The Role of Nutrition in Pressure Ulcer Prevention and Treatment: National Pressure Ulcer Advisory Panel White Paper

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Introduction

The purpose of this white paper is to review the currently available scientific evidence related to nutrition and hydration for pressure ulcer prevention and treatment in adults; introduce the nutrition recommendations from the new National Pressure Ulcer Advisory Panel (NPUAP)-European Pressure Ulcer Advisory Panel (EPUAP) Guidelines for Pressure Ulcer Treatment; and review research needs for the future.

Overview of Pressure Ulcers: Prevalence, Incidence, Cost and Nutrition

Estimates indicate that 1 to 3 million people in the US develop pressure ulcers each year (1). According to the Joint Commission, more than 2.5 million patients in United States (US) acute-care facilities suffer from pressure ulcers, and 60,000 die from pressure ulcer complications each year (2).

The NPUAP defines *prevalence* as "a proportion of persons who have a pressure ulcer at a specific point in time" (3). *Prevalence* of pressure ulcers in the US is widespread in all settings with estimates of 10% to 18% in acute care, 2.3% to 28% in long-term care, and 0% to 29% in home care (3). The NPUAP defines *incidence* as "the number of new cases of pressure ulcers appearing in a pressure ulcer - free population over a period of time" (3). *Incidence* of pressure ulcers ranges from 2.3% to 23.9% in long-term care, 0.4% to 38% in acute care, 0% to 17% in home care and 0% to 6% in rehabilitative care (3,4). In addition, new information from Agency for Healthcare Research and Quality (AHRQ) (5) indicates that pressure ulcer-related hospitalizations increased by an alarming 80 percent from 1993 to 2006.
Please note that the interpretation of incidence and prevalence numbers require caution as numbers are influenced by multiple factors including definition and method of calculation (3).

Pressure ulcers can reduce overall quality of life due to pain, treatments, and increased length of institutional stay, and may also contribute to premature mortality in some patients (6,7). Therefore, any intervention that may help to prevent pressure ulcers or to treat them once they occur is important to reduce the cost of pressure ulcer care and improve quality of life for affected individuals.

The burden of having a pressure ulcer is high, in physical, emotional and financial terms. Data from 1999 indicates that the cost of treating pressure ulcers may range from $5 to 8.5 billion annually (8). Factor in 7% per year for health care inflation, and this equates to approximately $9.2 to 15.6 billion dollars in 2008. AHRQ reported that pressure ulcer-related hospitalizations ranged from 13 to 14 days and cost $16, 755 to $20,430 compared to the average stay of 5 days and costs approximately $10,000 (5). The Centers for Medicare/Medicaid Services (CMS) reports the cost of treating a pressure ulcer in acute care (as a secondary diagnosis) is $43,180.00 per hospital stay (9,10). Contributing cost factors include increased length of stay due to pressure ulcer complications such as pain, infection, high tech support surfaces, and decreased functional ability (11).

In addition to the financial cost of pressure ulcers, mortality rates are disturbing. A recent AHRQ document (5) reports 503,300 pressure ulcer-related hospitalizations in 2006 which included 45,500 hospital admissions in which patients had pressure ulcers as the primary diagnosis. Of these admissions, one in 25 admissions ended in death. Another 457,800 pressure ulcer-related hospital admissions noted pressure ulcer as the secondary diagnosis. Of these admissions, the death rate was one in eight.

Litigation adds to the burden of health care costs. This is especially true in long-term care, where nearly 87% of verdicts and out of court settlements against facilities are awarded to the plaintiffs (12). One report reviewed 54 nursing home law suit cases from September 1999 to April 2002 involving pressure ulcers. The average monetary recovery was more than $13.5 million and included awards of up to $312 million in one case, when determined by a verdict or settlement (13). In litigation cases related to pressure ulcers, jury awards are highest for multiple causation factors. When awards were related to single causes, the highest awards were for those where inadequate nutrition was alleged to be the cause of pressure ulcers (12). However, it is important to note that in the past few years a few states have passed legislation limiting malpractice awards which may help to control these cost burdens in the future.

Nutrition and Pressure Ulcers

Although limited evidence-based research is available, general consensus indicates that nutrition is an important aspect of a comprehensive care plan for prevention and treatment of pressure ulcers (7,14,15), and it is essential to address nutrition in every individual with pressure ulcers. Adequate calories, protein, fluids, vitamins and minerals are required by the body for maintaining tissue integrity and preventing tissue breakdown. A large cohort study of 1524 residents in 95 nursing facilities documented that pressure ulcer incidence may be higher with increased age, frailty or severity of illness, pressure ulcer history or significant weight loss and eating difficulties (16,17).

