Redesigning Postdischarge Nutrition in the NICU

Overview

Preterm birth affects 1 of every 10 infants in the United States. Improper nutrition in the NICU can result in impaired neurodevelopment, delayed cognitive development, retarded growth, and an increased risk for type 1 diabetes and cardiovascular disease later in life. It is essential that the intake of protein, macronutrients, and micronutrients be provided at the right nutritional levels during their first hours, days, and weeks of life while in the NICU, followed by an individual feeding strategy at discharge.

Dr. Ian Griffin and **Dr. Tara Bastek** provide detailed information to underscore the significance of proper nutritional intake in the NICU. They review the latest nutrient intake recommendations and define optimal growth as an infant transitions from parenteral to enteral nutrition during the course of acute, convalescent, and discharge phases, with specific feeding strategies during each. Individualized formula fortification strategies are also discussed to help parents and providers follow prescribed feeding plans to optimize long-term outcomes.

Target Audience

This activity was developed for pediatric physicians, nurses, nurse practitioners, dietitians, and other healthcare providers who have an interest in newborns, infants and toddlers.

Learning Objectives

At the conclusion of this activity, participants should be better able to:

- Link nutrient intake recommendations for growing preterm infants with expected growth
- Describe the latest evidence supporting preterm infant convalescent and discharge nutrition
- Review novel approaches to convalescent and discharge feeds when a preterm infant is designated as at risk for growth failure or micronutrient deficiencies
- Customize nutritional interventions to help close the growth failure gap in the NICU and at discharge.

Faculty

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Faculty

Tara K. Bastek, MD, MPH
Speakers Bureau: Mead Johnson Nutrition, CAE Healthcare

Consultant: Mead Johnson Nutrition

Spouse Employer: Pfizer

Ian J. Griffin, MB ChB, has no relevant financial relationships to disclose.

The faculty for this activity has disclosed that there will be no discussion about the use of products for non-FDA approved applications.

Additional content planners

The following have no significant relationship to disclose:
Erin Allen, MS, RD, LDN (Dietitian Reviewer)
Victoria Anderson (Medical Writer)
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This activity is supported by an independent educational grant from **Mead Johnson Nutrition**.

This activity is an online enduring material. It has been edited to meet requirements for online learning. Successful completion is achieved by reading and/or viewing the materials, reflecting on its implications in your practice, and completing the assessment component.

The estimated time to complete the activity is 1.0 hour.

This activity was released on November 19, 2020 and is eligible for credit through November 19, 2022.

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Contact Information

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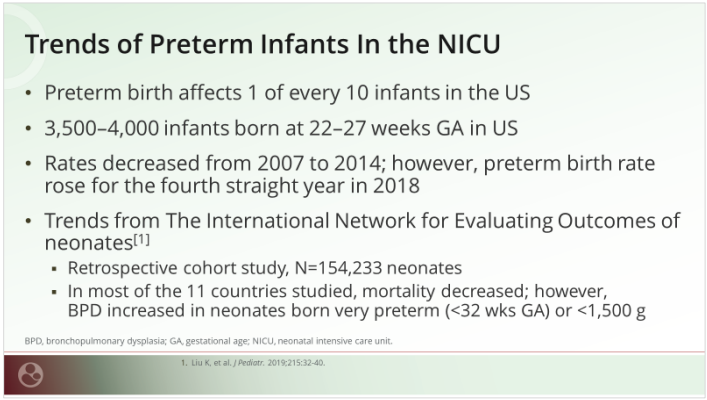
Editor's Note: This is a transcript of an audio webcast presented on November 12, 2020. It has been edited and condensed for clarity.

Nutrient Intake Recommendations

Tara K. Bastek, MD, MPH: Any conversation about nutrition and preterm infants really has to consider the arc of the infant's experience from birth all the way to discharge from the NICU. As we think about nutrient intake recommendations, it begins from the minute they are born and as we start our care, and we try—all of us—to implement the best recommendations from experts as we continue to move through that NICU experience across the continuum of care.

We will set the stage to talk about the scope of the issue with preterm infants in the United States. We know that preterm birth affects 1 out of every 10 births or infants in the United States. By looking at the average birth rate in the US and doing some statistical calculations, we can estimate that we have somewhere around the order of 4,000 infants a year who are born between 22 and 27 weeks gestation here in the United States.[1]



Slide 1 — Trends of Preterm Infants In the NICU

The babies at this gestational age—while that number doesn't seem very large, particularly when we think about the millions of infants that are born every year—however, we know that these infants consume considerable amounts of attention, love, resources, energy from their families, as well as all of us in neonatology that support them.

The trend across the United States had actually been improving—by improving I mean a decreasing preterm birth rate—for a good 7 years or so between 2007 and 2014. However, in the last 5 to 6 years we have seen a shift again in the preterm birth rate rising, and that reflects many, many different influences happening in the country. But it means we have work to do, and we have lots of individual lives that need our support and attention.

We will also take a look at some of the trends for what they survive with. These infants at the 22- to 27-week age range represent the youngest, the smallest, the most fragile of those preterm babies. And looking at trend data across the last 20 or so years, we know that there are some positive trends, and there is some sobering information.

For infants that are at the older end of this age range, those that are 26 to 28 weeks, surviving to hospital discharge *without* a comorbid condition, those numbers are improving. Meaning there are fewer children having a comorbid condition in that gestational age range. However, the infants that are born younger than that still have a significant comorbidity burden at the time of NICU discharge, and therefore, across the first couple of years of life.

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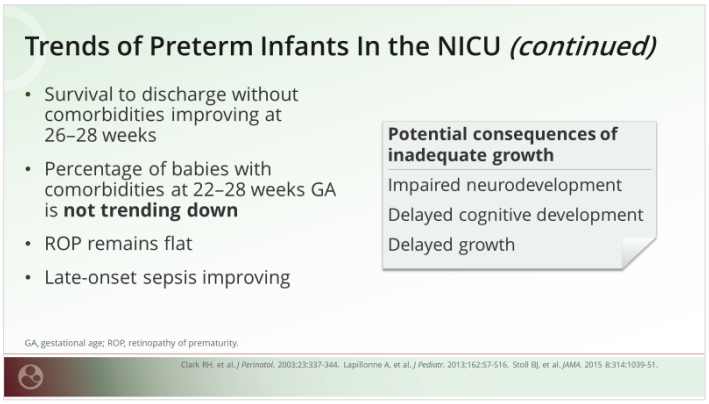
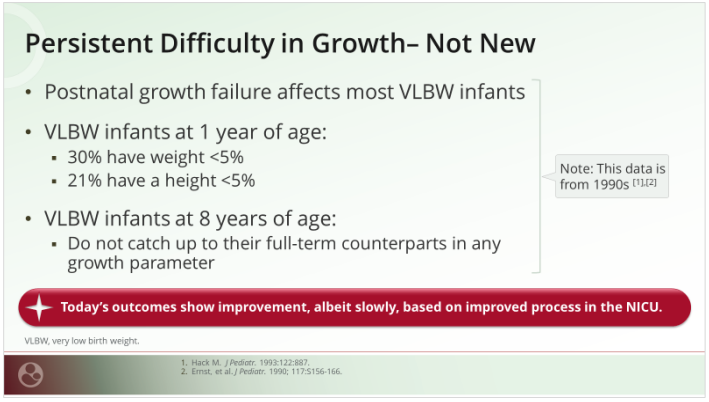


Slide 2 — Trends of Preterm Infants In the NICU (continued)

When you look across the percent of infants with comorbidities across that entire gestational age range of 22 to 28 weeks, we do not see downward trends in the percent of children with those comorbidities.

We do know that across the last 20 years, the absolute numbers of children who are surviving at any one of these given gestational ages is significantly greater now than it was 20 years ago. So, again, with percentages, we know there are—in absolute terms—more children we are needing to support and address.



Slide 3 — Persistent Difficulty in Growth– Not New

Very key comorbid conditions, like ROP [retinopathy of prematurity] and chronic lung disease, are remaining flat. Chronic lung disease may actually be rising a bit. Other things like late-onset sepsis, which has gotten much attention in the last 5 to 10 years, is beginning to improve. All of this wraps into nutrition in that if we do not have good growth and good repair and recovery for these children, we have information that it will impair long-term neurodevelopment. It can delay cognitive components. It can delay physical growth and stature.

We know from data that this is definitely not new. From back in the 1990s, we have always known in the field of neonatology that extrauterine growth has been a challenge for these babies.[2] This data you see before you [Slide 3] is actually from the late 1990s where even then they could demonstrate that VLBWs, which are 1,500 g and less at a year of age, show impairment in height and weight achievement, and that even to the 8 years of age range those children do not actually show a catch-up to their full term counterparts.[3]

Growth Shifts in the NICU

In particular, there had been some very interesting data about surviving preterm children in adolescent years and the impact of short stature on confidence and social interaction. These things have impact on these children *well* after they leave hospital NICUs.

We also know that in the last 30 years since those data were published, we have not been doing nothing. We have all—in the field—made substantial changes and improvement to how we are providing nutrition to these children. So, there are shifts happening across growth in the NICU, but they are slow, and sometimes getting that data clear can be challenging.

Extrauterine Growth

Extrauterine growth is pretty common. Certainly, surviving outside, in even the best NICU in the US, is not exactly the same as spending a third trimester in a human uterus. There are a lot of different things they must face, including increased metabolic demands; they may have poor tolerance of enteral feeds or the parenteral nutrition combination.

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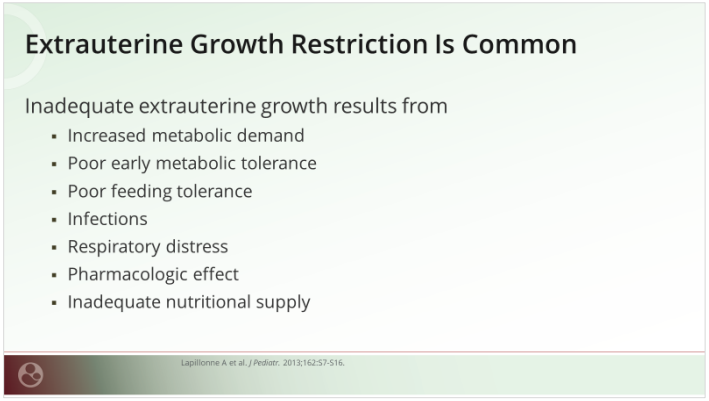
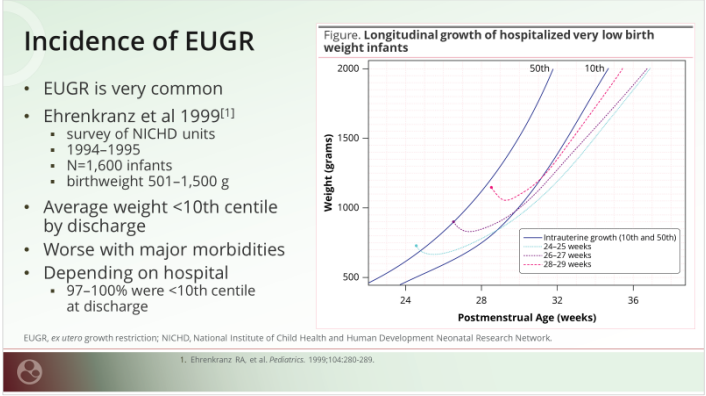
Intercurrent illness, like infection, is a major problem.



