Medical Staff Conference

Malnutrition in Hospitalized Patients—Diagnosis and Treatment

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from transcriptions, they are prepared by Drs Homer A. Boushey, Associate Professor of Medicine, and David G. Warnock, Associate Professor of Medicine, under the direction of Dr Lloyd H. Smith, Jr, Professor of Medicine and Associate Dean in the School of Medicine. Requests for reprints should be sent to the Department of Medicine, University of California, San Francisco, School of Medicine, San Francisco, CA 94143.

R. CURTIS MORRIS, JR, MD:* *This Medical Staff Conference is unique in that it is a Nutritional Conference. To my knowledge, this is the first time the Department of Medicine has ever had a Medical Staff Conference devoted entirely to nutrition.*

Our speaker is Robert B. Baron, MD. Dr Baron is the Director of the Screening and Acute Care Clinic, and he entered the field of nutrition in a rather interesting way. After having graduated from Princeton University in sociology and anthropology, he took a master's degree in nutrition at the University of Wisconsin in 1974. Immediately thereafter, he came here, was graduated in Medicine in 1978 and has been very active on this campus in nutritional matters. He will discuss malnutrition in patients in hospital, its diagnosis and treatment.

ROBERT B. BARON, MD:† The most important nutritional problem of in-hospital patients is protein-calorie undernutrition or, as it is more commonly called, protein-calorie malnutrition. In this review, I will discuss the epidemiology, pathophysiology, diagnosis and selected aspects of treatment of this condition. I will not be discussing other important nutritional problems such as micronutrient deficiency diseases or obesity.

Much of the material on this subject is controversial, and many of the most important questions in this field remain unanswered. Whenever possible, I will try to give practical suggestions to facilitate clinical decision making in the care of these patients. These are complex questions, however, that do not usually lend themselves to "cookbook" answers. Often we are left to rely on clinical experience and judgment.

Epidemiology of Protein-Calorie Malnutrition

Despite significant advances in prevention, detection and treatment, protein-calorie malnutrition remains an important problem in inpatients. Its prevalence has been estimated at 26% to 80% of patients admitted to hospital, depending on the type of patient population and hospital studied.[1-8] In these studies, however, nutritional assessment techniques are used that do not reliably differentiate changes in nutritional variables caused by a patient's nutritional state from those caused by the underlying disease itself. Additionally, reference standards were used that were developed from studies of healthy young adults that may not be appropriate for the population studied.[9] A more realistic estimate of protein-calorie malnutrition in adult inpatients is probably closer to 20% of all admissions.

The causes of malnutrition in these patients can be divided into three major categories: decreased oral intake, increased nutrient losses or increased nutrient requirements. Table 1 lists some of the conditions in each of these categories that can contribute to the pathogenesis of malnutrition in inpatients. Few patients are sick enough to require hospital care without suffering from at least one of these conditions. Most commonly, malnutrition is caused by a combination of decreased oral intake due to anorexia and increased nutrient requirements due to the underlying disease.

Physiologic Consequences of Malnutrition

The consequences of protein-calorie malnutrition are a direct result of negative nitrogen and caloric balance. As the malnutrition progresses, virtually every organ and system of the body undergoes morphologic and physiologic alteration.[10] The severity of these changes is related to the magnitude and duration of the nutritional deprivation.

The most obvious manifestation of protein-calorie malnutrition in most patients is loss of adipose tissue and body weight. Most patients can tolerate 5% to 10% weight loss with little functional derangement. Losses of 35% to 40%, however, make survival unlikely. In general, death from starvation occurs soon after adipose tissue stores are completely depleted. Patients who retain large amounts of sodium and water, however, can have significant protein-calorie malnutrition without weight loss.

