PRACTICE MANAGEMENT GUIDELINES FOR

NUTRITIONAL SUPPORT OF THE TRAUMA PATIENT

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Introduction

Nutritional support is an integral, though often neglected, component of the care of the critically injured patient. Our understanding of the metabolic changes associated with starvation, stress and sepsis has deepened over the past 20-30 years, and along with this has come a greater appreciation for the importance of the timing, composition and route of administration of nutritional support to the trauma patient. While supportive data do exist for many of our current nutritional practices, the trauma surgeon cannot assume that interventions which are successful in laboratory animals or even in the critically-ill *non*-trauma patient will necessarily produce the same results in critically ill trauma patients. Stanley J. Dudrick, MD, one of the forefathers of surgical nutrition in this country, put it this way. "…we do get ourselves into an awful lot of trouble and lack of consensus as a result of mixing in animal data together with normal, starved man data when we are talking about trauma, especially in burns." [1] For this reason, the recommendations provided in this guideline are based , where at all possible, on studies performed on trauma or burn patients. Nevertheless, a brief discussion of some of the basic science principles of nutritional support is provided in the following section as a backdrop for the clinical studies presented within this guideline.

This practice management guideline is actually a compilation of 6 separate guidelines, each of which addresses a specific aspect of the nutritional support of the trauma patient. These topics are presented in the following order:

I. Route of Nutritional Support (TPN vs TEN)
II. Timing of Nutritional Support ("Early" vs "Late")
III. Type of Nutritional Support (Standard vs "Enhanced")
IV. Site of Nutritional Support (Gastric vs Jejunal)
V. Macronutrient Formulation (How many calories, and what proportion of protein, carbohydrate and fat?)
VI. Monitoring of Nutritional Support (Which tests and how often?)
VII.

Each "sub-guideline" is a separate and free-standing document, with its own set of recommendations, evidentiary tables and references. However, recognizing the need to inocrporate the major recommendations from the sub-guidelines into a logical overall approach to the nutritional support of the trauma patient, a summary algorithm is provided at the conclusion of the guideline. Of necessity, many of the recommendations from the "sub-guidelines" could not be included within the algorithm, and there was no practical way to distinguish between the various levels of recommendations (I, II and III) within the algorithm. Nevertheless, the algorithm does provide a safe, reasonable and literature-supported approach to nutritional support and, we hope, will provoke constructive discussion and stimulate further investigation.

Experimental Background

The first suggestion that route and type of nutrition influence clinical outcome was noted in Alexander's study of severely burned patients randomized to a standard enteral diet or a protein-supplemented diet.[2] Children receiving the high protein enteral diet had a higher survival rate and fewer septic complications than children receiving the standard enteral diet. Although not discussed at the time, patients receiving the high protein diet were administered significantly less parenteral nutrition than the standard diet group. During the same time period, experimental observations depicted differences between enteral and parenteral feeding. In a model of septic peritonitis, both malnourished and well-nourished animals administered the TPN solution enterally survived peritonitis significantly better than animals pair fed the TPN solution intravenously.[3, 4] Since these initial studies, multiple clinical trials have studied the impact of route and type of nutrition comparing enterally fed patients (receiving a variety of enteral products) to 1) unfed trauma patients[5, 6] and 2) trauma[7-9] or burn patients[10] given IV-TPN. In addition, burn patients have been studied after receiving a variety of enteral formulas (high vs standard protein,[2] enhanced vs standard diet[11]) while patients sustaining severe head injury have been randomized to intravenous nutrition vs intragastric feeding[12, 13] or intragastric vs postpyloric feeding.[14, 15]

While the preponderance of these studies show benefits of the enteral route with additional improvement with various specialty substrates *in select patient populations*, investigators have searched for mechanisms to explain improved infectious rates with enteral feeding. Intravenous feeding increases gut permeability[16, 17] and increases bacterial translocation to mesenteric lymph notes,[18, 19] connoting a breakdown in the gut mucosal barrier which allows passage of small and large molecules from the intestinal lumen. Experimentally, bacterial translocation increases with intravenous nutrition, an enteral elemental diet, burns, hemorrhage and shock, but not with starvation alone unless a simultaneous inflammatory focus is created.[20] Inflammatory molecules, such as zymosan, also increase gut permeability to bacteria.[21] Reduction in IgA and increases in bacterial translocation occur with bacterial overgrowth within the gastrointestinal tract (primarily aerobic bacteria).[19] These permeability increases to macromolecules have been noted in burn patients[22, 23] and patients sustaining blunt and penetrating trauma to the torso.[24, 25] Numerous investigations into the significance of bacterial translocation have engendered a hypothesis that the permeable gut allows systemic entry of toxic substances with deleterious end organ effects, but this work has not shown any relationship between increased permeability and the development of intra-abdominal or pulmonary infectious complications. Recently, the gastrointestinal tract has been defined as a site for leukocyte "priming" following initial injury which up-regulates the inflammatory response within the lungs after a secondary hit.[26-28] Manipulation of this initial priming via the gastrointestinal tract remains a current focus of investigation.

Investigations into the nutrient manipulation of the mucosal immune system also provide an intriguing insight into the host defenses at mucosal surfaces. Mucosal associated lymphoid tissue which originated from gut-associated lymphoid tissue (GALT) accounts for approximately 50% of the total body's immunity and 70-80% of immunoglobulin production by the body, primarily in the form of IgA.[29] Experimentally, dietary conditions which increase bacterial translocation (IV-TPN or an elemental diet) are associated with significant reductions in GALT cells within the Peyer's patches, lamina propria, and intraepithelial space in association with decreases in intestinal and respiratory IgA levels.[30] Functionally, the hypoplasia of this GALT system induced by inadequate nutrient regimens impair IgA-mediated antiviral mucosal immunity[31] and resistance to established immunity against intratracheal *Pseudomonas*.[32] This deterioration may be associated with loss of systemic immunity with impaired function of polymorphonuclear cells and monocytes. Experimentally, reduction in IgA levels *in vitro* increase the virulence of intraluminal bacteria improving bacterial ability to attach—and potentially invade—mucosal surfaces.[33] These experimental manipulations serve as a backdrop for our understanding of the clinical studies of route and type of nutrition in patients sustaining severe trauma, burns, or head injury.

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A. Route of Nutritional Support

I. STATEMENT OF THE PROBLEM

The metabolic response to injury mobilizes amino acids from lean tissues to support wound healing immunologic response, and accelerated protein synthesis. The goal of aggressive early nutrition is to maintain host defenses by supporting this hypermetabolism, preserve lean body mass. Route of nutrient administration affects these responses, and benefits of early enteral feeding have been clearly shown. Laboratory and clinical studies reveal beneficial affects of early nutrition on the gut mucosa, immunologic integrity, survival of septic peritonitis, pneumonia and abscess formation.

Therefore the question arises as to the route to deliver nutrition to the traumatized hypermetabolic patient with multisystem injuries including severe head injuries, burns, blunt and penetrating mechanisms. There are certainly risks and benefits to enteral and parenteral nutrition in this complicated patient population. The purpose of this review is to determine the benefits and the risks of the route of nutrition in the severely injured patient through peer reviewed publications over the past 20 years. To develop recommendations and guidelines from the conclusions of these studies based on the scientific methodology of these studies.

II. PROCESS

A. Identification of References

References were identified using the computerized searched of the National Library of Medicine (NLM) using the NLM's search service to access Medline.

The search was designed to identify English language citations between 1976 and 2000 using the keywords: nutrition, enteral, parenteral, trauma, injury, and burn. The bibliographies of the selected references were examined to identify relevant articles not identified by the computerized search.

Ninety--five articles were identified. Literature reviews, case reports, editorials, were excluded. A cohort of three trauma surgeons selected twenty-seven articles for review and analysis.

B. Quality of the References

The quality assessment instrument applied to the references was that developed by the Brain Trauma Foundation and subsequently adopted by the EAST Practice Management Guidelines Committee. Articles were classified as Class I, II, or III according to the following definitions:

<u>Class I</u>: A prospective, randomized clinical trial. Fourteen articles were chosen and analyzed.

<u>Class II</u>: A prospective, non-comparative clinical study or a retrospective analysis based on reliable data. Ten articles were chosen and analyzed.

<u>Class III</u>: A retrospective case series or database review. Three articles were chosen and analyzed.

III. RECOMMENDATIONS

1) **Level I** (Convincingly justifiable on scientific evidence alone, usually based on Class I data, ie, randomized, prospective controlled investigations.)
   i) Patients with blunt and penetrating abdominal injuries sustain fewer septic complications when fed enterally as opposed to parenterally.
   ii) Patients with severe head injuries have similar outcomes whether fed enterally or parenterally.

2) **Level II** (Reasonably justifiable by available scientific evidence and strongly supported by expert critical care opinion usually supported by Class I or Class II data, ie, nonrandomized, concurrent, or historical cohort investigations.)
   i) There is insufficient evidence to support Level II recommendations.

3) **Level III** (Adequate scientific evidence is lacking by widely supported by available data and expert critical care opinion usually supported by class II or Class III data, ie, review articles, substantial case series or reviewed published opinion.)
   i) In severely injured patients, TPN should be started by day 7 if enteral feeding is not successful.
   ii) Patients who fail to tolerate at least 50% of their goal rate of enteral feedings by the seventh post-injury day should have TPN instituted, but weaned when greater than 50% of enteral feedings are tolerated.

IV. SCIENTIFIC FOUNDATION

The recommendations developed for the nutritional guidelines required multiple levels of discussion within groups and between groups, because there were a number of areas that the subgroups had common areas of interest, and artificial boundaries were often crossed in the six areas that were analyzed.

A. Patients with blunt and penetrating abdominal injuries sustain fewer septic complications when fed enterally as opposed to parenterally.

There are a number of studies that support this important guideline. Moore and Jones[1] reported the benefits of enteral feedings utilizing immediate jejunal feedings in 1986. The patients in this study had laparotomy for severe abdominal injuries (ATI >15). Nutritional parameters and overall complications were no different between the enterally and parenterally fed groups; the septic morbidity was higher in the parenterally fed group ($p < 0.025$). Peterson et al.[2] further evaluated this effect, and found that acute phase proteins increased from baseline to a higher extent in the TPN group compared to TEN in patients suffering abdominal trauma with an ATI > 15, < 40. The TPN group reached a nadir in constitutive proteins at day 10, while the TPN group saw a rise in serum albumin and retinol-binding protein ($p < 0.05$). In 1989, Moore et al.[3] revealed further evidence of the reduced septic complications in patients fed enterally versus parenterally (40 < ATI > 15). A meta-analysis of eight prospective randomized trials attests to the feasibility of early postoperative enteral feedings in high-risk surgical patients and these patients have reduced septic morbidity rates compared with those administered parenterally.[4] In 1992 and 1994, Kudsk et al.[5,6] showed further evidence of the effectiveness of enteral nutrition over parenteral nutrition. In the earlier study, the rate of septic complications including pneumonia, intra-abdominal abscess, and line sepsis were significantly reduced in the enterally fed group of patients with an ATI > 15. Furthermore, the sicker the patient (ATI > 24, ISS > 20, transfusions > 20 units, and re-operation) had significantly fewer infections. The latter study confirmed the previous report of Peterson et al.[2] concluding that enteral feeding produces greater increase in constitutive proteins and greater decreases in acute-phase proteins after severe trauma. This is primarily caused by reduced septic morbidity with enteral feeding. Other factors involved in the reduced septic complications include bacterial translocation, endotoxin, interleukins-1, 2, 6, 11 and 12, and macrophage stimulation. These effects are beyond the scope of this review.

One potential disadvantage regarding the enteral approach to nutrition of the trauma patient is the concern that adequate amounts of protein and calories cannot be delivered via this route, due to frequent interruptions in feeding necessitated by multiple operative procedures. Moncure et al have recently shown that enteral feedings can be safely administered up until the time of transport to the operating room. This approach resulted in delivery of greater amounts of protein and calories, without any increase in peri-operative aspiration events.[7]

B. Patients with severe head injuries have similar outcomes whether fed enterally or parenterally.

The route of administration in the head injured patient remains controversial, both routes are effective and each has its advantages and disadvantages. One of the earliest studies to show a benefit to the early use of parenteral feedings was Rapp et al.[8] In 1983, patients with severe head injury were randomly assigned to receive enteral or parenteral nutrition. Patients receiving TPN within 72 hours of admission had a lower mortality rate ($p<0.0001$). Haussman et al.[9] found in 1984 that combined parenteral and enteral feeding was comparable to parenteral feeding concerning mortality, N-balance, creatinine and 3-methylhistidine excretions, but brain injured patients with impaired gastric function, such as high tube reflux are better treated by parenteral nutrition. Hadley et al.[10] further demonstrated the equal effectiveness of each route. Although the parenteral nutrition group had higher mean daily nitrogen intakes ($p<0.01$) and mean daily nitrogen losses ($p<0.001$), there were no significant differences in serum albumin levels, weight loss, the incidence of infection, nitrogen balance, and final outcome. A series of studies performed by Young, Ott and colleagues[11, 12] further defined nutritional support in the head injured patient. In the laboratory, intravenous hyperosmolor solutions were found to potentiate cerebral edema following head injury. In 1987, Young et al.[11] found no significant difference in peak ICP, failed therapy of ICP, serum osmolality, morbidity or mortality, and patient outcome in patients receiving parenteral versus enteral nutrition. Young et al.[12] then reported on 51 brain-injured patients in a randomized prospective study between parenteral and enteral nutritional support. Following the outcome of these patients for one year, the patients receiving parenteral support had a better outcome at 3, 6 and 12 months. Furthermore, the enterally fed group had a higher septic complication rate ($p<0.008$), which was felt to be due to lower total protein intake, cumulative caloric balance, and negative nitrogen balance. The enterally fed group did not tolerate feedings a mean of 9 days, and received less calories and protein. Ott et al.[13] characterized the feeding intolerance in 1991. Gastric emptying was found to be biphasic, and a majority of brain injured patients displayed delayed gastric emptying during the 1st week post-injury. This delayed and biphasic response persisted through the second week in over 50% of the patients. By week 3, most patients exhibited rapid gastric emptying, and all patients tolerated full volume enteral feedings by day 16. Borzotta et al.[14] confirmed the efficacy of enteral and parenteral support utilizing early jejunal feedings in the enteral group and delayed gastric feeding (day 5-9) in the parenteral group. No difference was found regarding measured energy expenditure, protein intake, albumin, transferrin, nitrogen balance, infectious rates, or hospital costs. Much of this information has been summarized recently in an excellent review published by the Cochrane Library .[15]

C. In severely injured patients, TPN should be started by day 7 if enteral feeding is not successful.

The critical feature to nutrition in the severely injured patient is the implementation of nutrition. The lack of nutrition is far more deleterious than route of nutrition. Total starvation for less than 2 to 3 days in healthy adults results in only glycogen and water losses and only minor functional consequences. Functional deficits are evident in healthy normal weight adults who voluntarily restrict their food intake after about 15 days of semi-starvation. Many trauma patients are hypermetabolic, and depletion of nutrient stores will proceed more rapidly in the case of total starvation than it does in healthy adults. The functional consequences of total or partial starvation thus evolve more rapidly in the stressed and catabolic patient than they do in healthy individuals. A maximum period of 7 days for a severely limited nutrient intake is the empirical absolute limit most investigators set for trauma patients.[16]

D. Patients who fail to tolerate at least 50% of their goal rate of enteral feedings by the seventh post-injury day should have TPN instituted, but weaned when greater than 50% of enteral feedings are tolerated.

Similar to the above guideline, the goal of nutritional support in the injured patient is delivery of 50% of the caloric and protein needs of the patient by the 7th post-injury day. On the basis of the above recommendation, less than 50% of protein/calorie goal for 15 days leads to functional deficits in healthy volunteers. The functional consequences of partial starvation may evolve more rapidly in the stressed and catabolic patient. A maximum period of 7 days for a severely limited nutrient intake is the empirical absolute limit most investigators set for trauma patients.[16]

V. SUMMARY

Although the evidence is not abundant, it is significant and scientifically supported that patients with blunt and penetrating abdominal injuries sustain fewer septic complications when fed enterally as opposed to parenterally. The surgeon must be aware of the potential benefits of enteral feedings in these severely injured patients. The trauma surgeon caring for patients with head injury must weigh the benefits and the risks of the route of nutrient administration, as patients with severe head injuries have similar outcomes whether fed enterally or parenterally. As determined in studies of malnutrition and starvation, the hypermetabolic state of the severely injured patient requires that TPN should be started by day 7 if enteral feeding is not successful. Equally patients who fail to tolerate at least 50% of their goal rate of enteral feedings by the seventh post-injury day should have TPN instituted, but weaned when greater than 50% of enteral feedings are tolerated.

