NUTRITION

It is universally recognized that nutrition is an important component of medical care. Malnutrition is very common, present in at least 30% of hospitalized patients, and its presence or development is associated with worse clinical outcomes. Unfortunately, malnutrition is commonly under-recognized and de-prioritized in the acute care setting. This module will help the student recognize common signs of overall macronutrient (calories and protein) deficiencies, as well as physical manifestations of micronutrient deficiencies. Emphasis is placed on understanding the key components of the history and physical exam and common nutrition screening and assessment tools. A full detailed description of enteral and parenteral access follows to provide the student with a comprehensive understanding of these devices and common complications related to these devices. Next, the student is introduced to the different types of enteral formulas, with examples of how to tailor the exact formula to the needs of individual patients. A basic introduction to parenteral nutrition is provided. Finally, the module ends with a discussion of short bowel syndrome.

Physical Exam Signs of Protein-Calorie Malnutrition

Low body mass index (BMI)
Loss of muscle mass and subcutaneous fat, especially in the following areas: under the eyes, triceps, biceps, temple, clavicle, scapula, ribs, quadriceps, calf, interosseous muscle between thumb and index finger
Muscle weakness (especially hand-grip strength)
Peripheral edema
Hair loss
Temporal wasting

Most common signs of Vitamin, Mineral, and Trace Element deficiencies

Vitamin A – dermatitis, night blindness
Vitamin D – osteoporosis (bone demineralization) ➔ fractures with minimal trauma
Vitamin E – anemia (secondary to hemolysis and decreased RBC lifespan)
Vitamin K – easy bruising/bleeding
Vitamin C - scurvy
Vitamin B1 (thiamin) – Wernicke-Korsakoff syndrome, peripheral neuropathy
Vitamin B2 (riboflavin) – stomatitis, cheilosis, anemia
Vitamin B3 (niacin) – pellagra (dermatitis, diarrhea, and dementia)
Vitamin B6 – cheilosis, stomatitis, microcytic anemia
Vitamin B12 – macrocytic anemia, damage to spinal cord
Folate – macrocytic anemia
Iron – microcytic anemia; glossitis, brittle nails
Selenium – cardiomyopathy, weakness
Zinc – hair loss, dermatitis, altered taste

Nutritional Assessment

There is no single clinical sign or laboratory value that can provide an accurate and comprehensive picture of nutritional status. At minimum, a good nutritional assessment requires a thorough history and physical which may require help from the medical record or family members of the patient.

1. Historical Data

A. Weight History

Weight changes are an important part of the nutritional assessment. Specifically, it is critical to note if the weight changes were intentional, how much the weight changed, and over what time period the weight change occurred. Commonly, patients will not know exactly how much weight they have lost. Asking the patient about changes in how their clothes fit or changes in appetite or diet can provide clues.

B. Medical/Surgical History

Many acute and chronic medical conditions can alter metabolism and place patients at nutritional risk. Several acute conditions lead to an increased metabolic rate and decreased nutrient uptake along with poor utilization. Inflammation decreases the gastrointestinal tract’s ability to absorb nutrients and blunts the response to nutritional support interventions.

Acute conditions include sepsis, burns, trauma, and hemorrhage, among others. The commonality is that they all are associated with the systemic inflammatory response syndrome (SIRS).

Chronic conditions that affect nutrient absorption and utilization include diabetes mellitus, celiac disease, inflammatory bowel disease, pancreatitis, and chronic non-healing wounds. Patients may have congenital or surgical anatomical changes that lead to poor nutrient absorption. Fistulas, short bowel syndrome, ostomies, oropharyngeal disorders, poor dentition, esophageal disorders, or various oncologic conditions can interfere with nutrient uptake. Alcoholism places patients at risk for refeeding syndrome. Eating disorders, dietary practices, fad diets, over-the-counter supplements, social situations that lead to malnutrition, and restricted access to a good food source can also place a patient at risk for malnutrition.

C. Medication History

Some medications may affect metabolism and nutrient uptake. Therefore, when assessing a patient’s nutritional status, it is important to take a full medication history. Drug absorption and metabolism is also affected by nutrient uptake and association with mealtime.

D. Physical Exam

A thorough physical exam is a critical part of nutritional assessment. Temporal wasting and loss of tissue at high turnover areas - the hair, nails, and the mouth or gums - can indicate malnutrition. Note that obesity can exist simultaneously with malnutrition. It is important to understand that overweight individuals are usually *sarcopenic* and are at *increased* risk of malnutrition in the hospitalized setting. Vital signs that are consistent with malnutrition are fever or hypothermia, and tachycardia. These not only indicate severe malnutrition but also can indicate a higher metabolic demand necessitating more support. Grip strength is an excellent indicator of overall nutritional and functional status.

E. Anthropometric Data

Several body measurements can help us estimate nutritional needs and track nutrition over time.

1) Height

2) Body Weight

Actual body weight may not reflect actual nutritional needs if the patient is obese. Many calculations used to determine caloric needs are based on ideal body weight. Several methods exist to estimate ideal body weight based on gender and height. Caloric goals are based on adjusted body weight, which is between the actual and ideal body weight.

3) Body Mass Index (BMI)

Classically, BMI has been used to quantify nutritional status.

