Healthline VOLUME 16

Coram®* Continuing Education Program

Nutrition In Transplantation

Nutritional status tends to impact outcomes in all patient populations. In the chronically ill, nutritional compromise is common, and a nutrition assessment and nutrition planning are critical components of care. In the transplant population, dietary considerations must be addressed throughout the transplant continuum. While nutritional deficits and needs vary between individuals and according to disease state, type of transplant, post-transplant immunosuppressive protocols, and long-term self-care, the goals for care are the same:

1. To maximize pre-transplant nutritional status to best ensure ongoing candidacy pre-transplant and facilitate the post-transplant healing process,
2. To monitor both early and long-term nutritional intake and status to promote healing, manage weight, minimize medication side effects, and meet the body's needs, and
3. To educate patients regarding potential nutritional risks, negative outcomes associated with poor nutrition, and interventions that support long-term transplant success and optimum health.

Pre-transplant Phase

Patients who present to transplant often have a history of chronic illness and have experienced some or all of the following: a trajectory of failing health; decreased ability to perform their activities of daily living (ADLs), which may include eating; medication adverse effects; and organ/disease-specific nutrition challenges and interventions. For example, as liver dysfunction progresses, the ability to process protein and absorb nutrients decreases. Patients will likely be placed on a protein-restricted diet, with its oft-associated muscle wasting, for weeks or months prior to transplant. Patients with renal failure may develop protein-energy malnutrition and negative nitrogen balance, which cause loss of lean body mass and fat deposits. Since approximately half of potential kidney transplant candidates develop renal failure secondary to diabetes, the associated complications may exacerbate the nutritional compromise. The blood cell transplant patient presents after a pre-transplant conditioning regimen that includes high-dose chemotherapy and radiation, both likely to cause side effects that impact the patient's ability to eat and/or absorb nutrients.

While many patients present to transplant underweight and nutritionally compromised, it is equally important to evaluate the nutritional status of the obese patient. For example, severe obesity in the liver transplant candidate (body mass index, or BMI, greater than 35 kg/m^2) is associated with wound infection, multisystem organ failure, and increased transplant costs. In heart transplant recipients, a reduction of weight-to-BMI ratio to less than 27 kg/m^2 is suggested.[1]

Reported Incidences of Malnutrition in the Pre-transplant Patient[1]

Liver: Of patients with alcoholic cirrhosis, 34% to 82% have malnutrition, as do 27% to 87% of patients with nonalcoholic cirrhosis.

Kidney: Up to 40% of patients with chronic renal failure who require hemodialysis or long-term peritoneal dialysis reportedly have protein-energy malnutrition (PEM).

Heart: Of heart patients, 45% have malnutrition. These patients are at risk for developing cardiac cachexia.

The goals of nutrition therapy while preparing or waiting for transplant are to:

1. Replenish malnourished individuals,
2. Maintain the status of those with adequate muscle and energy reserve,
3. Promote weight loss in candidates with excessive weight based on BMI, and
4. Manage symptoms and maximize quality of life.[1]

Improvements in nutritional status, immune function, infection rates, length of stay, and post-transplant morbidity and mortality rates have shown positive benefits

*Coram CVS Specialty® Infusion Services

with aggressive pre-transplant nutrition intervention.[1]

Post-transplant Phase

Nutrition and the Immune System

Critical in the success of any transplant is modulating the immune system enough that the body will not reject the transplant, while not compromising the immune response so significantly that the patient develops serious infection. Immune response and specific immunomodulation strategies are unique to each patient, and "walking the tightrope" between too little and too much immunosuppression is a real challenge. Adding varying degrees of nutritional compromise significantly impacts that balance since nutrition works both independently and in concert with the immune system to help regulate immune function.

Adequate energy and protein stores are essential to both innate and adaptive immune responses. A depleted protein pool deprives the body of amino acids required to synthesize immune cells. Insufficient energy and protein stores limit the ability of natural killer cells to synthesize the toxic proteins that destroy pathogens. Reduced protein stores also result in a loss of complement proteins, which release the cytokines that coordinate immune reactions. Protein energy malnutrition (PEM) reduces the size of the thymus; the smaller thymus then causes a decrease in the availability of lymphocytes and macrophages. Adequate energy and protein stores help limit the ability of bacteria to adhere to cells such as respiratory epithelial cells.

