Assessing Relapses and Response to Relapse Treatment in Patients with Multiple Sclerosis
A Nursing Perspective

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There are currently no assessment tools that focus on evaluating patients with multiple sclerosis (MS) who are experiencing a relapse or that evaluate patients' response to acute relapse treatment. In practice, assessments are often subjective, potentially resulting in overlooked symptoms, unaddressed patient concerns, unnoticed or underrecognized side effects of therapies (both disease modifying and symptomatic), and suboptimal therapeutic response. Systematic evaluation of specific symptoms and potential side effects can minimize the likelihood of overlooking important information. However, given the number of potential symptoms and adverse events that patients may experience, an exhaustive evaluation can be time-consuming. Clinicians are thus challenged to balance thoroughness with brevity. A need exists for a brief but comprehensive objective assessment tool that can be used in practice to 1) help clinicians assess patients when they present with symptoms of a relapse, and 2) evaluate outcomes of acute management. A working group of expert nurses convened to discuss recognition and management of relapses. In this article, we review data related to recognition and management of relapses, discuss practical challenges, and describe the development of an assessment questionnaire that evaluates relapse symptoms, the impact of symptoms on the patient, and the effectiveness and tolerability of acute treatment. The questionnaire is designed to be appropriate for use in MS specialty clinics, general neurology practices, or other practice settings and can be administered by nurses, physicians, other clinicians, or patients (self-evaluation). The relapse assessment questionnaire is currently being piloted in a number of practice settings. Int J MS Care. 2012;14:148–159.

Relapses can be a defining feature of multiple sclerosis (MS) for patients. They involve acute physical and cognitive symptoms and present psychosocial and emotional challenges that can significantly disrupt a patient's life.[1,2] Relapses may contribute to disease progression and disability,

although some debate exists regarding whether and to what extent they may affect long-term outcomes.[3-7] They may be indicative of a suboptimal response to chronic treatment with disease-modifying drugs (DMDs)[8] or a sign of increased disease activity.[9]

Despite awareness of the impact of relapses on patients with MS, relatively little practical guidance is available with respect to the determination of the relapse severity, acute treatment response, and the extent of recovery. In the clinical setting, most clinicians recognize the importance of considering patients' perceptions. This perspective is often overlooked in research studies that shape clinical practice. Data from the North

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American Research Committee on Multiple Sclerosis (NARCOMS) Registry, for example, indicate that many patients are dissatisfied with corticosteroid treatment, the most common form of relapse management.[10] A more systematic approach to relapse evaluation that takes into account the patient experience may lead to improved management and clinical outcomes. Although several objective assessment scales for MS-associated symptoms and disability are available, the field lacks an assessment tool designed specifically to evaluate relapses. In particular, the need exists for an instrument that can be used to evaluate not only the acute changes in symptoms and the impact on daily functioning associated with relapse, but also the patient's perception of the degree of symptom resolution, restoration of function, and satisfaction with treatment and outcomes. Such an instrument will provide critical information regarding past and present symptoms and functional activities. It will also examine outcomes that include patient perceptions and satisfaction, and ultimately will contribute to the more optimal, patient-based approaches for resolving future relapses.

A working group of MS nurse experts from the United States and Canada convened in February 2011 to discuss the impact, evaluation, and treatment patterns of MS relapses in clinical practice. The purpose of the meeting was to arrive at a consensus on 1) criteria to consider when assessing an MS relapse, 2) how to evaluate treatment outcomes, and 3) the appropriate timing of such assessments. Consensus reached in these three areas led to the development of an instrument that can be widely used in the MS community for the assessment of relapses and response to treatment. This article was developed based on the meeting, and was intended to provide a nursing perspective on best practices in relapse management. It will briefly review data related to identifying, assessing, and managing MS relapses; describe challenges associated with assessing and managing relapses; and outline the creation of a new tool designed to facilitate assessment and response to the treatment of acute relapse.

