Nutritional Management in MND/ALS Patients: An Evidence Based Review.

Objective:

This systematic review addresses the evidence in regard to the management of nutrition for patients with motor neurone disease (MND), in particular amyotrophic lateral sclerosis (ALS). The aim is to help establish patient and carer based guidelines for the clinical management of nutrition for MND/ALS patients.

Justification:

Nutrition is an independent prognostic factor for survival in MND/ALS patients (Cameron & Rosenfield, 2002; Desport et al, 1999). The symptoms and progression of ALS can affect a patient's nutrition and hydration in three ways. Firstly, the upper extremity weakness limits a patient's dexterity so that cutting food and feeding can be difficult. Secondly, the onset of dysphagia impairs the swallowing of food. Thirdly there is a requirement for increased calorific intake and hypermetabolism is present. Patients can very quickly become deprived of protein, calories and vitamins as their food and fluid consumption may be greatly restricted. If nutritional support is not provided, patients will become malnourished, affecting many functions including respiratory function and the quality of life. The loss of weight has also been associated with shortened survival rates (Desport et al, 2001; Kasarskis et al, 1996; Lacomblez et al, 1996). Management of nutritional status throughout disease progression is important to enhancing the quality of life and optimising the timing of interventions (Silani, Kasarskis & Yanagisawa, 1998).

Miller et al (1999) conducted a systematic review on nutritional management as part of their development of guidelines (parameters) for the management of ALS. However, the management of nutrition incorporates a continual assessment and implementation of dietary modifications throughout the duration of the disease (Moxley & Kempf, 1980). This process warrants a more detailed systematic review of methods and recommendations. In the early stages, food fortification and oral supplementation is managed, food consistency modified and advice provided on safe swallowing but as the disease progresses, nutritional support may have to provide artificial nutrition (parenteral or enteral therapy). The issues of nutritional management in ALS patients, can be divided into three main areas of importance:

1. Management of dysphagia
2. Nutritional maintenance
3. Enteral feeding

Within these components, a list of review questions was developed, addressing the treatment goals of meeting the patients' nutritional requirements (Table 1). Through these questions, recommendations for guidelines and further research on the clinical management of nutrition for ALS patients can be yielded.

Table 1.
List of Review Questions.

Management of Dysphagia.

- ***I.*** What is the evidence for accurately evaluating dysphagia in MND patients?
- ***II.*** What are the recommended procedures for managing dysphagia?
- ***III.*** Are there any interventions that can help ease difficulties with swallowing and feeding?

Nutritional Maintenance.

- ***I.*** How common is malnutrition in MND?
- ***II.*** What is the evidence for accurately evaluating nutritional status?
- ***III.*** What is the evidence for managing constipation and other intestinal problems?
- ***IV.*** What are the fluid and caloric requirements of patients with MND at different stages of the illness?

Nutritional Management for Advanced Stages – i.e. use of gastrostomy.

- ***I.*** When should interventions such as PEG be implemented?
- ***II.*** What are the risks of PEG in patients with MND?
- ***III.*** What is the effect of PEG in preventing aspiration and aspiration pneumonia in MND?
- ***IV.*** Can PEG prolong survival and improve quality of life?
- ***V.*** What are the alternative methods of feeding?
- ***VI.*** What are the patients' views on PEG and other treatments?

Review Methods:

Studies were identified through computerized searches of 35 databases, including MEDLINE, CINAHL, PsychINFO, Cochrane Controlled Trials Register, National Research Register and Conference Papers Index. Internet searches of websites of drug companies and MND research sites, snow balling and hand searches were also employed to locate any unpublished study or other grey literature on nutrition and MND. Since management of ALS involves a number of health professionals and care workers, searches were made across multiple disciplines. No time frame was imposed on the search so that the articles would include everything ever published on MND and nutrition. This provided large catchments of literature, which increased probability of identifying all relevant studies. On initial screening of titles and abstracts, a large number of duplicates were found but once these were identified

and irrelevant articles deleted, a total of 659 articles were recorded. According to the protocol, only articles pertaining to nutritional management in MND patients could be included. All other managerial issues pertaining to MND, general and descriptive articles on MND, experiments on animal populations and nutritional management of other populations were excluded. The study selection process reduced the number of 659 down to 242 articles.

All studies selected addressed nutrition in ALS patients, though some were geared towards neuromuscular patients in general but had mentioned ALS patients or addressed the management of ALS disease. Most of the articles were on general nutritional management, which consisted largely of medical professionals' opinions or were part of a more general management article. Since the purpose of this review is to extract the best evidence, only articles that were graded as C and higher were extracted for the review (See Table 2 for the quality assessment grades). A large proportion of 'expert' opinion was extracted as there was a lack of higher level research in addressing some of the research questions. However only articles that were classed D+ (i.e. they were explicitly backed up by evidence from other literature or from the author's own primary research) were included. Opinions expressed in letters to editors on published studies were also removed from the systematic review, as these did not reveal any inconsistencies with the data that the systematic review had not already detected nor did they include primary research of the writer. Single case studies were also omitted, as these were descriptive and did not mention best practice in managerial issues. In addition, they varied so much in content that they could not be viewed cohesively. Literature on impaired glucose utilisation amongst ALS patients were also removed as the studies were at least 20 years old and had no practical applications for the current management of nutritional status. The resulting number of articles for data synthesis was 137.

The majority of studies were retrospective (mostly Class C evidence). There were no randomised controlled trials, although there was one well-conducted systematic review (Miller et al, 1999) – replicated in Miller (2001) – and six other systematic reviews of varying quality pertaining to issues of nutrition in ALS patients. A minimum number of patients and defined patient characteristics per observational or controlled quasi-experimental study were not set as criteria for inclusion. Firstly, the ALS sub-population in the general population is small so sample sizes will also be small. Secondly, the ALS population varies in demographics and disease severity, so compilation of all studies can help to identify the common issues of nutrition. Due to the variation in sample characteristics, study design and statistical tests used, it was deemed more suitable to report the results qualitatively rather than attempt to quantify the results. In regards to the development of the guidelines, each guideline was classified in relation to the quality of the evidence (Table 3). It is worth noting that most guidelines comprised of a consensus of 'expert' opinion (level III). This highlights the necessity for more experimental and observational research.

Table 2
Grading of Quality of Evidence:

A.+	High quality experimental studies without heterogeneity and with precise results. Also includes high quality systematic reviews of RCTs/meta-analysis.
A.	High quality experimental studies with heterogeneity or well conducted systematic reviews, meta-analyses of RCTs, or RCTs with a low risk of bias.
A.-	RCTs with a high risk of bias.
B+	High quality quasi-experimental studies, high quality controlled observational studies with a low risk of bias.
B	Quasi-experimental studies and controlled observational studies that were well conducted.
B-	Low quality quasi-experimental studies and low quality controlled observational studies that have a high risk of bias.
C+	High quality non-controlled observational studies & case series
C	Well conducted non-controlled observational studies & case series
C-	Low quality non-controlled observational studies & case series
D+	Valid expert opinion.
D	Inconclusive expert opinion
D-	Questionable/inconclusive expert opinion.

Table 3
Classification of recommendations for clinical management:

I.	Strong recommendation for use in clinical management, arising from strong evidence obtained from class A and B studies.
II.	Recommendation for clinical management that is based on Class B and/or Class C evidence.
III.	Suggestion for clinical management that is based on Class D evidence and/or where evidence is inconclusive.

Management of Dysphagia:

The management of nutrition in MND/ALS patients involves the management of dysphagia. A review of literature on nutritional management in ALS patients revealed a negative correlation between severity of dysphagia and caloric intake and weight loss (Silani, Kasarskis & Yanagisawa, 1998). This is because the symptoms of dysphagia - such as drooling, choking on fluid and food - impede oral feeding, resulting in a deficit in protein and caloric intake (Miller et al, 1999). Furthermore, dysphagia can lead to aspiration pneumonia (Leigh & Ray-Chaudhuri, 1994). Between 9% and 30% of patients with ALS initially present with dysphagia – particularly in those with bulbar onset - and nearly all will develop the condition eventually (Robbins, 1987; Desport et al, 2001).

What is the evidence for accurately evaluating dysphagia in MND patients?

When viewing the literature cohesively, a process of evaluation can be determined. A patient presents with a swallowing problem. This is examined through an initial bedside evaluation, followed as soon as possible by a specialist evaluation, if dysphagia symptoms are identified. Early referrals to speech & language therapists are advocated in the literature. Speech & Language therapists can determine the presence, severity and nature of dysphagia, prognosis for improvement and swallowing techniques to reduce risks of choking and aspiration (Borasio et al, 2001a; Langmore, 1999; Houde & Mangolds, 1999). Identification of problem foods, which cause the greatest difficulty in swallowing, can also be made (Gelinas & Miller, 2000; Langmore, 1999). From the specialist assessment, recommendations can be made in relation to the changes in food consistencies, feeding strategies and any further evaluations (Langmore, 1999; Carter & Miller, 1998). This is usually done in conjunction with the dietician. Once referred, ongoing assessment and communication between speech & language therapists, dieticians, physicians and other team members should be maintained throughout the disease progression (III).

Bedside Evaluation.

There is no single test to detect dysphagia in patients with ALS (Miller et al, 1999) and swallowing in ALS patients is difficult to assess objectively (Hardiman, 2000). In order to assess symptomatic dysphagia, a bedside evaluation of dysphagia should comprise of three components: (1) evaluation of swallowing during a meal, (2) a physical examination and (3) use of more objective techniques, such as video-fluoroscopy for specific questions such as aspiration.