VI. FUTURE INVESTIGATION

Many of the issues to the route of nutrition in the trauma patient are far from settled. Although some such as the benefits of enteral nutrition in the severely injured patient with abdominal trauma are well documented, the mechanisms (immunologic and physiologic) remain unclear. The route of administration of enteral feedings, the nutrient composition, and the long-term outcome of trauma patients are still areas for future evaluation by clinicians and scientists. The effectiveness of nutritional support of the severely head injured patient remains a difficult area to evaluate, as the injury remains a significant factor in the outcome of the patient. Prospective studies of nutritional support evaluating long-term outcome are still required. Previous work has demonstrated the safety and efficacy of enteral and parenteral nutrition in head injured patients, but their exact role or the preference of either route has not been demonstrated. Further study is required to determine a cost-effective delivery of nutrition that may improve the outcome of severely head injured patients.

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First Author	Year	Class	Conclusions
Rapp (8)	1983	I	38 patients with blunt/penetrating head injury randomized within 48 hours to TPN (n=20, age=29.2_4.1, GCS 7.7_0.6) or intra-gastric feeding (n=18, age=34.9_3.8, GCS=7.2_0.6) with defined formula diet. Enteral caloric intake ≤400 cal/day for 1st day, ≤600 cal/day for 1st 10 days, and <9000 cal/day for 14 days due to delayed gastric emptying. 8/18 enteral died within 18 days vs. 0 TPN patients. Prolonged gastroparesis with intra-gastric feeding post severe head injury.
Hausmann (9)	1985	I	20 patients randomized to enteral-parenteral (n=10) and TPN (n=10) after suffering severe brain injury (GCS 5-7). There were no differences in protein intake, nitrogen balance, or mortality between the groups. Both regimes nutritionally effective, but impaired gastric emptying hampered enteral feedings.
Adams (21)	1986	I	Multiple trauma patients post laparotomy were randomized to receive EN via needle catheter jejunostomy or TPN. There were no differences in nitrogen balance or postoperative complications. Early enteral nutrition is safe.
Hadley (10)	1986	I	45 head-injured patients with GCS ≤ 10 randomized to intra-gastric (n=21, GCS = 5.9) feeding with standard commercial diet or TPN (n=24, GCS = 5.8). Enteral patients achieved positive caloric balance (140% of BMR) in 5% on day 2, 45% on day 3, 70% on day 4, between 70 and 85% to day 11. TPN achieved > 80% by day 5 and 100% by day 9. Complication rate and infectious rate similar. Use TPN only when GI tract fails to work. Editorial: gastroparesis begins to resolve on day 3-4. Do not wait for NG drainage to drop or bowel sounds to return.
Young (11)	1987	I	96 severely brain injured patients were randomized to receive early TPN or enteral feedings when tolerated. There were no differences in the groups including: admitting GCS score, # of craniotomies, MOI, ICP>20, failure of conventional therapy, barbiturate failure nor serum osmolality. TPN can be used safely, but no outcome advantage to enteral feeding.
Young (12)	1987	I	51 evaluable of 58 consented patients with GCS 4-10 after blunt or penetrating head wounds randomized to TPN (n=23, age =30.3_2.7, GCS=7.0_0.3) or intra-gastric feedings (n=38, age=34.0_2.9, GCS=6.5_0.4) after bowel sounds return and NG drainage dropped below 100ml. Enteral patients received <500 cal/day for 1st 2 days (vs. 1221 kcal TPN group),

First Author	Year	Class	Conclusions
			<1500 cal/day for days 6-8 (vs. 2350 kcal in TPN group) due to gastroparesis. Infectious complications the same and neurologic outcome similar at 1 year. Prolonged gastroparesis after severe head injury.
Grahm (28)	1989	I	22 patients with blunt/penetrating wounds and GCCS, 10 randomized (by admission day) to nasojejunal feeding via fluoroscopy by 36 hours (age = 25.5_13.2, GCS = 5.1) and started at goal rate or intra-gastric feedings after day 3 if GI function returned (age =27.8_9.3, GCS = 7.1). Caloric intake matched measured needs by day 3 with jejunal tube and approached 75% of needs on day 5-7. With intra-gastric feedings, significantly fewer bacterial infections (bronchitis 3-4 plus WBC in sputum with positive cultures with jejunal feeds. Goal rates achieved faster with small bowel access. Gastric residuals limit intra-gastric feeding rate. No change in metabolic rate by indirect calorimetry.
Jones (26)	1989	I	123 patients requiring emergent laparotomy (ATI $\geq$ 15) were prospectively randomized to non-enteral feeding (n=52) or enteral-fed (n=71) by means of a needle jejunostomy catheter. 50% of control group had GI symptoms (12% moderate discomfort). 83% of enteral-fed had symptoms, 16% moderate symptoms, 13% required TPN. 87% tolerated enteral feedings, 35 cal/kg/d and 14.5gm N/d by day post-operative day 5.
Moore FA (3)	1989	I	Patients with major abdominal trauma were randomized to receive EN or TPN after laparotomy. Patients who received EN had fewer septic complications. In addition nutritional protein markers were restored faster in the TEN group.
Kudsk (5)	1992	I	Trauma patients were randomized to receive TPN or EN within 24 hours of penetrating or blunt abdominal trauma. There was a lower incidence of septic complications in the patients who received EN.
Eyer (25)	1993	I	38 evaluable patients randomized to early (starting 31_13 hours after ICU admission) vs. late (82_11 hours) feeding via nasoduodenal tubes. ISS similar but 58% of early had severe acute lung injury vs. 21% in late group. Target rates in most patients reached within 12 hours of start with advancement of 25 ml every 4 hours. Excellent small bowel tolerance with no intra-abdominal injury within 1.5 days of injury but no differences in ICU or ventilator days, organ system failure of infections (? Of infection rate. Higher with early

First Author	Year	Class	Conclusions
			group but included eye, sinus and urinary infections probably unrelated to enteral feeding).
Kudsk (6)	1994	I	68 patients randomized to enteral (n=34, ATI=28.0_1.7, ISS= 27.0_1.8) or parenteral (n=34, ATI=27.8_1.4, ISS=26.8_1.9) nutrition. Significantly higher levels of constitutive proteins and lower levels of acute-phase protein levels were noted in the enteral group. The more important factor related to route of nutrition was the significant reduction in septic morbidity (any infection, pneumonia, line sepsis) associated with enteral nutrition.
Borzotta (14)	1994	I	48 evaluable head injured patients (GCS<8) randomized to TPN (n=21, age 28.9_10, ISS=33.4_9.5, GCS 5.4_1.9) or enteral feeding via surgically placed jejunostomies (n=27, age=26.2_10.4, ISS=32.5_10.1, GCS=5.2_1.6) and started within 72 hours of injury. All TPN patients had initial attempts with intra-gastric feeding (and presumably failed). TPN transition to intra-gastric feedings started on day 5. Diarrhea more common in TPN patients. High rate of nasogastric tube dislodgment. In first 3 days, enteral delivered calories equaled 90.5% of measured resting expenditure by indirect calorimetry by day 3. With direct small bowel access, nearly achieved calculated goal by day 3 (and subsequently over) with little intolerance.
Spapen (20)	1995	I	Mechanically ventilated patients were randomized to receive cisapride 10 mg four times daily or no cisapride with tube feedings. Gastric residue was measured using bedside scintigraphy. Patients in the cisapride group had accelerated gastric emptying. This was statistically significant.
Page (24)	1979	II	Patients post elective major abdominal and emergent abdominal surgery were fed by needle-catheter jejunostomy and monitored for complications. Patients' nutritional status was adequately maintained. Complication rate was 2.5%. Jejunostomy feeding is safe in the postoperative period.
Moore EE (1)	1986	II	Patients post celiotomy for abdominal trauma were randomized to receive EN via needle jejunostomy or intravenous fluids. EN was started within the first 24 hours post-op. Nitrogen balance was improved in the patients receiving EN and there were fewer septic complications.
Norton (27)	1988	II	23 patients with blunt/penetrating head injury and GCS 4-10 (avg.6.6) followed for enteral

First Author	Year	Class	Conclusions
			tolerance. Feeds started when drainage <200ml/day and bowel sounds present. 7 tolerated feeds within 7 days, 4 between 7-10 days, and 12 never tolerated feeds with trend to greater intolerance with lower GSC. Tolerance did not correlate with bowel sounds. Gastroparesis in most patients with severe head injury.
Peterson (2)	1988	II	Hepatic synthesis of acute phase reactant proteins was evaluated in patients with major torso trauma. Patients who received TPN were compared with those who received EN. The group receiving EN had earlier attenuation of the acute-phase reactant protein production.
Ott (13)	1991	II	12 head injured patients (GCS=4-10) were evaluated during their hospital stay for liquid gastric emptying. 50% had delayed gastric emptying for up to 7 days, 40% normal within 14 days, and 80% normal or biphasic emptying by 16 days. Patients with normal or rapid emptying (30%) tolerated full feedings in 8.5_0.5 days, which was significantly earlier than the patients with delayed gastric emptying (50%, 13.7_3.2 days).
Moore FA (4)	1992	II	A meta-analysis of 8 prospective randomized trial to compare the efficacy of early EN and TPN in high risk surgical patients. Patients who received EN had fewer septic complications.
Hadfield (21)	1995	II	Patients were randomly allocated to receive TPN or EN. Gastrointestinal absorption was evaluated by measuring D-xylose, 3-O methyl glucose, and GIT permeability was determined by measuring lactulose and L-rhamnose. This study showed that all critically ill patients had GIT dysfunction however, mucosal integrity was restored by giving EN.
Heyland (18)	1995	II	A prospective cohort study which evaluated the factors associated with initiation and tolerance of EN in critically ill patients. The study found that EN was not initiated in all eligible patients and fifty percent of the patients receiving EN achieved tolerance of the regimen
Kalfarentzos (17)	1997	II	A prospective randomized trial of 38 patients with acute severe pancreatitis. 20 received TPN and 18 received elemental EN nutrition. EN feedings were tolerated well and patients had fewer complications.
Moncure (7)	1999	II	Trauma patients with J-tubes requiring non-abdominal surgery. Prospective, non-randomized study of 82 trauma patients, 46 of whom had tube feedings continued up until the time of transport to the operating room (fed group), and 36 who had their feedings

First Author	**Year**	**Class**	**Conclusions**
			stopped at midnight before their operation. Aspiration of tube feeds did not occur in either group, and the fed group received more protein and calories on the operative day as well as on post-operative day #1.
Bethel (23)	1979	III	EN was given to patients referred for TPN. Patients showed weight gain and improvement in serum albumin levels. Nasogastric feedings are a safe alternative to TPN.
ASPEN Board of Directors (16)	1993	III	Many trauma patients are hypermetabolic, and depletion of nutrient stores will proceed more rapidly in the case of total starvation than it does in healthy adults. The functional consequences of total or partial starvation thus evolve more rapidly in the stressed and catabolic patient than they do in healthy individuals. A maximum period of 7 days for a severely limited nutrient intake is the empirical absolute limit most investigators set for trauma patients.
Raff (19)	1997	III	A retrospective review of burn patients receiving early intra-gastric feeding. Patients who tolerated the early feeding had significantly lower mortality rates.
Yanagawa (15)	2000	III	Patients of all ages with traumatic brain injury of any severity, either isolated or part of multisystem injury. Review of all randomized controlled trials of timing or route of nutritional support following acute traumatic brain injury. 12 trials were reviewed. Authors conclude that early feeding may be associated with fewer infections and a trend towards improved survival and long-term disability. There was a trend towards better outcomes with parenteral nutrition (compared to enteral), but this finding may be related in part to the delay in starting enteral feeds due to associated gastric ileus. Overall the quality of the trials was poor, and the authors called for larger trials with more relevant clinical endpoints.

B. Early vs. "Delayed" Enteral Feedings

I. STATEMENT OF THE PROBLEM

Over the past two decades, impact of nutrition support on critically injured patients has received significant attention with research focus upon the importance of route and type of nutrition, timing of nutrition, severity of injury, and clinical outcome. With the diverse patient populations of blunt and penetrating torso trauma, severe burns, and head injuries, the metabolic and clinical effects of nutrition support are significantly different. This document summarizes published data describing the success and limitation of nutrition support in these diverse populations.

II. PROCESS

A computerized search of the National Library of Medicine was undertaken using “Key Server” software to identify English language citations during the period 1983 through 2000. In addition bibliographies from these articles were used to search additional relevant papers. Only articles which attempted to use specialized nutrition support as early as possible following injury were studied and the data analyzed for clinical success with the therapies.

III. RECOMMENDATIONS

A. Level I Recommendations

1. There is sufficient Level I and II data to support use of early intragastric feedings in <u>burns</u> as soon after admission as possible since delayed enteral feeding (> 18 hours) results in a high rate of gastroparesis and need for intravenous nutrition. A high success rate of intragastric feeding occurs when feedings are started within 12 hours of burn.

B. Level II Recommendations

1. Patients with severe head injury who do not tolerate gastric feedings within 48 hours of injury should be switched to post-pyloric feedings, ideally beyond the Ligament of Treitz, if feasible and safe for the patient.

C. Level III Recommendations

1. Patients who are incompletely resuscitated should not have direct small bowel feedings instituted due to the risk of gastrointestinal intolerance and possible intestinal necrosis.
2. In patients undergoing laparotomy for *blunt and penetrating abdominal injuries*, direct small bowel access should be obtained (via nasojejunal feeding tube, gastrojejunal feeding tube or feeding jejunostomy) and enteral feedings begun, if not contraindicated (see C1 above), within 12-24 hours of injury.
3. Intragastric feeding of *patients with severe head* injury should be attempted soon after admission unless NG drainage is excessively high (>300 cc/12 hours)

IV. SCIENTIFIC FOUNDATION

The clinical advantages of early enteral feeding have been noted in a number of Class I, randomized prospective studies of severely injured patient sustaining blunt and penetrating trauma of the torso (Table I) burns (Table II), and head injuries (Table III). Each of these patient populations poses unique problems in successfully feeding the gastrointestinal tract.

The randomized prospective studies of blunt and penetrating trauma investigating the route and type of nutrition which demonstrated clinical benefits have been limited to patients with direct small bowel access obtained at the time of surgery. Moore et al.[1] randomized patients to either needle catheter jejunostomy (NCJ) feedings with a chemically defined diet started 18-24 hours postoperatively or to no early enteral nutrition and demonstrated a significant reduction in septic complications, primarily intra-abdominal abscess. Patients were limited to an Abdominal Trauma Index (ATI) between 15 and 40 because of previous work[2,3] which demonstrated decreased gastrointestinal tolerance in patients with an ATI greater than 40 or direct viscus injury. In this study, enteral feedings were administered to a goal rate within 72 hours which limited successful advancement in the more severely injured. A second study of early enteral feeding versus TPN[4] confirmed a reduction in septic complications (primarily pneumonia with a trend toward reduced intra-abdominal abscess) in a similar population with mild to moderate severity of injury. In another study recruiting patients with moderate severity of injuries; i.e., ATI 18-40 or ISS 16-45,[5] diets were started within 24 hours and advanced to goal by 72 hours with GI intolerance in approximately 26% of patients but interruption or discontinuation in only 13.5% of study patients.

A randomized prospective study of enteral feeding via jejunostomy versus parenteral feeding demonstrated a significant reduction in both intra-abdominal abscess and pneumonia in moderate to very severely injured trauma patients receiving enteral nutrition in moderate to very severely injured patients without ATI or ISS limits.[6] Four percent of enterally fed patients failed enteral feedings (defined as 50% of nutrient goal by one week) because of severity of injury. As a result, parenterally fed patients received more nutrition than the enterally fed population. Benefits of enteral feeding were only noted in patients sustaining an ATI >24 or an ISS >20. Feedings were successfully started within 24 hours in both groups. A subsequent study randomized severely injured patients with an ATI >24 or an ISS >20 to one of two enteral diets.[7] Diets were started 1.5 to 2 days following surgery due to early hemodynamic instability in many of the patients. GI symptoms were common and occurred in 88% of enterally fed patients which required slowing the feedings in 45%. The more severe the blunt and penetrating trauma to the torso in patients requiring laparotomy, the greater the intolerance to feeding, the longer the delay before institution of feeding, and slower rate of progression necessary to improve tolerance.

