Pediatric Nutrition
CONTINUING EDUCATION FOR CLINICIANS

Intestinal Failure in Infants: Managing the Transition From Total Parenteral Nutrition—*A Case-Based Program*

✦ Course Transcript ✦

Overview

Mark R. Corkins, MD, CNSC, and **Anna Featherston Tuttle, MS, RD, LDN, CNSC,** provide an overview of intestinal failure (IF) in infants and a detailed, case-based discussion of nutrition management. Topics include causes and outcomes of IF, nutrition goals, assessment of infants with IF, pharmacotherapeutic options, and nutritional management. Practical recommendations for initiating and then weaning from parenteral to enteral nutrition are discussed, alongside the key guiding principles of maximizing enteral feeds in infants with short bowel syndrome and other forms of IF.

Target Audience

This activity was developed for neonatologists, nurses, advanced practice clinicians, dietitians, and other healthcare providers who care for preterm and term infants.

Learning Objectives

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

- Identify the key aspects of managing intestinal failure (IF) in infants
- Lay out a strategy to transition an infant with IF from total parenteral nutrition

Faculty

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Mark R. Corkins, MD, CNSC

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Anna Featherston Tuttle, MS, RD, LDN, CNSC

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This activity was released on June 24, 2022, and is eligible for credit through June 24, 2024.

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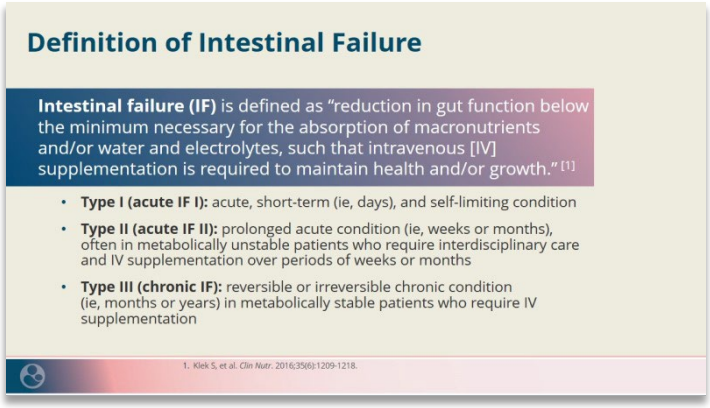
Abbreviations

G-tube	gastrostomy tube	**NICU**	neonatal intensive care unit
GI	gastrointestinal	**PN**	parenteral nutrition
GLP-2	glucagon-like peptide 2	**PPI**	proton pump inhibitor
NEC	necrotizing enterocolitis		

Editor's Note: This is a transcript of a live webcast presented online on June 9, 2022. It has been edited and condensed for clarity.

Overview of Intestinal Failure

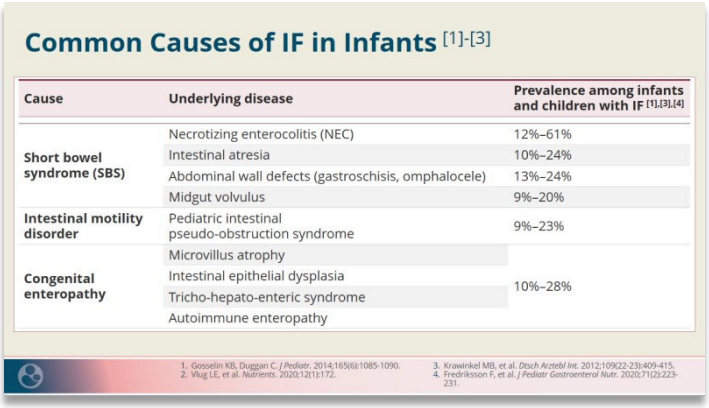
Mark Corkins, MD: What is intestinal failure? Basically, [it's] not enough gut that you can use it for all your nutrition, and that's kind of a high level. Basically, yes, we have a formal definition on [Slide 1], and you're not getting enough macronutrients or water or electrolytes. But basically, you need intravenous help. That's really the most simple [definition] of intestinal failure. Now, type I is acute, short-term, couple of days, self-limiting, and that's not really the focus here. Now, type II, that's a prolonged, acute condition. You know you've got something that's happened to your bowel. Usually, it's surgical or trauma, and you're unstable and you're going to require some multidisciplinary care, and it may take weeks or months to recover. But, hopefully, it's recoverable. Type III, now those are the ones we're really talking about here. This is irreversible, chronic—months to years. They're stable, but there's just not enough intestine to meet all their nutrition needs, and so they require some sort of intravenous help to meet their nutritional needs.



Slide 1 – Definition of Intestinal Failure

What are common causes? Well, I mean, if you look at [Slide 2], different people have different amounts, and that's that prevalence on the right. Most studies say necrotizing enterocolitis in former preemies is number 1. We do see some kids who have congenital atresia. We see some kids that have congenital defects in their abdominal wall. Some full-term kids who have malrotation and end up having midgut volvulus. Small numbers of kids with dysmotility, and then there's some congenital

things, like microvillus atrophy, intestinal epithelial dysplasia, trichohepaticenteric syndrome, autoimmune enteropathy—there are a whole bunch of different etiologies.



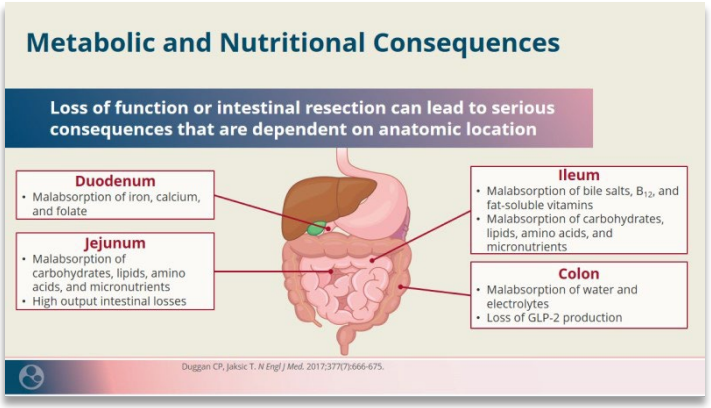
Common Causes of IF in Infants [1]-[3]

Cause	Underlying disease	Prevalence among infants and children with IF [1],[3],[4]
Short bowel syndrome (SBS)	Necrotizing enterocolitis (NEC)	12%–61%
	Intestinal atresia	10%–24%
	Abdominal wall defects (gastroschisis, omphalocele)	13%–24%
	Midgut volvulus	9%–20%
Intestinal motility disorder	Pediatric intestinal pseudo-obstruction syndrome	9%–23%
Congenital enteropathy	Microvillus atrophy	10%–28%
	Intestinal epithelial dysplasia	
	Tricho-hepato-enteric syndrome	
	Autoimmune enteropathy	

1. Gosselin KB, Duggan C. *J Pediatr.* 2014;165(6):1085-1090.
2. Vlug LE, et al. *Nutrients.* 2020;12(1):172.
3. Krawinkel MB, et al. *Dtsch Arztebl Int.* 2012;109(22-23):409-415.
4. Fredriksson F, et al. *J Pediatr Gastroenterol Nutr.* 2020;71(2):223-231.

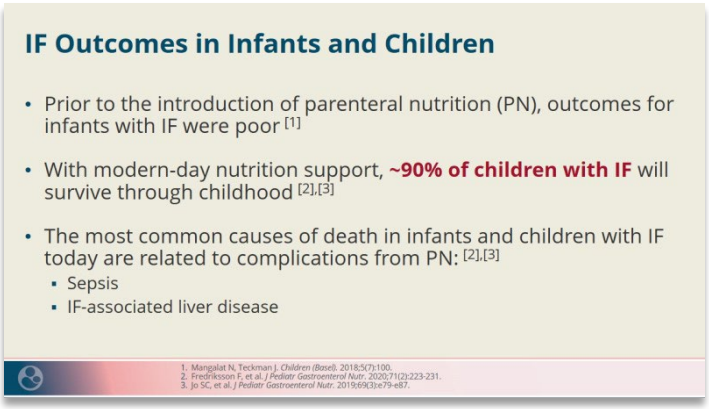
Slide 2 – Common Causes of IF in Infants

What are the consequences if you lose some intestine or the intestine isn't working well? It depends on what you lose (Slide 3). Let's just be honest, division of labor—different parts of the bowel do different things. For instance, the duodenum, that's where most of our iron, calcium, and folate gets absorbed. The jejunum in the middle, that's the workhorse; that's the longest section, and that's our macronutrients, getting enough carbohydrates, getting enough lipids, getting our amino acids—a lot of our macronutrients. Of course, also because that's the workhorse, if you don't have enough of it, you also tend to have a very high output. Ileum, that's where the bile salts, B12, the fat-soluble vitamins, and some of the other macronutrients get absorbed. The colon is where your water and your electrolytes are absorbed, and so it's mainly fluid and electrolyte management. But it's also where your GLP-2 is produced, and that's what helps drive adaptation. So, if you've lost your colon, you may have some issues there.