Defining an MS Relapse

Optimal management of MS relapses begins with determining what a relapse is. Generally accepted principles exist, but specific definitions vary considerably in the MS community. There are limited objective diagnostic criteria that can be used in clinical practice. The recently updated McDonald criteria[11] define an attack (relapse, exacerbation) as "patient-reported or objectively observed events typical of an acute inflammatory demyelinating event in the CNS [central nervous system], current or historical, with duration of at least 24 hours, in the absence of fever or infection." This definition is appropriate for use as a standard criterion for the purposes of documenting the occurrence of relapses in a uniform way, such as in clinical trials. However, the definition is somewhat ambiguous and, as such, may not be interpreted consistently by practicing clinicians.[12] Moreover, this definition may not necessarily capture the reality faced by MS clinicians. Additional considerations to verify a relapse or to determine the necessity of treatment may be required in certain circumstances.[13] For example, subjective findings may be necessary in order to identify a sensory relapse. A key consideration, noted in the definition of relapse above, is the need to rule out fever, metabolic issues, infections, or other physiological processes, as these all may be indicators of pseudorelapse.[7,9]

A pseudorelapse is defined as an acute worsening of symptoms that is typically associated with an increase in body temperature, which can be due to infection, exercise, or heat exposure.[7,9] In contrast to true relapses, which represent the manifestation of a demyelinating event, pseudorelapses produce symptoms that are associated with other physiological processes.[7,9,14] Additional characteristics of true relapses are that they generally last for at least 24 hours, can last up to weeks or months, and frequently require treatment. Pseudorelapses, on the other hand, are more transient and typically resolve when the causative physiological stress has been removed or resolved.[7,9,14] In clinical practice, however, the distinction between a true relapse and a pseudorelapse may not be as clear. For instance, in some cases, a true exacerbation may be the underlying cause of an infection (eg, an exacerbation associated with urinary symptoms/bladder retention can lead to a urinary tract infection), or an exacerbation can occur concomitantly with an infection. Although a comprehensive discussion of these issues is beyond the scope of this article, education of both patients and clinicians with regard to distinguishing between relapse and pseudorelapse would likely prove beneficial.

One reason for the difficulty in providing a more precise definition of relapse is that the presentation of an MS relapse is highly variable. Specific symptoms of

MS relapses can differ widely among patients, often depending on the body system(s) affected. Symptoms can also differ between relapses within a single patient, although some evidence suggests that subsequent relapses tend to occur in the same CNS location as the initial event.[15] In the London, Ontario, natural history cohort, sensory system involvement was reported most frequently (54%), followed by optic (22%), brainstem (21%), motor (18%), cerebellar (6%), and bowel/bladder (3%) involvement.[3] The London, Ontario, data also illustrate that a single relapse can affect multiple body systems. Changes in cognition and increased fatigue are also common and should not be overlooked, as they are likely to impair patients' activities of daily living (ADLs) and work productivity.[13,16]

The severity of an MS relapse is one factor to consider when determining an appropriate management strategy. As with other aspects of relapse, little guidance is available in the literature with respect to the definition of severity. Freedman and colleagues[17] developed a system that categorizes relapse severity as mild, moderate, or severe, depending on such issues as the number and type of body systems involved, effects on ADLs, whether treatment and/or hospitalization is required, and time to recovery. These suggested guidelines were developed to evaluate relapses retrospectively, however, not as guidance for the clinician who needs to determine whether treatment is necessary. Generally, a relapse that affects a patient's function, regardless of his or her particular symptoms, would be considered severe enough to recommend treatment.[7]

It is difficult to predict whether and when a particular patient will experience a severe relapse. One study showed that the risk for severe relapse was lower among patients receiving treatment with DMDs and higher among younger individuals.[18] Another study found that greater severity of an initial demyelinating event was predicted by younger age and brainstem/cerebellum or cerebrum involvement; this study also demonstrated that occurrence of a prior severe event was associated with an increased odds ratio for a subsequent severe event.[19] A relapse can be interpreted as an outward manifestation of damage in the CNS.[9] Although no data are available that identify a clear correlation between physical or cognitive findings and damage to the CNS, lesions may ultimately affect functioning. Conversely, even if a patient does not perceive severe symptoms, a significant lesion may nonetheless be present.[20]

