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Dysphagia

Can Protein-Calorie Malnutrition Cause Dysphagia?

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Abstract. Nutrient deprivation has previously been shown to cause alterations in muscle and nerve function. Although an effect has never been studied in the neuromusculature of deglutition, the authors argue that an effect is likely. The proposed result is an increase in swallowing impairment in dysphagic individuals and associated risk of aspiration. Research studying the relationship between malnutrition and dysphagia is needed to verify clinical significance. Until controlled studies are completed, the authors suggest alternative alimentation in repleting severely malnourished dysphagic patients prior to attempting oral diet. A review of nutritional status indices is included to aid in identifying dysphagic patients at nutritional risk. Early identification of nutritional compromise and intervention can prevent malnutrition and its deleterious effects.

Key words: Deglutition disorders — Nutrition disorders — Starvation — Muscle function — Nerve function — Deglutition.

The act of swallowing is a complicated event requiring the coordinated activity of over 20 different muscles for the movement of saliva or ingested foods from the mouth to the stomach [1, 2]. Any interference with the precise movements of the involved muscles (and their associated structures) may lead to swallowing difficulties. Neuromuscular disease, stroke, head and neck cancers and surgical procedures are well known for their potential to interfere with one or more components of the swallow and cause dysphagia. If malnutrition also interferes with the function of deglutitive muscles, then, malnutrition may similarly compromise the integrity of the swallow and cause or worsen dysphagia. After a thorough search of the literature, no research could be found that addresses the effect of malnutrition on the muscles or neural pathways of deglutition. Case studies, such as recently published by O'Gara [3], could be used to support an effect of malnutrition. O'Gara's study shows concomitant improvements in nutritional status and dysphagia. It is difficult, however, to separate the effect of nutritional repletion from those of the various therapies employed (including thermal stimulation and compensatory maneuvers). Observations of improved oral-motor function in children with cerebral palsy following nutritional rehabilitation have similarly been made [4], but await definitive study.

The question that we pose, therefore, cannot be answered at this point in time due to a lack of research support. It is our intent, rather, to direct attention to the argument that protein-calorie malnutrition (PCM) *may* negatively affect swallowing function and *may* achieve clinical significance in some cases. Many studies have been published that assess the effect of malnutrition on other muscle groups and nerve function in general. A review of this literature and a discussion of current nutritional assessment methodology and treatment are pre-

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sented here in an effort to (1) encourage early identification of nutritional compromise prior to the development of functional changes associated with malnutrition, (2) promote timely initiation of appropriate nutritional support, (3) recommend alternative alimentation in the early repletion of severe malnutrition in dysphagic cases, and (4) stimulate research directed specifically at the effect malnutrition may have on swallowing pathophysiology.

Clinical Relevance

Malnutrition is a common sequelae of dysphagia. An impairment in swallowing ability can interfere with an individual's food selection and total intake. If the impairment is severe, food intake may be inadequate to maintain calorie and protein balance inducing a catabolic state. Left unchecked, weight loss and malnutrition will ensue. Several studies have documented an association between dysphagia and malnutrition. Sitzmann [5] reported that over a 1-year period, 100% consecutive hospital admissions with a primary diagnosis of dysphagia (N = 90) were malnourished. Other researchers have advanced an association between dysphagia severity and the degree of nutritional depletion. Moghissi and Teasdale [6] found that the amount of weight loss present in patients with esophageal cancer is highly predictive of their dysphagia severity score. Sheppard et al. [7] achieved similar predictability using an index of body composition known as the body mass index (BMI = wt (kg)/ht $(m)^2$) in studying 108 mentally retarded adults. Although it is reasonable to assume that dysphagia preceded the development of malnutrition in these study patients, it is worth noting that it is impossible to rule out an effect of malnutrition on dysphagia severity.

If PCM does affect swallow function, the impairment must be of little consequence for the general population as it has not been recognized in the literature. However, in patients with underlying swallow impairments (due to disease or a disabling condition), the additional compromise in swallowing function caused by PCM may significantly raise aspiration risk and hinder an individual's ability to consume adequate nutrition. We surmise that an individual's risk of aspiration will increase only after exceeding a threshold level of impairment. In the dysphagic case, the PCM-induced swallowing impairment would be masked by the underlying pathological condition and, therefore, difficult to identify. It is the effect of PCM on the dysphagic individual that we believe may have clinical relevance.

Effect of PCM on Dysphagia Morbidity and Mortality

PCM can negatively affect dysphagia morbidity and mortality by either increasing the incidence of aspiration episodes and, therefore, risk for pneumonia, or by interfering with an individual's ability to recover from aspiration pneumonia. There are several ways by which PCM may enhance these processes. While impaired wound healing is a major concern in PCM, it will not be discussed here as it does not directly relate to dysphagia management.

Weakness is one of the cardinal symptoms of PCM [8]. General weakness and fatigue may affect a dysphagic individual's ability to learn or execute compensatory eating strategies. Weakness of the respiratory muscles, however, may have the greatest impact on aspiration risk. Excellent reviews of the adverse effects of PCM on respiratory function have been published [9, 10]. A loss of respiratory strength directly proportional to the degree of weight loss and distributed evenly between inspiratory and expiratory muscles has been demonstrated [11]. The consequences of malnutrition induced respiratory muscle weakness include reduced vital capacity, increased residual volume, and reduced maximal voluntary ventilation. In the malnourished dysphagic patient, these effects of PCM will limit the ability to clear aspirated material. Over time this may lead to an increased incidence of aspiration pneumonia.

Depression, irritability, mental confusion, and an inability to concentrate are among the host of psychological changes that occur in PCM [12]. These behaviors, like generalized weakness, will impair an individual's learning ability, but additionally will impair judgment and the ability to remain focused. These cognitive abilities are known to be essential for dysphagia training, safe swallowing, and successful self-feeding.