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TABLE 1.—*Pathogenesis of Protein-Calorie Malnutrition in Patients in Hospital*

Decreased Oral Intake	Increased Nutrient Losses
Anorexia	Malabsorption
Nausea	Diarrhea
Dysphagia	Bleeding
Pain	Glycosuria
Obstruction	Nephrosis
Poor dentition	Fistula drainage
Poverty	Protein-losing enteropathy
Old age	Increased Nutrient Requirements
Social isolation	Fever
Substance abuse	Neoplasms
Depression	Surgery
Unbalanced diet	Trauma
	Burns
	Medications

Loss of protein from skeletal muscle and from most organs parallels total body weight loss. Early investigators in this field thought that vital organs were spared during starvation. Unfortunately, this is not true. In starved rats, for example, a seven-day fast results in a 40% decrease in tissue protein from the liver, 28% from the gastrointestinal tract, 20% from kidneys and 18% from the heart.[11] Early in protein-calorie malnutrition, hepatic synthesis of serum transport proteins is depressed and levels of serum proteins decreased.

Immunologic changes are among the most important consequences of protein-calorie malnutrition.[12-14] The total lymphocyte count is decreased predominantly due to a fall in the number of T cells. Measures of T-cell function are also depressed. B-cell function is affected more variably. Some specific antibody responses remain normal while others are decreased. Both complement activity and granulocyte functions are depressed. Abnormalities in anatomic barriers add to the increased risk of infection. Virtually every aspect of wound healing is affected, including neovascularization, fibroblast proliferation, collagen synthesis and wound remodeling.[15]

As protein-calorie malnutrition becomes more severe, organ dysfunction may develop. The heart, lung and gastrointestinal tract are most affected. Cardiac function is depressed, with decreases in cardiac output and contractility.[16,17] An electrocardiogram may show prolonged QT intervals, decreased voltage and a rightward axis shift.[18] The patient becomes more susceptible to ventricular arrhythmias. At autopsy, the heart shows myofibrillar atrophy and interstitial edema.[16,19] Patients who have severe protein-calorie malnutrition should be refed slowly and carefully. Reintroducing calories, protein, salt and water can precipitate congestive heart failure.[17]

Pulmonary function is affected primarily by atrophy and weakness of the muscles of respiration. Mucociliary clearance is impaired and vital capacity and minute ventilation decreased.[18] The ventilatory response to hypoxia may be depressed.[20] Bronchopneumonia and respiratory failure are major causes of morbidity and mortality in these patients.

The gastrointestinal tract is affected throughout its entire length, but the most important changes occur in the small intestine.[21] Mucosal atrophy and edema, lymphocytic infiltration, loss of villi and decreased disaccharidase activity can develop. In combination with mild exocrine pancreatic insufficiency, these changes can result in progressive malabsorption and further malnutrition. Enteral refeeding of severely malnourished patients should also be initiated slowly due to these abnormalities in the gastrointestinal tract.

Clinically, progressive weight loss, hypoalbuminemia, anergy and mild normochromic normocytic anemia develop. As patients become progressively more debilitated, refractory bed sores, pneumonia and sepsis may develop.[22] Eventually, they may die from what Steffee has termed "nitrogen death."[23]

Nutritional Assessment

In the past 15 years, major technologic advances have enabled us to intervene in the development of protein-calorie malnutrition in almost any patient. Nutrients can be administered via central veins or small-bore enteric feeding tubes, and such support can be continued in a patient's home. But, like most new treatments, nutritional support is expensive and has its own associated risks. Our task is to select those patients in whom intervention will make an important difference in the clinical outcome.