BMI = weight kg/height m^2
Underweight = <18.5
Normal weight = 18.5–24.9
Overweight = 25–29.9
Obesity = BMI of 30 or greater

F. Other Body Composition Assessment Tools

Several other methods are available that are better at assessing nutritional status and body composition. However, due to limited availability, they are not in widespread clinical use. Water displacement can be used to determine body fat percentage, as can impedance analysis. CT, MRI, and ultrasound looking at the relative size and density of the psoas and soleus muscles are also being used as a measure of lean muscle mass.

2. Laboratory Data

As with the rest of the nutritional assessment, lab values can assist with the initial assessment and can help monitor progress during therapy but are not an absolute indicator of nutritional status and should be interpreted with caution. Many nutritional markers are acute phase reactants and are altered by the inflammatory response. Albumin, prealbumin, transferrin, and retinol binding protein can be used to gauge and monitor a patient's response to therapy once out of the acute phase. Trends over time are the most useful. Transferrin and retinol binding protein (RBP) are mentioned in textbooks but are not used in clinical practice to diagnose malnutrition.

Protein	Half-life	Normal Range
Albumin	21 days	3.5-5.0 mg/dL
Prealbumin	2-3 days	18-38 mg/dL

A. Assessment of Adequacy of Nutrition Therapy

Several factors can be monitored over time to determine the adequacy of nutritional supplementation.

1) Nitrogen balance

As proteins and amino acids are metabolized, nitrogen is produced and excreted in the urine as urea. Nitrogen balance is calculated as follows:

Nitrogen balance = (protein/amino acid intake (g) / 6.25) - (urine urea nitrogen + 4)

A positive nitrogen balance indicates adequate protein intake, and anabolic metabolism. Nitrogen balance calculation requires 24-hour urine collection.

2) Calorie counts

For patients receiving an oral diet, calorie counting can provide a measure of the adequacy of nutritional intake. Typically, the total calories provided in a meal are known, and an estimate based on the fraction of the meal consumed is used to calculate the caloric intake. The total count, averaged over 2-3 days, can help determine if a patient requires additional supplementation via tube feeding.

3) Catabolism to anabolism

The switch from catabolism to anabolism is signaled by mobilization of fluid from the third space and an increase in serum protein values and positive nitrogen balance.

Nutrition Screening and Assessment Tools

In addition to the history and physical, laboratory and anthropometric measurements, several scoring tools have been developed and validated to assess nutritional risk. The Nutritional Risk in the Critically Ill (NUTRIC) Score uses the patient's age, SOFA (sequential organ failure assessment) and APACHE II (acute physiology and chronic health evaluation) scores, comorbidities, length of hospital stay, and IL-6 level to stratify patients into high and low risk categories. The Nutrition Risk Screening 2002 (NRS) tool uses the nutritional history and severity of illness to stratify patients. These scoring systems have been validated and are recommended by the several nutritional guidelines are part of the nutritional assessment.

Nutrition to prevent complications:

Understand the importance of nutrition in preventing surgical complications
After surgery or trauma, the cytokine release and metabolic stress response force the body from an anabolic to a catabolic state. The inflammatory response to injury, indicated by the SIRS response with tachycardia, hyperthermia, elevated white blood cell count, and tachypnea, increases the metabolic stress in a fashion that is proportional to the severity of injury. The body switches to catabolism of skeletal muscle, fat, and glycogen to produce free fatty acids, glucose, and amino acids needed to keep up with the metabolic demands of the stress response. This leads to loss of lean muscle mass, which interferes with functional status outcomes after recovery. Additionally, as the healing process starts, inadequate nutrition can impair wound healing and recovery, and increase the risk of surgical site infection or other postoperative complications. Patients with significant comorbidities like diabetes, cardiopulmonary failure, cancer, or other chronic inflammatory syndromes are at additional risk of developing postoperative complications due to malnutrition.

How and when to adequately prepare patients nutritionally for surgery
Patients can be identified to be at increased risk of developing postoperative complications and delayed wound healing as a result of malnutrition by using the same nutritional assessment and screening tools outlined previously. Patients at increased risk include those who are purely malnourished due to poor diet, as well as those with previously good nutritional status but that also have a chronic inflammatory condition or cancer. These patients should undergo nutritional evaluation and optimization before surgery, if possible.

Patients identified prior to surgery to be at increased nutritional risk should have nutritional recommendations developed and instituted by a clinical dietitian. These interventions may range from "prehabilitation" diet and exercise in mild cases to admission to the hospital for full nutritional support via enteral nutrition (EN) or in extreme cases, parenteral nutrition (PN).

Options for Enteral Access

1. Device Selection

Several options exist for providing access for enteral nutrition (EN) support. The primary decision is whether the patient will require short-term support via a nasoenteric tube versus long-term feeding access via a percutaneous tube. If therapy is predicted to last less than 4 weeks, the nasoenteral route is appropriate. If longer support is anticipated, the clinician should consider offering a procedure for feeding tube placement, as a nasoenteral tube left in the nasal passage for a longer period can lead to sinus infection and skin necrosis at the nare. Nasoenteral tubes are also much longer and more predisposed to clogging and dislodgement, prompting the need for replacement. Nasoenteral tubes can be placed blindly, endoscopically, or radiographically. Feeding tubes can be gastric, jejunal, or gastrojejunal.