Infection is one of the most frequent and life-threatening complications of PCM. Death rates from measles and gastroenteritis and other infectious diseases are up to 50 times as high in protein- and calorie-deficient children as in well-nourished children [13]. Chandra and Chandra [14] have shown malnourished adults to have a five fold higher incidence of postoperative sepsis than their well-nourished controls. Several observed immunologic changes help to explain how PCM has these deleterious effects. PCM has been shown to impair cell-mediated immunity and neutrophil function, reduce the concentration of complement components, and decrease secretory IgA antibody response [14]. Niederman et al. [15] also observed enhanced gram-

negative bacterial adhesion and colonization of lower airway cells in nutritionally depleted humans. Reversal of these immunological outcomes has been demonstrated following nutritional therapy [15–17]. It may be reasoned that the malnourished dysphagic patient is impaired in his ability to ward off bacterial invasions and, therefore, is expected to be at an increased risk for pneumonia following aspiration of food or gastrointestinal contents. Furthermore, nutritional repletion can reverse this immunologic risk.

Protein-calorie malnutrition is common in the dysphagic population and should be avoided because of its deleterious effects on respiratory muscle strength, psychological behaviors, and immune function. These effects of PCM place the malnourished dysphagic individual at a higher risk for aspiration and subsequent pneumonia than either the well-nourished dysphagic or the malnourished nondysphagic. If a mechanical impairment in swallowing ability is shown to be caused by malnutrition, then it would add to this already high combined morbidity. As stated previously, the effect of PCM on deglutition is an area without evidence of study. Therefore, in support of our hypothesis, we will proceed to address this issue from a theoretical standpoint reviewing the general physiologic changes that occur in muscle and nerve function as a result of malnutrition. We use this argument to assert the need for early identification and treatment of malnutrition in the dysphagic population.

Alteration in Muscle Size and Function

Skeletal muscle wasting is an obvious effect of malnutrition and occurs at a rate proportional to the rate of weight loss [8]. A reduction in the temporalis, sternomastoideus, and cervical extensor muscles of the face is easily recognized by clinicians and is diagnostic of malnutrition. Less apparent, however, is the body's inability to spare internal muscles and viscera from catabolism. Early in the twentieth century, it was maintained that the most vital organs (heart and brain) were protected by nature from the degenerative effects of starvation. This idea, however, was not supported by factual data. In 1950, Keys et al. [8] summarized a large volume of animal and human observations to convincingly demonstrate that cardiac atrophy does occur during starvation. In fact, the loss of cardiac mass is nearly proportional to the weight loss of the whole body. More recently, this position has been confirmed in studies of laboratory animals [18–21] and humans with anorexia nervosa [22, 23]. It is currently recognized that cardiac mass and indices of cardiac function in PCM remain proportional to body mass and metabolic rate (i.e., workload) [21]. Thus an adaptation to undernutrition may be facilitating a reduction in cardiac mass as a means of energy conservation. This hypothesis is supported by the lack of reduction in cardiac mass observed in cancer cachexia, where metabolic demands remain high [23]. Liver [8, 18, 19, 23], spleen [23], and kidney [23] mass are similarly lost in isolated malnutrition and preserved in cancer [23].

The brain has also been shown to undergo gross morphological changes in PCM. Data gathered during the 1920s famine in the Soviet Union demonstrated a 2-cm reduction in head circumference in adult men and women over a 3-year period [8]. Furthermore, severe malnutrition within the first year of life has been associated with a reduction in total weight, protein, DNA, and RNA content of the brain [13]. While brain weight is proportional to degree of underweight in these children, a reduction in total brain cell number has occurred [13]. It is not known if a reduction in brain cell number impairs intelligence.

There is no evidence to suggest that the muscles of deglutition would be spared from degeneration during periods of nutrient deficits. While some deglutitive muscles may hypertrophy to compensate for disease-afflicted muscles, an overall decrease in workload is expected in most cases of dysphagia as intake of food declines. Furthermore, deglutitive muscles are mainly striated, suggesting their metabolic fate may more closely resemble that of peripheral muscles over internal organs. Peripheral muscle losses occur at a rate proportional to the rate of weight loss in both hypermetabolic disease states and isolated PCM [23].

An alteration in skeletal muscle function accompanies muscle degeneration in protein-calorie malnutrition [17, 24–37]. Tables 1 and 2 summarize recent studies that address muscle function after a period of restricted nutrient intake in animal and human subjects respectively. Interpretation of these data is complicated by the diversity of approaches employed. The animal studies listed in Table 1 differ in the duration and severity of nutrient deprivation, muscle selection, and preparation techniques. The human studies listed in Table 2 differ markedly in patient profile and criteria for diagnosing malnutrition.

In spite of the differences in study design, the results presented in Tables 1 and 2 affirm that a reduction in macronutrient intake leads to a reduction in muscle mass. Also apparent is a concomitant

Table 1. Summary of recent animal studies addressing the effect of malnutrition on muscle function

Subject/muscle	Investigator/year	Period of nutrient deprivation	Preparation method	Major findings[a]					
				Muscle wet weight	Fiber area	Maximum contractile force	F10/[b] Fmax	Post-tetanic relaxation time	Fatigability
Rat/diaphram	Dureuil [24] 1989	4 days	In vivo	↓	—[c]	↓	NS[d]	↑	↑
	Sieck [28] 1989	4 weeks	In vitro	—	↓	↓	—	—	↓
	Lewis [25] 1986	Until 50% control weight	In vitro	↓	↓	↓	↑	—	↓
Rat/gastrocnemius	Russell [29] 1984	2–5 days	In situ	—	—	↓	↑	↑	↑
		21 days	In situ	—	—	↓	↑	↑	↑
	Raju [30] 1974	13 weeks	In situ	↓	—	—	—	—	↑
Rat/gastrocnemius, plantaris, soleus	Ardawi [31] 1989	21 days	In situ	↓	—	↓	↑	↑	↑
Hamster/diaphram	Drew [27] 1988	Until 40% adult weight	In vitro	↓	↓	↓	NS	—	—
	Kelsen [26] 1985	4 weeks	In vitro	↓	↓	↓	NS	—	—

[a] All published results are listed, level of significance $P < 0.05$.
[b] F10/Fmax denotes the ratio of force at 10 Hz to 30–100 Hz.
[c] Information not available.
[d] NS indicates changes observed were not significant.

decrease in muscle fiber diameter, maximal isometric contractile force, and an increase in the percent force generated at 10 Hz to 30–100 Hz (high frequency reference values vary between studies, denoted F10/Fmax). The rate of relaxation following tetanic stimulation is significantly slowed in malnutrition while the fatiguability of a malnourished muscle appears to vary. Conflicting fatiguability results may be attributed to differences in muscle preparation techniques. The studies which maintained an intact blood supply to the issue (in vivo, in situ) report an increase in fatiguability, while studies using detached muscles (in vitro) report the opposite. This suggests in vitro preparations produce nonphysiologic responses.