Slide 4 — Extrauterine Growth Restriction Is Common

We know that complications with different comorbidities, like necrotizing enterocolitis (NEC) or pneumothoraces, and other things can actually add additional burden. Almost all of these neonatal infants—particularly the young,—all of them have surfactant deficiency injury and a significant metabolic demand on repair and recovery of that.

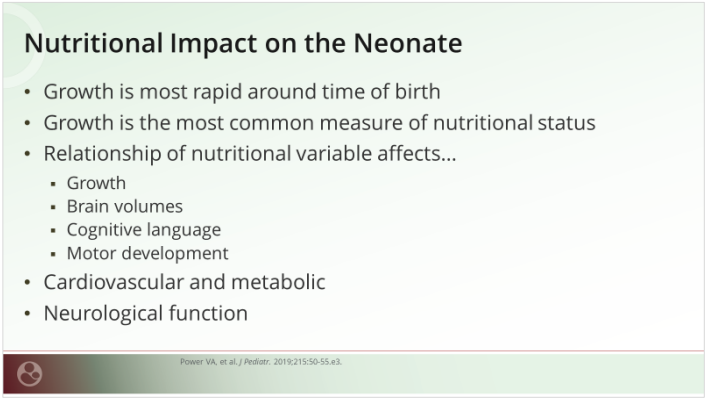
There are a number of competing factors that fit into that, with growth being one of the biggest. This is a graph [Slide 5] that actually—and this is again data that comes to us from right around '99, 2000, from Dr. Ehrenkranz—is just showing the impact of extrauterine growth restriction.[4] The vast majority of children, at the time they are discharged, are growing less than the tenth percentile, although they have had birth weights in much higher percentile ranges. We can see that all gestational age blocks have some impairment; some are just greater than others, and that has been actually tied into some of that long-term impact.



Slide 5 — Incidence of EUGR

Growth and Nutritional Status

We know that growth is the most rapid in the third trimester, which is the time that our premature children spend in neonatal ICUs if they are born early. Growth—and growth velocity—is the most common measure we have to look at nutritional status. It is easy; it is quick to have; it is something that is very trackable, but we know that there are some ties together with body growth as well as brain growth, and that's often noted in head circumference along with length. Those nutrition variables will also impact cognitive and motor development along the way. There is some data about long-term cardiovascular metabolic impact on those children that remain growth restricted.[5]



Slide 6 — Nutritional Impact on the Neonate

So, we know that looking in the long term, early data came out to tell us that higher protein intake,

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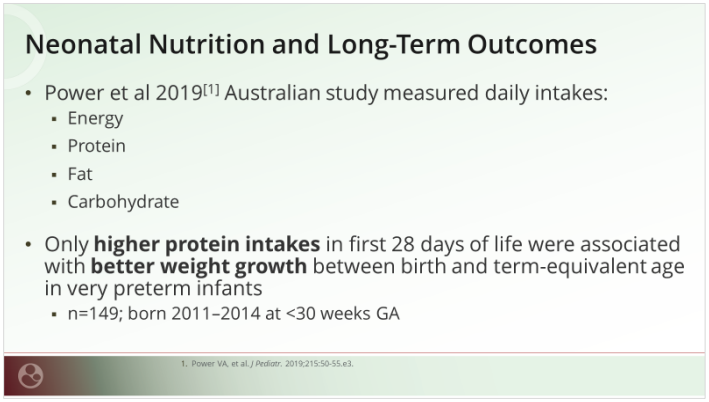
particularly in the first month of life, seemed to be associated with better weight gain, both early on as well as [when] they reached term-equivalent age.

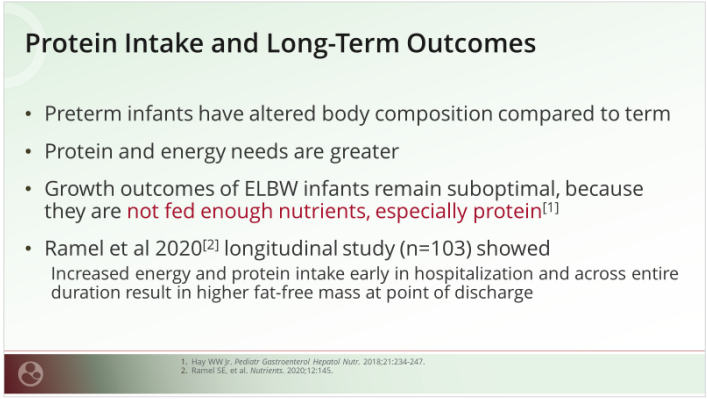
Many of us are aware of the challenges and impacts that we face. We begin here with a look at early feeding and then move into the more convalescent stages.



Slide 7 — Neonatal Nutrition and Long-Term Outcomes

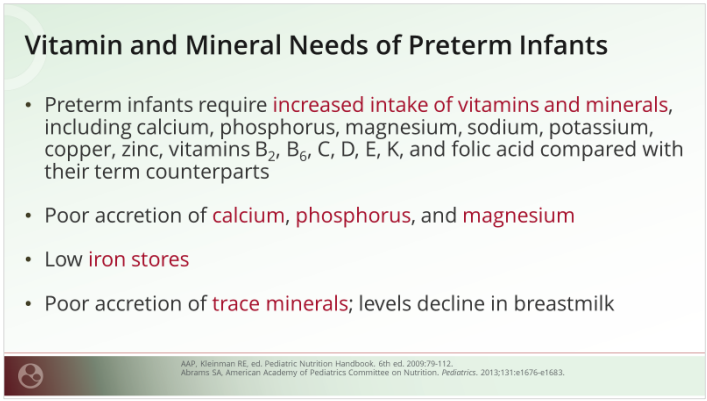
At this point, I can hand it over to Dr. Griffin, and I will meet you again near the end of the talk.

Ian J. Griffin, MB ChB: As Tara said, preterm infants have altered body composition compared to term infants, and their protein and energy needs are much higher. These 2 facts are related. There's data from this year from Sarah Ramel showing that if we increase the protein and energy intakes of preterm babies during their hospital stay,[6] they end up with higher lean tissue mass, or higher fat-free mass, at the time of discharge—a change that should be metabolically beneficial.



Slide 8 — Protein Intake and Long-Term Outcomes

In addition, preterm babies have increased needs for a range of vitamins and minerals—a list of which is shown here [Slide 9]. They have been shown to have reduced accretion of calcium, phosphate, and magnesium. They have reduced iron stores, and they have poor accretion of a number of trace minerals, in part due to the fact that levels in breast milk tend to decline with increasing lactation.



Slide 9 — Vitamin and Mineral Needs of Preterm Infants

The optimum intake of nutrients is essential for a range of reasons beyond growth. For example, long chain polyunsaturated fats are important to support neurodevelopment and immune function. Vitamin D is required for both neuromuscular function and bone mineralization; and iron status has shown a significant relationship with later neurodevelopmental outcome.

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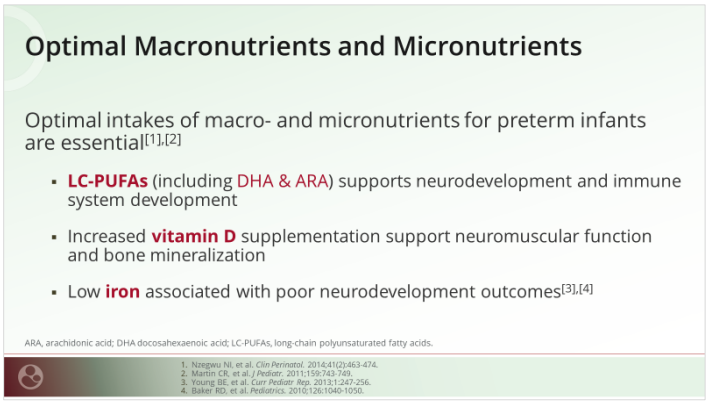


Slide 10 — Optimal Macronutrients and Micronutrients

In this [Table 1] we show some recommended intakes for some select micronutrients. This is from the review by Bert Koletzko from 2014.[7] Although it's a little old, I still think it's the very best work of its kind we have to refer to. I won't read this to you, but here you can see the data being shown in terms of per kg per day or per 100 calories of feed.

	Per kg body weight per day	Per 100 Cal
Calcium, mg	120–200	109–182
Phosphate, mg	60–140	55–127
Sodium, mg	69–115	63–105
Iron, mg	2–3	1.8–2.7
Zinc, mg	1.4–2.5	1.3–2.3
Vitamin D, IU	400–1,000[a] (per day)	100–350[b]

a. Total IU/day from milk and supplement
b. From milk only

Table 1 — Recommended Intakes of Select Micronutrients

Protein is Critical

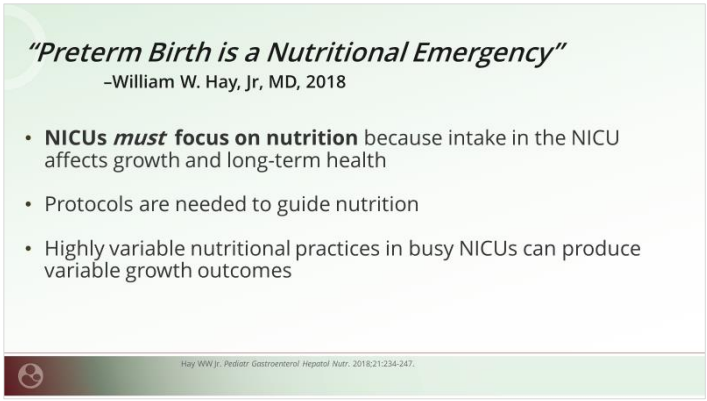
Here is similar data for macronutrients [Table 2]. The 1 macronutrient I would point out is protein, with here a recommendation of 3.5–4.5 g/kg/day of protein. Some subsequent recommendations, particularly European ones, have been on the lower side of that. But protein—I think, we've mentioned already a couple of times in this presentation [is critical]—and I think it's going to be an ongoing motif throughout the talk.

	Per kg body weight per day	Per 100 Cal
Fluids, mL	135–200	
Energy, Cal	110–130	
Protein, g	3.5–4.5	3.2–4.1
Lipids, g	4.8–6.6	4.4–6.0
DHA, mg	18–60	16.4–55
ARA, mg	18–45	16.4–41
Carbohydrate, g	11.6–13.2	10.5–12

ARA, arachidonic acid; DHA docosahexaenoic acid.

Table 2 — Recommended Intakes

Here's a nice quote from Bill Hay that's saying that preterm birth is a nutritional emergency,[8] and that is certainly true. NICUs must really focus very closely on nutrition, because the nutritional decisions we make, even early on, are going to have profound and long-term effects on growth and later health.



Slide 11 — Preterm Birth is a Nutritional Emergency

Need for Protocols

In order to do a good job nutritionally, we need to have protocols. We need to avoid, as much as possible, variations in practice, because variations in practice produce variable outcomes, and, almost invariably, variation in outcome is not good for the baby.