2. Tube Selection

A. Tube types

Nasogastric tubes come in a wide variety of sizes. Large-bore (18 French) tubes are typically used for decompression, feeding, and medication administration. Smaller-bore Dobhoff (8-12F) tubes can be placed if the patient has no need for drainage or decompression. These are more comfortable but are more prone to clogging due to the small inner diameter. These tubes use a stylet for placement that has hydrophilic coating that helps with removal. Weights at the bottom theoretically help with advancement into the pylorus for post-pyloric feeding. They are equipped with multiple ports for medication administration along with tube feeds.

Percutaneously placed tubes have a bolster at the distal tip, either a water-filled balloon or solid silicone. Which bolster is used usually depends on the method used for tube placement. Solid bolsters provide better longevity, however balloon-tipped tubes are generally easier to place and are used to replace dislodged tube.

B. Methods of access

1) Nasal tubes

Nasogastric tubes can be placed nasally or orally in an unconscious intubated patient. The appropriate length for insertion can be estimated by placing the tip of the tube at the patient’s xiphoid process, running the tube behind the ear and to the tip of the nose. This length is typically between 50-60 cm. Lubrication should be used. Tube placement can be facilitated by having the patient swallow air or a sip of water during placement, and by tilting the patient’s head forward. Tube placement for feeding must be confirmed radiographically prior to use to avoid the devastating consequences of initiating feeds using a tube that is misplaced in the airway. Proper verification on chest radiograph shows tube coursing in the midline with the tip below the diaphragm.

For placement of nasoduodenal or nasojejunal tubes, several techniques have been described to increase likelihood of passage of the tube past the pylorus. These include rotating the patient onto the right side, insufflating air to distend the stomach, and administering prokinetic medications.

2) **Enterostomy tubes**
Prior to placement of any surgically placed tube, a surgical history should be obtained, and knowledge of the anatomy must be known. Tubes can be placed endoscopically, using fluoroscopic techniques, or open or laparoscopically in the operating room.

3) Gastrostomy tubes (G-tube)
Gastrostomy tubes can be placed under fluoroscopic guidance, using simultaneous endoscopy, or surgically in the operating room. Percutaneous endoscopic gastrostomy (PEG) is most common. A PEG is a procedure that can be done at the bedside in the ICU or in an endoscopy suite. Contraindications include inability to transilluminate the abdominal wall with the endoscope placed in the stomach, ascites, esophageal obstruction, head and neck cancer, coagulopathy, gastric varices, or gastric ulcer disease.

Fluoroscopic techniques are performed by Interventional Radiologists. Since these procedures do not involve endoscopy, these can be performed under local analgesia with light sedation.

Lastly, gastrostomy tubes can be placed in the OR, either laparoscopically or open. These options are especially well suited for patients whose PEG procedure was aborted, or for patients who have had prior abdominal surgery with unknown or difficult current anatomy.

4) Gastrojejunal (GJ) tubes
When gastric decompression is also necessary, i.e., in pancreatitis, gastric outlet, or motility issues, a GJ tube may be desired. In this case, the tube can be placed using an existing gastrostomy or via a new procedure. The tube can be placed with endoscopic assistance, under fluoroscopy, or in the operating room. The patient benefits from enteral nutrition while draining the stomach in cases where the patient may still vomit or be a high aspiration risk.

5) Jejunostomy (J) tubes
A tube can be placed directly into the jejunum for feeding. This is typically performed surgically (open or laparoscopic), but endoscopic and percutaneous techniques have been described. Decompression is not possible with a jejunal tube.

3. Complications of Enteral Access

Complications for nasoenteric tubes include vomiting on insertion which can lead to aspiration or misplacement into the airway which can lead to pneumothorax. To minimize these risks, tube placement should be confirmed by chest X-ray. Long-term complications include ischemic necrosis or ulceration of the nare, sinusitis, malfunction of the tube, and unplanned removal of the tube. Bridles can be used to minimize the risk of accidental removal.

Complications of percutaneous enterostomy tubes are leakage, chronic skin and abdominal wall wounds, infection, buried bumper syndrome, and accidental removal. Jejunostomy tubes can cause internal hernia or volvulus.

Options for Parenteral Access

Higher blood flow is needed to administer hyperosmolar fluids to prevent thrombophlebitis. Therefore, parenteral nutrition requires central vein access.

1. Types of Access

Access type describes where the distal catheter tip is, not the insertion site.

A. Peripheral venous access

Peripheral venous access for lower osmolarity formulas is provided via a standard angiocatheter. These are capable of delivering formulas with osmolarity below 900 mOsm/L; formulas above that concentration can cause damage to the veins. Peripheral angiocatheters can cause thrombophlebitis, noted by pain, erythema, redness, or palpable cord. This finding necessitates urgent removal. Midline catheters provide similar access with a 20-25 cm catheter that is inserted in the larger veins of the arm with a distal tip that sits in the axillary vein. These are limited to delivering the same medications and subject to the same osmolarity limit but can stay in for up to 6 weeks.

B. Central access

For central venous catheters, the catheter tip lies in the SVC or right atrium. Insertion sites are in jugular, subclavian, femoral veins for standard multilumen catheters. Nontunneled peripherally inserted central catheters (PICC) are placed via a peripheral vein in the arm, i.e., the cephalic or basilic vein. These have the benefit of being able to stay in for several months, but have the disadvantages of being difficult for the patient to care for at home (only one free hand to manage the care and dressing). Additionally, extra consideration should be given in patients with renal failure, as long-term indwelling catheters can cause sclerosis of the veins and can compromise the function of vessels that would be used for dialysis access.