A careful history should be obtained at each visit with questions on oral intake and aspects that diminish quality of life including the frequency of choking, texture of foods that cause problems, drooling, duration of meals (Miller et al, 1999; Langton Hewer, 1995; Hillel & Miller, 1987). The first indication of dysphagia can be one of the following complaints: (1) difficulty with swallowing solids and/or liquids; (2) coughing or choking on liquids; (3) reduced ability in chewing; (4) liquids leaking around the lips or food spillage from the oral cavity; (5) eating more slowly; (6) increased saliva production or thick saliva and (7) postnasal congestion (Mitsumoto et al, 1998; Robbins, 1987; Hillel & Miller, 1987; Welntz, 1983). Dysphagia can be assessed using the bedside techniques of observing the patient swallowing very small amounts of water (e.g.: 50 ml) or eating a standard amount of food, such as a biscuit with butter and jam. Observations should be made on how the patient coughs or regurgitates liquids or solids and the activity should be timed. Assessing whether drinking style is continuous or made up of separated swallows is also helpful (Scott & Heughan, 1993). Mitsumoto et al (1998) recommend the use of two bedside tests. In the first examination, the patient is asked to swallow a 5 to 10 ml bolus of water or to swallow as fast as possible without any liquid or solid in the mouth. The normal patients should be able to swallow water on command without tipping the head back, drooling, choking or delaying. Dysphagia may be indicated by the difficulty the patient has in taking successive swallows without pausing between them (Campell & Enderby, 1984). In the second test, the patient is asked to swallow 3 to 5 times in 10 seconds. Here the elevation of the hyoid bone and thyroid cartilage is observed and presence of coughing or choking before and after swallows are also noted. Food spillage, food collections under tongue and on palate should also be checked (Mitusumoto et al, 1998).

As well as observing eating and drinking, a physical examination is recommended in the literature. Such an assessment is suggested to include the following: (1) lip closure and the ability to whistle; (2) tongue strength, mobility and tone; (3) palatal movement in response to tactile stimulation; (4) evidence of 'palatal escape'; (5) the quality and strength of the cough; (6) the presence or absence of exaggerated jaw and facial reflexes; (7) evidence of salivary pooling and the presence or absence of dysarthria (Langton Hewer, 1995). Speech evaluation is also a critical component of the physical examination (Hillel & Miller, 1987). Progression in swallowing difficulties has been shown to be indicated in patients where there is a worsening of speech symptoms (Strand et al, 1996). The examination of the causes of dysphagia in ALS requires an understanding of the anatomy and the physiology of normal swallowing, that is the oral, pharyngeal and oesophageal phases (Burns & Carr-Davies, 1996; Hillel & Miller, 1987). Any changes in swallowing over time should be noted.

Objective Measurements of Dysphagia.

For specific questions, video-fluoroscopy can provide a more objective measurement of swallowing (Gelinas & Miller, 2000; Hardiman, 2000; Desport et al, 2000a). Video-fluoroscopy involves the swallowing by the patient of barium suspension of varying consistency, fluid and semi-solid. An analysis of the various stages of swallowing in is made and laryngeal penetration can be reliably detected by video-fluoroscopy (Langton Hewer, 1995). In observational studies, video-fluoroscopy has been shown to be useful in defining abnormalities in deglutition and detecting aspiration (Higo et al, 2002; Cheldi et al, 1999; Chen et al, 1992; Wilson et al, 1990; Bevan & Griffiths, 1989; Hudson, 1987). Video-fluoroscopy can also help guide decisions about feeding regimes and estimate the patient's risk of respiratory complications from oral feeding (Wright & Jordan, 1997; Gilardeau et al, 1995; Buchholz, 1994). Briani et al (1997) compared the use of videoestimate-fluoroscopy with video-pharyngolarygoscopy and pharynogo-oesophageal manometry in 23 MND patients with different degrees of dysphagia. They concluded that video-fluoroscopy was the most sensitive technique in identifying oropharyngeal alterations of swallowing. It was also capable of detecting pre-clinical abnormalities in non-dysphagic patients who later developed dysphagia (Birani et al, 1997; Leighton et al, 1994; Robbines, 1987). However, if the patient cannot be positioned for video-fluoroscopy then a video-pharyngolaryngoscopic study of swallowing should be performed. It is less sensitive than video-fluoroscopy but can indicate presence of aspiration more reliably than clinical evaluation (Briani et al, 1997). As Leighton et al (1994) demonstrated, video-fluoroscopy could be used to assess risks of aspiration. The presence of laryngeal penetration on video-fluoroscopy in the setting of clinical dysphagia indicates a high risk of aspiration pneumonia. There is however, a large variance in interpreting video-fluoroscopy amidst speech pathologists (Hardiman, 2000; Miller et al, 1999).

Video-fluoroscopy could be combined with clinical evaluation. Chen et al (1992) found that using different examining materials during the fluoroscopic examination in addition to clinical assessment helped to direct feeding techniques as well as monitoring swallowing abnormalities. Other studies have shown video-fluoroscopy to be effective in evaluating dysphagia when utilised with other techniques. Bevan & Griffiths (1989) found the combined techniques of video-fibrolaryngoscopy and video-fluoroscopy were the best methods for evaluating dysphagia. Higo et al (2002) and Cheldi et al (1999) recommend use of video-fluoroscopy and manometry to accurately assess changes of swallow function and upper oesophageal sphincter spasm, which is an important cause of aspiration. Video-fluoroscopic examination in conjunction with barium swallow can help plan suitable feeding regimes (Wright & Jordan, 1997).

Another procedure for evaluating dysphagia in MND patients is the use of electrophysiological methods (EMG techniques). Erekin et al (1998) included 29 ALS patients as part of their controlled study on the use of EMG methods (177 neurological patients and 75 controls). They concluded that EMG methods were capable of diagnosing neurogenic dysphagia objectively and quickly. A modified barium swallow can be used to diagnose aspiration and for defining which food textures the patient can safely swallow (Gelinas & Miller, 2000; Carter &: Miller, 1998). Unlike a standard barium swallow, a modified barium swallow uses small amounts of barium or barium-impregnated foods and liquids. The aim is to simulate normal eating and drinking activities while pharyngeal and laryngeal functions are observed. Robbins (1987) compared liquid and semi-solid (paste) swallows of 23 ALS patients with bulbar symptoms with 9 ALS patients without bulbar symptoms and concluded that use of paste material should be part of the standard modified barium swallow examination because the failure to propel and direct paste materials signified an impending bulbar involvement with dysphagia symptoms. Sufit (1997) also recommends the use of modified barium swallow but in conjunction with an oropharyngeal examination by a speech pathologist.

Two recent studies have demonstrated effective use of clinical indices in evaluating dysphagia. Hughes & Wiles (1995) compared the three quantitative indices of swallowing in a MND population and in a non-MND population. They found that measuring average volume per swallow (ml), average time per swallow and swallowing capacity (ml/s) on a ratio scale and exposed as % of that predicted by age and sex, was an effective and practical way of monitoring change in patients with dysphagia. This study enables swallowing indices in patients to be expressed as percent predicted according to sex and age. Mari et al (1997) also assessed the use of clinical indices (3 oz water swallow test and history of cough on swallowing) against video-fluoroscopy and concluded that the items were a useful, cost-effective screening tool. Since inexpensive, reliable and simple 'bedside' assessments are practical for assessing dysphagia in MND patients, more research is needed on whether or not clinical indices can predict complications of dysphagia.

Recommendations:

1. If patient has a swallowing problem, then a bedside evaluation should be performed (III).
2. If dysphagia symptoms are present, the patient should be referred to Speech & Language Therapists for a specialist evaluation. (III). The Dietician should then work closely with the SLT to determine the appropriate modified diet and consistency of foods in order to maintain adequate nutrition.
3. For specific clinical questions such as detecting aspiration and defining abnormalities in deglutition, consider the more objective evaluation methods of video-fluoroscopy and EMG techniques (II).
4. Once referred, ongoing assessment and communication between the specialist team, primary care team and patient should be maintained (III).

What are the recommended procedures for managing dysphagia?

Good management of dysphagia in MND/ALS patients comprises of three main elements: (1) a multidisciplinary approach, (2) an ongoing assessment and management of dysphagia and (3) modification of foods and use of swallowing and feeding techniques. Education of the carer and patient is also emphasised.

(1) A Multidisciplinary Approach.

A multidisciplinary approach to the management of dysphagia is recommended throughout the literature (Cawadias, 2000; Sonies, 2000; Langmore, 1999; Carr-Davies & Visconti, 1993). Speech and Language therapists and dieticians have primary roles to play alongside the primary physicians, neurologists, nurses, physiotherapists, occupational therapists and respiratory therapists in addressing the different issues arising from dysphagia (Leigh, Williams & Abrahams, 2001; Langmore, 1999; Groher, 1996; Gilardeau et al, 1995; Carr-Davies & Visconti, 1993). The involvement of dieticians and speech pathologists in the early stages is highly recommended across the literature and their close collaboration is necessary in the assessment and treatment of dysphagia. Houde & Mangolds (1999) point out that the composition of the team will depend on the specific needs of the individual patient and add that a nurse practitioner may be an appropriate coordinator of the care provided by the multidisciplinary team. Carr-Davies & Visconti (1993) and Groher (1996) have noted that swallowing problems in MND patients are diverse, the progression of symptoms of ALS varies between patients and thus individualised approaches are required to dysphagia management. Briani et al (1997) also support an individualised treatment, arguing that it should be developed on the basis of the radiological findings and clinical evaluation.