Here again is an example [Slide 12] of some data by Rich Ehrenkranz.[9] This is data from the NICHD [National Institute of Child Health and Human Development]. What he's done here is look at the in-hospital growth of babies and divided it into 4 quartiles by weight gain. On the left we have the

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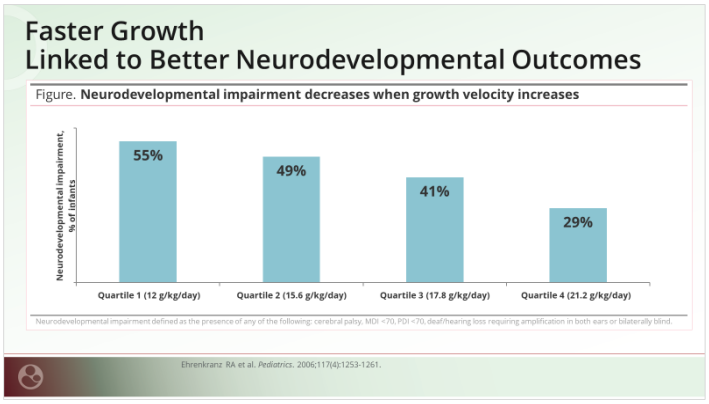
slowest growing quartile; on the right we have the fastest growing quartile. He's giving us the rates of neurodevelopmental impairments among these infants at 18–22 months. As you can see, as in-hospital growth improves from left to right, the rate of neurodevelopmental impairment falls.



Slide 12 — Faster Growth-Linked to Better Neurodevelopmental Outcomes

This is similar data [Table 3], looking at a range of other outcomes at 18 to 22 months. Again, as growth improves in hospital, moving from left to right, the rate of cerebral palsy at 18 months falls; the chances of having an abnormally low Bayley's MDI [mental developmental index] or PDI [physical development index] falls. The chances of having weight, length, or head circumference below the tenth centile at 18 months falls; and the rate of rehospitalization falls.

What does good growth look like?

I think it's clear that growth is dependent on nutritional intake, but we really need to ask ourselves, what does good growth look like in the hospital, and where are the vulnerable periods where babies may grow poorly and fall behind?

	Q1 (n=124)	Q2 (n=122)	Q3 (n=123)	Q4 (n=121)	*P*
Weight gain mean (SD) g/kg/d	12.0 (2.1)	15.6 (0.8)	17.8 (0.8)	21.2 (2.0)	
Normal neurologic exams	70	77	76	86	<.01
Q4 equates 2.53x risk of NDI					
CP, %	21	13	13	6	<.01
MDI <70,%	39	37	34	21	<.01
PDI <70,%	35	32	18	14	<.001
Weight <10 percentile, %	58	61	51	46	.03
Length <10 percentile, %	47	43	29	28	<.001
HC <10% percentile, %	31	18	18	22	.098
Rehospitalization, %	63	60	50	45	<.01

HC, head circumference; MDI, Mental Developmental Index; NDI, neurodevelopmental impairment; PDI, Psychomotor Developmental Index.

Table 3 — Evidence of the importance of growth in the NICU

Weight

We have 3 main measures of growth: weight, length, and head circumference. Obviously, length is the easiest to do, and most units are doing it every day. Because we do it so frequently, it's easy to see trends in weight gain relatively quickly. Importantly, growth as measured by weight gain has been clearly associated both with short- and long-term outcomes, including long-term neurodevelopmental outcome. The cons of measuring or relying on weight are that it is affected by fluid status, for example the use of diuretics, and people will say that it's not "real growth." But typically, a target of about 16–18 g/kg/d is probably appropriate.

	Pros	Cons	Target
Weight	• Easy to do • Done daily • Easy to see trends • Cleary associated with short- and long-term outcomes	• Affected by fluid status • Diuretics • Not 'real' growth	~16–18 g/kg/d
Length	'Real' growth	• Hard to do • Inaccurate • Often not a better measure of lean mass • Often not better related to outcome	~1 cm/wk
Head circumference	• Strongly related to developmental outcome • Easy to do	Confounded by change in head shape	~1 cm/wk

Table 4 — What to Measure: Pros and Cons and Target Goals

Length

Many people prefer length because they feel it more closely mirrors real growth, but it's hard to do, and it's inaccurate except in very experienced hands. Furthermore, it's not really much of a better measure of lean mass than weight is, and it's often not better related to long-term outcome than weight is.

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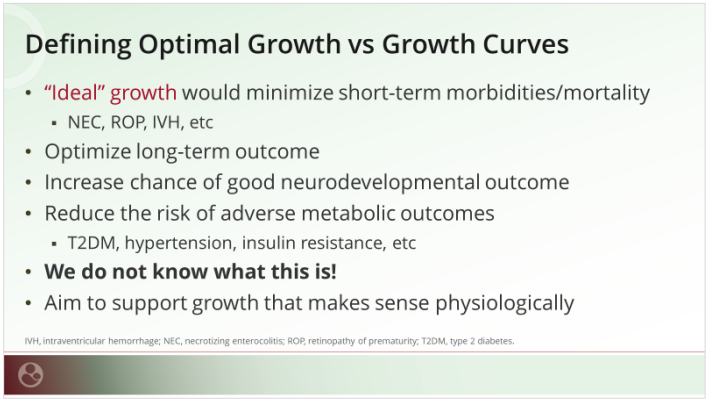
Head Circumference

Finally, there's head circumference. This is very strongly related to long-term developmental outcome and it's relatively easy to do, but it is confounded by changes in head shape that occur particularly in the most preterm of babies.

On the previous slide we gave some targets, but really one take home message is that growth charts are much to be preferred over targets of grams per kilogram per day, for example. Because those can change with corrected gestational age, and they also vary somewhat depending whether a baby is on the 90th or the 10th centile, for example.

What does ideal growth look like?

What does ideal growth look like? Ideally, it would be the growth pattern that minimizes short-term mortality and morbidity, so for example NEC, ROP and IVH [intraventricular hemorrhage]. It would also optimize long-term outcome; increase the chance of good neurodevelopmental outcome; and reduce the risk of adverse metabolic outcomes, like type-two diabetes, hypertension, insulin resistance, and the like. Unfortunately, we don't know what that growth pattern is, and absent that information, our aim can really only be to support growth that makes sense physiologically. We really have no better model of what growth should look like than that of the healthy fetus.



Slide 13 — Defining Optimal Growth vs Growth Curves

Growth Charts

As I mentioned before, we would prefer to use growth charts than numerical targets. We have a range of options: the Olsen chart from the US, the Bertino charts from Italy,[10] the Fenton charts,[11] and more recently the Intergrowth-21st charts.[12] Of these, I think that the most useful is the Fenton charts.[13] They spanned a period from a very preterm birth right through to 50 weeks corrected age. They've been validated as a growth monitoring tool in preterm infants. The definitions of poor growth made using the Fenton charts are strongly related to long-term outcomes, including neuro development, and are, in actual fact, more strongly related than definitions of poor growth made, for example, using the Intergrowth charts.

Olsen chart (developed from NICU growth data) Bertino chart (developed from 'ideal' growth data)	Up to 36 weeks GA	• Assess for GA, SGA, LGA • Not recommended for growth monitoring for preterm >36 wks
Fenton chart	Between 36–50 weeks correct age (10 weeks post-term)	• Best growth chart to assess longitudinal growth in preterm infants over this period • Validated as a growth monitoring tool in preterm infants • Definitions of poor growth are strongly related to long-term outcomes
INTERGROWTH-21st	Between 24–33 weeks GA	• International fetal growth standards • Show how fetuses should grow rather than how they have grown

SGA, small for gestational age; LGA, large for gestational age.

Table 5 — Growth Charts

Fenton Chart Specifics

The Fenton charts do have a couple of peculiarities about them, and it's important to remember that they use 2 references. Before the expected date of delivery, you are comparing your baby to newborn, healthy preterm babies, who typically haven't undergone the postnatal water loss that babies undergo. So, before the expected date of delivery, it's perfectly appropriate for your preterm baby to be 1 centile below their birth centile, because that baby has lost that postnatal water loss but is being compared to babies who haven't.

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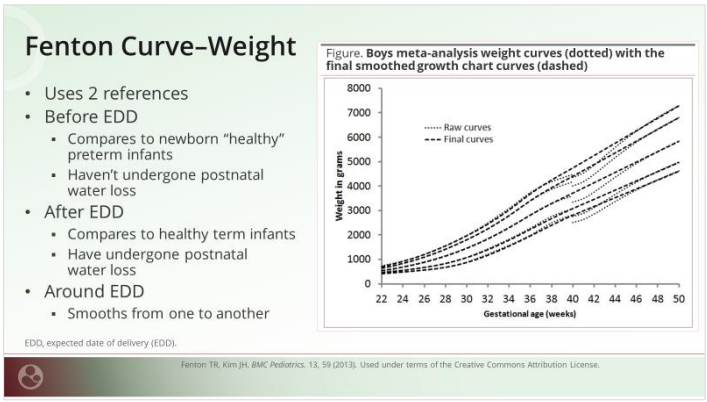
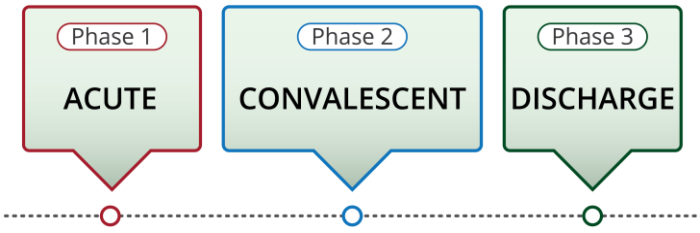


Slide 14 — Fenton Curve–Weight

After the expected date of delivery, we are making a comparison to healthy term infants who have already undergone that postnatal water loss. Then, at that time, you would hope that your baby was back to their birth centile. That obviously means that between those 2 periods there's going to be an upward crossing of centiles, usually between 36 to 40 weeks corrected gestational age. That looks like catch-up growth, but it's really just an artifact of how the charts were developed.

If you're uncomfortable with that, then your alternative is to use something like the Olsen charts before expected date of delivery, and something like the WHO charts, after the expected date of delivery.

