sparse (Figure 2) with thick, waxy flakes and scales on the scalp. He had patchy areas of ichthyosis, mostly on the trunk and antecubital fossa. He had shiny skin on his palms, thin, dystrophic nails (toes>fingers), and shallow, short, concave nails.

The geneticist referred him to Pediatric Hematology and Pediatric Immunology, recommended RSV vaccination, and ordered an absolute neutrophil count (ANC). He had neutropenia: WBC 5.2, hemoglobin 12.8, platelets 312, ANC 0.4 (normal range 2.2-9.2 bil/L), but the ANC had normalized two weeks later at 6.6.

At 11 months of age, he was hospitalized briefly for neutropenia (ANC 0.6), dry cough, and fever to 101.7 degrees without a documented source of infection (cultures were negative). The source of the infection was presumed to be viral. His differential had lymphocyte predominance without excess bands. His growth parameters then were still generally small for his age: Ht 70.5 cm, 2 %ile (Z= -2.10), Wt 7.11 kg, <1 %ile (Z= -2.71), HC 44 cm, 6 %ile (Z= -1.55), BMI 14.31 kg/m<sup>2</sup> 2 %ile (Z= -2.09). At 13 months of age, he had an in-person visit with the pediatric dermatologist who documented tiger-tail banding on polarized trichoscopy (Figure 3).

"ERCC2 is a protein that acts as a DNA helicase in transcriptioncoupled nucleotide excision repair and phosphorylation of nuclear receptors. Cells use nucleotide excision repair to fix damaged DNA, including damage from ultraviolet radiation."

#### Assessment and counseling:

ERCC2 is a protein that acts as a DNA helicase in transcriptioncoupled nucleotide excision repair and phosphorylation of nuclear receptors. Cells use nucleotide excision repair to fix damaged DNA, including damage from ultraviolet radiation. Pathogenic variants in *ERCC2* (*XPD*) are associated with a group of autosomal recessive disorders, including trichothiodystrophy (TTD) with sulfur-deficient brittle hair and developmental abnormalities but without skin cancer, xeroderma pigmentosum (XP) with pigmentary abnormalities and increased skin cancer, XP/TTD with combined

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"Signs and symptoms of TTD vary widely and include ichthyosis, abnormal fingernails and toenails, developmental delays, intellectual disability, dysmyelination, and cerebral atrophy."

Signs and symptoms of TTD vary widely and include ichthyosis, abnormal fingernails and toenails, developmental delays, intellectual disability, dysmyelination, and cerebral atrophy. Some patients with neurological abnormalities are described to have an outgoing, sociable personality), delayed growth, short stature, dry eye, microcornea, nystagmus, congenital cataracts, neutropenia,



Figure 1: This infant with trichothiodystrophy has sparse hair and eyebrows, short and down-slanting palpebral fissures and deep=set eyes



Figure 2: Note the broken hairs and waxy scales on the scalp

recurrent, sometimes life-threatening infections, and decreased fertility. Mild cases may involve only brittle, sulfur-deficient hair that displays a diagnostic alternating light and dark banding pattern, called 'tiger tail banding (Figure 3).

More severe presentation of TTD includes delayed development, significant intellectual disability, and recurrent infections. Severely affected individuals may have limited survival. Increased mortality is due to infection. In 2008, Faghri and colleagues published a comprehensive review of 112 patients with TTD, documenting recurrent infections in 35%. They noted early mortality with a 20-fold increased risk of death before the age of 10 years, the majority secondary to infection (pneumonia or sepsis). Randall and colleagues (2018) encourage IVIG or granulocyte colony-stimulating factor therapy for patients with TTD who have severe neutropenia or low levels of IgG. RSV immunization is recommended (personal communication, D.Tamura, NIH) because of the increased mortality associated with this viral infection among infants with TTD. The family was offered enrollment in a clinical trial at the NIH on TTD, xeroderma pigmentosum, and Cockayne syndrome.



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Figure 3: Tiger tail banding is evident on this polarized microscopic view of hair from this patient with trichothiodystrophy.