The objective of nutritional assessment is to identify those patients who are already malnourished or who are at increased risk of protein-calorie malnutrition developing. Dozens of assessment techniques are currently available and in common use. Blackburn and colleagues[24] have recommended an extensive panel of clinical and laboratory measurements. These include anthropometric measurements of height, weight, triceps skin-fold thickness and arm muscle circumference; laboratory analysis of serum albumin and transferrin levels; quantitative and qualitative measurements of lymphocyte function; 24-hour measurements of creatinine excretion as a function of height, and measurements of protein and energy intake and expenditure. Other authors recommend the use of serum proteins with shorter half-lives,[25] measures of protein turnover,[26,27] sophisticated measures of body composition,[28-30] dynamic measures of muscle function[31] and quantitative indices that combine various measurements.[32,33]

Unfortunately, data on the diagnostic accuracy of these tests have been extremely difficult to obtain. Most tests are unable to discriminate reliably between abnormalities due primarily to protein-calorie malnutrition and those due to an underlying illness. The serum levels of albumin and other transport proteins, for example, are usually low in patients with protein-calorie malnutrition but are also low in many additional disorders.[34,35] Similarly, anergy may be due to many factors other than malnutrition.[36] In short, there is currently no "gold standard" for protein-calorie malnutrition with which these tests can be compared.[37]

Abnormalities in these indices, however, can predict adverse clinical outcomes. Hypoalbuminemia, anergy and lymphopenia have each been shown to predict a twofold to fivefold increase in postoperative morbidity and mortality.[38-42] Poor outcomes and prolonged hospital stays have also been described in medical patients with abnormal nutritional assessment measurements.[8,41,43] Combining several of these tests into quantitative indices improves their ability to predict poor outcomes. Buzby and colleagues have used multivariate analysis to develop a quantitative "prognostic nutritional

index" using serum albumin and serum transferrin values, triceps skin-fold thickness and delayed hypersensitivity reactions.[32] In retesting the index prospectively in 100 different surgical patients, 13 of 15 deaths were found to have occurred in their high-risk group.

Other investigators have begun to reemphasize the utility of a nutritionally focused history and physical examination in predicting adverse clinical outcomes. As early as 1936, Studley showed that patients with severe weight loss had a fivefold increase in postoperative mortality following surgical treatment of chronic peptic ulcer disease.[44] Studying more than 4,000 patients, Seltzer and co-workers showed that a history of a 4.5-kg (10-lb) weight loss before a surgical procedure increases the surgical mortality 30-fold.[45] Detsky and associates suggest that a more complete history and physical examination can also accurately predict surgical complications.[46] Using receiver operating characteristic curves to compare the predictive accuracy of different tests, they showed that their "subjective global assessment" is more accurate than single laboratory tests or Buzby's "prognostic nutritional index."

Current recommendations for nutritional assessment are shown in Table 2. The nutritional history should emphasize nutrient intakes, changes in body weight and a patient's functional state. The physical examination should focus on fat and muscle stores, volume state and signs of micronutrient deficiency. Laboratory testing can be limited to measuring the serum albumin level. If already available, the total lymphocyte count or serum transferrin value may be helpful. Finally, a patient's nutritional state should be closely followed during stay in hospital. Body weights should be measured at least weekly and patients' nutrient intake observed as a function of their estimated requirements.

This form of assessment of the nutritional state is easy to do and inexpensive. It should be included as a routine part of the admitting history and physical examination of any patient at risk of protein-calorie malnutrition developing. Abnormal assessment values will help to identify patients at risk for adverse clinical outcomes that may be related to their nutritional state.

TABLE 2.—*Recommendations for Nutritional Assessment*

Nutritionally Focused History
Intake history
Weight history
Functional state
Nutritionally Focused Physical Examination
Fat and muscle mass state
Volume state
Signs of micronutrient deficiencies
Interpreting Readily Available Laboratory Data
Serum albumin
Serum transferrin
Total lymphocyte count
Observing Intake as a Function of Estimated Needs
Calories (1 to 1.5 × basal energy expenditure: 25 to 40 kcal/kg)
Protein (0.8 to 1.5 grams/kg)

TABLE 3.—*Conditions in Adult Patients for Which Nutritional Support Is Almost Certainly Indicated*

Inadequate bowel syndromes
Severe prolonged hypercatabolism, such as from extensive burns and multiple trauma
As adjunct to conditions requiring prolonged therapeutic bowel rest
Severe malnutrition—that is, >25% to 30% weight loss—and treatable disease