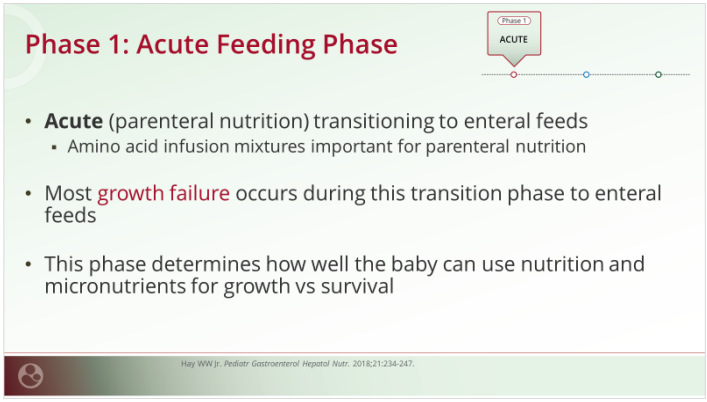
Feeding Methods in 3 Phases



Acute Phase

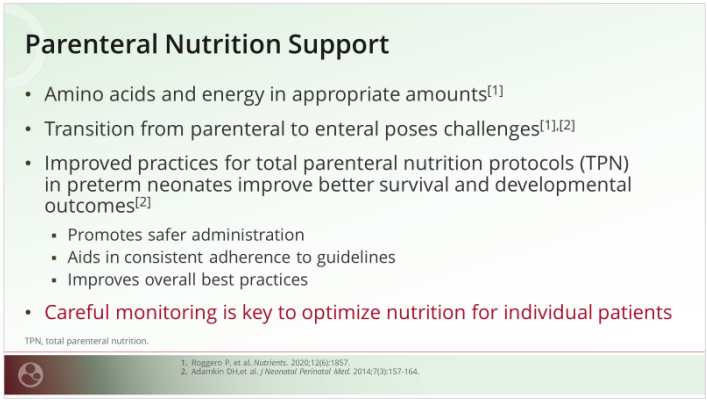
Now we're going to consider the 3 phases of growth. The first phase is the acute phase. This starts at the moment of birth and continues until the baby is on full enteral nutrition. The second phase is the convalescent phase. This is the period from full enteral nutrition until the baby goes home. And the discharge period obviously speaks for itself.

During the acute phase, as I say this is the period where we move from full parental nutrition to full enteral nutrition. This is the period where a lot of growth failure can occur.



Slide 15 — Phase 1: Acute Feeding Phase

With the modern products we have, full parenteral nutrition can supply good protein and energy intakes to even the most preterm of babies. With modern formulas and human milk fortifiers, full enteral nutrition can do the same. It can supply all the protein and energy a preterm baby needs. The difficulty is in the transition between those 2 approaches: the transition from parenteral nutrition to enteral nutrition.[14]

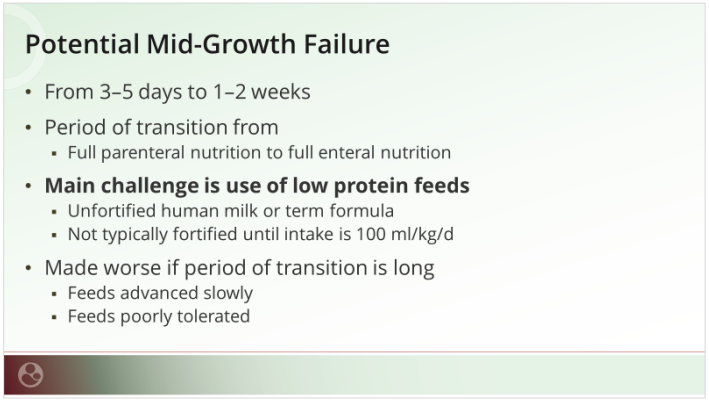


Slide 16 — Parenteral Nutrition Support

This period starts from maybe 1–2 days and carries on for 1–2 weeks, depending on how rapidly you

Redesigning Postdischarge Nutrition in the NICU

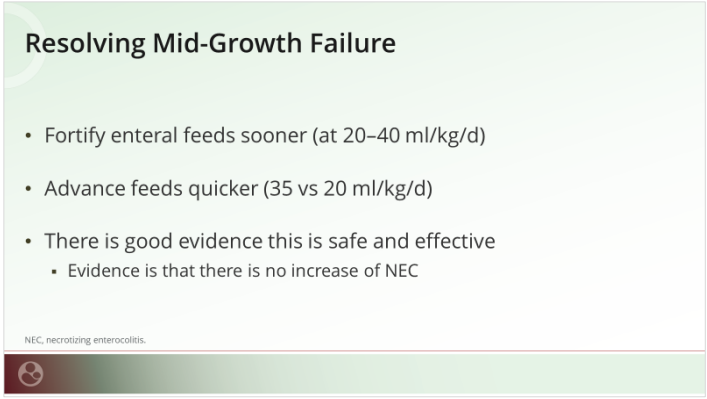
transition from parenteral to enteral nutrition. The main challenge during this period is the use of low-protein feeds. Most places will start feeds either with unfortified human milk or with a term formula, and not fortify that until the intake is 100 mL/kg/d. This means we're taking really good quality parenteral nutrition, that contains good amounts of protein, away from the baby, and we're replacing it with feeds that contain less protein. During this period, the baby is very liable to have inadequate protein intakes and accumulate a deficit in protein. This is obviously made worse if the period of transition is long; for example, if feeds are advanced very slowly or if feeds are poorly tolerated.



Slide 17 — Potential Mid-Growth Failure

Avoid Low-Protein Feeds

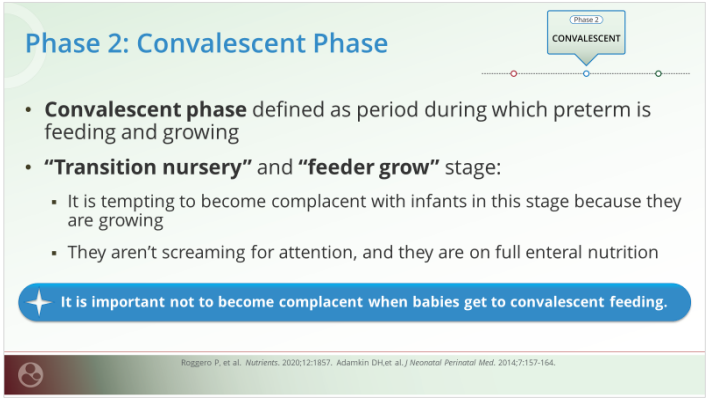
The way to avoid growth failure during this period is to avoid the use of low-protein feeds. I would recommend that we should fortify enteral feeds earlier, either at 20–40 mL/kg/d, and advance feeds more quickly, so at a rate of 30–35 mL/kg/d rather than 15–20 mL/kg/d. There is good evidence from well-designed randomized controlled trials that this is safe and effective, and evidence that there really is no identifiable increase in the risk of NEC by doing this.



Slide 18 — Resolving Mid-Growth Failure

Convalescent Period

The next period is the convalescent period. This is that period that people call the feeder-grower period, where babies are often in a transitional nursery or a special care nursery. And it's tempting and very easy to become complacent during this stage because the babies are doing good. They've gotten through the life-threatening things that challenge them early on; they're not demanding our constant attention, and we're not having to make the complicated and time-consuming kind of decisions that we had to make earlier on. So, it's very easy to just skip over these babies on rounds and really not give them the attention they deserve.



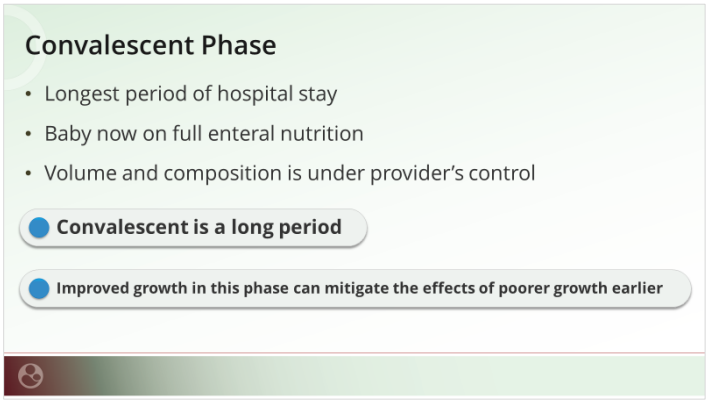
Slide 19 — Phase 2: Convalescent Phase

However, this convalescent period is the longest period during the hospital stay. As I say, the baby is on full enteral nutrition, and both the volume and

the composition that baby gets is pretty much entirely under our control.

Growth and Morbidity

It's easy during this period to blame poor growth on comorbidities. For example, the baby wasn't growing well because they had a NEC scare, they had sepsis, they had feeding intolerance. But that relationship is a little bit more complicated. There's increasing evidence that poor growth can predispose babies to acute morbidities. The relationship between growth and morbidity is a 2-way street: both can affect the other.



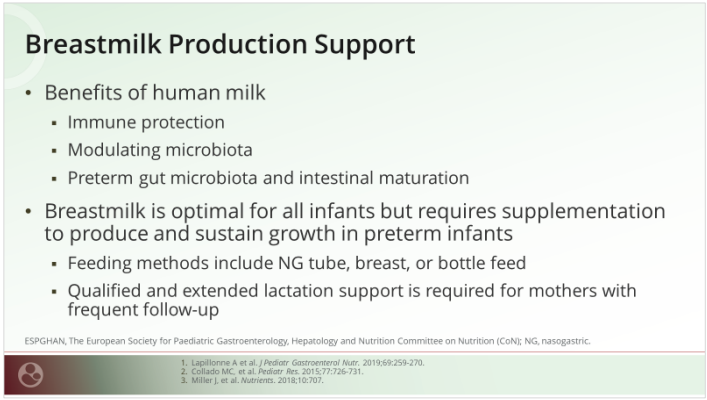
Slide 20 — Convalescent Phase

During this period, a lot of things will happen. I'm sure everyone who works on a NICU knows this. Overnight the baby had a residual. The belly was distended, so feeds were stopped overnight. People will come in in the morning and want to restart feeds but maybe not do it too quickly. So, they'll start feeds at 1/4 of the normal amount, then, a bit later, go up to 1/2, then 3/4, then full feeds. All the time we're doing this, the baby is probably just receiving D10 [infusion rate], so, we're taking away a really good source of nutrition and replacing it with a really poor source of nutrition.

That's okay if it happens just once, but if that happens as an ongoing thing and multiplied during a baby's admission, this can really develop into a significant problem and have a very profound effect on the baby's hospital growth. As I said before, just a reminder that sometimes poor nutrition and poor growth is the cause of morbidities rather than the other way round.

Human Milk in Convalescent Period

During this convalescent period, we really want to be using human milk. It has a lot of non-nutritional factors that formula is not able to duplicate. It leads to increased immune protection, modulates the baby's microbiota, and improves intestinal maturation. However, although breast milk is optimal for all preterm infants, it does require supplementation to provide and sustain adequate growth in preterm infants. We should also not forget that qualified, intensive, and extended lactation support is really required for mothers to allow them to produce milk for their babies.