Compromised nutritional status such as unintentional weight loss, undernutrition, protein energy malnutrition (PEM), and dehydration deficits are known risk factors for pressure ulcer development (1,18). Other nutrition-related risk factors associated with increased risk of pressure ulcers include low body mass index (BMI), reduced food intake, and impaired ability to eat independently (16,18,19).

The National Pressure Ulcer Long Term Care Study (NPULS) was a retrospective cohort study of detailed resident characteristics, treatments, and outcomes using a convenience sample of nursing home residents. Participants included 2,420 adult residents of nursing facilities, with a length of stay of 14 days or longer, who were at risk of developing a pressure ulcer. More than 50% of residents in the study experienced weight loss of at least 5% during the 12 week study, and 45.6% of residents were considered underweight (defined as a BMI of 22 or less). The highest percentage of weight loss occurred in the residents with a recent pressure ulcer. In addition, residents with the lowest BMIs also had existing pressure ulcers (20). Thomas (21) noted that recent weight loss in older adults was a key factor in mortality risk, and Murden and Ainslie (22) indicated that a 10% decline in weight over a 6 month period was a strong predictor of mortality in this population. Two studies supported the theory that individuals in long-term care whose body weight declined by 5% in 30 days were at increased risk for death (23,24). Thomas (25) described the “anorexia of aging” including appetite decline, weight loss and, decreased metabolic rate placing the elderly person at risk for undernutrition.

Undernutrition has been defined as pure protein and energy deficiency which is reversed solely by the administration of nutrients (26). This definition ultimately defines undernutrition by the ability to improve nutritional status and reverse the consequences of undernutrition.

Poor outcomes are associated with undernutrition including the risk of morbidity and mortality, hence the need to quickly identify and treat undernutrition when pressure ulcers are present. Undernutrition may also negatively impact pressure ulcer healing. Conditions that may lead to undernutrition include: increased dependence on others for eating, chewing and swallowing problems, decreased oral intake of food and fluid, unintentional weight loss and advanced age. Undernutrition may decrease the body’s ability to fight infections and have a negative impact on pressure ulcer healing.

Several other medical conditions may affect pressure ulcer healing. PEM has been defined as a wasting and excessive loss of lean body

mass resulting from "too little energy being supplied to the body tissue that can be reversed solely by the administration of nutrients" (27). Cachexia is another medical malady which may affect pressure ulcer healing. "Cachexia is a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults (corrected for fluid retention)… Anorexia, inflammation, insulin resistance, and increased muscle protein breakdown are frequently associated with wasting disease. Wasting disease is distinct from starvation, age related loss of muscle mass, primary depression, malabsorption and hyperthyroidism and is associated with increased morbidity" (28).

Yet another concern is hypermetabolism, a responsive increase in metabolic rate, which is triggered by trauma, severe illness, infection, pressure ulcers and other factors. The body utilizes calories at a rapid rate, first pulling from available glycogen stores, then from visceral protein stores in order to provide energy needed to keep the major organs functioning. At the same time, cytokines, the proteins that are liberated in tissue injury and that mediate the body's immune and inflammatory response, contribute to metabolic and gastrointestinal changes such as anorexia and malaise. The effect of increased cytokines and Interleukin 1-6 (pro-inflammatory cytokines) on nutritional status results in anorexia, muscle wasting, decreased nitrogen retention, and impaired albumin synthesis (29). Together, the above maladies may contribute to unintended weight loss, undernutrition and/or PEM which in turn are risk factors for pressure ulcer development.

Recommendations for Practice

Nutritional Considerations in Pressure Ulcer Prevention

Little specific evidence exists related to medical nutrition therapy (MNT) for preventing pressure ulcers. However, early nutrition screening and assessment is essential to identify risk of undernutrition, PEM and unintentional weight loss which may precipitate pressure ulcer development and delay healing. There are many physical, functional and psychosocial factors that can contribute to inadequate intake, unintentional weight loss, undernutrition and/or PEM, including cognitive deficits, dysphagia, depression, food-medication interactions, gastrointestinal (GI) disorders and impaired ability to eat independently. No clear method exists to determine when nutritional status decline begins, especially in older people. In spite of aggressive nutritional interventions, some individuals are simply unable to absorb adequate nutrients for good health.