(2) Ongoing Assessment and Management of Dysphagia.

Although largely drawn from level III evidence, ongoing assessment of dysphagia is advocated (Hardiman, 2000; Kasarskis & Neville, 1996). In a prospective observational study of 140 MND patients over a mean period of 11.8 months after diagnosis, Strand et al (1996) concluded that management of dysphagia should be based on disease progression and on the documentation of the level of swallowing impairment during successive outpatient evaluations. Initial stages of management involve monitoring food and fluid intake whilst later stages involve the evaluation for PEG or other gastronomies. As the disease progresses, changes in swallowing will mainly occur in five main stages moving firstly from normal eating habits to early eating problems (e.g. difficulty chewing, isolated choking episodes, mealtime has increased, smaller bite sizes being necessary). In the third stage, changes in dietary consistency are needed with the requirement for a soft diet and then later for a liquidised or pureed diet. In the final stages, the patient may progress from supplemental

tube feedings to tube feeding with the occasional oral nutrition and then to having no oral intake (Strand et al, 1996). This is echoed by Silani, Kasarskis & Yanagisawa (1998), who also stress the use of general education regarding nutrition and nutritional supplementation in the early stages. Buchholz (1994) advises the ongoing monitoring of medications to help treat the symptoms of dysphagia and the elimination of medications that may be contributing to dysphagia. Minimizing risk of aspiration and choking are additionally identified as essential features of the ongoing management of dysphagia (Borasio et al, 2001a).

(3) Modification of Foods and Use of Swallowing and Feeding Techniques.

The management of dysphagia involves the modification of the consistency of foods, monitoring swallows, positioning for feeding, use of oral motor exercises, use of safe eating methods such as the chin tuck and taking small frequent meals (Leigh, Williams & Abrahams, 2001; Gelinas & Miller, 2000; Langton Hewer, 1995; Gilardeau et al, 1995; Buchholtz, 1994; Campell & Enderby, 1984; Goldblatt, 1977). These procedures should help alleviate episodes of choking.

There is an emphasis on food texture being modified to soft, semi-solid or liquidised states as they are easier to swallow than liquids or solids. However, Perry et al (2002) in their observational study of 12 MND patients found that the elevation of the soft palate was lower when swallowing pudding then for liquids. They concluded that thickening liquids to prevent aspiration might induce less palatal elevation and result in nasal regurgitation. Nevertheless, foods should be easy to chew and rich in calories (Borasio et al, 2001a; Borasio et al, 2001b; Eisen & Weber, 1999). In relation to liquids, drinking through straws can help swallowing (Hillel & Miller, 1989; Goldblatt, 1977). The use of thicker liquids, semi-solid foods with a high water content, such as gelatine, or sucking ice cubes are suggested as better alternatives to thinner liquids and can help alleviate aspiration (Langmore, 1999; Hillel & Miller, 1989; Goldblatt, 1977). Room temperature water is generally the most difficult liquid to swallow (Hillel & Miller, 1989) and so frozen drinks are advised (Pall, 1995). Sherbets, custards and sauces can be used to prevent dehydration and aspiration, which can be caused by clear liquids (Norris, Smith & Denys, 1987). Irritating foods such as strong spices are advised to be avoided (Langton Hewer, 1995; Leigh & Ray-Chaudhuri, 1994; Norris, Smith & Denys, 1987). Strand et al (1996) stress the avoidance of caffeine products to help maintain hydration for patients with normal eating habits with some feeding difficulty. Use of high calorie desserts and high protein and calorie supplements and feeds are also widely recommended (Hardiman, 2000; Gorman, 2000; Sufit, 1997; Welnetz, 1983). Carr-Davies & Visconti (1993) and De Lisa et al (1979) point out that intake of milk products may increase mucus production, making it more difficult to swallow. However, others – such as Corden (1996) and Burns & Carr-Davies (1996) - recommend use of dairy products to boost calorie and protein intake.

Carr-Davis & Visconti (1993) recommend that patients should eat more slowly, take smaller bites and alternate bites of solid food with sips of liquid to ensure adequate oral and pharyngeal clearing. Sucking ice cubes a few minutes before a meal, swallowing two to three times per mouthful and postswallow clearing (coughing after each swallow) can also help to ease swallowing (Gelinas & Miller, 2000; Groher, 1996; Campell & Enderby, 1984). Chewing sweets or gum may help trigger the automatic swallow reflex if it has become depressed (Leigh & Ray-Chaudhuri, 1994). Smith, Forbes & Norris (1975) maintain that use of Neostigmine 30 to 45 minutes before meals may temporarily improve food intake, though this advice is not repeated in later literature. Willig et al (1995) report that 73% of ALS patients experience difficulty in bringing food to the mouth and this can be helped by the use of light-weight tableware, dishes and glasses designed to facilitate grasping. Eating in an upright posture with the neck flexed can also help (De Lisa et al, 1979; Goldblatt, 1977). Devices and positioning techniques can be obtained from an occupational therapist or physiotherapist. From a patient's point of view, Henke (1968) stresses that eating is tiring and that the patient should not be hurried when eating. Instead meals can be kept hot on a hot plate or modified to smaller but more regular meals.

Education of Patient and Carer.

Early education of the patient and carer in feeding and swallowing techniques, on hydration and nutrition and on enteral feeding helps to facilitate successful management of nutrition and dysphagia (Sonies, 2000; Groher, 1996; Gilardeau et al, 1995). General education regarding the principles of good nutrition is considered to be best accomplished by a dietician, though a close partnership between dietician and neurologist is recommended (Silani, Kasarskis & Yanagisawa, 1998). Patients should be encouraged to keep a daily record of caloric intake and weighed at every office visit (Sufit, 1997). Borasio et al (2001) and Gorman (2000) suggest

the involvement of a speech & language therapist in assessing the patient, giving advice on the consistency and quantity of food and fluid in the diet, timing of meals, patient's posture while eating and on swallowing techniques, for example the double swallowing to minimise aspiration. Occupational therapists can also help by providing information on energy-saving techniques and helpful devices, such as adapted eating utensils or a thumb shell splint to help a patient to hold a glass (Sinaki, 1987). Barium swallow has been suggested to assist the development of strategies to maintain oral intake for the patient (Miller et al, 1999). It may disclose difficulties in handling certain specific types of food textures, but ALS is not static and so patients should be educated in using all physical manipulation techniques to maintain oral intake (Silani, Kasarskis & Yanagisawa, 1998). Gilardeau et al (1995) advise that the patient's carer is also trained to observe for aspiration and how to minimize it by using proper feeding techniques.

Recommendations:

1. Management of dysphagia in MND patients involves a multi-disciplinary approach (speech and language therapist and dietician as key members of the team) and ongoing assessment (III).
2. To ease swallowing difficulties, it is recommended to modify the consistency of foods, monitor swallows and use safe eating methods such as the chin tuck (III).
3. Patients who have difficulties with feeding should be referred to an occupational therapist or physiotherapist for aids and positioning techniques (III).
4. Patients and carers should be educated in swallowing and feeding techniques (III).

Are there any interventions that can help ease difficulties with swallowing?

Some invasive and non-invasive procedures are available to help ease swallowing and siarlorrhea in ALS patients. However, these procedures are not suitable for all ALS patients and therefore careful patient selection is necessary. Leigh & Ray-Chaudhuri (1994) have suggested that some medications, such as baclofen and L-threonine, may also help to reduce swallowing problems but it should be noted that there is an absence of at least level II evidence on the use of medication for managing dysphagia in the ALS patient population.

Cricopharyngeal myotomy (CPM).

Cricopharyngeal myotomy (CPM), performed with a spastic sphincter, can be used to improve pharyngeal emptying in patients though the procedure is controversial amongst clinicians (Hardiman, 2000; Sonies, 2000). The evidence, though few in number, is largely favourable yet clinical opinion is divided on the merits. Perhaps, it is difficult to assess the effectiveness of CPM when ALS is a progressive degenerative disease.

Buchholtz (1995) undertook a somewhat biased review of CPM in neurological patients (i.e. restricted his searches to just one database, Medline, and did not follow a systematic review process). However, he noted that the outcomes of CPM in treating dysphagia in neurological disorders were favourable. This is echoed by Langton Hewer & Enderby (1990) in their review but they noted that there was a lack of measurement of improvements in eating, weight gain or reduction in frequency of choking. Lebo, Sang & Norris (1976) found that 64% of 38 ALS patients with aspiration improved after CPM and Loizou, Small & Dalton (1980) demonstrated improvement in 19 of 25 patients who had undergone CPM. Norris, Smith & Lebo (1977) performed CPM in 100 cases and concluded that to avoid treatment failure, suitable cases should be selected in accordance to a certain criteria. Their criteria included forced vital capacity being greater than 50%, recent weight loss of exceeding 15% of body weight and maximum voluntary ventilation being greater than 25% predicted. Leighton et al (1994) surveyed 17 ALS patients, who underwent CPM. Three responded well whilst six others reported reduced frequency of choking. Out of the overall 92 patients, 89% reported satisfaction with the procedure but Leighton et al (1994) argued that the procedure was not suitable for people who were unable to have general anasthesia.