Tamura and associates (2011) found a high risk of pregnancy and neonatal complications in their cohort of 27 TTD-associated pregnancies in 23 mothers. There were pregnancy complications in 81%: 56% had a preterm delivery, 30% had preeclampsia, 19% had placental abnormalities, 11% had HELLP syndrome, and 4% had an emergency c-section for fetal distress, while 44% had two or more complications. Only 19% of the pregnancies delivered at term without complications. Eight of the ten pregnancies tested had multiple abnormal screening markers, including elevated human chorionic gonadotrophin levels. Eighty-five percent of the neonates had complications: 70% were low birth weight (<2500 g), 35% had birth weight <10<sup>th</sup> centile for gestational age, 70% had NICU admission, 67% had a collodion membrane, and 31% of the 16 males had cryptorchidism. Cataracts were present in 54% of the TTD patients examined.

Although the diagnosis of this rare disease, trichothiodystrophy, was made quickly in this baby, he did not fully benefit from having an early diagnosis in the newborn period. He was discharged home from the NICU shortly after the diagnosis was made, and the focus of his subsequent care was on treating his ichthyosis, which was felt to be the major problem of his disorder. The mildness of his skin problems may have falsely reassured his family

and his care team. The primary threat to his health was neutropenia and a high risk of infection; these were not appreciated until we alerted his care team. As rapid whole-genome sequencing becomes more available, neonatologists will have to rise to the challenge to realize the benefits and care coordination of early diagnoses for their patients.

#### **Practical applications:**

- 1. Understand that the benefits of a rapid genome sequencing test in the neonatal period may not be fully realized without careful phenotyping and coordinated multispecialty follow-up
- 2. Appreciate that pathogenic variants in one gene can cause several disorders.
- 3. Realize that trichothiodystrophy poses severe risks of neutropenia, infection, and increased mortality for affected infants. Offer RSV immunization to infants with trichothiodystrophy and follow for neutropenia
- 4. Recognize that HELLP syndrome in the mother can be a sign of a genetic disorder, such as trichothiodystrophy, in the fetus.

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Disclosures: The authors have no relevant disclosures.

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#### **OPIOIDS and NAS**

When reporting on mothers, babies, and substance use LANGUAGE MATTERS



#### I am not an addict.

I was exposed to substances in utero. I am not addicted. Addiction is a set of behaviors associated with having a Substance Use Disorder (SUD).

#### I was exposed to opioids.

While I was in the womb my mother and I shared a blood supply. I was exposed to the medications and substances she used. I may have become physiologically dependent on some of those substances.



# NAS is a temporary and treatable condition.

There are evidence-based pharmacological and non-pharmacological treatments for Neonatal Abstinence Syndrome.



#### My mother may have a SUD.

She might be receiving Medication-Assisted Treatment (MAT). My NAS may be a side effect of her appropriate medical care. It is not evidence of abuse or mistreatment.

#### My potential is limitless.

I am so much more than my NAS diagnosis. My drug exposure will not determine my long-term outcomes. But how you treat me will. When you invest in my family's health and wellbeing by supporting

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Medicaid and Early Childhood Education you can expect that I will do as well as any of my peers!

Learn more about Neonatal Abstinence Syndrome at www.nationalperinatal.org





#### Editors: Martin, Gilbert, Rosenfeld, Warren (Eds.)



evidence-based, step-by-step approach for their diagnosis and management. *Common Problems in the Newborn Nursery* is an easy-to-use, practical guide, covering a full range of clinical dilemmas: bacterial and viral infections, jaundice, hypoglycemia, hypotonia, nursery arrhythmia, developmental dysplasia of the hips, newborn feeding, cardiac problems, late preterm infants, dermatology, anemia, birth injuries, ocular issues, and hearing assessments in the newborn.

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#### White Privilege & Why NICUs Should Care

Deb Discenza



The National Coalition for Infant Health is a collaborative of more than 200 professional, clinical, community health, and family support organizations focused on improving the lives of premature infants through age two and their families. NCfIH's mission is to promote lifelong clinical, health, education, and supportive services needed by premature infants and their families. NCfIH prioritizes safety of this vulnerable population and access to approved therapies.

" In the year 2020, where COVID showed the realities of the disparities among African American families, the brutality of those disparities, and the racism on which they were created, the Alliance for Black NICU Families was our part of making infrastructural change specifically in the NICU parent and professional communities ongoing."