When measured, the maximum contractile force generated by muscles in malnourished subjects was reduced in all studies reviewed with one exception [17]. The lack of change in muscle function observed by Lennmarken and Larsson [17] has been attributed to a relatively better nourished subject group. It is interesting to note, however, that these investigators did observe a significant rise in post-tetanic relaxation rate following nutrient repletion, suggesting an alteration in function was initially present.

The response of the adductor pollicis to ulnar nerve stimulation has been frequently used in humans to reflect muscle function as a whole. Moxham et al. [38] have demonstrated that the frequency-force curves of the adductor pollicis, quadriceps, and sternomastoid, and the force-pressure curve of the diaphragm are similar. Arora and Rochester [39] have also reported changes in respiratory muscle function paralleling those listed in Table 2. A reduction in diaphragm muscle mass and contractile force per unit area were two of the factors identified as contributing to muscle weakness.

It may be argued that the hospitalized patient could possess non-nutritional factors related to disease that would have an impact on muscle function. Brough et al. [32] studied the confounding effects of age, gender, nutrition status, steroids, surgery, and sepsis on muscle contraction characteristics. No significant effect could be attributed to gender, steroids, or surgery. A weak correlation between age and force of contraction was reported. Sepsis resulted in a rise in the ratio of the force of contraction, but this remained significantly less than the effect observed in hypocaloric patients. In addition, Brough's group noted a significant correlation between the reversal of all abnormal measures of muscle function and the duration of nutritional support. This study concluded nutrition status was the major factor contributing to the changes in muscle function observed in hospitalized patients.

Table 2. Summary of recent human studies addressing the effect of malnutrition on muscle function

Muscle	Investigator/year	Population/define malnutrition	Subject number	Major findings[a]			
				Maximum contractile force	F10/[b] Fmax	Post-tetanic relaxation time	Fatigability
Adductor pollicis	Brough [32] 1986	Inpatients/consuming <90% estimated needs	12	↓	↑	↑	—[c]
	Chan [33] 1986	Presurgical patients/ weight loss >10%	8	—	↑	↑	—
	Lennmarken [17] 1986	Presurgical patients/ weight loss >7% plus 2 other abnormal nutrition indices	9	NS[d]	NS	NS	NS
	Shizgal [34] 1986	Inpatients/increase in total body Na:K (16 receiving TPN)	21	↓	NS	—	NS
	Shizgal [34] 1986	Healthy volunteers after 48-h fast	8	↓	NS	—	↑
	Russell [35] 1983	Anorexia nervosa	6	↓	↑	↑	↑
	Russell [36] 1983	Obese patients after 2 weeks 400 kcal diet	6	NS	↑	↑	NS
		After additional 2-week fast	6	↓	↑	↑	↑
	Lopes [37] 1982	Inpatients/recent weight loss plus low serum albumin	10	↓	↑	↑	↑

[a] All published results are listed, level of significance $P < 0.05$.
[b] F10/Fmax denotes the ratio of force at 10 Hz to 30–100 Hz.
[c] Information not available.
[d] NS indicates changes observed were not significant.

The reduction in muscle weight following nutrient deprivation has been attributed to a reduction in muscle fiber diameter [18, 25–28, 40–42]. A decrease in sarcoplasmic volume is thought to be the primary contributing factor [40], although a reduction in myofibrillar protein has been recently demonstrated [43, 44]. In some cases of severe cachexia [41] a slight reduction in fiber number has been reported. Hegarty and Kim [19] report a reduction in fiber number in the skeletal muscle of young rats after a complete fast; however, more rigorous techniques have been unable to reproduce these results [18].

Muscle fibers are classified according to various biochemical and physiological characteristics into two main categories: type I (slow twitch) and type II (fast twitch) (see Table 3) [45]. Type I fibers are characterized by a small diameter, aerobic metabolism, and a rich capillary supply. They are the fiber type of slow twitch motor units which produce small twitch tensions and are generally recruited early in muscle contraction (low threshold). They also relax more slowly following tetany. Type II fibers are larger in diameter and are the components of fast twitch motor units. These motor units (higher threshold) are recruited after slow twitch units and generate higher tensions (see Table 4). Type II fibers can be divided into at least two subcategories known as IIa and IIb. Type IIa have a smaller relative diameter, produce moderate tensions, and can generate energy (ATP) by both aerobic and anaerobic metabolism. Type IIb have the largest diameter, produce the highest tensions, and derive energy primarily through anaerobic glycogenolysis. Fast twitch motor units comprised mainly of type IIb muscle fibers, therefore, fatigue rapidly.

Type II muscle fibers, and type IIb in particular [25, 42], are affected by PCM to a much greater extent than type I muscle fibers [25, 27, 28]. The relative sparing of slow twitch fibers in PCM likely stems from the basic differences between the fiber types. Type I fibers may be selectively maintained by their early and more frequent recruitment for low level activities. Alternatively, the high-oxidative capacity of type I fibers would allow more efficient use of available substrates [26].