One recent study[8] randomized multisystem trauma patients (ISS > 25, GCS = 12) to early (< 6 hours after resuscitation from shock) or late (= 24 hours after resuscitation from shock) gastric feeding using the same enteral diet for both groups. Parenteral feeding was provided to both groups to meet caloric demands. Within four days, the early fed group tolerated significantly more enteral feeding than the late-fed group, and by the end of one week, they were receiving 80% of their enteral feeding compared with 61% in the late-fed group ($p < 0.025$). The early-fed group sustained significantly fewer incidents of late multiple organ dysfunction.

Intragastric feedings has been studied the most closely in burn patients. In a population of pediatric patients with burns greater than 40% of their body, early intragastric feeding started soon after admission was highly successful.[9] This was duplicated in a larger population of pediatric patients with burns greater than 10%[10] and confirmed again in a group sustaining 25-60% body surface burn.[11] Although diarrhea occurred in 40%, intragastric feeding early following burn was well tolerated. In a population of patients with burns of 40-70%,[12] intraduodenal feeding was started within 48 hours and was well tolerated. Fifty-five intubated, ventilated patients with burns of approximately 45% were started on intragastric feedings with gastric stimulatory agents.[13] When diets were started within 15 hours, goals were reached in 82% of patients within 72 hours, but when feedings were delayed to 18 hours or greater, the majority of patients failed. A study of intraduodenal feeding in patients with 35% body burn started within 48 hours also was well tolerated with rare episodes of distension, reflux, or diarrhea.[14] In a retrospective study of 106 patients with burns of 20% or greater,[15] tolerance of intragastric feedings was greater than 90% in patients started within six hours of burn.

Success with enteral feeding of patients with severe head injuries is less encouraging. In two studies of patients with GCS values between 4 and 10,[16, 17] patients randomized to intragastric feeding received less than 500-600 kcal/day over the first two days, less than 800 cal/day on days 3-5, and less than 1,500 cal/day on days 6-8 due to gastroparesis. However, no attempts were made to feed patients until NG drainage had dropped below 100 cc. Similar results were noted in 23 patients sustaining blunt and penetrating trauma to the head with GCS between 4 and 10.[18] Although feedings were not initiated unless NG drainage was less than 200 cc per day and bowel sounds were present, only one-third of patients tolerated feedings within 7 days of injury and 12 never tolerated feedings. Resolution of this gastroparesis appears to occur on days 3 to 4 in many patients although it may occur sooner than the studies above since gastric emptying may occur despite higher NG drainage and prior to return of bowel sounds.[19] In another study,[20] nasojejunal feedings approached nutrient needs within three days but did not approach nutrient goals until day 5 to day 7 in patients receiving intragastric feeding due to high gastric residuals. Similar delays were noted in the study of 48 evaluable head-injured patients.[21] Recently, 82 patients sustaining head injury were randomized to either intragastric feeding or to intestinal feeding using a pH sensor tube. All patients required mechanical ventilation on the first day of hospitalization, had a GCS score > 3, and at least one reactive pupil. Intestinal tube placement was confirmed by abdominal radiography. Patients receiving the small intestinal tube had a higher percentage of energy and nitrogen administration during the study. Within three days of injury, the intestinal-fed patients achieved 70% of their nutrient goal and by six days achieved 90% of their nutrient requirements. Intragastric-fed patients achieved 30% of nutrient goals by day 3 and 55% by day 6. The intestinally fed patients sustained fewer complications and had an associated reduction in acute-phase protein production.[22] The Cochrane Library has recently summarized the available data concerning the timing of nutritional support in head-injured patients.[23]

V. SUMMARY

Direct small bowel access is necessary to successfully feed patients via the gastrointestinal tract who have sustained severe blunt and penetrating torso and abdominal injuries as well as severe head injuries. Intragastric feeding *at the earliest* becomes successful in the majority of head-injured patients at approximately the 3-4th day due to gastroparesis. Small bowel feedings are tolerated in this patient population with small bowel access. In patients with penetrating and blunt injuries to the abdomen who have small bowel access, enteral feeding can be instituted in most patients after resuscitation is complete and hemodynamic stability has been gained. Advancement to goal rate is slower as in patients with higher Abdominal Trauma Index scores, in particular if > 40. In addition, GI injury below the site of access may slow advancement of tube feedings but is not a contraindication to direct small bowel feedings. Intragastric feeding in patients with severe burns should be instituted *as soon as possible* during resuscitation to prevent or minimize the onset of gastroparesis which appears to occur with increasing incidence if feedings are delayed, particularly if delayed beyond 18 hours. In all patient populations, total parenteral nutrition can be instituted soon after injury, ideally after hemodynamic stability has been gained and resuscitation is complete.

VI. FUTURE INVESTIGATION

Several obstacles limit the successful use of early enteral nutrition. First, access to suitable sites in the gastrointestinal tract for the delivery of nutrition support requires clinical vigilance and planning. Although many patients can be successfully fed intragastrically, critical illness and critical injury often mandate placement of the tube beyond the ligament of Treitz. Unless access is obtained at the time of celiotomy, methods to successfully advance tubes beyond the ligament of Treitz are limited, and further research for solutions to this problem is warranted. Methods are needed to recognize dislodgment into the stomach and to keep the tube beyond the ligament of Treitz, particularly those advanced through the stomach. Second, protocols or markers which promote successful, safe advancement of feeding rate are needed, especially markers which identify patients who will be intolerant of enteral feeding due to distension, bloating, diarrhea, and the rare complication of intestinal necrosis. Third, development of pharmacologic or nonpharmacologic means to reverse or eliminate gastroparesis or ileus may be able to minimize progressive calorie deficits and maximize the benefits of early enteral delivery of nutrients.

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TABLE I: BLUNT/PENETRATING TRAUMA

First Author (Ref)	Year	Data Class	Conclusions
Moore EE (1)	1986	I	63 patients with ATI >15 prospectively randomized to IV fluids (TPN added at day 5 if still NPO) or enteral feedings started at 12 to 18 hours postop and advanced to goal by 72 hours. 12% of enteral patients switched to TPN vs 29% of controls. Postop infections: Control 29% vs enteral 9%, P<.05. Enteral failures: ATI >40. Conclusions: Enteral feeding feasible, reduces septic complications and costs, less well tolerated with ATI >40 if feeding rate advanced aggressively.
Moore FA (4)	1989	I	59 evaluable patients with ATI >5 and <40 prospectively randomized to TPN or jejunal feedings starting 12 hours postoperatively and advanced to goal rate by 72 hours. Major infectious complications 3% with enteral vs 20% with TPN, p<.03. Conclusions: Enteral feedings well tolerated and reduce serious infectious complications.
Kudsk (6)	1992	I	96 evaluable patients with ATI $\geq$ 15 prospectively randomized to enteral feeding started 24 hours postoperatively or TPN started 22.9 hours postoperatively and advanced as tolerated. Two patients failed enteral feeding; TPN patients received more nutrition over hospital course. Significantly lower pneumonia and abscess rates with enteral feeding; most benefit in patients with more severe injuries (ATI $\geq$ 25, ISS $\geq$ 20). More diarrhea with enteral feeding. Conclusion: Almost all patients received successful enteral feeding when advanced at slower rate as tolerated, even with high ATI, high ISS, and gut injury.
Moore FA (5)	1994	I	96 evaluable patients with ATI 18-40 or ISS 16-45 randomized to supplemented diet or standard diet and started within 24 hours and advanced to goal by 72 hours. GI intolerance of 22% in supplemented diets vs 30% in standard (overall = 26%) requiring interruption or discontinuation in 13.5%. Fewer intra-abdominal abscesses, less organ failure with supplemented diet. One bowel necrosis possibly related. Conclusion: Patients with moderate degree of injury tolerated GI feedings started within 24 hours of injury with rapid advancement.
Kudsk (7)	1996	I	Only high-risk patients with ATI >25 or ISS >20 included. If enteral access obtained at laparotomy, patients randomized to supplemented diet or isonitrogenous diet starting 1.63 and 1.97 days after operation, respectively, and advanced as tolerated. Third group without enteral access followed prospectively. GI symptoms

First Author (Ref)	Year	Data Class	Conclusions
			(distension, diarrhea, or cramps) in 88% of enterally fed patients requiring slowing of feedings in 45% of patients. Major infections most frequent in unfed and lowest with supplemented diet. Conclusions: Increased intolerance in most severely injured but septic morbidity reduced compared to unfed. “Early” is later as severity of injury increases.
Moore EE (2)	1981	II (non-randomized, prospective)	30 patients with two or more organs received jejunostomy feedings started at 18 hours postoperatively. All patients advanced to 2.4 L/day at full strength within 72 hours but slowed in 3 patients. Conclusion: No evidence of pancreatic stimulation with pancreatic injuries.
Jones (3)	1989	II (prospective)	123 patients (71 enterally fed with jejunostomy, 52 control given TPN or IV fluids) followed for GI symptoms. Feeds started 12 hours postoperatively. GI complaints in 50% of control patients and 83% of enterally fed patients. Moderate to severe complaints in 12% of control vs 51% of enterally fed. Risk factors for intolerance of enteral feedings: 1) ATI >40 (45% symptomatic), 2) gunshot wounds (73% symptomatic), 3) gut injury (82% symptomatic). Nine patients converted to TPN. Conclusion: Advance enteral feedings slower in high risk patients.
Kompan (8)	1999	II	28 patients were randomized to early (< 6 hours after shock resuscitation) or late (≥ 24 hours following resuscitation) gastric feeding and parenteral nutrition was used to supplement nutrient needs. The early-fed group tolerated significantly greater volumes of enteral feeding by the fourth day and reached 80% of their calculated nutrient goals by the end of the first week. The late-fed group only achieved 61% of their enteral goal by one week. Early patients had lower late (day4-14) multiple organ failure (MOF) scores compared with late patients. Intestinal permeability measured by the lactulose/mannitol (L/M) ratio was greater in the late group compared with the normal controls. On day 2, L/M ratios correlated with late MOF scores and with liver failure. Day 4 L/M ratios correlated with ISS from time of injury to initiation of enteral feeding. Conclusion: Multiply injured patients started on early intrgastric feeding following resuscitation from shock are more rapidly advanced to nutrient goals than patients whose feedings are delayed for more than 24 hours. The early enteral feeding patients sustained much less late MOF and maintained normal gut integrity.

TABLE II: BURNS

First Author	Year	Data Class	Subject Type	Conclusions
Alexander (9)	1980	I	Children	Randomization of 22 children with burns >40% (with 4 early deaths) to an enteral high protein or standard protein diet with IV-TPN supplementation and diet. 60-70% of intake successful via GI tract. Standard protein diet group received 14% of caloric intake as IV-TPN vs 6% in high protein group. Conclusions: Fewer bacteremic days, better immunologic and serum protein values and better survival in high protein group. GI tract usable in severely burned patients.
Gottschlich (10)	1990	I	Human	50 patients with burns >10% randomized to intragastric feeding via tube with standard diet (n=14, 38.3 _ 5.3% BSA burn, age 15.1 _ 4.9) vs supplemented diet (n=17, 45.0 _ 4.1% BSA burn, age = 21.3 _ 4.2) or stress diet (n=19, 38.6 _ 4.3% BSA burn, age = 21.3 _ 4.3 years) Started soon after burn (Group I 2.3 _ 0.5 day, group II 1.1 _ 0.3 days and group III 1.9 _ 0.5 days post admission). Patients needing TPN supplementation were group I n=3, group II n=5, and group III n=2. Diarrhea in 40% of patients. Significant reduction in LOS/% body burn and wound infectious episodes in group II with trend to higher mortality in Group III. Conclusion: Burned patients Tolerated early intragastric feeding.
Saffle J(14)	1997	I	Human	49 completers (of 50 enteral) randomized to supplemented diet (n=25, age = 35.0 _ 3, TBSA = 35.4 _ 4%) or standard high protein diet (n=24, age = 38 _ 4 years, TBSA = 34.7 _ 3.7%) fed intraduodenally within 48 hours of burn and advanced by 25 ml every 4 hours to goal. Discontinuation or reduced rate "rare" due to distension, reflux, diarrhea. Conclusion: No differences in outcome but successful feeding rates high. Discussion – Almost none started ≤ 12 hours after burn.
McArdle (12)	1984	II prospective	Human	12 patients with TBSA burns of 40-70% (2nd and 3rd degree) fed via intraduodenal tube with semi-elemental diet. 6/12 fed within 48 hours of burn. No distension or diarrhea and positive nitrogen balance at 9.8 _ 2.3 days. Conclusion: Early enteral feeding well tolerated when started within 48 hours of burn.
Chiarelli (11)	1990	II	Human adult	20 patients with 25-60% body surface burned started on intragastric

First Author	Year	Data Class	Subject Type	Conclusions
		(case control)		feeding of blenderized diet 4.4 _ 0.49 hours after burn (n=10, average burn = 38 _ 4.4%) or 57.7 hours postburn (n=10, average burn = 38.5 _ 3.9%). Probability of survival .71 vs .74, respectively). Urinary catecholamine and glucagon levels lower in first two weeks in early fed group. Conclusion: Intragastric feedings well tolerated early after severe burn.
McDonald (15)	1991	III	Human	Retrospective study of 106 patients with ≥ 20% TBSA burn started on intragastric bolus feedings within 6 hours of burn. Tolerance of feeding by day: day 1 – 82%; day 2 – 90%, day 3 – 92%, day 4 – 95%. Intolerance, usually vomiting (15%). Tolerant (TBSA = 35 _ 26%, p<.003 predicted mortality 73 _ 35% p<.0001). Patients ≤ 12 years exceeded goal by day 3 and > 12 years old by day 4. Conclusion: Immediate intragastric enteral feeding safe and effective after major burns.
Raff (13)	1997	II retrospective but reliable data III ?	Human	Retrospective review of 55 intubated, ventilated patients (≥ 5 days) with TBSA burn of 44.2 _ 17.4% (35.0 _ 1.7 3rd degree) and abbreviated burn severity index ≥ 7 (average = 9.1 _ 2.1) intragastrically fed with commercial, supplemented diet. Cisapride given via NG tid and metoclopramide given IV tid. Diet started 15.3 hours post burn 45 (81.8%) reached goal within 72 hours. 5 (9.1%) tolerated but missed goal and 5 failed entirely. Only 4 of 48 started within 18 hours failed while 6 of 7 started after 18 hours failed with no significant difference in % burn, ABSI or age between success and failure groups. Increased mortality with failure. Conclusion: Early feeding successful and should be started within 18 hours of burn.

TABLE III: HEAD INJURY

First Author	Year	Data Class	Conclusions
Rapp (16)	1983	I	38 patients with blunt/penetrating head injury randomized within 48 hours to TPN (n=20, age = 29.2 _ 4.1, GCS 7.7 _ 0.6) or intragastric feeding (n=18, age = 34.9 _ 3.8, GCS = 7.2 _ .6) with defined formula diet. Enteral caloric intake ≤ 400 cal/day for 1st day, ≤ 600 cal/day for 1st 10 days, and < 900 cal/day for 14 days due to delayed gastric emptying. 8/18 enteral died sithin 18 days vs 0 TPN patients. Conclusion: Prolonged gastroparesis with intragastric feeding post severe head injury.
Hadley (19)	1986	I	45 head injured patients with GCS ≤ 10 randomized to intragastric (n=21, GCS = 5.9) feeding with standard commercial diet or TPN (n=24, GCS = 5.8). Enteral patients achieved positive *caloric* balance (140% of BMR) in 5% on day 2, 45% on day 3, 70% on day 4, between 70 and 85% to day 11. TPN achieved > 80% by day 5 and 100% by day 9. Complication rate and infectious rate similar. Conclusion: Use TPN only when GI tract fails to work. Editorial: gastroparesis begins to resolve on day 3-4. Don't wait for NG drainage to drop or bowel sounds to occur.
Young (17)	1987	I	51 evaluable of 58 consented patients with GCS 4-10 after blunt or penetrating head wounds randomized to TPN (n=23, age = 30.3 _ 2.7, GCS = 7.0 _ .3) or intragastric feedings (n=38, age = 34.0 _ 2.9, GCS = 6.5 _ 0.4) after bowel sounds return and NG drainage droped below 100 cc. Enteral patients received < 500 cal/day for 1st 2 days (vs 1221 kcal in TPN group), < 800 cal/day for days 3-5 (vs 2367 kcal TPN group), < 1500 cal/day for days 6-8 (vs 2350 kcal in TPN group) due to gastroparesis. Infectious complications the same and neurologic outcome similar at 1 year. Conclusion: Prolonged gastroparesis after severe head injury.
Grahm (20)	1989	I	22 patients with blunt/penetrating wounds and GCS < 10 randomized (by admission day) to *nasojejunal* feeding via fluoroscopy by 36 hours (age = 25.5 _ 13.2, GCS = 5.1) and started at goal rate or intragastric feedings after day 3 if GI function returned (age = 27.8 _ 9.3, GCS = 7.1). Caloric intake matched measured needs by day 3 with jejunal tube and approached 75% of needs on day 5-7. With intragastric feedings, significantly fewer bacterial infections (bronchitis – 3 to 4 plus WBC in sputum with positive cultures with jejunal feeds. Conclusions: Goal rates achieved faster with small bowel access. Gastric residuals limit IG feeding rate. No change in metabolic rate by indirect calorimetry.