In late December, I received our new non-profit designation letter from the IRS. The Alliance for Black NICU Families (<u>https://Black-NICUFamilies.org</u>) was in place. My co-founder, Ashley Randolph, celebrated with me by phone. In the year 2020, where COVID



showed the realities of the disparities among African American families, the brutality of those disparities, and the racism on which they were created, the Alliance for Black NICU Families was our part of making infrastructural change specifically in the NICU parent and professional communities ongoing. It was beyond overdue and something I had spoken to during board and steering committee meetings regularly. I am not Black myself, but I saw too much that had yet to be addressed in our community, so I

"Mayhem occurred at every entrance to the building resulting in "patriots" breaking through doors and windows and entering with every intent of "taking back the country." Like you, I watched how the Capitol Hill Police were outnumbered and overwhelmed. "

stepped up to do what was needed.

Fast forward to Wednesday, January 6, 2021, our nation's Capital came under siege as the 2020 electoral votes were being certified for then President-Elect Joe Biden. Mayhem occurred at every entrance to the building resulting in "patriots" breaking through doors and windows and entering with every intent of "taking back the country." Like you, I watched how the Capitol Hill Police were outnumbered and overwhelmed. I also watched as some of the officers were high-fiving rioters and taking selfies, too. In the aftermath, the Capitol Hill Police chief resigned, feeling he had failed his officers. As it turns out, he had been requesting help for many days and weeks ahead of the certification. His Pentagon bosses deemed it not necessary as one of them felt that the "optics looked bad." Seriously? Well, the scene looked way worse, as it turned out. It was horrific and also the very definition of White Privilege on full display. As the rioters looted and destroyed congressional offices as they beat officers with various weapons, others chose to



**Safety.** Premature infants are born vulnerable. Products, treatments and related public policies should prioritize these fragile infants' safety.

**Access**. Budget-driven health care policies should not preclude premature infants' access to preventative or necessary therapies.

**Nutrition.** Proper nutrition and full access to health care keep premature infants healthy after discharge from the NICU.

**Equality.** Prematurity and related vulnerabilities disproportionately impact minority and economically disadvantaged families. Restrictions on care and treatment should not worsen inherent disparities. cement the moment in other ways with pictures alongside statutes as they waved a Trump 2020 flag or meandered down a hall with a large Confederate flag. For days I shook with anger and was equally devastated. I attended the Women's March in 2017 as 1.2 million people of every type of background attended and marched peacefully throughout the city filled with military trucks, tanks, and police vehicles. And note that all of this, plus full riot gear, rubber bullets, and tear gas was in place for the Black Lives Matter protests. The contrasts are glaringly apparent to this month's utter thuggery—shame on us.

So what does this blatant White Privilege have to do with Neonatology? A lot, as it turns out. Studies are now showing that Black newborn babies under the care of a white doctor are at a high risk of dying. 20% of the babies in the NICU are Black. Do the math. *It is painful.* 

"Add to this learning that my fellow Preemie Moms that were Black and the families they served never received any educational materials or given any sense of how to advocate for their child."

Add to this learning that my fellow Preemie Moms that were Black and the families they served never received any educational materials or given any sense of how to advocate for their child. Knowing that she was at high risk for preterm birth, my co-founder found out that the 17p shots were not going to be covered. She had to move states to get what she needed to help her baby have a safe start to life. I have one close friend whose son was supposed to be taken to the eye doctor for ROP follow-up, but no one had told the family at discharge. Today, he is blind, despite the family's heroic efforts after the fact. And, another family had security called on the father in the operating room as his wife had an emergency csection to save her life and that of the child just because he was asking questions. Imagine weeks later when this same family got a call from the NICU the morning of the baby's discharge date to tell them that their son died. All of these families were Black. Surreal.

White Privilege is receiving care without security being called. It

"White Privilege is receiving care without security being called. It is also getting the resources and educational materials needed to make informed decisions and appropriate follow-ups as well. It is not having to look over your shoulder all of the time while caring for your baby in the NICU. " is also getting the resources and educational materials needed to make informed decisions and appropriate follow-ups as well. It is not having to look over your shoulder all of the time while caring for your baby in the NICU. It is not having to endure microaggressions and outright racist behavior from a NICU provider simply because you have a different skin color. Add to this the White Privileged Moms who have enough means to buy their baby needed items and access to specialized healthcare outlets and equipment as well as time off from work and/or childcare for appointments, etc. And do not even get me started on the lack of access to decent housing, food, and medications as well as jobs, benefits, and equal compensation. The stark difference is horrific and shameful. I was one of those privileged Moms, and I had no idea that this was a problem 17 years ago. White Privilege is assuming that everyone else is treated as well as you are. It is time for a change.

