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REVIEW

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Podcast Issue

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VOLUME 10 – ISSUE 12: TRANSCRIPT

Nutritional Management Of Low Birth Weight Preterm Infants

Our guest author is Brenda Poindexter, MD, Professor of Pediatrics at Cincinnati Children's Hospital Medical Center.

After participating in this activity, the participant will demonstrate the ability to:

- Discuss nutrient requirements of extremely premature infants in the first week of life.
- Explain the benefits of standardized feeding guidelines for premature infants.
- Describe strategies to fortify human milk to optimize growth outcomes of premature infants.

This discussion, offered as a downloadable audio file and companion transcript, covers the important topic of nutritional management of low birth weight preterm infants in the format of case-study scenarios for the clinical practice. This program is a follow up to the [Volume 10, Issue 11 eNeonatal Review newsletter—Nutritional Management of Low Birth Weight Preterm Infants](#).

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Dr. Brenda Poindexter has indicated there will be no references to unlabeled or unapproved uses of drugs of products, with the exception of near- and mid-infrared milk analyzers.

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Faculty Disclosure

Dr. Brenda Poindexter has indicated that she has no financial interests or relationships with any commercial entity whose products or services are relevant to the content of her presentation.

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- Physicians may not be aware of recent evidence-based recommendations on recognizing and treating GERD in neonates.
- Current neonatal nutritional management practices may be enhanced to optimize and meet the specific needs of low birth weight preterm infants.
- Current neonatal nutritional management practices may be enhanced to optimize and meet the specific needs of low birth weight preterm infants.
- Clinicians who treat neonates are uncertain of optimal strategies for prevention and early recognition and treatment of necrotizing enterocolitis.

Respiratory-Related Issues

- Clinicians may be unfamiliar with some of the newest evidence-based approaches for treating neonatal persistent pulmonary hypertension.
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MR. BOB BUSKER: Welcome to this first *eNeonatal Review* podcast.

Today's program is a follow-up to our newsletter on Nutritional Management of Low Birth Weight Preterm Infants. With us today is that issue's author, Dr. Brenda Poindexter, professor of pediatrics from the Cincinnati Children's Hospital Medical Center.

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Learning objectives for this audio program include:

- Discuss nutrient requirements of extremely premature infants in the first week of life.
- Explain the benefits of standardized feeding guidelines for premature infants.
- Describe strategies to fortify human milk to optimize growth outcomes of premature infants.

Dr. Poindexter has disclosed that she has no financial interests or relationships with any commercial entity whose products or services are relevant to the content of her presentation. She has indicated as well that there will be no references to unlabeled or unapproved uses of drugs or products, with the exception of near- and mid-infrared milk analyzers.

MR. BUSKER: I'm Bob Busker, managing editor of *eNeonatal Review*. Dr. Poindexter, thank you for joining us today.

DR. BRENDA POINDEXTER: You're welcome. It's a privilege to be talking to your audience about the importance of nutrition in premature infants.

MR. BUSKER: In your newsletter issue, Dr. Poindexter, you reviewed some of the recent literature describing the challenges in providing optimal nutritional management for low birth weight preterm infants. Today I'd like to focus on how that information can impact clinical practice. So let me ask you to start things off, if you would please, by presenting a patient.

DR. POINDEXTER: Absolutely. So we have a 650 gm female who was delivered at 24 weeks' gestation to a

26 year old primiparous birth mother with an unremarkable pregnancy history until the time of presentation with premature rupture of membranes and preterm labor. Rupture of membranes occurred approximately 18 hours prior to delivery, and the mother did receive antibiotics and one dose of betamethasone prior to delivery. The infant required intubation in the delivery room and one dose of surfactant. Umbilical lines were placed in the NICU shortly after delivery.

MR. BUSKER: Very premature, very low birth weight. So immediately after birth, how important is nutrition?

DR. POINDEXTER: So it's a great question and the importance of nutrition is absolutely crucial. Although many people are focused on the respiratory management of extremely premature infants, we really have to consider extreme prematurity as a nutritional emergency. If you think about what is happening in utero up until the time of delivery, the placenta is actually supplying upwards of 3-1/2 gm/kg/d amino acids to the developing fetus. This is far in excess of what the fetus needs to accrete protein, and some of those amino acids are actually used as an energy source.