Other studies have noted the limitations of CPM in ALS patients. David (1985) maintains that CPM is only beneficial when performed early in the course of ALS, while Tayama (1995) found poor results for CPM in ALS patients who had severe aspiration. Although, this was disputed by MacDougall et al (1995) who found in their controlled study of 13 ALS patients with 13 age and sex matched healthy volunteers that CPM was inappropriate, since dysphagia in the ALS patients was not due to upper oesophageal sphincter spasm. More recently, a retrospective study on the use of CPM in 46 patients with different diseases found that treatment failure was more likely to occur in ALS patients relative to other diseases (St Guily, 1997). This could be due to

the main cause of dysphagia in ALS being a defective oral phase of swallowing, thereby resulting in a minority of ALS patients who show UES dysfunction benefiting from CPM (Costantini et al, 1996). Janzen et al (1987) found CPM helpful in their experience when dysphagia was due to cricopharyngeal spasm. Wilson, Bruce-Lockhart & Johnson (1990) found that use of video-fluoroscopy prior to CPM helps to accurately select suitable patients for CPM, thus, improving outcome. The literature thus suggests that CPM may be beneficial for some patients in the early stages of dysphagia but such patients would need to be screened for suitability prior to the surgery.

Management of Siarlorrhea.

In relation to drooling or siarlorrhea, this can be managed non-invasively through the administration of Atropine, Amitriptyline or Doxepin (Burns & Carr-Davies, 1996; Hillel & Miller, 1989; Kristjanson et al, 1987; Hudson, 1987). A survey of 2018 ALS patients in the USA by Bradley et al (2001) found that less than 50% received medications (e.g.: Attopine) to control moderate or marked sialorrhea. Although there were side effects like excessive dryness of the mouth and constipation, 73% found them helpful. Siarlorrhea can also be controlled surgically through the invasive methods of transtympanic neurectomy, radiation and through the injection of botulinum toxin A. Transtympanic neurectomy has been reported to be a successful intervention in the ALS population (Kristjanson et al, 1987; De Lisa et al, 1979). Hudson (1987) based his observations on 300 outpatients at his clinic over a period of 10 years and concluded that transtympanic neurectomy was an appropriate procedure but that the patient must have sufficient ventilatory capacity and emotional stability to endure the procedure under local anaesthetic. Janzen et al (1987) also found that transtympanic neurectomy and chorda tympanectomy were effective and but added that submandibular gland excision was disappointing in their patient population.

Radiation of the salivary glands is another suggested procedure. However, there were only three studies of sufficient evidence identified on the effectiveness of radiotherapy in controlling sialorrhea amongst ALS patients. Stalpers et al (2002) retrospectively observed 19 ALS patients who had undergone radiotherapy for drooling between March 1995 and January 1999. Fourteen of these patients had a satisfactory response after initial radiation, whilst two patients did not have any success despite three reirradiations. Ten patients did not report any side effects, six reported pain in the parotid area and another four had dryness in the mouth. Harriman et al (2001) examined the lowest dose of radiation necessary to control salivary production. Nine ALS patients were spilt into two groups, receiving two different doses of radiation (the first group received 8Gy in one single dose whilst the second group received a total of 12.5Gy in two doses). The low dose of radiation had few side effects and could effectively control secretions in the patients. Increasing the dosage was not seen as an improvement. Andersen et al (2001) conducted a prospective study on 18 MND/ALS patients and also concluded that low dosage external radiotherapy of the salivary glands was effective in reducing drooling. However, all these studies are small scale and more research is needed into the benefits of radiotherapy.

Injections of botulinum toxin A into or around the parotid glands is another proposed treatment for sialorrhea (Bushara, 1997). In a small uncontrolled study, Giess et al (2000) demonstrated in five patients that botulinum toxin A was a relatively safe and effective treatment in reducing drooling in patients with ALS. More research on the use of botulinum toxin is needed.

Recommendations:

1. Siarlorrhea may be improved through the invasive procedures of irradiation, transtympanic neuroectomy, chorda tympanectomy, submandibular gland excision and injections of botulinum toxin A (II).
2. Swallowing may be improved through use of cricopharyngeal myotomy (CPM) but careful patient selection in terms of overall medical stability and respiratory function (especially airway protection) is recommended (II).
3. Medication for drooling and other alternative methods can be considered, if in a convenient form for patients to swallow (III).

Research Recommendations:

1. More research, particularly prospective and randomised studies, is warranted on injections of botulinum toxin and irradiation in treating dysphagia in ALS patients.
2. Further studies are also needed on the use of medication and alternative therapies, for example pineapple and papaya.

Nutritional Maintenance:

Malnutrition is of great concern amongst ALS patients, as it not only results in the loss of muscle function, immunosuppression, impaired respiratory function and reduced tissue viability but it can also accelerate mortality (Worwood & Leigh, 1998; Mazzini et al, 1995). Desport et al (1999) found in their observation of 55 patients that malnutrition was significantly correlated with risk of death. The presence of malnutrition was also linked to nutritional surveillance rather than the onset of disease. Weight loss in MND patients can be attributed to a number of factors: muscle atrophy, a decrease in food intake due to dysphagia, physical inability to prepare food and feed oneself, chronic pulmonary infections, anorexia, urinary tract infections and psychological upset (Desport et al, 2001; Desport et al, 2000a; Worwood & Leigh, 1998; Mathus-Vliegen et al, 1994; Slowie et al, 1983). These factors influence the intake of food and fluid resulting in an inadequate caloric intake and subsequent malnutrition. In regards to nutritional management, it is important to observe weight loss and to manage dietary requirements in order to reduce the risk of malnutrition.

How common is malnutrition in MND?

In a number of studies, malnutrition was found to be prevalent in ALS patients. Patients with dysphagia were no more likely to be malnourished than those without dysphagia (Desport et al, 1999; Worwood, & Leigh, 1998; Kasarskis et al, 1996). Palmo et al (2002) found in their observations that malnutrition was common in all chronic neurological disorders with 20% of their ALS subjects being defined as being undernourished. In a cross-sectional sample of 47 British ALS patients, 21% were found to be moderately to severely malnourished (Worwood & Leigh, 1998). In a non-controlled observational study of 55 ALS patients (Desport et al, 1999), 16.4% were defined as being malnourished (BMI of less than 18.5kg/m2). Mazzini et al (1995) reported that 53% of the 66 ALS patients in their study had a BMI of less than 20kg/m2 and 55% had a weight loss of over 15% of their usual weight, indicating malnutrition. Shimizu, Hayashi & Tanabe (1991) found that the mean BMI of 11 ALS patients on ventilators was 15.3 kg/m2 with a standard deviation of 2.5 kg/m2.

Most nutritional status studies on ALS populations are cross-sectional (Slowie et al, 1983; Kanda et al, 1994; Nau et al, 1995). While cross-sectional studies provide information on the levels of malnutrition in a population, longitudinal data can offer evidence on the risk of malnutrition and the degree of weight loss as the disease progresses. Kasarskis et al (1996) provides a longitudinal observation of the changes in body composition and the increasing risk of malnutrition to the proximity of death. Over a six month period, 16 patients were observed with different severity of the disease and all experienced progressive reduction in BMI in relation to time of death. Further longitudinal studies are necessary to assess risk and incidences of malnutrition as the disease progresses. While studies on nutritional status have small patient populations and have heterogeneous patient characteristics, they do indicate that malnutrition is frequent amongst ALS patients.

The literature suggests that ALS patients have a decreased caloric intake and consume less energy than the recommended dietary allowance. A reduction in energy intake is associated with increased weight loss, degree of dysphagia and the reduction of the tricep-skin-fold thickness (Silani, Kasarskis & Yanagisawa, 1998). Worwood & Leigh (1998) found that all their patients had considerably lower dietary intake for energy than the Estimated Average Requirement (2,380 kcal/day for 60 to 64 year old men and 1,900 kcal/day for 60 to 64 year old women). From the observation of 20 randomly selected ALS patients aged 44 to 70 and a disease duration of 6 months to 11 years, Slowie et al (1983) concluded that inadequate caloric intake and significant weight loss were present in the early stages of ALS. They found that 70% of their patients had caloric intakes below the Recommended Dietary Allowances. Patients who had reported the lowest caloric intakes had experienced the greatest weight loss - 25% had lost 10% or more of their body weight (Slowie et al, 1983). Slowie et al (1983) maintain that a good indicator of nutritional risk is the weight loss of 10% or more of body weight in a group of patients who have unintentionally lost weight and who may be still above ideal weight. A drop of 10% from ideal weight levels is linked with loss of physiologic adaptability and morbidity (Willig et al, 1995). Gender differences occur in relation to degree of weight loss. Men have been found to have greater weight loss and changes in body composition than women (Kasarskis et al, 1996; Worwood & Leigh, 1998). Furthermore, men have been shown to be more prone to hypermetabolism (Desport et al, 2001).

Hypermetabolism is a feature of MND/ALS, although the origin is uncertain. This is paradoxical because due to the reduction in physical activity, MND/ALS patients often experience significant reduction in fat free mass and fat free mass is the principal determinant of resting

energy expenditure (REE)1. Hence, a lower metabolism rate would be expected not hypermetabolism. The literature suggests that ALS patients are not intrinsically hypermetabolic but that as the disease progresses, the increased effort of breathing and metabolic demands on the remaining functional muscles may increase energy requirements (Silani, Kasarskis & Yanagisawa, 1998; Kasarskis & Neville, 1996; Kasarskis et al, 1996; Shimizu, Hayashi & Tanabe, 1991). This is disputed by Desport et al (2001) in their investigation of hypermetabolism in an observational study of 62 ALS patients. They did not find any support for the condition being linked to increased respiratory muscular efforts in maintaining adequate breathing. They did find that a number of other factors correlated with a hypermetabolic state including fat-free mass, age, sex and weight. They also suggested that factors such as a sympathetic nervous system and mitochrondrial derangements (which cause excessive heat production and energy deficit) may play a role in hypermetabolism. The existence of hypermetabolism further exacerbates the risk of malnutrition for the ALS patient. When managing nutrition, it is a factor to be taken into account, thus further study into the causes of hypermetabolism is warranted.

