

Navigating Toward Neonatology: Infantile Spasms

Benjamin Hopkins, OSMIV, Donald M. Null, MD

“Welcome back to my fourth installment. My name is Benjamin Hopkins, and I am currently a fourth-year medical student at Western University of Health Sciences in Pomona, California. When ‘I grow up,’ I want to be a Neonatologist. Look at last month’s journal for my previous article and follow along with this column as I navigate my way to becoming a Neonatologist.”

Welcome back to my fourth installment. My name is Benjamin Hopkins, and I am currently a fourth-year medical student at Western University of Health Sciences in Pomona, California. When ‘I grow up,’ I want to be a Neonatologist. Look at previous months’ journals for my earlier articles and follow along with this column as I navigate my way to becoming a neonatologist.

Currently, I am submitting my rank order list for pediatric residency programs. Knowing that I am heading toward a fellowship, my rank list prioritizes programs with high match rates in neonatology, that offer me broad exposure to neonatal patients, have close connections to multiple hospitals with different levels of neonatal ICUs, and, of course, where I feel most comfortable.

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I am still rotating within pediatric neurology. It continues to be a fantastic experience, with various “bread-and-butter” and complex

patients and many unique patients in the inpatient and outpatient settings. The attending neurologist I work with is an excellent instructor who offers individualized patient care, exceptional treatment options, and education to each patient and their family. My time was spent diving deeper into the etiologies of neurologic disorders and the optimal treatments to help patients have the best quality of life.

One of my patients this month was a 15-year-old female who had intellectual disabilities due to infantile spasms as a newborn. She is receiving many therapies, including speech therapy, occupational therapy, and physical therapy and has previously had swallowing and behavioral therapy. She is currently taking risperidone for autism-like behavior, self-inflicted injuries, and behavioral outbursts. She is not presently taking any anti-seizure medication, as she has been seizure-free since the infantile spasms. The patient’s infantile spasms were unresponsive to a variety of medical treatments and ended up subsiding on their own. Of patients with infantile spasms, approximately 85% have significant developmental disabilities, often with other underlying diseases (1). Among the 85% of those with developmental disabilities, 50% are considered to have severely delayed development (1).

“Infantile spasms have been studied for over a century and belong to a group of early-onset epilepsies of infancy and childhood that include epileptic spasms and hypsarrhythmia. Infantile spasms are diagnosed on characteristic seizure patterns. Classification of infantile spasms has progressed to distinguish types of spasms (flexor, extensor, mixed), often confused with normal infant motor behaviors ”

Infantile spasms have been studied for over a century and belong to a group of early-onset epilepsies of infancy and childhood that include epileptic spasms and hypsarrhythmia (1–4). Infantile spasms are diagnosed on characteristic seizure patterns (1, 3, 4). Classification of infantile spasms has progressed to distinguish types of spasms (flexor, extensor, mixed), often confused with normal infant motor behaviors (3, 4). In infantile spasms, the neck, body, arms, and legs are often symmetrically contracted in the axial plane for 0.2–2 seconds (1). The spasms typically arise in 20–40 spasms with intervals lasting 5–30 seconds (1). With the spasms being shorter at the onset, electroencephalography (EEG) is essential in diagnosis (1–4). Performing an EEG early in the course is recommended to help support the diagnosis (1, 4). The typical pattern seen on EEG is hypsarrhythmia, which appears in about 70% of infantile spasm diagnoses (1, 4). Hypsarrhythmia is a chaotic, severe paroxysmal EEG pattern with abnormal background activity (1–4). If hypsarrhythmia is not seen, it may appear within the first week of symptoms; otherwise, a

variant of hypsarrhythmia may be seen (1, 4). The most common variant pattern seen on EEG is a generalized slow-wave transient followed by an attenuation of the background activity in all regions (4).

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The incidence of infantile spasms is 0.02–0.04%, with an average age of onset of six months (1, 4). There is no clear etiology of infantile spasms; the current understanding is that it has many causes consistent with structural, genetic, and metabolic abnormalities (1, 2, 5). With improved genetic testing and our increased ability to diagnose specific brain disorders, the etiology of infantile spasms can be found in roughly 60% of cases (1, 5). When an etiology is found, it can be pre-, peri-, or postnatal: prenatal causes make up roughly 55%, perinatal roughly 25%, and postnatal roughly 8%. Other causes, such as brain tumors, comprise 12% (1). Around 25% of patients with infantile spasms will have spontaneous resolution of them within one year of onset (4).

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Treatment for infantile spasms starts with adrenocorticotrophic hormone (ACTH) (1–3, 5). Other standard therapies include oral corticosteroids and vigabatrin (1–3). Non-standard therapies include the ketogenic diet, topiramate, zonisamide, clobazam, clonazepam, valproate, phenobarbital, oxcarbazepine, levetiracetam, and surgery (2, 3, 5). Prompt treatment is critical in improving long-term outcomes; however, treatment is often delayed and resistant to numerous medications (2, 5). For infantile spasms that are completely resistant to medication or have a single unilateral epileptogenic cortex, surgery is considered, though this is most often not a viable option (3, 5). Treatment efficacy is assessed with EEG at two weeks, and if spasms or hypsarrhythmia has not resolved, medication change is indicated (1). When not initially controlled, medications have been found to have response rates of 22% at two weeks, with the patient often having poor cognitive outcomes, frequently due to the delay in seizure control (2, 5). Collaborating with the patient's primary care provider is essential to monitor treatment potential side effects (2).