Traditional multi-lumen central venous catheters (“central line”) placed in the ICU, Emergency Department (ED), or operating room (OR) have the advantage of multiple ports. Critically ill patients may require access for other medications or for hemodynamic monitoring. These catheters are placed at the bedside with ultrasound guidance in the jugular or femoral veins, or by using anatomical landmarks for cannulation of the subclavian vein. Complications include pneumothorax, air embolism, hematoma, and bleeding. The primary long-term complication is catheter-associated blood stream infection (CLABSI).

Other options for central access are tunneled catheters, which separate the site of skin insertion from the vein. These usually have a cuff of fibrous material that produces an inflammatory response; the subsequent scarring secures the catheter in place. These catheters have a lower infection rate than non-tunneled catheters, but the infection risk is still significant and removal in the case of an infected catheter requires a minor surgical procedure under local anesthesia. They can be used for months to years with good care, just like dialysis catheters.

Lastly, there are implantable port devices used for chemotherapy that have an injectable port placed directly below the skin. These carry a lower risk of infection and are much more convenient and cosmetic. Non-coring needles can be used 100-200 times with a self-sealing silicone port. Ports are typical for intermittent central access needs, as in chemotherapy administration, and are not generally recommended for TPN infusion.

2. Device Selection and Patient Assessment

Device selection mostly depends on duration of therapy and setting. Shorter therapy in the ICU usually calls for a standard central line or PICC. Longer access requires a PICC for home use. Prior to any insertion procedure, a history and physical with specific consideration of any previous cannulation procedures should be performed.

3. Indications for Enteral or Parenteral Supplementation

The main goals of nutritional support of the surgical patient have been clearly defined by the Society of Critical Care Medicine (SCCM) and the American Society for Parental and Enteral Nutrition (ASPEN). These goals include the nutritional support for the preservation of lean body mass and immune function while preventing associated metabolic complications.

In order to determine which type of nutritional support is indicated for the surgical patient, it is necessary to determine the patient’s tolerance of either enteral or parenteral nutrition, the indications for enteral versus parenteral nutrition, as well as the patient’s overall clinical picture and the planned timing of nutritional support intervention.

There is a large body of literature describing the associated increases in overall morbidity and mortality when postoperative patients are subjected to prolonged periods of starvation.

The first step in selecting the type of nutritional support begins with the assessment of the patient's ability to tolerate enteral support: Can the patient eat by mouth? Can the patient tolerate enteral feeds, either gastric or small bowel? Are there postoperative considerations for prolonged starvation like significant metabolic and physiologic derangements? What was the preoperative nutritional state of the patient? The simplest way to decide is the old adage, "if the gut works, use it".

Once it has been determined that a patient can tolerate enteral feeding, the scientific evidence is clear: Early enteral nutrition (EN) is the preferred route over parenteral nutrition (PN). The benefits of EN when compared to PN include: no requirement for central venous access, prevention of gut mucosal atrophy, and reduced cost. EN is considered early when feeding is initiated within the first 24 to 48 hours postoperatively or after ICU admission.

Currently, accepted indications for PN include: intolerance of enteral feeding, inadequate EN support (as defined by EN achieving <80% of the 24 hour caloric goal for several days), pre-procedural nutritional support in malnourished patients, and in those patients with intestinal failure.

The timing of when to begin PN is controversial within the literature and in clinical practice. Multiple professional society guidelines have attempted to codify when to initiate PN. What is clear within the guidelines and literature is that the benefit of PN is most pronounced when the patient is either nutritionally deficient pre-procedure or has an extended period of post-procedural starvation, either due to disease process or EN intolerance. Guidelines set forth by SCCM, ASPEN and European Society for Clinical Nutrition and Metabolism (ESPEN) all recommend initiation of PN if the patient has been or will be intolerant of EN for 7 days or more, or if the patient is malnourished pre-procedure and able to undergo PN support for 7-10 days before an elective procedure.

Basic Enteric Formulations:

Enteral formulas come in multiple concentrations and preparations, often with specific diseases in mind when formulated. Selection of the formula for use can be simplified as long as one keeps in mind the protein requirements and the caloric needs of the patient. Additional factors in the consideration of EN formula prescription are current disease state and associated comorbidities, electrolyte and additional metabolic derangements, ability to tolerate, digest and absorb the specific formula and overall inflammatory state. The basic formula types include polymeric (standard), elemental and semi-elemental (predigested), blenderized, and specialty (disease-specific and modular).

Polymeric or standard formulas are designed to meet the needs of a healthy patient. Their nutrients are fixed and calorie densities (kilocalorie concentrations) are variable, thereby allowing for fluctuations in water content. Kilocalorie density can range from 1.0 kcal/mL to 2.0 kcal/mL. The concentrations and sources of carbohydrates, fat, and protein are varied by specific formulations as is the presence or absence of fiber. The fiber sources can be further divided into soluble or insoluble.

