

IJMSC Volume 2, Issue 1 March 2000

Letter from the Editor

Robert M. Herndon, MD

Editor-in-Chief



Dear Colleague:

As Founding Editor of IJMSC, I am pleased to announce that a decision has been made to provide free access to this very important publication. This will not change the nature of the journal but will make it available to almost all people who provide care or whose lives are affected by multiple sclerosis. IJMSC will remain the official journal of the Consortium of MS Centers (CMSC) and of Rehabilitation in MS (RIMS). It will continue to be peer reviewed and dedicated to the education and collaboration of MS professionals throughout the world.

Subscribers still must fill out a subscription form, which can be done on-line. This allows us to keep track of our readers, which is important to our current and future advertisers. Elimination of the subscription charge will make the journal much more available to international colleagues, many of whom would not be able to afford a subscription.

Our future plans include a continuing education section that will allow health care professionals to obtain continuing education credit on line. We welcome discussion and/or comment on any article in the journal and hope to include a "Letters to the Editor" section in the near future.

We would like to invite our readers to submit articles about all aspects of MS care: treatment of the disease process, symptom management, complications, rehabilitation, access issues, social issues, and research projects. As an international journal, we deal with a variety of healthcare issues, systems, and policies that differ among countries and even among regions within a country. They differ in scope as well, ranging from covered diagnostic services, mobility issues, access to public accommodations, available drugs, access to drugs, availability of other treatment modalities, to social services. These are important issues that impact our patients' quality of life and we welcome articles on any aspect of healthcare or patient services.

Our goal is to sustain a level of excellence in MS clinical care based on research, expert opinion, and the emerging models of care throughout the world. We would like to extend an invitation to you to join us in these efforts.

Instructions for authors can be obtained by visiting the journal on-line or by e-mail from either ijmsc@partmedcomm.com or robert.herndon@med.va.gov

Sincerely,
Robert M. Herndon, MD

Editor-in-Chief

Reduction of Relapses in Multiple Sclerosis After Anti-Alpha4 Integrin Antibody (Natalizumab)

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Abstract

Anti-alpha4 integrin antibody, natalizumab (Antegren), is a monoclonal antibody to a4b1 integrin adhesion molecules expressed on activated monocytes and CD4 cells. A 1-year followup of 28 patients with relapsing multiple sclerosis, randomized to 3 groups in a double-blind pharmacokinetic study, are presented. One group received placebo, a second group low doses (0.01–0.3 mg/kg) of natalizumab, and a third group high doses (1–3 mg/kg) of natalizumab. The observed reduction of relapses in all natalizumab-treated patients with multiple sclerosis suggests a potential range of doses to induce stabilization of the disease.

Presented in part at the American Neurological Association annual meeting, October 20, 1998, Montreal, Quebec.

Supported by Athena Neurosciences (now incorporated by Elan Pharmaceuticals).

Suggested citation: Minagar A, Sheremata WA, Vollmer TL, Willmer-Hulme AJ, Koller M. Reduction of relapses in multiple sclerosis after anti-alpha4 integrin antibody (natalizumab). *Int J MS Care* [serial online]. Mar 2000; 3:1–6. Available at <http://www.ms-care.com>.

Introduction

Multiple sclerosis (MS) is defined by its relapsing clinical course and by the presence of chronic inflammatory cells in demyelinating plaques.¹ The CD4 cells and macrophages which populate the lesions are of hematogenous origin.^{2,3} Migration of these cells across the blood-brain barrier (BBB) is a central issue in demyelinating disease.⁴ Anti-alpha4 integrin antibody (natalizumab; Antegren[®]) can inhibit egress of the CD4 cells and macrophages from the intravascular compartment by blocking binding of the cell adhesion molecule a4b1-integrin, on activated CD4 lymphocytes and macrophages, with its ligand vascular adhesion molecule (VCAM). Natalizumab is a humanized murine monoclonal antibody to a4b1 integrin. This drug has been shown to rapidly reverse experimental allergic encephalomyelitis.^{4,5} We have studied natalizumab in a prospective doubleblind pharmacokinetic (PK) study in patients with MS.⁶

We now report an apparent reduction of relapses in relapsing-remitting (RR) and secondary progressive (SP) MS for 1 year of follow-up after a single infusion of the study drug (71% placebo, 14% natalizumab).

Patients and Methods

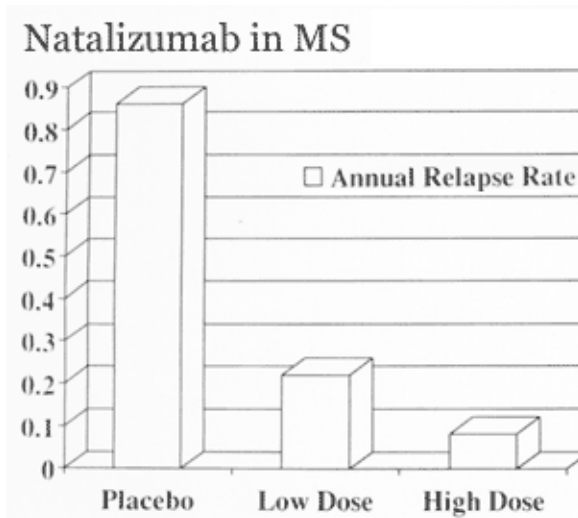
Twenty eight patients (mean age, 42 years; range, 18–55 years) with clinically definite, stable RR or SP MS had been included in the PK study and were the subject of the present inquiry. Briefly, they had a Kurtzke Expanded Disability Status Scale (EDSS) disability rating of ≤ 5.5 . Of these 28 patients, 15 were men and 13 women; 20 had RR, and 8 had SP MS. They had a mean duration of illness of 8.3 years. Prior to entry, all patients signed an institutional review board (IRB)-approved informed consent.

The 28 patients were screened by dose group and randomized to active drug (0.03, 0.1, 0.3, 1.0, or 3.0 mg/kg of natalizumab) or placebo and were sequentially placed in incremental dosage groups. For extended followup, they were assigned to one of three groups: group 1 (7 patients) received placebo; group 2 (9 patients) received a low dose (0.01–0.3 mg/kg) of natalizumab; and group 3 (12 patients) received a high dose (1.0–3.0 mg/kg) of natalizumab.

Patients were followed prospectively for 8 weeks and monitored by physical and neurological examination, EDSS and its component functional systems scores (FSS), laboratory tests, and electrocardiograms. Subsequent data collection was obtained retrospectively. Data were primarily obtained from the PK study records and by personal and telephone contact with the treating physicians and the patients themselves. The physicians and personnel reviewed any subsequent medical records. The patients were also contacted directly by the staff of the two centers regarding their health status. An exacerbation was defined as the appearance of a new symptom or reappearance of an old symptom of central nervous disease attributable to MS, with confirmation of new neurological signs by examination resulting in an increase in the EDSS by 1 grade.

Results

Clinical data were collected for 27 of the 28 patients. One patient was lost to follow-up after the initial 6 months of follow-up. Another left the New Haven area and moved to South Florida. The patients remained blinded until 9 months after initiation, an interval during which the majority of the relapses occurred. The accompanying figure charts the annual rates of relapses for all three groups.



Placebo, low dose, and high dose groups. The scale on the left indicates the annual relapse rates.

Figure. Annualized Relapse Rates for three study dosage groups.

In the placebo group, relapses occurred in 5 of 7 participants (71%), with 6 exacerbations recorded. Initial relapses in each of the 5 patients occurred after a mean period of 3.9 months (range 2.5 to 10 months) in the study. Two patients were treated with intravenous methylprednisone for acute relapses, which occurred 2.5 months and 10 months after entry.

In group 2, relapses occurred in 2 of 9 patients (22%). One patient who received a low dose (0.03 mg/kg) of natalizumab and another who received 0.1 mg/kg experienced one relapse each, at 5 months and 2.5 months, respectively, after study entry.

In group 3, only 1 of 12 patients (8%), who had received 3 mg/kg of natalizumab, experienced a relapse after 5 months. The relapse did not respond to intravenous methylprednisolone, despite two courses of treatment.

Discussion

While the majority (5 of 7, or 71%) of placebo recipients relapsed, only 3 (14%) of the 21 natalizumab-treated patients relapsed. These findings suggest that blocking of α 4b1-integrin binding by monoclonal antibody is associated with long-lasting beneficial effect in patients with MS.

A clear-cut dose-response relationship for natalizumab was also evident by dose grouping. The relapse rate for the low-dose natalizumab-treated patient groups was decreased to 22%, as compared to only 8% of the high-dose group. Thus, an increasing dose of natalizumab appears to be associated with a longer-term benefit over time.

Duration of natalizumab binding to α 4b1 integrin, and inhibition of binding to its ligand, is proportional to dosage of natalizumab.⁶ These observations suggest potential efficacy of natalizumab in preventing the relapse of MS and warrant further studies of this novel medication.

Our observation of a reduction of exacerbations following single doses of natalizumab, however, differ from those reported from a study in the United Kingdom.⁷ In that study, designed to evaluate use of magnetic resonance imaging (MRI) in natalizumab trials, a decrease in new lesion formation was seen by MRI in the first 12 weeks after drug infusion. Despite this, no decrease in relapses was seen in the first 12 weeks, but an increase was seen in the next 12 weeks, a time period when our patients also tended to relapse (more in the placebo group than in the natalizumab-treated groups). All groups subsequently stabilized. However, the next effect of natalizumab in our study was to reduce exacerbations for 1 year from the time of infusion. These differences are not explained on the basis of antibody to natalizumab, because antibody occurred in low titer in only 10% of both trials and was transient. Differences in definition of relapses in the two studies might explain these discrepancies, but the small number of observations in both studies suggest caution in the interpretation of the results. Larger pivotal studies are needed to further evaluate natalizumab in preventing clinical relapses and disability in MS.

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Ishihara's Tests for Color Blindness: A Useful Indicator of Visual Involvement in Multiple Sclerosis

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Abstract

Because vision commonly is affected in persons with multiple sclerosis, it would be helpful to have a bedside test capable of identifying abnormalities that are not readily apparent. This study evaluated the sensitivity and specificity of the first 11 plates of Ishihara's Tests for color blindness (1995 concise edition) as compared to visual evoked potentials in patients with multiple sclerosis reporting normal vision. Forty-five multiple sclerosis patients and 42 controls, aged 25 to 44 years, were assessed. After examination of vision by a neurologist, Ishihara's Tests for color blindness and visual evoked potential tests were administered under conditions similar to those encountered in a neurologic practice. The specificity for each test was defined by the responses of the control population. In differentiating individuals with multiple sclerosis from controls, Ishihara's Tests for color blindness was as sensitive (62%; 28/45) and specific (100%; 42/42) as visual evoked potentials (sensitivity = 58%, 26/45; specificity = 98%, 41/42). Ishihara's Tests for color blindness identified a different population of patients and probably measured a different aspect of visual function than did visual evoked potentials. Ishihara's Tests for color blindness appeared more likely to identify patients with a long disease duration, while visual evoked potentials better identified patients with a history of optic neuritis. Ishihara's Tests for color blindness may be a simple and cost-effective adjunct for detecting and following the visual abnormalities of patients with multiple sclerosis.

Suggested citation: Kaufman MD, Lutz DM, Norton J. Ishihara's Tests for Color Blindness: a useful indicator of visual involvement in multiple sclerosis. *Int J MSCare* [serial online]. Mar 2000; 3:7-12. Available at <http://www.ms-care.com>.

Introduction

In a neurologic practice, commonly encountered problems of the preretinal visual pathways, such as inadequate refraction, oscillopsia, and lens or vitreous opacities, compromise the use of the Snellen visual acuity (SVA) chart in detecting and following visual dysfunction related to multiple sclerosis (MS). Patients with MS, even those with a history of retrobulbar neuritis, frequently have normal visual acuity. Ishihara's Tests for color blindness (ITCB) is a collection of pseudoisochromatic plates that measures color vision and is largely independent of preretinal changes affecting SVA. The complete edition of ITCB contains 38 plates, while a concise edition, assembled in 1989, consists of a subset of 14 plates. The first 11 plates of the concise edition, identifying patients with red-green color deficiency, were used in this study. The concise edition can be purchased inexpensively and can be rapidly and reliably administered by a technician. Misreading up to 1 or 2 plates out of 11 is generally considered normal. Slight differences in color printing for different ITCB editions make it impossible to state categorically which plates may be misinterpreted by normal populations.¹

Color vision frequently is abnormal in patients with retrobulbar neuritis,² and tests of color vision have been used to monitor visual dysfunction in MS.^{3,4} The utility of these tests may

reflect particular vulnerability of color-carrying parvocellular fibers to injury.⁵ The sensitivities of the first 25 plates of the complete edition of ITCB and visual evoked potentials (VEPs) have been compared in 2 studies for patients with MS^{6,7} and for patients with optic neuritis⁸ in a third study. All 3 studies reported a sensitivity for the VEP that was about twice that for ITCB in distinguishing patients with MS (Table 1). In the 2 studies of patients with MS,^{6,8} approximately 10% of the eyes with good visual acuity had an abnormality by ITCB not identified as abnormal with VEPs. This observation suggested that ITCB might be a useful adjunct to the clinical examination. In a small pilot series of 24 patients, we administered the first 11 plates of ITCB, 1995 concise edition (Kanehara & Co, Ltd, Tokyo). This procedure required about 1 minute of technician time and was highly reproducible (data not shown). Based upon the results of that study, we compared the ability of ITCB and VEPs to uncover visual disturbances in MS patients with subjectively normal vision.

Table 1. Studies Comparing ITCB With VEP in Patients With MS and Optic Neuritis

Study	Patient Type	% Abnormal VEP	% Abnormal ITCB	Abnormal ITCB and Normal VEP
Frederikson et al, 1986	MS – good vision	88% (114/130) eyes	63% (82/130) eyes	7/65 patients
van Diemen et al, 1992	MS – normal vision	82% (36/44) eyes	32% (14/44) eyes	No data
Frederikson, 1997	Optic neuritis/MS	59% (34/58) patients	22% (13/58) patients	5/59 normal eyes

Methods

Thirty women and 15 men with MS were selected from a population followed at the MS Center at Carolinas Medical Center. To be eligible for the study, the following criteria had to be satisfied:

1. Aged 25 to 44 years, inclusive;
2. Kurtzke expanded disability status scale (KEDSS) score of 0 to 8.0, inclusive;
3. Clinically definite MS for at least 1 year;
4. Clinically stable vision by history for at least 90 days before testing;
5. Normal oral temperature at the time of the study (≤ 99.7 °F);
6. No dopamine precursors, agonists, or antagonists for 30 days before VEP testing;
7. No history of color blindness in the patient or a first-degree relative;
8. No known diagnosis unrelated to MS associated with a visual disturbance, such as glaucoma, cataracts, diabetes, or lens or retinal abnormalities; and
9. Subjectively normal visual acuity by self-report.

Subjectively normal visual acuity was defined by an affirmative answer to the question, "Is your vision normal?" After informed consent was obtained, a neurologist evaluated the subject's vision using confrontation visual fields, reaction of the pupils to light, and ophthalmoscopic examination. If these were normal, subjects underwent standardized visual acuity testing using a Snellen chart, 20 feet away, and a "near card." If the visual acuity using the patient's

corrective lens was not 20/20–1 or better, a pinhole correction was used. If near and far measures differed, the best visual acuity was used for the analysis. After the subject had rested for at least 30 minutes in the MS Center, VEPs and ITCB were performed by a technician on the same day as the neurologist's visual assessment.

ITCB was administered as it would be given in an office practice of neurology. Subjects were administered the first 11 plates of ITCB, concise edition, in a windowless, 8 x 10 foot room illuminated by fluorescent lighting. Two sets of three F40 Cool White/Rapid Start/Watt Miser bulbs with an average brightness of 2280 lumens and a color temperature of 4150 illuminated the room. The same booklet for ITCB was used to assess color vision for all subjects. Subjects then underwent monocular pattern-reversal VEPs using a checkerboard pattern generated by a black and white monitor at a distance of approximately 1.5 meters, which subtended a check size of 1 minute on the retina. A Cz-Oz bipolar montage referenced to Fpz averaged 150 potentials generated by pattern reversals with rejection of potentials for which the baseline was displaced significantly. The tests were performed using a commercially available CA 1000 machine (Cadwell Laboratories, Inc, Seattle, Wash).