Recommendations:

1. Weight loss of 10% or more of pre-illness body weight in a period of 3 to 6 months is a prognostic factor for malnutrition (II).
2. Caloric intake is to be continually monitored in order to avoid malnutrition - i.e. BMI of less than or equal to 18.5 kg/m2 (II).

Research Recommendations:

1. More longitudinal data, like Kasarskis et al (1996), are needed to indicate risk of malnutrition as disease progresses.
2. Cross-sectional data are warranted, which look at the effects of age, sex and other variables on risk of malnutrition.
3. More research is necessary into the causes and extent of hypermetabolism in ALS patients.

What is the evidence for accurately evaluating nutritional status?

Evaluating body composition (i.e. body fat and fat free mass) is a necessary component of nutritional management as it can detect malnutrition and provide a basis for appropriate nutritional advice throughout the disease progression. Mazzini et al (1995) recommend that nutritional status should be assessed immediately after the onset of bulbar symptoms. Clinical judgements about the degree of nutritional intervention should be based on serial measures of body composition (Nau et al, 1995). However, there is limited research on body composition and nutritional status of ALS patients.

It is recommended that in order to achieve accurate assessment of nutritional status, a combination of measures should be used. Single measures of body weight and composition can be unreliable. For example, Desport et al (2001) report that taking dietary histories (i.e. diet diaries usually cross-checked with 24 hour intake) can be biased or limited. This is due to the reliance on what information the patient's relatives provide and some patients can overestimate their intake, particularly if they will not accept the possibility of enteral nutrition. In addition, Palmo et al (2001) has argued that bioelectrical impedance analysis has not been validated against a reference method and hence the results can only be suggestive. Desport et al (2000a) point out that bioelectrical impedance analysis has yet to be validated for patients with ALS. From the literature, measures of body composition work best in combination as they can validate each other. Although the individual measures and criteria for malnutrition varied across the studies, using multi-measures heightens the precision in detecting malnutrition. Desport et al (2001) combined the results of bioelectrical impedance analysis, indirect calorimetry and calculation of body mass index. Slowie et al (1983) argued that risk of malnutrition in ALS patients can be adequately assessed in the early stages through a combination of dietary history, anthropometric measurements (i.e. individual's weight at time of the initial clinic visit compared to patient's usual weight and triceps skinfold and upper arm circumference to measure body fat mass) and biochemical tests (which screen for abnormalities, particularly glucose and cholesterol metabolism). Worwood & Leigh (1998) also used dietary histories, calculation of body mass index and anthropometric measurements as part of their assessments.

Anthropometry has been shown to be a valuable tool in detecting malnutrition in ALS patients (Worwood &

Leigh, 1998; Slowie et al, 1983). Malnutrition can be indicated by the triceps skinfold and arm muscle circumference measurements being below 30th percentile, with measurements below 24th percentile indicating severe malnutrition (Slowie et al, 1983). Desport et al (1999) dispute this anthropometric criteria as having too low a threshold for malnutrition. Worwood & Leigh (1998) indicated malnutrition by the measurement of under the 5th percentile for the mid-arm circumference, triceps skinfold thickness or mid-arm muscle circumference. The upper extremity anthropometrics of mid-arm circumference, triceps skinfold thickens and mid-arm muscle circumference are argued to be precise indicators of nutritional status when combined (Worwood & Leigh, 1998; Kasarskis et al 1996). Individually they are weak predictors of energy and protein stores. Reliability of body fat estimates is dependent on the skill of the examiner and is influenced by sex, race and age. However, anthropometry is quick, cheap, non-invasive and can be readily applied in the field or at the bedside. It reflects both the progression of muscle atrophy and the nutritional state of the patient (Worwood & Leigh, 1998; Kasarskis et al, 1997).

Body Mass Index (BMI) is another common tool, although there is some variance in the threshold level of malnutrition. Desport et al (1999) used a BMI of less or equal to 18.5 kg/m2 as being malnourished, while Palmo et al (2001) set their threshold of malnutrition as being under 18.5 kg/m2. Worwood & Leigh (1998) and Hillinger et al (2002) used a Body Mass Index of below or equal to 20kg/m2 to indicate malnourishment. However, according to Nau et al (1995) body mass index does not distinguish between or record changes within different fat and lean tissue types and thus is not an indicator of malnutrition. Nau et al (1995) conducted a case control study of 12 male ALS patients and 6 age-matched controls in order to quantify body composition changes during a 6 month period. There was no change in the control group. The ALS patients meanwhile had lost an average of 2kg of lean mass but gained an average of 0.55 kg of fat mass (an overall loss of 1.45kg). When converted to their energy equivalents, ALS subjects had a net increase of 3100 kcal being stored. Thus, while the patients had lost 1.5kg of body mass, they actually maintained the amount of energy stored in their bodies. This led Nau et al (1995) to conclude that due to restricted physical activity and increased fat stores, the amount of energy stored in the body could be preserved despite loss in lean and overall body mass. Thus monitoring changes in body mass requires the additional information gained from body composition analysis.

As well as the 'field techniques' of BMI and anthropometric approaches, nutritional status can also be assessed by reference body composition methods such as magnetic resonance imaging (MRI), ultrasound, computerized tomographic scanning, electrical impedance, and densitometry. These are costly, time consuming and not widely available (Worwood & Leigh, 1998). Furthermore, they may require specialised training. Dual X-ray absorptiometry (DXA) is becoming a popular method in assessing body fat and body composition in different clinical populations, as it has low operational costs, is non-invasive, easy to use and quick. Kanda et al (1994) and Tandan et al (1998) have demonstrated its usefulness in evaluating muscle mass for the estimation of the clinical stages in neuromuscular diseases including ALS. ALS subjects were shown to have had decreased total mass and soft tissue mass when compared to a non-age matched control groups. Nau et al (1995) and Hillinger at al (2002) used Dual X-ray absorptiometry to measure body composition in ALS patients and found it to be a reliable and accurate measurement of bone mass, fat mass and soft tissue. Nau et al (1997) determined the relative validity of anthropometry and bioelectrical impedance analysis (BIA) and concluded that both tended to overestimate lean mass and underestimate fat mass in the ALS patient when compared to Dual X-Ray absorptiometry. When combined with BMI or anthropometry, it can determine the aetiology of weight loss (Hillinger et al, 2002). This may help to differentiate between the presence of malnutrition, increased metabolism or loss of lean muscle mass from disease progression. However, the method is expensive and is primarily available for research (Nau et al, 1997).

Recommendations:

1. Ongoing assessment of nutritional status is recommended (II).
2. A combination of body composition measures (body weight dietary histories, BMI, biochemical tests, anthropometry) is recommended to achieve accurate assessment of nutritional status (II).
3. For routine measurements, more specialised techniques such as dual X-ray absorptiometry and computerized tomographic scanning are not recommended as they are expensive and require specialist training (II).

Research Recommendation:

1. More prospective studies are needed on what body compositional changes are to be expected in ALS patients. This would help determine the optimal energy intake.

What is the evidence for managing constipation and other intestinal problems?

Most evidence on managing constipation, diarrhoea and other intestinal problems are expert opinion based. Constipation plays a role in malnutrition because it can exacerbate appetite loss (Cameron & Rosenfield, 2002; Desport et al, 2001). It results from limited physical exercise, weakness of abdominal and pelvic muscles, diet lacking in fibre, dehydration and use of certain medical treatments, such as glycopyrronuum, methanthelinium or propantheline (Cameron & Rosenfield, 2002; Desport et al, 2001; Desport et al, 2000; Corden, 1996). Management suggestions include use of osmotic laxatives (such as lactulose), bulk-forming laxatives (such as methyl cellulose), suppositories, enemas, fixed meal times to produce bowel regularity and the augmentation of fluid and fibre intake (Borasio et al, 2001b; Evans & Shaw, 2001; Langton Hewer, 1995; Leigh & Ray-Chaudhuri, 1994; Moxley & Kempf, 1980; De Lisa et al, 1979). Fruit and milk of magnesia are also suggested to help relieve constipation (Rose, 1987). If bowel pains arise, an ileus should be suspected and appropriate tests performed (Borasio et al, 2001b).

In relation to gastric emptying and colonic transit time, Toefer et al (1997) noted in their controlled, non-randomised study measuring colonic transit time, that ALS patients had significantly delayed transits. This, they suggested, was linked to inactivity, inadequate fibre intake and possible gastrointestinal autonomic involvement due to nerval degeneration. A later controlled experiment also revealed delayed gastric emptying of solids (Toepfer et al, 1999). Both studies also demonstrated the applicability of non-invasive techniques such as C-octanoic acid breath test for measuring gastric emptying and radio-opaque markers for assessing colonic transit time in ALS patients (Toepfer et al, 1999a).

Recommendations:

1. Constipation and diarrhoea can be managed through monitoring dietary fibre intake, having fixed meal times, prescribable dietary fibre supplements, the use of laxatives and adequate fluid intake (III).
2. Delayed gastric emptying and colonic transit time may be assessed by a C-octanoic acid breath test and by radio-opaque markers (II).