Infection that occurs with depressed immune function diminishes the appetite and may result in gastrointestinal (GI) symptoms such as diarrhea, causing additional nutrient loss and nutritional insufficiency. Infection may also lead to hypermetabolism, increasing the body's nutrient needs.

Vitamins, minerals, and trace elements provide coenzymes for metabolic reactions important to the immune system and promote optimal levels of immune system cells such as natural killer cells, which target and eliminate bacteria. Some micronutrients serve as antioxidants; others are co-factors for enzymes important to macrophage function. Immune function and response can be further compromised by a reduction in vitamin, mineral, and trace element intake or an increased output of vitamins, minerals, and trace elements due to nausea and reduced diet tolerance, emesis, or diarrhea.

Some dietary fibers have a probiotic activity, which can promote a healthy ratio of indigenous to pathologic bacteria in the GI tract and create an intestinal environment unfriendly to pathogens. This is especially important because the gut is one of the most important immune organs in the body and home to hundreds of strains of bacteria. A deficiency of dietary fiber poses a risk for imbalance between healthy and pathologic bacteria.

Acute Post-transplant Phase

The first three months post-transplant are significant in terms of the degree of immunosuppression, prevention of infection, and impact on long-term outcomes. Nutritional compromise is a risk, as patients may present with such factors as post-operative pain or diminished GI motility, which can impact the ability to eat and/or absorb nutrients. Additionally, high-dose immunosuppressive medications have significant nutritional impact. In the blood cell transplant patient, effects of the pre-transplant conditioning regimen may persist, such as severe mouth sores, decreased appetite, and nausea and vomiting. Until these resolve, nutritional support may be needed.

Hemodynamic stability and proper hydration are critically important in the immediate post-operative phase. Fluid requirements for immediate post-transplant patients vary greatly, depending upon volume status, fluid administration, and renal function. Diarrhea, chest tubes, wounds, surgical drains, naso-gastric drainage, ostomy output, pancreatic secretions, and urine output are sources of fluid losses that can increase fluid intake requirements. Additionally, for renal transplant patients, the time to adequate diuresis may vary depending on time to full function of the transplanted kidney; fluid intake must be adjusted accordingly. For heart/lung post-transplant patients, fluid restriction is often needed, thus requiring the provision of concentrated (decreased volume) nutritional support.

The primary nutrition goals in the acute post-transplant phase are to:

1. Establish adequate nutrient intake,
2. Replete nutrient stores,
3. Reduce the impact of immunosuppressive medications,
4. Provide nutrient substrate to support the body's ability to fight infection,
5. Heal anastomoses and surgical wounds, and
6. Supply energy to allow the patient to participate in physical rehabilitation and activities of daily living.

For children, it is especially important to provide sufficient energy and protein for growth and development.[2]

It is important to minimize the adverse nutritional effects of immunosuppressive drugs. In the immediate post-transplant period, doses are high and hyperglycemia, fluid retention, electrolyte abnormalities, and wound healing are the focus of care. As the immunosuppressive doses taper to maintenance levels, the issues become weight and blood sugar control and lipid management. The table below illustrates key factors specific to immunosuppressive medications that impact nutritional care planning and patient education.

Nutrition Alterations in the Acute Post-transplant Phase

After organ transplantation, protein catabolic rate is accelerated. Protein requirements are directly related to steroid dose, nutrition status, stress state, losses from drains and wounds, and requirements for wound healing. Protein is lost from surgical drains, wounds, stomas, and dialysis, further increasing protein intake requirements. As steroid doses are decreased or discontinued, the need for dietary protein may also decrease.

Nitrogen losses result from malnutrition, steroid therapy muscle catabolism, and surgical stress. Nitrogen balance studies may be used to monitor protein needs, as long as renal function is adequate. Adult requirements range from 1.5–2.0 g/kg/day to maintain adequate nitrogen balance.[3]

Hyperglycemia is the most common abnormality in glucose metabolism occurring early in the post-transplant period. Risk factors include physiologic stress, infection, and use of medications. A transient decrease in lipid oxidation occurs within 30–45 days after transplant, but then increases and remains increased for several months. These two abnormalities are discussed below.