Forty-two normal controls were recruited from the clinic staff and from relatives accompanying patients to the MS Center of Carolinas Medical Center. After informed consent was obtained, 20 males and 22 females, aged 25 to 44 years, were questioned for a history of color blindness in themselves or in a primary relative, for a history of visual disturbance, and for the presence of a systemic illness that could affect vision. Following confirmation that there were no known visual disturbances, control subjects underwent the same series of tests as did the MS patients. The criteria for an abnormal VEP and for the ITCB were defined by data collected from the normal control population.

Data were assessed using standard statistical methods. Descriptive statistics including means and standard deviations or counts and percentages were calculated. The SAS™ System, version 6.12, was used to complete all analyses. A normal value for ITCB that yielded the maximum sensitivity for the detection of patients with MS as compared to the control group was calculated using a chi-square test. A Spearman correlation coefficient was employed to determine the relationship of correct responses on ITCB, versus the latencies of the P100 responses, versus the SVAs for the MS patients. Spearman correlation coefficients were determined among the number of correct responses to ITCB of the 2 eyes combined, age at the time of evaluation, KEDSS score, and duration of disease. The mean duration of disease was calculated for MS patients who correctly identified at least 20 of 22 plates when the scores of both eyes were combined (the "better" group) and for those that identified less than 20 plates correctly (the "worse" group). A *P* value of less than 0.05 was considered significant.

Results

Controls

Plate 5 was missed by 15 subjects, 5 in one eye and 10 in both eyes. One male and one female missed plates 5 and 8, with the female missing both plates in both eyes. No control missed any other plates or missed plate 8 without also missing plate 5. There was no significant correlation between the number of plates missed and the latency of the P100 when the controls were segregated into populations missing either no plates or 1 or 2 plates (*P* = .17 for the right eye and *P* = .22 for the left eye).

The mean P100 latency in the control population was 103.7 ± 4.6 milliseconds (msec). A value of greater than the mean plus 2.5 SD (115.2 msec) or an asymmetry of more than 8 msec was used to define an abnormal response for this study. Using this value, 1 of 84 eyes (1 of 42 controls) was determined to have an abnormal response (a latency for the P100 of 117.5 msec). This subject was noted by our technician to be sleepy. This value may be explained by

the observation that convergence of vision or inattention to the monitor, as might be produced in drowsiness, can lengthen the latency of the VEP.⁹

MS Patients

For the 90 eyes of the 45 patients, 69 were measured as having 20/20–1 or better vision, 15 had acuity worse than 20/20–1 but 20/25–1 or better, and the remaining 6 eyes were measured at no worse than 20/50–1. Pseudoisochromatic plate identification by the right and left eye was compared for controls and MS patients (Table 2). The MS patients read color plates less well than did the controls. Collectively, only 31 of the 90 eyes were normal when defined as the ability to read all ITCB plates correctly, misread only plate 5, or misread only plates 5 and 8. Only 8 of 45 patients identified all ITCB correctly with both eyes. Of these 8 patients, 5 had bilaterally normal SVAs and VEPs, 2 had normal SVAs and at least 1 abnormal VEP, and 1 had an abnormal SVA and an abnormal VEP. Fewer plates were misread by eyes with normal SVA as compared to eyes with abnormal SVA (Table 3). Asymmetric identification of plates between eyes was not a specific finding in MS. When only plates 5 and 8 were considered, lack of symmetry occurred in 29% (5/17) of controls and in 23% (11/48) of MS patients.

Table 2. Comparison of Control and MS Populations by the Color Plates Misread by Each Eye

Percent Plates Incorrect for Controls Versus MS Patients						
Plate	Left Eye Controls	Right Eye Controls	Combined Controls	Left Eye MS Patients	Right Eye MS Patients	Combined MS Patients
1	0	0	0	1/45 = 2%	0	1/90 = 1%
2	0	0	0	9/45 = 20%	6/45 = 13%	15/90 = 17%
3	0	0	0	6/45 = 13%	9/45 = 20%	15/90 = 17%
4	0	0	0	14/45 = 31%	12/45 = 27%	26/90 = 29%
5	14/42 = 33%	12/42 = 29%	26/84 = 31%	30/45 = 67%	34/45 = 76%	64/90 = 71%
6	0	0	0	9/45 = 20%	7/45 = 16%	16/90 = 18%
7	0	0	0	20/45 = 44%	22/45 = 49%	42/90 = 47%
8	2/42 = 5%	1/42 = 2%	3/84 = 4%	11/45 = 24%	10/45 = 22%	21/90 = 23%
9	0	0	0	10/45 = 22%	9/45 = 20%	19/90 = 21%
10	0	0	0	11/45 = 24%	11/45 = 24%	22/90 = 24%
11	0	0	0	5/45 = 11%	4/45 = 9%	9/90 = 10%
All	16/462 = 3%	13/462 = 3%	29/924 = 3%	127/495 = 26%	120/495 = 24%	247/990 = 25%

Table 3. Percentage of Individual Plates Misread by Patients With Normal Visual Acuity in Both Eyes and by Patients With Abnormal Vision in One or Both Eyes

Plates Misread for Eyes With Normal and Abnormal Acuity				
Plate	Eyes With SVA of 20/20-1 or Better	Percent Misread	Eyes With SVA Worse Than 20/20-1	Percent Misread
1	0/69	0%	1/21	5%
2	5/69	7%	10/21	48%
3	4/69	6%	11/21	52%
4	12/69	17%	14/21	67%
5	46/69	67%	18/21	86%
6	7/69	10%	9/21	43%
7	30/69	43%	12/21	57%
8	10/69	14%	11/21	52%
9	9/69	13%	10/21	48%
10	11/69	16%	11/21	52%
11	4/69	6%	5/21	23%
Total	138/759	18%	112/231	48%

Eight women and 4 men (27%, 12/45) gave a prior history of retrobulbar neuritis, 8 of whom had a history of involvement of only 1 eye. Of these 8 patients, the VEP in the historically affected eye was abnormal in 7 of them, and it was longer in the affected eye than the contralateral eye in all 8 subjects. ITCB was abnormal in 4 of the 8 eyes affected by optic neuritis.

The Spearman correlation coefficient was highest for the combined number of color plates correctly identified by either eye (ie, the combined ITCB correct reads versus duration of disease), showing a correlation of -0.492 ($P = .0007$). The negative correlation signifies that the greater the number of correctly identified plates, the shorter the duration of disease. The mean duration of the disease was 6.4 years for those MS patients with a "better" ITCB score ($n = 18$) as compared to 13.3 years for those with a "worse" ITCB score ($n = 26$) ($P = .003$). The duration of disease could not be determined reliably in 1 patient. The correlation coefficient found for combined ITCB correct reads versus KEDSS was -0.308 ($P = .042$) with higher (better) ITCB scores associated with lower (better) KEDSS scores. No statistically significant correlations were found for gender versus age at time of evaluation, KEDSS scores, disease duration, and combined ITCB correct reads.

Spearman correlation coefficients relating combined ITCB correct reads to P100 latencies were significant for the right eye (correlation = -0.333 ; $P = .025$) and nearly so for the left eye (correlation = -0.293 ; $P = .051$). Combined ITCB correct reads and far SVA for the right eye (correlation = -0.415 ; $P = .005$) and for the left eye (correlation = -0.34537 ; $P = .020$) were significantly correlated, but VEP latencies were not significantly correlated with SVA.

Because of the importance of detecting abnormalities of vision in patients with normal SVA, a subset of 29 of the 45 MS patients with normal SVA in both eyes (ie, SVA better than or equal to 20/20-1) was assessed. For these patients, the sensitivity of the VEP for discriminating patients with MS was 48% (14/29), while the specificity was 98% (44/45), because 1 control had an abnormal VEP. A comparatively favorable sensitivity of 55% (16/29) and a specificity of

100% (45/45) was observed for ITCB (Table 4). For the evaluation of this group of 29 patients with normal SVA, if a normal ITCB was defined as the correct identification of any 9 of 11 plates, the sensitivity of ITCB fell to 34% (10/29). On the other hand, if the normal response was defined as identifying all plates or misidentifying any 1 plate, the sensitivity fell to 48% (14/29). Seven of these 14 patients had normal VEPs bilaterally. The fall in sensitivity for this cutoff of ITCB, as compared to the cutoff using misidentification of plate 5 alone or in combination with plate 8, resulted from some MS patients missing a single plate other than plate 5.

Table 4. Abnormalities in the P100 Latencies (>2 Standard Deviations Above Normal) in the MS and Control Populations Versus Abnormalities in the ITCB as Defined by No Misses, Only Plate 5 Missed, or Plate 5 and Plate 8 Missed Together

SVA 20/20–1 or Better in Both Eyes for 29 Patients and 42 Controls	Normal VEP, P100 < 115.2	Abnormal VEP, P100 > 115.2
Normal ITCB		
Patients (13)	8	5
Controls (42)	41	1
Abnormal ITCB		
Patients (16)	7	9
Controls (0)	0	0

Comment

For this study, using misidentification of any plates other than plate 5 or plates 5 and 8 as abnormal, ITCB (1995 concise edition) discriminated MS patients with normal visual acuity from control subjects with a sensitivity and a specificity that were similar to those of VEPs. Twenty-seven of 42 controls missed no plates with either eye, 13 missed only plate 5, and only 2 missed both plates 5 and 8 in the ITCB concise edition series of 11 plates. This is consistent with a previous study showing that only 3 of 51 controls misread 2 of the first 25 color plates in the complete edition.⁶ In 45 MS patients with subjectively normal acuity at our Center, misidentification of any plate other than plate 5 alone or in combination with plate 8 had a sensitivity of 62% (28/45). In comparison, the sensitivity of the VEP was 58% (26/45). When 29 patients with normal visual acuity by examination were evaluated, the sensitivity of these tests was 55% (16/29) for ITCB and 48% (14/29) for VEPs.

As has been shown in previous studies, color discrimination provided different information about vision than did the VEP. VEPs were more sensitive than ITCB in identifying patients with previous retrobulbar neuritis. In 8 patients with a history of unilateral retrobulbar neuritis, 88% of VEPs and 50% of ITCB were abnormal. Since retrobulbar neuritis is a striking symptom, administration of VEP tests to this group is often not needed to diagnose MS. ITCB appeared equally sensitive in detecting visual abnormalities in those with and without a history of optic neuritis. It appeared most sensitive in patients with a long duration of disease and with visual acuity abnormalities. Others have also found that abnormalities of ITCB but not VEPs correlate with diminished visual acuity.⁸ Thus ITCB may have limited usefulness for the detection of early MS.

Because plate 7 was commonly the only plate other than plate 5 to be misread by patients with MS, it was especially sensitive in identifying patients with MS in this study. We did not,

however, find any systematic difference in plate identification of the transformation designs (plates 2–5) and the vanishing designs (plates 6–8, 10, and 11) for ITCB. Abnormalities in ITCB and VEPs frequently identified different individuals, so that 47% (7/15) of patients with normal SVAs and VEPs were identified only by ITCB. On the other hand, for patients with bilaterally normal SVAs and ITCB, 38% (5/13) had at least one abnormal VEP. Combining the abnormalities recorded by VEPs and ITCB, 72% (21/29) patients with definite MS and normal visual acuity in both eyes had at least one abnormal response.

A weakness of this study is the uncertainty to which these findings can be generalized. An ophthalmologist did not exclude other preretinal abnormalities that could have affected ITCB in patients with MS. Patients with known congenital deficiencies in color vision and systemic or ophthalmologic diseases that could affect vision were excluded from analysis. The abnormal responses for both ITCB and VEPs were defined using an age- and sex-matched control population. Because color printing varies in different editions of ITCB, all patients were tested with the same ITCB booklet under fluorescent lighting in 3 nearly identical rooms. The differences in relative sensitivities of ITCB and VEPs in this study as compared to previous studies may have resulted from differences in lighting, from a difference in patient selection (ie, fewer patients with a history of retrobulbar neuritis or more patients with a long disease duration), or from the definitions of an abnormal response for each test.

The purpose in reporting these results is to alert clinicians to a simple, inexpensive test—the concise edition of ITCB—that is valuable in detecting visual dysfunction in patients with MS. This study was not designed to define the most sensitive or specific means for detecting visual problems in MS. Abnormalities of ITCB are not specific for MS. Because ITCB appears to become progressively abnormal as the duration of MS increases, it may be a good way to follow disease of the optic pathways. An important caveat to the application of this study to clinical practice is that, just as VEP laboratories should establish their own unique normal values, criteria for abnormalities of ITCB may need to be individualized for each test setting to obtain maximum test sensitivity.

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The Evolution of Nursing Care in Multiple Sclerosis

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Abstract

Multiple sclerosis (MS) is a chronic, frequently debilitating neurologic disease that affects young adults in the prime of their lives. Until recently, treatment focused on symptom management rather than on disease modification. Patients' contacts with the health care system were limited to the diagnostic period, episodes of acute attacks, and periods of disease progression.

With the advent of disease-modifying agents, the focus of care in MS has changed from one of maintenance and crisis intervention to a more positive and proactive approach. The nurse working in the field of MS has emerged as an important member of the health care team, playing a vital role in the ongoing care of and interaction with patients and their families. Nursing care in MS is a collaborative effort whose goal is self-awareness and self-responsibility; its activities involve supporting a great deal of self-care by patients, families, and care partners.

The nurse working with MS patients is a care provider, facilitator, advocate, educator, counselor, and innovator. The challenges of the disease require many creative interventions in a wide variety of settings. The list of care needs is long and complex. Interventions range from instruction in the use of medications, both oral and injectable, to bowel and bladder management strategies, to the improvement of mobility. The dynamic nature of the disease, along with its psychosocial, economic, and physical implications, calls for ongoing skill development and up-to-date information on the part of the nurse interested in MS care.

Suggested citation: Halper J. The evolution of nursing care in multiple sclerosis. *Int J MSCare* [serial online]. Mar 2000; 3:13–20. Available at <http://www.ms-care.com>.

Introduction

Multiple sclerosis (MS) is a chronic disease of the central nervous system that affects young adults in the prime of their lives. It is diagnosed almost twice as frequently in women as in men.¹ Most patients initially experience a relapsing-remitting course in which exacerbations are followed by periods of remission. Often, the disease converts to a progressive course, in which chronic problems gradually accumulate and acute relapses no longer occur. Common symptoms of MS include fatigue, cognitive changes, emotional problems (particularly depression), altered mobility, visual abnormalities, bladder and bowel dysfunction, and sensory problems.²

A Brief Overview of MS

An international survey was conducted in 1996 to standardize the terminology used to describe the clinical course of the disease. This led to 4 major classifications of the disease: (1)

relapsing-remitting; (2) primary progressive; (3) secondary progressive; and (4) progressive-relapsing. Relapsing-remitting MS is characterized by clearly defined relapses followed by periods of lack of disease progression. Primary progressive disease is demonstrated by a nearly continuous worsening disease course that may be interrupted by occasional plateaus and temporary minor improvements. Secondary progressive MS is defined as an initial relapsing-remitting disease followed by progression with or without occasional relapses, minor remissions, and plateaus. Finally, progressive-relapsing MS is progressive disease from the onset with clear acute relapses, with or without recovery.³

The cause of MS is not known, although it is suspected to be the result of an autoimmune response to a viral infection in a genetically susceptible individual. Several viruses have been detected in patients with MS, but no single virus has been identified as a causative agent. It is possible that more than one virus is capable of triggering this response.¹

Nursing Assessment and Promoting Wellness

Assessment

The nurse has emerged a key member of a team of health care professionals tending to patients with MS and their families. Nurses see patients in the acute care setting, long-term programs, rehabilitation units, outpatient MS centers or clinics, neurologists offices, or in the home. Day-to-day contact, knowledge, and awareness of critical issues in MS make the nurse well-positioned to perform patient assessments. In addition, the nurse often serves as a liaison between the patient, family, and health care providers and can be instrumental in the design, implementation, and coordination of a comprehensive treatment plan for the patient.²

The first type of evaluation commonly made by the nurse is an assessment of the physiologic, emotional, social, and environmental needs of the patient. For example, a nurse is perhaps the best person to observe subtle changes in the patient's bowel and bladder function, mobility, swallowing, vision, and skin integrity. Keen observation makes it possible to treat such symptoms promptly, thereby preventing the development of serious complications.