Indications for Nutritional Support

The precise indications for initiating specialized enteral and parenteral nutritional support remain controversial. Like many new medical technologies, nutritional support has been widely used without clear clinical evidence that such intervention will reliably improve clinical outcomes. Some authors have advocated the use of nutritional support for every patient who is malnourished.[47,48] Others, however, emphasize the need for methodologically sound data to establish the efficacy of nutritional support in distinct clinical situations.[49,50]

Despite the lack of controlled trials, there are at least four groups of adult patients for whom nutritional support can currently be advocated (Table 3). Patients with inadequate bowel syndromes, including patients with short bowel syndrome, pseudo-obstruction or other severe disorders of the small intestine, clearly require nutritional support to sustain life. Patients with severe, prolonged hypercatabolism due to extensive burns, multiple trauma, prolonged ventilatory support and other similar conditions deserve aggressive and early nutritional support. Most trauma surgeons agree that nutritional support has at least in part contributed to improved outcomes in these patients. Somewhat more controversial are gastrointestinal disorders, such as enterocutaneous fistulas or severe Crohn's disease, for which many gastroenterologists recommend prolonged bowel rest as a therapeutic modality after standard treatments have failed. In these cases, nutritional support is a reasonable adjunct to the primary therapy. Patients with severe malnutrition who have lost greater than 25% to 30% of their body weight, are close to "nitrogen death" and who have a treatable disease also deserve nutritional support.

These four groups of adult patients represent a minority of patients for whom nutritional support is currently administered. Yet, it has been difficult to establish the efficacy of nutritional support in most other conditions. Koretz has recently reviewed 53 randomized controlled clinical trials of central vein parenteral support (Table 4).[50] Only 6 of the 53 studies showed improved survival, while 11 showed improvement in other clinical outcomes. The vast majority showed no significant effect of nutritional support at all. Interestingly, most of these studies showed improvement in nutritional assessment measures. Patients became better nourished but their outcomes were not affected. Thus, nutritional support has not been shown to clearly improve clinical outcomes in most clinical situations. These data, however, do not disprove an important role for nutritional support. Virtually all of these trials have significant methodologic weaknesses that make them very difficult to interpret. Almost uniformly, the sample size has been inadequate to ensure that a significant benefit has not been missed ("Type II" error)[51] and patient selection has been poor. Many studies have included treatment of well-nourished patients. The duration of treatment has often been much too short to show a significant reversal of

TABLE 4.—*Summary of Survival Data From Prospective Randomized Controlled Trials of Parenteral Nutritional Support**

Disease (No. Studies)	Survival				Any Clinical Outcome		
	Better	Not Different	Worse	Not Stated	Better	Not Different	Worse
Colitis (1)	0	1	0	0	0	1	0
Hepatic encephalopathy (6)	1	2	1	2	2	3	1
Alcoholic hepatitis (1)	0	1	0	0	0	1	0
Perioperative (17)	1	16	0	0	3	14	0
Cancer chemotherapy (12)	1	9	1	1	2	5	5
Radiation therapy (4)	0	4	0	0	1	2	1
Terminal cancer (1)	1	0	0	0	1	0	0
Acute renal failure (4)	1	3	0	0	1	3	0
Low-birth-weight infants (6)	0	6	0	0	0	6	0
Head injuries (1)	1	0	0	0	1	0	0
Total (53)	6	42	2	3	11	35	7

*Adapted from Koretz.[50]

malnutrition. Finally, the control groups have rarely been placebo controlled and control patients often receive significant amounts of dextrose, tube feeding or other parenteral solutions.

Currently, several large-scale, randomized controlled trials are in progress. Until these results become available, it seems reasonable to follow the recommendations of the American Society for Parenteral and Enteral Nutrition, listed in Table 5.[52] These recommendations emphasize the importance of evaluating the risks, benefits and costs to each patient before deciding to initiate nutritional support. They also underscore the importance of assessing nutrition to identify malnourished patients.