Table 3. Profiles of predominant muscle fiber types. (Adapted from Binder [45], Table 23-1, p 512)

Fiber types	I	IIa	IIb
Morphology			
Diameter	Small	Medium	Large
Capillary supply	Rich	Rich	Sparse
Mitochondria	Rich	Moderate	Sparse
Histochemical features			
Glycogen	Low	High	High
Phosphorylase	Low	High	High
Myofibril ATPase	Low	High	High
NADH dehydrogenase	High	Medium-high	High
Biochemical features			
Lactate dehydrogenase	Low	Medium	High
Hexokinase	High	Medium	Low
Myoglobin	High	Medium	Low

Table 4. Characteristics of motor unit types. (Adapted from Binder [45], Table 23-2, p 516)

Motor unit type	Slow	Fast fatigue resistant	Fast fatiguable
Muscle fiber type	I	IIa	IIb
Muscle fiber diameter	Small	Medium	Large
Tetanic tension	Low	Medium	High
Twitch contractiontime	Slow	Fast	Fast
Fatigue index[a]	1	0.75	0.25

[a] Force after 2 min stimulation/initial force.

The proportion of muscle fiber types in a muscle reflects the muscle's function. Muscles requiring rapid or forceful contractions contain a higher percentage of fast twitch motor units, and, hence, type II fibers. In animals, the gastrocnemius muscle, used in running or jumping, is ~95% type II fibers [29]; the diaphragm, whose activity is less forceful and more sustained, is comprised of ~60% type II fibers [28]; and the soleus, used in postural control, is nearly 100% type I fibers [45]. While the percentage of muscle fiber types is not known for the multiplicity of muscles involved in deglutition, it is reasonable to suspect that there is a moderate-high percentage of type II fibers present. Successful swallowing is characterized by synchronized, rapid contractions and relaxations of the individual muscles involved. The speed required is characteristic of fast twitch motor units and their type II fibers. Furthermore, the lack of sustained activity in swallowing suggests type IIb fibers may predominate. As previously mentioned, type II fibers are most susceptible to nutrient deprivation. If, indeed, the muscles of deglutition contain a high percentage of type II fibers, the answer to our question will most likely be "yes." Deglutitive muscles may be among the first to atrophy in the face of reduced food intake. The integrity of the swallow could be compromised by malnutrition and would be associated with a higher risk of aspiration.

The predominating opinion of the authors cited is that the atrophy and thinning of muscle fibers causes the reduction in maximum force-generating capacity. The selective atrophy of type II fibers has a large impact on contractile force since they contribute greater specific tension (i.e., force/unit area) than type I fibers [28]. The increase in percent maximum force achieved at 10 Hz and prolonged posttetanic relaxation time can be similarly explained. The observations may reflect the greater proportion of low frequency stimulated type I fibers relative to high frequency stimulated type II fibers [25, 35–37]. An alternative explanation is that, if muscle relaxation is prolonged, potentiation of the force would occur during repetitive stimulation producing tetany at a lower frequency of stimulation [29, 37].

If morphological changes in the muscle fibers were the primary cause of the observed functional changes, a decrease in muscle fatigue would occur. Type I and IIa fibers, which are better preserved in PCM, are fatigue resistant. An increase in fatiguability, however, is reported in 75% of the reviewed studies which maintained a blood supply to the muscle (the remaining studies report no change) [24, 29–31, 34–37]. This suggests other physiologic factors are involved. The observations that muscle dysfunction begins within 24 h of fasting in humans [33] prior to a significant loss of nitrogen (and, therefore, muscle size), and that muscle function is normalized sooner than expected with refeeding [33–37] further supports the presence of other factors.

Several changes in muscle fiber enzyme activity have been reported in animals [29, 30, 46, 47] and in humans [48] suffering from PCM (see Table 5). In general, a significant reduction in tricarboxylic acid cycle (TCA) and glycolytic enzymes, and an increase in glycogenolytic enzymes occurs early in nutrient deprivation. Fatty acid oxidation is increased initially and then appears to drop off as deprivation, presumably, results in sufficient substrate to stimulate enzyme synthesis [29]. These changes parallel the systemic metabolic adaptations known to occur in starvation [49].

A decrease in intracellular energy substrates could participate in muscle fatigue. A drop in muscle glycogen [31, 33, 34], phosphocreatine [29, 31], and an accumulation of adenosine diphosphate (ADP)

Table 5. Reported changes in enzyme activities in muscle fibers following nutrient deprivation[a]

			TCA cycle					Glycolysis					Other	
Investigator/ year	Muscle	Period of nutrient deprivation	Citrate synthase	Isocitrate dehydrogenase	Malate dehydrogenase	Pyruvate dehydrogenase complex	Succinate dehydrogenase	Aldolase	Hexokinase	Lactate dehydrogenase	Phosphofructokinase	Pyruvate kinase	Glycogen phosphorylase (glycogenolysis)	Beta-hydroxyacyl coA dehydrogenase (fatty acid metabolism)
Ardawi [31] 1989	Rat/gastrocnemius, plantaris	21 days	↓						↓		↓	↓	↑	
Denyer [46] 1989	Rat/heart, diaphragm, red quadraceps	48 h				↓								
Holness [47] 1989	Rat/heart	48 h				↓								
Russell [29] 1984	Rat/gastrocnemius	2–5 days					NS				↓			↑
		21 days					↓				↓			↓
Russell [48] 1984	Obese human gastrocnemius	14 days					↓				↓			NS
Raju [30] 1974	Rat/gastrocnemius	13 weeks		↓	↓			↑		↑			↑	

[a] All published results are listed, level of significance $P < 0.02$.

[29, 31] does occur in muscle cells following nutrient deprivation. Phosphocreatine serves as a source of high energy phosphate during anaerobic muscle contraction by donating its phosphate to ADP. Since the formation of myofilament cross bridges during muscle contraction uses ATP, a lack of renewable high energy phosphates would increase muscle fatigue.

The drop in muscle pH that occurs with increased conversion of glycogen to lactate has also been suggested to contribute to muscle fatigue [31]. An increase in muscle lactate has been observed in rat gastrocnemius muscle following 5 and 21 days of nutrient deprivation [29, 31].