Another important aspect of defining an MS relapse is patients' understanding of what relapses are and their perception of relapse symptoms, which can differ considerably from clinicians' perceptions. Some patients may not spontaneously report relapses, whereas others may report having experienced multiple "relapses" over a short period of time, particularly if they perceive fluctuations in symptoms as relapses. Further, patients have different thresholds for symptom tolerability and degree of disability that they find manageable. Therefore, patient education is an important component of MS management, particularly with regard to relapses. For example, patients should be given clear instructions regarding when new symptoms or changes in the severity or frequency of chronic symptoms warrant professional contact. In addition, it is advisable that the clinician develop a collaborative patient relationship in order to identify changes from the patient's normal baseline physical and cognitive functioning.

Assessing MS Relapse and Recovery: Standardized Scales and Practical Challenges

Standardized assessments used in clinical trials of MS include the Expanded Disability Status Scale (EDSS)[21]; the Multiple Sclerosis Functional Composite (MSFC, which comprises the Nine-Hole Peg Test [NHPT], the Timed 25-Foot Walk [T25FW], and the Paced Auditory Serial Addition Test [PASAT])[22]; the Symbol Digit Modalities Test (SDMT)[23]; and the Fatigue Impact Scale (FIS).[24] Characteristics and considerations regarding the use of each scale are summarized in Table 1.[21,23-32] Although use of these scales is common in clinical trials, their use in clinical practice varies, and their utility in evaluating relapse and response to relapse treatment is somewhat limited. The EDSS and MSFC are not used routinely in the context of evaluating relapses, but may be required for clinical trials, insurance authorization for coverage of DMDs, or, in some clinical settings, as standard documentation for monitoring patients over time.

Several other assessment instruments have been developed and may be used as alternatives to the EDSS or MSFC in clinical trials or clinical practice to quantify disease severity. For example, the Scripps Neurological Rating Scale (SNRS) is an assessment based on a neu-

Table 1. Selected standardized assessment scales used in clinical trials of MS

Scale	Description	Considerations
EDSS[21,25-27]	Assessment of disability in 8 functional systems (pyramidal, cerebellar, brainstem, sensory, bowel/bladder, visual, cerebral, other)	• Based on standard neurologic examination • Widely used in clinical trials • Limited sensitivity to acute change • Variable interrater reliability • Emphasizes lower extremities and mobility • Does not assess cognitive function and fatigue • Lack of agreement with patient perception
MSFC (T25FW, NHPT, PASAT)[23,28-32]	Quantitative measure of leg, hand/arm, and cognitive function	• Sensitive to change in the assessment of relapse • Correlates with quality-of-life measure • Requires a reference population, which can vary, thereby affecting interpretation of standardized scores • Practice effects, particularly on the PASAT • PASAT is difficult to administer
SDMT[23]	Assessment of cognitive function	• Does not require reading or mathematics ability • May be preferred over the PASAT • May become more common in MS studies
FIS[24]	Assessment of effects of fatigue on quality of life	• Assesses cognitive, physical, and social dimensions • Useful for discriminating between patients with and without MS-related fatigue

Abbreviations: EDSS, Expanded Disability Status Scale; FIS, Fatigue Impact Scale; MS, multiple sclerosis; MSFC, Multiple Sclerosis Functional Composite; NHPT, Nine-Hole Peg Test; PASAT, Paced Auditory Serial Addition Test; SDMT, Symbol Digit Modalities Test; T25FW, Timed 25-Foot Walk.

rologic examination[33]; it has been used in some studies (eg, Sipe et al.[34] and Lublin et al.[35]) but currently is not widely used in clinical trials or in clinical practice. An assessment tool for use in clinical practice was developed by Ross and colleagues.[36] This instrument was designed to be completed by patients prior to an office visit. Although not formally validated, it provided a relatively easy way for clinicians to evaluate patient perception and quickly identify issues on which to focus. All of these scales were designed to help clinicians assess disease severity but may be of limited usefulness in capturing the important nuances necessary for evaluating relapse recovery.