What are the fluid and caloric requirements of patients with MND at different stages of the illness?

There is some discrepancy over the actual level of caloric and protein requirements for MND patients. Some advocate a decrease in calorie intake by MND/ALS patients (Kasarskis et al, 1996). Shimizu, Hayashi & Tanabe (1991) measured energy metabolism and caloric intake in a sample of ALS patients using enteral nutrition and mechanical ventilation and found that 75% of the patients had excessive intakes of calories and had gained weight. Increasing protein intake rather than calories may address this problem. Slowie et al (1983) point out that caloric requirements for patients with ALS would be less than the Recommended Dietary Allowances due to reduced physical exercise. In opposition, Kasarskis et al (1996) recommend increasing energy intake not protein intake to maintain weight. They observed the energy consumed in both the early and later stages of the disease and associated the progressive decline in body fat with the oxidation of fat for energy. As a result, they recommend that the caloric intake should not only be sufficient to meet the metabolic needs of the individual, but it should also compensate the energy lost in muscle mass by building fat stores, hence adequate diet throughout the disease.

Energy intake should equal the changing requirements throughout the disease progression (Desport et al, 1999; Nau et al, 1997; Nau et al, 1995). In early stages of ALS, motor neurone loss contributes to loss of lean body mass but there is a corresponding gain of fat body mass. This results in a net increase in total calories stored even as total body mass drops. Nau et al (1995) recommend a well-controlled diet that includes enough calories to meet the metabolic needs of the individual plus a little extra to allow for just enough accumulation of fat to compensate for the energy lost in the muscle mass. This stored energy may be needed in the later stages of the disease. Nutritional supplementation is also recommended but timing, efficacy and extent of nutritional intervention is yet to be determined (Hardiman, 2000; Silani, Kasarskis & Yanagisawa, 1998). Stanich et al (2002) investigated the impact of a protein caloric supplement (Meritene) on the nutritional state of 20 ALS patients for a period of 6 months. Nutritional state was maintained throughout the period, although alimentary ingestion decreased as disease progressed.

Despite the discrepancies in the current literature and the dearth of knowledge on the fluid requirements of MND/ALS patients, it can be surmised that ongoing assessment of fluid and caloric intake is important. Until further research has been done, the aim should be to provide the patient with a well-balanced diet in consultations with a dietician and general education on nutrition should be provided to the patient and carer. Monitoring of weight and body composition may also help to determine the caloric requirements of the diet for an individual patient.

Assessment of dietary intake requires monitoring energy, fluid, vitamin and mineral needs of the patient, yet there is a lack of research on the vitamin and mineral levels at the different stages of the disease. A survey of 11 ALS patients by Sato et al (1997) highlighted that ALS patients were deficit in vitamin D due to poor dietary intake and being in a sunlight-deprived state (due being home bound or hospitalised). Consequently, the patients were at risk of osteoporosis. They recommend the use of vitamin D supplementation to correct vitamin-D deficiency in patients with ALS. Burns & Carr-Davies (1996) also recommend supplementation with vitamin D, adding that a multiple vitamin/mineral supplement should suffice if adequate dietary sources are not present. There is also little guidance in the literature when to recommend use of antioxidant vitamin supplementation. Cameron & Rosenfield (2002) undertook a review of the use of dietary supplements as primary treatments for MND and concluded that though the use of readily available dietary supplements, such as vitamins, herbs and minerals, is common amongst ALS patients, much of the evidence supporting their use is anecdotal. They argue that more research is needed into the interaction of disparate mechanisms underlying motor neuron degeneration before we can fully assess the usefulness of such dietary supplements in the ALS patient's diet.

Recommendations:

1. Ongoing assessment of fluid and caloric requirements is recommended throughout disease progression (II).
2. High protein and calorie intake is generally recommended but the energy intake should equal the changing requirements of the patient throughout the disease progression (II). Such an approach will involve tailoring the diet for each patient. Body composition measurements can help determine the dietary requirements (II).
3. General education on nutrition should be provided to the patient and carer (III).
4. Due to the lack of evidence on the role of supplements in the MND population, vitamins and minerals are recommended to come from diet rather than supplements (III).

Research Recommendations:

1. Further research (perhaps cohort studies) is needed on the fluid and caloric requirements of MND/ALS patients throughout disease progression, such as whether caloric intake should be increased or decreased.
2. Research is also warranted on nutritional supplementation, in particular, the use of vitamin, mineral and herbal supplements. Timing and extent of nutritional supplementation ought to be addressed.

Enteral Feeding:

There are two methods for delivering enteral feeding (1) parenteral nutrition and (2) enteral nutrition such as the nasogastric tube, which is entered through the nose into the stomach, and the percutaneous endoscopic gastrostomy (PEG) and jejunostomy (PEJ) tube, which are entered into the stomach through the abdominal wall (gastrostomy) or into the intestine (jejunostomy). PEG is the recommended choice for long-term maintenance of good nutrition in MND/ALS patients with pronounced dysphagia (Hardiman 2000; Silani, Kasarskis & Yanagisawa, 1998; Miller et al, 1999; Borasio, 1994; Park et al, 1992; Larson, 1987). PEG benefits the patient through adequate nutritional intake, weight stabilization and as an alternative route for medication (Miller et al, 1999; Silani, Kasarskis & Yanagisawa, 1998). Patients can often continue to eat and drink orally (Miller et al, 1999). In a survey of the members of the European ALS Study Group, Borasio et al (2001) found that PEG was widely available in 94% of the ALS centres. Strong, Row & Rankin (1999) add that PEG and PEJ are more common than nasogastric because of greater patient comfort. They can be facilitated in the home environment or in hospital because of the simplicity of enteral feeding and the minimal disturbance it causes the patient (Thornton et al, 2002).

When should interventions such as PEG be implemented?

Clinicians vary in practice for timing the implementation of enteral feeding. Chio et al (2001) reviewed the management of MND in neurological departments in Italy and found that contrary to the published recommendations of Silani, Kasarskis & Yanagisawa

(1998) and Chio et al (1999), clinical-subjective parameters (aspiration and choking) were considered more relevant for choice and use of enteral feeding than the objective measures of video-fluoroscopy, weight loss and body mass index. A survey of nutritional therapy for ALS patients in 53 Japanese national hospitals revealed that physicians were inclined to encourage tube feeding only when non-oral nutrition therapy became necessary (Seki et al, 2000). In France, PEG appears to be usually placed after 2 years of disease evolution and is indicated by malnutrition, swallowing disorders or when forced vital capacity is altered (Desport et al, 2000). Amongst patients, a cross-sectional survey of 2018 ALS patients in the USA found a significant relationship between forced vital capacity (FVC) and the percent of patients having a gastrostomy tube (Bradley et al, 2001). Of patients with FVC of less than 50%, 12% had gastrostomy tube compared to just 3.3% of those with FVC over 50%. Overall only 30% of patients with significant dysphagia (measured by ALSFRS swallowing scores) had a gastrostomy tube (Bradley et al, 2001).

Given the variance in practice, it is important to exact a time for intervention. The literature specifies a number of factors, which influence the timing of PEG: forced vital capacity (FVC), accelerated weight loss and dysphagia symptoms. However, there are no randomised controlled trials focusing on the use of PEG in ALS patients, apart from one randomised 28 day study comparing PEG with nasogastric tube feeding in 40 neurological patients including 16 ALS patients (Park et al, 1992). Most of the literature are based on observational studies or non-randomised controlled experiments. As a result, the self-selection of patients for the procedures in studies introduces biases, which affect the outcomes and subsequently, the recommendations for timing of interventions.

According to the US clinical guidelines produced by Miller at al (1999), the recommendation for PEG should be made before the forced vital capacity (FVC) falls to 50% of predicted and not in the preterminal phase. This is because the onset of dysphagia may occur with the decline of respiratory sufficiency. However, this recommendation is based solely on the findings of Mazzini et al (1995). Mazzini et al (1995) found a strong correlation between survival and forced vital capacity (FVC) at time of PEG placement. They recommended that the procedure be performed when a patient's FVC is greater than 50% of the predicted value. Since Miller et al (1999), there have been a number of studies which question the level determined by Mazzini et al (1995). Kasarskis et al (1999) found that the level set by Mazzini et al (1995) was applicable to their patient population. Patients with a FVC <50% had increased risk of death within 30 days of gastrostomy placement and were at increased risk of morbidity, e.g. aspiration pneumonia. However, two Italian studies found that a higher FVC threshold was significant for successful PEG placement. Finnochiaro et al (1998) demonstrated that survival after PEG was significantly associated with FVC being > 70% (Median survival was 302 days compared to 112 days of those with FVC < 70% predicted, $p = 0.03$). Chio et al (1999) indicated increased risk of death in patients with FVC less than 65% predicted.

Two recent small and uncontrolled case series suggest that PEG placement may be suitable in patients with a FVC less than 50%. Boitano et al (2001) examined the use of non-invasive positive pressure ventilation (NIPPV) during PEG placement in 5 patients with FVC less than 50% predicted. The 30 day mortality rate was zero and no respiratory complications were recorded. Gregory et al, (2002) replicated this success of PEG placement in 33 ALS patients with FVC below 50% predicted (Gregory et al, 2002). Deriving from other published works, successful implementation of PEG in patients with FVC < 50% maybe due to the low risk associated with the PEG procedure. Thornton et al (2002) also found no correlation between FVC and failure of PEG and suggested that this could relate to the compensatory activity by accessory muscles of respiration developing better in some patients than others[2]. This questions the importance of the use of FVC as the most important criterion for the timing of PEG.