Estimating Acute Post-Transplant Nutritional Needs

Patients may return from the operating room with an extra 10–20 kg of fluid. Specific nutritional recommendations should be based on the patient's estimated dry weight. Organ transplant recipients are typically not hypermetabolic unless secondary conditions such as sepsis are present. Importantly, children undergoing blood cell transplant exhibit a significant reduction in resting energy expenditure in the early weeks after transplantation, a phenomenon that places them at risk for overfeeding.[4]

Several studies have evaluated post-transplant energy needs. The time periods studied varied from 2 to 28 days post-transplant and it was found that resting energy expenditure (REE) at the time of analysis was 7% to 42% above predicted values. Based on these studies, 1.3–1.5 times the calculated basal energy expenditure (BEE), or 30–35 kcal/kg, were recommended. Absorption capacity should also be considered in the final calorie recommendation.[5, 6]

Specific recommendations for vitamin, mineral, and trace element supplementation have not been established for the post-transplant patient. However, factors that contribute to vitamin and mineral abnormalities in the organ transplant patient must be taken into consideration when developing a nutrition plan of care. For example, if the patient has bile drainage, copper loss is increased and fat-soluble vitamins may be malabsorbed. Patients with an ostomy may have increased zinc

Table 1: Potential Immunosuppressant Side Effects

Drug	Potential Nutrition Side Effects
Tacrolimus (Prograf®)	Nausea, vomiting, hyperkalemia, hyperglycemia, abdominal distress
Cyclosporine (Sandimmune®, Neoral®)	Hyperkalemia, hypomagnesemia, hypertension, hyperglycemia, hyperlipidemia
Mycophenolate mofetil (CellCept®)	Diarrhea, nausea, vomiting
Azathioprine (Imuran®)	Nausea, vomiting, diarrhea (less common), macrocytic anemia, pancreatitis
Prednisone (Solu-Medrol®)	Hyperglycemia, sodium retention, osteoporosis, hyperphagia, impaired wound healing, increased infection risk, hypertension, pancreatitis (rare)
Muromonab-CD3 (OKT3®)	Nausea, vomiting, diarrhea, anorexia
Anti-thymocite globulin (Atgam®, Thymoglobulin®)	Fever, chills, increased risk of infection, profound leukopenia, thrombocytopenia
Basiliximab (Simulect®)	Constipation, nausea, abdominal pain, vomiting, diarrhea, dyspepsia, peripheral edema, fever, viral infection, hyper or hypokalemia, hyperglycemia, hypercholesterolemia, hypophosphatemia, anemia
Sirolimus (Rapamune®)	Peripheral edema, hypertriglyceridemia, hypertension, hyper-cholesterolemia, elevated creatinine, constipation, abdominal pain, diarrhea, headache, fever, urinary tract infection, anemia, nausea, thrombocytopenia
Belatacept (Nulojix®)	Diarrhea, constipation, nausea, vomiting

loss. A comprehensive nutrition assessment post-transplant is indicated to identify potential factors that contribute to micronutrient aberrations. Once identified, an appropriate repletion or restriction regimen can be established. Ongoing monitoring of clinical status and micronutrient levels support adjustments to the nutrition care plan as needed. At one year post-transplant, it is suggested that patients receive a daily multivitamin and that specific patient considerations that would impact vitamin or mineral status, such as failure of the transplanted organ, recurrent disease, or treatment complication, be considered when assessing a patient's micronutrient status.[7]

Long-term Post-transplant Phase

During the chronic post-transplant phase, it is common for patients to be challenged by obesity, hypertension, hyperlipidemia, osteoporosis, and/or diabetes mellitus, in large part due to their immunosuppressive medications, but also caused by their diet. The nutrition goal of this phase is to prevent or treat these complications.

Hypertension is the most common post-transplant complication, affecting up to 85% of adult recipients. It is a significant risk factor for graft failure as well as for cardiovascular disease (CVD); thus, aggressive blood pressure control is critical. While the greatest contribution to hypertension is the prescribed immunosuppressants, obesity contributes significantly and must be prevented or managed.