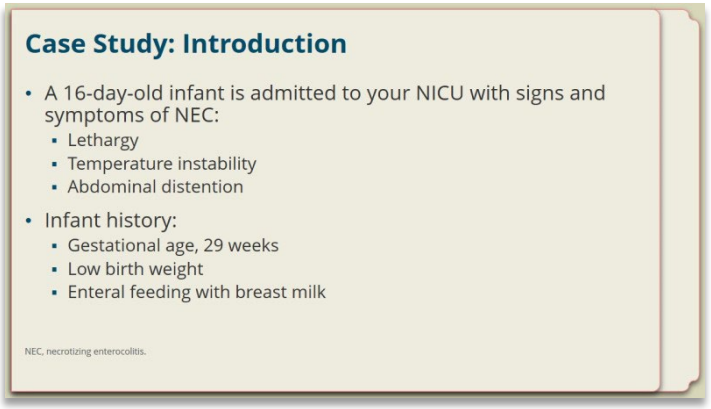


Slide 3 – Metabolic and Nutritional Consequences

What about outcomes? Okay, so we've talked a little bit about outcomes and what happens nutritionally here (Slide 4). Well, before parenteral nutrition was developed, man, it was not a good situation because we couldn't give them nutrition. If they didn't have enough intestine, there was no way, and so the outcomes were bad. But one of the modern-day miracles is parenteral nutrition, and 90% of kids with intestinal failure are going to survive through childhood because we can give them nutrition intravenously.[1,2] Most common causes of death and complications [in patients with intestinal failure] are complications from the parenteral nutrition. Sepsis, because you have a central line that's a portal right into your central blood system, and then the intestinal failure–associated with liver disease. Part of what makes the liver work is using your gut, and if you don't use your gut as much as you're supposed to, you end up with some liver disease.



Slide 4 – IF Outcomes in Infants and Children



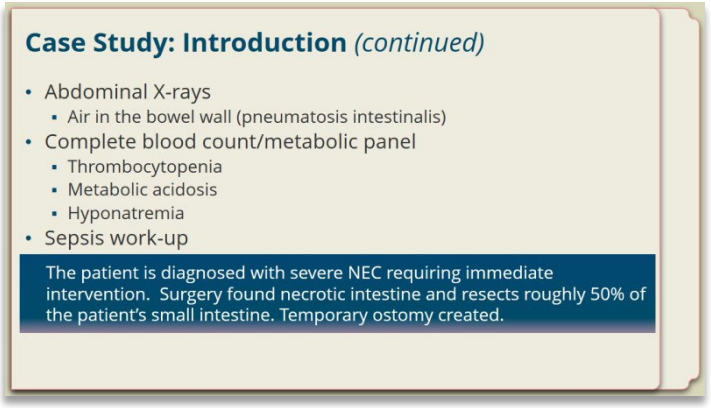
Slide 5 – Case Study: Introduction

That's kind of the high view of intestinal failure and some of the etiologies and the outcomes. So, now, to get us started with some of our case and some of the assessment things, I'm going to let Anna take over.

Case Part 1—Introduction

Anna Tuttle, MS, RD, LDN: Let's say you work at a high-level NICU and a 16-day-old infant is admitted from an outside hospital, from another NICU, with signs and symptoms of necrotizing enterocolitis or NEC, and those include lethargy, temperature instability, and abdominal distention (Slide 5). And a little bit of history on this infant, they were born at 29 weeks, so they had a very low birth weight, and since that time, they've been enterally feeding with breast milk.

Upon arrival, the team gets some abdominal x-rays, which show pneumatosis intestinalis (air in the abdominal wall or in the bowel wall) (Slide 6). They also get blood work with a complete blood count and metabolic panel, revealing thrombocytopenia (or a low platelet count), metabolic acidosis, and hyponatremia. So, therefore, the patient is diagnosed with severe NEC, which requires immediate attention. They are taken to surgery where they are found to have necrotic intestines, and approximately 50% of the patient's small intestine is removed, and a temporary ostomy is created.



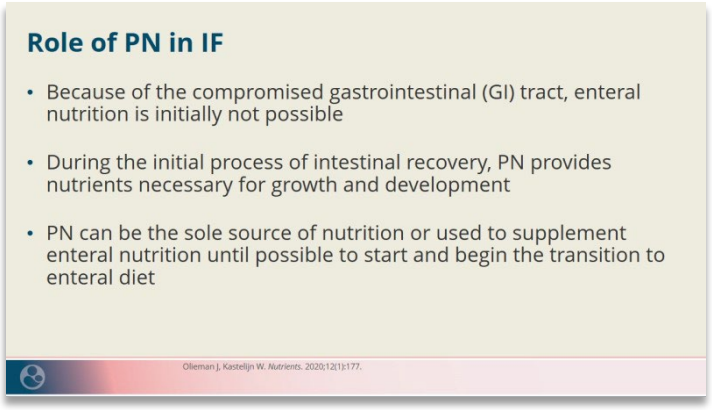
Slide 6 – Case Study: Introduction (continued)

Intestinal Failure Management

Anna Tuttle, MS, RD, LDN: How do we help manage these patients, like our case study and other patients like him or her? So, nutrition management of IF revolves around 2 main goals (Slide 7). These include safe provision of adequate nutrients to maintain lean body mass and function and help these fragile patients still grow, despite all of these things going on. And also, to support and accelerate intestinal adaptation to allow for weaning and hopeful discontinuation of their parenteral nutrition.

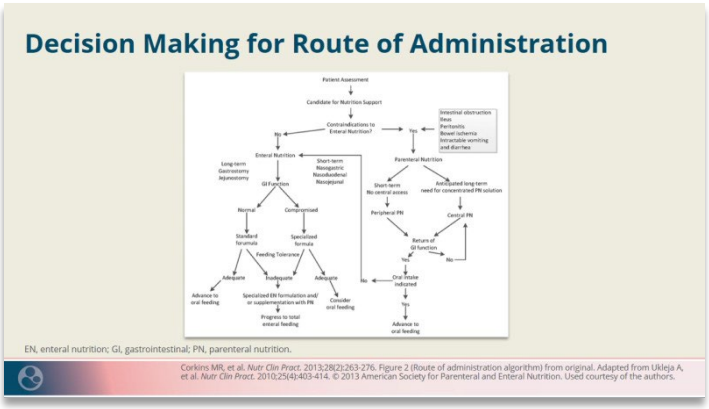
Slide 7 – Goals of Therapy

Because of the compromised GI tract, enteral nutrition is initially not possible (Slide 8). We have to allow that gut to heal some before we start enteral feeds and the patient has to show us that they're ready to start some enteral feeds. So, we need to start providing parenteral nutrition, which can give the nutrients necessary for growth and development to this population. So, we'll start that, and it can be a full source of nutrition, or it can be used to supplement the enteral nutrition until it's possible to start and really begin that transition to an enteral diet. So, that parenteral nutrition can really provide that balance in nutrients that's necessary to help heal these patients and to help them grow.



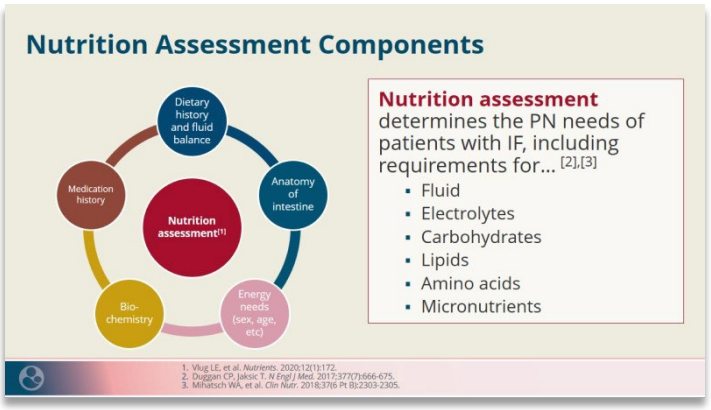
Slide 8 – Role of PN in IF

This is a great decision-making tree for route of administration as far as feeds go (Slide 9).[4] So you can kind of use this to help make those decisions, as if there is a contraindication to enteral nutrition. If there is, then, yes, you need to go on with parenteral nutrition, like with our case study. And then it also shows if you need long-term or short-term PN, you have to have different routes of administration there. And then, once we have return of our GI function, then maybe we can start some feeds. So, we have that on 1 side of the tree. And on the other side of the tree, we also have, if we can do enteral nutrition, what kind of GI function do we have? Is it normal or compromised? Which then helps guide what formula we should choose. So, I think this is just a good decision-making tree, not only for these patients but for others, as well, who have compromised GI tracts.



Slide 9 – Decision Making for Route of Administration

A nutrition assessment is vital to determine the right blend of nutrition components for the parenteral nutrition for these patients (Slide 10). So, a dietary history is important to know what they've been receiving: if it's been breast milk, what type of formula they've been on, how much they've been receiving, how they've been mixing the formula. Also, knowing the fluid balance: how much they've been taking in and how much they've been putting out as far as urinary output and things like that. To know the anatomy of the remaining intestines is very important. Like Dr. Corkins just mentioned, different parts of the intestines have different roles, so to know what is remaining is really important and to know how much is remaining is important to know what we need to supplement and how much fluid and other nutrients they may be losing. Calculating energy needs is very important. There are different calculations to use. I usually use sex, age, weight, and length, when determining those. And a lot of these patients have high energy needs because of many things (eg, prematurity, because now they are missing a large part of their intestines). With their prematurity, they may also have other comorbidities, such as cardiac defects. They may have pulmonary issues which also increase energy needs. So, that's also something to keep in mind as well. Keeping a close eye on biochemistry and labs to see what other things we need to add to the parenteral nutrition to provide the right mix for these patients is very important.