We need to do better for these families. Everyone entering the NICU deserves equal care, respect, equal access to help, and so much more. Racism is insidious, and if I hear from one more professional on social media that "Racism is not in our NICU," I will scream. Racism in the NICU happens quietly in rooms, behind doors with a word, a look, a feeling of unwelcome. It is not always the blatant encounters one sees in the movies.

Join us as we make real, positive change. Change happens when good people join hands in partnership and work together. The Alliance for Black NICU Families welcomes organizational partners across the country to help us mandate annual implicit bias training for NICU professionals state by state and endorses the Once Upon a Preemie Academy for its unique approach. We are also working to provide families and African American-led NICU/preemie organizations with grants to further their work.

Disclosures: Deb is a co-Founder of The Alliance for Black NICU Families (<u>https://blacknicufamilies.org</u>), and the Founder of PreemieWorld, LLC (<u>https://preemieworld.com</u>) as well as Crystal Ball Health, LLC (<u>https://crystalballhealth.com</u>)







# The Preemie Parent's SURVIVAL GUIDE to the NICU

By

*little man's* Nicole Conn

#### &

PreemieWorld.com's Deb Discenza

#### with

Medical Editor Alan R. Spitzer, M.D.

HOW TO second edition MAINTAIN YOUR SANITY & CREATE A NEW NORMAL





# National Statistics Respiratory Syncytial Virus

## **About Respiratory Syncytial Virus**

Respiratory syncytial virus, or RSV, is a contagious seasonal respiratory virus that can cause bronchiolitis and pneumonia. It is also the leading cause of hospitalization in babies less than one year old.<sup>1</sup> RSV can be deadly for premature infants and at-risk infants with congenital heart disease or chronic lung disease.

Preventive treatment called palivizumab can protect infants from RSV, but national claims data shows certain babies aren't getting access to this FDA-indicated therapy.

## National Health Plan Coverage & Access

A national data supplier provided palivizumab claims for Medicaid and commercial health plans across the nation from January 2019 through December 2019.



"Gap" Babies Commercial Plans Denied 40% Medicaid: 25%



Medicaid: 25% **"In-Guidance" Babies** Commercial Plans Denied **25%** Medicaid: **14%**  Health plans deny 40% of palivizumab prescriptions for premature infants born between 29 and 36 weeks gestation.

One in every four prescriptions is denied for infants who should qualify for coverage under standard insurance policies.

This includes severely premature infants born before 29 weeks gestation, babies born before 32 weeks gestation who have chronic lung disease, and babies born with congenital heart disease.







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# RSV AWARENESS: A National Poll of Parents & Health Care Providers

Respiratory syncytial virus, or RSV, is far from the common cold. It can lead to hospitalization, lifelong health complications or even death for infants and young children. **In fact, it is the leading cause of hospitalization in children younger than one.** 

Yet a national poll of parents and specialty health care providers reveals a startling divide in attitudes toward the virus. While both groups acknowledge RSV as a significant concern, the two populations vary widely in their reported ability to meet RSV's threat head-on. Health care providers vigilantly monitor for the virus, which they report seeing regularly in their practices. Parents, however, feel unequipped to protect their young children.

Meanwhile, specialty health care providers overwhelmingly report that health plan rules and insurance denials block vulnerable infants' access to preventive RSV treatment. Such barriers can put unprepared parents at a double disadvantage. The survey does suggest, however, that education can embolden parents to seek more information about RSV and take steps to protect their children.

## KEY FINDINGS

#### Preparedness

Parents of children age four and under report that understanding of RSV is lacking. That leaves them less than fully prepared to prevent their young children from catching the virus. Specialty health care providers reiterated these concerns; 70% agreed that parents of their patients have a low awareness of RSV. Meanwhile, specialty health care providers themselves actively monitor for RSV. They reported that:



#### SPECIALTY HEALTH CARE PROVIDERS

They treat RSV as a priority, "often" or "always" evaluating their patients (80% doctors; 78% nurses)

During RSV season, they are especially vigilant about monitoring patients for symptoms or risk factors for RSV (98%).

#### PARENTS

Only 18% said parents know "a lot" about RSV, reflecting an awareness level that's roughly half that of the flu

Only 22% of parents consider themselves "very well prepared" to prevent RSV.



