[MUSIC PLAYING]

ELISABETH KRAMER: I'm one of the new g.I. attendants. I just started here in August. And I specialize in nutrition. And I'm on the Inpatient Nutrition Support Service here at Presby. So I thought it was fitting that I was asked to give this talk to you all where I did my residency. The Nutrition Support Service was actually run by the endochronology division. So I hope by the end of this talk you have some idea of what goes into determining which patients are eligible for specialized nutrition support, how we decide between parenteral and enteral nutrition, get a general sense of what goes into a parenteral nutrition formulation, and some of the complications of parenteral nutrition.

So malnutrition is an important and under-recognized problem in the hospital. The prevalence is estimated to be as high as 30% to 50% of hospitalized patients. It's associated with poor wound healing, compromised immunity, impairment of organ functions, and increased mortality. And poor recognition and treatment of malnutrition is closely linked to a general lack of practitioner awareness and training. So this is from a study from *The New England Journal of Medicine* in 1991. IT looked at the effect of malnutrition on post-op complications.

They studied 395 malnourished patients undergoing laparotomy or non-cardiac thoracotomy. And based on comprehensive nutrition assessments, patients were classified as having either borderline, mild, or severe malnutrition. And as you can see from this chart, the rates of complications, especially noninfectious complications, which included wound dehiscence, anastomotic leaks, decubitus ulcers, GI complications, and renal failure among others were significantly higher in the severely malnourished patients.

So because there is no single clinical or lab indicator of comprehensive nutritional status, an assessment requires collection of information from a variety of sources, including history, physical exam, anthropometric data, lab indicators, and dietary factors. So in terms of the history, one of the most important historical elements is prior weight loss, including volitional weight reduction. So we ask about usual weight, peak weight, and deliberate weight loss. And generally, a 10-pound weight loss over a six-month time period is noteworthy.

A weight loss of 10% of usual body weight is prognostic of clinical outcomes. Many medical and surgical diagnoses and their associated interventions impact inflammatory and nutritional status, and they're often associated with characteristic malnutrition syndromes. And these diagnoses include critical illness, severe burns, major abdominal surgery, severe GI Bleeds, pancreatitis, IBD, enclosed head injury, among others.

So anthropometric measures, like height, weight, and BMI are relatively simple physical measurements that can provide an indirect assessment of body size and composition. BMI is very important. A BMI of less than 18.5 is generally felt to be screening for malnutrition based on NIH guidelines and a BMI of less than 15 is associated with mortality. So there are also several. And then we can measure skin folds, skin circumferences, which can be helpful. But unfortunately due to lack of proper training, It's hard to actually do that.

So in terms of lab indicators, unfortunately, there is no single lab that can diagnose somebody with malnutrition. And in the hospital, we frequently get called frantically that somebody has a low albumin or pre-albumin. And while these levels are very important in assessing malnutrition, there are limitations in just using them in a vacuum. They are also lowered in several disease states and inflammation, which is significant in our patient population. So it can be helpful to get a c-reactive protein, which can put things in perspective. And you can see the degree of inflammation that's present.

Electrolytes can be helpful to monitor for over or under hydration. The BUN is low in decrease cell mass. And looking at the CBCN differential, there are numerous nutritional deficiencies associated with anemias, like iron deficiency, foliate and b-12 deficiencies. Lymphopenias are associated with malnutrition. And thrombocytopenia can be seen in vitamin C deficiency and foliate deficiencies. PTINR is an indirect measure of vitamin K status.

And then micronutrient panels, just several different nutrients that can be sent in patients that you suspect of having malnutrition syndrome. And we generally send this on most of the patients that we see in the hospital prior to starting parenteral nutrition. So multi-item screening and assessment instruments have been developed as indicators of nutritional risk because no single measures have validity for this purpose. Global assessment tools should be used as part of the standard nutrition screening to identify at at-risk malnourished patients.

The most widely accepted of these is the subjective global assessment, which takes into account multiple nutrition-related factors, including functional status, dietary factors, multiple g-I symptoms, weight loss, and physical exam. And the components are combined to obtain an SGA rating, ranging from well-nourished to severely malnourished. So in an ideal world, we use this assessment. In the real world, we don't. We generally just ask about weight loss and some symptoms that they're having and what their dietary intake is, and obviously physical exam.