Fetal protein accretion at 26 weeks is the highest of any other time in life, and the fetus is accreting at least 2.2 gm/kg/d of protein at that time. So when the placental supply of amino acids is interrupted at the time of premature birth, then you really have to step in and try to supply the needed both protein and energy. And our goal here is really to prevent growth failure and if early parenteral and enteral nutrition is not provided, the deficits in both protein and energy that can accrue will be difficult if not utterly impossible to recoup.

MR. BUSKER: The suggested target for parenteral nutrient intake in the first 24 hours after birth — tell us about that, please.

DR. POINDEXTER: The suggested target from parenteral nutrition includes at least 2 gm/kg/d of amino acids, at least 2 gm/kg/d of lipids and a total energy intake of approximately 60 to 80 kcal/kg/d. These recommendations come from multiple bodies, including the American Academy Committee on Nutrition, the European Nutrition Society (ESPGHAN),

and also from the most recent book entitled Nutritional Care of Preterm Infants. Nick Embleton from the UK wrote those guidelines for suggested target intakes from parenteral nutrition.

This is just in the first day and so it's really important to have a plan for stock amino acid solution so that the very first IV fluids that are hung can provide a source of amino acids to this baby. By day 1 to 2, the suggested target intakes increase and a minimum of 3-1/2 gm/kg/d of amino acids should be supplied, and 3 gm/kg/d to 4 gm/kg/d of lipids to meet the baby's total energy requirements of 80 kcal/kg/d to 100 kcal/kg/d.

MR. BUSKER: What's known about the consequences if these early nutritional targets aren't met?

DR. POINDEXTER: So if early nutritional targets are not met, we've already talked about the deficits that can accrue, and they can be impossible to recover from later in the hospitalization. We know that both protein and energy intake in the first week are associated with growth outcomes at 36 weeks post-menstrual age. Furthermore, protein and energy intake in that first week of life is also associated with neurodevelopmental outcomes at 2 years corrected age.

And I think over the past decade or so the focus by neonatologists has really been on ensuring that these babies are receiving adequate intakes of protein. However, as summarized by the article by Alexander Lapillonne that was reviewed in this issue, there was also increasing awareness of the quality of lipid supply early in life that's an important determinant of development, and also the consequences of not having adequate energy intake.¹

We know that those long chain polyunsaturated fatty acids, or LCPUFAs, that come from fish oil and supply DHA and ARA are very important for both visual acuity and central nervous system development. And these particular fatty acids are only available from the parenteral fish oils, and the fish oil emulsions are not available routinely in the United States.

MR. BUSKER: Now one of our learning objectives is about standardized feeding guidelines. Why are they important in achieving these goals?

DR. POINDEXTER: Yes, so we typically think about standardized feeding protocols in terms of the provision of enteral nutrition, but they really are very important also to ensure that you have adequate delivery of nutrients via the parenteral route early on because it is going to be impossible to meet the targeted intakes without having parenteral nutrition. Having a feeding guideline ensures availability of the stock amino acid solution that we talked about that is readily available in pharmacy and isn't dependent on having a technician to prepare it in the middle of the night. I also think that having a guideline that addresses parenteral nutrition really reinforces this idea that we have a nutritional emergency every time we're caring for an extremely premature infant. And standardized feeding guidelines at their best should incorporate provision of both parenteral and enteral nutrition.

And as was highlighted in the Gephart article about standardized feeding guidelines, we know that a use of a standardized guideline will reduce the duration of TPN days and reduce the number of days to reach full enteral nutrition.²

MR. BUSKER: Thank you, doctor. And we'll return, with Dr. Brenda Poindexter in just a moment.

DR. MAUREEN GILMORE: Hello. I'm Maureen Gilmore, assistant professor of pediatrics and director of neonatology at Johns Hopkins Bayview Medical Center. I'm one of the program directors of eNeonatal Review.

eNeonatal Review is a combination newsletter and podcast program delivered via email to subscribers. Newsletters are published every other month. Each issue reviews the current literature in areas of importance to neonatologists, respiratory therapists, neonatal nurses and nurse practitioners, and other health care practitioners whose work/practice includes treating neonates.

Bimonthly podcasts are also available as downloadable transcripts, providing case-based scenarios to help bring that new clinical information into practice in the delivery room and at the bedside.