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# Clinical Pearl: COVID-19 in the Pregnant Women Close to Home

Joseph R. Hageman, MD, Mitchell Goldstein, MD

Our daughter lives in rural Illinois with her husband and three girls, ages 6, 4, and 2 years. They live on a farm and have been very careful, and have worked hard to remain healthy and safe. She is pregnant at 19 weeks' gestation, and things have been going well. That is, until eight days ago, when her husband developed a cough and some fever. His father also became symptomatic, and now she and her daughters have all developed some congestion and various signs and symptoms of COVID-19, including some fever, cough, diarrhea, muscle aches, and fatigue. She, her husband, and his father have all been tested and are positive by nasopharyngeal RCT-PCR test. The children are presumed to be positive. This morning when she awoke and tried to take a deep breath, she had pleuritic chest pain and dyspnea. They have had a pulse oximeter, and her oxygen saturation was 97% in room air. She called her obstetrician, who felt it best for her to go to the hospital's emergency department, where she had delivered her three daughters. She drove herself to the hospital. There she was afebrile and remained in room air. Her chest radiograph was unremarkable. She was given an albuterol inhaler with a spacer and took 2 puffs with subsequent improvement in her ability to breathe and increase her cough productivity. Her laboratory studies were all within normal limits, including her D-dimer and a negative myoglobin test, except for a potassium level of 3.2 mEg/L and her electrocardiograms were also normal. After a discussion with her physicians on oral hydration, she was discharged home, acetaminophen for the chest discomfort, and her albuterol inhaler with spacer q 4-6 hours, her pulse oximeter, and with close follow up. As of January 6, she continues to improve, and her baby is moving in utero.

"So what do we know about the clinical course and risks to pregnant women with COVID-19 infection/disease during Pregnancy during the second and third trimester?"

So what do we know about the clinical course and risks to pregnant women with COVID-19 infection/disease during Pregnancy during the second and third trimester?

First of all, there are changes in the immune system of pregnant women as described by Wadman et al.:

"Pregnancy does appear to make women's bodies more vulnerable to severe COVID-19, the disease caused by SARS-CoV-2. That is partly because of pregnant women's uniquely adjusted immune systems, and partly because the coronavirus' points of attack the lungs and the cardiovascular system—are already stressed in pregnancy" (1). Secondly, In the study by Ellington et al., SARS-CoV-2 infection in Pregnancy was associated with hospitalization and increased risk for intensive care unit admission and receipt of mechanical ventilation, but not with death (2). If a pregnant woman with SARS-CoV-2 is sick enough to be admitted to the hospital, she is considered high risk for developing severe SARS-CoV-2 disease.

*" If a pregnant woman with SARS-CoV-2 is sick enough to be admitted to the hospital, she is considered high risk for developing severe SARS-CoV-2 disease."* 

There is also a nationwide prospective cohort study, PRIORITY or Pregnancy CoRonavIrus Outcomes RegIsTrY, organized by Afshar, Gaw, Flaherman, Jacoby, and co-investigators at the University of California San Francisco. This study collected clinical data from 736 pregnant or recently pregnant women with SARS-COV-2 positive (N= 594) or patients under investigation (PUIs = 142 who tested negative) from across the United States to describe the clinical presentation, symptomatology, and disease course of known or suspected COVID-19 disease in Pregnancy who were enrolled and followed up for one year (3). This paper was just published in December and is different from Ellington's study in that most of these women had mild illness and were seen as outpatients (3). These patients were collected between March 20, 2020, and July 10, 2020. The most prevalent symptoms in the first week after diagnosis were cough (46%), fatigue (38%), and headache (25%), with symptoms usually resolving within a



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month (3). By week four after diagnosis, 60% were asymptomatic; however, 25% were still symptomatic at week eight post-diagnosis (3) in those patients who tested positive for SARS-CoV-2 (3).

"Early reports of decreased preterm birth and subsequent admission to the NICU must be looked at in context as well. As many have been heeding the orders to shelter and avoid crowds, could the incidence of very early loss be under appreciated and under reported?"