Because patients with MS are at increased risk for depression and suicide,¹ it is also important for the nurse to pay close attention to the psychological state and needs of the patient. Changes in behavior, expressions of helplessness, hopelessness, anger, or sadness, and suicidal statements should be noted and reported to other members of the health care team. A study of suicide among patients with MS found that those who had committed suicide were more likely to have been male, unemployed, experiencing financial stress, more severely disabled, in a progressive phase of the disease, experiencing unendurable psychic pain, withdrawn, and isolated from a support network.⁴

A nurse who is aware of signs of cognitive dysfunction in the patient (poor concentration, confusion, short-term memory problems, difficulty following directions)⁵ should alert the physician, who may suggest a formal cognitive evaluation. In addition, the nurse can enlighten the patient, family, and friends that this symptom is a part of MS rather than a sign of stubbornness, inattentiveness, or irritability. Social, vocational, and recreational needs are assessed by the nurse as well.

Nurses are able to assess the relationship between the patient and his or her care partners, and they can often determine whether the care partners are helping or hindering the patient. The educational level of the family (how much they understand about the disease process, symptoms, and treatments) can also be evaluated. It should be made clear to everyone involved that two thirds of patients with MS do not become severely disabled and that most people with MS live a relatively normal life. Any gaps in the patient's knowledge can be filled in with readings, support groups, or individual educational sessions with the nurse.⁶ Finally, it is

important for the nurse to evaluate the patient's motivation as well as that of the care partners. Success in the management of MS depends on the attitude and outlook of the patient and his or her support network.

Promoting Wellness

Although pharmaceutical remedies are generally the focus of disease management discussions, they are not the only way to manage MS. The proper combination of rest and physical activity is an integral part of good health and wellness,⁹ and it is an area in which nursing can strongly influence the patient's experience of the disease.

By scheduling activities during periods in which energy levels are high and by taking regular rest periods, patients can effectively conserve their strength. Exercise is essential to maintaining muscle strength and tone and joint mobility. Swimming is an ideal activity because cool water prevents elevation in body temperature and buoyancy facilitates movement. Other highly recommended physical activities are stretching exercises, yoga, and tai chi. Heat and humidity can intensify MS symptoms; therefore, it is recommended that the patient's living and working environments be kept as cool as possible, preferably with air conditioning. Should a patient have a fever, it is important to reduce body temperature and to treat the underlying cause as promptly as possible.⁸

A good diet can promote wellness, while inadequate nutrition can make a patient more prone to infection. Maintenance of proper body weight and a balanced intake of nutrients can promote a healthier state. Adequate fluids, fruits, vegetables, and fiber can prevent constipation, a common complaint in MS. Cranberry juice and prune juice can increase urinary acidity and act as bacteriostatic agents; orange and grapefruit juice have the opposite effect and should be limited in their intake. Many patients experiment with dietary modifications to manage their MS. Nurses are in an excellent position to promote nutritional wellness, taking into consideration the patient's opinions, cultural and economic constraints, and physical impairments.⁹

Disease-Modifying Treatments

Disease Modification and Nursing Care

During the past 7 years, three agents—the ABC drugs—have become treatment options for reduction of exacerbations and modification of the disease course. These include the interferons—IFN-b-1b (Betaseron[®]), IFN-b-1a (Avonex[®]), and glatiramer acetate (Copaxone[®]). Interferons are immunomodulating agents that are injected subcutaneously every other day (Betaseron) and intramuscularly once a week (Avonex).¹⁰

Glatiramer acetate, which mimics myelin basic protein competing for binding sites and may interrupt the inflammatory cascade in the demyelinating process, is a daily subcutaneous injection. Side effects of the interferons include a flulike reaction, spasticity, site reactions in IFN-b-1a, and altered hematologic profile. These can be minimized by timing the administration of drug in the evening, medicating with nonsteroidal anti-inflammatory drugs (NSAIDs), rotating injection sites, and using sterile technique.²³ Copaxone does not cause flu-like symptoms, but has been reported to occasionally cause a mild, transient systemic reaction that resolves spontaneously over a short period of time.¹¹ Education, emotional support, and skills development will assist the patient and family to successfully manage these complex procedures. Nursing care in patients who are assuming responsibility for self-injection includes education about the medication, management of side effects and how to minimize them, injection techniques, and reasonable expectations about the therapy. The nurse's role may also include assisting the patient to obtain insurance approval for these medications. Occasionally, patients will not have adequate coverage for treatment and may require assistance to access support programs that have been developed by the pharmaceutical industry.¹²

Acute Exacerbations and Nursing Care

Acute exacerbations are usually treated with oral or intravenous corticosteroids, which have been shown to shorten the duration of the attacks. Steroids have no long-term benefit on the disease course. Intravenous therapy is usually methylprednisolone, 1 to 3 g daily for 3 to 5 days. This may or may not be followed by an oral taper or dexamethasone or prednisone. Some physicians treat patients with a course of oral corticosteroids only. Long-term administration of corticosteroids is not recommended because of the significant toxic effect of these drugs. Side effects of long-term steroid use include susceptibility to opportunistic infections, hypertension, cataracts, muscle wasting, osteoporosis, and diabetes.¹³ Nurses play a role in the acute management of MS by educating patients about the proposed therapy, overseeing adherence to the prescribed regimen, monitoring patients for side effects, and encouraging patients during this difficult period.

Symptom Management in MS

Primary symptoms in MS are those that are the direct result of demyelination in the central nervous system.¹⁴ Symptoms most commonly experienced include weakness, fatigue, tremor, pain, bladder and bowel dysfunction, paralysis, spasticity, visual changes, and diminished sexual function, including impotence in men.

Secondary symptoms are complications that are caused by the underlying impairment in MS. These include falls, injury, reduced activities of daily living, lack of sleep, urinary tract infections (URIs), incontinence of bowel and bladder, skin breakdown, contractures, problems with the environment, and diminished opportunities for intimacy.¹⁴

Tertiary symptoms are psychosocial or vocational problems, occurring as a result of primary and secondary symptoms in MS, that are not treated and become an overwhelming part of the patient's life. These include loss of job; shift in roles; divorce; loss of financial, social, vocational, and environmental mobility; the stigma of disability; and reactive depression.¹⁴ The nurse and the MS team should take measures to alleviate primary symptoms, thereby dramatically reducing the incidence of secondary and tertiary symptoms. It is important to note, however, that the greatest impact on the patient's quality of life is taking measures to reduce social isolation and promoting participation and productivity despite the persistence of primary symptoms.¹⁷

Fatigue

Fatigue is a common symptom in MS that does not correlate well to the patient's physical status. Typically, a patient will become tired after exercise or as the day progresses. Some may also complain of sudden episodes of fatigue. Regular rest periods or short naps, performing moderate exercises, and using assistive devices such as motorized scooters are effective energy-conserving techniques. Medications for fatigue include amantadine, pemoline, and fluoxetine (amantadine, 100 mg bid; pemoline, 18.75 mg bid; fluoxetine, 20 mg qd, and modafinil, 100 mg or 200 mg).¹⁵ It has been found that depression can be a cause of fatigue, and treatments such as counseling and a supportive social environment can be therapeutic in combating this problem.⁸

Spasticity

Spasticity is caused by involuntary muscle contractions and is characterized by stiffness. This symptom can also result in pain and limitation of motion. Sudden stretching of muscles, changes in position, and use of tight clothing or equipment may trigger and worsen spasticity. Treatment consists of slow stretching programs, appropriate physical activity such as swimming, mechanical aids, medications such as baclofen, tizanidine, clonazepam, and dantrolene sodium. These medications may have sedative effects, and patients must be instructed about the potential side effects⁸ as well as dosage and administration.¹⁵ A baclofen

pump, in which medication is delivered continuously through intrathecal infusion, is the next step should these interventions prove ineffective. Surgical techniques such as nerve blocks and cutting of the tendons are infrequently used for intractable spasticity.⁸

Bladder and Bowel Dysfunction

Many patients with MS experience some type of bladder problem during the course of the disease. Symptoms may include urinary urgency, frequency, incontinence, nocturia, and frequent UTIs. Bladder dysfunction is managed by obtaining a careful history, ruling out a UTI through a urine analysis and culture and sensitivity test, and obtaining a post-void residual volume (PVR) of urine. This will help diagnose whether the patient has a failure-to-store bladder, a failure-to-empty bladder, or a bladder that combines the 2 problems. Treatment of the failure-to-store bladder (one that has a PVR volume of less than 100 ml) consists of anticholinergic agents such as oxybutynin, hyoscyamine sulfate, and propantheline bromide, avoidance of diuretic foods such as caffeine and aspartame, and maintaining a regular schedule for bladder emptying. Tolterodine, a muscarinic antagonist, may also be effective in a bladder that fails to store substantial amounts of urine.¹⁵ The failure-to-empty bladder is treated with intermittent catheterization by either the patient or a care partner, or with indwelling catheters. Combined dysfunction encompasses both the failure to store and the failure to empty. Treatment usually consists of anticholinergic agents along with a catheterization program, either self-care by the patient or family, or indwelling.¹⁶

Bowel dysfunction can manifest itself as either constipation or diarrhea. With constipation, an adequate intake of fluids and fiber, a bowel program that consists of regular and adequate time for evacuation, and stool softeners usually are effective in the management of this problem. Oral and rectal stimulants can also be used occasionally under nursing supervision, but frequent use of enemas and harsh laxatives should be avoided. Diarrhea is usually a secondary effect of overuse of laxatives or stool softeners or may occur with severe constipation when there is leakage of intestinal contents around stool impaction. Diarrhea may be treated with remedies that reduce gastrointestinal motility and fluid loss. Bulk-forming supplements may be of benefit.¹⁶

Sensory Symptoms

Sensory symptoms such as pain, numbness, burning, and tingling may be a great source of concern to the patient.⁸ Avoidance of noxious stimuli, investigation for underlying infections, and neurologic evaluation for exacerbations are recommended for these symptoms, especially if they occur acutely.⁸

Pain in patients with MS may be either a primary symptom or the result of the disability associated with the disease. Tension or migraine headache may be a primary symptom and is usually treated with prescription nonsteroidal anti-inflammatory agents or with the over-the-counter pain relievers. Retro-orbital pain may be due to optic neuritis, an exacerbation of MS. Treatment is with steroid therapy, usually given intravenously over 3 to 5 days. Trigeminal neuralgia or tic douloureux is a sharp facial pain associated with MS. Symptomatic relief can be achieved by treatment with gabapentin, phenytoin, amitriptyline, or carbamazepine.⁸ Intractable neuralgia can be treated with a surgical procedure called percutaneous rhizotomy, in which the sensory root fibers of the trigeminal nerve are severed. Dysesthetic pain, or a burning or electric shock sensation in the extremities or trunk, can be alleviated with the same medications used for trigeminal neuralgia or with topical application of capsaic acid cream. Secondary pain is usually musculoskeletal in nature and is the consequence of poor posture or balance. Patients who ambulate with inappropriate assistive devices, sit with poor posture, or fall frequently are subject to this symptom. Treatment consists of moist, moderate heat, massage, physical therapy, pain relievers, anti-inflammatory agents, and correction of the underlying problem.⁸

Cognitive Implications of MS

Cognitive dysfunction is common in patients with MS. It is estimated that up to 65% of those with the disease experience some degree of cognitive loss—some so mild that it does not affect their lives. Others have such a great degree of loss that they are no longer able to function independently. Temporary lapses in cognitive function may also occur during exacerbations.⁵ Cognitive disorders in MS often consist of retrieval deficits, difficulty with concept formation, problems with abstract reasoning, behavioral fluency, and planning and organizational skills. A nurse who suspects signs of cognitive dysfunction in a patient should consult other members of the health care team so that specific deficits can be diagnosed and interventions offered. A full battery of neuropsychologic examinations often reveals where the deficits lie so that compensatory strategies can be developed.⁵

At the present time there is no pharmacological treatment for cognitive dysfunction in MS, although some medications and rehabilitation activities are being investigated. Nevertheless, identification of cognitive dysfunction can lead to referrals for services. Documentation of a severe cognitive disorder may qualify patients for disability benefits. Frequently, behaviors in the patient that are caused by diminished cognition—stubbornness, crankiness, mood swings, and inattentiveness—must be interpreted to family members and coworkers. Education, along with individual and family counseling, can help the patient and care partner cope with this problem.⁵

The Nurse's Continuing Role

Planning for the Patient's Future

Nurses who care for patients with MS should be aware of specific concerns that the patients have about their disease, such as: What will happen to me and my family? Can I continue working? How disabled will I become? Often, preexisting insecurities in the patient become exaggerated. Nurses must assist these patients to become educated about their disease and suggested treatments. Patients should be encouraged to seek counseling to overcome depression and possibly to affiliate with support groups for an ongoing supportive social environment.¹⁷

Because MS usually strikes during the productive years of life, issues related to employment can be a prominent concern. It is estimated that 25% of patients with MS are working and that another 25% desire to return to the workforce.¹⁸ Fatigue and other symptoms experienced during relapses and in progressive disease and the unpredictability of future disease course in MS can impose major obstacles to employment. Nurses, social workers, and physicians can be supportive in encouraging a patient to continue to work, if possible. Working and productivity are important to a person's quality of life. Finding a job that does not require physically demanding work, staggering work hours, taking naps, and working from home are strategies used to assist patients to remain in the workforce. Those who are no longer able to work should be encouraged to find volunteer activities appropriate to their physical and mental function. Adaptive devices such as scooters, voice-activated computers, and visual aids can assist patients in these activities.¹⁹

The Nurse as an Educator

The nurse has a vital role in the education of patients and their family members. It is very important to encourage patients, who may be overwhelmed by their new diagnosis, to move out of a passive role and to assume a proactive stance about MS. The educated patient is more likely to feel a sense of empowerment, acceptance, and well-being.⁶ The nurse can assist in this process by referring patients to literature, newsletters, and short-term orientation groups, and by explaining the disease process, symptoms, tests, and technical terms. It is important for the nurse to help establish reasonable expectations for proposed treatments, to educate patients in self-care and wellness, and to prepare the patient for side effects. A nurse's support, advice,

education, and expertise as part of a therapeutic partnership can do much to advance MS from an overwhelming disease to a set of solvable problems in the lives of patients and their families.

Family Issues in MS

The patient and her partner must consider all aspects of parenting before deciding whether or not to start a family. Pregnancy has been shown to have a protective effect on MS, while the postpartum period results in a higher risk of relapses.²⁰ It is very likely that many couples would welcome information about this choice. A nurse should encourage couples to be realistic about the problems associated with MS; to evaluate their emotional, financial, and family support; to assess their flexibility with parenting roles; and to think beyond the initial stages of infancy. Couples should also be made aware of the resources available to them, including educational materials, family therapists, and support groups.²¹

A parent's diagnosis of MS can be difficult for a young child. A child's sense of security can be threatened by the disability of the parent. In addition, a child may have to shift roles and assume increased responsibility in the home. While a parent with MS should avoid giving elaborate details of symptoms and disability, children become more anxious when they sense that the truth is being kept from them. Parents should give age-appropriate answers to questions and seek supportive material from sources of information such as the National Multiple Sclerosis Society and the MS Society of Canada. Family counseling can allow family members the opportunity to air their concerns and develop strategies for coping.⁴

Nursing Care in Advanced MS

The severely disabled patient with MS has a need for intensive nursing care. Patients with dysphagia must be given dietary modifications to prevent aspiration and nutritional deficits. Thick fluids, soft foods, and special feeding techniques must be initiated and taught to care partners and providers. In patients who are no longer able to swallow safely, feeding must be done through a feeding tube, which is inserted into the stomach.²²

Skin care is another concern for the severely disabled. Pressure sores often occur over bony prominences such as on the sacrum, ankles, and elbows, and on pressure points such as on the heel. Measures to prevent pressure sores include the use of wheelchair cushions, wheelchairs that are well fitted to the patient, assistive devices (side rails, trapezes, etc) to promote repositioning, and good skin care to promote skin integrity.²²

With advanced MS patients, the nurse is challenged to provide the patients and families with a realistic hope and a message of caring. This is particularly difficult today in light of the new disease-modifying medications, which are offered to patients with MS but which are not appropriate for the severely disabled individual. Nursing care may consist of rehabilitation strategies, such as a program of stretching; linking patients to supportive services and networks; and intermittent appropriate psychosocial interventions as indicated by the needs of the patient and family.