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MR. BUSKER: Welcome back to this eNeonatal Review podcast. I'm Bob Busker, managing editor of the program. We've been talking with Dr. Brenda Poindexter from Cincinnati Children's Hospital Medical Center about improving the nutritional management of low birth weight preterm infants. So doctor, let's continue with the infant we've been discussing.

DR. POINDEXTER: Our 24 week gestation infant who was born yesterday is now 24 hours of age. After receiving one dose of surfactant, she weaned to less than 30 percent oxygen and was extubated to CPAP by 12 hours of age. Her blood glucose has been stable and she only required one normal saline bolus for some borderline hypotension, but her blood pressure has normalized since.

MR. BUSKER: So are we at the stage when this infant should receive should enteral nutrition? And how much?

DR. POINDEXTER: Ideally, enteral nutrition should be started today. The trophic volume, and when we talk about trophic feedings, or you may hear other people refer to these as minimal enteral feedings, we're really talking about small volumes, ranging anywhere from 10 mL/kg/d to 20 mL/kg/d, so the parenteral nutrition is meeting the bulk of the nutrient requirements, and the trophic or minimal enteral nutrition is priming the gut. It is designed to improve feeding tolerance and importantly has not been shown to increase the incidence of necrotizing enterocolitis.

Now the decision to start to initiate trophic feeds really should be part of those standardized feeding guidelines so that you're not making the decision to rely on the clinicians to remember to start them, and also so that you're taking out of the equation how ill they think the baby is. Because we're really just talking about feeding the gut and getting

the baby ready to tolerate increasing volumes of enteral nutrition.

MR. BUSKER: The infant we're talking about is fairly stable. But what if this extremely low birth weight preterm was less stable?

DR. POINDEXTER: If this baby were more unstable — by that some people might mean a baby still requiring ventilatory support or still having an umbilical line — certainly if she were requiring inotropic support, those might all be reasons people would be reluctant to start minimal feeds. This again is where having the standardized feeding guideline can help mitigate thinking a baby's severity of illness would preclude starting feedings.

The approach really should be similar for both a stable and an unstable baby in thinking about the timing of introducing minimal enteral feeds.

MR. BUSKER: If maternal milk, for whatever reason, is not available, should this infant receive donor breast milk? And if so, what are the differences between maternal and donor breast milk that need to be considered?

DR. POINDEXTER: That's a great question, and obviously the benefits for the premature infant of receiving mother's own milk can absolutely not be underestimated. And it's really important for all units caring for premature infants to develop support for initiation and maintenance of maternal milk supply. And I think the article by Gephart really highlighted the benefits that the attitudes of clinicians and their knowledge about moms both bringing in and maintaining supply, as well as just providing active support to the mother, has really, there is strong evidence to suggest that that increases the likelihood that the mother will continue to provide breast milk during the NICU stay.²

But for those moms where milk supply is not yet adequate or for those rare cases when mom, you know, maybe mom, herself, is too ill to be able to pump, donor milk certainly can be used as a bridge until maternal milk supply is available or adequate.

So knowing that, that donor milk or maternal milk may be, may be used in this population, it's really important to consider the variability of human milk.

And the article that was summarized by Dr. Groh-Wargo in the newsletter really speaks to the variability of human milk.³

I think that one of the most important things that clinicians caring for low birth weight babies need to know, is that the milk from a mother who delivers prematurely is very different from the milk composition if that same mother had delivered her baby at term. So we know that milk from a mother who has delivered prematurely is much higher in protein content and the, over time, as lactation progresses, that protein content gradually falls and approaches that of term milk. And the important thing to remember is that the donor milk banks in the US, the mothers who are contributing to these banks have typically delivered babies at term and may be many, many months into lactation. And so we would expect that donor milk would have both a lower protein and lower energy content than if the preterm baby were receiving her mother's own milk.

MR. BUSKER: Talk to us about fortification: at what point should human milk be fortified?

DR. POINDEXTER: That's a great question and one that is hard to answer. I think the bottom line is that the standardized feeding protocol developed for individual units must incorporate the answer to that question in their guidelines.