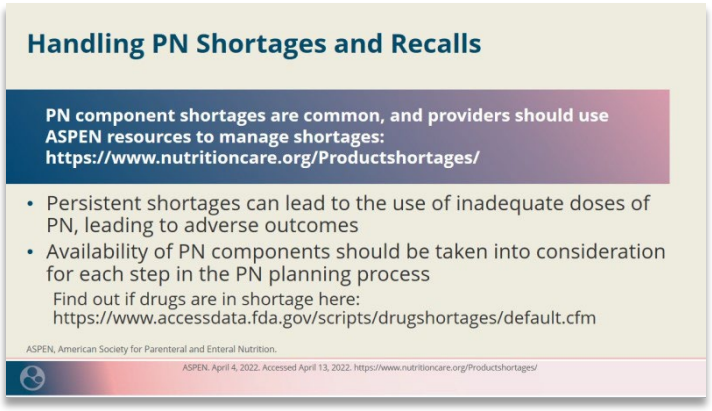
Slide 10 – Nutrition Assessment Components

Mark Corkins, MD: The role of the nutrition support team (Slide 11). Literally, this type of patient is very complex, and nobody wants to do this by themselves, or should do it by themselves, because we need all the expertise possible, for all of the possible input. And you should have some sort of a nutrition support team to help assess, prepare, and give parenteral nutrition, and the members of the team usually have some sort of supervising clinician. In most places, it's a pediatric GI doc, but not always. A surgeon, because you need somebody [to do] central lines or ostomies, or some need feeding tubes. An interventional radiologist sometimes does central lines. Anesthesiologists do it in some places. You need a dietitian for their expertise in assessing a patient's nutritional needs and the balances. A nurse specialist is very helpful to help oversee and manage their care; [someone who] knows about caring for ostomies and central

lines. A pharmacist, with the parenteral nutrition and the mixing and what's possible and what the various different nuances are. And then, social workers, because some of these kids have a lot of social issues. Speech pathologists, because you're going to hopefully also work on some oral intake as well, eventually. And a child life specialist to work with the family and work with the parents and get them some understanding and grasping of the import of all the things going on and help maybe teach some of the skills they need.

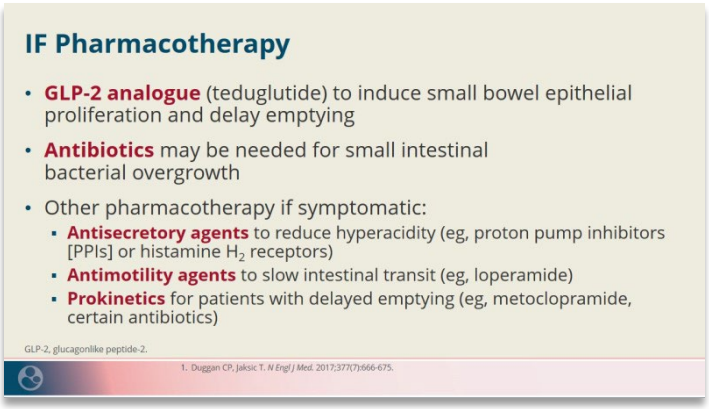
Slide 11 – Role of the Nutrition Support Team

Now, the bad news. If you do any kind of nutrition care, you're aware of [Slide 12], and I'm sighing. This will be permanently recorded, me sighing, because this is just a fact of life now. We have so many shortages and recalls in parenteral nutrition, and it's literally what's short this week and what's going to be short next week and what was short before, and we get things back and then other things go on backorder. There are some resources from the American Society for Parenteral and Enteral Nutrition and how to deal with [shortages].[3] We worry about it because it leads to some inadequate doses of some of our parenteral nutrition components. And we do worry, for instance, with calcium, well what about bone accretion? And you have to take that into account when you're planning your parenteral nutrition, and it's, like I said, almost a rolling issue what's short and when, how long is this going to be short, and how do we deal with it. Again, 1 slide doesn't handle how much grief this causes all of us, but on the other hand, since it changes almost daily, we can't give you much in the way of details because what's short today will be back tomorrow, but what's here today may be gone tomorrow. Here today, gone tomorrow.



Slide 12 – Handling PN Shortages and Recalls

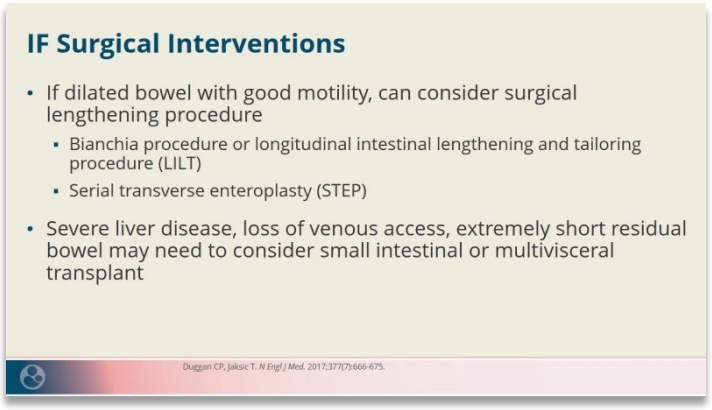
Alright, so let's talk a little bit about some pharmacology (Slide 13). Now, 1 of the biggest breakthroughs in the last few years for intestinal failure patients is a GLP-2 analogue available now. This is like glucagon-like peptide type 2, which is what drives adaptation. They've created an artificial form that's longer lasting than the natural form, and it actually induces small bowel epithelial proliferation. And it helps delay emptying a bit, and it actually is the first agent to directly treat intestinal failure by helping drive adaptation in the mucosa faster than it normally occurs.



Slide 13 – IF Pharmacotherapy

Now, antibiotics may be needed occasionally for small bowel bacterial overgrowth because that occurs, especially if they've lost their ileocecal valve (the valve between the small bowel and the colon). Other things: Antisecretory agents because 1 of the things, there's not a feedback loop now, and so you tend to make more acid because you don't have the feedback and so they need the acid blocked. Antimotility agents. Some of these kids, they're short, so you use an agent to slow down transit so it stays in longer. For instance, loperamide, we'll use that if they have some colon. But some kids, their actual GI tract, even though it's short because it got all beat up by the whole surgical and NEC process, they may have delayed emptying even though they're short, and sometimes we need some promotility therapy (eg, metoclopramide or low-dose erythromycin), which are used for motility to deal with some of these issues that we see in some of these kids.

What about surgical interventions (Slide 14)? Now, these kids, again, a lot of them—not all of them, but a lot of them—have had some sort of a surgery, which is why they have short bowel in the first place. However, if you have dilated bowel and it functions well, then there's some surgical interventions to try to lengthen the bowel, give you more surface area. The oldest one is the Bianchi longitudinal intestinal lengthening and tailoring procedure (or LILT), in which they basically take the bowel and divide it in half and then put it back-to-back. And then there's the serial transverse enteroplasty (or STEP procedure), which is where they literally do like paper dolls in the dilated bowel, cuts that are across from each other that serve to lengthen the bowel.

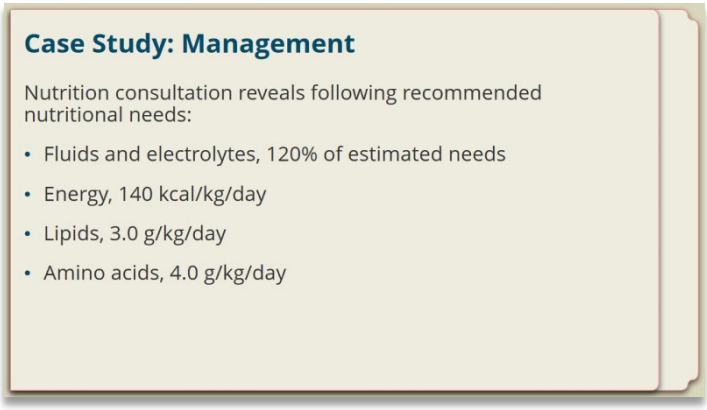


Slide 14 – IF Surgical Interventions

If you have a kid, though, that develops severe liver disease, and you're having venous access issues and they have extremely short residual small bowel, you may need to consider a small intestinal or multivisceral transplant. Again, the indications are on [Slide 14]. There are some kids that are just so short that you need to think about a transplant. Again, fewer and fewer kids are going to that nowadays with our newer interventions, but there are some kids where you need to think about surgery or transplant.

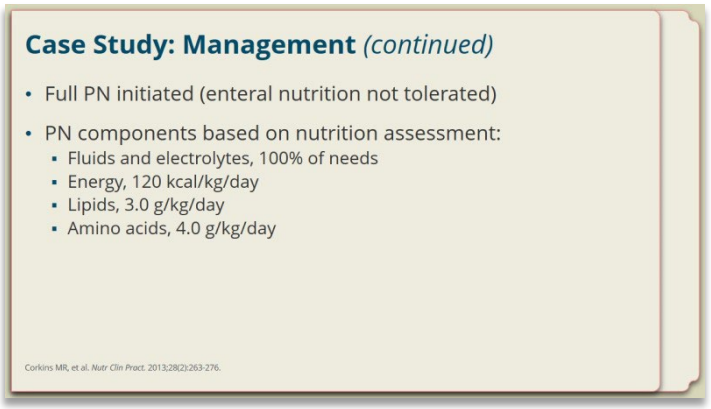
Case Part 2—Management

Anna Tuttle, MS, RD, LDN: Back to our case study. So, our nutrition consultation reveals the following recommendations (Slide 15). For our fluids, we want to meet about 120% of our estimated needs. We feel that this patient needs a little bit more fluid. This might be because of fluid losses—because of what was lost with our resection. We just want to make sure we're getting enough fluid to avoid dehydration. And then our energy needs are 140 kcal/kg, so a pretty decent amount for this individual. Lipids are at 3 g/kg, and our amino acids or protein is at 4 g/kg, which is a pretty typical recommendation for this population because they need that higher end of protein for growth and development and also for healing from the surgery. So, that's why it's on the higher end there.