Specialized nutrition support refers to the provision of nutrients, orally, enterally, or parenterally with therapeutic intent. It should be considered in patients who are found to be malnourished on nutrition assessment or are at significant risk for becoming malnourished. As we remind many of our consulting services, administration of nutrition support is never an emergency, and it shouldn't be initiated until the patient is hemodynamically stable.

So enteral nutrition refers to the non-volitional delivery of nutrients by tube into the GI tract. It requires a functional GI tract of sufficient length and condition to allow for adequate nutritional absorption. There are several contraindications to enteral nutrition. And they include peritonitis, intestinal obstruction, intractable vomiting, ileus, intractable diarrhea, and intestinal ischemia. Advances in the administration of enteral nutrition now make its use possible in patients with conditions that were previously felt to contraindicate its use, such as an acute pancreatitis and enterocutaneous fistula.

Oh, yeah.

AUDIENCE: I want to know why that is for acute pancreatitis. Is it because you're feeding lower in the gut?

ELISABETH KRAMER: Yeah, yeah, because now we put in-- in general, we put in NJ tubes. So when you're feeding distal to the ligament of Treitz, then you don't have the stimulation to release the pancreatic enzymes. And so that's generally, based on several studies, is shown to actually be better than giving parenteral nutrition in these patients. So enteral nutrition has many benefits, which make it the preferred route of nutrition support, including reduced cost, better maintenance of gut integrity, reduced infectious complications and decreased length of hospital stay.

However, there are circumstances when enteral nutrition is adequate and infusion of nutrition intravenously may be required to provide adequate nutrients. So major controversy in the field of nutrition support concerns the relative indications for the use of PN versus enteral nutrition. This is an algorithm from the American Society for Parenteral and Enteral Nutrition, or ASPEN guidelines. And it's helpful for determining whether the optimal route for nutrition support is enteral or parenteral in a specific clinical situation.

So after nutritional assessment, it's generally assumed that enteral support is preferable to parenteral support if the patient has a functional GI tract. So the purpose of this study was to investigate the importance of the root of nutrient administration on septic complications after blunt and penetrating trauma. 98 patients were randomized to either enteral or parenteral feeding within 24 hours of injury. The enteral group sustained significantly fewer pneumonias, inetera-abdominal abscesses, and line sepsis than the PN group, and sustained significantly fewer infections per patient.

The most significant changes occurred in the more severely injured patients. So if there's only one slide that you remember from this entire talk, I hope it's this one, the golden role of nutrition support. If the gut works, use it. Parental nutrition has been associated with complications and patient harm from infections due to the introduction of IV catheters and their manipulations, administration of essentially a viable growth medium into the bloodstream, metabolic complications, and errors that occurred during prescription of PN formulas.

And parenteral nutrition should therefore be reserved only for patients who were unable to tolerate enteral nutrients for prolonged periods of time. That being said, parenteral nutrition is a life-sustaining therapy that provides nutrients to patients with an impaired intestinal tract function and enteral access challenges. The first successful infusion of hypertonic parenteral nutrients was in the late 1960s. And since then, advances in central venous access and parenteral formulations have made its administration safer and more successful.

Indications for parenteral nutrition include contraindications for enteral nutrition, as we discussed earlier, or if a patient has failed in enteral nutrition trial with appropriate tube placement, including a trial of post-pyloric jejunal feedings. So the exact duration of starvation is unknown and the optimal number of days to wait before initiating parental nutrition is a controversial question. Unfortunately, there are no prospective randomized clinical trials available to address this issue.

But in general, the teaching is that it's unlikely that patients who were able to eat orally within six to eight days will benefit from a short duration of parenteral nutrition, even if they're malnourished. However, patients who don't eat or receive specialized nutrition support for more than 10 to 14 days after a hospital admission or surgery have been shown to have worse clinical outcomes, longer hospital stay, and higher costs. So therefore, it's reasonable to initiate nutrition support in patients with an adequate oral intake for seven to 14 days, or in those patients in whom inadequate oral intake is expected over a seven to 14-day time period.

And regarding the initiation and timing of specialized nutrition support, these are practice guidelines from ASPEN. And they say that nutrition support should be used in patients who can't meet their nutrient requirements by oral intake. When nutrition support is required, enteral nutrition should generally be used in preference to parenteral nutrition. Parenteral nutrition should be used when the GI tract is not functional or can't be accessed, and in patients who can't be adequately nourished by oral diets or enteral nutrition alone.