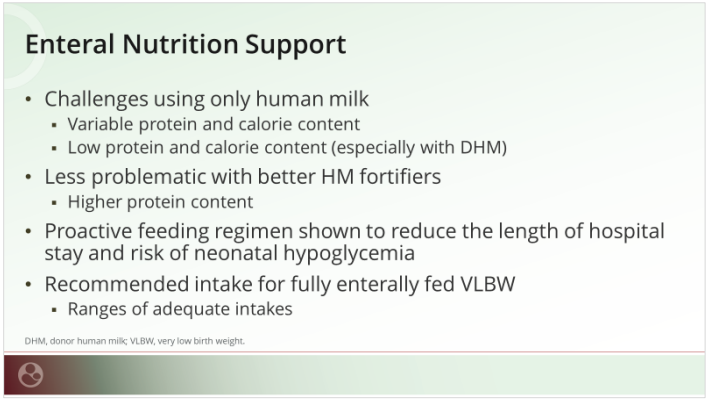


Slide 21 — Breastmilk Production Support

Challenges Using Human Milk

The challenges using human milk are twofold. First, the protein and energy content are very variable, and also on average it's relatively low. This is less problematic than it was even a few years ago because of the improving quality of human-milk fortifiers, which typically have higher protein contents than they used to. But still, this remains an issue, and you really need to be very cognizant of this as you're using human milk. This adds a little bit of complexity, but even so, the benefits of human

milk far outweigh the slight increase in work that we have to do to make it successful.[15,16,17]

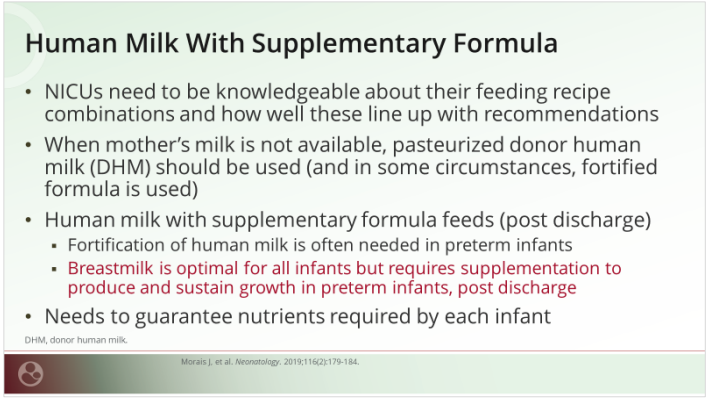


Slide 22 — Enteral Nutrition Support

Here again are some selected intakes of some micronutrients during this phase. Again, I won't read them to you, but they're available to refer to [Table 1]. Here again are the intakes of some selected macronutrients [Table 2].

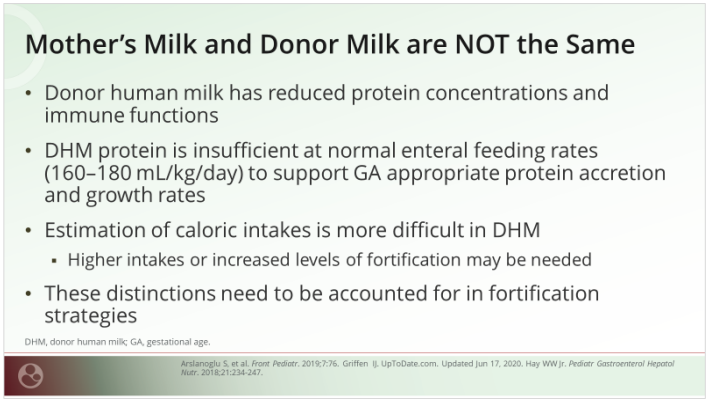
Know Your Feeding Recipe

NICUs need to be knowledgeable about their feeding recipe. You really need to understand how the milk is being fortified in your nursery, and what average intakes you can expect that to produce. Often mother's own milk may be inadequate in volume. In that case, pasteurized donor human milk is really the optimum substitute; although, for practical and economic reasons, sometimes fortified formulas will be used. The use of supplementary formula feeds is, of course, most common after hospital discharge where fortification and donor human milk is no longer available.



Slide 23 — Human Milk With Supplementary Formula

It is worth stressing that mother's own milk and donor human milk are not the same. Donor human milk has lower protein content, and the number of the immune factors are affected by pasteurization. Donor human milk, just like mother's own milk, is insufficient to meet the protein needs of preterm infants, even when fed at very high volumes. Also, donor human milk may be lower in calorie content than mother's own milk, and therefore, higher levels of fortification may need to be used. You need to consider these when you think about your fortification strategy.



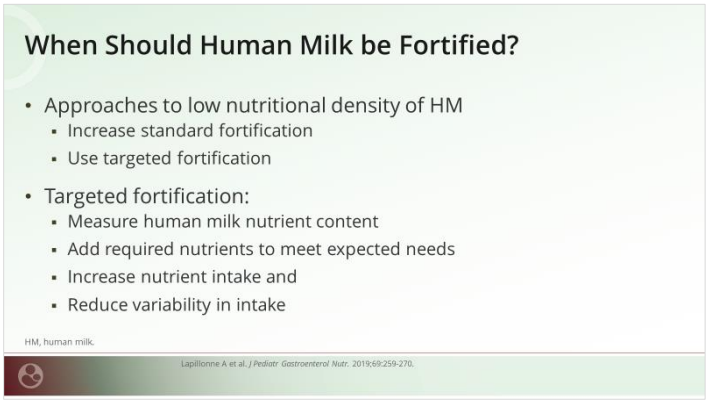
Slide 24 — Mother's Milk and Donor Milk are NOT the Same

Standard and Target Fortification

How should human milk be fortified? There really are 2 main approaches. One is standard fortification. This is where you add the same fortify recipe to every sample of human milk. The second

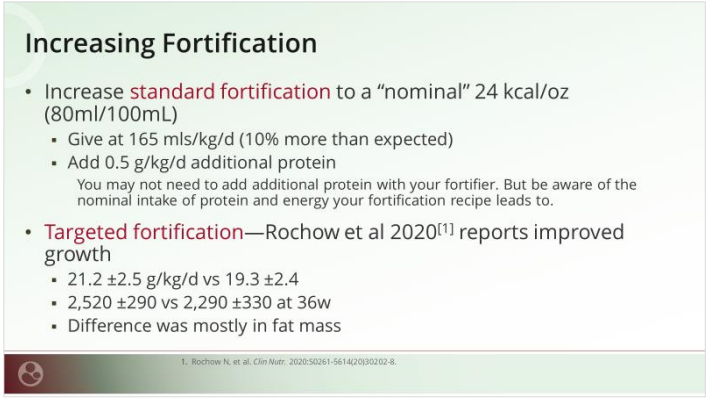
Redesigning Postdischarge Nutrition in the NICU

one, which is becoming increasingly fashionable is the use of targeted fortification. In this, one uses a human milk analyzer to measure the nutrient content of that particular sample of milk, and then you add the specific nutrients in the exact amount to get the level up to exactly where you want it to be. This has the theoretical benefits, but it may both increase the nutrient intake that comes from human milk and reduce the variability in content of protein and energy in human milk.



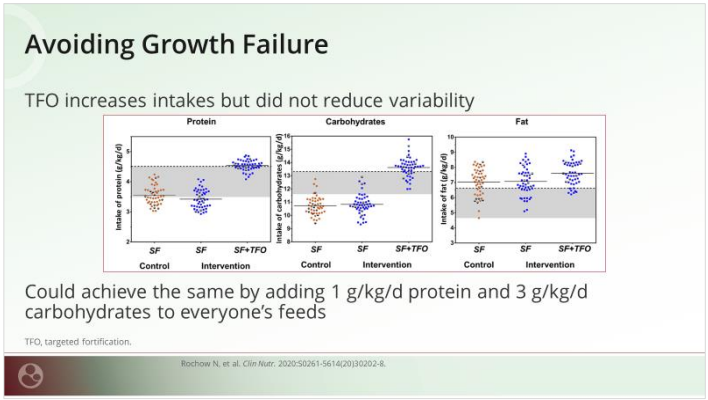
Slide 25 — When Should Human Milk be Fortified?

That is not our practice. Our practice has been to use standard fortification. We use a commercially available bovine human milk fortifier, fortify to a nominal intake of 24 calories per oz. I say nominal because as the mother's own milk or the donor human milk is very variable in composition, that variability in composition projects forward after standard fortification. We also add some additional protein. We do that based on the human milk fortifier we're using; it doesn't quite give us the protein intake we want, so we add more protein. You may not need to do that in your institution. It really depends on what human milk fortifier you're using and how you're putting it in the human milk. So again, you really need to understand how fortification works in your unit for your babies.



Slide 26 — Increasing Fortification

The alternative approach of targeted fortification has been examined by Christoph Fusch's group and they produced results earlier this year.[18] Their headline results looked relatively encouraging for targeted fortification. Targeted fortification improved weight gain from about 19–21 g/kg/d, and increased the weight of 36 weeks corrected gestational age from about 2.3 kg to about 2.5 kg. That difference was mostly in fat mass, which is only to be expected.



Slide 27 — Avoiding Growth Failure

However, if you dig into the results a little bit more, things are a bit more nuanced than those headline results suggest. I'll talk you through this slide [Slide 27]. We have 3 panels.[18] On the left, protein intake; in the center, carbohydrate intake; on the right, fat intake. The little red dots are the standard fortification. The first set of blue dots is the intervention group; what their intake got to with

standard fortification. And then the final set of little blue dots are after additional targeted fortification was done. So, really for this, you're comparing the little orange dots on the left of each panel to the little blue dots on the right of each panel. Shaded in gray is the target range for those macronutrients. You can see if you look at the protein group, their targeted intake of protein was 3.5–4.5 g/kg/d, exactly the same as the Koletzko recommendations.[7]

You can see that for the standard fortification group, about half of the babies were receiving protein intakes below the target range. For the targeted fortification, about half of them had protein intakes above the target range. What I think this chart shows most usefully is that the targeted fortification increased the nutrient intake but didn't really have very much effect on the variability of nutrient intake. The scatter of protein intake is relatively similar with the intervention and the control group.

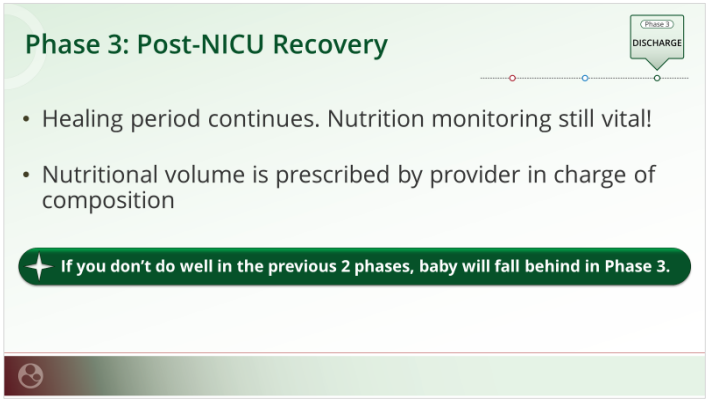
I think that these authors could have achieved something very similar just by better understanding their recipe for standard fortification and understanding that their recipe for standard fortification was only going to get half of the babies into their target range. I suspect that these authors could have had identical growth outcomes just by adding a little bit more protein, maybe 1/2 or 1 g/kg/d, to their fortification rather than going through all the cost, energy, effort and time of targeted fortification.

My plea, based on this study, is please don't go out and buy human milk analyzer; rather, sit down in your nursery and understand how you fortify human milk, and see if that gives you the intakes that you think your babies should need.

I will now turn the presentation back to Dr. Bastek to talk about the convalescent period.

Convalescent Period

Bastek: As we move through that journey, we come again to reaching the phase where… This slide is titled post-NICU recovery, but I really think of this as the transition period, as we are wrapping up a NICU experience and transitioning out the door, so it is much more of a continuum than it is a hard [period] when you walk out the door.