How about the rate of preterm birth and stillbirth during this pandemic? Concerning stillbirth, a study done by Stowe and colleagues in England comparing pre-pandemic and pandemic stillbirth rates revealed no increase in stillbirth rates (4). In Philadelphia, changes in preterm birth rates and stillbirth during the SARS-CoV-2 pandemic from March-June 2020 were examined, and no increase in preterm birth rate or increase in stillbirths was noted (5). This finding is in contrast to a study from a single London hospital by Khalil et al. that reported an increase in stillbirth rates (6).

Early reports of decreased preterm birth and subsequent admission to the NICU must be looked at in context as well. As many have been heeding the orders to shelter and avoid crowds, could the incidence of very early loss be under appreciated and under reported? Some of the symptomatology of CoV-2 infection may mask early spontaneous abortion.

There has been discussion about the differences in morbidity and mortality in Hispanic or black patients with SARS-CoV-2 infection. Here is a quote from the paper in the *Morbidity and Mortality Weekly Report (MMWR)* by Ellington and colleagues:

"Although data on race/ethnicity were missing for 20% of pregnant women in this study, these findings suggest that pregnant women who are Hispanic and black might be disproportionately affected by SARS-CoV-2 infection during pregnancy (2)." "During the study period, among pregnant women with laboratoryconfirmed SARS-CoV-2 infection who reported race/ethnicity, 46% were Hispanic, 22% were black, and 23% were white; these proportions differ from those among women with reported race/ ethnicity who gave birth in 2019: 24% were Hispanic, 15% were black, and 51% were white.††Although data on race/ethnicity were missing for 20% of pregnant women in this study, these findings suggest that pregnant women who are Hispanic and black might be disproportionately affected by SARS-CoV-2 infection during pregnancy" (2). In the PRIORITY study, an effort is ongoing to collect more patients of color to provide more clinical information about these women's course and provide ongoing follow up (3).

Disparity may play an important role in access to care and the circumstances that allow for CoV-2 disease to spread more rapidly. Crowded, shared living spaces in apartment complexes with common ventilation systems may ultimately be implicated, especially in expectant mothers experiencing poverty.

We will continue to closely follow the available literature to provide clinicians further perspective about the diagnosis, management, vaccination, and ongoing care of pregnant women with COVID-19 disease and their infants.

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The authors have no conflicts to disclose

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### OPIOIDS and NAS When reporting on mothers, babies, and substance use LANGUAGE MATTERS



#### I am not an addict.

I was exposed to substances in utero. I am not addicted. Addiction is a set of behaviors associated with having a Substance Use Disorder (SUD).



#### I was exposed to opioids.

While I was in the womb my mother and I shared a blood supply. I was exposed to the medications and substances she used. I may have become physiologically dependent on some of those substances.



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There are evidence-based pharmacological and non-pharmacological treatments for Neonatal Abstinence Syndrome.



### My mother may have a SUD.

She might be receiving Medication-Assisted Treatment (MAT). My NAS may be a side effect of her appropriate medical care. It is not evidence of abuse or mistreatment.

#### My potential is limitless.



I am so much more than my NAS diagnosis. My drug exposure will not determine my long-term outcomes. But how you treat me will. When you invest in my family's health and wellbeing by supporting Medicaid and Early Childhood Education you can expect that I will do as well as any of my peers!

Learn more about Neonatal Abstinence Syndrome at www.nationalperinatal.org



# Why PREMATURE INFANTS Need Access to an EXCLUSIVE HUMAN MILK DIET





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work with your medical team to create a plan

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with soap and water for 20+ seconds. Dry well.



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change into a clean gown or shirt.

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But **mixed messages** from the media and regulatory agencies cause pregnant women to sacrifice those benefits by eating less fish than recommended.

tilapia





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# **Letters to the Editor**

Letter to the Editor

Dr. Goldstein,

We live in unprecedented times, and I think we are all finding it difficult to make sense of where we stand in the course of our nation's history. But I hope you and your readers will indulge me in a thought exercise that went through my mind.

To date, our country has spent roughly \$4.5T fighting the coronavirus. Not all of it went to therapies, but paying people to stay at home reduces the spread and is appropriate to include in the cost.

"To date, our country has spent roughly \$4.5T fighting the coronavirus. Not all of it went to therapies, but paying people to stay at home reduces the spread and is appropriate to include in the cost."