Elemental and semi-elemental formulas are designed for patients with decreased absorptive and digestive capacity, e.g., active inflammatory bowel disease, radiation enteritis, or short bowel syndrome. These patients require pre-digested nutrient components which require less enzymatic activity. The proteins in these formulas have been prepared in a fashion such that the carbohydrates and amino acids are free (predigested) and much more easily absorbed. Additional nomenclature for these formulas include hydrolyzed or partially hydrolyzed formulas. These formulas are much more expensive than polymeric formulas and also less palatable to drink.

Specialty formulas include disease-specific and modular/immune modulating formulas (IMF). These formulas are designed for specific clinical entities and scenarios in which nutritional support must be tailored. Disease-specific formulas include formulas specifically designed for renal failure, liver failure, and diabetic patients, as well as specific clinical conditions such as acute respiratory distress syndrome (ARDS). The diabetic formulas contain lower carbohydrates and higher fat concentrations, whereas the specialty renal failure formulas have modified electrolyte concentrations (especially potassium and phosphorus). For liver failure patients, the formulas have elevated concentrations of branched chain amino acids and reduced concentrations of aromatic amino acids and sodium. IMF formulas were developed to augment or alter a patient’s inflammatory disease process. Much of the work regarding IMF was conducted with specific focus on trauma, surgical and septic patients. They included additional supplementation with substances such as glutamine, arginine, antioxidant micronutrients, and omega-3 polyunsaturated fats. While immunomodulation with EN was once a standard practice, the true efficacy of its use is unclear. There have been multiple meta-analysis and randomized control trials evaluating the use and the results have been mixed. Updated societal guidelines are changing and there appears to be an increased risk of mortality with IMF use.

Note that all commercially available tube feeding formulas (“medical food”) are Kosher, Hallal, lactose-free, and gluten-free.

Blenderized diets are, in essence, the original EN formulas. They were concocted in hospital kitchen by blending foods into a liquid which could then be delivered enterally. As nutritional support improved and EN formulas were specifically designed to meet the metabolic demands of the patients, this type of tube feeding had waned in use. Recently, however, there has been a resurgence of interest in these “home-made formulas”. Factors that must be considered when planning for blenderized diets include: patient’s ability to tolerate bolus feedings, stable weight and tolerance of commercially available formulas, adequate support system, and financial means.

Selection of Appropriate Formula:

Prescription of EN formula requires not only an understanding of the basics of nutritional support, such as timing of therapy, components of formulas, and EN route selection but most importantly, the metabolic demands of the patient. These metabolic demands are dictated by several factors including patient pre-hospital nutritional status, anthropomorphic characteristics, and changes in metabolism due to surgery, injury, and comorbidities, as well as conditions such as respiratory failure requiring mechanical ventilation, burns, spinal cord injuries, and obesity.

As previously discussed, the keys to selection of an EN formula begins with focus on meeting the caloric and protein needs. Understanding the metabolic and nutritional needs of the patient will guide EN formula selection. All patients undergoing surgery, post trauma or burn require increased amounts of energy; hence these patients require an increase in kilocalories as compared to the non-stressed healthy adult. Secondly, assessment for any additional nutritional support is required: what alterations to the GI tract have occurred? Is there evidence or suspicion for malabsorption?

Examples:

25-year-old man with a traumatic brain injury (TBI), respiratory failure requiring mechanical ventilation after a motor vehicle crash 24 hours prior. He has an intact GI tract and was in usual state of health (no preexisting malnutrition).

- EN formula selection for this patient would begin with a standard polymeric formula without the need for any supplementation. Goal nutritional support would be calculated by standard equations with slight correction for mechanical ventilation and TBI.

55-year-old woman status post esophagectomy for cancer with preceding 3 month history of 25 lb. unintentional weight loss and history of alcohol abuse. Intraoperatively a feeding jejunostomy tube was placed. Previously she underwent several small bowel resections for inflammatory bowel disease.

- This patient is clearly malnourished; not only from prior weight loss, but also the history of chronic alcohol abuse increases the risk of malnutrition. Given these components, she needs an EN formula with increased kcal density for the increased energy requirements. Further, use of an elemental or semi-elemental formula would be beneficial given the history of multiple bowel resections and deceased absorptive capacity secondary to inflammatory bowel disease.

40-year-old man admitted for liver failure due to chronic alcohol abuse who is intubated and has worsening oliguric acute kidney injury.

- The patient likely has preexisting malnutrition and increased metabolic demands due to renal failure and respiratory failure. This patient would require a concentrated formula with low potassium and phosphorus (i.e. renal-specific formula).

Initial PN Prescription (volume, carbohydrates, protein, lipids):

When initiating PN, one should make every effort to obtain an accurate *current body weight (CBW).* Using height and sex, one should also calculate the *ideal body weight (IBW)*. Finally, if the patient is obese, you should calculate the *adjusted body weight (ABW)*. ABW is calculated by subtracting the IBW from the CBW and dividing that value by 3 and then subsequently adding to the IBW. Feeding an overweight individual according to the IBW will result in underfeeding, while feeding an overweight individual according to the CBW will result in overfeeding because the excess weight is mostly adipose tissue and is metabolically inactive. As a general rule, if the patient is underweight (i.e., CBW is less than IBW), use the CBW in your calculations. If the patient is close to the IBW, use IBW in your calculations. If the patient is obese (more than 10 kg above IBW), then use the ABW in your calculations. Before initiating PN, it is important to measure a baseline triglyceride level and liver function panel. Thereafter, weekly monitoring is recommended.