Nutrition Screening and Assessment

The nutrition screening process can identify individuals at nutritional risk and assist in making referrals to the appropriate health care professionals for further assessment. Initial screening is completed on admission by a qualified health care professional.

Several tools may be utilized in the nutrition screening process. Langkamp-Henken and colleagues (30) concluded from a cross-sectional study that the Mini-Nutritional Assessment (MNA) and MNA Screening Form provided an advantage over using visceral protein in screening and assessing nutritional status (31). The Malnutrition Universal Screening Tool (MUST) is another potential screening tool which helps practitioners identify risk of undernutrition (32). However, these tools are not widely used in all practice areas.

The Braden Risk Assessment Scale: Predicting pressure ulcer risk (33) includes a nutrition subscale which yields additional data that can be used in the nutrition screening and assessment process. Individuals should be reassessed following a change in condition, e.g., surgery, NPO status, intravenous fluid therapy only, etc.

Based on the results of the nutrition screening, a referral is made for a formal assessment by a registered dietitian (RD), who then completes a thorough nutritional assessment on each individual and makes appropriate recommendations for interventions and management. The American Dietetic Association (ADA) Nutrition Care Process

includes four basic steps: Nutrition Assessment, Nutrition Diagnosis, Nutrition Intervention and Nutrition Monitoring and Evaluation (34). Nutrition assessment is a systematic and continual process of obtaining, verifying, and interpreting data upon which the decisions about the impact and cause of nutrition-related problems are made. The process includes review and analysis of medical, nutritional, laboratory data and food-medication interactions; obtaining anthropometric measurements; and reviewing physical examination results (assessment of visual signs of malnutrition, oral status, chewing/swallowing ability, and/or diminished ability to eat independently, etc.).

A German study conducted by Hengstermann et al. (35) concluded that the Mini Nutritional Assessment, a validated nutrition assessment tool, was "easy to use to determine the nutrition status in multi-morbid geriatric patients with pressure ulcers." The American Dietetic Association (ADA) Nutrition Risk Assessment is commonly utilized in long-term care, and was recently validated in a small study conducted by ADA (36,37). Further research is planned to complete the validation process.

Following the assessment, the registered dietitian (RD) identifies and determines a specific nutrition diagnosis or problem that the dietetics professional is responsible for treating. The intervention is specific to the nutrition diagnosis or problem. The monitoring and evaluation steps determne the progress made by the individual to meet the specific goals established. An example of the nutrition diagnosis for an individual with a pressure ulcer is: "Inadequate food and fluid intake related to less than 50% intake of meals as evidenced by non-healing Stage IV pressure ulcer and five pound weight loss in two weeks." The nutrition intervention is related to the specific nutrition diagnosis. The client/individual and the other members of the healthcare team would work together to develop appropriate and individualized interventions, and then monitor and evalutate for needed changes to nutrition interventions. In this case, an example of a nutrition intervention is: "Provide a regular diet with fortified foods at each meal and a 6 ounce nutritional supplement at 2:00 PM and HS" (34).

Biochemical Data

Biochemical data analysis is one component of the total nutrition assessment process. Although laboratory tests may help clinicians evaluate nutrition issues in patients at risk for a pressure ulcer or for those who already have a pressure ulcer, no laboratory test can specifically determine an individual's nutritional status. Serum albumin, prealbumin and other lab values may be useful to help establish overall prognosis; however, they may not correlate well with clinical observation of nutritional status (38,39).

Serum albumin levels have historically been used widely in practice, however they are a poor indicator of visceral protein status. This is due to albumin's long half-life (12 to 21 days) and multiple factors which decrease albumin levels even when protein intake is adequate (e.g., infection, acute stress, surgery, cortisone excess, hydration status). Decreases in serum albumin may reflect the presence of inflammatory cytokine production or other comorbidities rather than nutritional status (40). Cytokine production may result in albumin being pulled from the intravascular spaces into the extravascular spaces and circulating back to the liver until the inflammatory process is resolved. Recent studies show the hepatic proteins (albumin, transthyretin and transferrin) correlate with the severity of an underlying disease rather than nutritional status (41). Conversely, dehydration may falsely elevate albumin levels.

Due to its short half-life (2 to 3 days), prealbumin (or transthyretin and thyroxine-binding albumin) has historically been used by practitioners with the assumption that it may be a better indicator of the effectiveness of interventions used to improve clinical condition (including nutrition status). However, prealbumin is subject to the same influences that make albumin problematic when used as a nutritional indicator. Metabolic stress and inflammation may decrease levels; and converse to what practitioners may assume, prealbumin levels may be maintained during

states of malnutrition (42). For these reasons, it is not recommended as a marker for nutritional status (41,43-49).