But to what end? The best estimates are that 567,000 will die from COVID by April 1. But what if we had *not* spent \$4.5T and just let COVID run rampant. I'm not advocating for this; again, this is a thought exercise... 320 million Americans, 70% get infected before herd immunity kicks in, the case fatality rate is between 1.7% and 2.8% (so let's use 2.3%), and an infection rate per confirmed case is thought to be around 2.5x. That works out to 2M deaths.

So by spending \$4.5T, we will have averted 2M less 567K, or 1.4M deaths. That works out to \$3.2M per life saved. If further deaths occur beyond the 567K projected by April 1, the cost per life saved will be even higher.

I bring this up because I hear from time to time that HeRO monitoring is expensive. HeRO monitoring costs roughly \$8K to save the life of an ELBW, so it's about 400x more cost-effective to save a life with HeRO than we are spending to save a life from coronavirus using the conservative estimate.

And ELBW's leaving the NICU can expect to live  $\sim$ 75 years. The average age of a coronavirus victim is around 70, so averting death saves  $\sim$ 15 years, roughly a 5x difference. So HeRO monitoring is 400 x 5, or 2000x more cost-effective per life-year saved.

I bounced this idea off of a friend, who responded that babies don't vote.

Am I missing something, or do we, as a society, need to reevaluate our priorities? I would love to hear what you and your readers think.

Sincerely,

Will King

CEO

Medical Predictive Science Corporation

"I bring this up because I hear from time to time that HeRO monitoring is expensive. HeRO monitoring costs roughly \$8K to save the life of an ELBW, so it's about 400x more cost-effective to save a life with HeRO than we are spending to save a life from coronavirus using the conservative estimate."

Dear Dr. King,

The framers of the constitution believed in the concept of freedom of expression. In the 1700s, the concept that modern medical advances might in some way mitigate this freedom of expression or pursuit of happiness in a way that would require its most ardent champions to refrain from fully enjoying that right could not be imagined.

"The framers of the constitution believed in the concept of freedom of expression. In the 1700s, the concept that modern medical advances might in some way mitigate this freedom of expression or pursuit of happiness in a way that would require its most ardent champions to refrain from fully enjoying that right could not be imagined."

#### Or could it?

Smallpox was rampant in colonial America. George Washington's winter at Valley Forge is legend, but few know that his encampment was not only affected by cold and starvation but also by the ravages of what is now an "extinct" disease. In 1776, roughly half of the Continental army contracted smallpox. George Washington saw many of his soldiers weaken and die from a process that he was initially powerless to control. Faced with continued outbreaks and possibly bio-warfare from the British, Washington made a difficult decision to inoculate his troops, the process of variolization was dissimilar to Jenner's vaccination that was developed years later in that it had a fatality rate of up to 10%.

Washington put strict restrictions in place, required all those afflicted with smallpox to be placed in quarantine, restricted liberties including those involved in partaking of fresh water which might be used by the army, and for a certain period of time, locked down the town of Brookline, MA.

As we reflect on this nearly 250 years later, it is obvious that we are still fighting the same wars, only with a different pathogen and

a population divided on the concept of leadership and who controls what, where, and when.

In a quote often attributed to Thomas Jefferson, the "price of liberty is continued vigilance." Arguably, monitoring is that vigilance. Beyond just prematures, monitoring can help identify those at most risk of disease progression, likely to benefit from earlier intervention, and in need of quarantine to prevent further spread. And yes, monitoring is cheaper than disease.

"In a quote often attributed to Thomas Jefferson, the 'price of liberty is continued vigilance.' Arguably, monitoring is that vigilance."

Beyond the math, there is the sobering reality that we must as a society understand the risks, appreciate the benefits of the technology at our disposal, and vote accordingly. Until we follow what is best for the health of those most at risk and best of breed recommendation of our health care professionals, disease will progress. Runaway costs will continue. And yes, we will continue to miss the obvious priorities.

Sincerely,

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Mitchell Goldstein, MD Editor in Chief



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#### Erratum (Neonatology Today December, 2020)

Neonatology Today has identified no erratum affecting the November, 2020 edition.

Corrections can be sent directly to <u>LomaLindaPublishingCompany@gmail.com</u>. The most recent edition of Neonatology Today including any previously identified erratum may be downloaded from <u>www.neonatologytoday.net</u>.

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RSV is a respiratory virus with cold-like symptoms that causes 90,000 hospitalizations and 4,500 deaths per year in children 5 and younger. It's 10 times more deadly than the flu. For premature babies with fragile immune systems and underdeveloped lungs, RSV proves especially dangerous.