First Author	Year	Data Class	Conclusions
Borzotta (21)	1995	I	48 evaluable head-injured patients (GCS $\leq$8) randomized to TPN (n=21, age 28.9 _ 10, ISS = 33.4 _ 9.5, GCS 5.4 _ 1.9) or enteral feeding via surgically placed jejunostomies (n=27, age = 26.2 _ 10.4, ISS = 32.5 _ 10.1, GCS = 5.2 _ 1.6) and started within 72 hours of injury. All TPN patients had initial attempts with intragastric feeding (and presumably failed). TPN transition to intragastric feedings started on day 5. Diarrhea more common in *TPN* patients. High rate of nasogastric tube dislodgement. In first 3 days, enteral delivered calories equaled 90.5% of measured resting expenditure by indirect calorimetry by day 3. Conclusion: With direct small bowel access, nearly achieved calculated goal by day 3 (and subsequently over) with little intolerance.
Norton (18)	1988	II	23 patients with blunt/penetrating head injury and GCS 4-10 (avg.6.6) followed for enteral tolerance. Feeds started when drainage < 200 cc/day and bowel sounds present. 7 tolerated feeds within 7 days, 4 between 7-10 days, and 12 never tolerated feeds with trend to greater intolerance with lower GCS. Tolerance did not correlate with bowel sounds. Conclusion: Gastroparesis in most patients with severe head injury.
Taylor (22)	1999	II	82 patients receiving the same tube feeding were randomized to either intestinal feeding using a pH directed tube and started at goal rate, or to intragastric feeding at 15 cc/hour with gradual advancement as tolerated. Patients receiving the intestinal feeding advanced to their goal rate significantly faster than patients fed intragastrically. By the fourth post-injury day, these patients received more than 70% of their nutrient requirements (compared with 40% in the intragastrically-fed group) and by day 6 received more than 90% of their calculated requirements (compared with 55% in the intragastrically-fed group). Patients were similar with respect to GCS, APACHE II, CT scan findings, and age. Their neurologic outcomes at 6 months were similar with a trend towards better 3-month outcomes in the group fed into the intestine. Infectious morbidity was significantly better in the intestinal-fed group.
Yanagawa (23)	2000	III	Review of all randomized controlled trials of timing or route of nutritional support following acute traumatic brain injury. 12 trials were reviewed. Authors conclude that early feeding may be associated with fewer infections and a trend towards improved survival and long-term disability. There was a trend towards better outcomes with parenteral nutrition (compared to enteral), but this finding may be

First Author	Year	Data Class	Conclusions
			related in part to the delay in starting enteral feeds due to associated gastric ileus. Overall the quality of the trials was poor, and the authors called for larger trials with more relevant clinical endpoints.

C. Standard vs Enhanced Nutrition Support

I. STATEMENT OF THE PROBLEM

Enhanced formulations of enteral and parenteral nutrition support products have become available to support and "treat" injured patients. Is there a clinical benefit to the use of these products?

II. PROCESS

A. Identification of References

1. Medline search 1980-2000. Citations to include "enhanced nutrition," "nutrition support," "trauma," "burn," "enteral," "parenteral," "burn," and "micronutrients" were used.
2. Editorials and case reports were deleted. The list was culled to a total of 23 articles as listed.

B. Quality of the References

The quality assessment instrument applied to the references was that developed by the Brain Trauma Foundation and subsequently adopted by the EAST Practice Management Guidelines Committee. Articles were classified as Class I, II, or III according to the following definitions:

Class I – 19 articles were reviewed
Class II – 3 articles were reviewed
Class III – 1 article was reviewed

III. RECOMMENDATIONS

A. Level I

The use of enhanced enteral nutrition in a select group of severely injured patients (ISS>20, ATI>25) is beneficial to the trauma patient when given in conjunction with early feeding and adequate protein/calorie support. Level I evidence in nearly each one of the cited studies shows reduced incidence of multisystem organ dysfunction, infectious complications, and overall length of hospital stay. Mortality does not seem to be affected. There is no scientific evidence to support the use of enhanced products in less severely injured patients.

Literature regarding enhanced formulation in burned patients is not conclusive.

B. Level II

Administration of an "enhanced" formulation appears to reduce length of stay, septic morbidity and bacteremia in septic trauma patients.

C. Level III

1. There is not sufficient evidence to support the use of enhanced formulations of parenteral nutrition products on the basis of this literature review.

2. Micronutrients and trace elements should be monitored and replaced as indicated by laboratory data.

IV. SCIENTIFIC FOUNDATION

There have been twelve Class I randomized, prospective clinical studies of patients randomized to enteral nutrition support with diets supplemented with omega-3 fatty acids, arginine, nucleotides, betacarotene, and/or glutamine. Improvement in immunologic parameters,[1,2] reductions in the development of the systemic inflammatory response syndrome and multiple organ dysfunction syndrome,[2,3] and improved clinical outcome including reduced infectious complications and decreased length of hospital stay[2, 4-6, 7, 8] have been noted in the preponderance of these studies. One study[9] demonstrated a possible increase in respiratory compromise in patients administered the immune-enhancing diet, but at entry into the study, patients given the specialty diet had an increased incidence of existing severe pulmonary dysfunction. Patients receiving a specialized diet in one study[4] had more direct small bowel access with improved delivery of nutrients which may have explained the clinical outcome differences. Two Class I studies using isonitrogenous, isocaloric control diets[5,6] demonstrated that benefits are not secondary just to the increased nitrogen in these diets, an important factor shown in a study of burn patients.[10] There is conflicting data regarding the benefits of these specialty diets on outcome in patients with severe burns.[11, 12]

Mendez et al.[9] have summarized the effects of some of the individual elements of enhanced nutrition. Arginine may enhance immune response as a result of its involvement in the urea cycle,[13, 14] its role as a secretagogue,[13, 14] its ability to enhance T lymphocyte response to mitogens,[13-15] and its role in the production of nitric oxide.[15] Omega-3 rather than omega-6 fatty acid supplementation of enteral feedings may enhance immune responses by suppressing the production of proinflammatory and immunosuppressive prostaglandin products in response to stress and sepsis. Diets reduced in nuceotide content have been shown to cause suppression of cellular immune response[16] and reduces survival following septic insults. This effect is controversial because nucleotides are labile and the body synthesizes and reutilizes a large supply of nucleotides. Supplemental glutamine may act as a substrate for multiple immune functions.[17-22]

V. SUMMARY

A review of the literature regarding enhanced formulations revealed that there is adequate scientific evidence to support the use of enhanced enteral formulations as defined by the addition of omega 3 fatty acids, nucleotides, arginine, beta carotene, and/or glutamine when adequate calorie/protein requirements are met early in the course of treatment of a select group of severely injured patients (ISS > 20,ATI > 25). Similar, though less extensive, literature support exists for septic trauma patients. The improvements were demonstrated in decreased incidence of multisystem organ dysfunction, infection rates, and length of intensive care unit stay but not in overall mortality. No benefit is identified in less severely injured patients.

We found no evidence to support the use of enhanced parenteral formulations.

Laboratory evaluation of trace element levels and replacement as indicated seems prudent.

VI. FUTURE INVESTIGATION

Current literature does not address duration of time that enhanced formulations should be administered or are beneficial to trauma patients.

Conflicting data and reporting of the use of enhanced formulations in burn patients currently precludes recommendation. Further evaluation of the use of these nutrients in burn patients would be of interest.

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EVIDENTIARY TABLE

First Author	Year	Data Class	Conclusions
Alexander (10)	1980	I	18 children with protein supplemented diet, better survival, less infection
Jeevanandam (25)	1985	I	10 severely injured trauma patients, MCT-LCT may be preferential calorie source
Van Way (28)	1985	I	12 mixed group patients, both solutions promoted N retention, no outcome conclusion
Chiarla (24)	1988	I	16 septic post trauma patients, BCAA'a reduced proteolysis, no outcome conclusion
Gottschlich (11)	1990	I	Enhanced diet in 50 burned patients had decreased LOS and infection rate
Kuhl (26)	1990	I	10 trauma patients, no difference in HBC group
Cerra (1)	1991	I	Mixed group of patients, outcomes same, in vitro evidence of immune stimulation
Vente (29)	1991	I	100 mixed critically ill patients, no difference in groups
Brown (4)	1994	I	32 trauma patients, ISS 30, improved N balance, less infectious complications
Moore (2)	1994	I	98 trauma patients, ISS 20, reduced abd abscesses, MOF, vent days, ICU, and hospital days
Paawa (23)	1994	I	Persistent hypotaurinemia despite supplementation
Petersen (27)	1994	I	20 severely injured trauma patients, rhGH promotes protein anabolism, no outcome comment
Bower (7)	1995	I	A prospective randomized double-blind multicenter trial in 279 ICU patients (84% trauma patients) comparing Osmolite HN® with Impact®, the latter formula enhanced with arginine, nucleotides and ? -3 polyunsaturated fatty acids. The two formulas were neither isocaloric nor isonitrogenous. Overall mortality in both groups was less than predicted, but not significantly different between the two groups. Overall septic morbidity and length-of-stay (LOS) between the 2 groups was also similar. Significant differences were noted in LOS and in septic morbidity in 3 specific subpopulations; 1) 8 day shorter LOS in patients who received at least 5750 cc of "enhanced" formula over the first 7 days of feeding; 2) 10 day shorter LOS and significant reductions in overall septic morbidity and bacteremia in *septic* patients who received the"enhanced" formula compared to

First Author	Year	Data Class	Conclusions
			the standard formula; 3) 11.5 day reduction in LOS and significant reductions in overall septic morbidity in *septic* patients who received at least 5750 cc of "enhanced" formula over the first 7 days of feeding. Subgroup analysis is quite complicated and seems somewhat arbitrary.
Kudsk (5)	1996	I	35 trauma patients, ISS>20, shorter LOS and infectious complications
Mendez (9)	1997	I	43 trauma patients, ISS 30, enhanced diet on vent longer and LOS longer
Saffe (12)	1997	I	50 burns randomized, no difference in outcome
Atkinson (6)	1998	I	Mixed group of 101 patients, reduced vent days, LOS,SIRS
Houdijk (8)	1998	I	Prospective, randomized, controlled trial of standard vs glutamine-supplemented enteral feedings in 72 patients. Feedings were isocaloric and isonitrogenous. In patients who received at least 5 days of enteral feedings, the glutamine group had statistically fewer episodes of pneumonia, bacteremia, and overall sepsis. The glutamine group also had higher levels of glutamine and arginine, and lower concentrations of soluble TNF receptors.
Weimann (3)	1998	I	32 trauma patients, ISS 40, less SIRS and MSOF in enhanced group, vent days, length of ICU stay same
Hunt (31)	1984	II	Lower plasma Se in burn group despite supplementation
Paauw (32)	1990	II	9 trauma patients vs controls, taurine may be essential in the post injury state
Berger (30)	1994	II	10 burn patients, supplemented Cu,Zn,SD: shorter LOS in treated group
Nelson (33)	1992	III	Animal study-ascorbic acid may enhance body weight maintenance

D. Site of Enteral Support: Gastric vs. Jejunal

I. STATEMENT OF THE PROBLEM

Enteral nutrition is preferable to parenteral nutrition, and feeding into the stomach is convenient. Delayed gastric emptying may reduce the effectiveness and safety of gastric feedings compared to feeding into the small intestine.

II. PROCESS OF THE LITERATURE REVIEW

A Medline search was conducted for all articles published between 1973 through December 2000, using the key words "gastrostomy" and "jejunostomy." Another Medline search was conducted using the key words "enteral nutrition" and "trauma." Articles describing techniques, review articles, and case reports were excluded, although their references were reviewed to identify pertinent articles not found in the Medline search.

III. RECOMMENDATIONS

A. Level I

No recommendations.

B. Level II

In critically patients, early gastric feeding, is feasible, and clincal outcome is equivalent to patients fed into the duodenum. For this reason, and because access to the stomach can be obtained more quickly and easily than to the duodenum, an initial attempt at gastric feedings appears warranted.

C. Level III

No recommendations.

Patients at high risk for pulmonary aspiration due to gastric retention or gastroesophageal reflux should receive enteral feedings into the jejunum.Patients with moderate to severe brain injury demonstrate delayed gastric emptying (gastroparesis) as well as dysfunction of the lower esophageal sphincter. These abnormalities may limit nutritional delivery of calories and protein for the first two weeks following injury. Naso-jejunal feedings provide earlier success attaining nutritional goals compared to intra-gastric feedings, which are limited by high gastric residuals.

IV. SCIENTIFIC FOUNDATION

Since Moore and Jones[1] and Adams et al.[2] reported simultaneously that enteral nutritional support was feasible, and possibly associated with fewer complications than parenteral nutrition in the metabolic support of the trauma patient, feeding into the gut has become the preferred technique for nutrition following major injury. Access to the gut can be obtained by a variety of devices: surgically-placed gastrostomy or jejunostomy tubes if the patient has to undergo a laparotomy for abdominal injuries; nasogastric or nasoenteric tubes; and endoscopically- or radiologically-placed gastric or gastrojejunal tubes.

Patients with brain injuries often require early and prolonged nutritional support. Early experience with such patients suggested that parenteral nutrition was preferable to enteral feeding in patients with moderate-to-severe brain injury.[3-5] Support for this conclusion was obtained from studies in brain-injured patients which identified physiologic derangements such as delayed gastric emptying[6,7] and lower esophageal sphincter dysfunction.[8] Even if gastric feedings were given, they could not meet the increased metabolic requirements of the neurotrauma patient.[9] Feeding into the jejunum has been proposed to avoid some of the problems with gastric feeding, and has been shown to provide adequate calorie and nitrogen intake.[10] One recent study, however, has demonstrated that gastric feeding can be accomplished relatively soon (3.6 days in this series) following head injury without incurring significant complications.[11] Evidence regarding the optimal site of enteral nutrition in trauma patients is woefully inadequate. Although several studies have looked at complications rates of gastric versus jejunal feeding in nontrauma patients, these studies tend to be retrospective,[12-16,] have small numbers of subjects in each group,[12, 15, 17, 18] or compare nonequivalent procedures such as percutaneous gastrojejunostomy versus surgical gastrostomy.[13] Percutaneous gastrostomy (PEG) has recently been compared with percutaneous gastrojejunostomy (PEGJ) in a consecutive group of severely injured trauma patients, finding more rapid attainment of feeding goals in the PEGJ group, but no differences in outcomes.[14] One recently published randomized trial of gastric versus duodenal feeding demonstrated equivalent outcomes, but slightly earlier achievement of protein and calorie goals with duodenal feedings.[15] On balance, there does not seem to be a superiority of jejunal feeding over gastric feeding, but more prospective, randomized studies with larger numbers of patients are needed upon which to make a scientifically-supported decision.

V. SUMMARY

The need for nutrition following severe injury is intuitively apparent, especially in patients who will not be able to resume oral intake within a few days following injury. Enteral feeding is more physiologic and less expensive than parenteral feeding. Whether it is preferable to feed into the stomach or into the jejunum is not clear, but care must be taken in all patients to ensure that feedings are tolerated, and that aspiration is avoided.

VI. FUTURE INVESTIGATION

A multicenter, randomized, prospective trial should be conducted to evaluate the safety, efficacy, and cost of gastric feeding compared to post-pyloric enteral feeding in trauma victims. Patients with brain injury should be evaluated as a separate subgroup to avoid confounding issues.