One study of critically ill patients receiving total parenteral nutrition (TPN) failed to demonstrate that an increase in the prealbumin level indicated a better prognosis for this population (45). However, monitoring of low levels of serum hepatic proteins indicate that a person is very ill and therefore at high risk for undernutrition, PEM and unintended weight loss. In these cases, the individual would benefit from aggressive and frequent monitoring of weight and oral intake and appropriateness of nutrition interventions.

Current laboratory values are not always readily available, and waiting for test results may further delay nutritional intervention. Evaluation of lab values is only one aspect of the nutritional assessment process and should be considered along with other factors such as daily food/fluid intake, changes in weight status, diagnosis and medications.

Nutritional Considerations in Pressure Ulcer Treatment

Nutritional recommendations are primarily based on expert opinion, best practice guidelines and smaller studies. Each clinician must use expert clinical judgment based on a thorough medical and nutritional assessment to make appropriate individualized recommendations. The individualized care plan should focus on improving and/or maintaining the patient's overall nutritional status, acceptance of nutrition interventions, and clinical outcomes.

Macronutrients and Micronutrients Related to Pressure Ulcer Treatment

Macronutrients

Energy

Energy, or kilocalories, are provided through the macronutrients: carbohydrates, fats and proteins. Energy is essential for pressure ulcer healing. Providing adequate kilocalories promotes anabolism, nitrogen and collagen synthesis and healing (50). Increased calories are needed to overcome accelerated loss of energy and protein due to hypermetabolism which occurs in malnourished patients (14)

Carbohydrate in the form of glucose is the major fuel source for collagen synthesis, which is the building block of tissue. Providing sufficient carbohydrate as the primary fuel source is much more efficient than synthesis of glucose from protein and fat.

Provision of sufficient caloric requirements should be based on achieving individualized nutritional goals. Energy needs are currently assessed using several methods. The methods used for predictive formulas or energy needs measurement must be defined for individual populations (e.g., critically ill, obese). Recent research indicates that the Harris-Benedict equation is inaccurate for calculating energy requirements (51). The Mifflin-St. Jeor Equation may be more accurate and have a smaller margin of error when used to calculate resting metabolic rate for healthy obese individuals (52). Measured energy requirements (i.e. indirect calorimetry), if available, is a more accurate measure of energy expenditure but cost may be prohibitive in most settings. The National Academy of Sciences, Institute of Medicine, and Food and Nutrition Board in partnership with Health Canada (53) defined estimated energy requirements needed to maintain energy balance in a healthy individual. The requirements are defined by age, gender, weight, height and activity; and form the basis for determining baseline caloric requirements.

Calories may be adjusted upwards or downwards based on individual nutritional assessment. Individuals in a hypermetabolic state have caloric requirements above the baseline caloric requirements.

Caloric needs are ideally met by a healthy diet; however some individuals are unable or unwilling to consume an adequate diet. Overly restricted diets may make food unpalatable and unappealing and therefore reduce intake. The ADA's position statement indicates that quality of life and nutritional status are enhanced by the liberalization of the diet ordered by the physician (54). For example, an individual may not find a

sodium restricted diet appealing and therefore intake may be poor, leading to undernutrition and slowing the pressure ulcer healing process. The type and amount of food/fluid ingested daily should be reviewed periodically to ensure the individual actually ingests enough calories based on estimated needs. It is also important to examine the reasons for the intake being decreased. Oral nutritional supplements, enhanced foods, and food fortifiers can be used to combat unintended weight loss and undernutrition.

In a retrospective uncontrolled cohort study of 1524 residents in long-term care facilities, the prescription of an oral supplement was a predictor of pressure ulcer healing (16,17). Desneves et al. conducted a randomized controlled clinical trial (RCT) to measure pressure ulcer healing using the Pressure Ulcer Scale for Healing (PUSH) scores for three different groups of subjects (55). Group A received a standard hospital diet. Group B received a standard diet plus two high calorie supplements totaling 500 Kcalories, 18 grams of protein, 72 mg of vitamin C and 7.5 mg of zinc. Group C received a standard diet plus two high calorie supplements which provided 500 Kcalories, 21 grams of protein, 9 grams of additional arginine, 500 mg of vitamin C and 50 mg of zinc. Of the three groups, group C noted a 2.5 fold greater improvement in healing as measured by a lower PUSH score. However, this was a small three week intervention study of only 16 subjects and pressure ulcers were not described by stage. Therefore it is not possible to determine the impact of the diet by stage of pressure ulcer. A study conducted by Wilson and colleagues indicated that individuals who consumed oral nutritional supplements between meals experienced better absorption of nutrients with the least interference to meal intake (56). Nutritional supplements include products that supply nutrients such protein, calories, fat, vitamins, minerals and/or amino acids.

