
Trophic Feeds

Ekhard E. Ziegler

The Fomon Infant Nutrition Unit, Department of Pediatrics, University of Iowa, Iowa City, Iowa, USA

The question of when to start enteral feeding confronts the caretaker of very low-birthweight (VLBW) infants on a daily basis. Seemingly conflicting objectives enter into consideration. The desire to minimize the risk of necrotizing enterocolitis (NEC) argues for the delayed introduction of feeds. Or so it did until recently. On the other hand, the desire to provide nutrients argues in favor of the early introduction of feeds. In the 1960s and 1970s the argument for delayed introduction was considered compelling and regimens calling for the prolonged withholding of feeds were widely adopted. In more recent years, the focus of attention has shifted to the prevention of gut atrophy as an important consideration. Consequently, early feeding regimens have been devised and successfully tested.

Undernutrition is common in the preterm infant (1) and is perhaps to some degree unavoidable. Its potential for long-term adverse effects is generally not fully appreciated by neonatologists, who face the challenge of providing nutritional support while battling with a host of usually more pressing medical problems. In the overall nutrition of the VLBW infant, enteral feeding during the early days of life constitutes but one facet of a complex situation (2). What follows is a brief description, from a decidedly nutritional point of view, of the delayed feeding as practiced until recently. A review of the controlled studies of trophic (early) feeds shows that this modality is not only effective in preventing gut atrophy, but also appears safe in that it does not seem to increase the risk of NEC. Finally, the results of a survey of feeding practices at my own institution are presented, showing that gastric residuals are a common occurrence in the first week of life without being harbingers of NEC.

DELAYED FEEDING REGIMENS

With the advent of neonatal medicine in the 1960s and the increased survival of premature infants came NEC—until then an uncommon disease entity. Because this often devastating disease almost always occurred in infants who were being fed enteraly and hardly ever in infants who were not fed, feeds were suspected of causing NEC. Although the exact role of feeds in the etiology of NEC (obligatory bystander versus causative agent) remains unclear to this day, the fact that feeds are always
being given when NEC strikes is not in dispute. It is therefore understandable that preventive strategies focused on enteral feeding. Regimens were developed that called for graded periods of withholding of feeds, with infants at highest risk for NEC having feeds withheld for the longest time.

A prominent example is the regimen of Brown and Sweet (3). For low-birthweight infants with illness or a history of problems during delivery, they withheld feeds for the first 5 to 7 days of life before gradually introducing them. Frequent episodes of apnea or of bradycardia required cessation of feeds until 1 week after the last such episode. Marked abdominal distention, or occult fecal blood associated with other untoward signs, similarly necessitated withholding of feeds until a week after the abnormalities had cleared. If there were any gastric residuals of formula, a reduction in feed volume was mandatory, and persistent residuals required the cessation of feeding for 1 week. Brown and Sweet reported that before the introduction of their delayed feeding regimen, the incidence of NEC among low-birthweight babies had been 1.5%, but that it dropped to 0.11% after the introduction of the new regimen.

Only one prospective controlled trial tested the efficacy of delayed feeding regimens with regard to the incidence of NEC. In the study by La Gamma and colleagues (4), one group of infants with a birthweight of less than 1,500 g received only parenteral nutrition but no intragastric feeds for the first 2 weeks of life, whereas another group received parenteral nutrition plus intragastric feeds in gradually increasing amounts. A diagnosis of NEC required the presence of the clinical triad of abdominal distention or ileus, hematochezia, and bilious vomiting; radiologic confirmation was accepted but was not required. Using this definition, the incidence of NEC episodes was 60% in the group receiving no feeds for 2 weeks and 22% in the group receiving early oral feeds. The difference was statistically significant at $p < 0.02$. Although one might argue whether, in the absence of radiologic confirmation, all these episodes represented NEC, it is clear that the specific delayed feeding regimen that was tested did lead to an increase, rather than a decrease, in the incidence of NEC episodes.

Despite the absence of controlled trials showing the efficacy of delayed feeding regimens, such regimens were adopted widely and underwent a variety of modifications. Acceptance was probably facilitated by the soundness of the physiological principles invoked by proponents of delayed feedings, such as Brown and Sweet (3). The basic concept that any event causing gut ischemia increases the risk of NEC in a susceptible subject (e.g., a preterm infant) is certainly valid. What one may disagree about, however, is whether withholding of feeding is an effective countermeasure. Furthermore, from today’s perspective, one must ask whether, even if withholding were effective, its adverse effects might not outweigh its possible beneficial effects.