To begin PN support, you must decide upon amount of volume, calories, protein, and lipids to provide.

- Volume
  - Initial starting volume: 30-40 cc/kg/day (actual body weight)
  - Must take into consideration other sources of volume (e.g., sedative infusions, medication carrier volume, oral/enteral intake). Be careful not to fluid overload.
  - Adjust daily as needed to maintain relatively even fluid balance, accounting for daily insensible losses

- Energy (Calories)
  - Total caloric prescription can be calculated using Harris-Benedict equation or estimated as 25-30 kcal/kg/day

- Protein
  - Healthy, non-stressed adult: 1.0 g/kg/day
  - Stressed or malnourished adult: 1.5 g/kg/day
  - Stressed ***<u>and</u>*** malnourished adults: 2.0 g/kg/day
  - Even higher protein prescriptions (2.5 or even 3.0 g/kg/day) have been used for extremely catabolic patients (e.g., major burns, aggressive abdominal tumors, etc.)

- Lipids
  - An excellent source of calories, but lipid calories cannot comprise more than 30% of total daily calories (because of damage to the liver)

- Electrolytes
  - The daily sodium requirement is approximately 1-2 mEq/kg per day
  - The daily potassium requirement is approximately 0.5-1 mEq/kg per day

Common Complications of PN in the Short-term and Long-term:

Refeeding syndrome – was first described in cases of extreme starvation with World War II concentration camp survivors who were treated with extreme hyperalimentation (i.e., 75 kcal/kg/d). The full-blown syndrome includes cardiopulmonary failure, seizures, encephalopathy, and coma. Several electrolyte deficiencies may be seen, including hypomagnesemia, hypokalemia, hyponatremia, and hypocalcemia, though hypophosphatemia is nearly universal in true cases of refeeding syndrome. It is believed that the carbohydrate (dextrose) component in the PN is the culprit, as protein and lipid infusions have not been found to precipitate this syndrome. In the modern era, more moderate caloric prescriptions are standard and the full-blown refeeding syndrome is rarely encountered. However, refeeding hypophosphatemia is commonly encountered and should be aggressively treated with replacement.

Short-term:
Hyperglycemia is the most common complication. When initiating PN, the patient's blood glucose should be monitored at minimum every 4 hours until a stable trend has emerged. Elevated glucose values (>200) should be treated initially with sliding scale insulin (subcutaneous injection). For persistent insulin requirements over several days, you can begin to mix insulin directly into the PN. Practically speaking, it is prudent to only add 1/3 to 1/2 of the previous day's subcutaneous insulin requirements into the PN bag to avoid the risk of hypoglycemia.

Other short-term complications are usually related to the central access: central-line associated bloodstream infection and catheter-related thrombosis.

Long-term:
Parenteral nutrition-associated liver disease (PNALD) - PNALD is the end result of steatosis and liver dysfunction ultimately culminating in liver failure. This disease is mainly seen in neonates and children, but may manifest in adults after many years of PN support. Hyperbilirubinemia (direct bilirubin >2.0) is most suggestive, but definitive diagnosis is only achieved with liver biopsy. The two culprits that are implicated in development of PNALD are carbohydrates and phytoesterols. Chronic dextrose overfeeding has been shown to deposit into the liver as fat, leading to steatosis. Therefore, current recommendations are to limit carbohydrates to less than 7 g/kg/day. Additionally, recommendations are to try to "cycle" the PN to less than 24 h per day to avoid continuous exposure of the liver to glucose infusion. For chronic PN patients who are also able to tolerate some (but not enough) oral/enteral intake, one could consider alternating days off/on PN.

Phytoesterols are plant-based compounds (analogous to cholesterol in animals) which have been implicated in the development of PNALD. Up until recently, in the United States, the only type of intravenous lipid emulsion (IVLE) was 100% derived from soy.

Soy-based IVLE contain the two essential fatty acids (linoleic acid and alpha-linolenic acid) and thus you must provide at least *some* soy-based IVLE. However, with the essential fatty acids (EFAs) come phytoesterols and the risk of long-term liver damage. In 2016, a mixed lipid emulsion became available. This new IVLE (SMOFlipid®) contains soy, medium chain, olive oil, and fish oil. Preliminary studies in mostly neonates have demonstrated lower incidence of PNALD, and this option is now available to prevent or treat PNALD, though the evidence of benefit in adults is still forthcoming.

Metabolic bone disease - osteoporosis and osteomalacia have been reported in long-term PN patients and the incidence is as high as 50% after 6 months of PN therapy. These patients are at increased risk of fractures. Screening using bone mineral density measurements is recommended and, if diagnosed, supplementation with vitamin D and calcium should be initiated.

Special Considerations

1. Short Bowel Syndrome (SBS)

Traditionally, short bowel syndrome (SBS) has been defined as less than 200 cm of remaining small bowel. However, this length is arbitrary and many patients have been successfully “cured” of SBS through a process of intestinal rehabilitation. The majority of SBS cases are a result of extensive surgical resection and the remaining bowel may have three configurations: end-jejunostomy (with no colon in continuity), jejunocolic anastomosis with no ileocecal valve but part of the colon in continuity, and jejunoileal anastomosis with both ileocecal valve and colon in continuity.