#### But risk factors associated with RSV don't touch all infants equally.\*

\*Source: Respirator Syncytial Virus and African Americans

Caucasian Babies	Risk Factor	African American Babies
11.6%	Prematurity	18.3%
58.1%	Breastfeeding	50.2%
7.3%	Low Birth Weight	11.8%
60.1%	Siblings	71.6%
1%	Crowded Living Conditions	3%

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AFRICAN AMERICAN BABIES bear the brunt of RSV. Yet the American Academy of Pediatrics' restrictive new guidlines limit their access to RSV preventative treatment, increasing these babies' risk.

Af PA

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The 34<sup>th</sup> Annual Gravens Conference March 3, 4, 10, and 17, 2021 Virtual https://health.usf.edu/publichealth/ chiles/gravens-conference

37<sup>th</sup> Annual Advances in Therapeutics and Technology Conference March 24 -26, 2021 Virtual https://paclac.org/advances-in-careconference/

Annual Neonatal and Pediatric Airborne Transport Conference May 5 - 7, 2021 International Biomedical Austin, Texas https://www.int-bio.com/eventsnews/airborne-conference/

Pediatric Academic Society Virtual Meeting Phase 1: April 30 - May 4, 2021 Phase 2: May 10 - June 4, 2021 https://www.pas-meeting.org/ pas2021-virtual/

22<sup>nd</sup> Annual International Perinatal Bereavement Conference (IPBC) May 12 - 15, 2021 Pregnancy Death and Infant Loss Alliance (PLIDA) Chicago, Illinois https://www.plida.org/ipbc-2021

44<sup>th</sup> Annual Conference on Neonatal Perinatal Medicine June 17 - 21, 2021 AAP District VIII Section on Neonatal-Perinatal Medicine https://nm2020.district8sonpm.org/

#### Innovations in Neonatal Care Location: Santa Fe, New Mexico August 9 - 11, 2021 Mednax http://www.innovationsconference. com/

42nd Conference on Pediatric Health Care. Phase 1: March 10-13 (Orlando, Fl) Phase 2: March 24-27 (Virtual) NAPNAP https://www.napnap.org/nationalconference/

Location: Austin, Texas For up to date Meeting Information, visit <u>NeonatologyToday.net</u> and click on the events tab.

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#### Neonatology and the Arts

This section focuses on artistic work which is by those with an interest in Neonatology and Perinatology. The topics may be varied, but preference will be given to those works that focus on topics that are related to the fields of Neonatology, Pediatrics, and Perinatology. Contributions may include drawings, paintings, sketches, and other digital renderings. Photographs and video shorts may also be submitted. In order for the work to be considered, you must have the consent of any person whose photograph appears in the submission.

Works that have been published in another format are eligible for consideration as long as the contributor either owns the copyright or has secured copyright release prior to submission.

Logos and trademarks will usually not qualify for publication.

This month we continue to feature artistic works created by our readers on one page as well as photographs of birds on another. This month's original artwork is from Paula White, MD who shares another stunning image of Peonies. Our Bird for this month is a Shorebird by the ocean provided by Dr. Mita Shah.

> Herbert Vasquez, MD, Associate Neonatologist, Queen of the Valley Campus

Emanate Health, West Covina, CA VasquezH1@gmail.com

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1. Manuscripts are solicited by members of the Editorial Board or may be submitted by readers or other interested parties. Neonatology Today welcomes the submission of all academic manuscripts including randomized control trials, case reports, guidelines, best practice analysis, QI/QA, conference abstracts, and other important works. All content is subject to peer review.

2. All material should be emailed to:

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5. A brief biographical sketch (very short paragraph) of the principal author including current position and academic titles as well as fellowship status in professional societies should be included. A picture of the principal (corresponding) author and supporting authors should be submitted if available.

6. An abstract may be submitted.

7. The main text of the article should be written in formal style using correct English. The length may be up to 10,000 words. Abbreviations which are commonplace in neonatology or in the lay literature may be used.

8. References should be included in standard "NLM" format (APA 7<sup>th</sup> may also be used). Bibliography Software should be used to facilitate formatting and to ensure that the correct formatting and abbreviations are used for references.

9. Figures should be submitted separately as individual separate electronic files. Numbered figure captions should be included in the main file after the references. Captions should be brief.

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