ADVERSE EFFECTS OF DELAYED FEEDING

Undernutrition

When enteral feeding is withheld, nutrients must be provided by the parenteral route. Brown and Sweet (3) stressed that parenteral nutrition must be provided during
periods when enteral feeds are withheld, but they provided no specifics concerning nutrient intakes, either recommended or actually achieved. Since in those days peripheral veins were used almost exclusively, one has to assume that intakes of energy and specific nutrients were limited. It is not unreasonable to presume that VLBW infants subjected to delayed feeding regimens incurred a substantial price in terms of nutrients not received and complications of parenteral nutrition incurred. Although a quantitative risk/benefit assessment is, of course, impossible, it appears that a definite risk was incurred in exchange for uncertain and unknown benefits.

**Gut Atrophy**

There is a sizable body of data from animal studies describing the effects of the prolonged withholding of luminal nutrition (5). In the adult rat, parenteral nutrition in the absence of luminal nutrition leads to a decrease in gut weight, mucosal height and thickness, reduced crypt cell proliferation, shortened villus height, and lowered antral gastrin concentration (6,7), as well as to diminished disaccharidase and peroxidase activities (8). In the suckling rat, withholding of luminal nutrition leads to profound alterations of gut size and villus height (9), although these changes are readily reversible upon refeeding (10). Small amounts of luminal nutrients were shown to be required for prevention of gut atrophy in the rat (11). In the rabbit, Rothman et al. (12) showed that withholding luminal nutrition increased the permeability of the gut to macromolecules. Changes in permeability may play a role in the increased bacterial translocation observed during parenteral nutrition (13). Intestinal cellular immunity is also decreased (14). In children with protein/energy malnutrition, decreased local secretion of IgA has been reported (15). Groër and Walker (16) have pointed out that feeding is necessary for the normal maturation of the gut secretory immune system. Table 1 summarizes the important changes observed during luminal starvation.

**TROPHIC FEEDS**

In the early 1980s neonatologists began to question the wisdom of routinely withholding feeds. Some questioned its efficacy in reducing NEC (17), some were
concerned about the adverse effects of prolonged parenteral nutrition (18), and many were concerned about the intestinal atrophy resulting from a prolonged absence of luminal nutrition (18–20). They began to explore ways by which the alleged benefits of delayed feeding (i.e., a reduced risk of NEC) could be retained while at the same time preserving gut integrity. This explains the various terms applied to enteral feeds introduced earlier than had become standard practice. These terms include minimal enteral feedings (21), gastrointestinal priming (20), early hypocaloric feeding (18), trophic feeding, or early feeding. The terminology reflects the notion that small amounts of feed are sufficient to prevent gut atrophy while at the same time being small enough to keep the risk of NEC low. This belief rested in part on the finding by Lucas and colleagues (22) that small amounts of feed produce marked increases in plasma gut hormone levels in preterm infants, and in part on results of animal studies showing that small amounts of nutrients are sufficient to prevent intestinal atrophy (see earlier).

The effects of the early introduction of feeds were examined in several prospective controlled trials. In addition to looking for potential beneficial effects, investigators were careful to look for possible adverse effects (e.g., an increase in the incidence of NEC). The results of these controlled studies of early feeding are summarized in Table 2. It is worth pointing out that the age at which feeds were introduced in control subjects ranged between 7 and 18 days. Most probably these were the ages at which feeding was started in the respective nurseries as a matter of policy at the time. Table 2 shows that early feeding generally led to improved intestinal function, which may be interpreted as showing that gut atrophy was prevented or ameliorated. Most important, in none of the trials was there an increase in the incidence of NEC, nor were any other adverse effects noted.