The prognosis primarily depends on the etiology of the infantile spasms, and there is a better prognosis when no underlying etiology is found (1, 3). Poor prognosis is found when there is delayed development before the onset of infantile spasms or late initiation of treatment (1). Although the prognosis for most patients remains poor, new animal models and further studies that help identify favorable prognosis have been and are continuing to be developed (3, 4). Some conditions can be challenging to distinguish from infantile spasms: benign infantile myoclonus, infantile colic, Sandifer's syndrome, Ohtahara's syndrome, early myoclonic encephalopathy, and myoclonus associated with metabolic diseases (1). Any seizure in children under 18 months should be considered for infantile spasms, as earlier diagnosis and treatment are critical in providing the best care (1).

This month, I enjoyed talking with Dr. Donald Null, a neonatologist with over 50 years of experience who is currently an Emeritus Professor of Pediatrics in the Division of Neonatology at the University of Utah. We spoke about how to excel as a neonatologist, critical care physicians' mental wellness and burnout, and what to get involved in to offer the best treatment in all situations.*

1. What qualities are most essential to excel at as a neonatologist?

The most essential quality is listening to those around you—not just your colleagues but the nurses, respiratory therapists, nutritionists, consultants, and parents because if anyone knows their baby better, it's the parents. When the parent says, I'm concerned that something's going on, they have a much better idea than you as the doctor who spends five minutes doing an exam in the morning. The same thing applies to nurses; that's what I learned as an intern. My mentor in neonatology taught me that if Ms. Bess, one of our senior nurses, says the baby is sick, you better get off your butt and look at the baby because that baby is sick. If you looked at that baby 30 minutes ago, it doesn't matter; it's your job to sort out why. So, being an excellent physician requires listening to those around you and trying to understand and help what's going on with your patient.

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2. What do you now know that you wish you knew before going into neonatology?

We've learned that there will be changes in the care you provide because of technological advancements and medical treatment options. You have to remember that when I started, there was no pulse oximeter, high-frequency ventilation, or surfactant; it was just the beginning of blood pressure's ability to be managed noninvasively. That was developed in the Air Force when I was training there in 1972 and 1973. We know we will have better ways to manage things in the future.

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It taught me that an excellent physical exam and a visual and hands-on patient management ability became essential. After all, I was on the transportation team in a helicopter where you couldn't hear anything because of the helicopter's noise. We didn't have a pulse ox; we didn't have anything but our eyes and our hands to assess our patients and try to be able to manage them.

As things have advanced, there have become significantly more ways to manage patients. Now, you can manage patients differently in transport because you have indwelling arterial catheters with a monitor that continuously monitors blood pressure. You have high-frequency ventilation, or conventional, where you can better understand the pressures being delivered to the patient from that standpoint. You can carry a device with you that can measure the blood gas. In the 1970s, you needed almost a cc of blood to get blood gas; now, we can do it with a few drops. These things have become extraordinarily beneficial, but what has been lost between you and me is the physical exam and assessment of the patient because everybody's relying on the blood gas they get back, the pulse ox, the ventilator findings, a chest X-ray, et cetera. They don't assess the patient with a physical exam, and when you're doing transport, you better have that because you won't have access to an x-ray.

If you don't know how to assess the patient for risk factors such as pneumothorax, for instance, then you won't do an excellent job with your patient. Being more skilled at doing a physical exam and what it means becomes very important. So you better be able to assess the patient for whether you're confident they have a pneumothorax and you're going to stick a needle in their chest to get rid of the air. You can know several things that assist you in making that decision.

3. What would you encourage a future neonatologist to prioritize and be involved in?

That's a good question because some of it depends on your primary interests. I will tell you that respiratory was what you wanted to be involved in when I started. After all, you have to remember that in 1970, if you were a two-kilo baby, and you were a male and you were 34 weeks, and you had significant respiratory distress, the likelihood of you dying was about 80%. Today, a two-kilo baby has a 98% or 99% chance of surviving. And if he doesn't, it's because of infection or another reason. As time has changed, we've gone to other areas. A neonatologist has to do all those areas; you have nutrition, which has changed considerably. You have respiratory, which has also changed significantly to where we now do a lot

of less invasive inhalation. In short, we have done lots of things, and we've brought the survival rate up. When I was a resident, they would tell me that if the baby weighed less than a thousand grams, the baby wasn't going to survive. In some facilities, they had a scale in the delivery room, put the baby on it, and if the baby weighed 900 grams, they'd hand it to the mother, say, here, your baby won't live; comfort your baby. I mean, now people would gasp at that from that standpoint. And we should, because 900 grams are way into the 70, 80, 90 percent [survival] range at this point, depending on how they start.