Protein

Protein is the basis of the human body structure. Proteins are uniquely different from carbohydrates and fats (lipids) as only protein contains nitrogen. Protein is responsible for the synthesis of enzymes involved in pressure ulcer healing, cell multiplication, and collagen and connective tissue synthesis. All stages of healing require adequate protein. Caloric (energy) needs must be met first in order to spare protein from being utilized as an energy source.

Protein is essential to promote positive nitrogen balance. Increased protein levels have been linked to improved healing rates (57-61). Dietary protein is especially important in the older adult due to body composition changes that occur with aging and reduced activity levels. These changes may include sarcopenia and decreased immune function, which can lead to impaired wound healing and the inability to adequately fight infection. Sarcopenia, normal age-related loss of muscle, can be accelerated due to hyper-catabolic disease states and production of inflammatory cytokines which are liberated in tissue injury. Recent studies indicate the basic requirement for exogenous protein in older adults is a minimum of 1.0 gram per kilogram body weight, rather than 0.8 gram per kilogram of body weight for healthy adults (62).

The recommended range of protein associated with healing currently is between 1.2 to 1.5 grams per kilogram of body weight per day (63). Past studies have indicated that protein levels as high as 2.0 grams per kilogram body weight may not increase protein synthesis and may contribute to dehydration in the elderly (64).

Wolfe and Miller (65) noted that a protein level above the recommended 0.8 per kilogram of body weight for healthy adults is appropriate under conditions such as wound healing. Campbell, Trapp, Wolfe, et al. suggest a protein allowance of at least 1.0 to 1.2 grams per kilogram of body weight per day for healthy elderly individuals (66). The Agency for Health Care Policy and Research (AHCPR, which has been renamed Agency for Healthcare Research and Quality, or AHRQ) pressure ulcer treatment guidelines recommend 1.25 to 1.5 grams per kilogram of body weight per day for patients with pressure ulcers (67). The European Pressure Ulcer Advisory Panel (EPUAP) guideline

recommends 1.0 to 1.5 grams per kilogram of body weight per day (50).

Some recent studies have focused on increasing the amount of protein provided for wound healing. In one study, 89 nursing home residents with Stage II, III and IV pressure ulcers were randomized into a treatment group which received standard care plus a concentrated, fortified, collagen protein hydrolysate supplement three times a day (providing an additional 45 grams protein per day), and a control group which received standard care plus a placebo three times a day. PUSH scores were used to analyze wound healing. In the eight week study period, those in the treatment group had a fifty percent reduction in the PUSH scores compared to those in the control group (58). Additional studies are needed to determine whether higher amounts of protein are safe and effective in promoting pressure ulcer healing.

It is also important to note that nitrogen losses may occur from exudating pressure ulcers, possibly increasing protein needs. Clinical judgment is required to determine the appropriate level of protein for each individual, based on the number of pressure ulcers, overall nutritional status, comorbidities, and tolerance to nutritional interventions. For example, individuals with chronic kidney disease may be inappropriate candidates for high levels of protein (68).

Amino Acids

Amino acids are the building blocks of protein. Certain amino acids such as arginine and glutamine become conditionally essential amino acids during periods of severe stress such as trauma, sepsis, and/or pressure ulcers.

Arginine

Arginine stimulates insulin secretion, promotes the transport of amino acids into tissue cells and supports the formation of protein in the cells. Studies related to wound healing appear to be controversial and there is no definitive research study specifically related to arginine's impact on pressure ulcer healing in humans. A randomized controlled clinical trial in elderly nursing home residents with pressure ulcers reported that arginine supplementation was well tolerated but did not enhance mitogen-induced lymphocyte proliferation or healing (69). In a small 3 week interventional RCT, Desneves et al. noted a reduction in PUSH scores for individuals with pressure ulcers who consumed high calorie supplements containing arginine (55). Maximum safe dosages of arginine supplementation in humans have not been established. Additional research is needed to recommend the use of arginine alone or combined with other nutrients for pressure ulcer healing (70).