A related diagnosis is *intestinal failure* (IF), which is defined as “the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth.” IF may be divided into three types according to duration. *Type 1* is short-term and self-limiting, usually in the postoperative period in the setting of ileus. *Type 2* is more prolonged and often lasts for weeks to months. *Type 3* is a chronic condition lasting months to years (or lifelong).

The cause of SBS is nearly always extensive small bowel resection for various reasons such as Crohn’s Disease, mesenteric ischemia, trauma, and radiation enteritis. Patients may exhibit the syndrome (with intestinal failure) while having >200 cm of remaining bowel because the remaining bowel is of poor quality and unable to function normally.

Intestinal adaptation generally occurs in the first 2-3 years after surgery and includes microscopic and macroscopic changes which ultimately result in increased fluid and nutrition absorption. Adaptive changes include increases in villi height, crypt depth, and enterocyte mass, as well as changes in intestinal motility and size. Luminal nutrients have been shown to stimulate the adaptive process and thus resuming tube feeding or oral intake is important once the acute fluid/electrolyte imbalances have been corrected.

Symptoms and Complications of SBS

The symptoms and complications of SBS are those related to fluid, electrolyte, macronutrient, and micronutrient deficiencies. Thus, patients may have signs of dehydration, electrolyte deficiencies, and physical manifestations of malnutrition and trace element/mineral deficiencies. (See section above).

Complications may be divided into:

Malabsorption-related:

Fluids and electrolytes: dehydration secondary to excessive diarrhea or ostomy output, electrolyte imbalances (especially sodium, potassium, magnesium, and phosphorus)

Nutrition:

Macronutrients: calories, protein, lipids (i.e., essential fatty acid deficiency)
If the patient is unable to meet the nutrition requirements through some combination of oral, enteral, and parenteral nutrition, catabolism will ensue, and the patient will lose weight in the form of adipose tissue and skeletal muscle loss. (See the above section for signs of malnutrition.)

Micronutrients:

Fat-soluble: vitamin A, vitamin D, vitamin E, vitamin K
Essential fatty acid deficiency
Water-soluble: vitamin C, vitamin B1, vitamin B2, vitamin B6, vitamin B12, folate
Trace elements: zinc, selenium

Medical treatment of SBS

Medical treatment of SBS may be divided into antimotility agents (loperamide, diophenoxylate/ atropine), anti-secretory agents (proton pump inhibitors, octreotide), and medications to promote intestinal adaptation (teduglutide). Teduglutide is a long-acting analog of glucagon-like peptide 2 (GLP-2) which was recently approved by the FDA after Phase 3 studies demonstrated significant improvement in liberation from TPN and improved quality of life. Because teduglutide induces intestinal growth, its use is discouraged for patients with known gastrointestinal malignancy as it may enhance neoplastic spread.

Surgical treatment of SBS

Surgical treatments for SBS have been described but have not been well-studied in high quality trials. For patients with an enterocutaneous fistula, resection of the fistula with primary anastomosis of the bowel may cure the SBS if the overall remaining length and quality is sufficient to maintain health and hydration.

For patients with rapid transit and short intestinal length, reversing a segment of intestine (such that peristalsis of the reversed segment is retrograde) has been described to increase the contact time and improve nutrient absorption. Bowel lengthening procedures such as the Kimura, Bianchi, and STEP (serial transverse enteroplasty) procedures have been described but are seldom performed. For patients with dilated intestine (resulting in poor contractility), intestinal tapering or plication may be considered to reduce the size and improve motility.

Intestinal transplantation is increasingly performed for SBS, especially when concomitant liver failure (from chronic parenteral nutrition use) is present. For appropriately selected patients, graft survival is high and patient survival after intestinal transplant exceeds the natural history of SBS at that point.

Questions

1. A 40-year-old polytrauma patient has been hospitalized in the Trauma ICU after being struck by a passenger vehicle. He was reported to be homeless with an unclear medical history other than multiple prior ER visits for acute alcohol intoxication. He remains mechanically ventilated and has been unable to tolerate tube feedings because of elevated gastric residual volumes and emesis. After 7 days, the ICU team decides to start him on total parenteral nutrition (TPN). After several days, he develops frequent premature ventricular contractions and displays increased work of breathing. His daily laboratory studies show a precipitous decrease in his potassium, phosphorus, and magnesium levels.

   What is the most likely diagnosis?

   What therapy or treatment would you recommend?

2. You have been asked to evaluate a patient who is planned to undergo pancreatico-duedonectomy (Whipple Procedure) for an obstructing pancreatic mass. The patient reports an unintentional 30-pound weight loss during the preceding 3 months.

   What further data should be obtained from the patient's history?

   What physical exam findings would you look for?

   What is your differential diagnosis?

   What work-up would you recommend?

   What therapy or treatment would you recommend?

Answers

1. A 40-year-old polytrauma patient has been hospitalized in the Trauma ICU after being struck by a passenger vehicle. He was reported to be homeless with an unclear medical history other than multiple prior ER visits for acute alcohol intoxication. He remains mechanically ventilated and has been unable to tolerate tube feedings because of elevated gastric residual volumes and emesis. After 7 days, the ICU team decides to start him on total parenteral nutrition (TPN). After several days, he develops frequent premature ventricular contractions and displays increased work of breathing. His daily laboratory studies show a precipitous decrease in his potassium, phosphorus, and magnesium levels.