In the trials listed in Table 2 the initial feeds consisted of water, various formulas (both dilute and full strength), and breast milk. No conclusions regarding an optimal type of feed can be drawn from these trials. However, breast milk must be considered the preferred type of feed for all the reasons normally put forward in support of breast milk, including the documented protection it affords against NEC (24) and sepsis (25) in the LBW infant.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Age at start: experimental</th>
<th>Age at start: control</th>
<th>Adverse effects</th>
<th>Beneficial effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ostertag et al. (17)</td>
<td>1 d</td>
<td>7 d</td>
<td>None</td>
<td>↑ Nutrient intakes</td>
</tr>
<tr>
<td>Slagle &amp; Gross (19)</td>
<td>8 d</td>
<td>18 d</td>
<td>None</td>
<td>↑ Feeding tolerance</td>
</tr>
<tr>
<td>Dunn et al. (18)</td>
<td>2 d</td>
<td>9 d</td>
<td>None</td>
<td>↓ Serum bilirubin</td>
</tr>
<tr>
<td>Berseth (23)</td>
<td>3-5 d</td>
<td>10-14 d</td>
<td>None</td>
<td>↑ Gut motility maturation</td>
</tr>
<tr>
<td>Meetze et al. (20)</td>
<td>3 d</td>
<td>15 d</td>
<td>None</td>
<td>↑ Feeding tolerance</td>
</tr>
</tbody>
</table>

TABLE 2. Controlled studies of trophic feeds
EARLY FEEDING—IOWA 1997

Although most neonatologists have now abandoned regimens involving prolonged withholding of feeds as a matter of routine and have moved toward the early introduction of enteral feeding, there is no documentation of actual contemporary feeding practices in VLBW infants. A survey was therefore conducted at my institution, one purpose of which was to obtain data on the actual feeding practices during the first week of life. Because gastric residuals are often the earliest sign of illness in NEC and precede other manifestations of the disease, their occurrence is usually considered to indicate NEC until proven otherwise. However, in the first week of life gastric residuals seem to be common and without apparent connection to NEC. A second purpose of the survey was therefore to obtain data on the volume and color of gastric residuals.

Methods

The records of all 101 infants with birthweights of less than 1,250 g who were admitted in 1997 were reviewed. We excluded 11 infants who died within the first week of life, three who were admitted after the first week of life, one who had atresia of the sigmoid colon requiring surgical resection, and a set of conjoined twins born after a gestation of 32 weeks. The records of one infant could not be located. From the records of the remaining 83 infants the following information was extracted for each of the first 7 days of life:

• Type and amount of any feeding
• Mode of administration (bolus or continuous drip)
• Periods of withholding of feeds
• Volume and color of gastric residuals

Where recorded, actions taken in response to gastric residuals and reasons for withholding of feedings, where applicable, were ascertained. The records were also searched for episodes of NEC, or suspected NEC, during the first week of life, as well as during the entire hospital stay.

At the University of Iowa there is not an established feeding protocol. Rather, decisions regarding feeding are individualized and are made by the attending neonatologist. However, there is a consensus that feeding should be started early and that feed volumes should be increased slowly. Prevention and early recognition of NEC are overriding concerns, and in infants considered to be at increased risk of NEC, enteral feeding may be withheld for some period of time. The presence of signs compatible with NEC naturally prompts the usual steps, including temporary cessation of feeding until matters are resolved. Transpyloric feeding is not used. Feeds are mainly given as boluses, continuous feeding only being used occasionally.

The nursing staff are highly supportive of breastfeeding, and 75% to 85% of mothers initiate lactation and provide expressed breast milk for at least some period of time. During treatment with indomethacin, feeds are withheld for 48 to 72 hours. With few exceptions, VLBW infants receive parenteral nutrition, starting within 24
to 36 hours of birth. As a nursery routine, all infants have nasogastric or orogastric feeding tubes inserted soon after admission, and gastric contents are routinely aspirated every 3 hours whether the infant is fed or not. Volume and color of residuals, if present, are recorded.

**Results**

We found that the first feed was given at a mean age of 60 hours of age (range 9 to 156 hours). The reason for late initiation was often the continued presence of gastric residuals (see later), but in some cases a history of birth asphyxia was noted as the reason. The vast majority of infants received bolus feeds. Initial feed volume ranged from 0.2 to 5 ml per feed. The starting feed volume was most commonly 1 ml. The frequency of feeds ranged from one a day to one every 3 hours, the most common frequency being every 8 hours. Continuous-drip feeding was used as the initial feeding mode in only two infants, at an initial rate of 0.5 ml/h.