Low intracellular energy stores can alter calcium fluxes. Russell et al. have observed a significant rise in intracellular calcium concentration associated with acute nutrient deprivation in humans [48] and rats [29]. This is particularly interesting since muscle contraction is a calcium-mediated process [45]. In sequence, motor neuron transmitter release triggers an action potential in the muscle cell plasma membrane, the electrical signal is transmitted to the sarcoplasmic reticulum which responds by releasing its calcium pool into the sarcoplasm, the rise in free calcium initiates myofibril contraction, and finally, relaxation of the muscle cell follows the re-uptake of calcium by the sarcoplasmic reticulum (an ATP-dependent process). Russell's group hypothesizes that the decreased [phosphocreatine]/[ATP] and [ATP]/[ADP] ratios reduce the available energy for calcium efflux and sequestration into the sarcoplasmic reticulum. The resulting intracellular accumulation of calcium would reduce the muscle relaxation rate and alter contraction characteristics [29].

It is clear that protein-calorie malnutrition negatively affects muscle function. As a consequence of PCM, there is a reduction in muscle weight, muscle fiber diameter, and impairment in the force of contraction and rate of relaxation of muscle fibers. As noted earlier, no tissue is immune to nutrient deprivation. Perhaps the best anatomical analogy for swallowing musculature can be drawn to the effect of PCM on respiratory muscles. Although few studies have looked at respiratory muscle function in malnutrition, they consistently demonstrate a reduction in muscle size and contractile force proportional to the loss of body weight. It seems reasonable, then, that the deglutitive muscles would be altered by PCM. Furthermore, muscles with a high percentage of type II fibers have been shown to be affected by PCM more than type I predominant muscles. If deglutatory muscles fall in the moderate to high type II classification (as we reason to be likely), then they would be at the greatest risk for nutritional compromise.

The cellular biochemical changes noted to occur in nutrient deprivation may prove to be more clinically relevant than the morphological changes observed. Intracellular energy substrates appear to be quickly repleated with nutritional therapy and may permit normalization of muscle function prior to full regeneration of muscle tissue. This suggests that a relatively short-term supply of adequate nutrition may reverse most of the functional effects of PCM on swallowing and respiration. In the case of moderate to severe dysphagia with concomitant PCM, this may reduce the risk of aspiration sufficiently to permit oral feeding.

Alteration in Nerve Function

The highly coordinated muscular events of the swallow depend on the activity of the central nervous system (CNS). Fibers from the cranial nerves and higher cerebral centers send input signals to the brainstem swallowing centers [1]. This information is processed in the brainstem swallowing center and if appropriate, triggers a swallow response via efferent cranial nerves. PCM could potentially interfere with execution of the swallow response by altering action potential generation, propagation, or transmission in any component neuron.

A large amount of literature has been published describing the effect of PCM on brain and nervous system development. In general, children with PCM are irritable, apathetic, and listless. Their head circumference and brain weights are significantly reduced [13, 50–53]; 30% to 40% experience hypotonia [54, 55] and more than half present with tendon areflexia [55]. A significant reduction in motor nerve conduction velocity has also been demonstrated in the ulnar, median, peroneal [53–57] and posterior tibial nerves [51, 53–57] of malnourished children. The amount of peripheral nerve involvement seen in early childhood has been directly related to the degree of PCM present [50, 53, 55]. The effect is greater if the onset of PCM is earlier in development or longer in duration [53]. While deficiencies in B vitamins are known to cause peripheral neuropathy, clinical symptoms of B vitamin deficiencies did not correlate with the neural changes observed by Chopra et al. [50]. The potential interference of subclinical vitamin B deficiencies, however, cannot be ruled out.

Microscopic evaluation of neuronal tissue shows

a reduction in myelin sheath thickness and a widening of the nodes of Ranvier in experimental animals deprived of nutrition early in development [58]. A predominance of small diameter fibers has also been observed in children with PCM [50, 52, 57]. In addition, anterior horn and brainstem nuclei of malnourished animals show several morphologic changes [58] which include an excessive concentration of neuroglial nuclei, an increase in the proportion of neuroglial cells with nuclei of large diameter, and the presence of elongated, vesicular, and horseshoe-shaped nuclei.

Nutrient deprivation can be expected to have a much greater effect on the nervous system during the early stages of neuronal development than during adulthood. Dobbing and Sands [59] have described a critical period for brain and nervous system development that occurs in humans during the few months preceding and following birth. Failure to provide for adequate growth and development during this time period is associated with permanent damage to the CNS. The myelination of peripheral nerves in humans is also known to continue for several years after birth [60], suggesting an increased susceptibility to nutritional deficits during this time period as well. The applicability of results from developmental studies is, therefore, very limited when addressing PCM in adult humans.

Unfortunately, few recent studies have assessed the effect of PCM on nerve function after myelination has been completed [61–66]. A review of these studies suggests a functional decline in CNS performance in adults does occur in PCM; however, the effect is small. Keys et al. [8] reports that 6 months of low nutrient intake causes a diminution of the tendon reflex response. More recently, Mattson and Lecocq [61] studied the effect of a 28-day fast on obese subjects. Although 24% developed paresthesias, no significant change in mean motorneuron conduction velocity or range of velocities was found in the peroneal, median, or ulnar nerves. It is erroneous, however, to equate fasted obese subjects with malnutrition as a 28-day period may be insufficient to induce a truly deficient state.

Idiaquez [62] and Doekal et al. [63] have reported altered autonomic reflexes in association with malnutrition in adults. Idiaquez [62] describes a significant lack in heart rate response to postural changes (standing to lying down positions) in patients suffering from PCM. Doekel et al. [63] have observed a reduced or absent respiratory response to hypoxia after acute starvation. These changes are more likely attributed to an adaptive decrease in sympathetic activity [64, 65] rather than to degenerative changes in nervous tissue. Reduced sympathetic activity is believed to contribute to the reduced metabolic rate and, thus, to the enhanced fuel utilization known to occur in starvation.

