

Total parenteral nutrition: potion or poison?<sup>1-3</sup>

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**ABSTRACT** The role of nutritional support in clinical care has burgeoned over the past 40 y. Initially, total parenteral nutrition (TPN) was considered to be the standard of care. Later, the concept that enteral nutrition (EN) promoted gut function and prevented the translocation of intestinal bacteria resulted in EN becoming the standard of care. Furthermore, TPN was considered to be a dangerous form of therapy. Critical review of the data suggests that, in humans, TPN does not cause mucosal atrophy or increase bacterial translocation. Increased sepsis with TPN can be ascribed to overfeeding; the dangers of TPN-induced complications have been exaggerated. TPN is an equally effective alternative to EN when a risk of malnutrition is present and EN is not tolerated or when gut failure is present. *Am J Clin Nutr* 2001;74:160-3.

**KEY WORDS** Total parenteral nutrition, enteral nutrition, TPN, EN, nutritional support, malnutrition, review

**INTRODUCTION**

Gastrointestinal diseases often prevent adequate nutrition because of associated malabsorption, anorexia, and an inability to eat without discomfort. In addition, several disease states, such as sepsis, trauma, and cancer, alter nutrient utilization, resulting in loss of body weight and wasting. These phenotypic effects are similar to those observed with malnutrition caused by an inadequate food intake. About 40 y ago the role of malnutrition in the above-mentioned conditions was recognized to be associated with increased morbidity and mortality in hospitalized patients. This realization resulted in the development of total parenteral nutrition (TPN) and the philosophy that if some nutrition is good, more is better, and the coining of the term *hyperalimentation*. A flurry of studies then appeared in the literature extolling the virtues of superfeeding through a central venous catheter in promoting recovery from conditions ranging from anorexia to cancer. However, this enthusiasm gave way to reality when it became obvious from controlled studies that not only did TPN not cure cancer, but it also increased complications under certain circumstances.

In another development, the concept of bacterial translocation through the injured and malnourished intestine was raised as the cause of the sepsis resulting in multisystem organ failure in critically ill patients. It was hypothesized that, by not feeding the intestinal tract, TPN caused atrophy of the intestine, resulted in increased bacterial translocation, and promoted sepsis. A series of studies suggested that feeding nutrients through the intestinal tract prevented this sepsis and resulted in less morbidity and mortality than did TPN.

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Thus, the pendulum has now swung the other way and a flurry of studies and meta-analyses in the literature have characterized TPN as a poisonous form of therapy and have extolled the virtues of enteral nutrition (EN), or tube feeding, as a panacea of all ills. In this review, I critically examine the relative merits of EN and TPN.

**PARENTERAL NUTRITION COMPARED WITH STANDARD CARE****Gut failure**

Before the availability of TPN, severe malnutrition leading to increased morbidity and mortality was documented in patients with extensive intestinal resection. Several publications showed that these patients can lead useful lives with use of TPN at home (1-3).

**Critical illness**

Heyland et al (4) performed a meta-analysis of 26 randomized controlled trials in which TPN was compared with standard care. These trials included 2211 patients undergoing surgery, patients with burns, patients with pancreatitis, and patients in the intensive care unit. Although TPN did not reduce mortality and overall morbidity, Heyland et al found that it significantly reduced morbidity in malnourished patients.

To show that TPN reduces complications, it must be studied in patients in whom complications are increased; attempting to measure a difference in complications when the complication rate is already very low is a statistical nonstarter. Naber et al (5) showed that malnutrition increases the risk of morbidity in hospitalized patients. Therefore, it is not surprising that the only benefit of TPN seen was in malnourished patients.

By pooling data from 13 randomized controlled trials involving 1100 patients, Twomey [in Klein et al (6)] showed that there was a 10% reduction in risk of complications in patients receiving preoperative TPN, but that postoperative TPN increased complications. In a well-controlled trial of preoperative TPN in

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**TABLE 1**  
Total parenteral nutrition (TPN) and intestinal atrophy in humans<sup>1</sup>

Reference	Finding
Guedon et al, 1986 (11)	No atrophy after 21 d of NPO
Rossi et al, 1993 (12)	Atrophy after 9 mo of NPO
Pironi et al, 1994 (13)	Atrophy after 2–3 mo of TPN
Sedman et al, 1995 (14)	No atrophy with TPN compared with enteral nutrition for $\geq 10$ d
Groos et al, 1996 (15)	Atrophy after 7–12 wk of TPN

<sup>1</sup>NPO, nil per os (nothing fed by mouth).

patients undergoing hepatectomy, preoperative TPN reduced the incidence of overall complications, sepsis, and diuretic use (7). Note that in this trial, sepsis was reduced. In contrast, in a Veterans' Administration trial, the use of preoperative TPN increased the risk of sepsis (8), but a further analysis in a subgroup from that trial showed that malnourished patients receiving TPN had fewer nonseptic complications. Finally, in a trial of only malnourished patients, Bozzetti et al (9) found that TPN reduced noninfectious complications and did not increase sepsis.

## THEORY OF THE BENEFITS OF ENTERAL NUTRITION

### Prevents mucosal atrophy

Enteral nutrition is believed to be beneficial because it protects the gut from mucosal atrophy. This concept was developed from the results of animal studies showing that the administration of TPN resulted in significant intestinal villus atrophy within a few days (10). However, human studies have not shown any intestinal atrophy with complete bowel rest and TPN, even 1 mo after the withdrawal of food by mouth (Table 1). Atrophy was observed only when TPN was given to children for several months, during which time the children did not receive any food by mouth.