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TABLE 1 – ENTERAL FEEDING IN THE BRAIN-INJURED PATIENT

First Author	Year	Data Class	Injury Type	Conclusions
Rapp (3)	1983	II	CNS injury	20 brain-injured patients randomized to early TPN, 18 randomized to delayed gastric feedings. GCS scores were similar in the two groups, but 8 enterally-fed patients died within 18 days or injury, while none of the TPN patients died in the same time span. TPN patients had more positive nitrogen balance, higher serum albumin levels, and higher total lymphocyte counts than enterally-fed patients.
Young (4)	1987	II	CNS injury	51 brain-injured patients with GCS score 4 to 10 were randomized to TPN or enteral nutrition. TPN patients had higher mean intake of nitrogen and calories, but there were no differences in rates of pneumonia, urinary infections, septic shock, or all infections. Anergy screens, lymphocyte counts, and serum albumin levels were not different between the two groups. TPN patients had greater initial improvement in GCS scores and more favorable outcomes at 3 months, but outcome differences at 6 months and 1 year were not significant.
Borzotta (10)	1994	II	CNS injury	48 patients with severe brain injury were randomized to early TPN (n=21) or jejunal feeding (n=27). Measured energy expenditure and nitrogen excretion were similar in the two groups. Both routes of nutrition were equally effective in meeting nutritional goals, and infections were equal in frequency in the two groups.
Clifton (9)	1985	III	CNS injury	20 brain-injured patients were randomized to enteral feeding with either 14% or 22% of calories as protein. Those fed with higher protein formula had improved nitrogen retention, but nitrogen equilibrium was rarely achieved in either group.
Hadley (21)	1986	III	CNS injury	45 brain-injured patients randomized to TPN or gastric feedings. TPN patients had greater daily nitrogen intake and greater daily nitrogen losses than gastric-fed patients. There were no differences in maintenance of serum albumin levels, weight loss, infection rates, nitrogen balance, or mortality.
Norton (5)	1988	III	CNS injury	23 patients with acute brain injury and GCS scores of 4 to 10 were fed enterally. Tolerance of feeding was inversely related to increased

First Author	Year	Data Class	Injury Type	Conclusions
				intracranial pressure and to severity of brain injury (low GCS scores).
Ott (6)	1991	III	CNS injury	12 patients with brain injury and GCS scores of 4 to 10 were evaluated with liquid gastric-emptying scans. These showed delayed gastric emptying in the first week after injury, and rapid emptying by the third week. All patients tolerated full-rate feedings by post-injury day 16 except 2 patients with persistent delayed gastric emptying.
Saxe (8)	1994	III	CNS injury	16 patients with acute brain injury and GCS < 12 underwent esophageal manometry within 72 hours of admission and 5 patients had repeat studies 1 week after injury. All had minimal or no gastric-to-esophageal pressure differential initially, and 4 of 5 had normal differential at 1 week. Aspiration rate was not studied.
Kao (7)	1998	III	CNS injury	Gastric emptying of liquids was prolonged in 35 patients with moderate-to-severe brain injury, especially in females, older patients, and patients with lower GCS scores.
Klodell (11)	2000	III	CNS injury	118 head-injured patients were started on gastric feedings at an average of 3.6 days post-injury. 80% were fed via a percutaneous endoscopic gastrostomy tube (PEG), while 20% via small-bore naso-gastric tube. All patients received prokinetic agents initially. Overall, 97% of patients were able to tolerate gastric feedings, and only 2 of 118 patients required conversion to jejunostomy feedings. The incidence of aspiration was 4%.

TABLE II – GASTRIC VERSUS JEJUNAL FEEDING

First Author	Year	Data Class	Injury Type	Conclusions
Korbeck (15)	1999	I	ISS > 16	Prospective randomized (not blinded) study of 80 patients. Forty-three received gastric feeds and 37 received duodenal feeds via a fluoroscopically-placed naso-duodenal tube. Patient groups were similar with respect to injury severity, age, gender, APACHE II scores, narcotic/paralytic use, and energy requirements. There was no difference noted in ICU or hospital length of stay, ventilator days, overall morbidity or mortality. The incidence of pneumonia was 42% in the gastric group and 27% in the duodenal group, not statistically significant, but this may represent a type II statistical error. Patients in the duodenal group tolerated full-strength feeds 10 hour earlier on average than did the gastric group in this study.
Montecalvo (20)	1992	II	Non-trauma	38 selected medical and surgical ICU patients randomized to gastric (n=19) or jejunal (n=19) feeding. Patients fed in the jejunum received a higher proportion of their daily goal caloric intake and had a greater increase in serum prealbumin. Although pneumonia incidence was lower in jejunal (n=0) than in gastric-fed patients (n=2), this difference was not significant.
Strong (19)	1992	II	Non-trauma	33 patients randomized to gastric (n=17) or postpyloric (n=16) feedings. Pulmonary aspiration occurred in 31% of the gastric-fed patients, versus 40% of the postpyloric-fed patients.
Burtch (12)	1987	III	Non-trauma	Retrospective comparison of complications with surgical gastrostomy and surgical jejunostomy. Nine of 26 (35%) patients with gastrostomy had pulmonary aspiration, which was fatal in 2 patients. Only 2 of 30 (7%) patients with jejunostomy had aspiration (both nonfatal). Overall survival at one year was 4% and 10%, respectively.
Ho (13)	1988	III	Non-trauma	Retrospective review of 133 patients who underwent radiologically-placed percutaneous gastrojejunal catheters, compared with 100 patients who underwent surgical gastrostomy. Complication rate was 5.2% in the gastrojejunal catheter group, with no pulmonary

First Author	Year	Data Class	Injury Type	Conclusions
				aspiration, and a 7.5% 30-day mortality. Complications occurred in 33% of the gastrostomy patients, including 8 episodes of postoperative aspiration. Mortality in the gastrostomy group was 12%.
Kadakia (17)	1992	III	Non-trauma patients	Retrospective review of 79 patients who underwent percutaneous endoscopic gastrostomy or, percutaneous endoscopic jejunostomy (the latter procedure was chosen in 6 patients because of prior aspiration). Aspiration occurred in 9 patients, including 6 of 7 treated with jejunostomy.
Mullan (16)	1992	III	Medical-surgical (10% trauma)	Retrospective review of 276 patients receiving enteral nutrition. Only 12 (4.3%) episodes of aspiration occurred, and there was no difference in the risk of aspiration between nasoenteric, gastrostomy, or jejunostomy tubes.
Fox (22)	1995	III	Non-trauma patients	Retrospective study of medical/surgical patient population. Four of 69 (5.8%) of gastrostomy patients had aspiration pneumonia (respiratory symptoms, leukocytosis, and an infiltrate on chest radiograph), compared with 2 of 86 (2.3%; not significant) jejunostomy patients.
Spain (18)	1995	III	CNS trauma	Retrospective review of 74 patients with brain injury who received nasogastric tubes. They remained intragastric in 42, and were transpyloric in 32 patients. There were no differences in days to full feeding, ventilator days, ICU length of stay, incidence of pneumonia or incidence of aspiration.
Adams (14)	2000	III	Trauma	Prospective, non-randomized study of 89 trauma patients fed by either percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic gastrojejunostomy (PEGJ). Although the latter reached feeding goals earlier (80% at goal rate by day 3 vs. 65% of PEG patients; 93% vs. 79% by day 15, respectively), there wer no differences in complications between the groups. The only complications tracked were pneumonia, ileus and sepsis. There were no differences in ventilator days or hospital LOS.

E. Assessment of Energy and Substrate Requirements for the Trauma Patient

I. STATEMENT OF THE PROBLEM

Provision of adequate calories and protein to the hypermetabolic injured patient is of paramount importance to achieving optimal outcomes in this patient population. Failure to meet caloric requirements leads to erosion of lean body mass and subsequent negative nitrogen balance as the body attempts to provide sufficient energy and nitrogen to carry out vital functions. Conversely, overzealous nutritional support is associated with derangements in hepatic, pulmonary and immunologic function, and may lead to outcomes that may be nearly as detrimental to the injured patient as malnutrition.

II. PROCESS

A Medline search was conducted to identify all English language citations from 1973 through 1998 that contained one or more of the following keywords: “nutritional support”, “trauma”, “critically injured”, “head injury”, “spinal cord injury”, “paraplegia”, “quadriplegia”, “burns”, “energy expenditure”, “energy intake”, “enteral”, “parenteral”, “dietary proteins”, “dietary fats”, “dietary carbohydrates”, “protein”, “carbohydrate”, “fat”, “lipid”, “requirements”, and “nutrition”. Bibliographies of selected references and standard textbooks or other educational material were also examined to identify articles that might not have been retrieved in the computerized searches. Studies involving laboratory animals were excluded from our review, as were studies where the patient population was exclusively or predominantly pediatric so as to avoid the effect of growth and maturation of the patient upon energy and substrate requirements. Also excluded were letters to the editor, isolated case reports and most collected reviews. This resulted in a total of 9~~1~~**3** articles which, when classified according to the criteria initially proposed by the Brain Trauma Foundation[1] and subsequently adopted by the EAST Practice Management Guidelines Committee, yielded the following distribution of articles:

Class I (a prospective, randomized clinical trial) 19 Class I articles were identified and reviewed.

Class II (a prospective, non-comparative clinical study or a retrospective analysis based on reliable data) 45 Class II articles were identified and reviewed.

Class III (a retrospective case series or database review) 30 Class III articles were identified and reviewed.

III. RECOMMENDATIONS

1) **Level I**

a) There appears to be NO advantage to the routine use of calorimetry to determine the caloric requirements of burn patients.

2) **Level II**

a) For moderate to severe trauma injury patients (ISS range 25-30), energy requirements are estimated to be 25-30 total kcal/kg/day or 120-140% of predicted BEE (per Harris-Benedict equation).

b) There appears to be no consistent relationship between ISS and measured resting energy expenditure (MREE) in trauma patients.

c) For severe head-injury patients (GCS < 8), energy requirements may be met by replacing 140% of MREE (~30 total kcal/kg/day) in non-pharmacologically paralyzed patients and 100% of MREE (~25 kcal/kg/day) in paralyzed patients.
d) Within the first two weeks after spinal cord injury, nutritional support should be delivered at 20-22 total kcal/kg/day (55-90% of predicted BEE by Harris-Benedict equation) for quadriplegics and 22-24 total kcal/kg/day (80-90% of predicted BEE by Harris-Benedict equation) for paraplegics.
e) For patients with burns exceeding 20-30% TBSA, initial caloric requirements may be estimated any of several available formulas.
f) The Curreri Formula (25 kcal/kg + 40kcal/TBSA burn) overestimates caloric needs of the burn patient (as estimated by calorimetry) by 25-50%.
g) The Harris-Benedict Formula underestimates the caloric needs of the burn patient (as estimated by calorimetry) by 25-50%.
h) In patients with burns exceeding 50% TBSA, TPN supplementation of enteral feedings in order to achieve Curreri-predicted caloric requirements is associated with higher mortality and aberrations in T-cell function.
i) Caloric requirements for major burns fluctuate throughout the hospital course, but appear to follow a biphasic course with energy expenditure declining as the burn wound closes. Therefore, direct measurement of energy expenditure via calorimetry on a once or twice weekly basis may be of benefit in adjusting caloric support throughout the hospital course.
j) Intra-operative enteral feeding of the burn patient is safe and efficacious, leads to fewer interruptions in the enteral feeding regimen, and therefore more successful attainment of calorie and protein goals.
k) Approximately 1.25 grams of protein per kg body weight is appropriate for most traumatized patients.
l) Up to 2 grams of protein per kg body, weight per day is appropriate for severely burned patients.
m) In the burn patient, energy as carbohydrate may be provided at a rate of up to 5 mg/kg/min (~25 kcal/kg/day); exceeding this limit may predispose patients to the metabolic complications associated with overfeeding. In the non-burn trauma patient, even this rate of carbohydrate delivery may be excessive.
n) Intravenous lipid or fat intake and should be carefully monitored and maintained at <30 percent of total calories. Zero fat or minimal fat administration to burned or traumatically injured patients during the acute phase of injury of may minimize the susceptibility to infection and decrease length of stay.
o) Proteins, fat and carbohydrate requirements do not appear to vary significantly according to the route of administration, either enterally or parenterally.
p) Fat or carbohydrate requirements do not appear to vary significantly according to the type of injury, i.e., burned versus traumatically injured.

3) **Level III**

a) Provision of excess calories to trauma patients may induce hyperglycemia, excess CO_2 production, fluid/electrolyte abnormalities, lipogenesis, and hepatic steatosis.
b) Energy requirements for patients with less than 20-30% TBSA burns are similar to those of patients without cutaneous burns.
c) Protein requirements in burn patients and in those with severe CNS injuries may be

significantly greater than anticipated, up to 2.2 grams/kg body weight per day. However, the ability to achieve positive nitrogen balance in a given patient varies according to the phase of injury. Provision of large protein loads to elderly patients, or to those with compromised hepatic, renal or pulmonary function may lead to deleterious outcomes

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IV. SCIENTIFIC FOUNDATION

Calorie requirements of trauma patients have been debated for years. The gold standard for determining the caloric needs of patients incurring traumatic injuries is to measure their energy expenditure with indirect calorimetry. By measuring oxygen consumption (V_{O2}) and carbon dioxide production (V_{CO2}) via indirect calorimetry, resting energy expenditure can be calculated using the abbreviated Weir equation: $REE = [3.9 (V_{O2}) + 1.1 (V_{CO2})] \times 1.44$. Despite the availability of this technology, there have been few prospective, randomized clinical trials conducted specifically to determine the optimal amount of calories for this patient population. The best study to date that has addressed this issue with Class I evidence compared the effect of three different parenteral nutrition (PN) regimens (hypercaloric, isocaloric, hypocaloric) on protein catabolism and nitrogen loss when protein administration was fixed at 1.7 g/kg/day.[2] Caloric needs were provided at 125% of measured resting energy expenditure (MREE) in the hypercaloric group, 100% of MREE in the isocaloric group, and 75% of MREE in the hypocaloric group. The mean ISS was 27 for all three groups, and patients with burn, spinal cord, or isolated head injuries were excluded from study enrollment. Despite significant differences in caloric provision, no significant differences were observed in nitrogen balance, 3-methylhistidine excretion, or visceral protein status among the groups. The mean MREE was approximately 28 kcal/kg/day for all patients on day 4 of the study. However, 80% (24/30) of the patients were sedated with fentanyl and 7% (2/30) of the patients were pharmacologically paralyzed. Both of these treatment interventions have been associated with a hypometabolic response in neurologically injured patients. The only other Class I evidence available is derived from a trial comparing the metabolic effects of a carbohydrate-based diet versus a fat-based diet in critically ill patients with infections or trauma.[3] Only 2 of 12 patients were identified as suffering traumatic injuries. The mean MREE was approximately 26 kcal/kg/day for patients while receiving the different nutritional regimens. Demographic data describing the severity of illness or injury of the patients were not provided in the study.

Several methods have been used to estimate energy requirements of patients suffering traumatic injuries as an alternative to measuring actual energy requirements with indirect calorimetry. These include calculating basal energy expenditure with the Harris-Benedict equation (HBEE), multiplying the HBEE by an activity factor and a stress factor depending on the type of injury (i.e., blunt trauma, skeletal trauma, head trauma), and using 25 kcal/kg/day. A number of clinical trials have been conducted to evaluate the accuracy of these predictive methods for estimating MREE in trauma patients. The MREE of trauma patients has been reported to be approximately 26 kcal/kg/day (range 21-32 kcal/kg/day), 33 kcal/kg/day (postabsorptive state [range 25-41]), 37 kcal/kg/day (while receiving PN [29-46 kcal/kg/day]), 25 kcal/kg/day, and 38-48 kcal/kg/day (requiring insulin in TPN), and HBEE x 1.2 (activity factor) x 1.75 (stress factor).[4-7] One recent study noted a biphasic metabolic response to injury, with total energy expenditure (TEE) peaking during the second post-injury week at 59 kcal/kg/day, compared to only 31 kcal/kg/day during the first post-injury week.[8] Furthermore, these studies have attempted to determine a relationship between MREE and scoring systems used for evaluating the severity of disease and injury. Although some investigators[9, 10] have found no correlation (r=-0.042) between MREE and injury severity score (ISS), others[4] have claimed to identify a relatively high correlation between ISS and MREE/kg (r=0.84).