Glutamine

Glutamine's role in pressure ulcer healing may be its function as a fuel source for fibroblasts and epithelial cells needed for healing. The safe maximum dose for glutamine supplementation has been established as 0.57 grams per kilogram of body weight per day (71). Supplemental glutamine has *not* been shown to improve wound healing (72). More studies are needed to determine glutamine's impact on pressure ulcer healing.

Fluids

Fluids serve as the solvent for vitamins, minerals, glucose and other nutrients and the transport medium for nutrients and waste products though the body. Preliminary data from Stotts and Harriet (73) indicate that fluid administration may increase low tissue oxygen. Tissue oxygenation is needed for proper healing.

The RD calculates individual fluid requirements and determines nutritional interventions. Various formulas have been used to calculate adequate daily fluid intake. One general formula utilizes 1 mL per kcalorie consumed (50) initially. Practitioners must assess for tolerance and reassess as condition changes.

Health care practitioners should monitor individuals' hydration status, checking for signs and symptoms of dehydration such as: changes in weight, skin turgor, urine output, elevated serum sodium or calculated serum osmolality (74).
Individuals consuming high levels of protein may require additional fluid. Elevated temperature, vomiting, profuse sweating, diarrhea and heavily draining wounds contribute to fluid loss which must be replaced (74).

In generally healthy individuals who are adequately hydrated, food accounts for any where from 19 to 28% of total fluid intake (75). Total fluid needs include the water content of the food consumed (75). Nutritional supplements and enteral feedings are generally 75% water. For specific amount of free fluids refer to the individual product nutrition labeling.

Micronutrients

The Institute of Medicine (IOM), National Academy of Sciences (NAS) Dietary Reference Intakes indicate the level of each micronutrient needed at each stage of life for healthy individuals (53,76). Most nutrient needs can be met through a healthy diet. However, individuals with pressure ulcers may not be consuming an adequate diet to meet established nutritional reference standards.

Micronutrients that are "hypothesized" to be related to pressure ulcer healing include vitamin C, zinc and copper.

Ascorbic Acid

Ascorbic acid (vitamin C), a water soluble vitamin, is a cofactor with iron during the hydroxylation of proline and lysine in the production of collagen. Thus ascorbic acid is important for tissue repair and regeneration (77). Deficiency can be associated with impaired fibroblastic function and decreased collagen synthesis, which can result in delayed healing and capillary fragility. Ascorbic acid deficiency is also associated with impaired immune function which can decrease the ability to fight infection (77). However, mega doses of vitamin C have not been shown to accelerate wound healing (78). One blinded, multicenter trial included 88 patients with pressure ulcers who were randomized to receive 10 mg or 500 mg of vitamin C twice daily. The study did not result in improved healing in either of the two groups (79). The inclusion of fruits and vegetables such as citrus fruits in the diet can achieve the desired recommended daily amount. However, vitamin C at physiological doses should be considered when dietary deficiency is diagnosed.

Zinc and Copper

Zinc is a mineral that functions as an antioxidant and is associated with collagen formation, synthesis of protein, DNA and RNA, and cell proliferation. Inflammatory cells, epithelial cells and fibroblasts are proliferating cells (80). Zinc is transported through the body primarily by albumin, therefore, zinc absorption declines when plasma albumin declines, such as in PEM, trauma, sepsis or infection (81).

Deficiency of zinc may be the result of wounds with increased drainage, poor dietary intake over a long period of time, or excessive gastrointestinal losses. Zinc deficiency may cause loss of appetite, abnormal taste, impaired immune function and impaired wound healing. Good sources of zinc include high protein foods such as meat, liver, and shellfish.

No research has demonstrated an effect of zinc supplementation on improved pressure ulcer healing. When clinical signs of zinc deficiency are present, zinc should be supplemented at no more than 40 mg of elemental zinc per day which is the Daily Reference Intakes (DRI) upper limit (82). Zinc supplementation should be stopped once the deficiency is corrected. High-dose zinc supplementation (above 40 mg per day) is not recommended (76) because it can adversely affect copper status possibly resulting in anemia. High serum zinc levels may inhibit healing, impair phagocytosis, interfere with copper metabolism, and induce a copper deficiency since both minerals compete for binding sites on the albumin molecule (15,83, 84). Copper deficiency may be harmful as copper is essential for collagen cross-linking.

To determine if additional supplementation is necessary and before recommending additional supplementation, practitioners should review any comprehensive vitamin/mineral supplements, enteral formulas, oral nutritional supplements or fortified foods which contain additional micronutrients.