In the newsletter, the article by Gephart that summarized different approaches with standardized feeding protocols, delayed fortification until the infant was receiving 100 mL/kg/d.² In the more recent recommendations from the Nutritional Care of Preterm Infants book I mentioned earlier, we recommend beginning human milk fortification earlier than 100 mL/kg/d. The thought behind this is, if the baby is receiving unfortified human milk, it's impossible to meet the targeted recommendations, particularly for protein intake.

The Tillman pilot study in the newsletter demonstrated the feasibility of fortification as early as the first feed.⁴ Now clearly we need more studies in this area. I will add a caveat is that for the commercially available human milk fortifiers to be used, you need a minimum of 25 mL total volume to be able to add the fortifier and make the appropriate recipe. This is a little less challenging when you're using donor milk and you have a large volume of

pooled donor milk that you can fortify to be given to multiple babies in the NICU.

So we would never want to withhold mother's own milk simply because we didn't have enough to fortify, but really we need to, we need to conduct more studies to find out the optimal timing of when to add fortifier and also need to be thinking about the fact that human milk doesn't stay at one particular concentration of protein. And knowing that the protein content of mother's milk is changing while the baby's in the NICU, I think we perhaps need to think about future studies that could look at strategies for fortification that take into account the dynamic composition of human milk as lactation progresses.

MR. BUSKER: Donor milk versus maternal milk: should the donor milk be fortified differently than the mother's own milk?

DR. POINDEXTER: So another great question and at present we typically only have one recipe for how the commercially available fortifiers are added to human milk. But knowing that the composition of donor milk is different than maternal milk, I think that the answer is that we do need to think about different strategies for fortifying donor milk.

A lot of people, including Dr. Rochow, whose article was summarized in this newsletter, have used near-infrared spectroscopy to actually analyze the composition of both maternal milk and donor milk.⁵ And these analyzers are not yet approved for clinical use in the US, but a number of them are being used by different groups of investigators as part of research studies.

And so from some of these studies we know that the donor milk is not always the same composition of the assumptions that we are making. And, in fact, in the, in the Rochow study they found that at least one macronutrient in the pooled breast milk samples that they were analyzing, needed an adjustment every 12 hours.⁵ And it wasn't always the protein that needed to be increased, they found that there were other times where it was the fat content or the carbohydrate content.

So really whether we are using donor milk or maternal milk, we need multicomponent fortification and it's obvious that we need different strategies depending on what that base composition of the milk is. One of

the studies that we reviewed in this newsletter did a randomized trial of fortifying simply with human milk cream as a supplement to standard fortification in infants who were receiving an exclusive human milk-based diet. They demonstrated slight improvement in weight gain in the infants who received the cream supplement, but I would argue that the weight gain of 14 gm/kg/d that Dr. Hair and her colleagues found in this study is probably still suboptimal.⁶ It's important that we look not only at the absolute weight gain velocity, but also how that baby is tracking along their percentile on the growth curve. We need many more studies looking at the optimal fortification strategies, which I think will be different if the baby is receiving donor milk versus maternal milk. The strategies may also be different at different times, whether it's in those first weeks of life or in a baby who's been in the NICU for 8 to 10 weeks and has suffered the consequences of growth faltering.

MR. BUSKER: Let's continue with this same baby girl, doctor. How did her nutritional management proceed as she got older?

DR. POINDEXTER: In our unit we have a standardized feeding guideline, and our baby was able to advance on her enteral feeds per the protocol. By 3 weeks of age was receiving full gavage feeds with fortified donor human milk. Bovine liquid human milk fortifier was added when her enteral volume reached 150 mL/kg/d. The fortification recipe was intended to supply 24 calories per ounce.

At 3 weeks of age her weight is now 790 gm, her length is unchanged from birth, and her head circumference is up 1 cm from birth.

MR. BUSKER: When you consider this infant's birth weight, which as you said was 650 gm, is her growth at 3 weeks of age appropriate?

DR. POINDEXTER: If we look at this baby's growth on a standard growth curve such as the Fenton curve or the Olsen curve, her growth is certainly not ideal. It's not terribly surprising and is consistent with data from Tarah Colaizy's study that was also highlighted in this newsletter, which found the highest rates of growth failure in infants receiving the highest volume of donor human milk.⁷ So even though this baby is 140 gm above her birth weight, we can assume that she initially lost weight and perhaps regained it by day of life 7. That would mean that for the last two weeks

she's gained an average of 15 gm/kg/d, but her weight percentile for her corrected gestational age has clearly fallen off. This highlights why we can't simply look at the absolute weight or even gm/kg/d; we have to look at how she's doing in the context of her growth curve.