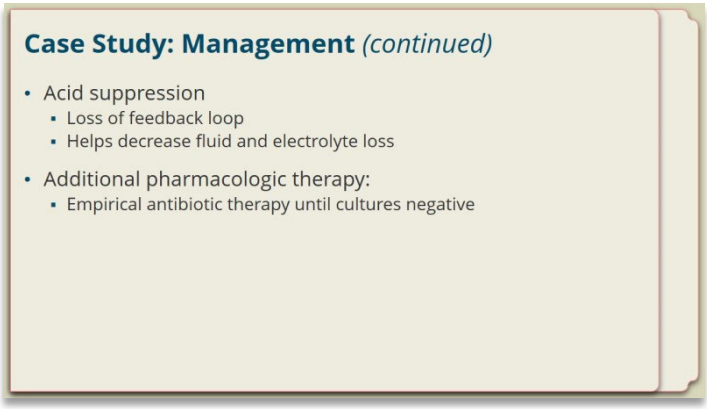
Slide 15 – Case Study: Management

They decide to go with full parenteral nutrition (Slide 16). Enteral nutrition is started, it seems, but is not tolerated, so that's why we decide to get all of our needs met by PN. So, then that mixture is made based on the following, the fluids are at 100% of needs. Since it's going intravenously, we know that we're getting all of those, so we just do the 100% of needs for that. For energy, it's 120 kcal/kg. For the most part, for parenteral nutrition calorie needs, we estimated that it's 90% of the enteral calorie needs, since you don't have the thermogenic effect of feeding or breaking down those calories, so it's usually at 90% of those needs. That's why it's the 120 instead of the 140 kcal/kg. And the lipids and the amino acids remain the same.



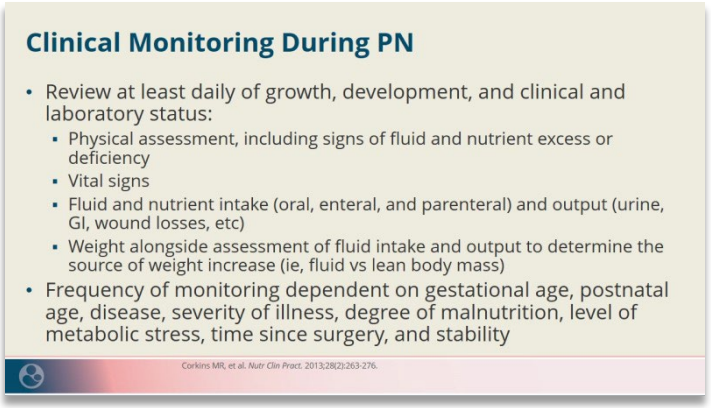
Slide 16 – Case Study: Management (continued)

As far as the acid suppression [in Slide 17], Dr. Corkins just mentioned this, but a lot of these patients lose that feedback loop, so we want to suppress that acid so we're not losing an excessive amount of fluid and electrolytes, since these patients are already set up to get dehydrated easily. So, whatever we can do to help keep that dehydration at bay, we will do. We usually start them on a PPI and other pharmacological therapy. They'll be on the empirical antibiotic therapy until cultures are negative, so that's what this case study did as well.



Slide 17 – Case Study: Management (continued)

In regards to clinical monitoring, very close attention is paid to their growth and development (Slide 18). Daily weights are taken while they are in the NICU. Usually, you try to do it at the same time, a dry diaper, and the same scale. You want it to be as similar to the previous day and the day before that as possible so that you don't have any outlying fluctuations. Do a physical assessment: put your hands on the patient, feeling around, feeling for any signs of malnutrition, seeing any signs of edema. Also, vital signs are taken on a regular basis. Strict attention to [inputs] and [outputs], of course. Make sure anything going in orally, enterally, or parenterally is documented. Pay close attention to output, so all urine output is documented as well as ostomy output. If a patient does have not have any ostomies or mucous fistulas, anything like that, weighing the diaper so that they can get a weight of the diaper. And then, if they can fractionate between the stool and the urine to get a better picture of how much they are stooling out. We just need to get an idea of how much output they are having. So, whatever we can do to do that. We also just need to know how much fluid they're getting in and out because we also want to know if their weight increase is true body weight or if it's fluid weight. So, that's something that we need to keep in mind as well. That's why it's always good to visually see the patient and evaluate for any edema or fluid weight gain.

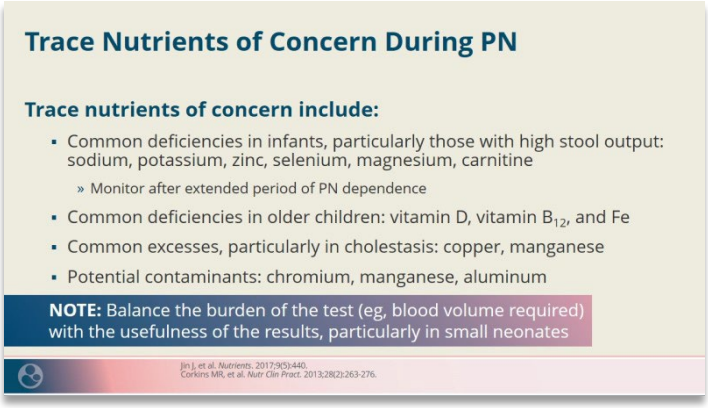


Slide 18 – Clinical Monitoring During PN

The frequency of monitoring can vary as they get older, and it also just depends on the severity of their disease, the time from surgery, their malnutrition status and just the team's decision. But initially, it's very close monitoring and that daily weight.

Mark Corkins, MD: Alright, well so I'm going to talk a little bit about trace nutrients (Slide 19). So, the macronutrients. We have some guides for that, and there are some with a little bit of data and different amounts [of data] with different trace elements because some people have interest and have studied them and some have very little studies and very little data. But it's pretty common in infants with a high output from their GI tract that sodium, potassium, zinc, selenium, magnesium, and carnitine, need to be monitored. They tend to lose those in a high output. And, initially, when you're started on parenteral nutrition, it's usually not a problem, but after they've been on it for a little while, you need to keep this in the back of your

head that you need to monitor these. And we try to have a scheduled approach where we just know that on a regular time-interval basis, we need to check these trace nutrients. Of course, we check them sooner if, for instance, we find a deficiency and we put them on supplements, we'll check them sooner to make sure it's normalizing.

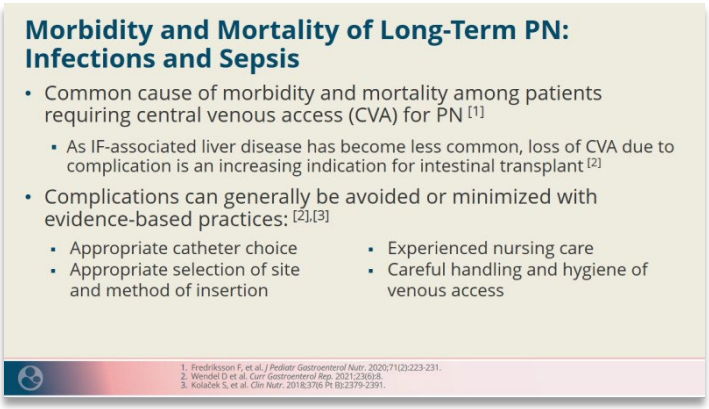


Slide 19 – Trace Nutrients of Concern During PN

In older kids, we see a lot of vitamin D, B12, and iron deficiency. There are some that actually we worry about when they get a little cholestatic: copper and manganese. Although, a few years ago, everybody was taking the copper all the way out when they got cholestatic, and then we had copper deficiencies. So, again, the best way to know what's good or bad is to monitor it and check a copper level on a regular basis if you're worried about it. It's interesting, there are also contaminants in parenteral nutrition: chromium, manganese, and aluminum. Chromium and manganese are trace nutrients that we do need in our body, but because most parenteral nutrition is contaminated, we actually worry about getting too much. Aluminum has no biologic function and unfortunately, in parenteral nutrition, tends to be high, and there are some concerns about a high aluminum content and effects on especially bone growth and the growth plates.

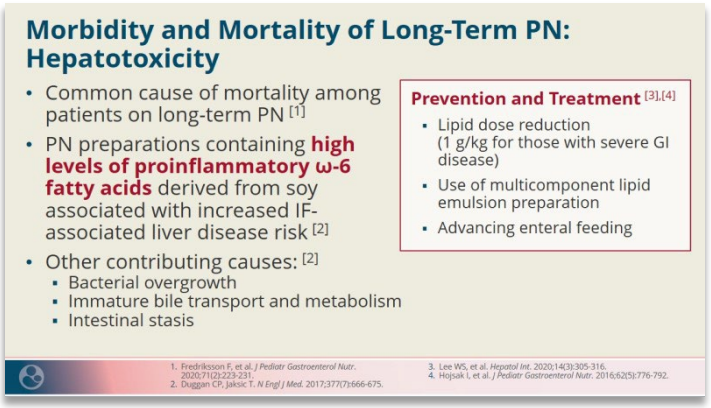
You have to balance, of course, your need to monitor with the amount of blood required to do this. And so, we tend to do it in stages and on a thoughtful schedule, especially in small neonates. You've got to think about this, and it's a balance. And you have to know when to do it and how often you need to do it.

Morbidity and mortality (Slide 20). Again, common causes of morbidity and mortality among the patients who have intestinal failure are parenteral nutrition which, again, is life-saving. Before, the outcomes were abysmal without parenteral nutrition, but that, in and of itself—our therapy—is the most common cause of mortality and morbidity. We see lots of issues, primarily infections and, again, parenteral nutrition–associated liver disease. And so, you've got to be careful. Where do you put the catheter? How is it put in? Good nursing care. There is great literature that, with experienced care and some of the bundles that are approached, handling and hygiene, you have less issues.[5] In fact, again, if you remember on my slide talking about surgical interventions, loss of vascular access is an indication for going to intestinal transplant. I think part of the reason we're seeing less intestinal transplants is because we're doing a better job of taking care of the central lines.