Current Recommendations for Medical Nutrition Therapy for Pressure Ulcer Treatment

The following recommendations are taken from the NPUAP-EPUAP Pressure Ulcer Treatment Guideline, published in 2009. The Treatment Guideline was developed following a systematic, comprehensive review of the peer-reviewed, published research on pressure ulcer treatment from 1998 through January 2008. Supplemental searches were conducted on related nutrition issues. Evidence tables from previous guidelines were reviewed to identify relevant studies published prior to 1998. All studies meeting inclusion criteria were reviewed for quality, summarized in evidence tables and classified according to their level of evidence using a schema developed by Sackett (85).

Sackett Level of Evidence Rating System for Individual Studies

Level	
I	Large randomized trial with clear-cut results (and low risk of error)
II	Small randomized trial with uncertain results (and moderate to high risk of error)
III	Non randomized trial with concurrent or contemporaneous controls
IV	Non randomized trial with historical controls
V	Case Series with no controls. Specify number of subjects.

Adapted from Sackett DL/ Evidence based medicine. What it is and what it isn't. Br Med J 1996;312:71-72.

Strength of Evidence Supporting Each Recommendation

Next the cumulative strength of evidence supporting each recommendation was rated according to the following criteria:

A – Recommendation supported by direct scientific evidence from properly designed and implemented controlled trials on pressure ulcer in humans providing statistical results that consistently support the recommendation (Sackett Level I studies).

B – Recommendation supported by direct scientific evidence from properly designed and implemented clinical series on pressure ulcers in humans providing statistical results that consistently support the recommendation (Sackett Level II, III, IV, V studies).

C – The recommendation is supported by expert opinion or indirect evidence (e.g. studies in animal models and/or other types of chronic wounds).

A complete description of the NPUAP-EPUAP guideline development methodology has been previously published (86).

Additional research is needed to determine the effects of various medical nutrition therapy (MNT) interventions on pressure ulcer healing. The goals of MNT must also be based on the individual's prognosis and goals of treatment. For some, aggressive intervention is appropriate. However, for others, such as those at end of life, the goal may simply be to maintain comfort to the extent possible based on the patient's wishes.

For individuals who have a pressure ulcer, the NPUAP-EPUAP guidelines are:

All individuals should have a nutritional assessment upon admission and with each condition change. This is particularly true for individuals with pressure ulcers.

1. **Screen and assess nutritional status for each individual with a pressure ulcer at admission and with each condition change and/or when progress toward pressure ulcer closure is not observed. (Strength of Evidence = C.)**

    1.1. **Refer all individuals with a pressure ulcer to the dietitian for**

early assessment and intervention of nutritional problems. (Strength of Evidence = C.)

1.2. Assess weight status for each individual to determine weight history and significant weight loss from usual body weight (≥ 5% change in 30 days or ≥ 10% in 180 days). (Strength of Evidence = C.)

1.3. Assess ability to eat independently. (Strength of Evidence = C.)

1.4. Assess adequacy of total nutrient intake (food, fluid, oral supplements, enteral/parenteral feedings). (Strength of Evidence = C.)

2. Provide sufficient calories. (Strength of Evidence = B.)

2.1. Provide 30-35 Kcalories/kg body weight for individuals under stress with a pressure ulcer. Adjust formula based on weight loss, weight gain or level of obesity. Individuals who are underweight or who have had significant unintentional weight loss may need additional Kcalories to cease weight loss and/or regain lost weight. (Strength of Evidence = C.)

2.2. Revise and modify (liberalize) dietary restrictions when limitations result in decreased food and fluid intake. This is to be done by a dietitian or medical professional. (Strength of Evidence = C.)

2.3. Provide enhanced foods and/or oral supplements between meals if needed. (Strength of Evidence = B.)

2.4. Consider nutritional support (enteral or parenteral nutrition) when oral intake is inadequate. This must be consistent with individual goals. (Strength of Evidence = C.)

3. Provide adequate protein for positive nitrogen balance for an individual with a pressure ulcer. (Strength of Evidence = B.)

3.1. Offer 1.25 - 1.5 grams protein/kg body weight for an individual with a pressure ulcer when compatible with goals of care, and reassess as condition changes. (Strength of Evidence = C.)

3.2. Assess renal function to ensure high levels of protein are appropriate for the individual. (Strength of Evidence = C.)

4. Provide and encourage adequate daily fluid intake for hydration. (Strength of Evidence = C.)

4.1. Monitor individuals for signs and symptoms of dehydration: changes in weight, skin turgor, urine output, elevated serum sodium or calculated serum osmolality. (Strength of Evidence = C.)

