Signaling Factors for Gut Adaptation

Akira Okada

Department of Pediatric Surgery, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

Introduction – Intestinal Failure

With the increasing number of patients safely receiving long-term total parenteral nutrition (TPN), it has become clear that there is a group of patients, in whom treatment is totally dependent on TPN for a prolonged period of time. This disease entity is referred to as ‘intestinal failure’, well defined as ‘conditions, which lack a functioning intestine necessary for adequate digestion and absorption’ [1].

Intestinal failure may roughly be divided into two types: one characterized by an absolute reduction in normally functioning gut mass (short bowel syndrome), and the other marked by an intestine with extensive lesions or functional insufficiency (intestinal dysfunction). Possible etiologic diseases or disorders are listed in Table 1. Short bowel syndrome occurs when the length of bowel available to achieve digestion and absorption has become inadequate as a result of massive bowel resection or congenital short bowel. Intestinal dysfunctions occur, when a large part of the intestinal tract does not function normally due to reduced motility or impaired digestion and absorption. Regarding survival following massive bowel resection in humans, an extensive review was made by Wilmore [2] in 1972. This indicates that, in infants with an intact ileocecal valve, none with small intestinal segment measuring less than 15 cm survived, while, in infants receiving ileocecal resection, this length is extended to 40 cm. However, patients with an even shorter length of remaining intestine can nowadays be maintained and successfully weaned from parenteral nutrition, if an appropriate nutritional regimen is administered concomitantly. The lower limit of remaining gut length compatible
with successful weaning from enteral feeding is estimated to be 30 cm or less in children. In adults, on the other hand, the extent of compensatory hypertrophy of the remaining intestine is becoming very limited, and the lower limit of remaining intestinal length is said to be at least 50–70 cm. Good recovery of intestinal function can be expected from efficient use of numerous factors stimulating regeneration and hypertrophy of the remnant intestinal mucosa, in addition to prolonged nutritional management with appropriate enteral and parenteral nutritional regimens. It should be noted that both short bowel syndrome and intestinal dysfunction are not only associated with the loss of digestive function, but also with the loss of the gut barrier function. Recent advances and the wide use of home parenteral nutrition have made it possible for patients with intestinal failure to return home and live a normal life. However, in association with the increased use of long-term TPN, adverse effects have become evident that were not recognized previously. These are problems related to intravenous catheter care, the supply of micronutrients and the occurrence of irreversible hepatic failure. The incidence of catheter-related sepsis increases with the prolonged use of TPN, so that well-trained and careful management is necessary. With respect to irreversible hepatic failure, we have treated about 128 patients with intestinal failure among whom 8 patients (6.2%) developed serious hepatic dysfunction and eventually died of hepatic failure [3]. Postmortem examination showed advanced liver fibrosis. The cause of such fibrosis is still unknown, but clinical and basic studies performed in the later 1980s suggested that bacterial translocation may be the mechanism underlying the development of fibrosis. Bacterial translocation is a phenomenon, in which intestinal
bacteria or bacterial toxins penetrate the intestinal mucosa and enter the blood vessels in particular situations, i.e., TPN-induced intestinal mucosal atrophy, intestinal congestion, sepsis, etc. [4]. The resultant bacteremia leads to hepatic and renal dysfunction, with the eventual development of multiple organ failure. Another mechanism proposed recently is injury of remote organs, i.e., lung, liver and kidney, induced by cytokines or other mediators generated from the intestine, when the intestine succumbs to sepsis, inflammation or ischemia [5]. There is still not enough evidence to support any of these hypotheses.