Obesity often develops as patients are able to eat and enjoy foods that may have been restricted prior to transplant. They typically feel better and again may eat foods that are not the healthiest. In addition, prednisone, a key immunosuppressant in most transplant protocols, increases one's appetite. Patients are often tempted to eat above their caloric needs.

As stated above, diabetes is a common cause of renal failure leading to kidney transplant. Both type 1 and type 2 greatly increase the risk for ischemic heart disease, CVD, and peripheral vascular disease. An additional risk for all transplant recipients is new-onset diabetes after transplant (NODAT). Both tacrolimus and cyclosporine have been associated with impaired glucose metabolism, compromised long-term graft function, increased risk of cardiovascular morbidity, and decreased patient survival. While the risk of NODAT is greatest during the first 3 to 6 months following transplantation, there is a continuous increase in NODAT incidence over time. In one study, the cumulative incidence of NODAT within 3 years of transplant was 16.2% overall — 17.7% with maintenance steroids and 12.3% without.[8] The International Consensus Guidelines on New-Onset Diabetes After Transplantation provide recommendations for management strategies to reduce diabetes onset and complications. A multifaceted approach for tight glycemic control is recommended and includes diet, exercise, weight control, monotherapy or combination therapy with an oral agent, and insulin.[9]

Resting energy expenditure represents the amount of calories required by the body during a non-active, 24-hour period.

Basal energy expenditure describes oxygen consumption during rest and fasting and extrapolated to 24 hours.

Osteoporosis develops in approximately 60% of transplant recipients. Maximum bone loss occurs during the first 3 to 6 months following transplantation, but then continues at a slower rate. Osteoporosis in transplant patients can cause significant morbidity and mortality, including fracture and avascular necrosis.

Hyperlipidemia occurs in about 60% to 80% of transplant patients. Post-transplantation dyslipidemia is a risk factor for long-term graft loss as well as for cardiovascular disease. Monitoring protocols vary by transplant program, but typically recommend evaluation for dyslipidemia at baseline, 2 to 3 months after a change in treatment, and at least yearly thereafter. Patients may require statins.

Patients post-allogeneic blood cell transplant are also at risk for graft-versus-host disease (GVHD), either acute or chronic. GVHD primarily affects the liver, skin, and GI tract, with varying degrees of liver dysfunction, skin reaction and diarrhea in the acute phase, and such symptoms as dry mouth, esophageal stricture and/or web formation, recurrent diarrhea, and weight loss if chronic. A rise in glucogon and norepinephrine seen in chronic GVHD patients can cause REE and changes to the speed of fat and carbohydrate oxygenation.[10, 11] Nutrition support is critical in this patient subset because >40% is malnourished.[11, 12] Additionally, oral magnesium supplements, infection, and pancreatic insufficiency contribute to post-transplant malabsorption and nutrition issues.

Monitoring a patient's progress through the transplant continuum includes evaluation of body weight and intake and output, and serial monitoring of laboratory parameters. Additionally, activities of daily living must be assessed periodically to ensure the

Long-term Post-transplant Nutrition Recommendations

- Obtain and maintain a healthy body weight.
- Limit sweets, sugar, and alcohol.
- Maintain a diet low in fat (including saturated fat), and cholesterol, with mild to moderate sodium intake. Include foods rich in magnesium, calcium, and phosphorus.
- Exercise regularly.
- Obtain a yearly DEXA scan.
- Maintain serum cholesterol levels <200 mg/dL.
- Maintain blood glucose levels between 70 and 125 mg/dl.
- Maintain bone density at levels normal for age.
- Maintain blood pressure <130/85.

individual's ability to ambulate and eat adequately.