Slide 20 – Morbidity and Mortality of Long-Term PN: Infections and Sepsis

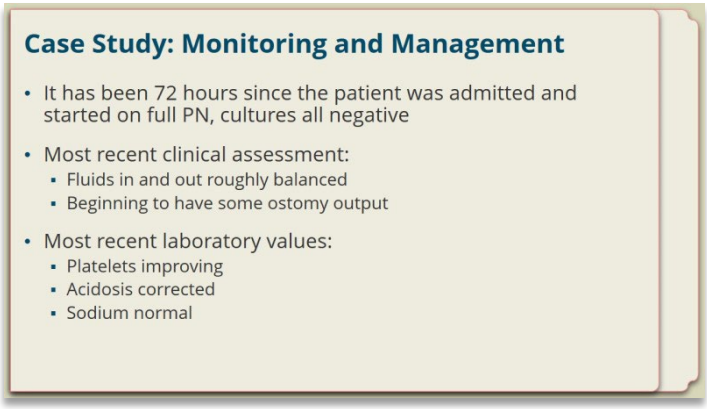
Long-term parenteral nutrition also has some effects on the liver (Slide 21). And again, it is a common cause of mortality for patients on long-term parenteral nutrition. There have been a lot of concerns about parental nutrition. For years, we had 1 type of parenteral nutrition lipid product approved in the US. It was high in omega-6, and it was from a soybean product and that seems to be associated with an increased risk of liver disease. Of course, there are other contributions: intestinal stasis, small bowel bacterial overgrowth, probably the immature bowel transport metabolisms. And some of the things that have been done that seem to reduce the risk of parenteral nutrition–associated liver disease include doing a lower dose of lipids. Now again, you have to worry that you're not getting them enough calories and enough lipids because, again, those are essential macronutrients. So, this is a balance. And then, using some of the newer lipids, some of the multicomponent lipid emulsions. There are some omega-3 lipid emulsions that are now available. There's this multicomponent lipid emulsion now available. And the biggest thing is advancing enteral feedings—using the gut, stimulating the bile flow—that's probably the absolute best intervention ever for preventing any kind of hepatotoxicity from your parenteral nutrition.



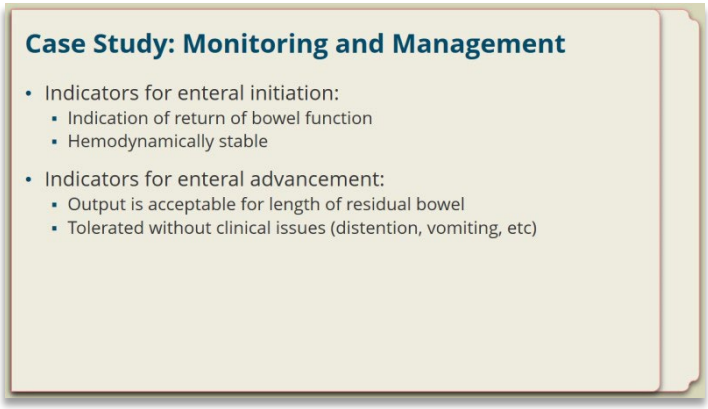
Slide 21 – Morbidity and Mortality of Long-Term PN: Hepatotoxicity

Case Part 3—Management

Anna Tuttle, MS, RD, LDN: It has been 72 hours since the patient was admitted and started on full PN (Slide 22). So far, the cultures have been negative, so that is great. So, our most recent clinical assessment shows that the fluids (the in and out) are roughly balanced, which is good, and the patient is starting to have some ostomy output. So, we're showing that the intestines are starting to work again. And the most recent lab values show the thrombocytopenia's resolving, so our platelets are improving. Acidosis has corrected, and our sodium is now normal.



Slide 22 – Case Study: Monitoring and Management



Slide 23 – Case Study: Monitoring and Management (continued)

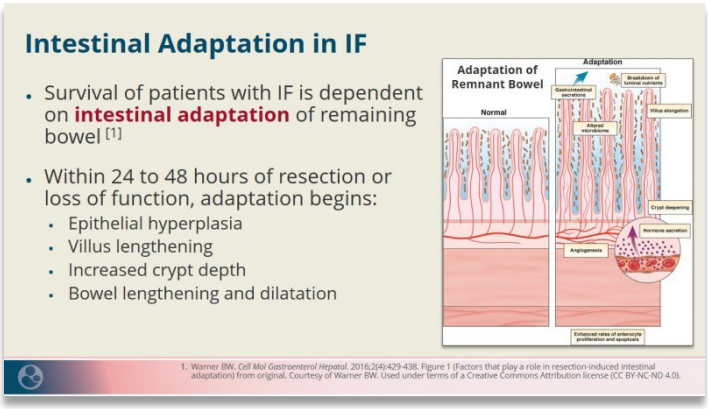
Our indicators for enteral initiation (Slide 23). We see that we are having return of bowel function with that ostomy output, and the patient is hemodynamically stable since our acidosis has resolved, our hyponatremia has resolved, and our platelets are improving. So, all of those are indicators that we can start some enteral feeds. Those are usually started at a very slow rate; you don't want to go too hard at the beginning. You just start very slowly, and then you have to listen to the patient and their body, basically, as far as the indicators for enteral advancement. One of the main indicators is output. So, you have to also see what output is acceptable based on the length of residual bowel. Knowing what is left as far as their bowel goes will help guide you as far as what their output might be. For instance, if they don't have a colon, they might have a higher output because they don't have a colon to help absorb the fluid of the output. So, they might have high output if they have an ileostomy compared to if they have a colostomy. That's something to keep in mind for your parameters of what the output should be.

Another indicator is knowing if they tolerated these increases without clinical issues. So, if you increase the feeds and then they are having abdominal distention or if they're having emesis, then maybe we need to slow down a little bit and go back to our previous rate and give them time to adjust. That's something to guide you (the output), and just make sure we're not showing any distention or vomiting or intolerance issues or just basic discomfort. And that helps guide if you can advance the feeds any further.

Weaning From PN to EN

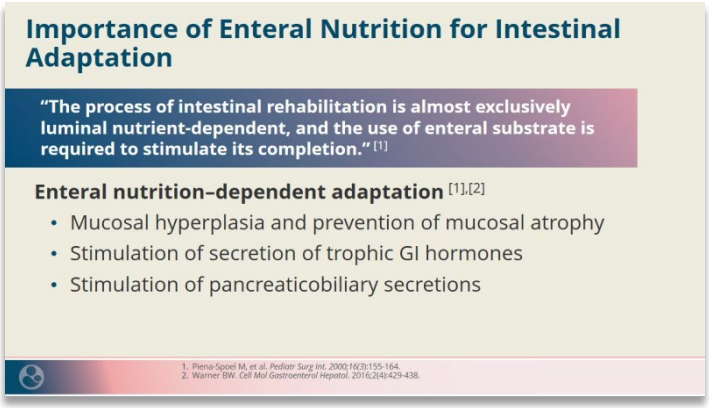
Mark Corkins, MD: Alright, so now we're going to talk about weaning from parenteral to enteral nutrition. We've kind of got this neonate, we've got some nutrition going and we've been able to start a little enteral nutrition. Now, we want to move forward, and this is where, for me as a GI doc and somebody who likes to do intestinal rehabilitation, this is where we want to go (Slide 24). We want some intestinal adaptation, and that's how these patients are going to survive and make progress as that remaining bowel adapts. In fact, within 24 to 48 hours after you resect bowel or lose function, the

bowel begins to adapt. The epithelial cells become hyperplastic; the villi get longer; the crypts get deeper; and the bowel gets a little longer and dilates a bit, which is helpful over time because it gives you more surface area. It all has to do with surface area. It's kind of like physics, which you thought you'd never use again if you ever took a physics class. Unfortunately, you still have to think about physical things, even if you don't do actual physics.



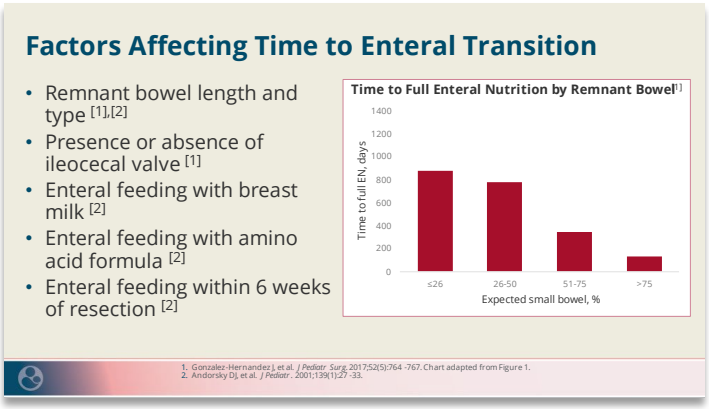
Slide 24 – Intestinal Adaptation in IF

One of the key things, of course, is the importance of enteral nutrition for intestinal adaptation (Slide 25). That intestinal rehabilitation is almost exclusively luminal nutrition dependent. And those enteral substrates are required to stimulate its completion. Basically, the fuel for the enterocytes is the enteral nutrition, and so you have to put enteral nutrition in there to get adaptation. If you don't feed them, the gut doesn't hypertrophy—it does the opposite. It hypertrophies when you feed it. What happens is you actually get atrophy when you're not feeding it. When you feed it, it stimulates the liver to flow. You get trophic GI hormones, and those help adaptation. You stimulate, again, the pancreatic and the biliary secretions, help prevent cholestasis in the liver and make the liver much happier—we like a happy liver.