**Historical Overview of Studies on Gut Adaptation**

In the first half of the 1970s, Wilmore et al. [6] performed an interesting experiment on central venous nutrition. After 90% resection of the small intestine, puppies were divided into 2 groups. Both groups were given nutrition with the same nutrient content, but 1 group was treated by TPN and the other by continuous enteral nutrition (EN). As expected, the puppies in the EN group showed less weight gain because of impaired digestion and absorption, when compared to the TPN group. However, the EN group showed marked proliferation of the intestinal mucosa despite inadequate weight gain. From this result, the authors suspected that something in EN was able to prevent atrophy of the digestive tract. Eastwood [7] in 1977 continuously administered a nutrient solution with the same calorie and protein content enterally to 1 group of rabbits and parenterally to another group. The result was an obvious difference in the proliferative activity of the intestinal mucosa. In 1979 Buts et al. [8] performed 50% resection of the small intestine in rats and raised the animals using 4 different methods to provide nutrition. The group showing the least mucosal proliferation was the TPN group, followed by the group given enteral administration of a glucose solution, and the group given an elemental diet. The group given macromolecular diet (i.e., EN with the addition of residue) showed the best mucosal proliferation. The above findings showed that atrophy of the small bowel mucosa occurs in association with TPN, and that it can be prevented through addition of certain factors into the TPN fluid. Further studies demonstrated various substances or factors to enhance mucosal proliferation and prevent atrophy. This was well summarized by Dowling [9] in his extensive studies (Table 2). Advanced studies in this area have shown that growth factors, cytokines and various nutrients have such an effect. Advances in genetic engineering have made it possible to produce recombinant growth factors and cytokines for use in humans, so that rapid progress could be made in this area of research.
Table 2. Summary of major and minor factors to promote intestinal adaptation according to Dowling [9]

<table>
<thead>
<tr>
<th>Major influences</th>
<th>Minor influences</th>
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<tr>
<td>Luminal nutrition</td>
<td>Changes in mucosal blood flow</td>
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<tr>
<td>Pancreaticobiliary secretions</td>
<td>Neural (including peptidergic) factors</td>
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<td>Hormonal factors</td>
<td>Changes in luminal and mucosal bacteria</td>
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<td>Other factors (e.g. salivary epidermal growth factor)</td>
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Table 3. Substances demonstrated to enhance enterocyte and/or colonocyte proliferation

<table>
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<tr>
<th>Peptides</th>
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<tr>
<td>Epidermal growth factor</td>
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<tr>
<td>Transforming growth factor-α</td>
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<tr>
<td>Insulin-like growth factors I and II</td>
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<tr>
<td>Keratinocyte growth factor</td>
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<tr>
<td>Peptide YY</td>
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<tr>
<td>Glucagon-like peptide 2</td>
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<tr>
<td>Neurotensin</td>
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<td>Hepatocyte growth factor</td>
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<tr>
<th>Nutritional factors</th>
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<tr>
<td>Fiber</td>
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<td>Short-chain fatty acids</td>
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<td>Glutamine</td>
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<td>Triglycerides</td>
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<td>Polyamines</td>
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<td>Lectins</td>
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<th>Cytokines</th>
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<td>Interleukins 3, 11, 15</td>
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Growth Factors and Other Modulators

A number of specific factors that enhance the proliferative response of the enterocyte have been identified and their effect was demonstrated in animal studies, but only limited trials are available in human subjects. Table 3 shows the factors demonstrated to enhance enterocyte and/or colonocyte proliferation.

Human Growth Hormone

Human growth hormone (hGH) has been known to reduce protein catabolism since the era of Cuthbertson in 1941. But particular attention was paid when Wilmore et al. [10] in 1974 first reported on the clinical effects of hGH. They reported that administration of hGH extract from
the pituitary gland to burn patients resulted in an improved nitrogen and potassium balance, enhanced wound healing, and a reduced incidence of complications. Since the production of purified recombinant, GH became possible through the evolution of gene engineering techniques in the mid-1980s, a number of clinical studies using GH have been performed. Vara-Thorbeck et al. [11] and Kissmeyer-Nielsen et al. [12] administered GH to TPN patients with gastrointestinal diseases and reported its protein-sparing effect, a reduced incidence of infection, and a decrease in malaise. Concerning the proliferating effect of GH on intestinal mucosa, a number of animal studies have demonstrated its beneficial effect on structural maintenance, adaptation and wound healing [13]. The function of GH is considered to act through endocrine and paracrine mechanisms via an insulin-like growth factor (IGF) [15].

**Insulin-Like Growth Factors I and II**

IGF-I (or II) is another growth factor similar in structure to insulin, which is primarily involved in the regulation of normal growth and development. The major source of circulating IGF-I and II is the liver, and their effects are more direct than that of GH.

IGF, previously described as a promoter of whole body anabolism, enhances DNA and protein synthesis in intestinal crypt cells in vitro, maintains intestinal integrity, and enhances intestinal mucosal adaptation after intestinal resection. Recombining IGF has been produced by genetic engineering techniques, and its anabolic effect and enhancement of intestinal mucosal growth have attracted attention. Localization of IGF receptors in the intestinal epithelium suggests a functional role of IGF-I in intestinal epithelial cell growth and differentiation and thus a possible role for IGF-I in gut repair. Our recent study using rats demonstrated that administration of IGF-I enhanced epithelial restitution after intestinal mucosal injury. In this model, increased thymidine uptake, cell migration and increased TGF-β mRNA expression were noted in intestinal epithelial cells.