    What is the most likely diagnosis?

    Refeeding syndrome caused by overly aggressive carbohydrate administration in a chronically malnourished patient.

    What therapy or treatment would you recommend?

    Aggressively treat the electrolyte imbalances (hypokalemia, hypomagnesemia, and hypophosphatemia) and decrease the carbohydrate in the TPN. Protein and lipid calories may be increased in compensation.

2. You have been asked to evaluate a patient who is planned to undergo pancreatico-duedonectomy (Whipple Procedure) for an obstructing pancreatic mass. The patient reports an unintentional 30-pound weight loss during the preceding 3 months.

    What further data should be obtained from the patient's history?

    When confronted with a patient experiencing unintentional weight loss, it is important to obtain a thorough dietary history, including frequency and size of meals, as well as types of food the patient usually eats and types of food the patient avoids. If the patient has voluntary dietary restrictions (e.g., vegetarian, lactose-free, etc.), it is helpful to understand the exact reason. That is, some may follow religious instructions (e.g., avoiding all pork) whereas others may have medical allergies, and others may have misconceptions about the harms of certain types of food (e.g., gluten). For the latter group, dietary counseling and patient education may convince the patient to loosen his/her dietary restriction and improve your ability to treat malnutrition without artificial nutrition therapy.

    It is also important to obtain a detailed history of the patient's bowel habits, including the frequency, caliber, consistency, and color of bowel movements.

Not all patients have regular soft, daily, brown, formed bowel movements at baseline. If the patient's stool habits are currently different from their baseline, it may be indicative of a GI motility issue or malabsorption. Thus, nutrient intake may not be the problem, but rather nutrient uptake.

What physical exam findings would you look for?

Common physical exam findings of overall macronutrient (calories and protein) deficiency include temporal muscle wasting; loss of normal buccal fat pad; loss of subcutaneous fat resulting in abnormally prominent neck musculature, clavicles, ribs; thenar muscle wasting; fragile and thin skin; brittle hair and nails. Severe malnutrition resulting in hypoalbuminemia can manifest as bilateral lower extremity edema and ascites.

What is your differential diagnosis?

Malnutrition in this patient can be a result of either inadequate oral intake or malabsorption. Inadequate oral intake may be due to nausea (for example, secondary to chemotherapy), anorexia secondary to cancer cachexia, early satiety due to extrinsic compression of the stomach, or gastric outlet obstruction due to the mass itself. Because of the pancreatic insufficiency secondary to an obstructing pancreatic mass, the patient is assumed to have some degree of fat malabsorption. This may be inferred from a history of pale colored stools and steatorrhea. Even without pancreatic duct obstruction, patients may experience exocrine pancreatic insufficiency if the secretion of digestive enzymes is mistimed with food intake.

What work-up would you recommend?

A food and stool journal would be the first step to work-up the cause of the malnutrition. Traditional biomarkers of nutrition such as albumin and transthyretin (also known as prealbumin) are commonly ordered and trended, but it is important to also concomitantly measure inflammation with C-reactive protein (CRP) to properly interpret the trends. This patient may also have micronutrient deficiencies, so a full vitamin and trace element panel is recommended: vitamin A, D, E, K (if concerns about bleeding diathesis), C, B1, B2, B6, B7, B9, B12, zinc, selenium, copper, and essential fatty acid panel.

Additional work-up includes a 24-hour urine collection to calculate the nitrogen balance, and indirect calorimetry to measure the resting energy expenditure (REE). The usual caloric prescriptions are either weight-based (e.g., 25 *kcal/kg/day) or equation-based (e.g., Harris-Benedict equation). However, in patients with cancer, their actual metabolic requirements may be much higher.*

What therapy or treatment would you recommend?

The nutritional intervention will depend upon the urgency of operative intervention. In some cases, the surgeon is eager to excise the tumor while it is still locally contained and potentially curable. Waiting too long will risk metastatic spread of the cancer during the interval that you are trying to "optimize" the patient for surgery. Strong evidence supports pre-operative TPN in malnourished patients undergoing elective GI procedures, as in this case example. However, if there is no plan to operate within the next month or two, TPN may not be the best option.

If the patient is able to eat normally and has normal bowel movements, then it is appropriate to prescribe supplemental oral nutritional supplements (ONS) such as Boost® or Ensure® as well as modular protein supplements. If the patient is absorbing properly, weight gain should proceed at a rate of approximately 0.5 to 1 kg per week. If there are concerns about pancreatic insufficiency, the patient may be prescribed pancreatic enzyme replacements to be ingested with meals and snacks.

If the patient is unable to eat normally due to gastric outlet obstruction, anorexia, or early satiety, then placement of a post-pyloric feeding tube is indicated. In this case, it is presumed that the rest of the gastrointestinal tract distal to the duodenum is intact and normal. Initially, a nasojejunal feeding tube may be inserted and the patient is assessed for tolerance. If the patient is able to tolerate jejunal feedings and has a positive response, then the nasojejunal tube may be converted to a percutaneous jejunal tube (either direct jejunal or transgastric). In these patients, if they demonstrate evidence of intolerance to standard polymeric enteral formulas, then it is appropriate to change to an elemental or semi-elemental enteral formula.

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