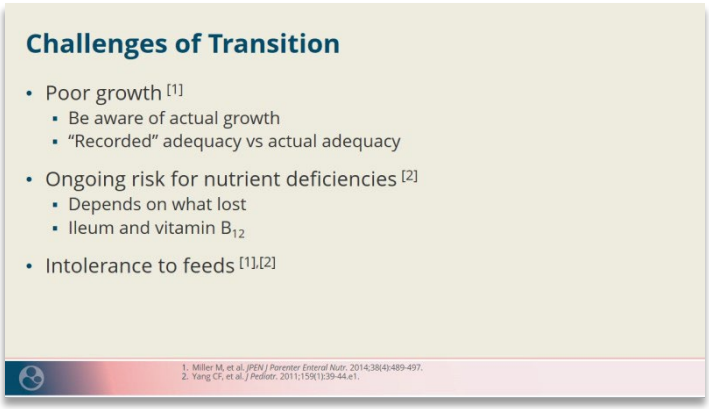


Slide 25 – Importance of Enteral Nutrition for Intestinal Adaptation

How long is adaptation going to take? Well, we've said this a billion times already I think (that might be a slight exaggeration), but it depends on what you've got left and [how much] is left (Slide 26). How much time is it going to take? Well, if you have more bowel, it's not going to take as long for the adaptation to take you off parenteral nutrition. So, the graph is from a study, and it shows that if you have less than a quarter of your bowel, it may take over 800 days. But if you have over 75% of your bowel, you know, it's going to take less than 200 days, basically, to get there.[6] Do you have the ileocecal valve? That valve at the end of the small bowel, between the small bowel and the colon, it closes—it keeps things in the small bowel longer so they can be absorbed. So, that actually means you can be shorter in your small intestine. It also is helpful for preventing bacteria from the colon from getting into your small bowel.



Slide 26 – Factors Affecting Time to Enteral Transition



Slide 27 – Challenges of Transition

Enteral feedings with breast milk [can affect time to transition]. Breast milk, to be honest with you, is not just the macronutrients. There's a lot of growth factors and other helpful things in breast milk that will help with adaptation. Sometimes, enteral feedings with amino acid formulas—they don't have to be digested, just absorbed. And then enteral feeding sooner rather than later—there are studies that basically say if you start within 6 weeks of resection, you'll do better. Of course, sooner is always better in just about everything in life. Sooner is better for most things.

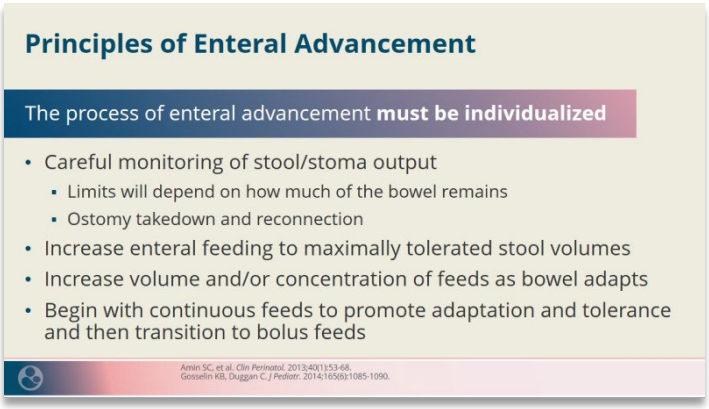
What about challenges (Slide 27)? So, we're talking about going to enteral nutrition. The problem is if you push it too fast, and they aren't ready and their bowel isn't adapted and they aren't absorbing well, you're not going to grow well. And you have to be aware of their actual growth. And also, you have to be aware of what I call the paper tolerance. There are kids, their output doesn't seem to be that bad—they don't seem to be not tolerating their feedings—but they aren't growing, and we see that fairly frequently. "Hey, they look pretty good," but they aren't getting there.

There are also some risks for ongoing nutrient deficiencies, again depends on what's lost. The ileum, for instance, with B12 is a good example.

And then [there is] intolerance to feedings.

Strategies for Parenteral to Enteral Nutrition

Anna Tuttle, MS, RD, LDN: As far as strategies for transitioning from parenteral to enteral (Slide 28), some basic principles—one of the things to always remember is that all of these guidelines that we might have at our different institutions, they're great to use as guidelines, but everything is very, very individualized and based on the patient. I know different hospitals have guidelines based on residual intestinal length of these patients and also how early they were born and their weight as far as how often they will advance feeds. And that's great to use as a guideline, but sometimes patients don't go according to the guidelines, so that's something just to really keep in mind. One of the best indicators, as I mentioned before, is stool or stoma output. So, paying really close attention to what their output is—that can be an indication of how much you can push feeds, and that also is sometimes limited on how much of the bowel remains.

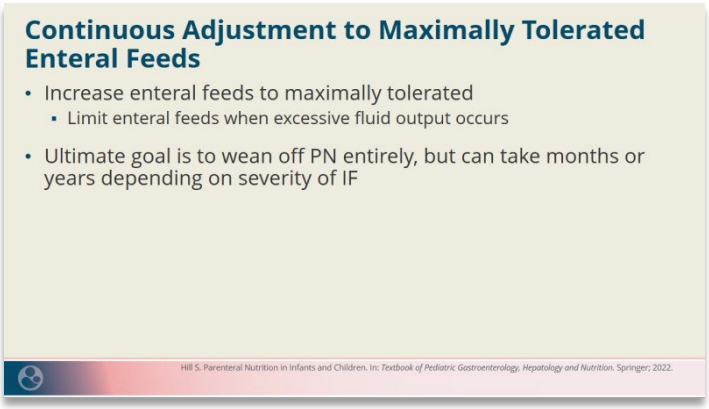


Slide 28 – Principles of Enteral Advancement

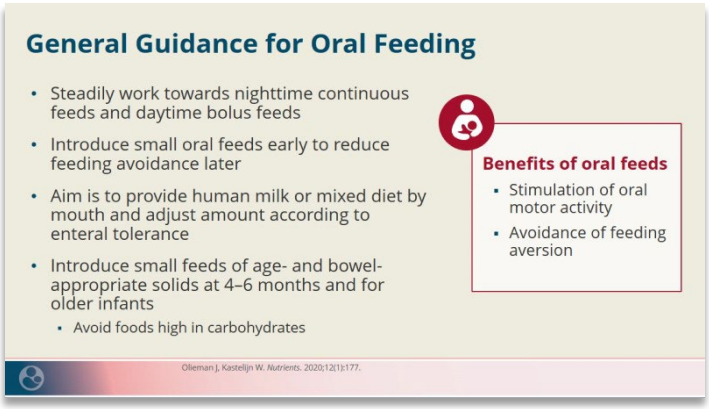
Later on, at a certain point, there usually is an ostomy takedown and reconnection, but for a while they will have that stoma that you'll measure the output of as well. You'll increase the enteral feeding to maximally tolerated stool volumes. So, every different child has a threshold, you don't really know what that threshold is until you kind of reach it. So, you'll slowly increase the volume. And it might be that you're increasing like 1 mL an hour every few days; it might be every week—it just really is patient-dependent. But it just really depends on what their output is and if they're showing any of those other signs and symptoms, such as distention or emesis or just basic discomfort.

And also, you might not be able to reach a certain volume for a while and have to stay at a certain volume for a few weeks or so until the bowel is able to adapt a little bit more, and then you can start increasing the volume again. So, you're not always going to be committed to maybe that one rate forever. You have to allow intestinal adaptation to continue to occur. We usually begin with continuous feeds. We like the constant contact of the breast milk or formula with the intestines, with the villi, so that helps promote adaptation and tolerance. And then, once we get to a certain level, then you can start talking about transitioning to bolus feeds.

Like I mentioned, you increase those enteral feeds to maximally tolerated (Slide 29). Then you'll just have to limit those feeds when there's excessive fluid output. And sometimes, you have to take a step back. Sometimes, you might get to a certain level and then that patient gets a GI bug or they get sick with something else and then you might have to decrease the rate a little bit and then bump up the PN again to make sure they're getting enough calories. And that can definitely happen, and it's not the end of the world. We just have to let that patient recover. We don't want them to lose weight, so we have to make sure they're still gaining weight appropriately, and then, once they recover from whatever viral illness or whatever is going on, then we can start increasing those feeds again. So that's something to keep in mind as well, that just basic things happen like that, and we just keep on increasing those feeds and listening to our patients and to their body because our ultimate goal is to wean off PN entirely, but this really takes time. It's not instantaneous; it can take months or years, really just depending on the severity of the intestinal failure and really just depending on the patient.



Slide 29 – Continuous Adjustment to Maximally Tolerated Enteral Feeds



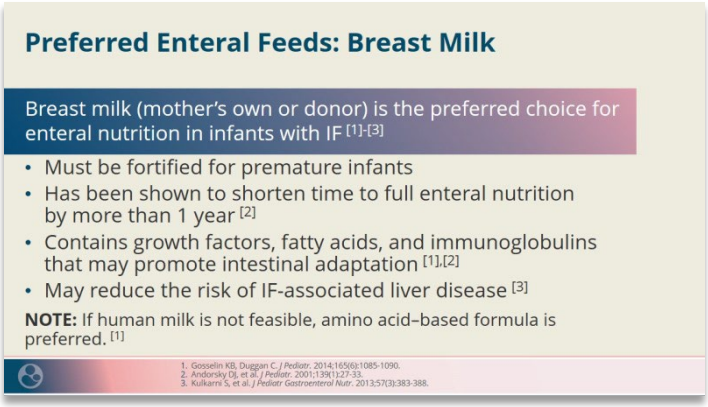
Slide 30 – General Guidance for Oral Feeding

Guidance for oral feeding (Slide 30)—and this is something great to talk about because a lot of premature babies are prone to oral aversion. So, something that can help with that is, once we're working up on those feedings (eg, eventually we get to nighttime continuous feeds and daytime bolus feeds), that will allow for some time off the pump, which will allow the patient to get a little hungry and allow for some oral feeds or even some of those bolus feeds to be given as oral feeds. Because we love to do some small oral feeds as early as we can to reduce feeding avoidance later because we don't really want to create this oral avoidance or oral aversion later on in life. The aim is usually to provide human milk or, even if the human milk would not be enough for this patient or the mother doesn't have enough milk or donor milk isn't an option, there could be a mixed diet, such as formula with human milk, as an option as well.