Although markedly beneficial effects of IGF-I have been observed in animal studies, its clinical effects on protein metabolism and gut integrity have not yet been clearly demonstrated and further analysis from the standpoint of cost-benefit effectiveness is required.

**Epidermal Growth Factor**

Epidermal growth factor (EGF), extracted from the mucous gland and Brunner’s glands, is a low molecular weight polypeptide that is known to enhance the growth of the intestinal mucosa. A number of animal studies have shown that it enhances growth and stimulates absorption [17, 18]. While a single dose of EGF does not enhance cell proliferation, repeated daily injections or parenteral nutrition with EGF greatly enhances cell proliferation in the small intestine and colon. EGF receptors are present throughout the intestinal
tract and located on both basolateral and bush-border membranes. EGF given enterally does not stimulate cell proliferation in the colon, whereas intravenous recombinant EGF reverses the marked intestinal hypoplasia characteristically found in TPN-fed rats. Furthermore, EGF upregulates electrolytes and nutrient absorption in the small bowel. Thus, EGF mediates the absorptive capacities of various nutrients. On the contrary, several clinical trials to augment intestinal adaptation have been made without success.

**Glucagon-Like Peptide-2**

Glucagon-like peptide-2 (GLP-2) is a peptide consisting of 32 amino acids and is secreted from the ileum. It has been demonstrated to enhance the growth of the intestinal mucosa [19–21]. In experiments on massive bowel resection or ischemia/reperfusion injury, administration of GLP-2 significantly increased DNA and protein content of the intestinal mucosa (unpublished data). However, such effects have not yet been confirmed in humans.

**Keratinocyte Growth Factor**

Keratinocyte growth factor (KGF) is a kind of fibroblast growth factor that is synthesized by the interstitial cells in the epithelium of the skin, lungs, and digestive tract. It is known to enhance the growth of the intestinal mucosa [22]. An animal study by Estivarez et al. [23] showed that KGF inhibits atrophy of the duodenal and ileal mucosa induced by fasting.

**Neurotensin**

Neurotensin is one of the peptides that are widely distributed in the intestinal wall [24]. It is known to prevent atrophy of the intestinal mucosa associated with TPN and to promote the release of secretory IgA and IgM into the bile [25].

**Interleukin-11**

Interleukin (IL)-11 is a growth factor extracted from the interstitial cells of bone marrow. It has been shown to enhance the growth of bone marrow progenitor cells and to be effective in restoring peripheral lymphocytes and platelets that have been damaged by chemotherapy and radiotherapy [26, 27]. IL-11 also enhances the growth of intestinal epithelial cells. Furthermore, it not only increases the weight of the intestinal mucosa in the remnant bowel after massive resection, but it also increases the absorption of galactose and glycine [28].

**Transforming Growth Factors α and β**

Transforming growth factor (TGF)-α stimulates intestinal cell proliferation and may promote cell migration and modulate intestinal membrane transport. TGF-α and EGF share the same intestinal cell-surface reception. In a way,
TGF-β inhibits cell proliferation \textit{in vitro} and \textit{in vivo}. No clinical studies have been performed to demonstrate clinical efficacy.