And nutrition support should be initiated in patients with inadequate oral intake for seven to 14 days, or in patients in whom inadequate oral intake is expected over a seven to 14-day period. So central parenteral nutrition or total parenteral nutrition, or TPN, is what I'm referring to when I say parenteral nutrition. It's called total nutrition because the entire nutrient needs of the patient can be delivered by this route. A complete and balanced formulation includes dextrose, amino acids, lipids, electrolytes, vitamins, and trace elements. And it provides this complete nutrition in a reasonable fluid volume.

It's a hyperasmolar formulation that has to be delivered into a large diameter vein. The rate of blood flow in the superior vena cava rapidly dilutes the hypertonic parenteral feeding formulation to that of body fluids. So it minimizes the risk of complications associated with IV infusions of hypertonic solutions, notably rumbo phlebitis. I'll touch on peripheral parenteral nutrition, or PPN briefly. We don't use it here, and we didn't use it where I trained.

PPN has a similar composition as central parental nutrition, but lower concentrations of nutrient components allow for peripheral venous administration. There's a lower dextrose dose and amino acid content. There are many drawbacks to PPN, which makes it inferior to central parenteral nutrition. Large fluid volumes need to be administered to provide comparable calorie and protein doses. It may cause phlebitis, given the hyper osmolarity, and it often requires frequent peripheral IV site rotations. It's contraindicated in significant malnutrition, large nutrient, or electrolyte needs, fluid restriction, or the need for prolonged parental nutrition generally more than two weeks.

So its use is therefore controversial, and many believe that the complications outweigh any benefits, especially because the patients have to only have minor nutritional deficits. So parenteral nutrition is a complex therapy. It's dependent on an adequate system to order, transcribe, prepare, compound, dispense, and administer. And the outcomes are optimized when PN is managed by an interdisciplinary care and nutrition support team compared to a single practitioner. And I'm not just saying that because I work on the nutrition support service. There's data to support it.

In this study, PN use was evaluated prospectively in 209 patients at a major tertiary care center managed by either individual, medical, or surgical services, or a metabolic support service. The study looked at the appropriateness of PN initiation, as well as metabolic complications and time on PN. And the study found that metabolic complications occurred less frequently in patients who received a metabolic support service consultation compared with those who did not.

Parental nutrition use of less than five days-- oh, sorry-- duration was also significantly less frequent among patients who received metabolic support service consultation. So the study also looked at the appropriateness of PN starts. It was considered to be indicated or not indicated based on ASPEN guidelines, and preventable if the GI tract was functional, but not accessed when possible. The therapy was considered to be not indicated or contraindicated. If the patients were classified as well-nourished, or if they had inadequate or enteral nutrition for fewer than seven days, had a DNR status, or were terminally ill, or were receiving adequate enteral nutrition.

Significantly more metabolic service PN starts were indicated than on the non-metabolic service. And fewer metabolic PN starts were preventable or not indicated. So PN that was not indicated or preventable resulted in excess annualized patient charges. So that translated into more than $130,000 in preventable PN starts, an almost $50,000 in starts that were not indicated or contraindicated.

So again, parenteral nutrition is a complex therapy that has nearly 40 different components. This is a picture of our order sheets here at Presby that are filled out by the dietitians every day. The components used in formulating PN typically include energy substrates, such as carbohydrates and fat, protein, as amino acids, as well as electrolytes and vitamins, trace elements, minerals, and water. Careful consideration of patient-specific needs, including age, nutrient requirements, BMI, and condition-specific concerns, like wounds, infection, critical illness, kidney or liver dysfunction need to be incorporated into determining energy and protein requirements.

Newer approaches to macronutrient dosing have emerged. They include strategies, such as permissive underfeeding and hypocaloric high protein feeding. It's somewhat beyond the scope of this talk. But basically, permissive underfeeding critically ill patients has been associated with fewer infectious complications and reduced mortality. Also, hypocaloric, high protein feeding in critically ill obese patients has been shown to be as effective as eucaloric feedings.

In PN formulations, crystalline amino acids are used to provide protein. So a mixture of essential and non-essential amino acids are commercially available. Modified or specialty amino acid products are specifically formulated for certain disease states or special conditions, such as renal failure, or hepatic failure, or fluid restriction. These products are, of course, much more costly, and they have controversial, clinical benefit. Studies have been mixed when compared to just a protein dose modification using our standard amino acid formulations. So we don't use them here.