Head and spinal cord injury patients represent a subset of trauma patients with unique metabolic requirements. Data from a majority of clinical trials have found hypermetabolism to occur in head injury patients with an average increase of 40% above that predicted with HBEE. The increases in energy expenditure are related to the increased oxygen consumption caused by the stress hormone flow in response to brain injury and may further be increased by hyperventilation, fever, seizures, and posturing. Patients with decerebrate or decorticate posturing have demonstrated elevations in energy expenditure at 200-250% of predicted energy expenditure.[11] Pharmacologic treatments have also been shown to have a dramatic impact on energy expenditure. High-dose barbiturates have been used to control increased intracranial pressures refractory to standard therapy. However, barbiturate therapy can decrease energy expenditure by as much as 40% below predicted energy expenditure with HBEE.[12] Other pharmacologic interventions, such as neuromuscular blockade with pancuronium bromide, have reduced energy expenditure by 42% below predicted energy expenditure with HBEE.[11]

In contrast to trauma and head injury patients, spinal cord injury patients exhibit a decrease in energy expenditure. Within the first three weeks following spinal cord injury, metabolic rates 94% (range 55-129%) of those predicted by HBEE have been observed.[13] An inverse relationship has been identified between the location of injury and energy expenditure. Thus, the higher the lesion, the lower the energy expenditure measurement. Nutrition support recommendations for quadriplegics is 20-40% below HBEE (20-22 kcal/kg/day) and 10-20% below HBEE for paraplegics. The importance of recognizing the hypometabolic response in spinal cord injury patients is that adverse effects may result from overfeeding with excessive calories. Providing calories in excess of energy expenditure in any patient may cause: (1) impaired glucose control, (2) suppression of chemotactic/phagocytic actions of monocytes due to hyperglycemia, (3) respiratory dysfunction from excessive CO_2 production, (4) lipogenesis, and (5) hepatic steatosis.

Energy requirements in the burn patient are difficult to determine because of the number of factors that impact upon this calculation. Early studies demonstrated a relationship between the percentage of total body surface area (TBSA) burned and energy requirements in these patients as determined by indirect or direct calorimetry. Wilmore[14] was the first to document this relationship in his study of twenty patients with burns ranging in size between 7% and 84% TBSA. He further noted that this hypermetabolism appeared to be mediated by catecholamines and appeared to plateau at 60% TBSA. During that same year Curreri,[15] in a prospective study of 9 patients, derived a formula, now bearing his name, relating energy expenditure to preburn weight and the %TBSA burned. Although subsequent studies have shown that this formula frequently over-estimates actual energy requirements, it remains one of the most, if not the most, commonly used method to determine energy requirements of patients in burn centers in the United States today.[16]

Since this time, multiple formulas have been proposed as more accurate predictors of caloric requirements of the burned patient. These formulas tend to fall into two broad categories, those, which include a factor for TBSA burned, and those, which do not. The majority of formulas within this latter category are based upon calculations of basal energy expenditure (BEE) as determined by this Harris-Benedict equation, which takes into account patient age, sex, height, and weight. To this BEE, are multiplied mathematical factors for the degree of stress (injury) and for the level of patient activity to arrive at an estimate for the patient's overall caloric requirement. Many studies have been carried out comparing the Curreri formula with formulas based upon the Harris-Benedict-derived BEE. Turner[17] carried out one such prospective study in 35 patients with second and third-degree TBSA burns ranging between 10 and 75%, noting that the Harris-Benedict-derived BEE underestimated actual energy expenditure by 23% while the Curreri formula overestimated energy expenditure by 58%. Long[18] measured energy expenditure in 39 critically ill patients and in 20 normal volunteers, finding that energy expenditure in burned patients exceeded that predicted by the Harris-Benedict equation by 132%. He thus suggested that the Harris-Benedict equation be multiplied by a stress factor as well as an activity factor to arrive at a more accurate estimation of caloric requirements. In fact, the values for stress and activity factors, which he proposed nearly 20 years ago, are still widely employed today.

However, even with these correction factors, Harris-Benedict predictions seem to perform no better than the Curreri formula. In a prospective study of 21 patients with between 21 and 81% TBSA burns, the Curreri formula overestimated actual energy expenditure by 25-36%, while the Harris-Benedict predictions modified by stress and activity factors, overestimated actual energy expenditure by 32-39%.[19] Other Harris-Benedict derived formulas have attempted to simplify matters by simply multiplying the Harris-Benedict derived BEE by either 1.5[20] or by a factor of 2.[21] Each of these authors claim superiority over Curreri based predictions which, as indicated above, seem to consistently overestimate actual energy expenditure as determined by indirect calorimetry.

The other major category of energy-predicting formulas in burn patients includes those which, like the Curreri Formula, are based upon the patient's TBSA and/or TBSA burned. Both Xie[22] and Allard[23] have compared their TBSA-based formulae to the Curreri and claim superior results, though the overall number of patients studied is quite small.

Despite the many published studies which claim superiority of a particular formula over the Curreri Formula in the prediction of energy requirements in burn patients, the Curreri Formula remains the most commonly used despite its well-documented propensity to overestimate energy requirements.[16] One would suspect, therefore, that actual determination of energy expenditure by indirect calorimetry, might be the most accurate and commonly used method of determining caloric requirements of burned patients. However, in an interesting study documenting actual burn practices in North American burn centers, Williamson noted that indirect calorimetry is infrequently carried out on a routine basis, being used only occasionally or for research purposes only. *More importantly, there appear to be no differences in patient outcome when calories are provided on the basis of direct measurement of energy expenditure or on the basis of a mathematical formula*. In a prospective randomized study of 49 patients, patients received feedings based upon the Curreri Formula or upon indirect calorimetry-determined energy expenditure. Despite the significant difference in the number of calories *prescribed* to each group, the actual number of calories *received* by each group were the same, and there were no differences in clinical outcomes or complications.[24] An important finding in this study was the discrepancy between the number of calories prescribed and the number of calories delivered to these burn patients. Regardless of whether the Curreri Formula is used or the BEE is multiplied by an activity factor and/or a stress factor, it is frequently difficult, if not impossible, for any given patient to ingest this number of calories. Indeed, in Ireton's study mentioned above,[20] patients received a caloric intake of only 81% of the calculated Curreri-predicted caloric requirement. Thus, it is perhaps advantageous that many of these formulas overestimate caloric need to compensate for the less-than-prescribed caloric load that these patients end up receiving.

At the same time, however, it seems unwise to attempt to achieve these high caloric loads by supplementing enteral nutrition with TPN. In a prospective randomized study of 39 patients with TBSA burns exceeding 50%, Herndon[25] demonstrated a significantly higher mortality and greater depressions in T-helper/suppressor ratios in patients receiving TPN.

Thus, the available data supports the use of some formula to determine the *initial* caloric requirements of burned patients, recognizing that such formulas may well over-estimate a patient's actual caloric need but that it is unlikely that this entire caloric load will be able to be delivered. One of the more common reasons for the inability to deliver the prescribed caloric load is the necessity to having to interrupt the tube feeding regimen for frequent trips to the operating room for debridement and grafting in the burn patient. The Williamson survey[16] documents that most patients in North American burn centers are kept NPO for at least 6-8 hours before surgery. Jenkins,[26] however, has demonstrated the feasibility and safety of continuing enteral feedings throughout operative procedures in a very select group of burn patients with enteral access established beyond the pylorus, and airway access established via an endotracheal tube or tracheostomy. These investigators were able to demonstrate significant caloric deficits and an increased incidence of wound infection in the unfed group as compared to the group who underwent intra-operative enteral feeding.

Finally, it should be mentioned that the caloric requirements of the burn patient do fluctuate over the course of burn wound healing as a result of closure of the burn wound, as well as other yet-to-be identified factors. Saffle[27] demonstrated the biphasic character of measured energy expenditures in burn patients. Energy expenditures actually rise from the time of admission through the 10th to 20th post-burn day and then decline thereafter but remain elevated at the time of discharge. This finding was confirmed by Cunningham[21] as well as by Ruten,[28] who noted a trend towards decreased energy expenditures with excision and coverage of the burn wound. Ireton-Jones,[29] however, was unable to demonstrate such a relationship between the percent of burn wound remaining open and the measured energy expenditure. Suffice it to say that, even in the absence of a demonstrated relationship between the percentage of burn wounds remaining open and energy expenditure, that the caloric needs of the burn patient will fluctuate from day to day depending upon other factors such as temperature, activity level, degree of anxiety, pain control, ventilator dependency, caloric intake, the presence or absence of sepsis, and other yet-to-be defined factors. Therefore, provision of the same caloric requirement over time runs the risk of overfeeding or underfeeding the burned patient. This has led some authors to recommend the use of indirect calorimetry to determine actual caloric requirements on a weekly or twice-weekly basis.[19, 30, 31]

At this time, there are insufficient data and on protein, fat and carbohydrate requirements in traumatically injured or burned patients to provide any Level One recommendations. A major problem appears to be the difficulty encountered identifying specific groups of patients for study.

For this reason, guidelines can only be applied broadly to patients within these two general categories. Another issue is that the current focus of nutrition and metabolic support has necessarily changed. The state of the art is such that we are less concerned with how to provide adequate quantities of macronutrients. The bulk of available evidence would suggest that, perhaps with the exception of the risks of overfeeding, we currently provide patients with sufficient calories and protein to avoid the detrimental effects of malnutrition. Our attention has shifted toward manipulating a patient's physiological and biochemical environment to his or her advantage through the administration of specific nutrients, growth factors or other agents, often in pharmacological doses.

A few "Class I" reports--randomized, prospective and adequately controlled trials-- have presented "convincingly justifiable" data. However, in these instances, either the number of patients studied has been too small or the particular population investigated has been too specialized to warrant inclusion in this practice management guideline.

Protein requirements have been largely established by reports from the early 80's that typically have presented dose ranges felt to be appropriate. These reports have been largely Class II studies.[6,32-35] More recent publications have confirmed these dose ranges based on extensive research conducted by a leading investigator,[36, 37] studies of protein requirements using state of the art measurements of body composition,[38] measurements of substrate metabolism and energy requirements,[39] or from expert opinion based on reviews of available literature.[40, 41]

The focus of other investigations has not been on specific protein requirements, but these studies do provide a reference point for the range of protein intakes that appear to be efficacious.[2, 42-45] Variations in protein requirements as a function of time after burn or injury have been acknowledged illustrating that current recommendations are only estimates of averaged needs.[46]

The question of whether the contribution from protein should or should not be included in calculations of *total* caloric intake has not been specifically addressed. However, the preponderance of evidence available from detailed studies of actual energy expenditure[21, 47] or nutrient utilization,[48, 49] reviews of published reports,[50] or prospective trials[51, 52] suggest that the majority of calories should be administered as carbohydrate. Although the exact percentage of total calories that should be provided as fat is unknown, consensus opinion would suggest that this quantity should be 30% or less under most circumstances. This conclusion does not obviate the need to modify carbohydrate administration to minimize CO_2 production in selected instances,[47, 49, 50] but the specific range under which these modifications should occur has not been established. Some reports, though not all,[52] especially the Class I report by Battistella,[54] suggest that minimizing fat intake or altering the type of fat administered[55-57] may decrease morbidity and improve outcome or favorably alter metabolic profiles.

A few reports suggest that the specific macronutrients administered[56, 58] or the use of growth factors[45, 59-61] may favorably influence metabolic responses. However, recent preliminary reports suggest that the use of growth hormone for this purpose in critically ill patients may be associated with deleterious outcomes.

V. SUMMARY

Multiple formulae exist that will provide an estimate of an individual patient's energy and substrate needs. While many of these provide accurate estimates, many do not and can lead to overfeeding with all of its inherent complications. It is best to remember that these formulae provide at best only an estimate of an individual patient's initial energy and substrate needs, and that these requirements will vary throughout the course of illness and recovery. Ongoing assessment of the appropriateness of nutritional support is crucial in avoiding under- and over-feeding.

VI. FUTURE INVESTIGATION

It is unlikely that there exists the ideal energy or substrate formula which will perform better than those that currently exist. However, more reliable and easier-to-use means of measuring energy expenditure and substrate utilization would provide significant advantages over the current state of technology with indirect calorimetry. Identification of these markers of metabolism will provide not only better means of assessing a given patient's initial requirements, but will better enable the clinician to modify nutritional support throughout the course of illness and recovery. It is equally unlikely that prospective, randomized, double-blinded controlled trials will be performed to study the effects of the administration of different quantities of protein, fat or carbohydrate. In our present health care environment, there is a demand for a clearer delineation of the indications for nutritional or metabolic support and for unequivocal demonstrations of efficacy with regards to decreasing costs and improving outcomes. Important questions that need to be examined include the: 1) effects of the nature of injury and its time course on requirements with an eye toward minimizing the effects of nutritional, especially parenteral, interventions; 2) effects of macronutrients administration on cellular biology and organ function during critical illness; and 3) identification of subpopulations that will benefit from the administration of specific nutrients or growth factors, who needs them, what kind and when?

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TABLE I: ENERGY REQUIREMENTS IN TRAUMA PATIENTS

First Author	Year	Data Class	Injury Type	Conclusion
Frankenfield (2)	1997	I	Blunt and penetrating trauma	Prospective, randomized study evaluating the effect of energy balance on N_2 balance in multiple trauma patients (ISS>25). Achievement of energy balance (NPC or total) failed to decrease catabolic rate or N_2 loss at a fixed protein intake of 1.7 g/kg/day
Schneeweiss (3)	1992	I	Polytrauma	Prospective, randomized, cross-over study comparing fat-based vs CHO-based enteral nutrition in critically-ill patients. Only 2/12 patients were trauma patients. Approximately 35% of enteral CHO was stored as glycogen and 50-60% of energy needs were met by fat oxidation. MREE ~ 26 kcal/kg/day.
Brain Trauma Foundation (1)	1996	I & II	Head injury	Replace 140% of REE in non-paralyzed patients and 100% of REE in paralyzed patients receiving enteral or parenteral nutrition containing at least 15% of kcal as protein by the 7^{th} day after injury.
Long (79)	1979	II	No trauma patients	
Iapichino (6)	1982	II	Trauma	Maximum protein sparing effect reached when caloric intake was = 130% MEE (~38-48 kcal/kg/D). Increased doses of insulin were used with TPN.
Paauw (7)	1984	II	Blunt trauma (n=8) Total patients n=119	Caloric intake of 25 kcal/kg/D(~ MREE) ~ 7% of patients were trauma
Dempsey (12)	1985	II	Head injury	Patients with severe head trauma without barbiturate therapy exhibit an average REE 26% above predicted by HBEE.
Kosanovich (72)	1985	II	Trauma (n=8) and Surgery (n=11)	Prospective, nonrandomized observational study. Increased caloric intake from 27.8 to 34.2 kcal/kg/Day on fixed protein of 1.27 g/kg/Day decreased the protein catabolic rate. Only 42% of patients

First Author	Year	Data Class	Injury Type	Conclusion
				were specifically trauma patients.
Mollinger (83)	1985	II	Spinal Cord Injury	20-30% below REE for quads and 12-15% below REE for paraplegics; however, patients were 3.8 to 8.6 yr from injury.
Clifton (11)	1986	II	Head injury	The authors recommend use of a nomogram to estimate REE at the bedside of comatose patients.
Swinamer (69)	1987	II	3/10 patients were trauma	Mean MREE was 47% above predicted EE based on Harris-Benedict equation
Kolpek (84)	1989	II	Spinal Cord Injury and head trauma	44% below BEE (22kcal/kg/D) for spinal cord injury pts during the 1st week after injury vs 144% x BEE (35 kcal/kg/D) for head trauma patients during 1st week. Protein losses for both groups were between 1.3-1.4 g/kg/day
Shaw (10)	1989	II	Blunt Trauma	The use of TPN in trauma patients results in an increase in glucose oxidation and decreased fat oxidation, and attenuation of protein synthesis. Recommend regimen of 2000-2500 kcal/day and 1.7 g/kg/day.
Dickerson (67)	1990	II	Head trauma	Protein requirements are accentuated in excess of kcal needs in head injury patients. UUN excretion of 16.5 g/Day
Jeevanandam (5)	1990	II	Blunt trauma	Prospective, nonrandomized observational study REE = 33.4 to 37.7 kcal/kg/Day for trauma patients with mean ISS = 34. Daily protein losses ~ 1.34 g/kg/D. Also found traumatic injury increased rate of fat mobilization.
Sedlock (85)	1990	II	Paraplegics	~21kcal/kg/day for MREE of 4 paraplegics with a mean of 7.4 years post injury
Rodriguez (63)	1991	II	Spinal Cord injury	Nonrandomized, prospective comparative trial. N_2 losses are obligatory in spinal cord injury patients. Recommend protein at 2 g/kg/day IBW due to losses.
Rodriguez (4)	1995	II	AMultisystem@ trauma (no	Prospective, observational study. Demonstrated no correlation between ISS and MREE. Suggested correlation between predicted