\textit{Glutamine (Gln)}

Glutamine (Gln) is the most abundant amino acid in the body (accounting for about 60% of the total free amino acid pool) and is a nonessential amino acid. The most important function of Gln lies in its metabolic role as a nitrogen carrier between major organs. It is known to prevent the degeneration of muscle protein, to maintain body protein levels at the time of surgical stress, and to be involved in maintaining intestinal epithelial cell function as an energy source. Other effects of Gln include the maintenance of the renal tubular function, enhancement of the immunocompetence of peripheral lymphocytes as an energy source, and promotion of wound healing. Gln is said to be effective via enteral or intravenous administration, but intravenous administration has not been used, because commercial crystalline amino acid preparations were not available due to its low stability. Various methods have been tried to stabilize Gln, including administration in an acetylated form or as a dipeptide. We formulated a dipeptide alanyl-glutamine-enriched TPN solution, and studied its effect on the intestine using various animal experimental models. It was confirmed that it could increase the growth of the intestinal mucosa in animals with intestinal atrophy due to TPN [29] and massive bowel resection [30], as well as having a protective effect on the mucus covering the surface of the intestinal mucosa [31]. For the clinical efficacy of Gln, several studies have been performed. Ziegler \textit{et al.} [32] administered Gln-supplemented parenteral mixtures to patients undergoing bone marrow transplantation and observed a decreased incidence of infection, reduced hospital stay, and less expenses. These findings, accompanied with the possibly enhanced immunocompetence, have been supported by the other study groups. For severely ill septic patients, Tremel \textit{et al.} [33] administered TPN with dipeptide glutamine, and noted that Gln-supplemented TPN prevents intestinal atrophy and increased permeability associated with Gln-free parenteral nutrition. A multicenter clinical trial was performed in Japan to study the effect of TPN containing alanyl-glutamine on permeability in patients who had undergone total gastrectomy [34]. No significant difference was found, and it was judged that further studies in larger series are necessary. In intensive care unit patients, Griffiths \textit{et al.} [35] also observed a significantly higher rate of survival (57%) in the Gln-supplemented TPN group as compared with that (33%) in the control group. Regarding gut barrier function, Neu \textit{et al.} [36] reported a significantly reduced bowel-related infection rate in premature infants receiving a Gln-enriched enteral formula. As such, a number of clinical trials of Gln-enriched parenteral and enteral formulas have already been performed with mostly favorable results. Concerning the effect of Gln on intestinal functions, Wilmore \textit{et al.} [37] treated 300 short bowel patients with a combination of GH, glutamine and high carbohydrate diet, and reported that 60% of the patients could be weaned from TPN, in
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30% TPN could be reduced, and the remaining 10% still required the same quantity of TPN. This is a remarkable result and tells us how important such combination therapy is in the adaptive process of short bowel syndrome. However, further clinical studies need to be conducted to confirm its efficacy.

**Short-Chain Fatty Acids**

The short-chain fatty acids (SCFAs), particularly butyrate, are formed in the gastrointestinal tract of mammals by microbial fermentation of carbohydrates, and are readily absorbed by intestinal and caloric mucosa, and are trophic to intestinal mucosa. TPN supplemented with SCFAs has been shown to reduce the small bowel mucosal atrophy induced by standard TPN. This effect is seen particularly in massive small bowel resection. The availability of these recombinant modulators facilitates the significant progress in this field. These growth factors also interact with specific nutrients to enhance the proliferative response of the intestinal mucosa. Experiments that utilize these growth factors or appropriate nutrients to animal models or clinical cases support the concept that intestinal function can be enhanced by this approach. It is expected that such therapy will be useful in the future for treatment of intestinal failure; i.e., short bowel syndrome and bowel dysfunctions.

**References**


Discussion

Dr. Becker: I am sure that we would like to enter into the practicalities of the short bowel syndrome. We know that the reason why children do so well is that normal growth is still taking place. In adults, growth has finished and recovery is a matter of adaptation and hypertrophy. How do you manage the gastric hypersecretion that you get with short bowel syndrome?

Dr. Okada: There are several approaches. One that we use effectively is a very small nasogastric tube that is aspirated continuously. Another approach is to use drug treatment, but this can be a very difficult problem.

Dr. Becker: Do you use somatostatin?

Dr. Okada: Somatostatin is good for controlling pancreatic secretion.

Dr. Heymsfield: We know that food is the most potent stimulus for bowel growth. What about mechanical factors? If you put a balloon in the gut and inflate it to change the mechanical load, does that help it to grow?

Dr. Okada: The technique of Bianchi is very famous, but I don’t have any experience with it. According to various reports by surgeons it appears to work in some cases but not all. If not managed properly, it can lead to obstruction.

Mrs. Bowley: My experience is in neonates, particularly after necrotizing enterocolitis. We use a mixture of total parenteral nutrition (TPN) and either breast milk or a semi-elemental formula. Supplements of glutamine are given. Anecdotally, we have found that infants fed breast milk do much better clinically than those given artificial nutritional support. Are you aware of any work on this subject? I realize it would be a very difficult subject to study.

Dr. Okada: I don’t believe that any kind of milk is easily assimilated by such patients in the early stages. However, I know that breast milk contains many growth factors, so if it can be tolerated it may be beneficial.

Dr. Becker: We have a dietician in the audience, Mrs. Annatjie Smith, who might like to comment on this. About 20 years ago her son was one of my patients with short bowel syndrome. We couldn’t get breast milk but we used cow colostrum. Annatjie went from dairy to dairy getting colostrum and she fed her son on this successfully for about 2 years. What Ms. Bowley was saying is that maybe there are growth factors in colostrum and in breast milk that promote additional growth of the gut in these cases. Would you like to comment, Annatjie?