Selecting Nutritional Support Methods

Available nutritional support methods permit adequate nutrient delivery to all patients. Enteral techniques include giving supplements orally, the use of nasogastric and nasoduodenal tubes and tube enterostomies. Parenteral techniques include peripheral vein parenteral nutrition and central vein parenteral nutrition. In most instances, nutritional support can and should be delivered through the gastrointestinal tract. Enteral feedings are safer, cheaper and offer significant physiologic advantages.

TABLE 5.—*Recommended Indications for Nutritional Support**

Normally nourished patients who are eating enough:
no additional therapy

Normally nourished patients who are not eating enough:
if less than 5 to 7 days, no therapy
if more than 5 to 7 days, consider nutritional support

Malnourished patients who are eating enough:
no additional therapy

Malnourished patients who are not eating enough:
consider nutritional support

Selected hypermetabolic patients may need nutritional support before 5 to 7 days

*Adapted from "Standards for Nutritional Support: Hospitalized Patients."[52]

TABLE 6.—*Nutritional Support at University of California, San Francisco—1985 Charges to Patients*

Enteral	
2 liters standard solution (intact protein/lactose-free, 2,120 kcal plus 75 grams protein)	$ 0
Peripheral vein	
2 liters 10% dextrose solution plus 4.25% amino acids plus 500 ml 20% soybean emulsion (1,900 kcal plus 85 grams protein)	$255
Central vein	
2 liters 25% dextrose solution plus 4.25% amino acids (2,040 kcal plus 85 grams protein)	$200

All methods of nutritional support, however, add some additional risks to patients. A recent large prospective study of patients fed by nasogastric tube showed an 11.7% complication rate.[53] Most of these complications, including diarrhea, tube dysfunction and minor metabolic abnormalities, were mild and easily correctable. Aspiration pneumonia developed in 1% of patients, however, a serious complication of enteral feeding. Other studies in higher risk patients show a significantly higher rate of aspiration.[54] Limiting nasogastric feedings to alert patients who can sit up and protect their airway will minimize the rate of aspiration.

Complications of central vein parenteral nutrition occur in more than 50% of patients.[55] Most are minor abnormalities of liver enzymes, electrolytes or blood sugar. Most studies, however, show a 5% rate of serious complications even under the best of circumstances. Severe complications include catheter insertion problems, particularly pneumothorax, and catheter-related sepsis.

Cost comparisons of enteral and parenteral nutrition are also striking (Table 6). At the University of California, San Francisco, patients are not charged additional fees for enteral solutions. Parenteral solutions with amino acids, however, cost $100 per liter. When lipids are given intravenously, the cost to patients goes up even further.

Careful patient selection and close monitoring of patients receiving nutritional support will keep costs and complications to an acceptable rate. A number of studies have shown that close and early involvement of a multidisciplinary nutritional support team can effectively decrease the incidence of complications.[56] The earlier the contact among patient, primary physician and nutritional support team and the greater "control" the team has in the care of these patients, the lower the complication rate.

Summary

Malnutrition is prevalent in hospitalized patients, occuring in about 20% of adult inpatients. Malnutrition results in significant abnormalities of body structure and function.

Current nutritional assessment techniques provide reliable prognostic information but are poor diagnostic techniques. Nutritional support can reverse nutritional deficits in most patients but the benefit of nutritional support on most clinical outcomes remains uncertain. Nutritional support should be considered in normally nourished patients who are not eating enough for more than five to seven days, malnourished patients who are not eating enough and selected hypermetabolic patients. Selection of the nutritional support method should be tailored to each patient, taking into consideration the overall clinical condition, cost and risk of complications. In most circumstances, if the gut works, it should be used. Finally, the use of nutritional support is facilitated by close interaction with a multidisciplinary nutritional support team.

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