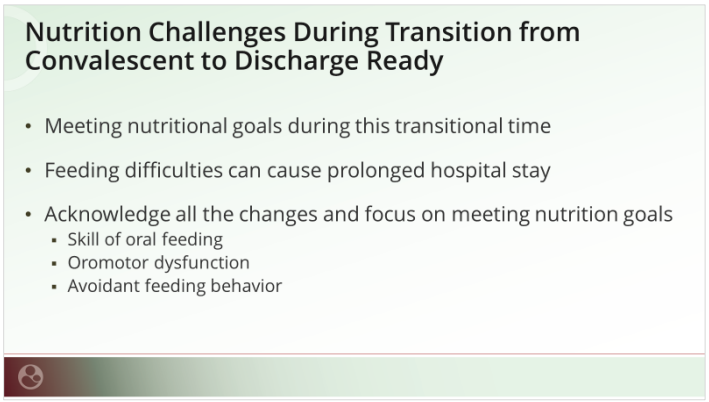
Slide 28 — Phase 3: Post-NICU Recovery

I think there are a few things that are really worth underscoring here as we reach the late convalescent window in a NICU and look towards home. And that is to remember that the growth needs of the baby sustain themselves. The healing period of cell repair and issues related to being premature, surfactant deficiency, and any other complication that may have arisen, that all continues for these infants. There are significant metabolic demands on the baby from those 2 things alone.

Oral Feeding

As they approach the ability to be discharged home, the third new event that occurs for them is the addition of oral feeding and the skill and complexity and metabolic demand that comes with that. This would be a range where the providers… we are still managing the components and the volume of their feeds and being mindful of how this transition goes.

Redesigning Postdischarge Nutrition in the NICU



Slide 29 — Nutrition Challenges During Transition from Convalescent to Discharge Ready

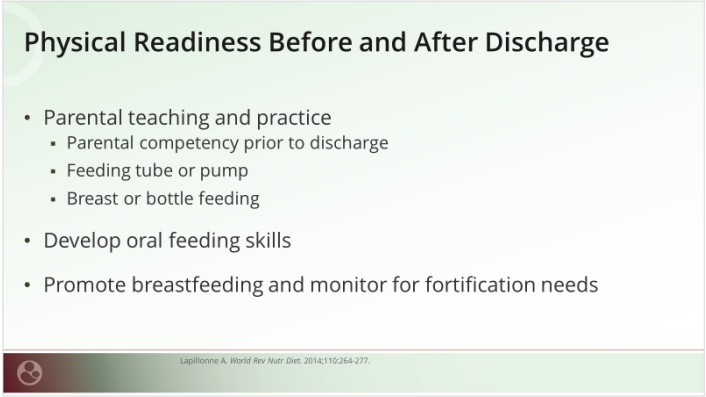
Transition-to-Home Feeds

The last piece to underscore, which is how we started this, is to say that as we look towards the discharge window for these babies with nutrition, how we have all supported them in the acute and interim convalescent phase will have direct bearing on how they enter this transition-to-home phase, whether they are growing well or [are] behind, and that has significant impact for these infants. We're going to talk a little bit about some ways to think through setting them up for transition-to-home feeds.

Remember that in an ideal world, while they were in this very long convalescent phase, we have been meeting their nutritional needs throughout that whole time. We now have to be aware that those needs and demands may be shifting. We know that oral-feeding challenges can be significant, particularly for the youngest and the smallest infants. And that the complicated motor components of integrated suck, swallow, breathe—sequencing those correctly. Negative experiences that [they] may be fostering. Avoidant feeding behavior… There are a number of potential challenges that come simultaneously with this change.

Physical Readiness

We can think of readiness for discharge and the setting of nutrition and feeding in sort of 2 ways. One is physical readiness, and that is the skill of oral feeding. How are these infants able to sequence? How are they being impacted by stamina with recovering lung injury and other things? Are there parental education needs and skill sets that we need parents to develop and be comfortable with? That may be feeding tubes or pumps. That might be lactation support, and comfort with latching and bottle feeding, and finding the right balance between those, and still promoting breast feeding with good nutrition. In many ways, it feels like that is a complicated task.



Slide 30 — Physical Readiness Before and After Discharge

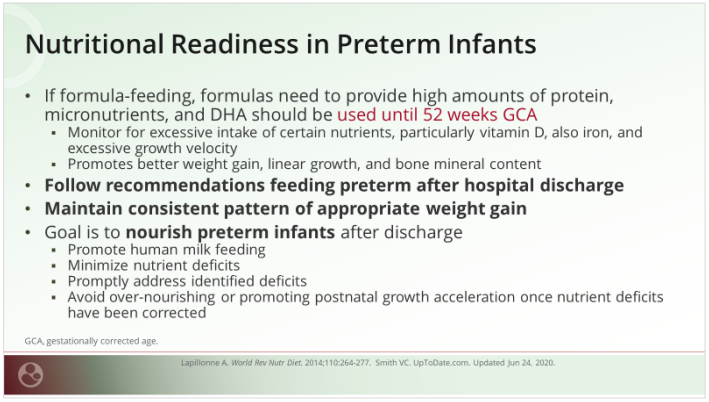
Nutritional Readiness for Discharge

The second component, I would argue, is a nutritional readiness for discharge in these preterm infants. Really beginning to think of having, just as we discharge plan for many other aspects of a premature infant's care, to think about having a planning conversation about what are the nutritional needs as we transition to home. For infants that might be formula feeding or enhanced breast milk feeding, the guidelines and things that support enhanced nutrition would also suggest that continuing that enhanced nutrition all the way out until 52 weeks corrected gestational age may indeed be very important for these infants to help them continue to show good convalescent growth

and help them continue to recover from the impact of preterm birth. That will take a little bit of oversight, which we'll talk about.

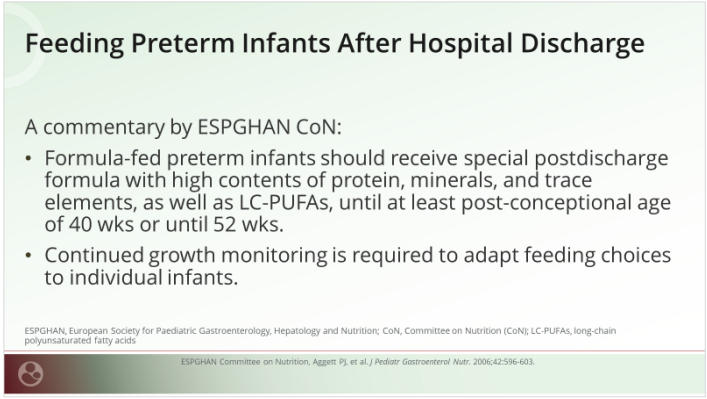
Maintain Weight Gain and Growth Velocity

The goal would be to try to maintain this consistent pattern of weight gain and growth velocity, and to look at meeting those goal needs of promoting human milk feeding to the greatest extent we can while minimizing other nutritional deficits. In the Goldilocks approach, we don't really want to over nourish and have accelerated excessive growth, that's largely excessive fat, but nor do we want to under-nourish and leave these infants without adequate nutrients and energy reserves for the new efforts that they are making.



Slide 31 — Nutritional Readiness in Preterm Infants

ESPGHAN and the other national and international guiding bodies have given us some very good direction on this,[19] and have for a while now talked about having postdischarge feeding needs, try to have higher contents of protein and minerals and certain trace elements, including the long-chain fatty acids extending beyond a 40-week due date sought.

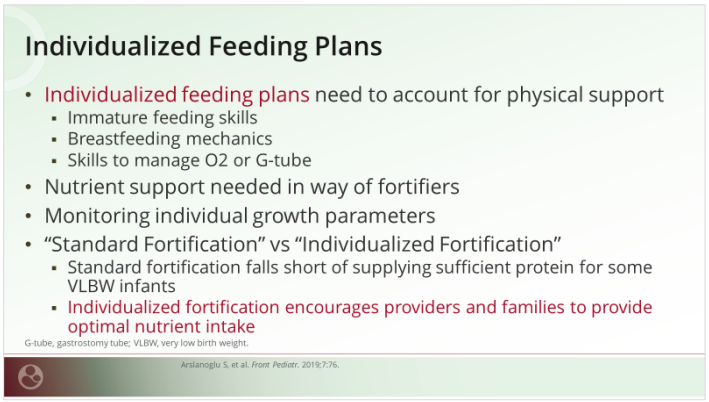


Slide 32 — Feeding Preterm Infants After Hospital Discharge

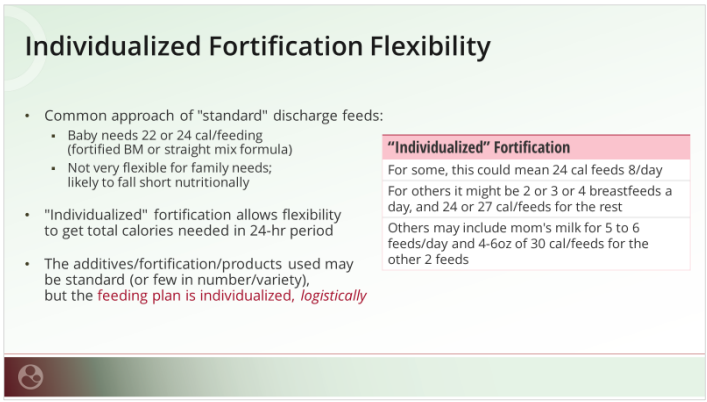
Some of the commercial formulas that are available on the market that many babies transition to over the course of the first 6 months or year of life are designed to meet those goals and needs. The downside is that they were designed to meet those needs if they were being used as 100% of the feeding. As we have more and more children, gratefully, wonderfully, going home breast feeding and having strong maternal feeding supplies, having a different strategy to make sure we are reaching nutrients is something that we need to think about.

The goal, of course, for all of us is to not lose any of the gains that families and NICUs have worked so hard to achieve for these premature infants. It is a crushing blow to think about having these infants, in celebration, go home only to have them failing to thrive or growing poorly as they are home, across those first months at home.

Redesigning Postdischarge Nutrition in the NICU



Slide 33 — Individualized Feeding Plans



Slide 34 — Individualized Fortification Flexibility

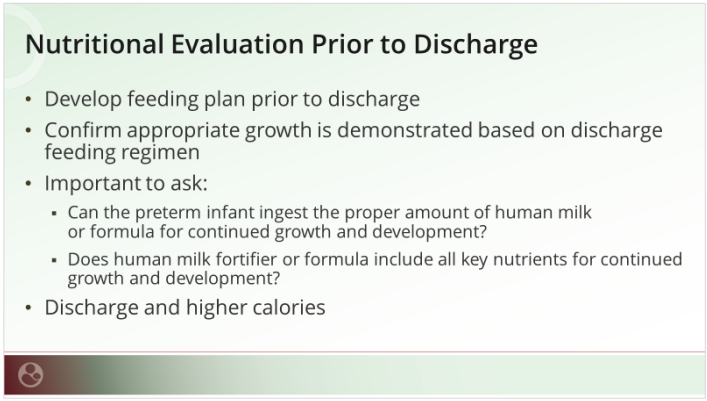
A similar concept to what Dr. Griffin brought up about individualized plan vs standard plan is something that we have been encouraging folks in our unit and others to really begin to think about. Rather [than] having a standard calorie-goal feeding plan that everybody is on—and we don't think too much about what additives are used to get there or what energy the baby is expending—that we really actually individualize that plan to account for the nutrient needs and physical support. So, if they are expending more energy, if they need to be able to have time with breastfeeding, how do we think about the micronutrient fortification support for these infants?