Timing of PEG placement to maximise survival and quality of life can also be assessed by onset of dysphagia and associated eating difficulty, the identification of early unintentional weight loss and ongoing nutritional assessment (Cameron & Rosenfield, 2002; Miller, 2001; Miller et al, 1999; Silani, Kasarskis & Yanagisawa, 1998). Accelerated weight loss is a key indicator of PEG timing, however like FVC levels, there is a variance in the measurement of weight loss. Kasarskis & Neville (1996) and Gregory et al (2002) recommend enteral feeding when the weight loss relative to usual weight reaches 5% while Leigh & Ray-Chaudhuri (1994), Mazzini et al (1995), Finocchiaro et al (1998) and Chio et al (1999) recommend a threshold of 10%. Chio et al (1999) found that the risk of death from PEG procedure is significantly higher in patients with more than 10% weight loss. Body Mass Index (BMI) appears to be a

more stable indicator of PEG placement. Desport et al (2000), Desport et al (2000a) and Finnochiaro et al (1998) have observed that BMI less than 18.5 kg/m2 is an unfavourable survival prognostic factor after gastrostomy. Thus they recommend enteral feeding via a nasogastric tube for patients with a BMI of less than 18kg/m2.

Throughout the observations, it is evident that the earlier the implementation, the more successful the PEG placement. Miller et al (1999) even recommend that PEG should be considered for patients with ALS who have symptomatic dysphagia soon after the symptom onset. However, in practice, patients can delay enteral feeding for a number of reasons, including the association of PEG with terminal stages. Until more evidence is gathered (particularly from larger scale studies) and a consensus reached on the timing of PEG, patients and physicians should be aware that PEG placement may not be applicable in the later stages of the disease. Furthermore, a number of factors influence timing of PEG and although the number of studies is small, they indicate a variance in thresholds for each factor. It is advised that each patient be assessed individually on the basis of these factors.

Recommendations:

1. Percutaneous endoscopic gastrostomy (PEG) helps to stabilise weight, combat malnutrition and is a suitable means for long term nutritional maintenance (II).
2. A number of factors influence the timing of PEG – FVC, dysphagia symptoms, malnutrition and condition of patient. Taking into account these factors, an individualised approach to timing of PEG is advocated (II).
3. On the basis of the PEG placement in later stages of the disease decreasing survival rates, it is recommended that the patient be informed that PEG may not be applicable later on in the disease progression (II).

Research Recommendations:

1. Ultimately there is a need for prospective and randomised controlled trials to accurately determine the timing of PEG3.

What are the risks of PEG in patients with MND?

Mathus Vliegen et al (1994) showed that PEG placement was well tolerated and safe among a group of advanced stage ALS patients with impaired respiratory function. Although the procedure-related mortality was 1.8% and 24 hour hospital mortality was 3.6%, these deaths were related to disease severity (in this case respiratory insufficiency) and not the PEG procedure. Cortez-Pinto et al (2002) observed 144 patients who underwent a PEG procedure over a period of seven years and while the 30 day mortality rate was 18%, PEG–associated mortality was found to be influenced by disease severity rather than the actual procedure. The placement of PEG in ALS patients does appear to relatively safe and survival and morbidity rates are reported to be more affected by disease severity than the actual procedure. Some complications do occur during the preoperative period and within the first month but according to Desport et al (2000), these are rarely severe. However there are a number of studies that have reported surgery related risks. Wolfsen et al (1990) reported a 36% incidence rate of tube dysfunction i.e. tube fracture, plugging and peri-tube leakage. Del Piano et al (1995) found that 17.7% of their ALS population had minor complications of pneuomperitoneum, wound infections, buried bumper syndrome, mechanical, gastro-oesophageal reflux, diarrhoea and impaired gastric emptying. Rozier et al (1991) found 7.1% of their patients developed periostomial infection during the 6 months of PEG-assisted nutrition. Although sourced from clinical opinons, Borasio et al (2001a) indicate that overfeeding on PEG may induce gastroesophageal reflux disease. Like all surgical procedures, PEG does bring risks but careful patient selection should minimise those risks, in particular the suitability of patients for sedation, which can lead to respiratory failure in ALS patients (Louwerse et al, 1997).

Recommendations:

1. Careful patient selection is recommended for PEG, as there are surgical risks and due to use of sedation, risks of aspiration and respiratory depression (II).

What is the effect of PEG in preventing aspiration and aspiration pneumonia in MND?

A systematic review of clinical applications of PEG and its risk factors for pneumonia, concluded that PEG or percutaneous endoscopic jejunostomy does not prevent aspiration pneumonia (Miller et al, 1999). However, the papers used in this review did not focus on the use of PEG in ALS patients. Their patient populations included cancer, stroke and other neurological disorders. Further evidence is needed on the incidence of PEG in ALS patients and on the presence of post-PEG aspiration. Kasarskis et al (1999) and Larson et al (1987) concluded

that patients with a history of aspiration are at greatest risk of aspiration during and immediately after surgery. Presence of reflux oesophagitis during endoscopy and concurrent infection are also considered the major risk factors for post-PEG aspiration pneumonia (Kasarskis et al, 1999). According to Miller et al (1999), recurrent aspiration pneumonia in aphonic patients with ALS may be treated with conservative laryngectomy or laryngeal diversion, however this evidence was obtained from a single case study[4].

Research Recommendation:

1. Research is needed on the effects of PEG on preventing aspiration and aspiration pneumonia in MND/ALS patients.

Can PEG prolong survival and improve quality of life?

Impact of PEG on quality of life has not been studied in detail (Miller et al, 1999).[5] Weight gain has been reported, which has implications for combating malnutrition. Finocchoiaro et al (1998) in non-randomised trial of 44 ALS matched by age, gender and severity of disease, showed that nutritional status improved after PEG. Mazzini et al (1995), Park et al (1992) and Del Piano et al (1999) found an increase in BMI and weight after starting enteral nutrition via PEG with suggestions of an increase in fat mass. In the Mazzini et al (1995) study, patients with PEG gained an average of 2.5kg in weight and after one year, 65% of the patients had normal BMI, while in the control group, BMI decreased. Briton et al (1997) in their observations of PEG in patients with neurological disorders (including 12 MND patients) reported that all patients gained weight after PEG, ranging from 3.5 to 13.6kg. Chio et al (1999) and Kasarskis et al (1999) also support the benefit of PEG in stabilising or increasing weight among ALS patients.

In relation to survival rates, results of controlled and non-controlled studies vary in the effect of PEG on survival. The first study on PEG in an ALS population, Mathus Vliegen et al (1994) reported a 30-day mortality rate of 11.5%. Median survival did not differ between treated and untreated groups, though no analysis by site of onset was given. Mazzini et al (1995) compared 31 ALS patients with PEG with 35 ALS who declined PEG and found no significant difference in mortality for either group for the first 6 months, but it was significantly lower in the PEG group thereafter. Finocchoiaro et al (1998) found that total survival was significantly lower in the PEG group than in the control group when measured from ALS onset (median 730 days compared to 915 days). Del Piano et al (1999) have also shown better survival rates in PEG groups when compared to non-PEG ALS populations but Desport et al (2000), Desport et al (2000a) and Strong et al (1998) did not find improvement. Strong, Rowe & Rankin (1999) in their retrospective study compared 73 ALS patients (41 with initial bulbar symptoms) with percutaneous gastrojejunostomy (PEJ) with 295 who did not require nutritional support or refused PEJ. The 30-day mortality rate was 9.6% while the morbidity rate was 4.1%. Survival time was significantly shorter (8.6 months) in the bulbar onsetting patients with PEJ than in the comparable control group. In relation to limb onsetting patients, those requiring enteral nutritional supplementation with PEJ early in their disease had a significantly short survivorship than those receiving a feeding tube later in the disease course. It was suspected that the patients requiring enteral support earlier in the disease were in a prognostically less favourable subgroup. In a study on PEG placement in 55 ALS patients with pulmonary function, the procedure-related mortality was 1.8% but was mainly due to respiratory failure (Louwerse et al, 1997). They concluded that while it is a safe procedure compared with nasogastric tube feeding and may improve quality of life, it does not prolong survival.

When compared to other populations with neurological disorders, ALS patients display shorter survival rates on PEG (Palmo et al, 2002). However, this could be due to ALS patients not being given enteral feeding until the terminal stages, whereby survival is determined by disease severity and progression. As Chio et al (1999) argue, the primary goal is to improve nutritional status rather than life prolongation and so, the emphasis should be on the quality of life.

Research Recommendations:

1. While studies like Mazzini et al (1995) did not randomise control subjects for ethical reasons, self-select controls does introduce uncontrolled variables such as the patient's psychological status, which affects survival. Therefore in order to accurately assess the effects of PEG on survival, we need to control for the other factors that may have an influence on survival. Randomised Controlled Trials are recommended.

What are the alternative methods of feeding?

When PEG is not appropriate, there are two alternative methods of feeding – percutaneous radiologic gastrostomy and nasogastric tube feeding – which can be considered for ALS patients.

Percutaneous Radiologic Gastrostomy (PRG).