First Author	Year	Data Class	Injury Type	Conclusion
			description of blunt vs penetrating)	and MREE
Klein (62)	1997	II	Trauma (no specific description of blunt vs penetrating)	Study which evaluated the quality of nutrition care provided to trauma patients at risk for MODS. Endpoints included dietitian documentation, %kcal/protein goals met based upon Harris-Benedict.
Uehara (8)	1999	II	Trauma patients with ISS > 16 (median ISS=33.5)	Derived Total Energy Expenditure (TEE) in 12 trauma patients by measuring energy intake and changes in total body fat, protein and glycogen. Authors noted a significant rise in TEE, which averaged 31 kcal/kg/day during the first week, but peaked at 59 kcal/kg/day during the second week. Based on this, authors recommend multiplying the HBEE by factors of 1.4 and 2.5, respectively for the first two post-injury weeks.
Blackburn (82)	1976	III		REVIEW
Wieman (81)	1978	III		REVIEW
Bistrian (80)	1979	III		Outlines a procedure to estimate stress based upon a 24 hr UUN.
Elwyn (78)	1981	III	Surgical patients	REVIEW
Kudsk (77)	1982	III	Trauma and burns	REVIEW
Stoner (76)	1982	III		REVIEW
Abbott (74)	1983	III		REVIEW
Schmitz (75)	1983	III		REVIEW
Jensen (73)	1984	III	Critical illness	REVIEW
Lemoyne (71)	1986	III		REVIEW
Woolfson (70)	1986	III		
McCarthy (64)	1991	III	Critically illness	REVIEW

First Author	Year	Data Class	Injury Type	Conclusion
Anonymous (68)	1989	III		REVIEW
Meguid (65)	1990	III	Trauma	REVIEW
Turner (66)	1990	III	Trauma	REVIEW

TABLE II: ENERGY REQUIREMENTS IN BURN PATIENTS

First Author	Year	Data Class	Conclusions
Ruten (28)	1986	I	Prospective, randomized study of 13 patients w/ burns >45% TBSA. One group had burn excised within 72 hours and covered with auto- or allograft. Second group treated with hydrotherapy and dressings. No significant difference in REE at any time up to 30 days post-burn, but trend towards decreased REE w/ excision. Small # patients, and groups not comparable.
Herndon (25)	1989	I	Prospective randomized study of 39 patients w/ > 50% TBSA burns. 16 received intravenous supplementation of enteral nutrition to achieve Curreri formula predicted requirements. Supplemented group had significantly higher mortality and greater depressions in T-helper/suppressor ratios. Patient groups questionably comparable.
Saffle (24)	1990	I	Prospective randomized study of 49 patients with 25-79% TBSA burns. Patients received feeds based on Curreri Formula or on indirect calorimetry. Curreri-based caloric goals exceeded MEE by 43%. Caloric goals for calorimetry patients were MEE X 1.2 (activity factor). Caloric *intakes* were the same for both groups .No differences in outcomes or complications.
Jenkins (26)	1994	I	Prospective, randomized study of 80 patients w/ burns > 10% TBSA. 40 patients fed peri-operatively; remainder had feedings held pre-, intra- and immediately post-op. No aspiration in either group. Same LOS, mortality and % pneumonia. Unfed group had significant caloric deficit, increased incidence of wound infection and required more albumin supplementation.
Curreri (15)	1974	II	Prospective study of 9 patients w/ TBSA between 40 and 73%. Used regression analysis to determine equation for caloric requirements using preb-burn weight, weight at 20 days post-burn, and actual caloric intake over the 20 day period. Formula derived: Caloric Intake = 25 kcal/kg + 40 kcal/% burn (Curreri Formula).
Wilmore (14)	1974	II	Classic paper relating increases in burn wound size to increased energy expenditure**.** Prospective study of 20 patients w/ 7-84% TBSA burns and 4 unburned controls. Noted hypermetabolism to be modified by ambient temperature and infection and to be mediated by catecholamines. Increase in energy expenditure is maximal w/ ~ 60% TBSA burn.
Bartlett (90)	1977	II	Prospective study of indirect calorimetry (IC) in 15 patients with 20-70% TBSA burns. IC

First Author	Year	Data Class	Conclusions
			performed once or twice daily until burn wound coverage. Oxygen consumption and caloric expenditure was 1.5 to 2 times normal, and was consistent hour-to-hour and day-to-day. MEE correlated best with the extent of full thickness burn.
Long (18)	1979	II	Measured energy expenditure in 39 sepsis/trauma/burn patients and 20 normal volunteers. Energy expenditure of burn patients exceeded that predicted by the Harris-Benedict (HBEE) equation by 132%. Developed equation: Caloric Expenditure = HBEE X Stress Factor X Activity Factor. Values for stress and activity factors are given and are still in use today.
Saffle (27)	1985	II	Prospective study of indirect calorimetry in 29 patients with 3-80% TBSA burns. Actual MEE was only 76% of Curreri-predicted requirements, and was 1.47 times the Harris-Benedict-predicted requirement. Neither formula addresses biphasic character of actual MEE, which rises from admission through day 10-20, and then declines but still remains elevated at discharge.
Turner (17)	1985	II	Prospective study of 35 patients w/10-75% $2^o/3^o$ TBSA burns. Calculated energy expenditure predicted by the Harris -Benedict equation (HBEE) underestimated actual energy expenditure by 23%. Curreri-derived energy requirements overestimated actual energy expenditure by 58%. In patients w/ TBSA > 20%, HBEE was a better predictor of actual energy expenditure.
Ireton (20)	1986	II	Prospective study of indirect calorimetry (IC) in 17 patients with 26-79% TBSA burns. Each patient had IC only once between PBD 2-26. Actual MEE best estimated by HBEE X 1.5. Curreri formula (CEE) overestimated MEE by a factor of 1.53 and HBEE underestimated MEE by 0.72.Mean caloric *intake* was only 81% of CEE, indicating difficulties attaining this goal.
Ireton-Jones (29)	1987	II	Prospective study of 20 patients w/ 31-74% $2^o/3^o$ TBSA burns. Serial MEE=s and UUN excretion determined as wounds were reduced to <15% TBSA w/ healing and grafting. No correlation between % open wound and MEE or UUN excretion. Also poor correlation between MEE and caloric require- ment as predicted by Curreri formula,even modified for reduced burn size.
Schane (19)	1987	II	Prospective study of 21 patients w/ 21-81% TBSA burns. Curreri formula derived energy requirements (CEE) overestimated actual MEE by 25-36%. Harris-Benedict predictions

First Author	Year	Data Class	Conclusions
			(HBEE) modified by stress and activity factors overestimated actual MEE by 32-39%. CEE and HBEE were good estimates of maximal MEE. Serial determinations of MEE are recommended.
Allard (92)	1988	II	Prospective study of indirect calorimetry in 23 patients with 7-90% TBSA burns. Curreri formula overestimated MEE by 52%, and Harris-Benedict formula (HBEE) underestimated MEE by 29%. Energy expenditure increased from 6.5% to 34.1% above HBEE with feeding, suggesting that 25% of the caloric intake is used to increase MEE.
Cunningham (21)	1989	II	Prospective study of indirect calorimetry in 122 patients with 2-98% TBSA burns. Actual MEE best estimated by 2 x HBEE, not by Currrei formula, BEE x activity factor x injury factor, or 2000 x body surface area. Confirms biphasic MEE noted by Saffle (26). TBSA burns < 30% are associated with MEEs which are difficult to differentiate from normal variability in MEE.
Allard (23)	1990	II	Prospective study of 10 patients with 30-90% TBSA burns. Compares actual MEE with energy requirements predicted by the Curreri and the Toronto formulas and twice the Harris-Benedict (HBEE)formula. Best approxi- mation of actual MEE was Toronto Formula which utilizes TBSA burned, caloric intake of prior 24 hours, # days post-burn, temperature and HBEE.
Ireton-Jones (88)	1992	II	Developed equations predicting energy expenditures based on 200 patients w/ a variety of diagnoses, including burns. Tested equation on 100 patients and found a high correlation with MEE. Factors predictive of energy expenditure included age, sex, ventilator dependency, weight, presence of obesity, trauma or burns. Burn size, however, was not a predictive factor.
Xie (22)	1993	II	Prospective study of 75 patients w/ 5-98% TBSA burns. Compares new formula [1000 X m^2 (surface area) + 25 X %TBSA] to Curreri formula and to [2000 X m2], [2 x BMR] and [20 X Kg + 70 X %TBSA] . Data suggest Chinese formula more closely approximates actual MEE.
Khorram-Sefat (31)	1999	II	Resting Energy Expenditure (REE) determined in 27 patients, daily for the first post-burn week and twice a week thereafter. Patients grouped according to predicted mortality [PM] (< 20%, 20-80%, and >80%), and REE patterns in the 3 groups compared. REE similar in all

First Author	Year	Data Class	Conclusions
			groups for first 20 days (~ 50% above HBEE), after which it declined in patients with PM < 80%, but continued to be elevated up to the 45^{th} day in patients with PM > 80%. Finding no clear relationship between REE and TBSA burn during the first 15 days post-burn, the authors conclude that the only reliable way to calculate the caloric needs of burn patients is to perform indirect calorimetry. If this is not feasible, a caloric load of no more than 50-60% above HBEE is recommended.
Schumer (86)	1979	III	Expert panel discussion of the metabolic effects of burn injury and some of the treatment strategies required to overcome them. Despite being written almost 20 years ago, still quite applicable current discussions of burn nutrition.
Williamson (16)	1989	III	Interesting study documenting actual burn nutrition practices at North American burn centers. Most centers use a Curreri-based formula to determine energy requirements. Those that use metabolic carts do so only occasionally or for research purposes. Most centers keep patients NPO at least 6-8 hours before surgery.
Mancusi-Ungaro (89)	1992	III	Retrospective study of 12 patients with 7-82.5% TBSA burns. Measured caloric balance (calories consumed - calories expended as determined by weekly calorimetry). Positive caloric balance correlated with good patient and nutritional outcomes and was easier to determine than nitrogen balance. Caloric expenditure did not correlate with burn size.
Curreri (91)	1990	III	Concise overview of many of the issues surrounding the estimation and administration of appropriate nutritional support to the burn patient.
Waymack (30)	1992	III	Recommends weekly or preferentially twice-weekly measurement of resting metabolic energy expenditures using indirect calorimetry for patients with severe burns.
Deitch (87)	1995	III	General review making the folowing points: - no proven outcome benefit of MEE vs caloric estimates. - data derived from pediatric burn patients may not apply to adults. - energy requirements may increase or decrease throughout hospitalization. - avoid overfeeding, control pain /anxiety and optimize thermal conditions.

TABLE III: MACRONUTRIENT REQUIREMENTS IN TRAUMA AND BURNS

First Author	Year	Data Class	Injury Type	Conclusion
Moore (42)	1986	I	ATI > 15	Protein intake estimated from body weights was 1.5 - 2.0 gm/kg BW/day
Hausmann (59)	1990	I	Polytrauma	Nandrolone decanoate improved nitrogen balance by reducing nitrogen excretion and 3-methylhistidine and renal AA losses.
Kuhl (93)	1990	I	Polytrauma	N balance, IGF-1, fibronectin and prealbumin levels measured in patients randomized to receive standard (21% branched chain AA's) or enriched formula (46% BCAA). No differences in these variables were detected.
Cerra (58)	1991	I	Critically Ill	Enteral diets supplemented with arginine, fish oil and RNA stimulated in vitro lymphocyte proliferative responses and reduced 3-methyl histidine excretion but had no observed beneficial effects at follow-up 6 and 12 months later.
Brown (56)	1994	I	Trauma	An enteral formula enriched with arginine, linolenic acid, beta carotene and hydrolyzed protein led to a decreased incidence of infection and better nitrogen balance.
Petersen (45)	1994	I	Trauma	Protein given as 1.6 g/ Kg BW/day. Recombinant human growth hormone increased the efficiency of protein synthesis.
Garrel (57)	1995	I	Burns	3 groups: control 35% fat, low (15%) fat, low fat plus fish oil (15%). Low fat nutrition support decreases infectious morbidity and length of stay. Fish oil composition did not matter.
Jeevanadam (60)	1995	I	Trauma, ISS = 31∀2	Recombinant human growth hormone + TPN in the period immediately after traumatic injury improves nitrogen retention (less negative) and normalizes plasma AA levels.
Jeevanadam (48)	1995	I	Polytrauma	AA's as 20% of energy needs, CHO@ 50% and lipid as 30%. A medium chain triglyceride-long chain triglyceride mixture may be better for trauma pts because the formula allows more rapid

First Author	Year	Data Class	Injury Type	Conclusion
				and efficient fuel utilization.
Jeevanadam (61)	1996	I	Trauma, ISS = 31∀2	Less negative nitrogen balance, increased whole body protein synthesis, increased efficiency of protein synthesis, increase plasma glucose levels and enhanced lipolysis in patients treated with recombinant human growth hormone.
Battistella (54)	1997	I	Polytrauma	Pts. receiving TPN randomized to receive standard fat emulsion or to have fat withheld for 10 days who received the same AA and CHO dose. IV fat increased the susceptibility to infection, prolonged pulmonary dysfunction and delayed recovery (? 2° underfeeding or fat?)
Frankenfield (2)	1997	I	Trauma	Randomized prospective study of patients to 3 groups: 1) CHO + lipid = measured energy expenditure [MEE]; 2)CHO, lipid, + protein = MEE; and 3)CHO + lipid = 50% of MEE. Protein = 1.7 g/Kg BW/day. Achieving energy balance did not decrease the catabolic rate or nitrogen loss.
Bernier (53)	1998	I	Burns > 20% BSA	Low fat feeding with or without fish oil did not change IL-6 production.
Iapichino (6)	1982	II	Trauma	Caloric intake of 130% of energy needs provided maximal protein sparing effect. AA's should be provided as 20% of energy requirements.
Kagan (51)	1982	II	Burns: 1-10%, 11-30% and 31-60% BSA	Calorie:nitrogen ratio's of 150:1 may not provide adequate nitrogen to achieve equilibrium.
Matsuda (52)	1983	II	Burns	Calorie:nitrogen ratios of 150:1 ok for patients with BSA less than 10%. Patients with > 10% wounds need ratios of approximately 100 to 1
Nordenstrom (34)	1983	II	Mixture of trauma and septic patients	Nitrogen sparing effects of lipid and glucose based systems are similar. Factors other than N balance should be used to decide which system to use.

First Author	Year	Data Class	Injury Type	Conclusion
Wolfe (35)	1983	II	Burns (Av. = 70% BSA)	Protein intake was 1.4-2.2 g protein/Kg BW/Day With the higher dose there was additional increase in protein synthesis but N excretion was decreased.
Twyman (33)	1985	II	Head Injuries	Suggestive data indicating that protein requirements are higher in head injured patients at approximately 2.2 g/Kg BW/day.
Cunningham (21)	1989	II	Burns	For burns exceeding 30% BSA, 2 X the resting metabolic rate most closely approximated the measured energy expenditure. Cal:nitrogen ratio of 150:1 preferred.
Jeevanadam (39)	1990	II	Trauma	Prospective study suggesting that 0.35 g N or ~2.2 g protein/Kg BW/day required to minimize loss of lean body mass.
Larsson (46)	1990	II	Burns or fracture of > 2 long bones	Nitrogen requirements vary over time. 0.20 grams N/kg BW/day or 1.25 g of protein/ Kg BW/day is optimal.
Jeevanadam (47)	1992	II	Trauma, ISS 32 ∀ 2	Study suggests that intravenous glucose should given at a rate that does not exceed the resting energy expenditure (REE).
Eyer (43)	1993	II	Blunt Trauma, ISS ; 10	Purpose of this randomized controlled study was to evaluate metabolic responses to "early" enteral feeding (unaltered) but protein was set at 1.5 g/kg BW/day
Guenst (49)	1994	II	Potpourri	Use indirect calorimetry to measure energy expenditure or give total calories up to 140% of the basal energy expenditure with glucose infusions less than or equal to 4 mg/Kg BW/minute. Fat can be given as 40-60% of calories.
Chuntrasakul (44)	1998	II	Trauma, Burns and Cancer (ISS = 24, Av. % TBSA burned = 48	Goal of study was not to determine CHO, protein or fat requirements but energy provided as 35-50 Kcal/kg BW/day and protein @ 1.5-2.5 g/Kg BW/day.
Homsy (32)	1983	III	Critically Ill and Marasmic Patients	30 - 40 kcal and 1.5 g protein/kg BW/Day recommended.
Alexander (55)	1990	III	Burns	Authors suggest that optimal enteral diet provides 20% energy

First Author	Year	Data Class	Injury Type	Conclusion
				from Whey, 2% from arginine, 0.5% from histidine and cysteine with lipids as 15% of non-protein calories. Lipid should be 50% fish oil and 50% safflower oil. This diet is believed to improve outcome.(decr wound infections, hospital stays, and death).
Tredget (50)	1992	III	Burns	CHO's are an important fuel source for burned patients. The theoretical maximum is 5-6 mg/Kg BW/min.
Wolfe (37)	1997	III	Critically Ill	Review by leading researcher in the field suggests that carbohydrate should be the "predominant" source of non-protein calories.
Ishibashi (38)	1998	III	Immediately post-trauma or severely septic patients (ISS = 16)	Retrospective study that used very sophisticated techniques. 1.2 g protein/kg pre-illness wt is optimal amount.
Debiasse (40)	1994	III	Critically Ill including Burns and Trauma Patients	Authors suggest that 70% of energy should be provided as CHO, 30% or less as Lipid and 1.5 g - 2 g protein/Kg BW/day (the latter for burned patients).
Wolfe (36)	1996	III	Critical Ill including Burns and Trauma Patients	Non-protein energy should be provided largely as CHO. Protein should be set at 1.5 g/Kg BW/day.
Pomposelli (41)	1994	III	Critically Ill	Protein should be provided between 1.5-2 g/Kg BW/day. Calories should be limited to the patient's energy expenditure.