We usually introduce small feeds of age- or bowel-appropriate solid foods at 4 to 6 months, usually avoiding like foods that are, of course, high in sugar, since that can increase output. So, it's usually something high in pectin or fiber, such as green beans. But we really love to start those oral feeds as soon as we can. The stimulation of oral motor activity and avoidance of feeding aversion is just really helpful, even if it is just the oral stimulation, such as dipping a pacifier in breast milk and just like having some sort of oral stimulation so that they're not just going to be totally averse to putting anything in their mouth, is really important. And that's where speech [pathology] can really come in handy as well in the hospital.

As I mentioned, breast milk (mother's own or donor) is the preferred choice for enteral nutrition (Slide 31). Mother's milk is really the best choice, since it is perfectly tailored for their infant, but sometimes that is not an option. So, there is donor milk available in a lot of different hospitals. A lot of times, breast milk does need to be fortified for premature infants. It doesn't have enough protein for what we estimate. Breast milk has lower protein, so we usually add some fortifier to bump

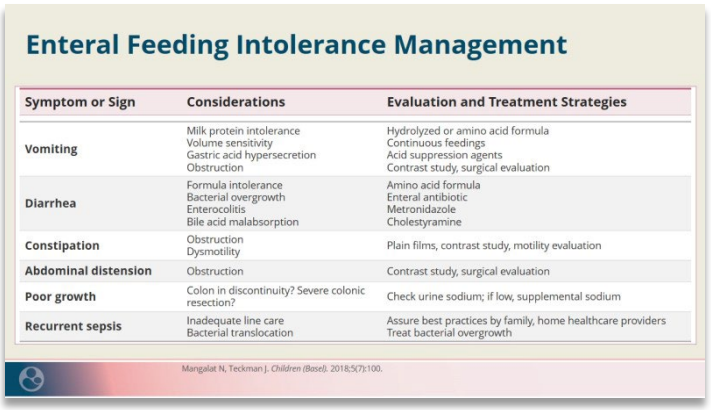
up the protein to meet those requirements for the premature infants. But breast milk has been shown to shorten time to full enteral nutrition by more than a year in these babies.[7] Breast milk contains growth factors, fatty acids, and immunoglobulins that can really help promote that intestinal adaptation, and it may also reduce the risk of intestinal failure-associated liver disease.



Slide 31 – Preferred Enteral Feeds: Breast Milk

Mark Corkins, MD: How do you manage intolerance (Slide 32)? We've mentioned several times, sometimes something happens and they aren't tolerating the feedings, and these are different things that we can see that show up sometimes in these kids. Remember, these are preemies, and they can also get other things besides short bowel. If life was fair, having intestinal failure would be all you get, but unfortunately life is not fair, as I keep telling my children. Life is not fair. It should be fair, but it's not. Life is not a Disney movie.

So, vomiting. That can actually turn out to be protein intolerance if they're getting, for instance, breast milk, and there's some dairy products in mom's breast milk. They can have some sort of dysmotility, like I said, some of this bowel's beat up, and it's dysmotile. They have that gastric acid hypersecretion if they're not on a good acid suppression. They have surgery; they maybe have some scarring and have an obstruction. Again, the diarrhea can be if they're not tolerating the formula. They may have small bowel bacterial overgrowth if they don't have an ileocecal valve and the bacteria have gotten into the small bowel. Constipation, again, it can just be dysmotility, or they can have an obstruction. Distention [could be] obstruction, again. Poor growth: is their colon in continuity? Do they have a severe colonic resection? Are they keeping up with their sodium, their fluids? Again, sepsis: is the line getting good care? Are they getting bacterial translocation because their bowel isn't adapting? Lots of different issues that you have to think about.

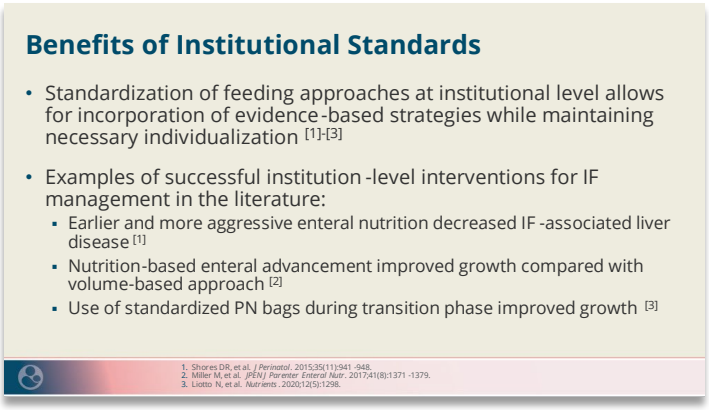


Slide 32 – Enteral Feeding Intolerance Management

Anna mentioned that a lot of institutions have standards and, again, while every patient needs a tailored approach, a standardized approach does 1 thing and that means that you are thinking about advancing the feedings (Slide 33). And that is a good thing. And it makes you think, even though you might have to tailor it for the patient, you're thinking, okay, I need to advance the feedings.

Well, there's this and this and this, maybe we need to take a day off, but it's driving you to think and protocolizing advancing the feedings.

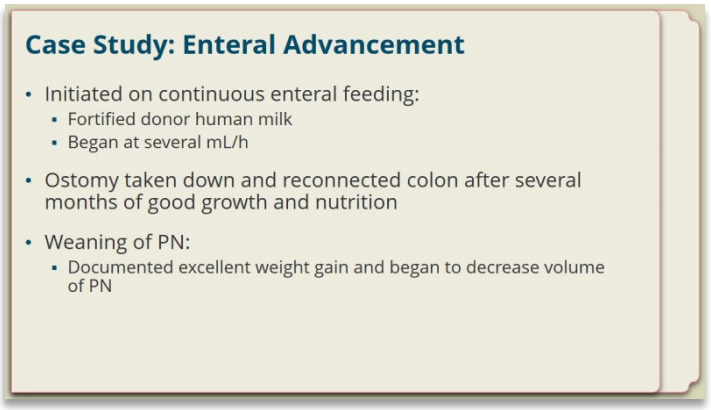
Again, some examples of institutional-level interventions that have been found in the literature. For instance, if you give earlier and more aggressive enteral nutrition, you have less intestinal failure–associated liver disease.[8] Makes sense. A nutrition-based enteral approach improves growth compared to a volume-based approach.[9] And then a standardized PN bag—you have standardized parenteral nutrition during your transition phase and you are going to end up getting better growth.[10] So again, some of these standards, they're good things; they help drive us. You may have to adapt for the patient, but it's not bad to have a standard protocol that you can adapt as you need to.



Slide 33 – Benefits of Institutional Standards

Case Part 4—Enteral Advancement

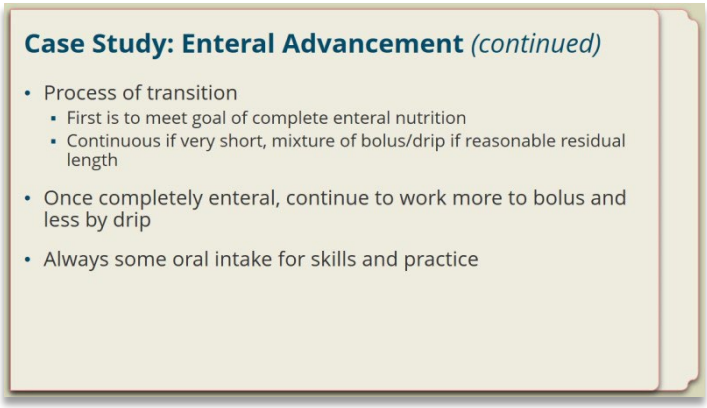
Anna Tuttle, MS, RD, LDN: He was initiated on continuous enteral feeding (Slide 34). They chose to use fortified donor human milk, began at several mL per hour. This might've been based on his weight, sometimes they will do that based on how much weight will be however many mL per hour. He had an ostomy takedown and reconnected colon after several months of good growth and nutrition. He was able to wean some of his parenteral nutrition. They documented excellent weight gain and began to decrease the volume of PN as he was able to increase his enteral feeds.



Slide 34 – Case Study: Enteral Advancement

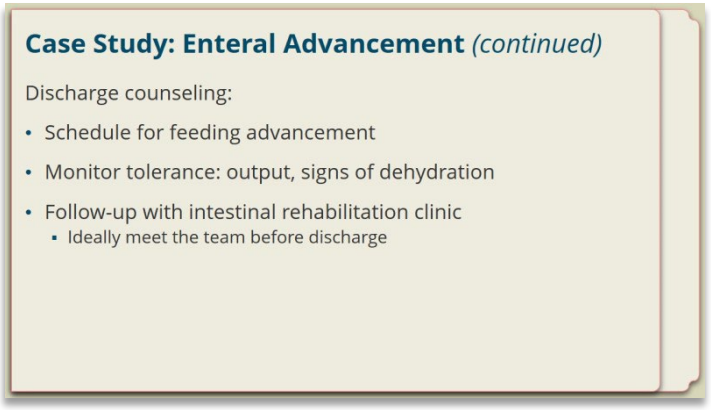
Regarding the process of transition, the first is to meet the goal of complete enteral nutrition (Slide 35). So, first he did that via continuous and then, after that, they did some short, a mixture of bolus feeds. A lot of times, you'll do an overnight continuous feed and then a few daytime bolus feeds. If that works for these patients, there are some patients who really can't tolerate high volume at 1 time, so it's really patient-dependent. But usually, a lot of these patients can tolerate those overnight feeds and then a few small bolus feeds during the day. And so, after we show tolerance of that, then we can start chipping away at the overnight continuous feeds as well, because regularly, most people aren't eating continuously overnight. So, ideally, we want to get to a more normalized pattern of eating if we can. And then we always want to work on some oral intake for skills and practice, and it might be that we're not really relying on this oral intake for calories. We just

consider anything maybe taken in orally as a bonus, but just to work on those skills and practice to get used to different tastes and textures of food, to also getting them involved in the family experience of eating. So, even if they're only on G-tube feeds and it's time for a bolus feed, put them at the table with their family, put them in a highchair and put them on their pump so they're at least getting that experience that they're getting fed while the rest of the family is eating, so that it's still like a family experience.