If oxidized for energy, amino acids yield four kilocalories per gram. And we generally use caution or decrease the dose significantly if a patient has a serum B1 of over 100. So carbohydrates are the primary energy source in the human body, and they provide about 45% to 65% of daily energy requirements. In PN, the most commonly used carbohydrate substrate is dextrose. It's an acidic solution, and it provides 3.4 kilocals per gram.

Central venous access is required for concentrations above 10% due to the risk of thrombophlebitis in peripheral veins. It's generally not started or started a much lower concentration in the setting of hyperglycemia, and that's generally when we also frantically call you guys for help. In PN, intravenous fat emulsions are used to provide energy as well as essential fatty acids. Lipids provide 15% to 30% of non-protein calories in PN. Fat emulsions compounded in the same containers, as other IV nutrients is referred to as a three-in-one admixture or a total nutrient admixture. And it's what makes the bag of PN white instead of yellow, if you see these patients.

Lipids in TNA can run for 24 hours as opposed to given separately, where they have to be infused within 12 hours to decrease the risk of contamination. Fat emulsions also contain egg yolk phospholipids, which functions as an emulsifier. So we have to be careful in patients with egg allergies. And it has glycerin to adjust the osmolality. Glycerin also adds caloric content. Each gram of fat provides nine kilocals, so very calorically dense. And lipids are generally held or modified if the triglyceride level is greater than 400.

Maintenance or therapeutic amounts of various electrolytes are added to PN formulations depending on a patient's requirements, which are listed in this table. Acetate and chloride do not have specific ranges for intake. They're rather adjusted as needed to maintain an acid/base balance. Electrolytes are available in various salt forms, and they're manufactured as either single salts or combination products. Certain salts are preferred for use in PN admixtures because they're less likely to cause incompatibilities compared with alternative salts.

So this very complex slide, which I don't expect you to read, just shows the recommended systematic approach to prescribing electrolytes and PN. And the point of the slide is just for you to get an idea of how complicated it can be to order and balance electrolytes in the PN. And even after following this, we generally get calls from pharmacies saying that our calcium phosphate balances are off and we don't have enough potassium.

So commercially available vitamin products for use in adult PN preparations include single-vitamin and multi-vitamin products with both fat and water soluble vitamins. And this is the content of the multi-vitamin used in most PN preparations. Fat soluble vitamin daily dose and multi-vitamin products is about the same as the oral recommended daily allowance, or the RDA. In contrast, water soluble vitamins in PN doses are 2.5 to five times greater than the oral RDA, and the rationale for the increased requirements of the water soluble vitamins is the increased urinary losses compared with oral administration.

Parental formulations for single vitamins are not available for several vitamins, including biotin, pantothenic acid, riboflavin, vitamin A, vitamin D, and vitamin E. And we've run into these issues where patients are deficient in these vitamins, and we generally have to just double the multi-vitamin dose. But it can be an issue. And commonly used trace elements in PN formulations include zinc, copper, chromium, manganese, and selenium. And other trace elements can be supplemented into the PN as needed.

There are several injectable iron products available on the market. But only iron dextrin is approved for addition to PN. And it can only be used in lipid-free admixtures because it can de-stabilize lipids. So in general, for our patients who have iron deficiency, We usually give them a separate IV iron infusion. Copper and manganese are mainly excreted in the bile. So they should be reduced or omitted in patients with cholestasis.

We don't use them here, but there are commercially available pre-mix dextrose amino acid products for central and peripheral vein administration. And they come with or without a standard package of electrolytes. And dextrose and amino acid components are mixed just prior to use. They can be preferred in settings where there is infrequent or irregular use of PN, such as in rural hospitals or long term care facilities. They have a reasonably stable shelf life. They require minimal admixing.

All pre-mixed products require addition of vitamin injection shortly before administration because vitamins are not stable when they're added for more than 24 hours in advance of use. So the monitoring of parenteral nutrition should include a routine evaluation and assessment of clinical condition with the focus on nutrition and metabolic effects of PN therapy. So this shows recommended monitoring for our patients. And serial documentation is helpful to guide adjustments to fluid electrolytes and nutrient therapies.