Individualizing Strategy

The other idea would be to think about a flexible strategy. A common approach for standard feedings near the time of discharge would be having either a set caloric intake with either fortified maternal milk or formula, and that we do the same thing at every feed around the clock. Individualizing that might actually mean considering which one of those infants might be able to nurse without supplementation behind it, once or twice or 3 times a day. Then how do you offset that with enhanced fortified feeds for the other part of the day? How does that work with family logistics, and does that help better meet the needs for these infants?

But maybe thinking of it as tailoring it on a logistical level, as opposed to, we're using lots of different products for those infants. An example would be we have the same thing 8 times a day, but maybe we are actually adjusting for mother's milk supply and the infant's ability to breastfeed well or poorly.

We think there are a few very important questions to ask that help prompt this conversation: can the preterm infant nearing discharge take the goal volume that we want them to take of either human milk or formula? Which fortifiers can we add key elements to? We have been exploring use of some of the fortification strategies that we use in the neonatal ICU and being able to transition them to families as they go home, continuing to use the same products in the community as we try to get close to that 52-week goal of strong growth.

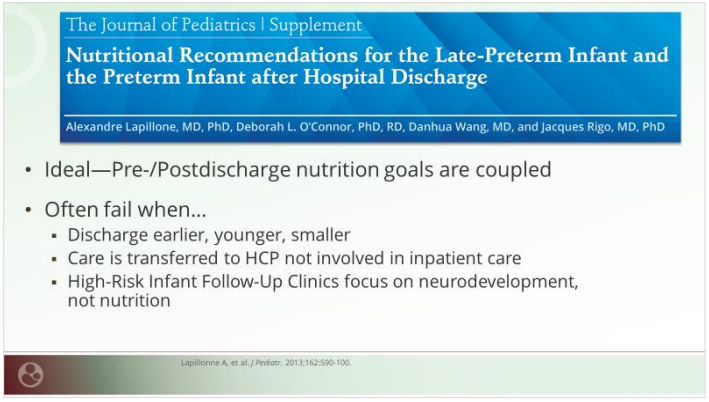


Slide 35 — Nutritional Evaluation Prior to Discharge

Redesigning Postdischarge Nutrition in the NICU

Lapillonne and his group had published a tremendous body of work supporting this kind of nutrition concept but had published this very influential paper about thinking how we support the late-preterm and preterm infant as they transition to home, and things that are happening after the neonatal ICU may transition to community providers.[20] They raised the awareness that as we are discharging infants earlier and younger and smaller, which is often seen as a success by our families as well as our administrators, it carries with it some risk that these infants do not have a good transition of care.

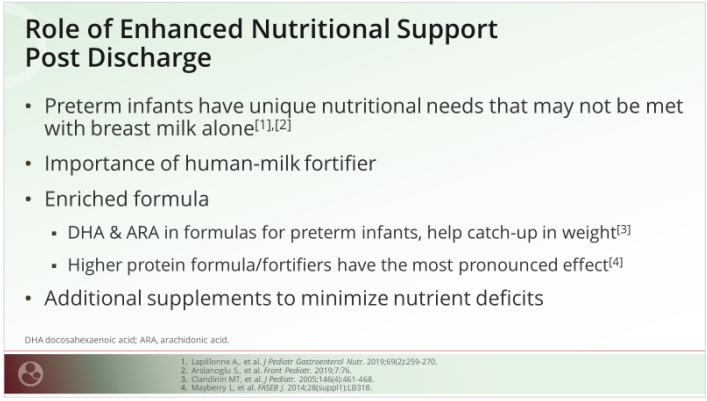
The community health providers may not understand all those nuances. There are competing interests, and our typical safety nets for these preterm infants generally are focused more on neurodevelopment and they do not think of themselves as, nor are they structured to be, nutrition-assessment places, particularly in the early weeks of transitioning home. That actually really prompts a consideration for how we might be using our discharge resources for these infants.



Slide 36 — Nutritional Recommendations for the Late-Preterm Infant and the Preterm Infant after Hospital Discharge

Again, we've underscored that mother's milk alone does not have the nutritional complexity to be able to meet the needs of the preterm infants who are still recovering from the significant impact that premature experience has on them. Human milk fortifiers have gotten much better, and we are supplementing. All of those things we need to continue to think about as we set them up for home.

One of the things we would underscore is that having some ability to follow that and structure it is very important. The idea that there is a mechanism to follow growth, including weight and length, to follow them on a weekly or biweekly basis for the first several weeks outside of the hospital is an important way to make sure that concerns and questions are addressed, but also to kind of keep them on the right track.

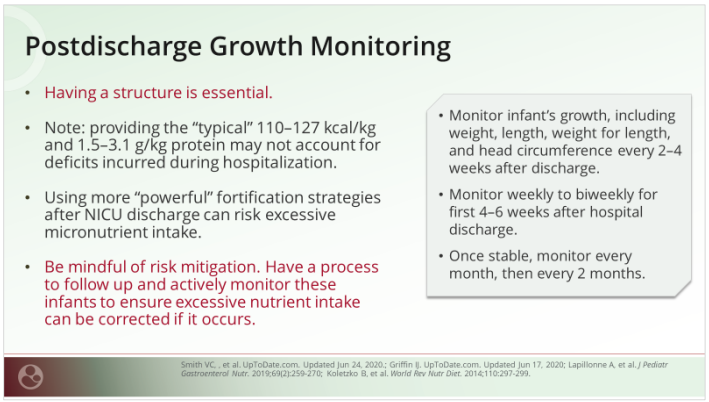


Slide 37 — Role of Enhanced Nutritional Support

Breastfeeding Support

As I mentioned before, using some of these more powerful fortification strategies after discharge can be helpful. The biggest benefit of that is in the ever-increasing support for breastfeeding, in particular, and breast milk intake going home. The upside of our traditional—I would call them traditional—NICU fortifiers is that they are very concentrated, and they preserve the majority of human milk and displace it less and less, and that is a reason to consider them.

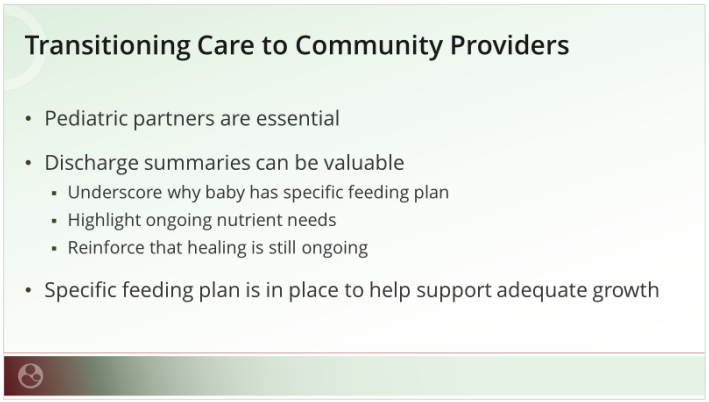
Redesigning Postdischarge Nutrition in the NICU



Slide 38 — Postdischarge Growth Monitoring

Monitoring Intake of Micronutrients

However, it means that we also need to be mindful of where there might actually be risk, and particularly excessive intake on some of the micronutrients. Vitamin D is the one that comes to mind the most. There are certainly children who have excellent vitamin D levels and would become vitamin D, sort of, excessive, and then make those NICU-based fortifiers less desirable—something we would want to avoid in the long term, several weeks out of the hospital. The idea that there is a location or a place to have these infants followed up, in a cohesive way, where there are people aware of these balancing factors, it would be a very helpful support for them.



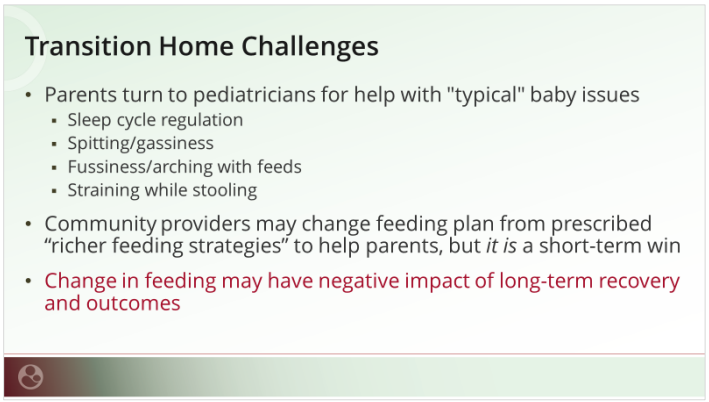
Slide 39 — Transitioning Care to Community Providers

I also would underscore that our community pediatricians and family medicine doctors, and those who are supporting these preterm infants and their families as they go home, are essential. They are essential to the transition process home and to keeping the care strategies on track. Discharge summaries can be very valuable, although we have all seen unwieldy discharge summaries of infants who have spent months, literally, in ICU. So, finding ways in our electronic records and communications to highlight the specifics of a feeding plan, whether that's bolded or boxes or other things that will call someone's attention to it. And to underscore that there's a rationale for wanting to continue this for weeks beyond the NICU so we can try to protect that adequate growth.

Balancing Changes

We know from a developmental perspective that premature infants, as they transition home, they struggle with a lot of behavioral changes. Some of that is just their developmental neurological complexity allowing them to demonstrate a more complicated repertoire of behaviors, but we know that parents struggle, often with a nervous family. Although they are not a new baby, they may have been in a NICU for a long time, they are new to them at home, and these infants are changing. So concerns about sleep cycle regulation, crying, fussiness, whether that be everything is related to reflux or not, the straining while stooling, whether that is true constipation or just low abdominal muscle tone. Balancing those concerns from parents is a real challenge. Our community pediatricians and family medicine providers and others are often faced with trying to help families navigate that.

Redesigning Postdischarge Nutrition in the NICU

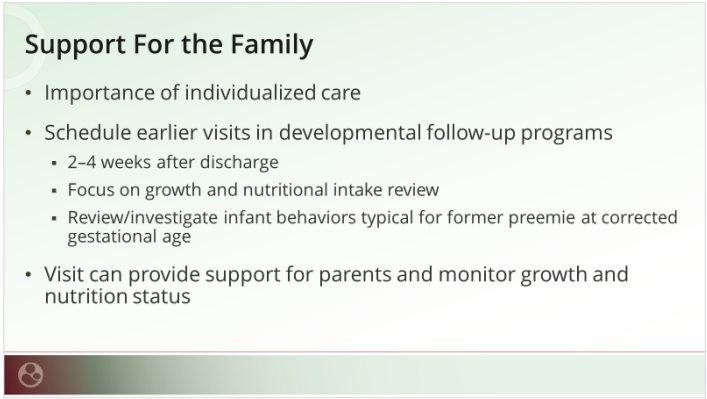


Slide 40 — Transition Home Challenges

A common event is to see infants changing their feeding strategies. Doing that might actually provide what is perceived to be a short-term win; however, taking them off some of these richer feeding strategies may have significant long-term negative impact in undermining their ability to recover from the issues of prematurity. Specifically, I think about things where we may be trying to avoid a particular component, whether that be protein or sugar structures, like lactose, and they are shifted to one of those formulas designed for term infants and do not in any way have the ability to make up the deficits that a preterm infant has.