### Prevents bacterial translocation

Rigorous studies were performed in human subjects in which bacterial translocation from the intestine was identified by culturing the same organism in the blood as in the intestine and the mesenteric lymph nodes. These studies showed that translocation occurs, especially in patients with intestinal obstruction, but that its incidence is no different between patients receiving TPN or EN (16). Even most trauma patients did not have septicemia from organisms found in the gut and only 2 of 132 patients had translocation (17). In summary, therefore, there is little evidence in humans that TPN causes atrophy of the intestinal mucosa and that EN prevents bacterial translocation.

## NUTRIENTS AND SEPSIS

Although it is true that progressive starvation will ultimately lead to death and that malnutrition is associated with an increased risk of complications, the available trials have not clearly shown that artificial nutrition reduces complications or mortality. On the other hand, these trials did not specifically select patients with severe weight loss, ie, those most likely to show benefit from nutritional support or to die from starvation. Furthermore, it is not as well recognized that in the presence of sepsis an increased intake of energy (carbohydrates or fats) increases the risk of complications (18). The risk of complications with increased energy

intake is especially associated with the development of hyperglycemia (19), and hyperglycemia tends to occur in septic patients who are insulin resistant. The possible mechanism of increased complications induced by increased energy intake is an increase in the expression of tumor necrosis factor receptors (20) associated with an increase in nuclear factor  $\kappa$ B binding to the nucleus (N Raina and KN Jeejeebhoy, unpublished observations, 2000). Furthermore, in septic guinea pigs, increased energy intake caused an increase in mortality (21). In animals infused with tumor necrosis factor, simply feeding sufficient energy to promote normal growth caused increased complications (22).

The trials comparing EN and TPN should be examined with a view toward determining whether the nutritional support was comparable in terms of energy intake. Excess energy intake with either EN or TPN influences the risk of sepsis.

## ENTERAL COMPARED WITH PARENTERAL NUTRITION: OUTCOME ANALYSIS

### Pancreatitis

McLave et al (23) randomly assigned 32 patients to receive either TPN or EN and observed no significant differences in rates of infection or morbidity. Windsor et al (24) randomly assigned 34 patients with acute pancreatitis to either TPN or EN and observed no significant differences in incidence of sepsis, length of hospital stay, computerized tomography scores, or organ failure. Kalfarentzos et al (25) randomly assigned 38 patients to either EN or TPN and showed that patients receiving TPN had a higher incidence of sepsis. However, twice the number of patients receiving TPN were hyperglycemic and therefore the difference in increased energy intake and hyperglycemia may explain the increased sepsis with TPN. On the other hand, administration of TPN did not increase the length of stay in the intensive care unit or in the hospital. Giving TPN also did not increase the need for antibiotics or ventilator support.

### Inflammatory bowel disease

In a randomized controlled trial comparing TPN with EN or TPN given together with an oral diet in patients with Crohn disease, no increased complications were observed as a result of TPN, and the rate of remission between the 2 modalities of Crohn disease was the same (26). In patients with acute colitis it was shown that TPN resulted in an increased rate of sepsis; however, other complications such as the rate of colectomy or remission of disease activity were not significantly different between the 2 groups (27). In that trial, however, only 44 of 82 patients were studied and very sick patients were excluded, biasing the results.

### Trauma

In a study of nutritional support after major abdominal trauma, Moore et al (28) randomly assigned 29 patients to EN and 30 patients to TPN. The investigators found a significantly increased incidence of sepsis in patients receiving TPN. However, patients given TPN received significantly more energy and had higher concentrations of plasma glucose than did patients given EN. They also had significantly increased concentrations of plasma insulin, suggesting that they were overfed. Kudsk et al (29) randomly assigned 98 patients to either EN or TPN; again, in this study, the patients given TPN received significantly more energy. The patients randomly assigned to TPN who had high

injury severity scores or high abdominal trauma index scores had increased sepsis. Despite the increased sepsis rate, patients receiving TPN did not receive more antibiotics nor did they remain longer in hospital.


### Sepsis

Cerra et al (30) randomly assigned 66 patients who were septic and hypermetabolic to EN or TPN and found that there was no significant difference in the incidence of multisystem organ failure or death between the 2 groups.

### Procedure-related complications

In theory, it would be expected that procedure-related complications would be much greater in patient receiving TPN because of catheter-related problems. However, in 7 of 9 randomized trials of EN compared with TPN in which procedure-related complications were reported, the incidence was higher during EN (31).

### Conclusion

TPN is the form of nutritional support most suited to patients with gut failure, in whom it is lifesaving. It is obviously beneficial when malnutrition is present in several clinical conditions. On the other hand, overfeeding, which can easily occur with TPN, increases complications—especially sepsis. There is little evidence that several processes described in animals and ascribed to TPN, such as intestinal atrophy and increased bacterial translocation, occur in humans. Unlike the general belief, TPN undertaken by experienced teams does not cause more complications than does EN. In fact, it appears that TPN is associated with fewer procedure-related complications. In short, when indicated because of the inability to give EN, TPN is beneficial in the treatment of malnutrition but is not a cure for all illnesses. These conclusions are supported by the results of a recent 562-patient trial of EN compared with TPN that concluded that TPN did not increase sepsis, EN delivered less than the target nutritional intake, and the procedure-related complications were greater with EN (32). 

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