The fact that her length hasn't changed is also a really important consideration and likely tells us that she hasn't received enough protein in those early weeks of life. This degree of growth failure could potentially have been avoided if her, if the human milk that she was receiving had been fortified earlier. And perhaps similar to the strategy as Dr. Tillman utilized in his pilot study.⁴

MR. BUSKER: This baby's growth rate seems to be faltering, if not actually failing. What might be some of the potential causes of suboptimal growth in this patient?

DR. POINDEXTER: Sure. So there, there are a number of factors to consider. You know, we have already touched on the variability in the composition of human milk and so we may not be delivering the intended nutrients, and this would be true for both donor and maternal milk. This baby didn't reach full-volume feedings until well after the second week of life, so the duration to reach full volume could potentially have been achieved sooner with a feeding guideline by advancing enteral volumes of 20 mL/kg/d.

We also haven't talked about whether she ever had feedings held, perhaps based on gastric residuals. And I would make the point that measuring gastric residuals is really not an evidence-based practice and can cause significant interruptions in feedings, which can then prevent the baby from actually receiving the intended nutrition and can also add to those early deficits that may be hard to recover from.

MR. BUSKER: What about measuring the composition of the donor milk she's receiving? Would that be helpful?

DR. POINDEXTER: I think it certainly would be helpful, but as I already mentioned, the human milk analyzers are not yet approved for clinical use in the United States and also lead to a very labor-intensive process. But, you know, knowing the composition of what this infant was receiving might have prompted clinicians to either fortify sooner or to actually try an

individualized fortification strategy where they would perhaps have added more protein or more calories based on knowing what the milk they were giving the baby was actually providing her with.

MR. BUSKER: This baby is already receiving fortified donor milk. Are there additional strategies to improve her growth?

DR. POINDEXTER: The best strategy that I can suggest, in the absence of having a way to measure in real time the composition, is that we need more of the multicomponent fortification. So she probably needs more calories and protein. We know that just adding protein or just adding carbohydrate, as was the case in the cream fortifier study we talked about, is not ideal. The bottom line is that we need further studies on optimal fortification strategies, and these studies need to look not only at short-term growth outcomes, but also provide more data about long-term outcomes such as neurodevelopment. That's going to be very, very important as we strive to provide better nutrition to these babies.

We also need to think about the fortification strategy and what level of growth faltering is going to prompt us to increase fortification. That should definitely be incorporated into standardized feeding guidelines.

MR. BUSKER: Dr. Poindexter, thank you for today's case and discussion. Let's wrap things up by reviewing what we've been talking about in light of our learning objectives. So to begin: the nutrient requirements for extremely premature infants in the first week of life.

DR. POINDEXTER: The most important take-home message is that extreme prematurity is a nutritional emergency. Meeting the targeted intake for protein and energy in that first week of life is one of the most important tasks a clinician has. Ensuring that the baby receives adequate protein and energy will affect not only their in-hospital growth but also their neurodevelopment after they leave the hospital.

MR. BUSKER: And our second learning objective: the benefits of standardized feeding guidelines for premature infants.

DR. POINDEXTER: Standardized feeding guidelines ensure that the baby will receive immediate parenteral nutrition. They give guidelines for when to start to feedings and how to advance them, as well as how to

handle intolerance of feeding and when and how to fortify human milk feedings. These are all critically important for ensuring optimal growth and for preventing necrotizing enterocolitis.

MR. BUSKER: And finally: strategies to fortify human milk to optimize growth outcomes.

DR. POINDEXTER: So, clearly, the strategy that will be most helpful is to understand the inadequacy of unfortified human milk, particularly if you are using a large volume of donor human milk. I think a strategy that starts earlier than what we have traditionally done is important and then also looking to the future and hopefully having new fortifiers that are available that will allow us to better meet the needs of our premature infants, particularly fortifiers that supply extra protein to accommodate for the lower protein content of donor human milk.

MR. BUSKER: Dr. Brenda Poindexter from the Cincinnati Children's Hospital Medical Center, thank you for participating in this eNeonatal Review Podcast.

DR. POINDEXTER: Absolutely, you're very welcome.

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