Conclusion

The nurse working with patients with MS has many roles: care provider, facilitator, advocate, educator, counselor, and innovator. Additionally, the nurse often serves as a liaison between the patient, family, and health care providers and can be instrumental in the design, implementation, and coordination of a comprehensive treatment plan for the patient. A nurse's support, advice, education, and expertise as part of a therapeutic partnership can do much to advance MS from an overwhelming disease to a set of solvable problems in the lives of patients and their families.

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Impact of a Comprehensive Long-Term Care Program on Caregivers and Persons With Multiple Sclerosis

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Abstract

The goal of this project was to evaluate a comprehensive model of long-term care in multiple sclerosis (MS). This model consisted of workshops designed to assist participants cope with caregiving demands; medical day care to provide rehabilitation and group therapy; home visits by a psychotherapist or nurse to assist with practical and psychological issues; and case management and liaison services.

Thirty patient-caregiver units receiving treatment were compared with 29 control subjects, with data being collected on 3 occasions over a 2-year period. Repeated measures analysis of variance found that physical functioning declined for MS subjects as indicated by Kurtzke score, Incapacity Status Scale score, and number of hospitalizations. The experimental group reported an increase in perceived cognitive deficits and decreased anxiety. Control subjects reported a greater decline in perceived health than experimental subjects as assessed by the SF-36 general health subscale. All caregivers reported increased overcommitment. Caregivers of controls reported significant decreases in perceived health and that health problems and caregiving activities interfered with social activities. Persons with MS in both groups reported increased satisfaction with caregiver help, while control subjects reported greater satisfaction with the timeliness of help received.

These results provide valuable information about effective ways to use and integrate community resources in the provision of long-term care for persons with MS.

This study was supported in part by grant #RTC84-133 from the National Institute on Disability and Rehabilitation Research (1993–1998) and grant #817-5463A from the Paralyzed Veterans of America's Spinal Cord Research Foundation (1998–1999).

Presented in part at the Multiple Sclerosis Centers annual consortium, September 6, 1997, Calgary, Alberta, Canada; October 3, 1998, Cleveland, Ohio; and May 15, 1999, Kansas City, Mo.

Suggested citation: Guagenti-Tax EM, DiLorenzo TA, Tenteromano L, LaRocca NG, Smith CR. Impact of a comprehensive long-term care program on caregivers and persons with multiple sclerosis. *Int J MSCare* [serial online]. Mar 2000; 3:21–28. Available at: <http://www.ms-care.com>

Introduction

The goal of this project was to develop, implement, and evaluate a comprehensive model of long-term care for individuals with multiple sclerosis (MS) and their caregivers. This comprehensive program was designed to provide individuals with MS and their families with the support, knowledge, and resources they need to live as comfortably as possible with a chronic illness. The program also sought to help caregivers maintain the family member with MS in the community as long as possible, while maintaining or improving the health status and quality of life of patients and caregivers.

MS is a chronic, progressive disease of the central nervous system. Its symptom profile differs widely from patient to patient but can affect virtually every body system. The outcome of MS is variable, with some individuals having a mild course with few symptoms and others having a more debilitating disease leading to significant disability.¹

Advances in symptom management and the treatment of acute complications have resulted in longer life expectancy for people with MS,^{2,3} leading to a growing population of chronically ill individuals requiring long-term care. This long-term care begins within the family setting, with a gradual shifting of roles and responsibilities within the family to accommodate the demands of the illness.⁴ In most instances, the care continues within the home until the demands become too great, and family caregivers are no longer willing or able to provide care at home.

Families differ significantly in their ability to cope with the challenges of chronic illness. This variation among families has significant implications for long-term care because "the manner in which families meet these challenges has a profound impact on family health, and on the patient's adjustment and rehabilitation course."⁵ It is therefore incumbent on health care providers working with these families to identify those who are likely to need support in their coping efforts.

Recently, more information about younger people with disabilities and their caregivers has been available. A study examining the caregivers of MS patients⁶ found them to differ from the typical caregiver of the frail elderly on a number of dimensions. Caregivers of MS patients tended to be spouses who were unassisted in caregiving activities. In addition to caregiving, the majority worked full time and had child care responsibilities. In contrast, caregivers of the elderly tended to be daughters who were not working and received assistance with caregiving. Another study of MS caregivers examined the use of respite services.⁷ Although caregivers felt that their regular activities had been curtailed by caring for their relative, only 55% had ever used any of the respite options available to them, including admitting the patient to the hospital, using day care programs, hiring assistants, or calling on family or friends for help. The reasons cited for not availing themselves of respite services included (1) lack of awareness, (2) lack of confidence in available resources, and (3) guilt and/or anxiety about letting go of any aspect of their family member's care. Unfortunately, this reluctance to use respite services limits their potential value in forestalling or preventing residential placement. These results highlight both the multiple demands placed upon MS caregivers and the support they need for respite care services.

One of the resources of greatest potential benefit to disabled individuals and their family caregivers is adult day health care (ADHC). ADHC refers to community-based programs that provide a range of coordinated social, health, and therapeutic services to the elderly and the chronically ill in order to maximize functional ability and well being.^{8,9} A central goal of ADHC is the promotion of optimal self-care and independence to maintain residence in the community and prevent or delay institutionalization. Of equal importance are the potential benefits for family members of periodic respite from the stresses of caregiving. The consensus is that adult day care has the potential to promote the health and independence of the patient, reduce the

stress on family members, and reduce the stress on the health care system by appropriately limiting the use of outpatient office visits and the need for hospitalization or institutionalization. However, little has been published about the effectiveness of these programs.^{10,11} Furthermore, it appears that few MS patients or their families make use of available services.

ADHC programs designed specifically for individuals with MS have been reported on in the literature. The MS Achievement Center (MSAC) is an ADHC program for MS patients designed to maintain individuals in the community. A primary goal is to ease caregiving responsibilities, thereby preventing or forestalling burnout and premature institutionalization. Participants attend 1 day per week for 5 hours, for at least 1 year. Services include physical therapy, occupational therapy, chaplaincy-led support groups, social work, therapeutic recreation, skin care programs, accident prevention programs, seating and positioning clinics, and nutritional education.

In program evaluation reports,^{12,13} subjects in the MSAC were reported to have fewer symptoms, less fatigue, and a lower rate of decline in physical function than a wait-list control group.¹³ In terms of quality of life, MSAC attendees had better outcomes than did controls on the energy/fatigue, social function, social support, and general health dimensions of the SF-36.¹² Participation in the MSAC was associated with less time spent caregiving and higher use of community services; however, no differences were found in caregiver well-being.¹⁴ These results provide support for the effectiveness of the MSAC in terms of participant, but not caregiver, outcomes. No data were reported on the impact of the program in terms of outside use of medical services (eg, long-term-care residential admissions). Because one of the underlying goals of MSAC is to prevent placement, it would be important to assess this variables in future studies.

The long-term-care program in the present study differs from that of the MSAC by having fewer day health sessions, but it provides individual case management services on a regular basis to both clients and their caregivers.

Method

Forty-three patient-caregiver experimental units participated in the comprehensive program, and 30 patient-caregiver units served as the control group. Data on medical, social, and psychological status at entry, 12 months, and 24 months after enrollment in the program, as well as data on the impact of the program on caregivers, were collected. This completed project represented the first randomized controlled trial of the impact of a comprehensive program of care for MS patients and caregivers.

The study utilized a 2-group, longitudinal design with both subjects and investigators unblinded. Randomization followed the Zelen (1979)¹⁵ "randomized consent" procedure for years 1 and 2 of the funded grant period. In this procedure, subjects who meet entrance criteria are randomized without their knowledge or consent to receive either standard care or a new form of treatment. The randomized consent design has frequently been used when a new treatment is being compared to standard care and when blinding is not possible because of the nature of the treatments. The underlying assumption of the design is that the vast majority of subjects will agree to participate. Following an intent-to-treat model, subjects who decline to participate in the new treatment must still be followed and remain part of the experimental group. The investigators considered a single-blind design, in which the assessments would be done by a staff person blinded to group assignment. However, this alternative was rejected for 2 reasons. First, the in-depth nature of the interview would make it extremely difficult to maintain blinding. Second, the cost involved in maintaining both blinded and unblinded staff in a study of this size would be prohibitive. In year 3 of the project, randomization was changed to

a conventional randomization rather than the Zelen procedure. This change was initiated because higher refusal rates were calculated for the experimental group.

Subjects randomized to the control group received the standard care available at 2 participating MS care centers and a local MS society chapter. Subjects randomized to the experimental group were invited to participate in the new long-term-care program. Both groups executed informed consent before entering the study.

The program targeted subjects with MS who required some assistance with basic life activities such as bathing, dressing, grooming, feeding, etc, and who lived with a caregiver. Eligible subjects included people with clinically definite or laboratory-supported definite MS, between 18 and 65 years old, requiring at least 4 hours per day of caregiving by a family member for at least 1 year, and with a Kurtze Expanded Disability Status Scale (EDSS) score between 6.0 and 8.5.

Instruments were administered to clients and caregivers by trained interviewers either in the client's home (n=69), at the caregiver's place of employment (n=3), at the MS center (n=2), or by telephone (n=2). To ensure confidentiality, clients and caregivers were interviewed separately. Interviews lasted from 2 to 4 hours, depending on the cognitive and physical abilities of the client-caregiver units. It was sometimes necessary to complete an interview in 2 parts.

The treatment program consisted of 4 coordinated components designed to provide a comprehensive response to the medical, educational, and psychosocial needs of severely disabled persons with MS and their family caregivers. They included (1) a twice-monthly medical day-care program, (2) a series of semiannual workshops for persons with MS and family caregivers, (3) monthly home visits by a social worker, nurse, or volunteer, and (4) case management and liaison services. These 4 components are described in detail below.

Medical Day-Care Program.

Only experimental subjects attended the medical day-care program, which was held 2 days per month for 12 months. The medical day care program provided group-based physical, occupational, and recreational therapy, group counseling with a social worker, socialization, nursing services as needed, and lunch. The goals of the program were (1) to maintain the current level of functioning, (2) to prevent secondary and tertiary complications, (eg, contractures, skin breakdowns, infections), (3) to provide respite for family caregivers, and (4) to maintain and strengthen marital and family relationships.

Group physical and occupational therapy sessions included energy conservation and stress reduction, upper body movement, range of motion and instructions for home exercises, cognitive exercises, adaptive equipment, and fall prevention. Topics of group psychotherapy included hidden fears, loss, grief and other emotions, relationship with one's doctor and health care providers, cognitive changes, positive solutions, changing negative patterns and behaviors, communicating with a care partner, charting support networks, and saying good bye to group members.

Workshops.

Family caregivers and persons with MS attended 10 workshops that addressed coping with social, psychological, and medical aspects of MS and their impact on the caregiver.

Social Work/Nurse Home Visit.

Once a month, the social worker or nurse conducted a home visit with the person with MS and/or the primary family caregiver to identify problem areas in the functioning of the patient-

caregiver unit; to assess the impact of the chronic illness on the family system and identify points of stress needing to be addressed; to facilitate communication between patient and caregiver; to teach coping strategies and improve problem-solving skills; to provide emotional support; and to help families learn how to recognize and make effective use of their available options.

Case Management and Liaison Services.

The social worker and nurse provided a wide range of assistance to experimental patient-care giver units, from obtaining medical care, home services, transportation, and health insurance to resume assistance and letters of recommendation.

Outcome Measures

Four sets of measures were used, covering medical, psychological, social, and economic factors.

Medical Measures for Persons with MS

1. The EDSS,¹⁶ which is a single index of severity of MS, in half-unit increments ranging from 0 (normal) to 10 (death);
2. The Incapacity Status Scale (ISS),¹⁷ which uses a 5-point Likert-type format to assess functional capacity in 16 areas of physical disability. Scores can range from 0 to 64, with higher scores indicating greater disability; and
3. The number of acute hospital admissions.

Psychological Measures for Persons with MS

1. The Perceived Deficits Questionnaire (PDQ),¹⁸ which assesses perceived cognitive deficits from the client's perspective. It contains 20 items that describe situations in which a person may encounter problems with memory, attention, or concentration. Clients indicate how frequently these events are experienced on a Likert scale ranging from 0 (none) to 4 (almost always). Higher scores indicate greater perceived cognitive impairment;
2. The Hopkins Verbal Learning Test (HVL),¹⁹ which tests verbal learning and memory. It consists of 3 trials of free recall of a 12-item, semantically categorized word list, followed by yes/no recognition. The test is used in patients too impaired for more comprehensive memory assessments and where repeated testing is necessary. Each patient was administered 3 forms of the HVL test;
3. The Mental Health Inventory (MHI),²⁰ which is a measure of overall emotional functioning. It is a valid measure of mood that evaluates both positive well-being and psychological distress. The instrument consists of 38 items that measure affect, depression, loss of behavioral/emotional control, general positive affect, and emotional ties. Clients are asked to rate the above-mentioned attributes on a scale of 1 (least) to 6 (most) over the past month.

Social and Economic Measures for Persons with MS

1. The social interaction subscale from the Sickness Impact Profile (SIP),²¹ which evaluates the impact of illness on role functioning;
2. The Revised UCLA Loneliness-Companionship Scale,²² which assesses quality of social relationships. It is a 20-item 4-point scale ranging from (1) "I have never felt this way" to (4) "I have felt this way often." The scale consists of 10 positively worded statements reflecting satisfaction with social relationships. Scores can range from 20 to 80. The higher the score, the greater the loneliness;

3. The Questionnaire on Resources and Stress (QRS)²³ (for caregivers only), which measures several dimensions of family stress associated with the care of a dependent family member. The QRS consists of 285 true/false items organized into 15 nonoverlapping subscales, such as "excessive time demands," "overprotection/dependency," "lack of social support," "overcommitment (martyrdom)," "limits on family opportunity," and "lack of financial support";
4. The Health Status Questionnaire of Client and Caregiver (SF-36),^{24,25} which includes 8 multi-item measures of functioning and well-being that represent physical and mental health status on the following dimensions: general health perception, physical function, energy/fatigue, emotional well-being, social functioning, bodily pain, role limitations due to emotional problems, and role limitations due to physical problems. All item scores are summed and transformed onto a scale of 0 to 100, with 0 representing the poorest and 100 the best health. The period of coverage by the SF-36 was the preceding 4 weeks;
5. Satisfaction With Care,²⁶ which is a 3-part scale. Part 1 includes questions regarding the client's satisfaction with his or her doctor and other health care providers in terms of health care, ability to get an appointment, and understanding his or her treatment plan. Part 2 involves satisfaction with personal care and help with client's daily routine provided by caregivers. Satisfaction With Care uses a Likert-type format ranging from "sometimes" to "always." The third part of the scale assesses client satisfaction with the caregiver;
6. Cost of health care and home assistance¹⁴ inquired about out-of-pocket costs due to MS;
7. Information about length of stay and reason for nursing home placement was obtained during the interview;
8. Demographic and financial information was obtained for both clients and caregivers; and
9. A Qualitative Final Program Evaluation was given to experimental subjects only on the last 2 sessions of the medical day-care program. Part 1 of the 1-hour client evaluation assesses the extent to which program services are (1) very helpful, (2) helpful, or (3) not helpful, regarding group occupational and physical therapy, recreation, psychotherapy sessions, case management and health care services, monthly home visits, workshops, volunteers, and nursing and social work services. Questions are also asked about how helpful program services are in terms of learning practical information, ways to cope with MS, providing closeness to other members, and identifying resources. Part 3 evaluates program components according to (1) excellent, (2) very good, (3) adequate, or (4) poor, regarding day and time of program, rest room and group room accommodations, and food quality. Three open-ended questions about program expectations and ways to improve the program are also included. The final question asks if participants would continue in the program, if they could.