Healthy lifestyle habits are invaluable and the importance of self-care cannot be overstated. While specific protocols and recommendations may differ between transplant centers and per the individual needs of the patient, general long-term nutritional self-care is important. As stated in one article, "A healthy perspective on nutrition is to think of food as medicine, as important as the medications you will take after your transplant. Eat what your body needs, as recommended, without overdosing on any one thing or neglecting any particular food group."[13]

Conclusion

Transplantation may improve both survival and patient quality of life in individuals requiring organ or blood cell transplantation. However, the surgical and medical treatments used in transplantation influence nutrition status and the timing and type of nutrition delivery. Pre-existing malnutrition due to disease is also a concern that needs to be identified and treated to optimize post-transplant outcomes. Nutrition therapy varies with the transplant type, nutrition status and tolerance, stage of transplant, organ function, medical management, and presence of complications. Each transplant patient requires his or her own unique nutrition care, monitored and adjusted throughout the transplant continuum.♦

References

1. Weseman RA. Nutritional requirements of adults before transplantation. Medscape Reference. http://emedicine.medscape.com/article/431031. Updated Sept. 26, 2012. Accessed Oct. 3, 2012.
2. Hasse JM, Matarese LE. Solid Organ Transplantation ch 31 *The A.S.P.E.N. Adult Nutrition Support Core Curriculum.* 2nd ed 2012.
3. Shanbhogue RLK, Bistrian BR, Jenkins RL, et al. Increased protein catabolism without hypermetabolicm after human orthotopic liver transplantation. *Surgery*. 1987;101:146-149.
4. Bechard LJ, Feldman HA, Venick R, et al. Attenuation of resting energy expenditure following hematopoietic SCT in children. *Bone Marrow Transplant.* 2012 Feb 20. doi: 10.1038/bmt.2012.19. [Epub ahead of print]
5. Plank LD, Metzger DJ, McCall JL, et al. Sequential changes in the metabolic response to orthotopic liver transplantation during the first year after surgery. *Ann Surg.* 2001;234,245-255.
6. Delafosse B, Faure JL, Bouffard Y, et al. Liver transplantation-energy expenditure, nitrogen loss and substrate oxidation rate in the first two post-operative days. *Transplant Proc.* 1989;21:2453-2454.
7. Hasse JM, Roberts S Transplantation, In: Rombeau JL, Rolandelli RH (eds). *Parenteral Nutrition.* 3rd ed. Philadelphia: WB Saunders 2001, 540.
8. Luan FL, Steffick DE, Akinlow OO. New-onset diabetes mellitus in kidney transplant recipients discharged on steroid-free immunosuppression. *Transplantation.* 2011; 91:334–341.
9. Ghisdal L, Van Laecke S, Abramowicz MJ, Vanholder R, Abramowicz D. New-onset diabetes after renal transplantation. *Diabetes Care.* Jan 2012 35; 1:181-188.
10. Zauner C, Rabitsch W, Schneeweiss B, et al. Energy and substrate metabolism in patients with chronic extensive graft-versus-host disease. *Transplantation.* 2001;71:524-528.
11. Couriel D et al. Ancillary Therapy and Supportive Care of Chronic Graft-versus-Host Disease: National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: V. Ancillary Therapy and Supportive Care Working Group *Report Biology of Blood and Marrow Transplantation.* (2006)12:375-396.
12. Jacobsohn DA, Margolis J, Doherty J, Anders V, Vogelsang GB. Weight loss and malnutrition in patients with chronic graft-versus-host disease. *Bone Marrow Transplant.* 2002;29:231-236.
13. United States Department of Veterans Affairs website. Nutrition: Liver Transplant. www.hepatitis.va.gov/patient/complications/transplant-nutrition.asp. Accessed Feb. 12, 2012.

Self-Assessment Quiz: Nutrition in Transplantation

LEARNING GOAL

To understand the complexities of and responsibilities for nutrition in transplantation.

LEARNING OBJECTIVES

At the end of this program, the reader will be able to:

1. State three potential contributors to malnutrition in the pre-transplant phase.
2. State three potential contributors to malnutrition in the post-transplant phase.
3. Identify the nutritional implications of immunosuppressant medications.

SELF-ASSESSMENT QUESTIONS

In the Quiz Answers section on the next page, fill in the correct answer for each question. To obtain two (2.0) contact hours toward CE credit, the passing score is 100%. Return your Self-Assesment Quiz to Coram via email or fax. See the next page for details on how to return to your quiz. Please allow approximately seven days to process your test and receive your certificate upon achieving a passing score.