4.2. Provide additional fluid for individuals with dehydration, elevated temperature, vomiting, profuse sweating, diarrhea or heavily draining wounds. (Strength of Evidence = C.)

5. Provide adequate vitamins and minerals. (Strength of Evidence = B.)

5.1. Encourage consumption of a balanced diet which includes good sources of vitamins and minerals. (Strength of Evidence = B.)

5.2. Offer vitamin and mineral supplements when dietary intake is poor or deficiencies are confirmed or suspected. (Strength of Evidence = B.)

Research Needs

Undernutrition is associated with increased morbidity and mortality. Early identification and treatment of nutritional problems is critical. There were no studies specifically addressing the obese individual with pressure ulcers. Additional research is also needed for pediatric patients and neonates. Appetite stimulants and anabolic steroids may have a role in improving body weight; however, more research is needed to determine effectiveness in promoting pressure ulcer healing.

Research is needed to better define appropriate caloric range for obese individuals (those with BMI ≥30) with pressure ulcers. Although weight loss is usually recommended for obese individuals, weight loss efforts may need to be modified or postponed temporarily to provide sufficient nutrients for pressure ulcer healing.

It is essential to meet minimal recommended dietary intake (RDI). Protein levels for patients with wounds should be 1.25-1.5 grams of protein. Randomized clinical trials indicate increased protein levels promote pressure ulcer healing. The research to date does not demonstrate the effectiveness of branched chain or individual amino acids, such as arginine and glutamine, in the treatment of pressure ulcers. Further study is needed.

Recommendations are based on good clinical practice as the evidence specific to fluid requirements and pressure ulcers is lacking.

There is no research to justify administration of vitamin/mineral supplements that are above the US RDI or comparable European or international standards.

Ethical and Clinical Implications for Practice

Clinicians need evidence-based research results to develop appropriate clinical guidelines for nutrition assessment and intervention. Nutrition and hydration can have a positive impact on the quality of life. Poor health outcomes may be associated with even small amounts of unintended weight loss. Early nutrition interventions can help to prevent and/or delay undernutrition, PEM and hydration deficits and their impact on risk of pressure ulcer development and delayed healing. Refer the patient to the RD as soon as risk is identified or upon identification of a pressure ulcer. If medically possible, early aggressive nutrition interventions should be implemented to prevent or correct nutrition deficits. For individuals at the end of life, however, nutrition interventions must be weighed against the burdens versus benefits and patient preferences.

If oral intake is inadequate, the registered dietitian may recommend consideration of enteral or parenteral nutrition consistent with the patient's wishes. Enteral (tube) feeding is the preferred route if the gastrointestinal tract (GI) is functioning. The risks and benefits of nutrition support should be discussed with the individual and caregivers early on, and should reflect the individual's preferences and goals for care. Studies that have reviewed enteral nutrition for improved outcomes for pressure ulcers have been disappointing (60,87,88). If enteral feeding is provided, health practitioners should routinely monitor feedings to ensure individuals are actually receiving the amount of tube feeding solution prescribed.

Acknowledgements

Becky Dorner, RD, LD, is President, Becky Dorner & Associates, Inc, and Nutrition Consulting Services, Akron, Ohio; Mary Ellen Posthauer, RD, CD, is a Consultant Dietitian and Chief Executive Officer of MEP Healthcare Services, Evansville, Indiana; David Thomas, MD, CMD, FACP, is Professor of Medicine, Saint Louis University, Saint Louis, Missouri.

The authors thank the National Pressure Ulcer Advisory Panel board for its approval of this document on December 22, 2008: Joyce Black, PhD, RN; Mona M. Baharestani, PhD, ANP, CWON, CWS; Evan Call, MS; Janet Cuddigan, PhD, RN, CWCN, CCCN; Teresa Conner-Kerr,

PhD, PT, CWS, CLT; Becky Dorner, RD, LD; Laura Edsberg, PhD; Aimee´ Garcia, MD; Susan Garber, MA, OTR, FAOTA, FACRM; Diane Langemo, PhD, RN, FAAN; Laurie McNichol, MSN, RN, GNP, CWOCN; Barbara Pieper, PhD, RN, CS, CWOCN, FAAN; Catherine Ratliff, PhD, APRN-BC, CWOCN; Steven Reger, PhD, CP; and Greg Schultz, PhD.

The authors also thank the reviewers of the document: Diane Langemo, PhD, RN, FAAN; Janet Cuddigan, PhD, RN, CWCN, CCCN; Steven Black, MD; and Lynn Moore, RD, LD.

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