Results

One hundred eighty-seven patient-caregiver units from a local chapter of the National MS Society and from 2 MS care centers were contacted. Groups were comparable at Time 1 (N=73); no statistically significant differences were noted between experimental and control groups on outcome and demographic measures. Differences on demographic measures were noted at Time 3 (N=59) (see control group results). Fourteen patient-caregiver units dropped out of the study. Five patient-caregiver units (35.7%) dropped out before the inception of the Medical Day Care Program, and 8 (57.1%) dropped out during program operation. Reasons for dropping out included death of the caregiver (n=1, 7.1%), death of the person with MS (n=4, 28.6%), disease progression (n= 4, 28.6%), and transportation problems (n=5, 35.7%). Reasons for nonparticipation of the majority of the sample were as follows: lived too far away (n=28, 24.6%), transportation problems (n=18, 15.8%), MS patient not interested (n=17, 14.9%), caregiver not interested (n=8, 7.0%), still working, part or full time (n=8, 7.0%), and no caregiver (n= 8, 7.0%).

Subjects

Experimental Group (Patients). Of the 59 patient-caregiver units who remained in the study at 24 months, the majority of MS clients were female (86.7%), with a mean age of 44 years (SD=8.4). Disease course, as rated by the client, was chronic progressive (66.7%). Sixty-three percent were married and 83% were Caucasian. Twenty-seven percent had no children, and 46.9% had children still living at home. The mean education was 14.4 years (SD=2.9). Financial information revealed that clients were receiving Medicaid, Medicare, and disability (6.7%, 70%, and 83.3, respectively).

Experimental Group (Caregivers).

Of the experimental group caregivers, the majority (56.7%) were female, with a mean age of 44.9 years (SD=13.0). Relationship to the client included spouse or partner (66.7%), parent (16.7%), sibling (6.7%), and child (10%). Eighty-three percent of the caregivers were Caucasian. Experimental group caregivers were receiving Medicaid, Medicare, and disability (6.7%, 10%, and 36.7%, respectively). Significant differences were noted for caregiver education, with experimental group caregivers having more education (experimental mean=14.7; control mean=12.8; $P = .03$).

Control Group (Patients).

The majority (69%) were female, with a mean age of 49 years (SD=10.4). Control group patients were significantly older ($P < .05$). Significant differences were noted on years since first MS symptoms appeared (experimental mean=12.9, control mean=18.3; $P = .03$) and years since diagnoses (experimental mean=8.9, control mean=14.2; $P = .013$), with the control group scoring higher. Seventy-two percent of the control group were married and 1 control group client-caregiver unit was a member of a religious order. The majority (89.7%) were Caucasian. Seventeen percent had no children, and 53.1% had children still living at home. Disease course, as rated by the client, was chronic progressive for the majority (86.2%). The mean education level was 13.4 years (SD=3.7). Clients were receiving Medicaid, Medicare, and disability (13.8%, 69%, and 69%, respectively).

Control Group (Caregivers).

Of the control group caregivers, the majority were female (51.7%), with a mean age of 51.8 years (SD=14.3). Relationship to client included spouse or partner (69%), parent (13.8%), religious order (3.4%), and child (13.8%). Eighty-six percent of the caregivers were Caucasian. Control group caregivers were receiving Medicaid, Medicare, and disability (13.8%, 10.3%, and 44.8%, respectively).

Table 1a. Demographic Information: Client (N=59)

Demographic Information	Experimental Group (%)	Control Group %
Gender Female	86.7	69.0
Age Mean (SD)	44 years (8.4)	49 years (10.4)
Ethnicity Caucasian	83.0	89.7
Disease course (client rated)		
Chronic progressive	66.7	86.2
Years since MS	12.9	18.3
	8.9	14.2

symptoms (mean) Years since diagnoses (mean)		
Education Mean (SD)	14.4 years (2.9)	13.4 years (3.7)
Financial information Medicaid Medicare Disability	6.7 70.0 83.3	13.8 69.0 69.0
Marital status Married	63.0	72.4
Children No children Children at home	27 46.9	17 53.1

Table 1b. Demographic Information: Caregiver (N=59)

Demographic Information	Experimental Group (%)	Control Group (%)
Gender Female	56.7	51.7
Age Mean (SD)	44.9 years (13.0)	51.8 years (14.3)
Ethnicity Caucasian	83.0	86.2
Education Mean (SD)	14.7 years (3.3)	12.8 years (3.3)
Relationship to client Spouse or partner Parent Sibling Child Religious order	66.7 16.7 6.7 10.0 —	69.0 13.8 — 13.8 3.4
Financial Information Medicaid Medicare Disability	6.7 10.3 36.7	13.8 10.3 44.8

Statistical Analysis

The analytic strategy of repeated measures analysis of variance (ANOVA) was used with SPSSPC/PC+ statistical software.²⁷ There was a single within-subjects factor, time. The between-subjects factor was group assignment. Significance tests were performed on the

between-subjects factor, the within-subjects factor, and the interaction. The level of significance for all tests was set at .05.

All Subjects (Main Effects).

Repeated measures ANOVA revealed that physical functioning declined for all MS subjects as indicated by the EDSS (F [2,114]=3.14, p=.047), the ISS (F [2,114]=9.22, P =.000), and the number of MS-related hospitalizations (F [2,114]=17.06, P =.000). The MS sample displayed an increase in perceived cognitive deficits (F [2,114]=3.87, P =.024) and a decrease in anxiety (F [2,114]=32.49, P =.000). Subjects with MS, as a whole, declined in verbal recall but improved in yes/no memory recognition, as evidenced by the HVL test. Their ability to recall verbally in 2 trials of free recall significantly decreased: Trial 1 (F [2,110]=4.57, P =.012) and Trial 3 (F [2,110]=7.54, P =.001). On yes/no recognition test, both groups made significantly better false-positive errors (F [2,110]=4.4, P =.014) and did not differ on the true-positive rate (F [2,110]=.20, P >.05). Overall, decision bias (the false-alarm rate for related and unrelated distractors) significantly declined for both groups (F [2,110]=4.48, p=.014). All subjects reported an increase in satisfaction with the help they received in their daily routine from their caregivers (F [2,114]=5.47, P =.005) and in getting help with their daily routine, within a reasonable time frame, when they needed it (F [2,114]=3.34, P =.039). On the QRS, caregivers reported an increase in overcommitment martyrdom (F [2,114]=8.73, P =.000).

Control Group (Interaction Effects).

A significant interaction was found on the SF-36 general health subscale, with control persons with MS reporting greater decline in perceived health (F [2,114]=3.35, P =.039). Caregivers of control group individuals also reported significant decrease in perceived health. Significant main and interaction effects on the SF-36 general health subscale (F [2,114]=6.49, P =.002) (F [2,114]=4.80, P =.010) were noted. Caregivers of the control group reported their physical health problems interfered with normal social activities over time. Their ability to carry out normal social activities with family, friends, or groups also significantly decreased. Significant interaction effects on social functioning (F [2,114]=5.74, P =.004) and role physical (F [2,114]=3.25, P =.042) were reported. Control group subjects reported greater satisfaction with getting help with their daily routine, within a reasonable time frame, when they needed it (F [2,114]=5.85, P =.004). Means and SDs of significant results are displayed in Tables 2a and 2b. Significant main and interaction effects are found in Tables 3a and 3b.

Table 2a. Client Mean Score by Outcome Measure and Experimental Condition (N=59)

Measure	Pretreatment Mean SD N	12 Months Mean SD N	24 Months Mean SD N
EDSS			
Experimental	7.06 .81 30	7.13 .92 30	7.25 .96 30
Control	7.24 .92 29	7.29 .95 29	7.34 .94 29
ISS			
Experimental	22.60 9.38 30	22.87 11.59 30	26.07 12.05 30
Control	28.93 9.14 29	29.66 11.22 29	33.04 11.20 29
Acute hospital MS hospitalization			
Experimental	2.80 2.75 30	3.67 3.22 30	4.67 3.83 30
Control	4.00 2.95 29	4.45 3.50	5.93 4.81

		29	29
SF-36			
General health	63.27 23.04	56.03 21.50	61.47 26.07
Experimental	30	30	30
Control	51.34 27.91	57.14 26.59	50.86 27.60
	29	29	29
Satisfaction w/care			
Help w/routine		3.33 1.75	
Experimental	4.27 .94 30	30	4.43 .94 30
Control	4.34 1.04 29	4.45 .87 29	4.48 .87 29
Help reasonable time			
Experimental	4.10 1.06 30	3.47 1.57	4.23 1.14
Control	4.45 .78 29	30	30
		4.28 1.22	4.38 .90 29
		29	
Mental health			
Anxiety	68.53 21.44	57.33 14.49	72.93 17.59
Experimental	30	30	30
Control	68.83 21.63	50.89 17.49	65.67 22.39
	29	29	29
PDQ			
Experimental	19.97 12.47	19.63 15.16	20.03 16.88
Control	30	30	30
	23.10 16.12	27.59 19.03	27.07 21.00
	29	29	29
HVL free recall			
Trial 1	53.74 16.15	56.32 16.62	50.57 18.08
Experimental	29	29	29
Control	50.00 14.87	47.62 16.64	41.67 17.71
	28	28	28
Trial 3			
Experimental	77.30 18.08	81.32 18.59	72.41 24.31
Control	29	29	29
False positive	66.37 18.07	72.32 20.92	63.69 21.78
Experimental	28	28	28
Control			
Decision Bias (BR)	.06 .04 29	.09 .10 29	.05 .03 29
Experimental	.09 .10 28	.10 .08 28	.06 .06 28
Control			
	.53 .12 29	.55 .15 29	.50 .09 29
	.57 .17 28	.52 .16 28	.44 .19 28

Table 2b. Caregiver Mean Score by Outcome Measure and Experimental Condition (N=59)

Measure	Pretreatment Mean SD N	12 Months Mean SD N	24 Months Mean SD N
SF-36	80.10 13.76 30	77.13 18.62 30	78.63 20.37 30
General health	87.07 11.31 29	81.31 14.11 29	72.48 21.28 29
Role, physical	80.00 34.99 30	95.83 14.80 30	86.67 28.42 30
Social function	93.10 23.05 29	89.66 23.64 29	81.90 33.34 29
Experimental	87.92 19.55 30	82.08 24.27 30	93.99 15.39 30
Control	93.10 18.17 29	92.24 15.09 29	83.62 24.57 29
QRS overcommitment			
Experimental	3.77 1.17 30	3.9 1.39 30	4.8 1.05 30
Control	4.24 1.02 29	4.4 1.32 29	4.6 1.29 29

Table 3a. Results of Repeated Measure Analysis of Variance for Client

Measure	Main Effect	Interaction Effect
Medical measures		
EDSS	F 2, 114 = 3.14 p=.047	N/A
Acute MS Hospitalizations	F 2, 114 = 17.06 p=.000	
Incapacity Status Scale	F 2, 114 = 9.22 p=.000	
Psychological Measures		
Perceived Deficits Quest.	F 2, 114 = 3.87 p=.024	N/A
Hopkins Verbal Learning	F 2, 110 = 4.57 p=.012	
-verbal recall trail 1	F 2, 110 = 7.54 p=.001	
-verbal recall trail 3	F 2, 110 = 4.40 p=.014	
-false positive rate	F 2, 110 = 4.48 p=.014	
-decision bias	F 2, 110 = 4.48 p=.014	
Mental Health Inventory	F 2, 114 = 32.49	
-anxiety subscale		

	p=.000	
Social Measures		
Health Status Quest.		
General health	F 2, 114 = 5.47 p=.005	F 2,114 = 3.35 p=.039
Satisfaction with Care		
Help with daily routine		
Help in reasonable time	F 2, 114 = 3.34 p=.039	F 2, 114 = 5.85 p=.004

Table 3b. Results of Repeated Measure Analysis of Variance for Caregiver

Measure	Main Effects	Interaction Effects
Social Measures:		
Health Status Quest.		
-general health	F 2, 114 = 6.49 p=.002	F 2, 114 = 4.80 p=.010
-role physical		F 2, 114 = 3.25 p=.042
-social functioning		F 2, 114 = 5.74 p=.004
Quest. on Resources & Stress	F 2, 114 = 8.73 p=.000	N/A
-over commitment/martyrdom		

Qualitative Final Program Evaluation of Experimental Subjects with MS

Medical Day Care Program. Ninety-seven percent of the experimental patients said they would continue in the program if they could, and 100% said the group was extremely helpful or helpful in providing a sense of closeness with other people. The majority of program participants had never participated in a formal day program (96.7%) and were extremely isolated. A great portion of their day, prior to attending the program, was spent tending to their activities of daily living (ADL) needs and watching television.

In group therapy sessions, many reported that they had lost their friends because of MS or that their social network significantly decreased when their disability worsened. Didactic group psychotherapy sessions, rated as extremely helpful or helpful by 100% of the participants, were originally scheduled for 1 hour; however, participants enthusiastically requested that the sessions continue for 2 hours. The nurse and volunteers also participated in these sessions. Family members were requested to participate on an as-needed basis. Group occupational therapy was rated as extremely helpful or helpful (90%). Group recreational services were rated as not helpful (72%).

Workshops for Persons With MS and Caregivers.

Workshops were rated by persons with MS as extremely helpful or helpful (90% of the sample). Further use of workshop presenter services occurred for 26 patient-caregiver units (87%); for example, family units used the services of an attorney (n=2), clinical psychologist (n=4), nutritionist (n=2), manicurists (n=2), computer technology specialist (n=5), occupational therapist and assistive technology specialist (n=5), exercise (n=2), and urology (n=3). Most

significant were the opportunities that family members had to meet with one another and the friendships that ensued.

Case Management and Liaison Services for Caregivers and Persons With MS.

Case management and health care services were seen as extremely helpful or helpful for nursing services (100%) and extremely helpful or helpful for social work services (97%). Case management services most frequently required for the day program by persons with MS were arranging ambulette, taxi, or car-pooling services (74%). It was necessary for the staff to be actively involved in this activity, which also entailed frequent telephone calls on the day before the program, to remind clients and caregivers of the actual program day and of the arrangements made. Feeding assistance (51%) and transfer assistance (51%) were an integral part of program activities. Informational MS educational sessions (58%) were led by the nurse, social worker, or occupational therapist during group therapy or before program activities.

Caregiver support service (44%) occurred during day program operation, during home visits, or by telephone by the social worker or nurse. Services included off-hour crisis intervention telephone calls, divorce mediation, couple's therapy, bereavement support, insurance company intervention, letters of recommendation, resume writing, medication information, doctor-patient intervention, transportation assistance, and respite services.

Benefits of the long-term-care program, as reported by 83% of the experimental program participants, included the following: enjoyed being with people with the same condition and discovered how they coped (76%), learned we were not alone (76%), made some friends (40%), being involved in many activities and got out of the house (28%), and staff was great (12%). Suggestions by 73% of the sample to improve the program included the following: provide transportation to the program (64%), weekly meetings instead of bimonthly (64%), change recreational activities (41%), more vigorous structured physical therapy (32%), increase length of the program with no ending date (32%), and not mixing more disabled persons in groups with the less disabled (5%).

Discussion

Modest beneficial effects were found for persons with MS in terms of anxiety reduction and satisfaction with caregiver interactions. Experimental subjects did not report a decline in perceived general health as did the control group. Important results were found for caregivers of persons with MS in the control group. These caregivers reported a greater decline in perceived health and that health interfered with social activities. It seems that participation in the program may have prevented similar decline in caregivers of individuals with MS.

The most serious limitation of the program is that the conclusions to the study as they are described are not supported by the experimental design and data analyses. Despite the limited results on scientific outcome measures, success of the program was demonstrated in other ways. As evidenced by the final program evaluation, experimental clients looked forward to attending the bimonthly program and made new and lasting friendships. Workshops were originally designed for caregivers only; however, participants wanted not only to attend but also to introduce their family members to the new friends that they met in the program. The bimonthly meetings served as mutual aide groups and provided a new opportunity for socialization. The groups provided a forum for persons with MS to discover that they are not alone, to share feelings, and to make new friendships to compensate for their many losses. The program was novel for staff as well, many of whom had little or no experience with MS. Because this was a new model, rehabilitation staff was resistant to program start-up. Once staff participated, they were impressed by the efficacy of the program and became knowledgeable about the ramifications of the disease process.