There are many areas that you can focus on. One of my best friends was a neonatologist; his deal was the follow-up. He did incredible work with follow-up and after-discharge management. You can become interested in nutrition, follow-up, respiratory and cardiac issues, etc. And now, with the ability to do ultrasound findings, you can do ultrasounds of the chest, looking for pneumothoraces, ultrasound of the heart to look at the function and what kind of medications you're going to use for the patient and how it's going to fix or not fix the patient from this additional view.

I suggest to trainees or individuals like yourself who want to do neonatology there are multiple areas you can focus on. Those are areas you can get into when you rotate through other specialties, see what stands out to you and what area you have passion for. As a resident, you're rotating through neurology, nephrology, cardiology, and many more. You can expand your knowledge base, and in this day and age, you can go to a meeting or get on a video and look at how you look at the heart, not like you're looking at the heart as a cardiologist, but just as an extra tool. You can use it to see if something needs to be done, like a pneumopericardium or a hemopericardium. These are the things you can start to learn early on that will assist you in deciding what areas you want to focus on.

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You must decide a couple of things when you go into neonatology. One is where do I want to be? Do I want to be at a level four center, or do I want to be at a level two center? You must remember that if you're at a level two center and a patient gets sick, you've got to go to the level four center for it. So, will you be comfortable sending your patients to a level four? My boss said to me, do you want to refer your patients, or do you want to be the person they refer patients to? I very quickly knew what I wanted. That helps you with how you will practice and what you need to know when you practice from that standpoint.

It is essential to consider all aspects, though; being in a level two NICU, sometimes you have to have a lot more skills than you do in a level four because in a level four, you've got cardiology, nephrology, GI, you've got all those things at the hospital with you. Whereas in a level two NICU, you don't; however, you can contact somebody, and they will drive over there the next day and look at a patient for you, but you need the skill to say, I can't wait till tomorrow. I've looked at this patient, and this patient's sick enough

that I need to get this patient somewhere else. That means that if you say, well, I want to go to a level two NICU because I want to have a little more time with my family from that standpoint, but I'm going to learn how to use an echo machine so that I know when I need to send a patient to a level four NICU.

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4. How do you think the critical care scenario of the NICU affects the chance of burnout? And how should we counter it?

It depends on your basic personality with how much you can work and how many hours you can work. I grew up with way different schedules than are currently present, and I loved what I did. To me, going into the NICU and helping a patient, talking to parents, and when the baby isn't going to survive, sitting with the parents when we withdrew support from the baby was what I liked to do.

I have never had burnout, sometimes working 80 or 90 hours a week just because that's who I am, what I enjoy doing, and helping parents with what they do. You have to decide how much of your time and energy you will invest in your job as a physician. How much of your time is invested outside of the hospital and outside of what you do for work? You have to look at that balance. In an ICU setting, you will have to spend more time inside than outside from that standpoint. Some concerns are how you tolerate caring for patients who may not survive. That's not because you did something wrong, but occasionally, you'll do something wrong, and the patient will die. You still have to say, I did the best I could, and this is what I've done, and this is how I've helped people, and this is how I've helped families.

However, you have to be cut out for that because that's where many people have burnout. The burnout is because you might lose patients and don't think you can return to work this week. For myself, having grown up in the military, it was a little different because you had the kind of stuff where I had to deal with families whose husbands died overseas. I was caring for the kids, so it was a different environment.

Being okay with having patients who might die is only part of it. I was talking with some friends of mine who are physicians, and he said we talk about this work-life balance, but I am still waiting to hear anybody talking about adding work on the work side. They're always adding balance on the other side. That is something that people must start focusing on, making the work side a good place for you.

“If you’re going to be a neonatologist and want to be in a level three or four facility, you’ll have plenty of coverage, but you’ll have the sickest of the sick. You’re going to lose patients, and you’re going to have to work through it. When somebody is ill, you will have to cover for them. Sometimes, that’s the way life is, and if you don’t want to do that, you ought to be, but if you still want to be a neonatologist, you should be in a level two facility where you’ll have less of that.”

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5. What are you currently working on?

I have retired from being in the newborn ICU; however, I do research in the lamb lab. What we're trying to do now is to look at certain medications that can be given to reduce the risk of developing chronic lung disease and not hurt the patient with side effects.

So, I developed the ability to take the preterm lamb and put them on a high-frequency nasal support. With that, they don't develop chronic lung disease, and they don't develop injury to the brain, lungs, kidneys, or other organs. One thing that the model enables us to do is if you have a new medication that you are concerned about that could harm the patient; while it might fix the lungs, it might hurt the kidneys, liver, or brain.

We now have a model that we can use on the animal model that gives us chronic lung disease. We can provide it to that animal and see if it reduces the chronic lung disease they typically develop from a conventional ventilator.

You can give it to an animal that isn't going to get chronic lung disease or lung injury and is still preterm. You can give that medicine to them and see if it causes any injury to the other organs, which would have no injury in normal development without the medication.

With the knowledge we gain through this model, you can then take that medication and be much more confident that it's a reasonable medication to try in humans and will not very likely—you can never say never—but rarely would cause an injury to the human. So that's the kind of stuff I'm working on right now.

*Answers paraphrased from video/voice call.

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