Magnetic resonance imaging (MRI) can be used in the context of evaluating MS relapse; its value depends on the individual patient history and presentation. It is used more often to monitor disease progression or to evaluate whether chronic treatment needs to be altered.[17] It can prove useful, however, in patients with vague, persistent symptoms, in order to determine if an increase in disease activity is present.

Practical challenges are often encountered in the initial assessment to determine whether a patient is experiencing a relapse and whether treatment is needed. A clinician may be unable to see a patient in the office for evaluation of an acute attack for a number of reasons.

Relapses may occur outside of normal office hours, or a clinician may be unavailable for a patient to schedule an appointment with. Patients may be physically unable to get to a physician's office because of lack of transportation, bad weather, or severe symptoms, or they may be deterred by insurance limitations on the number of covered visits or co-payment requirements. Alternatives to an in-office assessment can include a telephone consultation, referral to a primary-care physician or to a hospital emergency department, or telemedicine (eg, via an Internet video service like Skype). The acceptability and frequency of use of these alternatives vary by practice. The relapse evaluation tool that was developed as a result of this nursing consensus initiative was designed to address the aforementioned limitations of the existing models, as a versatile option for acquisition of information.

In the context of evaluating recovery from relapse, establishing a baseline prior to relapse is necessary for later determination of the extent of recovery.[35] For example, it is not sufficient to simply calculate the change in EDSS score from the assessment during the relapse to the assessment after the relapse. This change in score can indicate significant improvement even though the patient may have experienced an incomplete or partial recovery with residual disability based

on the change from the pre-relapse baseline.[14,37] Because the presence of residual symptoms or disability may have implications for the overall disease management strategy, it is important that clinicians accurately assess recovery in terms of a return to baseline.

Differences in the timing of post-relapse follow-up assessments can affect the degree of symptom improvement or residual disability observed.[14,35,38] For example, in studies by Lublin et al.[35] and Hirst et al.,[14] mean EDSS scores were higher during the second month after relapse (days 30 to 59) and decreased during the third month (days 60 to 89), suggesting that disability may be largely stabilized by 3 months post-relapse. However, mean EDSS scores increased again at assessments conducted after 3 months. A practical consideration with regard to timing is that the post-relapse follow-up should be conducted within a reasonable amount of time; patients may be unable to accurately recall their response to treatment and/or side effects several months after an MS relapse, and a patient's clinical status can change during that time.

An important aspect of the assessment of relapse and treatment response is the patient's perception of symptoms and disability. As previously noted, the effect of symptoms varies according to the patient and is a key component in determining whether treatment is necessary. Similarly, it is important to ascertain how patients feel about their response to treatment. They may note a change in the severity of their symptoms but still experience considerable disability or side effects from the treatment. Some evidence suggests that a lack of agreement exists between scores on standardized assessments and patients' perceptions. For example, data from a 2010 study by van Winsen et al.[26] indicated that EDSS scores do not accurately reflect patients' perceptions of improvement, with 42% of participants who were identified as experiencing significant improvement on the EDSS reporting that they felt little or no improvement. In addition, data from the NARCOMS Registry indicate that a substantial percentage of patients treated with intravenous (IV; 30%) or oral corticosteroids (39%) reported that their treatment had no effect or made their relapse symptoms worse.[10] Considering previously reported evidence that many patients experience an incomplete recovery from relapses, even with treatment,[14,18,35] these findings are not entirely surprising.