So this table shows suggested monitoring parameters, and frequency for critically ill, stable, inpatient, in-home patients on PN. Again, this should be used as a guide. It says that stable inpatient serum chemistry should be checked only one to two times a week. We get nervous if a patient hasn't had labs from that morning. So we don't follow this so strictly.

So the goal of PN therapy is always to return to using the GI tract with oral or enteral feeds whenever possible. And we're constantly assessing patients for their ability to take in oral or enteral feedings. Transitional feeding is considered to be the period between oral diet or enteral nutrition initiation and PN discontinuation. And this transition should be planned to avoid a potential decline in nutrition status when PN is discontinued. This figure details a suggested approach for transition and discontinuation of PN.

For many patients, that can be discontinued as soon as they're able to tolerate a diet that's been advanced beyond clear liquids. But others may require a more detailed transitional feeding plan, especially those with significant nutritional compromise. So then we generally overlap the PN with enteral nutrition for a longer period. As I alluded to earlier, there are many complications associated with PN. Complications associated with vascular access devices can be divided into infectious and noninfectious etiology, such as catheter thrombosis.

Macronutrient-related complications include hyper and hypoglycemia, essential fatty acid deficiency, and hypertriglyceridemia. And other complications I'll touch on are refeeding syndrome, hepatobiliary complications, and metabolic bone disease. PN administration is an important risk factor for bloodstream infections. And this is a dreaded but all too common complication in our patients, especially those on long-term home PN therapy. Bloodstream infections associated with central venous catheters have been attributed in mortality, ranging from 12% to 25%. And central venous catheter infections can originate from endogenous skin flora, contamination of the catheter hub, hematologinous seeding of the device from a distant site, or contamination of the infuseIT.

And hub contamination is the most frequent cause of enteral luminal contamination in long term use. Migration of skin flora from the insertion site is more prevalent and short term catheters. And contamination of the infuseIT actually rarely causes sepsis. This was an observational study of patients receiving long term PN from January, 1981 to July, 2005 to describe the epidemiology and microbiology characteristics of bloodstream infections in this population.

47 patients receiving long term PN were evaluated. 38 patients or 80.9% developed 248 bloodstream infections while receiving parenteral nutrition. The incidents of bloodstream infections for all patients were 0.83 per catheter year. More than one bloodstream infection episode occurred in almost 79% of these patients, and 23.8% of bloodstream infections were polymicrobial. 55% of microorganisms identified were gram positive. And that was followed by gram negative and fungal infections. The most prevalent pathogen was coagulase negative staph.

The incidence of bloodstream infections is high. And a significant proportion of polio microbial bacterial and fungal infections occur in long-term PN patients. So careful management of the infusion line is essential to reduce the risk of infections in this population. And central line infections are also a big problem in our own PN patients. We do our best to educate them and their family members on the proper care of their line. And this is a sheet that we give to our patients on discharge and the practice that we recommend nurses follow in caring for these lines on the floors.

Catheter occlusion is the most common non-infectious complication of PN. The occlusion can be secondary to thrombotic or non-thrombotic causes. Non-thrombotic clauses include drug interactions, PN formulas with an inappropriate calcium phosphate ratio, and lipid residue. Also, mechanical occlusion can occur from external clamps, kinking of the catheter, occluded port needles, or constricting sutures. And the treatment depends on the extent of thrombosis, severity of symptoms, as well as the need to reestablish access and available alternatives.

And as you know all too well, hyperglycemia is a very common complication of PN therapy. Often, multifactorial increases with age, obesity, severity of illness, rates of dextrose infusion, and concomitant diabetes diagnosis. A multi-center study of 605 non-critically ill patients receiving PN demonstrated that patients with a mean blood glucose level above 180 were 5.6 times more likely to die while hospitalized compared with those with mean blood glucose of less than 140.

So these observations indicate that prevention and correction of hyperglycemia via modification of nutrient composition, use of insulin, or a combination of both should be strongly considered during PN therapy. In these patients, it's important to limit dextrose infusion rates until control of serum glucose is attained. And obviously, insulin is the treatment of choice to control hyperglycemia, either subcutaneously, IV, or directly into the PN formula. Generally, a treatment with continuous insulin infusion is preferred in critically ill patients and patients with multifactorial hyperglycemia because it allows for more frequent dose adjustments.