Mrs. Smith: My son was 22 months old so no breast milk was available. I fed him colostrum, which was quite easily obtained, when one really searched for it via the radio and through the newspapers. We also gave him elemental feed, which at the time was not available in South Africa and different components had to be imported in powder form and mixed. In addition he had TPN, but without the lipid component. He did well on this combination and he is now 22 years old and graduating from university.
Ms. Downs: I’m sure that everyone is familiar with the work on preventing necrotizing enterocolitis by using breast milk in premature infants. I think that growth factors and nucleotides in breast milk may be important for that action. Alluding to glutamine, if you use it enterally, do you recommend giving it as a bolus? And what dose do you recommend in an adult with short bowel syndrome?

Dr. Okada: We give it in a dose of 30–40% of the total amino acids as a continuous infusion.

Dr. Soeters: I would like to make a short comment on the effects of glutamine, growth hormone, and fiber on short bowel. The studies of Wilmore and Byrne [1] were anecdotal. Their patients were admitted to a center, where they were very well treated and had excellent dietary advice, and their results were spectacular—in fact, a lot of the patients were weaned off parenteral nutrition. However, this work was repeated on two separate occasions, and one of those studies, by Scolapio [2], was a randomized crossover design. In those studies the results were not so impressive, though I think an effect could still be shown. In particular, there appeared to be an effect on electrolyte absorption, which is a crucial factor in the short bowel syndrome. Such patients are depleted of potassium, phosphorus, and magnesium—three crucial elements. So if you can improve retention of these minerals that is very important. The problem, however, is that the benefit is short lived—as soon as you stop the treatment you revert to the former situation. The other problem is that we do not know whether it is growth hormone, glutamine, or fiber that is having the effect. There are indications that it might be growth hormone rather than glutamine or fiber, but that cannot be confirmed by this kind of multimodal treatment.

Dr. Segal: In a recent issue of Gastroenterology there was an important study showing that growth hormone significantly improves patients with short bowel Crohn’s disease. The reason it was important is that all the emphasis up to now has been on immunomodulatory treatment of Crohn’s disease, whereas this study showed a significant improvement using growth hormone alone.

Dr. Soeters: Did the growth hormone have to be continued? That would make it a very expensive treatment.

Dr. Segal: I think it was a preliminary short-term study only.

Dr. Pichard: To follow up that point, I would say that if you are considering chronic supplementation with recombinant growth hormone in short bowel Crohn’s, the dose is likely to be very low. You don’t need pharmacological treatment, you need substitution therapy. Also, you are unlikely to need to treat the patient every day. Three times a week would probably be sufficient, as in other conditions, where substitution is needed. Then you need to look at the ratio in terms of cost between home TPN and growth hormone treatment with oral feeding. My guess is if you look at the global cost, including the complications of TPN, it is likely to be more economical to use growth hormone, and maybe even glutamine.

Dr. Soeters: Your point is well taken, but it would be even better if you could just give a single course of growth hormone for a long-lasting effect, though that probably is not the case.

Dr. Silvis: Have you looked at the use of probiotics?

Dr. Okada: I have no experience of these myself. Several Japanese surgeons are interested in probiotics and are doing clinical trials, but I don’t have any results of these.

Dr. Waitzberg: I would like to hear from Prof. Okada about the Japanese experience of intestinal transplantation for short bowel syndrome.

Dr. Okada: We have recently had a case in my department who is doing very well after about one and a half years. The indications for transplantation for intestinal failure can be classified in two categories: excessively short bowel and intestinal dysfunction (such as intractable diarrhea or chronic idiopathic pseudo-obstruction).
This procedure was a very dangerous one several years ago, but now that we have good immunosuppressant agents the problems are much reduced. There have been five bowel transplants in Japan – a very small series I know – but all are doing well. The problem is that we need a follow-up of at least 5 or 6 years, because intestinal transplant rejection may occur after several years.

Dr. Labadarios: You said that you use TPN to start treatment in the short bowel syndrome, followed by the introduction of semi-elemental enteral feeding. Do you give that feed on a bolus basis or on a continuous basis?

Dr. Okada: We give it as a continuous infusion. I accept that there may be advantages to bolus administration, but we have no data on that.

Ms. Downs: Has anyone looked at the role of glutathione in short bowel, especially in older adult patients who might not be able to synthesize it naturally?