The volunteer department at the medical center was extremely helpful in recruiting dedicated and caring volunteers and social work students to assist in program activities. Volunteer services were rated as extremely helpful or helpful (90%). All volunteers remained throughout program completion, and the majority (98%) continued their relationships with clients and caregivers after the program was completed. It was not uncommon for volunteers to continue to visit in the home or at the medical center when clients were hospitalized or waiting for medical appointments. The volunteer department of the medical center also provided monetary grants for transportation, meals, holidays, and seasonal events. The most recent grant was awarded to an MSW student to continue social work intervention for 3 clients who needed transitional services.

MS educational sessions at the medical day-care program were beneficial. Clients frequently asked questions about medication, catheterization, urinary tract infections, and recent news proclamations. The nurse also involved participants in ongoing clinical trials at the medical center. The one-stop shopping approach was used. Neurologist visits, urology, dental, assistive technology, and speech and swallowing evaluations were arranged while the participant attended the day program. MS physicians and nurses frequently made drop-in visits at group therapy sessions and entertained questions.

In addition to the changes described above in study outcome measures, the success of the program can also be measured by the establishment, and ongoing success, of the 3-year running "graduate group," a newsletter (written by graduates), attendance by experimental patient-caregiver units at various MS Society-supported programs, peer support groups, other adult day programs, and the continued social interaction between program clients, caregivers, and volunteers.

The amelioration of loss and feelings of connectedness are invaluable results of the interventions provided by this research project. Further studies are needed using research measures that tap change in social support, socialization, knowledge of resources, and caregiver burden. Additionally, MS patients require services from many systems and service providers. It would be beneficial to initiate controlled studies that explore whether comprehensive case management services would ease the burden for patient-caregiver units. Ideally, case managers would be at the MSW level, capable of coordinating services and intervening therapeutically when necessary—for example, providing couple therapy, family therapy, and acting as a liaison between professionals and clients.

There are several important additional limitations to the study. First, denial is a primary line of defense to the reality of the disease.²⁸ Both the caregiver and the person with MS can unconsciously collude in denying the severity of the symptoms and the emotional and physical devastation caused by the disease. The self-report measures that were used in this study could be influenced by denial. The unconscious use of defensive denial by people responding to self-report mental health questionnaires can result in false-positive results.²⁹ More objective measures that evaluate disease process and mental status by means of professional evaluation and observation would perhaps be more accurate than the self-report measures used in this study. Second, a gender bias toward the interviewer may have influenced responses. It appeared that patients replied more honestly to sensitive questions from the female interviewers. For example, questions about sexuality, intimate relationship issues, and bowel and bladder functions appeared to elicit a differential pattern when asked by a male versus a female interviewer. Next, the standardized instruments did not capture the impact of the program, in particular, the decrease in isolation, the continued socialization and long-lasting friendships that resulted for subjects in the experimental group. Lastly, attrition was a problem. The sample consisted primarily of people who had chronic progressive MS. The original sample size was 73 patient-caregiver units; attrition resulted in a sample size of 59 patient-caregiver units. In fact, this mortality rate had the consequence of reducing statistical power of the data

analysis to below what was desired at the outset of the study. Given the severity of the disease and individuals eligible for the study, mortality was a contributor to attrition.

Conclusion

Development of effective programs to address progressive disabling conditions remains one of the most significant challenges for the field of rehabilitation. This challenge is most notably manifested in MS, where a seemingly unpredictable course can wreak havoc on many traditional intervention methods. In the future, the challenge will grow with the increasing number of people affected by other progressive conditions such as spinal cord dysfunction, arthritis, leukemia, acquired immunodeficiency syndrome, diabetes, and others. The majority of people disabled by MS have significant spinal cord dysfunction; therefore, the research that addresses problems of MS will also be applicable in many ways to people with spinal cord injuries and other causes of spinal cord dysfunction. The results of this project provided valuable information about effective ways to use and integrate community resources in the provision of long-term care for persons with MS.

Acknowledgment

The authors would like to thank Larry Cohen, Paul Goodheart, and Henry Bangser for their dedicated assistance. Appreciation is also extended to Laura Lennihan, MD, volunteers and staff of Helen Hayes Hospital, and Fordham University social work interns.

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Drug-Induced Dysphagia

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Abstract

Dysphagia is commonly defined as difficulty swallowing. Although the disorder can have several causes, the patient's medication is often overlooked as a source of the problem. This type of dysphagia, one of the most readily corrected, is known as drug-induced dysphagia. A thorough literature search was undertaken to determine the potential for drug-induced dysphagia.

Drug-induced dysphagia can be classified into one of three categories: dysphagia as a side effect, dysphagia as a complication of therapeutic action, and medication-induced esophageal injury. Examples of medications in each category are provided based on therapeutic classification. Specifically, the role of dysphagia in multiple sclerosis and the agents that have been linked with dysphagia are discussed.

The most valuable method of preventing drug-induced dysphagia is obtaining a thorough and accurate medication history from each patient. Other prevention strategies and compensatory techniques are also explored.

Suggested citation: Balzer KM. Drug-induced dysphagia. *Int J MSCare* [serial online]. Mar 2000; 3:29–34. Available at <http://www.ms-care.com>.

Introduction

Dysphagia is defined as the subjective sensation of difficulty swallowing.¹ Dysphagia itself is not a disease; rather, it is a symptom of an underlying disorder. The word dysphagia is derived from the Greek roots *dys* (meaning "with difficulty") and *phagia* (meaning "to eat").¹ It is estimated that up to 15 million people in the United States suffer from some form of dysphagia.²

The seemingly simple act of swallowing is actually a highly complex process. Approximately 30 facial muscles and 8 cranial nerves are involved in a normal swallow.³ Impairment of these muscles or nerves from any mechanism may lead to a swallowing disorder.

Symptoms of dysphagia are widely varied, ranging from difficulty initiating a swallow to the feeling of complete esophageal obstruction.¹ Early symptoms may include frequent throat clearing, drooling, a hoarse or weak voice, choking or coughing while eating, problems with speech, or regurgitation of food.²⁻⁶ The patient may report fullness, pressure or burning in the sternal area after eating, a loss of pleasure in food, or that food is "sticking" in the throat.³⁻⁶ Progressive dysphagia may result in lifestyle changes, such as decreased food intake or alterations in diet.^{5,6} Potentially damaging complications of dysphagia include coughing, choking, dehydration, malnutrition, and bronchitis or other upper airway infections.⁵ In extreme

cases, aspiration of food may result in pneumonia, which can have serious or even fatal consequences.^{2,5}

What Causes Dysphagia?

The most frequent causes of dysphagia are neurologic in origin. Common examples include cerebrovascular accident, Parkinson disease, myasthenia gravis, muscular dystrophy, Alzheimer disease, and multiple sclerosis (MS).^{1,2,5-8} However, dysphagia may also be caused by neuromuscular disorders or by obstruction of the esophagus. These causes include scleroderma, esophageal tumors or strictures, acquired immunodeficiency syndrome (AIDS), and head or neck injuries.^{2,9}

An often overlooked cause of dysphagia is the patient's medication. This is known as drug-induced dysphagia. Drug-induced dysphagia is far more common than reports in medical literature suggest, and it is one of the most readily corrected causes of dysphagia.

Drug-Induced Dysphagia

The first reported case of drug-induced dysphagia occurred in 1970.¹⁰ Through additional reports, 3 major mechanisms have been identified:

1. Dysphagia as a side effect of the drug;⁸
2. Dysphagia as a complication of the drug's therapeutic action;^{8,11} and
3. Medication-induced esophageal injury.^{8,11}

Each of these mechanisms will be discussed in detail, and both prevention strategies and compensatory techniques will be explored. However, it is important to note that the most valuable tool in determining the potential for any type of drug-induced dysphagia is the collection of a thorough and accurate medication history from each patient.^{2,5}

Dysphagia As a Side Effect

The esophagus is composed of both smooth and striated muscle.¹¹ Smooth muscle function and coordination are dependent on both cholinergic and muscarinic innervation. Therefore, drugs with anticholinergic or antimuscarinic activity have the potential to cause dysphagia (Table 1).^{8,11} Management techniques for this type of dysphagia usually include discontinuing the offending agent, if possible. In addition, the use of saliva substitutes or frequent sips of water to facilitate transport may be beneficial.

Table 1. Drugs That Have Anticholinergic or Antimuscarinic Effects¹¹⁻¹⁴

<p style="text-align: center;">Atropine (Atropar) Benztropine mesylate (Cogentin) Dicyclomine (Bentyl) Hyoscyamine (Cytospaz) Ipratropium (Atrovent) Oxybutynin (Ditropan) Propantheline (Pro-Banthine) Scopolamine (Transderm-Scop) Trihexyphenidyl (Artane) Tolterodine (Detrol)</p>

Conversely, a direct effect on striated muscle is seen with neuromuscular blocking agents, used as muscle relaxants during surgery (Table 2).^{8,11} Management techniques for this type of dysphagia are minimal, as the effect typically decreases as the agent wears off.

Table 2. Neuromuscular Blocking Agents¹²⁻¹⁴

<p>Atracurium (Tracrium) Cisatracurium (Nimbex) Doxacurium (Nuromax) Mivacurium (Mivacron) Pancuronium (Pavulon) Pipecuronium (Arduan) Rocuronium (Zemuron) Succinylcholine (Anectine, Quelicin) Tubocurarine (Tubarine) Vecuronium (Norcuron)</p>

Drugs that cause dry mouth (xerostomia) interfere with swallowing by impairing food transport.^{8,11} The medications that most commonly cause xerostomia include tricyclic antidepressants, antihistamines, and diuretics.^{8,15} However, numerous other medications have been implicated (Table 3). Management strategies include changing to another agent, if possible; the use of a saliva substitute;¹⁵ and frequent sips of water between meals.

Table 3. Drugs That Cause Xerostomia^{8,11-15}

Angiotensin-converting enzyme (ACE) inhibitors	Captopril (Capoten) Lisinopril (Prinivil, Zestril)
Antiarrhythmics	Disopyramide (Norpace) Mexiletine (Mexitil) Procainamide (Procan)
Antiemetics	Meclizine (Antivert) Metoclopramide (Reglan) Ondansetron (Zofran) Prochlorperazine (Compazine) Promethazine (Phenergan)
Antihistamines and decongestants	Chlorpheniramine (Chlor-Trimeton) Cyproheptadine (Periactin) Diphenhydramine (Benadryl) Hydroxyzine (Atarax, Vistaril) Pseudoephedrine (Sudafed)

Diuretics	Ethacrynic acid (Edecrin)
Selective serotonin reuptake inhibitors (SSRIs)	Citalopram (Celexa) Fluoxetine (Prozac) Nefazodone (Serzone) Paroxetine (Paxil) Sertraline (Zoloft) Venlafaxine (Effexor)
Tricyclic antidepressants (TCAs)	Amitriptyline (Elavil) Desipramine (Norpramin) Imipramine (Tofranil)

Local anesthetics, commonly used for nasogastric tube insertion, endoscopy, or dental manipulation, may also cause dysphagia (Table 4). These drugs cause a loss of sensory afferent input, which results in a feeling of impaired or uncontrolled swallowing by the patient.^{8,11} This effect resolves as the medication wears off; therefore, management strategies are minimal.

Table 4. Local Anesthetics¹²⁻¹⁴

<p>Benzocaine (Americaine, Dermoplast) Benzonatate (Tessalon) Lidocaine (Xylocaine)</p>

Finally, antipsychotic (or neuroleptic) medications represent a unique class of drugs that may cause dysphagia as a side effect (Table 5). Antipsychotics work by blocking dopaminergic transmission, which can result in an extrapyramidal syndrome similar to Parkinson disease. This pseudo-Parkinsonism can contribute to dysphagia.¹¹ Over time, the resultant dopaminergic supersensitivity may lead to an irreversible syndrome known as tardive dyskinesia (TD).⁹ Clinically significant TD occurs in 10% to 20% of patients who take these drugs for longer than 1 year.¹⁵ Since TD usually involves the orofacial and lingual muscles, the syndrome may progress until the patient is unable to chew or swallow.¹⁵

Table 5. Antipsychotic/Neuroleptic Medications^{9,12-14,16,17}

<p>Chlorpromazine (Thorazine) Clozapine (Clozaril) Fluphenazine (Prolixin) Haloperidol (Haldol) Lithium (Eskalith, Lithobid) Loxapine (Loxitane) Olanzapine (Zyprexa) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trifluoperazine (Stelazine)</p>

Management of these patients is difficult, because use of the medication is imperative in many patients. Decreasing the dosage may also prove a challenge: drug-induced Parkinson-like dysphagia usually resolves on decreases in dosage, whereas the opposite is true for TD due to dopaminergic supersensitivity.⁹ However, several strategies can still be employed to manage dysphagia from an antipsychotic drug. First, use an atypical antipsychotic agent (such as risperidone, quetiapine, or olanzapine), which has less association with pseudo-Parkinsonism and TD.¹⁵ The patient should be observed carefully for pseudo-Parkinsonism; a reversing agent such as diphenhydramine, benztropine, or amantadine can be administered if such symptoms occur. Finally, monitoring the patient for TD is of utmost importance. The drug must be discontinued at the first signs of TD; if the drug is still given after the development of TD, the only treatment is to administer larger doses of the antipsychotic.^{9,15}

Dysphagia As a Complication of Therapeutic Action

Agents used to treat cancer or suppress the immune system may cause dysphagia through 2 different mechanisms. First, chemotherapy directly injures the esophageal mucosa due to cytotoxic effects on the rapidly dividing cells of the gastrointestinal tract. Second, prolonged use of immunosuppressants predisposes the patient to viral and fungal infections of the esophagus.^{8,11} Because these mechanisms often occur in combination, dysphagia in the oncology or transplant patient may be quite severe. A list of such medications is provided in Table 6. Management techniques for this type of dysphagia are twofold: using a therapeutic mouthwash to prevent infection and anesthetize the area, and treating the underlying infection, if present.¹¹

Table 6. Antineoplastics and Immunosuppressants¹¹⁻¹⁴

<p>Azathioprine (Imuran) Carmustine (BiCNU) Cyclosporine (Sandimmune, Neoral) Daunorubicin (Daunomycin) Lymphocytic immunoglobulin (Atgam) Paclitaxel (Taxol) Porfimer (Photofrin) Vinorelbine (Navelbine)</p>

The therapeutic effects of corticosteroids can also contribute to dysphagia. When used over a long period of time and in high doses, steroids can cause skeletal muscle wasting (Table 7).¹⁵ Although not usually the primary sight of deterioration, the skeletal muscles of the esophagus may be affected, resulting in dysphagia. Unfortunately, at this stage of muscle wasting, compensatory techniques may be the only viable option for dysphagia management. In such cases, a speech-language pathologist can offer suggestions beyond the scope of this discussion.

Table 7. High-Dose Corticosteroids¹²⁻¹⁴

<p>Dexamethasone (Decadron) Methylprednisolone (Medrol, Solu-Medrol) Prednisolone (Delta Cortef) Prednisone (Deltasone)</p>

Medications that depress the central nervous system have been cited as a serious potential cause of dysphagia. Agents such as antiepileptics, benzodiazepines, narcotics, and skeletal muscle relaxants place the patient at greater risk for dysphagia due to decreased awareness, decreased voluntary muscle control, and difficulty initiating a swallow.^{8,15} A list of such medications is provided in Table 8. Approaches to managing this type of dysphagia involve advising the patient to take other medications prior to taking the offending agent, if possible. If this is not a realistic option, stress the importance of using caution when swallowing and to do so under close supervision.