Radiologically inserted gastrostomy (RIG) – now known as percutaneous radiologic gastrostomy (PRG) - can be used in patients in the terminal phases of the disease or when patients have poor respiratory function. It does not require sedation and the patient can remain upright, unlike PEG. Chio et al (2002) investigated whether PRG was a safe alternative in ALS patients with respiratory impairment. They compared 16 ALS patients with PRG to 25 ALS patients with PEG placements. All PRG placements were successful, whereas 2 cases of PEG were not. PRG had the advantage of having a minor impact on respiratory function and could be used without sedation. PRG was also cheaper (350 Euro) and quicker (mean time of placement was 5 minutes, standard deviation of 2 minutes) compared to PEG (800 Euro, mean time of 22 minutes). There were problems with the procedure including difficulties of evaluating the conditions of gastric mucus during the intervention but they concluded that PRG was a safe alternative to PEG in patients with serious respiratory impairment. Thornton et al (2002) retrospectively compared PEG and PRG in 36 ALS patients over 3 1/2 years. (20 opted for PEG and 16 for PRG). Out of the 20 patients for PEG, 11 were successful. The procedure in the other nine failed due to inability to trasilluminate the abdominal wall. These nine patients then underwent successful PRG. All 16 of the original PRG cases were successful. No significant differences in survival rates between PEG and PRG groups were observed. While one patient aspired with PEG, no one did with PRG. This is due to the avoidance of the endoscopic route of placement, which lowers the risk of aspiration. They also found that PRG required less sedation so less associated chance of respiratory suppression. They concluded PRG as the preferred primary gastrostomy technique in ALS patients.

Wollman et al (1995) conducted a meta-analysis of the literature on gastrostomy cases from 1978 to 1995 in order to evaluate the effectiveness and safety of radiologic, percutaneous endoscopic and surgical gastrostomy. Although, literature on ALS was absorbed into a larger population group of neurological disorders, overall results are worth observing for future research on PEG and RIG in ALS patients. Firstly, Wollman et al (1995) found a lack of prospective, randomised studies on the procedures and of trials comparing the methods for a certain population. Secondly, PEG and RIG were both found to be safe and effective procedures though the rate of tube placements was more successful in radiologic gastrostomy than PEG (99.2% versus 95.7%, $p < 0.001$). Additionally, radiologic gastrostomy had lower rates of major complications (5.9%) versus 9.4%) and tube-related complications (12.1% versus 16%). It also significantly lowered risk of aspiration (PRG 0.6%, PEG 2.1%).

Nasogastric Tube Feeding.

In relation to use of nasogastric tube feeding (NGT), the evidence is not as favourable as for PEG or PRG. Louwerse et al (1997) found that placement of nasogastric tube can lead to aspiration of tube feeding and is not convenient to patients who drool or choke. Scott & Austin (1994) performed a retrospective study of 4 years on MND patients with severe dysphagia and compared 13 with a nasogastric tube with 18 who continued to feed orally. They found that nasogastric tube feeding presented a number of problems. Firstly, survival time from onset of bulbar symptoms were not significantly different between the two groups. Secondly, those with nasogastric tube reported increased oropharyngeal secretions, requiring suction more often than those who did not have a tube and they also had an increase in nausea and feeling of hunger. However, while both groups had incidences of aspiration and weight loss, it was not as pronounced in the nasogastric tube group.

Clinical opinion based literature, such as Leigh & Ray-Chaudhuri (1994), were favourable to the use of nasogastric tube feeding for temporary feeding when dysphagia is made worse by oral or upper respiratory tract infection. Short-term nasogastric tube feeding of 2 to 4 weeks can also help clinicians to determine the patient's response to feeding and help the evaluation of safety for gastrostomy insertion. Furthermore, other clinical opinion such as Mitusumoto et al (1998) and Silani, Kasarskis & Yanagisawa (1998) view the nasogastric tube as an adequate short term to maintain nutrition over a period of several days, weeks or months, if tubes are removed and replaced regularly. This recommendation is supported by a comparative observational study of 72 patients with dysphagia using a nasogastric tube and 62 others on PEG feeding (Ehler et al, 2002). The nasogastric tube may sometimes be

used as long-term support if the patient is not suitable for PEG, has markedly reduced vital capacity or if the patient chooses the procedure. Nasogastric tube feeding has additional advantages of being less invasive to place, shorter hospital stays and may be placed in the home environment.

Recommendations:

1. For those patients where PEG is not appropriate, percutaneous radiologic gastrostomy (PRG) is a suitable alternative (II).
2. Nasogastric tube feeding (NGT) may be considered for short-term feeding and where PEG or PRG is not suitable (III). NGT also offers a window to evaluate the patient response to enteral feeding and allows non-invasive ventilation to be established.

Research Recommendation:

1. While PEG is the current choice for artificial nutrition, the few studies on PRG suggest that PRG may be an appropriate, safe alternative to PEG, especially in patients with poor respiratory function or in the terminal stages. It is possible to explore this further in either a randomised controlled trial or a well conducted quasi-experiment comparing the two treatments.

What are the patients' views on PEG and other treatments?

There is a need to identify the factors that are important to patients when choosing PEG and other treatments. Decision-making regarding nutritional status involves the patient and if guidelines are to be successfully followed, they should incorporate patients' wants as well as the best clinical evidence. Albert et al (2001) used the Project on Death in America ALS cohort and followed 121 patients over a 2 to 4 year follow up period in order to examine timing of PEG placement. 61% of the patients enrolled on the study. When adjusting for differential length of follow up and loss to follow up and death, cumulative incidence of PEG was 48%. Patients' attitude toward PEG at baseline was a significant predictor of PEG choice over follow-up. Less than 10% who said they did not want PEG went on to have it later as their disease progressed. People who opted for PEG were proactive in relation to disease management. In an earlier publication of the same project (though follow up period was one year), Albert et al (1999) found a total of 28.2% were in favour of PEG placement and that those in favour and those unable to specify at baseline were significantly more likely to undergo PEG placement in the follow up period than those opposed ($p<0.001$). Time to onset of PEG was also significantly earlier among subjects in favour of or unable to specify a preference. Preferences were unrelated to age, gender, level of education or severity of disease at baseline. It is worth noting that 28.2% is a small proportion of people who want intervention and it would to beneficial to find out whether this is representative of the population.

Current literature indicates a reluctance of patients to use PEG yet a satisfaction when using artificial nutrition. In a retrospective study of MND patients in the advanced stages in a Taiwan hospital, only one of eighteen patients on tube feeding opted for a gastrostomy despite gastrostomy being the clinically preferred form. Mazzini et al (1995) had 35 patients refuse PEG because they thought it was too invasive. Schneider et al (2000) surveyed 38 patients using home enteral nutrition including 3 ALS patients. All patients reported feelings of home enteral nutrition (HEN) being beneficial to them, despite the technical considerations. Smith (1995) did a review of the literature on home care technology including home enteral nutrition. The studies had heterogeneous samples containing sub-populations with varying demographics, medical disorders and enteral feedings of different calorie amounts. Yet, throughout the studies, patients using parenteral nutrition did express feelings of frustration, depression, embarrassment and role changes with familial relationships. Silani, Kasarskis & Yanagisawa (1998) argue that in Italy the main obstacle encountered in utilising PEG is the reluctance of patients who have not been given adequate information about dysphagia and its nutritional implications by their neurologist or GP. Further information is warranted on patients' reasons for choice or declination of PEG and other treatments.

Research Recommendation:

1. Research is required for identifying patients' perceptions and for providing patient and carer education.

Conclusion:

The purpose of this systematic review was to develop evidence based guidelines for the nutritional management in MND/ALS patients. In the process, we have unearthed gaps in the literature and a subsequent need for further research, in particular randomised and non-randomised controlled trials on the uses of enteral feeding and other interventions to improve swallowing. Until more evidence is produced these guidelines are based on current evidence of best practice, which largely comprises clinical opinion. This is not an ideal situation and this review has highlighted the need for more systematic research in the field of nutritional management in Motor Neurone Disease.

Development Group

Gene Feder, Chair
Catherine Heffernan, Guidelines Researcher
Tricia Holmes, MND Association
Crispin Jenkinson, Professor of Health Services Research
Richard Kupfer, Consultant Radiologist
Nigel Leigh, Professor of Clinical Neurology
Sue McGowan, Clinical Specialist in SaLT
Alan Rio, Senior Dietitican
Paul Sidhu, Consultant Physician/Geriatrician, Gastroenterologist

Peer reviewed by:
Beverley Hopcutt, Speech and Language Therapist

A condensed version of this review is available in published form:

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Hefffernan, Jenkinson, Holmes, Feder, Kupfer,Leigh, McGowan, Rio, Sidhu

1 Resting Energy Expenditure is the energy required for the maintenance of normal bodily functions and for homeostasis.
2 There is a study in progress on whether PEG has an adverse effect on respiratory function in bulbar onset ALS patients led by Dr. Kinnear, University Hospital, Nottingham. Results are pending.
3 Currently, there is a project being led by Professor Mitchell, Royal Preston Hospital, Preston on the delay in diagnosis and timing of gastrostomy in MND. Results are pending.
4 Carter, G. T., Johnson, E.R., Bonekat, H. W. & Lieberman, J. S. 1992. "Laryngeal diversion in the treatment of intractable aspiration in motor neuron disease". Arch Phys Med Rehabil., vol 73, no 7, pp 680-682.
5 There is a study in progress on the impact of enteral nutrition on the quality of life of ALS patients. Initiated in 1999 by Dr Michael Strong at the London Health Science Centre, London, Ontario, Canada, results are still pending.

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