Microscopic evaluation of adult nervous tissue does support an effect of PCM. Keys et al. [8] observed an increase in vacuolation, chromatolysis, and fibrolysis in both central and peripheral nerves with starvation. Degeneration of the myelin sheath has also been observed in peripheral nerves of mature humans and animals [8, 66, 67]. Experimental protein deficiency in monkeys has produced irregular thickening and infoldings of the myelin sheath and formation of myelin nodules that protrude into the axoplasm [66]. This was associated with a marked slowing of conduction velocities after 9 weeks of nutrient deprivation. Oldfors [67] observed a degeneration of nerve fibers in the spinal cord and distal portions of the longitudinal tail nerves of protein-deficient rats. The anatomical and functional changes observed in these studies are not attributable to concomitant B vitamin deficiencies as an adequate intake of B vitamins was assured.

Neurotransmitter synthesis is known to be susceptible to precursor control. A deficiency in tryptophan, tyrosine, and choline has been shown to reduce the synthesis of serotonin, norepinephrine, and acetylcholine, respectively [68]. Serotonin [69, 70] and norepinephrine [70, 71] participate in the swallow at the level of the nucleus solitarius. A reduction in these neurotransmitters might impair the fidelity of synaptic transmission causing a failure to produce the action potentials necessary for muscular contractions. This situation could theoretically be amplified by a reduction in neurotransmitter receptors due to the substrate limitations imposed by PCM. Conversely, it can be argued that synaptic neurotransmitter action could be heightened by either a reduction in degratory enzymes or an increase in amino acid precursors made available from muscle catabolism. Which physiologic factor will dominate in malnutrition is unknown.

The impact of PCM on nerve function is significant during development of the central and peripheral nervous system. Providing infants and children with adequate nutrition is imperative to assure optimal intellectual and physiologic function in adulthood. Although the data are limited, a negative effect of PCM on mature neuronal tissue is probable. Whether the effect causes an alteration in function in the network of swallowing neurons, however, is only speculative. Certainly, the effect is less apparent than the alterations in muscle size and contractile properties caused by PCM.

Table 6. Nutritional assessment parameters

Parameter	Level indicative of malnutrition	Measures
Body weight	60%–80% ideal = moderate <60% = severe	Calorie and protein stores
Weight loss	5%–10% of usual weight over 6 months	Calorie and protein stores
Triceps skinfold	<10th percentile for gender and age	Calorie reserves
Midarm muscle circumference	Loss of 15–20 percentiles	Somatic protein
Creatinine-height index	60%–80% = moderate <60% = severe	Somatic protein
Serum albumin	3.0–3.5 g/dl = mild 2.1–3.0 g/dl = moderate <2.1 g/dl = severe	Visceral protein
Serum transferrin	150–200 mg/dl = mild 100–150 mg/dl = moderate <100 mg/dl = severe	Visceral protein
Serum prealbumin	10–15 mg/dl = mild 5–10 mg/dl = moderate <5 mg/dl = severe	Visceral protein/adequacy of recent calorie and protein intake
Total lymphocyte count	1200–1500 = mild 800–1200 = moderate <800 = severe	Immune function
Cutaneous hypersensitivity	<5 mm induration in response to three antigens	Immune function

Nutrition Status Assessment

If PCM has the potential to alter neuromuscular function, early identification of nutritional compromise is of primary importance to the dysphagic patient whose swallowing is already impaired by a neuromuscular condition. Although it may be easy to identify the severely malnourished patient, the patient with subtle undernutrition is difficult to recognize. Furthermore, a major difficulty in assessing the nutritional status of individuals is the need to differentiate between alterations in assessment parameters caused by a lack of nutrients versus metabolically induced changes caused by the disease process. A discussion of these parameters is presented here to underscore their usefulness, complexity, and limitations, and provide the health care professional with the ability to identify dysphagic patients at risk for developing nutrient deficiencies. This discussion is limited to indices of macronutrient deficiencies as the parameters for assessing vitamin and mineral deficiencies are beyond the scope of this article.

Nutritional assessment involves the ongoing evaluation of nutrient intake and losses and the evaluation of nutrient stores. Protein stores are the structural and functional proteins themselves; adipose, glycogen, and proteins comprise the caloric reserve [72]. Detecting alterations in macronutrient stores traditionally uses an estimation of intake, anthropometry, hepatic protein synthesis, cellular immunity, and the creatinine-height index [73]. Table 6 lists these common parameters used in nutritional assessment and the levels indicative of malnutrition.

In the adult, maintenance of usual body weight is expected. Therefore, weight loss over time is a helpful measure of nutrition status [74]. In the child, both weight gain and growth are desired. Failure to maintain expected rates of growth and appropriate weight gain is one indicator of PCM [13]. In acute weight loss, catabolism of tissue proteins provides energy for daily caloric requirements [75]. A weight loss of 5% to 10% of usual body weight over 6 months indicates loss of lean body mass and macronutrient deficiency [74].

Body fat and muscle stores may be assessed by measurement of skinfold thicknesses. Adipose tissue comprises approximately 25% of total body weight and half of this tissue is found in the subcutaneous compartment [76]. Triceps skinfold measurements have been most frequently used in assessing fat stores. Triceps skinfold, along with midarm circumference is used to calculate a midarm muscle circumference as an indicator of somatic protein status [76]. These measurements, however, can vary significantly among observers [77]. Additional problems with fat fold measures include the arbitrary grading of depletion severity and assumptions made regarding tissue compartments in calculating results [77].

Endogenous creatinine production and excretion indirectly measure muscle mass [78]. In nutrition assessment, the patient's creatinine excretion is compared with the value expected from a healthy subject of similar age, height, and ideal body weight. This test requires normal renal function, which can limit its use in the hospitalized patient population.

Depressed serum levels of protein synthesized and secreted by the liver may reflect visceral protein depletion. It is assumed that decreased values reflect reduced levels of amino acid precursors and decreased hepatic (and other visceral) mass [79]. Serum albumin, transferrin, and prealbumin (transthyretin) are three hepatic proteins used as indicators of visceral protein status. Mullen et al. [16] prospectively studied the immunologic and nutrition

status in 64 patients consecutively admitted for elective surgical procedures and found that the visceral protein compartment was the most prognostic indicator of surgical morbidity and mortality. A serum albumin of less than 3 g/dl had a two and one half-fold increase in morbidity compared with those patients with a serum albumin level of greater than 3 g/dl. Serum transferrin levels below 220 mg/dl were associated with a fivefold increase in complications.