MS Relapse Management: Treatment Considerations

Relapses are generally considered self-limiting, tending to resolve over time even if not treated. However, as mentioned earlier, the relationship of unaddressed or poorly managed relapses to disease progression and disability is an area deserving of investigation. Importantly, MS is not only an inflammatory process but also a degenerative one.[39] In addition to addressing the inflammation associated with relapses, it is possible that relapse treatments protect against neurodegeneration via a mechanism that is not yet well understood. For example, the anti-inflammatory actions of relapse treatments may provide indirect protection from neuronal damage,[39] or there may be neuroprotective or neurotrophic effects mediated via factors such as brain-derived neurotrophic factor (BDNF) and cytokines or through direct actions on immune cells.[40-46] Research on the treatment of MS relapses is incomplete in this respect. In addition, there remain many uncertainties around the relationship between relapse symptoms, lesions, and disability, as well as the effects of relapse treatment. As noted earlier, MRI can detect lesions indicative of inflammatory activity (ie, gadolinium-enhancing lesions) even in the absence of clinical relapse symptoms.[20] Further, changes in MRI do not necessarily mirror the clinical course of symptom resolution associated with relapse treatment.[47,48] Finally, there is currently no published evidence to demonstrate conclusively that treatment of relapses has an effect on the progression or long-term course of MS.[49,50] Nonetheless, treatment has been shown to shorten the duration of a relapse and promote recovery,[7,37,50] induces short-term immunologic effects,[49] and may reduce residual disability in the short term.[14] Based on this premise, treatment of relapses is part of MS standard practice.

Several treatment options for a relapse—including possible dosing regimens, adverse events, and corresponding references—are summarized in Table 2,[50-73] with a brief description of each of these options noted below. Detailed descriptions of the clinical trials evaluating each relapse treatment are outside the scope of this assessment-focused review. We refer the reader to a recent review by Repovic and Lublin[74] for a comprehensive summary of the literature supporting the efficacy and tolerability of various MS relapse treatments.

High-dose corticosteroid treatment is accepted as the standard of care for MS relapses.[51] The efficacy of high-

Table 2. Treatment options for MS relapses

Treatment	Place in therapy	Dosing regimens	Adverse events
IV corticosteroids[51-59]	First-line	• IVMP 500 mg/d to 2 g/d × 3–5 d[a] • Dexamethasone[b] 8 mg/d × 7 d, 4 mg/d × 4 d, 2 mg/d × 3 d	• Common: GI symptoms, insomnia, dysphoria, anxiety, edema, hyperglycemia, headache, myalgia, palpitations, metallic taste, increased appetite, acne, flushing • Less common but important: mental disturbances (eg, psychosis), avascular necrosis of bone, hypokalemia, GI perforation, menstrual irregularities, and exacerbations of preexisting peptic ulcer disease, diabetes, hypertension • Potential long-term effects: osteoporosis, cataracts, glaucoma, Cushingoid features, immune suppression
Oral corticosteroids[52,57,60-63]	First-line	• Prednisone 1250 mg/d × 5 d • Methylprednisolone 1000–1400 mg/d × 5 d • Methylprednisolone 48 mg/d × 7 d, 24 mg/d × 7 d, 12 mg/d × 7 d • Dexamethasone 4 mg 4 times daily × 5 d	• See above
ACTH[50,64-69]	First- or second-line	• 80–120 U/d IM or SC × 2–3 wk[a] • 120 U/d IM × 7 d, 80 U/d × 7 d, 60 U/d × 1 d, 40 U/d × 1 d, 20 U/d × 1 d • 80 U/d IM × 7 d, 40 U/d × 4 d, 20 U/d × 3 d • 80 U/d IM × 7 d, 60 U/d × 7 d, 40 U/d × 7 d, 20 U/d × 7 d • 80 U/d IM or SC × 5 d	• Similar to adverse events with corticosteroids • Common: fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain • Less common but important: increased susceptibility to new infection or risk for reactivation of latent infections, Cushing's syndrome, elevated blood pressure, salt and water retention, hypokalemia, GI perforation and bleeding, euphoria, insomnia, irritability, mood swings, personality changes, depression, psychosis • Potential long-term effects: cataracts, ocular infections or glaucoma, decreases in bone density
Plasmapheresis[70-73]	Second- or third-line	• Multiple treatments, separated by 48 h	• Nausea, hypotension, paresthesia, complications related to the use of central venous access, anticoagulation, replacement fluids, or filtration techniques

Abbreviations: ACTH, adrenocorticotropic hormone; GI, gastrointestinal; IM, intramuscular; IV, intravenous; IVMP, intravenous methylprednisolone; MS, multiple sclerosis; SC, subcutaneous.
[a]± oral steroid (prednisone or dexamethasone) tapering.
[b]Dexamethasone can also be administered intramuscularly.