1. **Nutritional deficits in the pre-transplant phase are impacted by:**
   a. The presence of comorbidities
   b. The type of dysfunctional organ
   c. The ability to perform activities of daily living
   d. A and B
   e. All of the above

2. **Diabetes is common in the pre-renal transplant patient population.**
   a. True
   b. False

3. **The goals of nutrition therapy for the patient awaiting transplant include to:**
   a. Replenish any nutritional deficits
   b. Support patient weight loss in candidates with excessive BMI
   c. Maximize quality of life
   d. A and C
   e. All of the above

4. **Nutrition and nutritive substances work competitively with immune function regulation.**
   a. True
   b. False

5. **Adequate energy and protein stores are essential to immune system function.**
   a. True
   b. False

6. **Hypertension is a significant risk for failure of the transplanted organ.**
   a. True
   b. False

7. **The cumulative incidence of NODAT within 3 years of transplant is approximately 10%.**
   a. True
   b. False

8. **Contributors to excessive weight gain in post-transplant patients include each of the following EXCEPT:**
   a. Patients over-eating foods that were previously restricted to them
   b. Hyperlipidemia
   c. The use of prednisone, which often increases a patient's appetite beyond what their body needs

9. **Contributors to malnutrition in the blood cell transplant patient include:**
   a. Adverse effects of the pre-transplant preparatory protocols
   b. Acute graft-versus-host disease
   c. Chronic graft-versus-host disease
   d. A and C
   e. All of the above

10. **Monitoring a patient's progress through the transplant continuum includes evaluation of body weight and intake and output, and serial monitoring of laboratory parameters.**
    a. True
    b. False

Healthline VOLUME 16

Coram®* Continuing Education Program

Nutrition In Transplantation

QUIZ ANSWERS

Fill in the key below with the correct answers to receive 2.0 Continuing Education credits.**

1. (a) (b) (c) (d) (e)
2. (a) (b)
3. (a) (b) (c) (d) (e)
4. (a) (b)
5. (a) (b)
6. (a) (b)
7. (a) (b)
8. (a) (b) (c)
9. (a) (b) (c) (d) (e)
10. (a) (b)

**Accreditation Information

- Provider approved by the California Board of Registered Nursing, Provider Number 15200 for 2.0 contact hours.
- Coram CVS Specialty® Infusion Services is approved by the Delaware Board of Nursing, Provider Number DE-14-010517.
- Coram CVS Specialty Infusion Services is approved by The Commission for Case Manager Certification to provide continuing education credit to CCM® board certified case managers.
- Coram CVS Specialty Infusion Services is a Continuing Professional Education (CPE) accredited provider with the Commission on Dietetic Registration (CDR). Registered Dietitians (RDs) and Dietetic Technicians Registered (DTRs) will receive 2.0 continuing professional education units (CPEU) for completion of this program/material. CDR Provider CO100.
- Provider approved by the National Association of Social Workers (Approval Number 886613245).
- Coram CVS Specialty Infusion Services is an approved provider for the American Board for Transplant Certification (ABTC). Coram CVS Specialty Infusion Services will grant one Continuing Education Point for Transplant Certification (CEPTC) for this offering. Provider Number 147.
- Coram CVS Specialty Infusion Services is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

*Coram CVS Specialty Infusion Services

COR16048-0716

To obtain Continuing Education credits, please complete this information in full. Please print clearly.

Name: _____

Address: _____

City: _____ State: _____ ZIP: _____

License Number *(required to receive CEs)*: _____

❑ RN ❑ LPN ❑ Certified Case Manager ❑ Social Worker

Employer: _____

Work Phone: _____

Coram Representative: _____ Date: _____

Was this material:

Useful in your practice? ❑ Yes ❑ No

Comprehensive enough? ❑ Yes ❑ No

Well organized? ❑ Yes ❑ No

Certificate delivery:

❑ I would like my certificate mailed to the address provided above.

❑ I would like my certificate emailed to me at: _____

(ex: john.smith@coramhc.com)

Fax this page to Coram at 949-462-8990, or

SUBMIT FORM VIA EMAIL: CEDept@coramhc.com

Clear Form Fields