In 63 infants (76%) breast milk was the intended feed. It was not uncommon for mothers to provide little or no milk (colostrum) during the first 3 to 5 days. In four of these cases and at the explicit request of the mother, some supplemental formula was fed until sufficient breast milk became available. In two cases the breast milk supply remained low and the feeding of formula was started, at the mother’s request, during the first week of life. At their mothers’ decision, 20 infants received only formula.

Gastric residuals were considered to be present if any volume of 0.1 ml or more was recorded, or to be absent if the record indicated 0 or trace. Gastric residuals were a common occurrence before the first feed was offered. Thirty-nine infants (47%) had one or more records of a gastric residual volume of more than 0.1 ml. On the other hand, most infants (n = 44) had no gastric residual before feeds were initiated. Most residuals were of modest size (1.0 ml or less), but in 21 infants larger residuals were obtained on one or more occasion. The largest aspirate was 4 ml. Bilious residuals (green or yellow) were recorded in 17 infants on one or more occasion before feeds were initiated, including seven infants with residuals that were of trace volume but were nevertheless described as green. It appears likely that the preponderance of nonpropagating clusters characteristic of the preterm infant’s duodenal motor activity pattern (26) is responsible for the frequent bile-stained gastric residuals.

Although the size and color of residuals undoubtedly influenced decisions about the initiation of feeding, documentation is for the most part not readily available. Nevertheless, in infants with no residuals, feeding was started at a mean age of 53 hours, compared with 68 hours in those with residuals, and this difference was statistically significant (p < 0.05). Infants who had bilious residuals were started on feeds somewhat later (mean age of 73 hours) than infants who did not have bilious residuals (mean age of 58 hours); this difference was not statistically significant.

Although after the first feed there was almost always a residual, in most infants (n = 55), there was no appreciable change in the overall size or frequency of residuals after the start of feeds. On the other hand, in 22 infants there was a marked increase in size or frequency of residuals. Although the increase was transient in most infants,
TROPHIC FEEDS

in a few cases it prompted temporary discontinuation of feeds. In seven infants there was a definite decrease in the size or frequency of residuals once feeding was started. Bilious residuals were recorded in 28 infants (33%) on one or more occasions. Bolus feeds were changed to continuous-drip feeds in three infants as a matter of routine and in two infants because of sizable residuals with bolus feedings.

In 39 infants, feeds were discontinued for 24 hours or longer on at least one occasion during the first week of life. Although in 15 infants the reason for withholding was treatment of a persistent ductus arteriosus with indomethacin, in 24 infants there were other reasons. In 12 of these infants, bilious residuals preceded withholding of feeding. This represented 43% of the 28 infants with bilious residuals, whereas only 22% of infants without bilious residuals had feeds withheld for longer than 24 hours. Feeds were withheld once or twice for periods of less than 24 hours in 15 infants. Thus only 29 infants (35%) did not have feeds withheld for one reason or another during the first week of life.

In Table 3, data are summarized by chronological age (24-hour intervals). It is evident that the proportion of infants who were fed at a given age plateaued from about the fourth day. This illustrates the fact that, although all infants were started on feeds by 156 hours of age (6.5 days), by that time some infants had had feeds withheld for the reasons listed earlier. The average number of daily feeds and the total amount of milk or formula received increased throughout the first week of life. On the other hand, the proportion of infants with residuals, as well as the frequency and size of the residuals, essentially did not change during the first week of life.

**Necrotizing Enterocolitis**

None of the infants (including those who died in the first week of life) had signs suggestive of NEC, and in no infant was this diagnosis made during the first week of life. It is thus evident that none of the many gastric residuals was associated with NEC. Three infants had signs compatible with NEC when they were between 26 and 36 days old. None had radiologic evidence of pneumatosis intestinalis, although in two of these infants other clinical signs were suggestive of NEC and feeds were withheld for 10 days. One additional infant was admitted from another hospital at age 22 days with a radiologically confirmed diagnosis of NEC.