Family Support

Supporting the families, in general, this is a really important and exciting time for families as they are discharged home, and we would not want to sell and underscore the message that something is wrong, or they have failed. Everyone is trying to do the best for these babies. But really thinking of a way to help support them through the nervous excitement of learning their infants 24/7 and their nuances, while underscoring that we all are invested in the best long-term outcome. Supporting them by having our developmental follow-up programs begin to get some nutritional expertise. Scheduling their visits sooner, a week or 2, and every couple of weeks after discharge, so they will get the support of those folks can be very helpful for families to understand that balance.

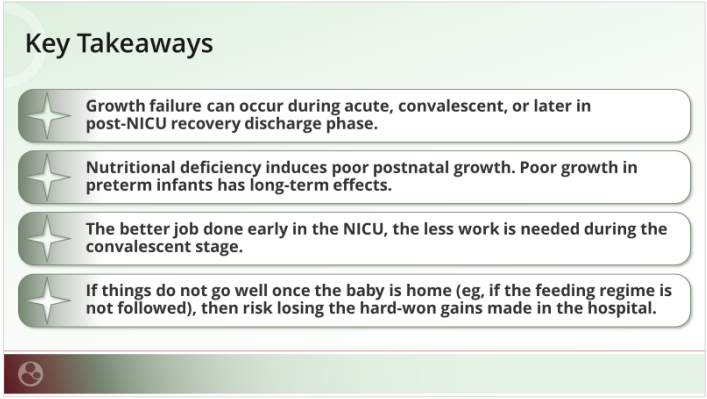


Slide 41 — Support For the Family

In conclusion, in the scope of this talk we have a few key takeaways:

- Growth failure can occur at any time during the NICU care, whether that is acute, convalescent, or as we transition to home.
- Deficit can induce poor postnatal growth, and poor growth in preterm infants clearly has long-term effects on both cognitive and motor development.
- The better we do early in the NICU, the less work is needed in the convalescent stage. I always say that if we don't fall as far down the hill, we don't have as far to climb up.
- If things do not go well once we transition to home, particularly if feeding strategies are changed, then we need to be aware that we may lose some of those hard-won gains in the hospital. It is really incumbent on us to help families find the right balance so we are meeting all needs in the best balanced way possible.

Redesigning Postdischarge Nutrition in the NICU



Slide 42 — Key Takeaways

That brings us to the end of our talk, and we are happy to take any questions you may have.

Question & Answer

Editor's Note: This is a transcript of audience questions together with presenter responses from the November 12, 2020 audio webcast.

Dr. Griffin, what strategies do you use in your NICU to get accurate growth for weight and length, and do you use or advocate for length boards?

Griffin: First of all, weight is not difficult, but you're completely right that length is the difficult one. You can't measure length without a length board. You can generate a number, but it has no meaning. Unfortunately, simply having a length board in and of itself isn't enough. It really is a 2-person job to measure length, and it really needs to be done by people who do it a lot and are motivated and invested in doing it properly. It truthfully is something that probably should be done by the nutritional team, on an ongoing basis, rather than something that's done Sunday morning at 2 AM by the night shift because that's when it's convenient.

But it is difficult, and that does speak to why, although a lot of people don't like relying on weight, weight probably for most babies is the way to go. If weight is really bad, then probably you'd want to get some good lengths, but for a lot of babies, weight is probably your way to go.

Dr. Bastek, what criteria is useful for describing to parents why their body is high, moderate, or low risk for nutritional deficits?

Bastek: I think that's an excellent question. We have, in terms of trying to target the nutritional needs for these infants, come together in our NICU to have some basic markers of what is successful growth or less successful growth. And so we have some birth weight break-up criteria. For instance, a birth weight less than 1,500 g will automatically be an infant we would put in a high-risk category for the long term. Other components that might set you up for concern for less successful growth would be slower growth velocity. For "less" evaluation, we use a sort of in the middle of the goals of g/k/day. Which is less ideal, I know, than daily weights, but, as we are trying to make a prediction, we've used some other markers of severe illness, like alk phos [alkaline phosphatase] levels, or prolonged time on parenteral nutrition.

The more medium and low-risk groups are by, sort of reverse, the older gestational ages and the bigger infants. If they are having poor growth velocity, then we would make some accommodations for that. So, we break it up by those evidence measures as we come close to the discharge window.

Dr. Griffin, could you comment on the AAP's recommendation that consideration should be given to fortification of human milk and use of fortified infant formula for a minimum of 12 weeks after discharge?

Griffin: Yes. I should say that before I came to the States, in the UK , we were involved in one of the big studies on postdischarge nutrition. We used the low-birth weight formula that carried on until babies were 6 months corrected age. We also had a group that were on the low-birth weight formula until their expected date of delivery, then changed

with term formula. We dropped that growth during analysis or during interim analysis, because that group did really poorly. When they stopped the low-birth weight formula, they weren't able to seem to upregulate their volume intake, so they were actually nutritionally more deprived after term. So, I think if you're going to do it, you *really* need to use the most enriched formula that you have access to, and you need to carry it on beyond their expected date of delivery. I would carry it on probably until 3 or 6 months corrected gestational age.

Dr. Bastek, what is the next course of action for infants who are not growing badly, but are not growing great either?

Bastek: What will seem like an unhelpful answer would of course be, we should take some action! I think the question actually represents maybe the toughest infant that we come across, where I would concur nothing is egregiously wrong, but nothing is super great either. Do we "rock the boat," change feeding strategies where tolerance and all those things might be less good than they were before? Are we okay to say it's good enough? I think the data—and what we're seeing in all of the information we've presented, particularly if we look at the long term—indicate that the answer to "do we rock the boat," is yes. Yes, we need to. How one goes about that would really depend on the specific feeding combination for that infant.

Some NICUs are using... Some individual babies have Mom's own milk in great supply, and that is a base that we can build off of. The things you might use to build with may look different than for an infant who is having a large component of donor human milk. As we think about risk-balance for these infants, the older they become and their necrotizing-enterocolitis risk drops, if they are having significant impairment of growth, shifting from donor milk to more of the NICU-based true preterm formulas, with richer components of protein and micronutrients, particularly their calcium and phosphorus intake, may be very much an advantage for those infants.

I think the specifics of how you would go about doing it really depend on the specifics that are available to that particular infant. It is, in many ways, becoming aware and knowledgeable about what the different available additives would bring to the table. So that in the kind of compilation or total recipe, we feel more confident, rather than saying, "This is what they say to do so I'm doing it," if that makes sense.

Griffin: Could I just add something to that? Well, first of all I agree with everything that Tara has said, but I would say that good enough isn't good enough, because this is going to determine how the baby is going to do for the rest of their life. So, good enough isn't good enough.

Usually, the reason babies aren't growing as well as we want them to is that they're not getting enough. We really, particularly if we're using human milk, we really don't know what we're giving. We think our recipe is producing 24 calories per oz. The truth is it's probably producing something between 20 and 27 calories per oz, so if the baby is not growing, they probably need either more volume or more fortification.

If you've done that and been aggressive on that side, I would point out that hyponatremia is a really—particularly in hospital—hyponatremia is a really good reason not to grow. So, it doesn't hurt to look for that, and I think that's underappreciated as the cause of poor growth.

Bastek: I would underscore that, and I'm going to tag on one more thing, Dr. Griffin, to say that I do not have as many gray hairs as my mentors had, of course. But I think for a very long time in our field the efforts made to *avoid* known comorbidities, like necrotizing enterocolitis [NEC] and chronic lung disease, have been many, and they are important efforts to reduce those complications. However,

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several, if not many, of those risk-reduction strategies had direct negative impact on the ability to adequately give nutrition to these infants. Low-volume intake strategies for chronic lung flow, fortification, as you mentioned, for necrotizing enterocolitis. I think many of us in neonatology welcome being able to shift our mindset to a more balanced approach while appreciating the impact of previous strategies. It is shifting, but sometimes it can be really difficult for NICUs to move away from a minimization of NEC-risk-at-all-costs type of strategy, but I feel like we are on a journey in the field of finding a better balance across all competing factors.

Griffin: I agree. This is becoming an "agree fest" but I agree with you completely. I think that the fear of NEC has damaged and harmed far more babies than NEC ever has, and if NEC really had anything to do with the way we fed babies, we would have cured NEC 30 years ago.

Dr. Griffin, does your NICU verify and confirm on a regular basis that your donor milk is the kcal/oz purchased per your purchase agreement?

Griffin: No. No, our human milk supplier doesn't analyze it for us. I think that is done in some places in the US. It's done, I think probably, more in Canada, but no, we get what we get. They will tell us whether it's term donor human milk or preterm donor human milk, but there's no nutritional analysis. We have human milk analyzers for research use, but from our human milk bank, it doesn't come with a composition.

Dr. Bastek, what iron dose do you recommend for preemie graduates?

Bastek: Well, if I had my neonatal dietitian with me, we could describe to you the very elaborate algorithm that exists for the combination of human milk and fortifier and additional vitamin D and iron. I will say that we generally supplement vitamin D and iron separately on our infants until they are close to 2,500 g or more. Then we will shift over to using the combination multivitamin product. Occasionally, we will fortify separately, but their volume of intake by that weight generally gets them enough vitamin D without the multivitamin solution. At lower weights, this will give you too much iron, particularly if there's a substantial amount of formula in the infant diet already.

Balancing that is significant, and I will say also the vitamin D intake, the Koletzko guidelines that were put out in 2014 give a range of 400 up to 1,000 IU a day.[7] So, we balance the iron and vitamin D intake, particularly as we use some of these higher powered, more concentrated fortifiers in the convalescent, transition-to-home window, that they are infants who are taking more than 400 IU a day.

Yes, we would check vitamin D levels, and we usually once a month will do what we call nutrition lab check-in: calcium, phosphorus, alk phos, vitamin D, things that would be looking at bone health and also as we get to the one that would be close to discharge, assessing where vitamin D levels are to see what sort of room we have to work with there.

Large numbers of infants who have vitamin D levels on the low end, where getting a 1,000 IU a day is perfectly fine and safe for them, if they're above vitamin D levels of 100, we would alter the fortification strategy so that we are not giving them high doses of vitamin D in those cases.

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Abbreviations

AAP	American Academy of Pediatrics	**NEC**	necrotizing enterocolitis
Alk Phos	alkaline phosphatase	**NICHD**	National Institute of Child Health and Human Development
ESPGHAN	The European Society for Paediatric Gastroenterology Hepatology and Nutrition	**NICU**	neonatal intensive care unit
EUGR	extrauterine growth	**PDI**	physical development index
IVH	intraventricular hemorrhage	**VLBW**	very low birth weight
LC-PUFAs	long-chain polyunsaturated fatty acids	**ROP**	retinopathy of prematurity
MDI	mental developmental index		

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