F. Nutrition Monitoring

I. STATEMENT OF THE PROBLEM

The monitoring of patients receiving nutritional support and specifically: parenteral nutritional support varies from institution to institution. The same variables are usually measured, however the frequency of obtaining laboratory tests and other measurements such as, nitrogen balance, vary. It is evident that patient's receiving nutritional support should be monitored. The goals of monitoring are to improve the efficacy of nutritional intervention and to prevent complications related to nutritional support.

II. PROCESS

A MEDLINE search was done from 1974 to present using the following terms: nutrition, monitoring, enteral nutrition, parenteral nutrition, albumin nitrogen balance, indirect calorimetry, trauma, critically ill and electrolytes. Only English language literature was reviewed. A total of 211 references were cited. Of these only 34 references were found to be directly relevant to the topic of nutrition monitoring. In addition literature was reviewed from non-MEDLINE sources. Several textbooks and other reports were reviewed. Six hospitals were polled to determine their protocols for monitoring of nutrition support. The result of this review was then incorporated into the following analysis.

III. RECOMMENDATIONS

A. Level I

No recommendations.

B. Level II

Compared to other visceral proteins, serial determination of serum pre-albumin is the most sensitive indicator of appropriate nutritional support

C. Level II

1. Patients receiving nutritional support should be weighed regularly, and accurate measurements made of intravenous volume infused, oral intake and urinary output.
2. Prior to the initiation of nutritional support baseline levels of the following should be obtained: blood urea nitrogen (BUN), creatinine, plasma electrolytes, glucose, calcium, magnesium, inorganic phosphorus, total protein, albumin, pre-albumin, hemoglobin, white blood cell count (WBC), platelet count, triglycerides, transaminases.
3. Patients must have an assessment of their nutritional needs. This assessment should be based on the patient's history, physical examination, laboratory values and the patient's disease process. Caloric and protein requirements should be based the overall assessment. Adjuncts such as, the Harris-Benedict Equation (HBE), indirect calorimetry, nitrogen balance calculation, and the creatinine-height index (CHI) should also be used to estimate caloric and protein requirements.

4. After the initiation of nutritional support, the following should be monitored daily until levels are stable: plasma electrolytes, glucose and magnesium. BUN, creatinine, calcium, inorganic phosphorus and, for patients receiving total parenteral nutrition, transaminase and triglyceride levels should be monitored 2-3 times per week until levels are stable. Total protein, albumin and pre-albumin should be monitored weekly until the levels are stable. Continued monitoring of these laboratory values should be dictated by the patient's clinical course.
5. A reassessment of the patient's nutritional needs e.g. nitrogen balance and indirect calorimetry measurements, should be done weekly until the patient has reached a steady state.

IV. SCIENTIFIC FOUNDATION

There are no prospective randomized trials, which evaluate the process of nutrition monitoring. Clinicians assume, and rightly so that periodic monitoring is an essential part of nutrition support.[1-4] Monitoring is essential to prevent complications such as hyperglycemia or electrolyte imbalances. Monitoring is also essential to determine the efficacy of nutritional intervention.[5,6] Patients receiving nutritional support are usually monitored daily. Electrolytes, nitrogen balance, indirect calorimetry, serum proteins and a plethora of tests are obtained on patients receiving nutritional support. The frequency of monitoring and the efficacy of laboratory examinations in determine the adequacy of nutritional support has yet to be clearly determined.[6]

Clifton et al.[7] found nitrogen balance to be practical and reliable when used to monitor head injury patients receiving nutrition support. Long et al.[8] also found nitrogen balance and indirect calorimetry to be useful tools in monitoring nutritional support. However, Moore and Jones[9] found that in trauma patients, the abdominal trauma index was a better predictor of septic morbidity than nitrogen balance or transferrin levels. Several authors also found that nitrogen loss in trauma patients correlated with the catabolic rate, not nitrogen intake.[10-12] Konstatanides[13-16] evaluated the efficacy of using nitrogen balance as a guide for nutritional support, and found that the total urea nitrogen (TUN), when used instead of the UUN to calculate nitrogen balance, was more reliable. Several studies have looked at the efficacy of measuring serum proteins. The albumin level was found to be good a prognostic indicator.[17, 18] Pre-albumin and transferrin levels were noted to be good monitoring tools.[17,19-22] One recent prospective, randomized trial compared serial determinations of serum albumin, pre-albumin, retinol binding protein, and transferrin, along with nitrogen balance determinations. Of these, serum pre-albumin emerged as the most sensitive indictor of appropriate nutritional support.[23] Clinicians must remember however that measurement of any acute-phase visceral protein may be affected by liver disease,[17,21-22] as well as by the patient's hydration status. Other factors monitored included insulin-like growth factor-1, fibronectin, retinol binding protein and tumor necrosis factor. These were not found to be efficacious for routine monitoring.[22, 24, 25]

The Harris-Benedict Equation is often used to estimate energy needs. When its efficacy was compared to the use of indirect calorimetry in determining caloric requirement, indirect calorimetry was noted to be more accurate.[26-29] There are some disadvantages, however, to using indirect calorimetry in patients with underlying lung disease.[28, 29] The monitoring of electrolytes was also noted to be essential in the management of patients receiving nutrition support.[1, 3, 30] Blood and urine glucose levels were also noted to be important in treatment of patients receiving nutritional support.[31,32] A class III study by Baker et al.[33] suggested that clinical judgment correlated well with laboratory values and anthropometric measurements. This study, however, did not address sequelae associated with inappropriate use of nutritional support. There were no studies which addressed the issue of the frequency of monitoring. The type of laboratory examinations which were done were similar in all the hospitals surveyed; however, the frequency of obtaining tests varied from institution to institution.

V. SUMMARY

Patients receiving nutritional support should be closely monitored. Current data however does not address the frequency of monitoring or the efficacy of monitoring.

VI. FUTURE INVESTIGATION

There are two major issues in nutrition monitoring. One is the frequency of obtaining laboratory tests and other measurements, such as indirect calorimetry. The other is the efficacy of intervention based on the values measured or calculated. The answers may be found by examining whether or not specific interventions are being made based on changes in values measured or calculated. A prospective randomized study with varying time intervals for obtaining laboratory and other measurements should provide guidelines for establishing the frequency with which these tests should be done.

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NUTRITIONAL SUPPORT OF THE TRAUMA PATIENT

LITERATURE REVIEW — NUTRITION MONITORING

First Author	Year	Data Class	Conclusions
Cerra (37)	1991	I	A prospective, blind, randomized trial which evaluated immune function and nitrogen balance. Two nutritional formulas were used. Patients achieved nitrogen balance with both regimens, however resolution of anergy was seen only in the group given the immune boosting formula.
Collins (1)	1979	II	Anthropometric measurements were compared to in vivo neutron activation analysis to determine body nitrogen stores. Anthropometric measurements were unreliable.
Faintuch (34)	1979	II	Anthropometric measurements can effectively detect changes in body constitution if the change is greater than 10%.
Tuten (11)	1985	II	Pre-albumin levels correlated with anabolic metabolism and nitrogen balance. Transferrin had similar results.
Moore (9)	1983	II	Nitrogen balance and transferrin levels were compared to the abdominal trauma index (ATI) as predictors of post injury septic morbidity. The ATI was found to be more accurate.
Antonas (35)	1987	II	CPK levels remained depressed as long as insulin levels were elevated. CPK-MM may be useful in short term monitoring of stressed patients receiving TPN.
Konstantinides (13)	1991	II	Nitrogen balance was measured using the urine urea nitrogen (UUN) and total urea nitrogen (TUN). TUN was found to be more accurate when used in the measurement of nitrogen balance than UUN.
Konstantinides (14)	1992	II	Urinary urea nitrogen (UUN) was compared to the direct measurement of total urinary nitrogen (TUN) in the calculation of nitrogen balance in burn patients. TUN was found to be more accurate and was recommended to replace the use of UUN
Rodriquez (26)	1995	II	The energy requirement of 35 trauma patients was estimated using the Harris-Benedict equation. The energy expenditure was then measured using indirect calorimetry. There was no correlation between the injury severity score and the measured energy expenditure.

First Author	Year	Data Class	Conclusions
Clark (25)	1996	II	A prospective study which analyzed insulin-like growth factor 1(IGF-1) as well as transferrin and pre-albumin levels in critically ill patients. These levels were compared to total body proteins and energy expenditure measured by indirect calorimetry. IGF-1 transferrin and pre-albumin levels did not correlate with changes in the protein stores in the acute phase of illness.
Long (32)	1996	II	Hepatic glucose output (HGO) was examined in 8 control subjects and 12 trauma patients after a fasting period of 60hrs. Glucose kinetics was measured after amino acid infusion and glucose infusion. Increasing the supply of gluconeogenic precursors did not stimulate enhance HGO.
Phang (5)	1996	II	Mechanically ventilated patients who received nutritional support were routinely assessed using albumin, pre-albumin, lymphocyte count, weight and bio-electric impedance analysis. Nutrition assessment parameters were not specific indicators of adequacy of nutrition support.
Frankenfield (12)	1997	II	Nitrogen loss in critically injured patients correlated with catabolic rate not nitrogen intake. The achievement of energy balance did not decrease nitrogen loss in the first few days post trauma.
Rady (19)	1997	II	A cohort study looking at preoperative albumin levels and outcome after cardiovascular surgery. Hypo-albuminemia was associated with a higher incidence of post-operative complications.
Smyrnios (29)	1997	II	A prospective study which compared 30-minute measurements of energy expenditure with 24-hour measurements of energy expenditure. The 30-minute measurements were variable, but the variability was acceptable for clinical purposes.
Nataloni (23)	1999	II	Data prospectively collected on 45 patients placed into 1 of 3 groups according to whether they received purely enteral or purely parenteral nutrition, or a combination of the two. All patients underwent serial determinations of serum albumin, prealbumin, retinol binding protein (RBP), and transferrin, as well as nitrogen balance determinations. In all 3 groups, only prealbumin and RBP in-creases significantly over the course of the 11-day study, and positive nitrogen balance was only achieved in the "enteral only" group. Significant increases were noted for both prealbumin and RBP

First Author	Year	Data Class	Conclusions
			as early as the third day in the enteral group compared to both the parenteral group and the enteral-parenteral group.
Blackburn (30)	1977	III	Malnutrition was assessed by using triceps skin folds, muscle circumference and weight, in 50 patients with cardiac disease. Patients who were severely malnourished did poorly.
Long (8)	1979	III	The energy expenditure in trauma patients and patients undergoing elective surgery was determined using indirect calorimetry and nitrogen balance calculation. This was found to be effective in determining the patients' energy needs.
Reines (31)	1979	III	Complications from the use of TPN in septic patients were analyzed. Hypoglycemia and hypophosphatemia were prevalent. Dextrostix monitoring of glucose levels was recommended.
Ching (18)	1980	III	Nutritional parameters were studied in critical ill patients receiving parenteral and enteral nutrition. Patients with trauma injuries had the greatest loss body weight and nitrogen excretion. The response of serum albumin levels to nutritional support was a good predictor of survival.
Baker (33)	1982	III	Clinical judgment was compared to laboratory and anthropometric measurements in assessment of nutritional requirements. Clinical judgment correlated well with laboratory values.
Bourry (17)	1982	III	Albumin, pre-albumin, retinol binding protein and transferrin were measured in 39 cancer patients receiving TPN. Pre-albumin was the most effective in monitoring nutrition intervention.
Iapaichino (10)	1984	III	Nitrogen intake and total energy intake were the major determinants of nitrogen balance.
Clifton (7)	1986	III	Nutritional requirement of patients with severe head injury was assessed using indirect calorimetry, nitrogen balance and weight. Nitrogen balance was balance was found to be practical and reliable.
Larsson (36)	1990	III	Nitrogen requirements and nitrogen balance were measured in patients within the first week post trauma. A nitrogen supply of 0.2 kg per body weight was recommended.

First Author	Year	Data Class	Conclusions
Mattox (24)	1991	III	The utility of biochemical markers was evaluated. TUN, UUN, 3-methylhistidine, acute phase reactant proteins, plasma amino acid, lactate-pyruvate ratio were examined for utility and efficacy in nutrition monitoring. Their values must be interpreted in light of the patient's clinical condition. They were not found to have extensive clinical use.
Konstantinides (15)	1992	III	The utility of nitrogen balance (NB) in nutritional assessment was examined. In addition the efficacy of using urine urea nitrogen (UUN) versus total urea nitrogen (TUN) to calculate the NB was evaluated. Twenty-four hour collection of urine samples was also compared to obtaining randomized urine samples. TUN was found to be more advantageous than UUN and 24-hour urine samples, than random collections of urine.
Adami (38)	1993	III	Body composition of patients undergoing pancreatico-biliary diversion was measured using bio-electric impedance (BIA) analysis. Clinical and BIA findings were similar.
Guirao (39)	1994	III	Extra-cellular water was monitored in patients receiving TPN. Tetrapolar bio-impedance analysis was shown to be accurate in measuring body fluid changes.
Konstantinides (16)	1994	III	This report examines the efficacy of nitrogen balance as a monitor for nutrition support. Partial urine collection was compared to 24-hour urine collection. Urine urea nitrogen was compared to total urea nitrogen. Nitrogen balance was found to be an effective means of monitoring nutritional intervention.
Spiekerman (22)	1994	III	This report reviewed the use of 8 nutritional markers: albumin, transferrin, pre-albumin, retinol-binding protein fibronectin, insulin-like growth factor-1, C-reactive protein and tumor necrosis factor. The advantages and disadvantages of each marker were discussed.
Manning (20)	1995	III	A review of multiple methods of nutritional assessment. This review examined the efficacy of measuring nitrogen balance, biochemical tests, visceral proteins, immunologic function and anthropometry. There was no single test which proved to be more effective than the others. A combination of tests and monitoring is recommended.

First Author	Year	Data Class	Conclusions
Russell (21)	1995	III	Nitrogen balance, albumin, transferrin, retinol-binding protein, fibronectin and Insulin-like growth factor-1 were evaluated as monitoring tools for nutritional support. The cost of these tests was significant. Monitoring trends rather than "normal" values was found to be more efficacious.
Brandi (27)	1997	III	A literature review of the usefulness of indirect calorimetry in critically ill patients. Indirect calorimetry is most effective in the evaluation of patients who fail to respond to nutritional intervention. It was also found to be useful in patients with prolonged ventilator dependence and, or multi-system organ failure.
Cutts (28)	1997	III	A study comparing the use of the Harris-Benedict equation (HBE) to estimate the energy requirements in obese patients with the actual energy expenditure as measured by indirect calorimetry. The HBE overestimated the energy requirements in obese patients.
Mizock (2)	1997	III	A review article discussing nutritional assessment and which patients received nutritional support.
Souba (4)	1997	III	A review article discussing the indications, monitoring and route of administration of nutritional support. Electrolytes should be monitored periodically.
Souba (6)	1997	III	An editorial which discussed the evaluation of the efficacy nutritional intervention.