Hypoglycemia with parenteral nutrition is multifactorial, and it's been associated with an increased risk of complications, length of hospitalization, and mortality. Abrupt discontinuation of PN is associated with a rebound hypoglycemia, especially in patients in whom the PN is cycled over 12 hours, like our home patients versus given over a 24-hour infusion. So to reduce the risk of rebound hypoglycemia, when it's being shut off, we recommend a one-to-two hour taper down of the infusion or half the infusion rate. If the PN solution has to be discontinued quickly, then a dextrose-containing fluid should be infused for one to two hours.

Another macronutrient-related complication of PN is essential fatty acid deficiency. Two polyunsaturated fatty acids, lonaic and alphalonaic acid cannot be synthesized by the body, and are considered to be essential. Clinical manifestations of essential fatty acid deficiency includes scaly dermatitis, alopecia, hepatomegaly, thrombocytopenia, fatty acid, and fatty liver-- sorry-- and anemia. And it's diagnosed by a triene-to-tetraene ratio of more than 0.2.

While rare, it can occur in adults receiving fat free PN within one to three weeks. And to prevent essential fatty acid deficiency, 1% to 2% of daily energy requirement should be derived from linoleic acid and 0.5% from alphalinoleic acid. So that basically translates into giving 500 cc's of lipids once a week. Hypertriglyceridemia occurs if the infusion rate of the IV fat emulsion exceeds the capacity of plasma fat clearance. There are several risk factors, including drugs such as steroids, cyclosporin, tacrolimus, and probofol, as well as many medical conditions, such as renal failure, sepsis, pancreatitis, dextrose overfitting, or hyperglycemia, diabetes, obesity, alcoholism, and multiple organ failure.

The rapid infusion of lipids may also put patients at risk for intolerances. hypertriglyceridemia, secondary to PN therapy can impair immune response. It increases the risk of pancreatitis and altars pulmonary hemodynamics. So strategies to reduce hypertriglyceridemia during PN therapy include temporary discontinuation, reducing the infusion rate to no less than eight to 10 hours, and limiting provision to provide only essential fatty acids. And serum triglyceride should be monitored in all patients receiving PN and withheld if serum concentrations exceed 400.

Refeeding syndrome is generally described as the metabolic and physiologic shift in fluids and electrolytes after the introduction of nutrition in severely malnourished patients. And it can occur with oral nutrition, enteral nutrition, or parenteral nutrition. The classic study describing refeeding syndrome was conducted in 1944 on male conscientious objectors of World War II. The participants had undergone semi-starvation for six months. And upon nutrition replenishment, several of the subjects developed cardiac failure.

And with the advent of modern day PN and enteral nutrition, reports of similar complications were noted in severely undernourished patients who received aggressive nutrition supplementation. So basically, what happens is carbohydrate introduction stimulates insulin secretion, which causes electrolytes to shift intracellularly. And this shift leads to a dramatic decrease in potassium, magnesium, and serum phosphorus, as total body stores are depleted. And then to maintain osmotic neutrality within the plasma, the body retains sodium and water, which can lead to the development of fluid overload and its clinical consequences, like congestive heart failure, pulmonary edema, and arrhythmias, especially in critically ill patients.

There can also be underlying vitamin and mineral deficiencies in refeeding syndrome, in particular, thiamine, which is co-factor for glycolysis can quickly become depleted with weight loss and malnutrition. And thiamine deficiency in malnourished patients has led to Wernicke's encephalopathy in patients given PN with high carbohydrate loads without supplemental thiamine. So the prevention treatment and monitoring of refeeding syndrome should include identifying at-risk patients and conservative carbohydrate initiation and advancement.

Examples of patients at risk for refeeding syndrome are those with anorexia nervosa, history of excessive alcohol consumption, and those with chronic disease states, causing under-nutrition, like cancer, COPD, or malabsorptive syndromes. So to prevent refeeding syndrome, we generally give 50% of the goal kilocalories on days one and two, and advance very slowly to 75% at the three, and finally to the goal kilocals at one week. And we replete electrolytes vigorously, especially IV, phosphate, magnesium, and potassium, which is why we're always crazy about having a phosphorus level prior to initiating PN.

And we monitor daily, sometimes twice daily electrolytes, closely watch ins and outs, and frequent vital checks. And in addition to the daily requirements provided by the IV multi-vitamin preparation, we additionally supplement with 50 to 100 milligrams a day of thiamine for five to 10 days for patients who are at risk of thiamine deficiency or refeeding syndrome.