The rate of synthesis and degradation of hepatic proteins determines their specific use in nutritional assessment. Albumin has a half-life of 20 days, transferrin 8 days, and prealbumin 2 days [79]. Prealbumin, therefore, is able to detect changes in visceral protein status earlier than albumin, with transferrin's ability being intermediate. In other words, prealbumin will fall rapidly when calorie or protein intake is less than metabolic needs and will be the first to return to normal following the initiation of adequate nutritional therapy. Unfortunately, hepatic protein serum levels may be affected by factors other than nutritional status. For example, prealbumin drops rapidly during infection and will not respond to nutritional therapy until the infection is cleared [80]. Serum hepatic proteins are also affected by the metabolic response to trauma or surgery, liver and renal function, age, and alterations in hydration status [81, 82]. Conversely, chronic PCM is characterized by normal serum hepatic protein levels in spite of visceral protein compromise [83]. In the semistarved or starved state, the body adapts to reduced synthetic capabilities by increasing the half-life of hepatic proteins. Serum levels are also maintained under these conditions by a reduction in total blood volume. Interpreting a transferrin level is complicated by its role in iron transport. Transferrin will rise in iron deficiency in spite of a relative lack of protein or calories [84].

Due to PCM's effect on immune function, immunologic indices such as circulating numbers of T-cells and lymphocytes and cutaneous hypersensitivity response to skin-test antigens are useful in assessing nutritional status. These parameters have been shown to correlate well with measures of visceral protein status [76] and predict risk of sepsis and mortality [85, 86]. While it is felt that energy is closely related to body cell mass, failure to respond to antigens may be due to non-nutritional factors, such as infection, immunosuppressive drugs, edema, and lack of prior exposure to the antigens.

Grip strength (dynamometry) has been shown by some [87, 88] to be a sensitive test for detecting early malnutrition. Watters et al. [89], however, failed to show a strong correlation between dynamometry results and other nutritional parameters. The authors speculate that dynamometry may correlate better with muscle metabolism than muscle mass. Serial readings of dynamometry, however, may prove to be useful in documenting improved nutritional and metabolic status.

Several investigators have attempted to develop panels of nutritional parameters which have a higher prognostic ability than isolated parameters [90]. These panels range from the very simple to the very complex. Seltzer et al. [91, 92] have proposed the combination of serum albumin and total lymphocyte count. These investigators observed that when both of these parameters are abnormal upon hospital admission they are associated with a four-fold increase in complications and a 20-fold increase in death. Mullen et al. [93] found a four parameter model (serum albumin, triceps skin fold, serum transferrin, and cutaneous hypersensitivity) accurate in predicting operative morbidity and mortality. When tested prospectively [94], Mullen's method (called the prognostic nutritional index or PNI), correctly predicted 72% of subsequent hospital mortality with a sensitivity of 74% and specificity of 66%. The difficulty in obtaining cutaneous hypersensitivity results has limited the application of this method. Jeejeehboy's group [95, 96] reports the combination of weight history and visual assessment of subcutaneous adipose and muscle wasting is equal in accuracy to laboratory measures of nutritional status. This technique is necessarily limited by the skill level of the diagnostician. Linn [97] has combined several subjective and objective parameters of nutritional assessment to create an intricate protein-energy malnutrition scale. This tool involves rating 23 items under the categories of anthropometrics, clinical history, physical exam, and laboratory tests. While this method has been validated, its major drawbacks are its cost and complexity. No nutrition panel has achieved wide acceptance. Parameters continue to be selected on an individual or institutional basis.

Malnutrition in patients with degenerative neuromuscular diseases or congenital defects is especially difficult to identify. Low body weight is frequently expected as a result of skeletal muscle atrophy. The question is, to what degree is malnutrition contributing to muscle atrophy? Some recent observations suggest the effect of malnutrition may be more significant than previously appreciated. Nutritional support in children with Duchenne muscular dystrophy [98] and cerebral palsy [99] has shown that an increase in muscle mass can occur where it was previously thought impossible. The fact

that not all patients with amyotrophic lateral sclerosis (ALS) lose weight [100] also suggests that nutrient deficits may promote the muscle atrophy observed in this progressive disease. Furthermore, the pattern of pulmonary compromise seen in ALS is identical to the decline in respiratory function reported in association with poor nutritional status [100].

The objective parameters of nutritional assessment including dietary history, anthropometric, and biochemical parameters maintain their effectiveness in diagnosing malnutrition in patients with neuromuscular diseases. Weight loss can also be used when interpreted in light of what can be reasonably attributed to disease specific muscle atrophy. The techniques of nutritional monitoring necessarily gain added importance. Frequent assessments of nutrient intake via food or formula intake records and rapid turnover hepatic proteins (e.g., prealbumin) will direct nutrition interventions prior to the development of malnutrition.

In our experience an admission weight, weight history, serum albumin, and prealbumin are sufficient to identify the majority of patients requiring nutritional attention. Rescreening hospitalized patients frequently for poor meal intakes and weight changes will identify patients at risk for developing nutritional compromise. In the acute care setting, weighing the patient every 2 to 3 days is recommended. Serum albumin can be checked every 2 to 3 weeks and prealbumin every week if there is cause for concern. Consulting a registered dietitian for a full nutritional assessment should follow the identification of abnormal nutritional parameters. A dietitian can identify specific nutrients at risk and direct further nutritional diagnosis and care. Prompt initiation of nutritional support, when indicated, will avoid the development of malnutrition and its adverse effects on wound healing, immunocompetence, neuromuscular function, cognition, and sense of well-being.