Dr. Soeters: I can comment on glutathione. Glutathione is effective on the enterocyte and is locally synthesized. My guess is that it is not produced in the gut, so that it can be released into the circulation to work elsewhere. Nevertheless I think glutathione kinetics are severely changed in short gut patients, as a result of many disturbing factors. For instance, in short gut patients there is a diminished bile acid pool, and even though the gut is short, there may be synthesis of secondary bowel acids that can be harmful to the gut itself and also to the liver. So I think it is very likely that in many patients of this kind glutathione kinetics will be severely disturbed.

Dr. Becker: May we now hear from the Red Cross? Mrs. van der Spuy, would you like to comment? I'm sure you have considerable experience of feeding very small babies.

Mrs. van der Spuy: My experience is in line with Nadia Bowley’s. If the mother can express her milk, we use the expressed breast milk, initially as a continuous enteral infusion. Parenteral nutrition is ongoing. If we don’t have breast milk available, then we use a semi-elemental diet.

Mrs. Smith: I have concern about the baby who is given parenteral nutrition without any enteral stimulation. There has been quite a lot of work done at the Kluger Institute in Canada by speech pathologists showing that such infants lose their oral sensitivity. It appears to be a lengthy process to restore the sensitivity to oral stimulation. We need to bear that in mind.

Mrs. Bowley: We always use dummies to maintain the suck response and build up the sucking muscles. If you put children on enteral or parenteral nutrition, for whatever reason, without giving anything orally, I think it is very important to use dummies.

Mrs. van der Spuy: I would add that we also give L-glutamine in powdered form, usually in a dose of 0.1–0.3 g/kg body weight. We mix it into the feed just before feed time, and generally give it once a day.

Dr. Soeters: Do you have any impression that it tastes unpleasant to the babies?

Mrs. van der Spuy: We haven’t experienced any rejection. I think age is important in this. Young infants don’t even reject semi-elemental feeds, which taste very unpleasant to us.

Mrs. Bowley: We give the glutamine as a bolus, because the amount is so small. If it was given continuously, it would be hard to get the amount right, as the concentration would be so small.

Dr. Winter: We can anticipate some gut adaptation in a patient with a short gut. Over what period of time in your experience does that occur, and when can we say that we can no longer expect any further gut adaptation? What is the optimal period of time to encourage enteral feeding?

Dr. Okada: It depends on the patient’s condition but usually 1–2 months.

Mrs. Bowley: Practically, it has got a lot to do with whether or not there is an ileocecal valve, the length of the remaining gut, and the way the patient responds. Some patients respond as though they have a short gut and others respond as though
they don’t have a short gut – for unknown reasons – so it’s very difficult to give an actual time, at which you can expect to get off TPN, or how much enteral feed can be given at any point in time.

Dr. Winter: My interpretation of the literature is that although we can anticipate some gut adaptation in humans, it is not as dramatic as the adaptation we see in experimental animals. The question is how much adaptation would we expect in a patient with, say, a gut length of 50 cm; could we anticipate that that patient would improve to an equivalent gut length say of 75 or 100 cm?

Dr. Waitzberg: Our experience of short bowel syndrome shows that recovery depends on the age of the patient, the size of the remnant, the presence of the cecal valve, and if there is any other disease. The old concept that if you have 50 cm of gut you will have to be on permanent TPN is no longer valid. We have seen such patients recover after 2 years of TPN, to the extent that they can be free of TPN, while still needing some intravenous supplements occasionally. In our experience, more than 35% of the patients with severe short bowel are eventually freed from TPN.

Dr. Soeters: In the Dutch experience of short bowel, it is not the length of the bowel that is the major determinant of remaining on TPN; it is the presence of the colon and the age of the patient. Thus in young people recovery, or regeneration potential, is much greater than in older people, especially those who have had a spontaneous vascular accident to the bowel. With regard to the presence of the colon, patients have been described who have only duodenum remaining, which is connected to the colon, who have graduated to exclusive enteral nutrition, if at the expense of loss of body weight. A new equilibrium is established, in which they can just manage, because when body weight decreases, the energy expenditure also decreases, and at some point the ability of the gut to absorb energy matches expenditure. The question is, how low a body weight is acceptable? In general, people with extremely low body weight lack vitality and do not perform well. If people cannot work or do sports, maybe one should consider giving them partial home parenteral nutrition.

Dr. Okada: I agree with that. The duodenum is very important for adaptation. We have seen this in several cases.

References