So PN-associated liver disease encompasses a multitude of conditions, including hepatic steatosis, or fat accumulation in the liver, cholalithiasis, or gall stones, and as well as colestasis or decreased in bile flow. And these complications range from self-limited to life-threatening, especially concerning for patients dependent on long term support. So steatosis is a common complication of overfeeding, and it's generally thought to be non-progressive. We see modest elevations in serum AST and ALT concentrations, usually within two weeks of PN therapy.

These mild elevations may return to normal, even while the patient is still receiving PN. But it almost always normalizes when it's discontinued. While generally self-limited, progression to steatohepatitis, fibrosis, or cirrhosis can become an issue in patients who are receiving long term home parenteral nutrition. Gallbladder stasis and cholecystitis is actually related more to a lack of enteral stimulation rather than to the PN formula itself. A decrease in cholecystokinin release and impaired bile flow and gall bladder contractility leads to formation of biliary sludge and stones.

In rare cases, it can progress to acute coliasistitis and the absence of gallstones. Or also called acalculous cholecystitis. And PN-associated cholecystitis occurs primarily in children, but it can also occur in adults receiving long term PN. It manifests as elevation of alkaline phosphatase, GGT, and conjugated bilirubin. It's probably the most severe of these complications, as it can progress to cirrhosis and hepatic failure.

So when a patient receiving PN develops liver complications, which is not uncommon, a review of all aspects of all aspects of care is necessary to identify and eliminate or treat other contributing factors. So some non-PN factors include hepatotoxic medications, which most of our patients are also on, herbal supplements, biliary obstruction, hepatitis, and sepsis. And since hepatic staetosis is related to overfeeding, the first step in management is decreasing the concentration of dextrose and lipids.

And' a continuous PN infusion over 24 hours can result in hyperinsulinemia and fat deposition in the liver. So cycling the PN infusion instead over 12 hours has been shown to reduce serum liver enzyme and biliary concentrations when compared to 24-hour continuous PN. And in addition to causing gallstones, not using the enteral root has also been associated with mucosal atrophy and decreased immunity, causing an overgrowth of hepatotoxin, producing anaerobic intestinal bacteria.

Introducing enteral nutrition early is the best method to prevent this complication, even giving tube feeds at a trickle rate. But other methods, including using deoxycholic acid, and exogenous cholecystokinin, as well as treating small intestinal bacterial overgrowth with rifaximin have been proposed. Intestinal transplant is last resort, but can be considered for patients with significant or progressive liver disease. And Medicare is actually approved payment for intestinal transplantation in patients who fail PN therapy. And one of their criteria for PN failure is the development of impending or overt liver failure.

So osteoporosis and osteomalacia are associated with long term PN use. And also, as you know, metabolic bone disease is multifactorial and associated with many medical conditions, which overlap with our patients, including diabetes, cirrhosis, pancreatic insufficiency, short bowel syndrome, Crohn's disease, as well as immobilization and many medications. The prevalence of PN-associated metabolic bone disease is unknown, but it's of concern in all patients receiving long term PN.

It's also unclear if PN accelerates or causes bone loss because most of our patients have at least one other risk factor for developing this condition. So numerous elements of PN nutrient composition have been postulated to affect bone metabolism. So therefore, careful PN admixture design for the long term PN patient is important to minimize risk. To maintain optimal bone health, it's important to have adequate amounts of protein, energy, calcium, phosphorus, magnesium, and vitamins D and K. So we always take this into account.

So in summary, malnutrition is a common and under-recognized problem among hospitalized patients. And this is associated with poor clinical outcomes, including post-op complications, poor wound healing, prolonged hospital stay, and increased mortality. Malnourished patients, or those with the potential to become malnourished should be evaluated for specialized nutrition support, especially those who haven't eaten or expected to not be able to eat or take enteral nutrition for seven to 14 days.

And the decision as to whether to use enteral or parenteral nutrition support can be complicated. But in general, if patients have a functional GI track, they should be fed enterally, given the benefits of enteral feeding, as well as the reduce costs and decreased complications. Parenteral nutrition is a complex formulation that's best ordered, compounded, and managed by a nutrition support team. And there are many complications associated with PN administration, including catheter-related bloodstream infections, hyper and hypoglycemia, refeeding syndrome, hepatobiliary complications, and metabolic bone disease.