**TABLE 3.** Feeds and gastric residuals by chronologic age during first week of life in 83 very low birthweight infants (successive 24 hour periods)

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of infants fed</td>
<td>6</td>
<td>36</td>
<td>61</td>
<td>67</td>
<td>70</td>
<td>66</td>
<td>73</td>
</tr>
<tr>
<td>Number of feeds (mean)*</td>
<td>1.2</td>
<td>2.9</td>
<td>3.1</td>
<td>4.0</td>
<td>4.7</td>
<td>5.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Feed volume (mean, ml/d)*</td>
<td>1.4</td>
<td>2.9</td>
<td>5.3</td>
<td>8.4</td>
<td>12.4</td>
<td>18.0</td>
<td>20.6</td>
</tr>
<tr>
<td>Number of infants with residuals</td>
<td>29</td>
<td>23</td>
<td>38</td>
<td>42</td>
<td>41</td>
<td>35</td>
<td>38</td>
</tr>
<tr>
<td>Number of residuals (mean)†</td>
<td>1.6</td>
<td>1.6</td>
<td>1.9</td>
<td>1.5</td>
<td>1.8</td>
<td>1.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Residual volume (mean, ml/d)†</td>
<td>1.4</td>
<td>1.2</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.4</td>
<td>1.4</td>
</tr>
</tbody>
</table>

* Among fed infants.
† Among infants with residuals.
Conclusion

Gastric residuals were a frequent occurrence in VLBW infants during the first week of life, whether the infants were fed or not and regardless of age. Since none of the infants had NEC, gastric residuals must have had other, more benign explanations (e.g., immature motility). Although many gastric residuals were bilious, none of the infants had intestinal obstruction. Appropriate responses to the largely benign gastric residuals during the first week of life have yet to be defined. Because immature intestinal motility is most likely to be responsible for the frequent gastric residuals, and because feeding has been shown to promote the maturation of intestinal motor activity (23,27), it may not be advisable to withhold feeds in response to benign gastric residuals.

Feeds were started on average at 60 hours of age. This is early by the standards of just a few years ago. An obstacle to the still earlier introduction of feeds, apart from the frequent presence of residuals, is that breast milk is often not available during the first few days of life. Feed volumes were increased very slowly, a practice that is designed to keep the risk of NEC low (28).

SUMMARY

Feeding regimens involving delayed introduction of feeding in VLBW infants were designed to reduce the risk of NEC. Because they were never shown convincingly to be effective in this regard, and because of concerns over the adverse effects of prolonged withholding of enteral feeding, including the adverse effects of prolonged parenteral nutrition, the earlier introduction of feeding (trophic feeding) has been proposed. A series of controlled trials showed that early (trophic) feeds not only are safe with regard to NEC but also seem to be effective in forestalling gut atrophy. Although documentation is not available, the impression is that early feeding protocols of one form or another have been widely adopted in nurseries across the country. At my own institution, early feeding has generally been adopted. The frequent occurrence of gastric residuals prevents early feeding in many infants. Strategies to overcome this obstacle need to be developed.

REFERENCES

TROPHIC FEEDS


DISCUSSION

Prof. Polberger: If we are using bolus feeding during the first weeks of life, do you have any comments on how often we should supply the feeds—every 2 or 3 hours, perhaps every hour?

Prof. Ziegler: We start by giving 1 ml every 8 hours on the first day of life. Then we increase the frequency. Don’t ask whether that is rational; it’s just the practice in our nursery! Quite possibly shorter feeding intervals might be better.

Dr. Walker: To what do you attribute your success in having no cases of necrotizing enterocolitis?

Prof. Ziegler: I think giving colostrum may play a big part in that.

Prof. Lucas: Many people think that babies below 26 weeks of gestation are very difficult
to feed, even minimally, so they are compelled to go on for weeks and weeks with intravenous feeding. If you say that atrophic changes start to be significant within a few days, then I would regard it as failure of minimal enteral feeding if it is not established by, say, 4 or 5 days. On that basis, what is the failure rate in your unit in babies below 26 weeks of gestation? That is, where you actually give up minimal enteral feeding because of unacceptable aspirates or because something happens to make you feel you can’t go on with it. I’m told all the time by neonatologists that they have failed to establish minimal enteral feeds in babies of that gestation.