Table 8. Medications That Cause Drowsiness or Confusion^{8,12-15}

Antiemetics	Droperidol (Inapsine)
Antiepileptic drugs	Carbamazepine (Tegretol) Gabapentin (Neurontin) Phenobarbital (Luminal) Phenytoin (Dilantin) Valproic acid (Depakote)
Benzodiazepines	Alprazolam (Xanax) Clonazepam (Klonopin) Clorazepate (Tranxene) Diazepam (Valium) Lorazepam (Ativan)
Narcotics	Alfentanil (Alfenta) Codeine (Tylenol #3) Fentanyl (Duragesic) Hydromorphone (Dilaudid) Meperidine (Demerol) Morphine (Astramorph, MS Contin, Roxanol) Oxycodone (OxyContin, Roxicodone) Propoxyphene (Darvon, Darvocet)
Skeletal muscle relaxants	Baclofen (Lioresal) Cyclobenzaprine (Flexeril) Tizanidine (Zanaflex)

Medication-Induced Esophageal Injury

The first case of medication-induced esophageal injury was reported by Pemberton in 1970.¹⁰ Medication-induced esophageal injury is typically caused by local irritation of the esophageal mucosa by orally ingested drugs.¹¹ Symptoms are quite characteristic, including a sudden onset of dysphagia, retrosternal chest pain, and odynophagia within 4 to 12 hours after ingesting the medication.^{10,11,16} A thorough medication history often reveals one of the agents listed in Table 9. The most common site of esophageal injury from medication is near the level of the aortic arch or left atrium.¹

Table 9. Drugs Associated With Medication-Induced Esophageal Injury^{1,8,10-14,16}

Acid-containing products	Clindamycin (Cleocin) Doxycycline (Vibramycin) Erythromycin (Ery-tabs, E-mycin) Minocycline (Minocin) Pentamidine (NebuPent) Tetracycline (Sumycin)
Antiarrhythmics	Quinidine (Quinaglute, Cardioquin)
Aspirin	Bayer Aspirin, others
Bisphosphonates	Alendronate (Fosamax) Tiludronate (Skelid)
Iron-containing products	FeoSol, Feratab, Slow FE, Fer-Iron, others
Methylxanthines	Theophylline (Theo-Dur, Unidur, Slo-Bid)
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Ibuprofen (Advil, Motrin) Indomethacin (Indocin) Ketoprofen (Orudis) Naproxen (Aleve, Naprosyn)
Potassium chloride	K-Dur, K-Tabs, Klor-Con, Micro-K, Slow-K, others
Vitamin C (ascorbic acid) products	Allbee with C, others

Increased risk of developing medication-induced esophageal injury is associated with several activities. Swallowing medications in a supine position promotes withholding of the medication in the esophagus and prolongs contact between the drug and the esophageal mucosa.^{8,11} Taking medications immediately prior to sleeping also increases risk, because both saliva production and frequency of peristalsis decrease during sleep.^{11,16} Patients who take medication without enough fluid are also at increased risk, as limited or no fluid intake promotes esophageal retention of the drug.^{8,11,15,16}

Elderly patients are at the highest risk for the development of medication-induced esophageal injury.¹¹ This is due to a combination of predisposing factors. First, the elderly are more likely to take an increased number of medications; the sheer volume of drugs ingested makes injury more probable. Second, the elderly have decreased esophageal motility and decreased production of saliva, which both contribute to impaired transport of medication and increased contact time with the offending agent. Finally, the elderly are more likely to have cardiac enlargement from congestive heart failure, which can compress the esophagus and delay the passage of medication.¹¹

Medications that are most frequently implicated in this type of dysphagia include agents containing acid or those with a pH less than 3.^{8,11,16} Other characteristics of caustic medications include those with a prolonged dissolution time, large pill diameter, or circular (versus oval) shape.^{10,15} These types of medications are also listed in Table 9.

There are several strategies that should be employed to prevent the development of medication-induced esophageal injury. These include the following:

- Having the patient take the medication sitting up at a 45- to 90-degree angle.^{1,10,15,16}
- Taking the medication with at least 100 mL of water or other appropriate carrier.^{10,11,15,17}
- Taking a small sip of water or other appropriate carrier *before and after* taking the medication.^{15,16}
- Taking medications that must be taken "at bedtime" at least 30 minutes before sleeping or 10 minutes before reclining.^{10,15,16}
- Taking one medication at a time.¹⁵
- Consulting a pharmacist before crushing tablets or opening capsules.¹⁵
- Requesting the liquid form of the medication—consult with a pharmacist regarding equivalent doses.^{10,15,16}

Miscellaneous Medications

Several other medications have been cited in the literature as having an association with dysphagia (Table 10). The mechanisms by which these agents cause dysphagia are unknown.

Table 10. *Miscellaneous Agents Associated With Dysphagia*¹²⁻¹⁵

Anti-Parkinson agents	Amantadine (Symmetrel) Bromocriptine (Parlodel) Pergolide (Permax) Ropinirole (Requip) Selegiline (Eldepryl)
Antiretroviral agents	Ritonavir (Norvir) Saquinavir (Invirase) Zalcitabine (Hivid)
Antiviral agents	Foscarnet (Foscavir) Ganciclovir (Cytovene) Rimantadine (Flumadine)
Migraine agents	Zolmitriptan (Zomig)
Multiple sclerosis agents	Interferon -1a (Avonex) Interferon -1b (Betaseron)
Myasthenia gravis agents	Edrophonium (Tensilon)
Rheumatoid arthritis agents	Penicillamine (Cuprimine)
Toxins/toxoids	Botulinum A toxin (Botox) Tetanus toxoids

Management strategies for these miscellaneous medications include changing to another agent (if possible), and educating the patient about the potential for dysphagia with the use of these drugs.

Dysphagia and MS

It is highly unlikely for MS to present as dysphagia. Dysphagia is usually observed in MS patients who already have an established diagnosis, and it is more likely to be evident in the MS patient with prior fluctuations of sensory, motor, visual, or bladder symptoms.⁴ An MS patient with dysphagia will usually have brain stem lesions or bilateral corticobulbar tract

involvement;⁷ this can interfere with muscle control of the lips, tongue, and soft palate.³ Dysphagia in the MS patient is thought to be multifactorial: it may be caused by lack of oropharyngeal control, delayed swallowing, delayed peristalsis, or poor laryngeal closure.⁵

Patients with MS are likely to be on a large number of medications, many of which have the potential to cause or exacerbate dysphagia. A list of MS medications that have been linked to dysphagia is found in Table 11.

Table 11. Multiple Sclerosis Medications Associated With Dysphagia

Anticholinergics and antimuscarinics	Oxybutynin (Ditropan) Propantheline (Pro-Banthine) Tolterodine (Detrol)
Antiepileptics/antineuralgics	Carbamazepine (Tegretol) Gabapentin (Neurontin)
Antipsychotics/neuroleptics	Lithium (Eskalith, Lithobid) Risperidone (Risperdal)
Benzodiazepines	Clonazepam (Klonopin) Diazepam (Valium)
Corticosteroids	Dexamethasone (Decadron) Methylprednisolone (Solu-Medrol) Prednisone (Deltasone)
Disease-modifying agents	Interferon -1a (Avonex) Interferon -1b (Betaseron)
Immunosuppressants	Azathioprine (Imuran)
Selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs)	Amitriptyline (Elavil) Fluoxetine (Prozac) Imipramine (Tofranil) Paroxetine (Paxil) Sertraline (Zoloft)
Skeletal muscle relaxants	Baclofen (Lioresal)

Management of the MS patient with dysphagia will vary with both the offending agent and the patient's symptoms. As expected, the offending agent should be discontinued; however, this may not be possible due to the limited number of medications available to treat MS and the

potential benefits of such drugs. If discontinuation is not realistic, the patient should be thoroughly educated regarding the potential for dysphagia and possible use of the compensatory techniques previously mentioned for each agent. If the dysphagia is especially severe or if the patient is at significant risk, a speech-language pathologist should be consulted.

Conclusion

Dysphagia is a potential side effect of numerous medications. The most valuable tool in identifying drug-induced dysphagia is obtaining a thorough and accurate medication history from each patient. Ideally, the offending agent should be discontinued; however, in the MS patient this may not always be feasible. If it is not possible to discontinue the agent, dysphagia management strategies may include taking the medication with adequate amounts of fluid, ingesting the drug in an upright position, taking the drug at least 30 minutes before sleeping, and spacing the offending agents and other medications to allow for recovery time between doses. Most important, however, is educating the patient regarding his or her medication's potential to cause dysphagia and its avoidance.

Acknowledgments

I am deeply indebted to the June Halper, MSN, RN, CS, Executive Director Consortium of Multiple Sclerosis Centers; Shirley A. Brown, CCC-SLP; and the entire staff of the Bernard W. Gimbel Multiple Sclerosis Comprehensive Care Center for their kindness and patience, and for providing me with a tremendous educational experience.

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Mobility in Multiple Sclerosis: More Than Just a Physical Problem

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Abstract

Mobility restriction is a common physical disability among individuals with multiple sclerosis (MS). Psychological, sociocultural, environmental, political, and economic influences are among the factors that affect the mobility of a person with MS. These factors have also been identified as elements of the determinants of individual and population health. Health care professionals providing services to the MS population often prescribe appropriate mobility devices for those with mobility restrictions. The goal is to enhance activities and participation in all domains of the individual's life. In addition to directing their services at the individual level, health care professionals addressing mobility issues of individuals with MS should include the additional factors and other determinants of health at the population and societal levels. Therefore, mobility is not only an individual's physical problem, but it is also a population health issue and a societal issue.

Suggested citation: Chan A, Heck CS. Mobility in multiple sclerosis: more than just a physical problem. *Int J MSCare* [serial online]. Mar 2000; 3:35–40. Available at: <http://mscare.com>.

Introduction

Mobility difficulty is an inevitable complaint for individuals with multiple sclerosis (MS). Primary neurologic symptoms that lead to mobility impairment are decreased motor control, impaired muscle strength, spasticity, impaired balance, and ataxia. As time progresses, any one or a combination of several of these symptoms will lead to reduced endurance, inability to walk a set distance, impaired gait pattern, or inability to support body weight, resulting in dependency on a wheelchair or other mobility device. Fatigue, which is a common symptom of MS, also affects the person's mobility.¹ Mobility impairment is the main factor contributing to physical disability. It restricts the individual's ability to participate in normal family, social, vocational, and recreational activities.

A number of objective tools are used to measure impairments and/or disability in the MS population, including the Kurtzke Expanded Disability Status Scale (EDSS)² and its original Disability Status Scale (DSS)³. The scale ranges from 0 to 10, where 0 is no impairment and 10 is death due to MS. EDSS scores of 4 and lower provide an indication of the degree of neurologic impairment. A score of higher than 4 is an indication of locomotion disability.⁴ At an EDSS/DSS score of 6, the individual requires the use of a unilateral ambulatory aid.^{2,3} At an EDSS score of 8, the individual requires a wheelchair for mobility. Weinschenker et al⁵ reported that the median time from onset of MS to reach a DSS score of 6 was 15 years. Of the MS population in this study, 33% had a DSS of 6 at 10 years from onset of MS.⁵ Within 30 years after onset of MS, 83% of the population had a DSS of 6. Therefore, depending on the type of

MS (relapsing-remitting or progressive), most individuals will experience mobility difficulties at some time during the course of the disease. With the progressive type of MS, 50% are likely to have an EDSS score of 6 in 5 years.⁵

For the MS population, one of the most common reasons for referral to rehabilitation professionals is to improve gait/mobility. It has been reported that patients with MS entering a short-term inpatient rehabilitation program identified gait/mobility as one of the 12 goals of rehabilitation.⁵ The roles of rehabilitation professionals and the management strategies generally used by these professionals for improving the mobility status of individuals with MS have been described in the literature.^{1,6-8} Physiotherapists prescribe, educate, and instruct in exercise programs and in use of walking aids and other mobility equipment;^{9,10} provide gait analysis and gait correction; and educate MS clients on fatigue management.^{1,9} Occupational therapists review the individual's ability to perform activities of daily living (ADLs) at home, work, and in social settings, and they make recommendations and provide instructions to improve the mobility status of the individual.^{11,12} The progressive nature of MS and its symptoms present significant challenges to the individual, health care teams, and society at large.

Factors Affecting Mobility

Are the strategies that address the physical disability of the disease sufficient to improve the mobility status of individuals with MS? Individuals and their families, as well as health care professionals experienced in working with the MS population, know there are additional important factors that also affect the mobility of an individual. These factors are

- Fatigue
- Cognitive impairment
- Psychological perspective
- Sociocultural factors
- Environmental factors
- Political factors
- Economic factors

This article reviews each of these factors and discusses how each factor affects the mobility of an individual with MS.

Fatigue

Fatigue is the most common symptom of MS.¹³ It affects individuals across the spectrum of the disease regardless of the level of disability.^{13,14} The impact of fatigue has both physical and psychological components.

Physical Component of Fatigue. Physically, fatigue can manifest itself as a reduction in endurance. Fatigue exacerbates existing symptoms and affects the physical functioning of the individual.^{15,16} Jonsson et al¹⁷ reported that one outcome of an inpatient rehabilitation program was the reduction of disability related to fatigue and mood. In Rossiter's study,¹² patients with MS identified reducing fatigue and improving gait/mobility as rehabilitation goals. This reflects that these 2 impairments are of major concern to these patients. For an individual who has impairment of balance or weakness of the legs, fatigue will magnify existing symptoms, thereby affecting gait and mobility. When walking distance is severely limited by fatigue, the person's activity level and ability to participate in society are restricted. Use of a mobility device (eg, a motorized scooter)^{7,10} is one strategy to overcome this restriction to mobility.

Psychological component of fatigue. Fatigue has also been described as a lack of energy and/or concentration¹⁸ that affects the motivation of the individual and his or her ability to enjoy an active life. When traveling short distances or participating in activities requires a lot of preparation or adaptation and consumes a lot of physical and psychological energy, the individual's motivation to participate in activities outside of the home is severely challenged. This is another example of the impact of fatigue on mobility of an individual.

Cognitive Impairment

MS-related cognitive impairment was reported in 43% of members of a large community-based MS Society¹⁹ and 59% of a large clinic-based sample²⁰ of the MS population. Cognitive impairment is moderately or strongly correlated with physical disability.²¹ Individuals with cognitive impairment are significantly less likely to be involved in social activities and more likely to need assistance in personal care and homemaking.²² Impaired recognition of recently learned information and diminished problem-solving skills are common cognitive deficits experienced by individuals with MS. The ability of an individual to recall and apply learned information and the ability to solve problems are necessary cognitive skills in learning to use a mobility device properly, whether it be a cane, scooter, or wheelchair. Thus, the presence of cognitive dysfunction has an impact on the mobility of individuals with MS.

Psychological Perspective

Individuals use different mechanisms and strategies to cope with changes in their health. Their responses range from facing each change and making positive adaptation to denying change or choosing inappropriate or ineffective strategies to cope with change. Adaptation to change is particularly taxing for the MS population, because for many there is daily variability in symptom presentation as well as variations along a time continuum due to progression of the disease. It has also been shown that individuals with MS exhibited greater levels of depression and psychological distress than did a cohort group of individuals.²³ A high level of psychological distress has positive correlation with the use of emotion-focused coping strategies.²³

In conjunction with symptoms presentation, especially those symptoms that cause mobility restrictions, there are corresponding changes in the individual's body image and ability to perform ADLs. This has a psychological impact on the person and challenges his or her acceptance of an altered level of functioning. Individuals who do not have strategies or the ability to cope with change will subsequently have difficulty accepting an altered level of functioning, and they may not be able to manage their MS symptoms effectively. An example of this is when an individual refuses to use a cane to compensate for poor balance, lower extremity weakness, or when fatigue limits walking distance. By refusing to use a cane, walking distance is significantly reduced and/or the incidence of falling is significantly increased. Another example of poor adaptation skills and management strategies is when persons with severe limitation in walking distance refuse to use a wheelchair because of their perception that using a wheelchair implies disability. Refusing to use a wheelchair restricts the person's ability to participate in activities in the community. Therefore, how a person adapts psychologically to changes has a significant impact on mobility status.

Thus, the coping strategies a person adopts have an impact on his or her ability to positively or functionally adapt to an altered level of mobility.

Sociocultural Factors

Although social factors and culture factors are two separate elements, they are often so interrelated that it is difficult to separate their distinct influence. In this article, therefore, these 2 factors are reviewed together. Some of the sociocultural factors that influence a person's behavior include gender, role within the family, ethnic background, culture, religious beliefs, and personal and group values. Behavior is also influenced by expectations of the society or the cultural and/or ethnic groups to which the person belongs. For example, in some patriarchal

cultural groups, the female is expected to assume a passive role, to be subservient, and to be "taken care of." In that particular cultural group, a female with mobility problems due to MS would be dependent on the male members of the family to take her outside of the home and to make decisions for her. Should the male members choose not to support her, this female could not go outside of the home even if she had an appropriate mobility device.