Nutrition Support

Nutrition support refers to the specific modification of nutritional therapy when oral intake is inadequate. In planning an appropriate nutrition support approach, several considerations must be included. The extent of macronutrient inadequacy must be assessed, including an estimate of the protein and calorie requirements versus intake. Once the protein and energy balance has been determined, the degree of protein and fat depletion should be assessed. A quick assessment of the degree of depletion may be made on the basis of nonvolitional weight loss. As previously discussed, a 5% to 10% weight loss over a 6-month period is indicative of malnutrition. The adequacy of nutrient stores and oral intake determines the urgency of nutritional support. For patients with significant weight loss, nutrition support should be initiated immediately and advanced as rapidly as tolerated to the level required to replete deficiencies. Serum phosphorus and magnesium should be monitored closely during the early refeeding period as levels commonly fall to critically low concentrations with induction of anabolic processes. A registered dietitian should be consulted prior to initiating nutrition support for a complete nutritional assessment and recommendations for mode of support. Dietitians are knowledgeable in the composition of available nutritional products and can design therapy to meet individualized needs.

Patients without evidence of malnutrition and little risk of aspiration may be effectively supported by oral means. This often requires specific modifications in posture, diet texture, and consistency. Several publications describe individualized methods to maintain nutritional status via oral diet in dysphagia [3, 101–104]. Special attention needs to be given to meeting the dysphagic patient's fluid needs. Fiber can also be a dietary component of concern.

Patients suffering from moderate malnutrition and mild-moderate dysphagia may best be treated with a short course of nutrition support either by total parenteral nutrition (TPN) or tube feeding prior to attempting an oral diet. As discussed above, an effect of malnutrition on muscle function occurs early in deprivation [34] and may be related to the energy-depleted state of the muscle cells. Impairment of the swallow caused by a lack of available energy, therefore, should improve quickly with nutritional support. Chan et al. [33] observed a return to normal muscle function parameters in malnourished surgical patients after 2 days of intravenous glucose and potassium administration. This quick response to energy substrate may explain the normal muscle function parameters observed by Shizgal et al. [34] (see Table 2). While Shizgal's subjects were malnourished, 75% were receiving TPN during muscle function testing. Attempting to achieve a level of oral intake sufficient for repleting the malnourished dysphagic will, by our hypothesis, be associated with a higher risk of aspiration. Nutritional repletion prior to the initial swallowing trial will minimize this risk and optimize the patient's chance of success.

Severe malnutrition and mild–moderate dysphagia require aggressive nutritional support. Believing our hypothesis to be true, we assert it would be in the patient's best interest to withhold oral diet until energy stores and some regeneration of muscle fibers has occurred. It is not possible to estimate the extent of repletion necessary to reverse the effect of PCM at this point in time. Russell et al. [35] describes normalization of maximal relaxation rate and fatiguability in patients with anorexia nervosa following 4 weeks of refeeding, and all parameters of muscle function returning to normal within 8 weeks. While patients with anorexia nervosa present with extreme malnutrition, they cannot be equated with the severely malnourished hospital patient due to the additional stress of disease and treatment. Frequent assessments of swallowing function should be used to determine when a maximum response has been achieved. Clearly, this is an area in need of research. However, before data can be generated and analyzed we believe there is sufficient argument to support this conservative approach.

Most clinicians believe that dysphagic patients who are unable to meet nutritional requirements by oral means may be safely supported enterally, provided they have a functioning gastrointestinal tract [105, 106]. Recent evidence, however, questions this standard practice. Sitzmann [5] has found a 40% complication incidence and a 30% mortality rate associated with continuous nasoenteric (nasogastric and nasoduodenal) feeding of dysphagic patients. This was significantly greater than the complication incidence and mortality rates observed in dysphagic patients receiving nutrition via gastrostomy, jejunostomy, or TPN. Since mortality was most frequently (80%) a result of respiratory failure from aspiration pneumonia and commonly associated with abnormal pharyngeal sensation, gastroesophageal reflux is a probable cause. A recent report by Jacobs et al. [107] has also found nasogastric tube feedings to be associated with a high incidence of pneumonia in intensive care patients. These researchers assert that continuous infusion of formula into the stomach leads to bacterial overgrowth, upwards migration, and subsequent respiratory infection. Feeding distal to the pylorus is believed to reduce the risk of gastroesophageal reflux and subsequent pneumonia [108]. Jejunostomy feedings have been successfully used in the nutritional support of patients with cystic fibrosis [109, 110], a population at high risk for gastroesophageal reflux. In light of these recent reports, to minimize aspiration risk we suggest the following: if presented with a dysphagic individual in need of nutritional support who has impaired alertness or sensation in the pharyngeal and laryngeal areas, the preferred delivery routes are jejunostomy or TPN, followed by gastrostomy. Nasoenteric tube feedings are a last resort. If the individual is also severely malnourished with compromised immune and respiratory functions, then avoiding oral or nasoenteric tube feedings is further warranted.

Conclusion

The studies reviewed demonstrate a marked functional decline in a variety of muscles as a result of PCM, and these changes are accompanied by biochemical alterations within the muscle cells characteristic of an energy-depleted state. Several etiologic theories have been developed which can explain the observed changes in muscle function. Changes also occur in nervous tissue as a result of PCM although the effect appears to be less significant. The question remains whether these changes occur in the neuromusculature of deglutition and, furthermore, if the effect is dysphagia. The information presented here suggests that this could be the case. We propose that this information be considered in the treatment of malnutrition in dysphagic patients, recommending the practice of withholding oral intake until some nutritional repletion has been accomplished by nonoral means. Furthermore, early detection of nutritional deficits and the establishment of an aggressive nutrition care plan can avoid malnutrition and its undesirable effects on wound healing and on immune and neuromuscular function. All health care professionals can participate in identifying dysphagic individuals at risk for malnutrition.

Research in the area of malnutrition and dysphagia is greatly needed. Electromyography, as described by Palmer [2], can provide an objective measure of swallow performance which may find applicability towards this aim. Correlating electromyographic results with nutritional assessment parameters may determine if a significant relationship exists. Patients with neuromuscular diseases, such as ALS or cerebral palsy, would be appropriate groups to study. Unlike stroke or surgical patients, the swallowing function of patients with neuromuscular diseases is not expected to improve. An effect of nutritional support on the degree of dysphagia present could, therefore, be directly observed.

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