Prof. Ziegler: There were no cases of outright failure the way you describe it. But feeding was frequently stopped for short or longer periods because of gastric residuals. There was one baby who had aspirates of some quantity over 5 or 6 days, but then it was decided to feed the baby anyway, and from that moment on there were no more aspirates. Neonatologists are scared of necrotizing enterocolitis. Every gastric aspirate constitutes NEC until proven otherwise. Because of that, babies are often not fed for as long as there are any aspirates at all.

Dr. Rashwan: What is your policy about the quantity of aspirate?

Prof. Ziegler: We have a rule that if the residual volume is greater than 20% of the feed volume, that requires a medical decision. It’s a purely arbitrary rule. I think a more important distinction is the type of aspirate—is it pure gastric juice, is it pure milk, is it mixed?

Dr. Chessex: As a neonatologist, I’m one of the bad guys. But like every neonatologist in this room I’m the one who has to go and explain to parents who have just lost a child that increasing the feeds on the day before had no relationship with the death of the child on the next day. It is difficult to make the parents believe it. The principal point of my comment is to say that there is a Canadian multicenter trial on trophic feeding that started about 18 months ago. The protocol has tried to tackle all the points you have raised. The endpoints of the study are necrotizing enterocolitis and the frequency of feeding stops. The study is ongoing and we’ll have to await the results.

Prof. Ziegler: I applaud you for undertaking such a task. It is very difficult to identify all the reasons feeds are withheld. When there is an aspirate, feeds may be held automatically for one or two cycles. That is certainly not the same as withholding feeds until a radiographic examination of the baby’s abdomen has been done.

Prof. Pohlandt: I’m not happy with using the term early trophic feeding synonymously with any early feeding. We would need a third term for those neonatologists who like to feed the baby early for real nutrition, not in these very small amounts for trophic purposes. What should we call that type of feeding? You gave the impression that most of the American neonatologists are afraid of early feeding. On this side of the Atlantic, at least in Germany, many neonatologists think that it is advantageous to give early feeding. We conducted a multicenter randomized trial 5 years ago where babies between 500 and 1,000 g birthweight were fed from the second day on according to a strict feeding protocol. By day 10, 62% of these babies were able to accept 100 ml of undiluted preterm formula, which is much more than trophic feeding. I think the majority can be fed.

Prof. Ziegler: I said at the outset that my remarks were colored by experience in the United States. I would not say that all neonatologists are afraid of early feeding. There is the notion that feeding babies increases the risk of NEC. I’ve been aware that in Germany and other countries, feeding is begun earlier.

Prof. Nem-Yun Boo: We recently completed an analysis of a case control study looking at predictors of food intolerance on VLBW babies. We started feeding at a volume of at least 0.5 ml per feed at 3-hour intervals. If the feed volume was less than 6 ml/ feed, we defined intolerance as an aspirate of 2 ml or more at the time of the next feed; if the feed volume was more
than 6 ml/feed, we defined intolerance as an aspirate of more than 33% of the feed volume. On this basis we found a very high rate of feed intolerance, around 64%. We looked at a number of potential risk factors, including the age of initiation of feeding, the volume fed, and a whole variety of neonatal management factors. On logistic regression analysis, the only significant predictor of feed intolerance was the age when the first feed was given—the later we fed the baby, the greater the risk of intolerance. We are preparing the data for publication.

Prof. Ziegler: Thank you very much for that interesting contribution. I look forward to seeing the data.

Dr. C. Kind: Did you look at the relation between tolerance of early feeding and the passage of meconium?

Prof. Ziegler: That’s a good idea. I haven’t looked at that, but I will.

Prof. De Vonderweid: Is there any sound reason for stopping minimal enteral feeding in babies who receive indomethacin or inotropes?

Prof. Ziegler: In our nursery, it’s been a rule for many years that babies must not be fed until 24 hours after the last dose of indomethacin. The rationale is that if the baby perforates and is being fed, he gets worse peritonitis than if he is not being fed. In relation to inotropes, usually if there is great cardiovascular or respiratory instability, we will not feed. But it’s getting more and more accepted that instability is not a contraindication to small feeds. However, this is a gradual process, and there are big differences of opinion among neonatologists.