The literature has indicated that family, and the role of the individual with MS within the family, can affect how the person with an illness adjusts and adapts to a change in his or her ability.²⁴ In cultures in which the family role is very traditional and clearly defined, the male of the family is expected to be the primary economic provider and decision maker for the family. On the one hand, an individual with MS in this family dynamic may strive and struggle to continue working even though his mobility problems may severely tax his ability to continue with full-time employment. This drive can be a facilitator for the person to adopt the use of mobility devices. Alternatively, this attitude can be a barrier if the person is too fatigued and puts himself at risk by continuing with full-time employment. On the other hand, a higher level of independence in the family has been shown to be associated with better psychological and physical functioning in patients.²⁴

A family is greatly affected by chronic illness or disability of a family member. The impact is dependent on a number of factors, including the type and severity of the illness/disability, as well as the mechanisms and strategies that have been adopted by the ill/disabled individual and family members. May²⁵ provided examples of the structural and psychological impact on families when a family member has a chronic illness. The effects of chronic illness/disability and its impact on relationships between the person with MS and different family members are interdependent.²⁴ Therefore, a chronic illness or disability has an extensive impact on the family system.

The society in which the person resides also has an impact. There are informal social attitudes and formal social rules toward ability/disability that affect the individual who is mobility challenged. For example, in some societies, disease or disability is considered an illness that should be cared for and nurtured at home. Participation of disabled persons in society is not a generally accepted norm in this type of society. Thus, the person with mobility difficulty is not only physically challenged but also has to overcome social attitudes in order to participate fully in the community.

This section clearly demonstrates that an individual's mobility must be viewed within the sociocultural framework of the family and the society.

Environmental Factors

Environmental factors can be considered at the micro level, which takes into account an individual's home and social environment. They can also be considered at the macro level, which pertains to the structural and physical environments of the local, regional, or national community. These two levels will be discussed separately.

Individual Level. At the micro individual level, the environment must be adapted for an individual using a mobility device. If a scooter or wheelchair is used, then barriers such as stairs, narrow door widths and hallways, and narrow turning angles must be modified to allow for the use of a mobility device. Even the floor coverings need to be examined for appropriateness of accommodating mobility devices. Modifications of the micro environment apply to the person's home, work, school, church, or other buildings frequented by the individual.⁹

Macro Level. Macro environmental factors are at the community level where the individual resides and at the regional and national levels. Climatic, geographic, and structural factors and physical environment could influence the mobility of an individual or population.

Snow, ice, and wind are major climatic changes experienced by individuals residing in communities located in northern latitudes. For individuals with mobility difficulties, these natural phenomena present a significant challenge to their participation in activities outside the home. Similarly, the monsoon weather has a major impact on individuals residing in communities located near the equator. Geographically, countries with mountainous terrains also pose challenges for individuals with mobility difficulty and influence the choice of appropriate or preferred mobility devices. Heat and humidity are other climatic factors that have a serious impact on the physical functions of individuals with MS. Studies have shown that fatigue in individuals with MS is worsened by heat.^{14,16,18,26} As discussed earlier, fatigue affects the physical functioning of an individual with MS.^{15,16}

Structural environmental factors are less dependent on nature and therefore can be modified by the community through policy development. Political and economic factors have a major impact on structural factors that affect individuals who are mobility challenged. Enabling policies for the disabled and a favorable economy can result in removal of a significant number of structural barriers in the community. Policies such as the one that requires all buildings to be made accessible for the mobility challenged are examples of removing structural barriers for the physically disabled. The 2 factors of policy and economy are discussed in more detail in the following sections.

Physical environment has been identified as one of the determinants of the health status of the individual and of population health.²⁷ Physical environment incorporates housing, workplace, and community, including road design.²⁷ Street and curb modifications and prolonging the timing of traffic light changes are some examples of making positive changes to the physical environment to enhance mobility and health for those with mobility difficulties.

Political Factors

Public policies concerning disability and the social welfare system can be major enablers or barriers for the disabled population. Policies also provide direction for acceptable social attitudes and behaviors for individuals, groups, organizations, and businesses.

Awareness and enabling policies for the disabled population exist in many industrialized countries. The Americans with Disability Act (ADA) in the United States,²⁸ the Canadian Charter of Rights and Freedom,²⁹ and the Ontario Human Rights Code³⁰ (Canada) are some examples of policies that set guidelines and standards for what is expected of society regarding disability. The 5 sections of the ADA²⁸ address the removal of different types of barriers for the disabled population. These sections pertain to:

- Employment
- Public services, including transportation
- Public accommodation, including services operated by private entities
- Telecommunications
- Miscellaneous provisions.

The ADA legislates the rights of the disabled to employment and financial, environmental, and structural changes. It also defines socially acceptable attitudes that influence the sociocultural factors affecting mobility, as discussed earlier. This enabler policy ensures the rights of the disabled through legislation. Similarly, the Canadian Charter of Rights and Freedom²⁹ is another example of an enabler policy.

At the international level, the World Health Organization (WHO) also sets standards for accommodations for the disabled and disadvantaged. In the International Classification of Impairment, Disability and Handicap-2 (ICIDH-2) document, services and systems that affect those with disabilities are identified under environmental factors.³¹ Since the formal structures and services in the community and even the informal rules, attitudes, and ideologies can be directed and modified by policies, these 2 levels of environmental factors of the ICIDH-2 are discussed under political factors in this article. The ADA is a good example of a policy providing direction to communities toward implementation of services (eg, accessible transportation) and systems (eg, employment rights) to accommodate the disabled. Thus, an individual's mobility is enhanced when policies exist to remove structural, environmental, and financial barriers.

Economic Factors

As with environmental factors, economic factors can be analyzed at the individual level (micro) and at the societal/community levels (macro), and they should also be considered both from a direct and an indirect perspective. The direct cost of MS, which can be calculated for an individual and for society, includes the costs of all insured health services, provision and purchase of equipment, modification of home, work, and social environments, and income support.^{32,33} The indirect cost of MS accounts for items such as loss of income and productivity and loss of ability to participate in leisure time and social activities.³³

Individual Level.

Individuals with mobility difficulties frequently use one or more mobility devices such as a cane, walker, wheelchair, scooter, etc. To ensure accessibility of the home or work environment, ramps or elevators may be required. In some countries, health or work insurance plans may provide some funding toward the purchase of mobility equipment, but frequently the individual has to bear a significant portion of the cost of purchasing this equipment. In addition to the purchase of mobility device(s), modification of the home and work environment to ensure accessibility can be very costly. Those with low income or with poor financial resources are significantly disadvantaged when it comes to getting the appropriate mobility devices and/or modification of their immediate environment as required.

A study from the United States³² reported that the overall average cost for an individual with MS was \$34,000 annually (1994 data). Fifty-seven percent of this cost was in nonpersonal health care cost, which included the loss of potential earnings, equipment purchase, environmental alterations, and formal and informal care expenses.³² A Canadian study³³ reported that the annual cost in 1995 for individuals with MS was \$14,523 for mild MS (EDSS \leq 2.5) and \$37,024 for those with severe MS (EDSS of 6.5 and greater). This cost included the direct cost of health services and indirect cost from loss of daily and leisure time activities and lost productivity. In this study, it was reported that for the severe group, between 74% and 88% of the total cost is borne by the person and not by society.³³

In addition, should individuals be unable to work full time or work at all, their income may be significantly affected. Thus, an individual with mobility difficulty is often in a financially compromised situation due to possible reduction in income and the increased cost associated with maintaining activity and mobility. In a longitudinal population study conducted over 10 years in Norway, 42.7% of individuals with MS were able to continue with full-time work, while 49.2% received external support to maintain their financial standard.³⁴

Income and its associated social status have been proved to be determinants of individual and population health.²⁷ Thus, a reduction in income has a negative impact on the health and well-being of the individual. It was found that poor quality of life was associated with unemployment and mobility limitation on stairs and was strongly related to interference by MS in social activities.³⁵

Societal Level.

At the societal level, the amount of funding available to ensure that the community and environment are accessible could be either an enabler or a barrier to individuals with mobility difficulties. "Enabler communities" for those with mobility difficulties are ones that mandate that all buildings are fully accessible, ensure that curbs and sidewalks are modified, and require that the timing of traffic lights is appropriate to accommodate slow walkers and wheelchair users. There are major costs associated with these progressive social policies that must be assumed, accepted, and supported by society.

In addition to equipment purchase and renovation, another economic factor is income replacement. Some countries have guaranteed income for those who are unable to work. For example, in Canada, which has a social safety net, individuals who are unemployed or unable to be employed are entitled to a basic living income with health care benefits. Countries without this basic guaranteed income impose additional economic hardship for individuals with mobility difficulties who are unable to continue with their usual employment. Depending on the type of work, in many cases, there is an inverse relationship between disability and the ability to work full time. For many, as disability increases, the ability to work full time decreases. Vocational retraining for those who are unable to meet the normal physical demands of their jobs is another economic demand on society. In some countries, social benefits include financial coverage for transportation, medical and social services for the disabled, and retraining cost. Because the disabled population is frequently the recipient of these services, their financial burden is significantly reduced when such funding is available.

A percentage of the cost of MS reported in the Canadian³³ and American³² studies were attributed to government-insured health care cost. The Canadian³³ and Norwegian studies³⁴ discussed income replacement and/or supplement. These are costs assumed by society for individuals with MS.

This discussion serves to illustrate the close linkage and relationship among structural, political, and economic factors. Structural factors are dependent on enabling policies and designated funding to remove physical barriers and to enhance accessibility.

Discussion

Health care professionals provide assessment and develop strategies to improve and/or enhance ambulation and mobility of individuals with MS. Using appropriate mobility devices as prescribed by health care professionals does not automatically result in increased activities and participation by the individuals in society. As reviewed in this article, many external factors affect the individual's activities and participation.

According to the 1997 revision of WHO's ICDH-2,³¹ *impairment, activity, and participation* are the new classifications for the consequences of and the impact on the lives of individuals with health conditions.

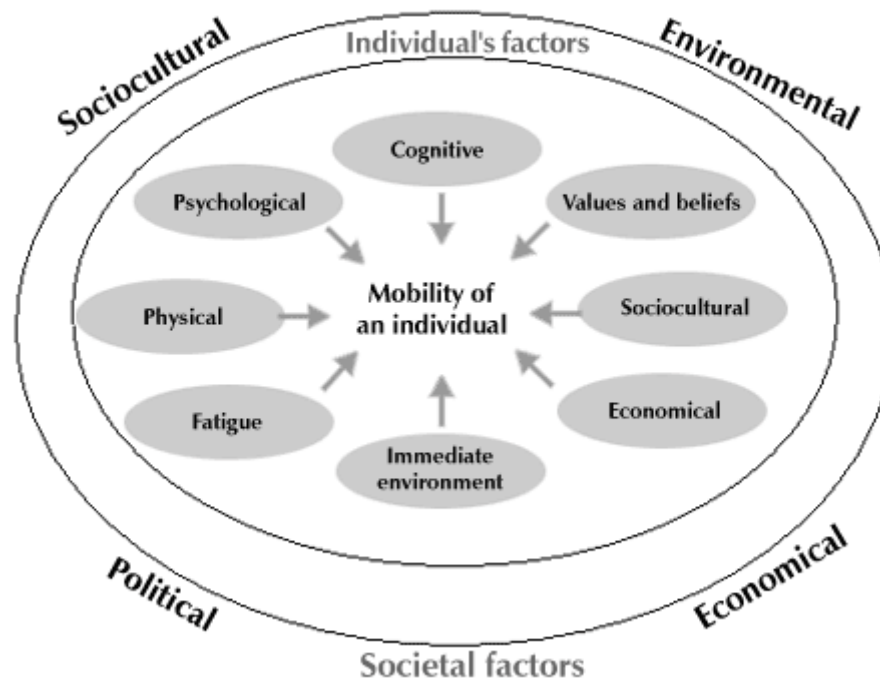
- *Impairments* are problems in the physiological or psychological functions or body structures.
- *Activity* is the performance of a task or action by an individual.
- *Participation* is an individual's involvement in life situations in relation to health conditions, body functions and structures, activities, and contextual factors.

In application of the ICDH-2³¹ conceptual model to the condition of MS, impairments at the individual level are often numerous, rarely static, and usually progressive. The constant state of change becomes a challenge for the individual with MS to adapt and to accept. The fluctuating

physical and psychological status of individuals with MS also poses a challenge to the health care professionals in their work with this unique population. As impairments and disability change, management strategies need to be re-examined and possibly modified. When impairments result in mobility restriction, activities of the individual can be severely curtailed, and participation by the individual as a member of society can be restricted.

An individual's activity and participation levels can be greatly enhanced through the use of appropriate mobility devices and by removing environmental barriers at the individual level. But one must be cognizant of the strong influence of the sociocultural factors and the psychological status of the individual in determining the success of these strategies. Political, economic, and environmental factors at the society level either enhance or limit the individual's activities and participation. The scope of the influence of the various factors is depicted in the figure.

Figure. Factors Affecting Individuals with Mobility Disability.



Although health care practitioners address mobility at the individual level, the additional factors as discussed in this article must be considered and addressed by clinicians when developing appropriate mobility management strategies for the individual. This means that the health care professionals must address the broader determinants of health.

According to the "Health for All"³⁶ document of WHO, population health encompasses more than health care or health services; it includes the broader determinants of health. The following factors have been identified as determinants of an individual's and a population's health by Canada's health ministers:²⁷

- Income and social status
- Social support networks
- Education
- Employment and working conditions
- Physical environments
- Biology and genetic endowment

- Personal health practices and coping skills
- Healthy child development
- Health services

This article reviewed several determinants of health and their impact on mobility of an individual with MS.

Conclusion

This article has shown that there are many factors, at the individual (micro) and societal (macro) levels, that affect the success of the management strategies developed to enhance an individual's mobility. One of the recommendations of the Pew Health Professions Commissions³⁷ is that the new health care system includes population-based perspective. Modifying political, sociocultural, environmental, economic, and societal factors that affect mobility would benefit the population as well as the individual.

Kuhn³⁸ defined a paradigm as an accepted framework that governs the way any system operates. Thus, a paradigm shift is required of health care professionals when providing care to the MS population. They must include considerations of the determinants of health and strive for positive enabler changes at the societal level to enhance mobility of the population. This in turn enhances the care and service provided at the individual level.

To conclude, it can be seen that mobility in MS is more than just a physical problem and more than a problem for the individual . It must be viewed as an issue that affects other dimensions, at the individual, population, and societal levels. Therefore, health care professionals addressing mobility issues in individuals with MS should direct their services not only at the individual level but also at the population and societal levels.

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Book Review

Multiple Sclerosis in Clinical Practice

By Stanley van den Noort and Nancy Holland.

234 pp. New York, Demos Medical Publishing, Inc, 1999. \$34.95 US. ISBN 1-888799-25-0.

This new book focusing on clinical care issues ranks as one of the best for clinicians that I have read. Experts in their field of practice cover a wide range of topics. It is written clearly and concisely, and it is well referenced. Furthermore, algorithms make it easy to follow clinical care paths.

Family physician A. H. Strelnick has written a preface to the book explaining its usefulness to physicians practicing in primary care settings. Chapter 1 provides information on history, pathogenesis, natural history, and clinical course as well as many other subjects related to diagnosis.

Chapter 2 focuses on treatments to alter the course of the disease. The majority of people with MS will need symptom management; therefore, up-to-date management strategies for the major symptoms of the disease are included in this book. In a recent survey by the International MS Society, people with MS ranked psychosocial issues as being of importance in their care. Chapters 9 and 10 of this book address these issues in a knowledgeable way. Chapter 11 deals with important primary care issues and makes it clear that not every symptom is related to MS.

Chapters with relevant case studies, community resources, and frequently used medications complete the book.

This book became an important reference in recent writings with MS clinic coordinators in Canada. In my opinion, it would make a useful addition to the office of anyone who cares for people with MS.

–Reviewed by Pauline Weldon, BN, RN
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