Slide 35 – Case Study: Enteral Advancement (continued)

Indicators when the patient is ready for discharge (Slide 36). Stable growth and output is very important. So, we want to document that they're still growing appropriately, have appropriate z scores for their corrected gestational age, make sure our output is appropriate, we're not having an excessive amount of output because, of course, we don't want to send them home before they're ready. And sometimes, patients aren't completely weaned off of parenteral nutrition. There are a lot of patients who go home on PN. It's not unheard of. Ideally, they are not on parenteral nutrition anymore, but sometimes they do have to go home on a little bit of parenteral nutrition.



Slide 36 – Case Study: Enteral Advancement (continued)

Regarding discharge counseling, the dietitian will meet with the family and talk about a schedule for feeding advancement. If they're on formula, talk about mixing instructions because sometimes they might be on a concentrated formula; they might not be on a standard 20 calorie per ounce, but might be on a more like 24 calorie per ounce or something like that. Or, if we're adding calories to mom's milk, just discuss how to mix that appropriately. And then just to talk about how to advance the feeding to keep our weight gain going upon discharge and also just talking about monitoring tolerance, what to look out for, looking out for signs of dehydration, any excessive output. Also, scheduling a follow-up with an intestinal rehabilitation clinic usually pretty soon after discharge (I'd say within 2 weeks after discharge) just to make sure everything's going well. And then you can space it out a little bit, but still, I would say while they're an infant, we would be seeing them monthly, ideally. But ideally, also they meet with the team prior to discharge just to get to know this team who will be following them very closely on the outpatient basis.

Mark Corkins, MD: Some of the key takeaways from this presentation. Number 1, short bowel

syndrome is the most common cause of intestinal failure in infants, and it requires initial management with parenteral nutrition very uniformly. They've had a major surgery and resection of intestine. Although lifesaving, long-term parenteral nutrition has morbidity and mortality with it. It's funny, it's a mixed blessing. Intestinal adaptation is necessary for positive outcomes for patients who have short bowel syndrome leading to intestinal failure. And again, we know that that's the long term. It's not going to be overnight. Enteral feedings should be initiated as soon as tolerated, preferably using human milk, and the enteral feedings should be constantly advanced and maintained at the maximum level tolerated for each patient. I mean, transition—you should be constantly transitioning because you should be constantly using the bowel to the maximum level you can, and minimizing your parenteral nutrition. And that's probably the best care that you can provide to these patients.

Key Takeaways

- SBS is the most common cause of IF in infants and requires initial management with PN
- Although lifesaving, long-term PN can lead to morbidity and mortality
- Intestinal adaptation is necessary for positive outcomes for patients with SBS
- Enteral feedings should be initiated as soon as tolerated preferably using human milk
- Enteral feedings should be constantly advanced and maintained at the maximum level the patient can tolerate

Question & Answer

Editor's Note: This is a transcript of audience questions together with presenter responses from the June 9, 2022, webcast.

With the use of antibiotics for bacterial overgrowth or as prokinetic agents, what is the impact on the microbiome and the growth of the epithelium?

Mark Corkins, MD: I mean, we do not do like continuous antibiotics in these folks. We only do it when we need it. For instance, if they have an episode of overgrowth, you have to treat it, and that's when we use antibiotics. We usually use it in short-term situations. Very rarely, we have kids who we put on cycled antibiotics. That's pretty rare. We don't do that very often. Of course, a lot of times the concern is that they don't have the ileocecal valve. Some of them also have overgrowth because the bowel is dysmotile. So, if we get better motility, of course that helps prevent overgrowth by kind of sweeping the bacteria out. So, again, we'll treat it in the short-term to get rid of the overgrowth, and then, if they have dysmotility, put them on a promotility agent to try to prevent overgrowth.

What is the typical range of acceptable stoma output in the advancement stage of EN?

Anna Tuttle, MS, RD, LDN: I would say we usually want it less than 40 to 50 mL/kg/day, but we also, and Dr. Corkins, you can jump in too, but I'd say if it's an ileostomy or jejunostomy, we would expect higher than that. But we usually, we want it less than 40 to 50 mL/kg/day.

Mark Corkins, MD: Right. So, for a jejunostomy, very high in the small bowel, normal may be up to (if it's very short) maybe 50 mL/kg/day, and that's

what you'd expect. Now, if you do little feedings, now you have to watch their fluids very carefully because you don't want them to get dehydrated. Now, if you have more bowel, higher is a problem, that means they're not tolerating. If you have the majority of your bowel, it should be less than 10 mL/kg/day. If you have some sort of a colostomy, it's usually 20 mL/kg/day. Like a cecostomy or ileostomy, you're talking like 20 to 30 mL/kg/day. Again, you have to know your anatomy to know what's acceptable for output.

In the case presented, the enteral nutrition started with fortified donor breast milk. Is it common to start with fortified breast milk or plain breast milk and how is the tolerance on fortified vs unfortified?

Mark Corkins, MD: Well, basically we would love to start with mom's own, but a lot of times, we end up with donor. We know that any kind [of breast milk], mom's own or the donor, doesn't meet the needs because this baby is not full-term; they are premature. So, we usually do have to fortify it, and usually they will tolerate that fairly well. Again, remember, we're starting very low and very slow.

Anna Tuttle, MS, RD, LDN: Right, right. Usually, the milk does need to be fortified to meet those protein requirements, and so we would just probably start with a low dose of fortification, and sometimes it is patient-dependent. They might start with only the breast milk, but usually they will add a little bit just to make sure we're meeting those protein requirements and then just slowly build up the best we can and then chip away at the parenteral nutrition as they're showing tolerance to those feeds.

In parenteral nutrition, are dietary fiber-derived short-chain fatty acids provided as an important nutrient for endothelial growth?

Mark Corkins, MD: Well, to be honest, the enterocytes actually get their nutrition by what passes through the GI tract and, yes, the short-chain fatty acids are important, and they are important sources of nutrition. But every nutrient is actually important. You can't neglect any of the nutrients because one thing about the enterocytes, they get their nutrition by pass-through. So, there's been lots and lots and lots and lots—over my years of doing intestinal rehab—lots of studies of all sorts of nutrients, and there's all sorts of things we thought were going to be the silver bullet.—"this is going to be the magic nutrient that's going to drive adaptation faster or better." To be honest, after looking at all those studies for all these years, there's no 1 magic nutrient. They're all important. You need all the nutrients. Now, the GLP-2 analog, again, is a hormonal approach that drives adaptation because it's missing when you have bowel resection. So, yes, the short-chain fatty acids are important, and they are very crucial, but I would say you don't get focused on 1; you need all of them.

Have you seen iodine deficiency in babies with intestinal failure who are primarily fed through TPN?

Mark Corkins, MD: Yes. Now, I could go more into depth, but yes. We've seen it. And to be honest with you, we didn't see it as much as when we used to use, in the old days, with central lines, we used betadine under the dressings. We cleaned the central line site when we changed the dressings with betadine, which contains iodine, and it's

funny: we never saw iodine deficiency. Now, in the modern era, we have gone away from betadine, and we're using other agents to clean the sites, and we've actually seen some iodine deficiencies, interestingly enough. Which, again, if we have some signs of that, that's 1 of the micronutrients we may look for if we're seeing clinical signs that make us curious that they may be deficient in iodine.

Another question about micronutrients: do you have any recommendations on how frequently to check trace elements in an infant on long-term parenteral nutrition?

Mark Corkins, MD: Well, we try to check every trace element roughly every 6 months, but remember, as I said, it's a small child, and so we tend to do it staggered. In other words, every trace element will get checked every 6 months, but we're actually checking usually about every 3 months. So, in other words, we'll check a set at 3 months, and then in 3 months we'll check another set. We're not checking the same set every 3 months, but we're making sure we try to check every 1 of the trace nutrients at every 6 months. Hopefully, that makes sense. It made sense in my head when I was saying it!

Anna Tuttle, MS, RD, LDN: Right, and when they initially go home, we might check it more frequently too, and just space it out as they're showing more normalization of labs. It's just dependent.

Mark Corkins, MD: It's a good thing to protocolize. That's one thing it's very helpful if you think in terms of a protocol, mentally, to follow this. That way, you don't miss it. If you rely on clinical signs or whatever, you will tend to miss it.

Anna Tuttle, MS, RD, LDN: True.

How are parents and caregivers of preterm infants being counseled when they are transitioning to at-home partial parenteral nutrition?

Anna Tuttle, MS, RD, LDN: It's a big process. We usually have a care conference, usually the case manager on the inpatient side sets it up with the parents, our intestinal failure team, the surgeon, the infusion company who will be handling the parenteral nutrition, the pharmacist, the dietitian, and the GI doctor, our intestinal failure coordinator. So, we have everybody meet with the parent, discuss what it will look like going home and answer any of the parent's questions, and then we outline what a training will look like, and they have to go through a whole training of central line care. They have to train with the home infusion company, do dressing changes, show that they can start the PN, stop the PN. Also, if the patient has a G-tube—most likely if they're on parenteral nutrition, they probably also have a G-tube—do that training as well. And then they'll also have to do a 24-hour stay to show that they can do all of the care. While they're there, they'll still be, of course, in the hospital and have the nurses and providers there for back-up, but to show that they would be able to do it on their own before they can be discharged home.

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