Dr. Berseth: The major dilemma we have in dealing with necrotizing enterocolitis is that we can’t predict the infants who are at risk. As a result, we’re left dealing with the lowest common denominator—that is, we develop our feeding protocols for all infants in the nursery in an attempt to prevent a disease that is only going to occur in 8% of them. The price we pay as a result is that we are artificially holding back the other 92%. There were two abstracts presented last year at the pediatric research meetings indicating that if one were more aggressive with increasing the feeds, one could achieve full enteral feeding sooner at a lower cost. My other point relates to what volume to use. We approached this as a dose/response question. We used a chronically hyperalimented puppy model and gave varying small increments of enteral feeds to those puppies. We could not demonstrate increased growth, as measured by intestinal weight or DNA content, until the enteral feed volume exceeded 30% of the fluid intake of the puppies. However, we could achieve maturation of motor function and some other functional indices in the gastrointestinal tract at volumes of 7.5% or more of the daily fluid intake, which is in the range of what many of us are using when we give minimal enteral feeding. So it appears that we can probably achieve at least part of what we want to achieve using a very low volume.

Prof. Pereira: In the two hospitals of my university in Chile, we start oral feeding in the first 6 to 12 hours at a volume of between 2 and 4 ml/kg.d. This is given as a bolus every 2 or 3 hours. Colostrum is given in 90% of the newborns. We increase the feeds gradually over 4 to 5 days if the baby looks well and doesn’t have more than 30% of gastric aspirate. On day 7, more than 90% of our babies are receiving feed volumes of about 60 to 80 ml/kg.d. More than 70% of the feed is own mother’s milk. We have about five or six cases of NEC per 10,000 live births each year.

Prof. Ziegler: Those are very impressive figures.

Prof. Koletzko: One explanation for the apparent difference in feeding routines between the United States and Europe could be the marked difference in the cost of malpractice insurance. This might make American neonatologists a bit more defensive. Another possible reason for the difference could be the more common use of breast milk for establishing enteral feeding in Europe, and when formulas are used, the predominance of hydrolysates, which give more
rapid intestinal transit and less hard stools. Maybe that could be an advantage in establishing early feeding. My other comment relates to NEC incidence. Published data on NEC rates seem to show a lower incidence in Europe than in the United States, though this may reflect different diagnostic criteria. Do you have any comment on this?

Prof. Ziegler: I'm very cautious when I compare incidence data of NEC, since the criteria for diagnosis vary so widely. I don't think malpractice costs have anything to do with our feeding policies, nor do I think the type of feeds currently used are likely to be a factor in NEC incidence. I do think the claim of the early studies that postponing enteral feeding reduces the incidence of NEC was uncritically accepted as proven fact, and this is the reason why feedings were withheld in the United States. You Europeans probably never accepted that at face value, and maybe that is the reason you have persisted with early feeding.

Prof. Lucas: There is very little experience of using hydrolyzed formulas in America and Britain, but I understood that about 90% of the preterm formulas used in Germany are partially hydrolyzed. Prof. Koletzko therefore raised an important issue, that maybe there is a reduction in one particular sort of morbidity as a result of using that kind of formula. I'd be interested to hear of any more evidence on the use of these in preterm infants. There has evidently been much more clinical experience of their use than many of us are aware of.

Prof. Pohlandt: One of the main problems with feeding ELBW infants is constipation, and linked with that, how to establish faster transit of the stools. Gastric emptying is thought to be facilitated by hydrolysates, so we did a randomized prospective study in 19 (babies that was the precalculated sample size) and found that the transit time of the hydrolysate was 9 hours shorter than that of whole cow's milk protein. But that doesn't prove that we can move up to a full enteral intake more rapidly on a hydrolyzed formula. That study has not yet been done.

Dr. Sedaghatian: We use only breast milk for early feeding in infants of less than 1,000 g. We start at 24 hours with 0.5 ml every three hours, not every eight hours, but we don't give any foreign protein for at least 2 or 3 days. Do you think you should specify in your protocol that early feeding should only be with human milk, or do you think it is acceptable to use a formula from the start?

Prof. Ziegler: I do not see a reason for not introducing a milk-based formula in the first 24 hours. I would still start with very small feeds. It is possible that milk formulas carry a higher risk of necrotizing enterocolitis, but it's still unproven whether it makes a difference when we start feeding very early. I don't see a reason for withholding a formula when breast milk is not available.