dose corticosteroids in speeding recovery from relapses has been demonstrated in several studies,[52,56-58,75] including the Optic Neuritis Treatment Trial.[54] The anti-inflammatory and immunosuppressive effects of corticosteroids are achieved through multiple mechanisms, including inhibition of inflammatory cytokine production, inhibiting activation of macrophages or microglia, reducing leukocyte chemotaxis, and increasing function of regulatory T cells; generally the actions of exogenous corticosteroids are mediated via binding to glucocorticoid receptors.[76] Although IV administration of corticosteroids has been the most common approach, evidence of comparable efficacy and tolerability[52,57] has led to increased use of orally administered high-dose steroids for the treatment of MS relapses.[63] Potential benefits of high-dose oral corticosteroids include ease of initiating treatment, lack of need for home care or hospitalization, convenience, and low cost.[61]

Another US Food and Drug Administration (FDA)–approved therapy for the treatment of relapse is long-acting adrenocorticotropic hormone (ACTH) gel, a formulation of pro-opiomelanocortin peptides including ACTH(1-39).[64] ACTH is a native melanocortin peptide that contains 39 amino acids.[77] Historically, ACTH gel was thought to produce anti-inflammatory action indirectly, solely through physically increasing the release of cortisol from the adrenal gland (corticotropic effects) via a melanocortin receptor found in the adrenal cortex.[78] However, the effects of ACTH gel are likely more than adrenocorticotropic in nature due to additional melanocortin receptor–mediated mechanisms.[79,80] Melanocortin receptors as a class have been shown to exhibit various physiological actions in the body, including a variety of anti-inflammatory actions such as decreasing proinflammatory factors (cytokines and chemokines, nitric oxide, and adhesion molecules), inhibiting white blood cell migration, and increasing anti-inflammatory factors that may help to restore immune balance.[79,80] According to the National Multiple Sclerosis Society (NMSS), ACTH gel may be appropriate in certain situations, such as when IV infusion is impractical, or in cases in which positive effects on bone via stimulation of 5-dehydroepiandrosterone (DHEA) and mineralocorticoids may be desirable.[51] Other patient types who may benefit from ACTH gel treatment are those who do not tolerate or do not respond to steroids.

Other treatment options that are used less frequently include plasmapheresis and intravenous immunoglobulin (IVIG). Plasmapheresis (therapeutic plasma exchange) is typically reserved for those patients who experience an incomplete recovery with other treatments. Recently updated guidelines from the American Academy of Neurology suggest that plasmapheresis is probably effective as adjunctive therapy and possibly effective for exacerbations that fail to respond to high-dose corticosteroids.[70] Intravenous immunoglobulin is generally considered to be second- or third-line therapy for patients in whom corticosteroids are contraindicated or ineffective, or for the treatment of relapses during pregnancy or the postpartum period.[81,82]

With regard to the timing of relapse therapy, the NMSS recommends treating major relapses as quickly as possible but notes that minor relapses may be monitored initially.[51] However, some clinicians will begin treatment for minor relapses immediately if requested to do so by the patient. Usually this is done if symptoms have affected the patient's ADLs in ways that are significant to the patient. Treatment can be initiated several weeks into a relapse (eg, in the case of a patient who experiences a relapse but cannot obtain an appointment for 3 weeks); however, it may not be necessary to initiate treatment several months into a relapse or in those patients whose relapse symptoms appear to be improving.[51]

In practice, determination of the need for treatment is highly dependent on the individual patient. Certain symptoms that are not bothersome to some patients may cause significant impairment in others, depending on a person's occupation, home responsibilities, or leisure activities. For example, sensory relapses may require treatment, as these symptoms can have a significant impact on some patients' functional ability.[13] Patient preference with regard to benefits versus risks associated with steroids and other treatments must be considered; relapses during pregnancy or breastfeeding can be particularly challenging in this respect. Other factors that contribute to the decision to initiate therapy and to the selection of appropriate treatment include cost, insurance coverage, and prior experience.

It is difficult to predict how well and how quickly a patient will recover from a relapse. For example, although some evidence suggests that patients with more severe relapses experience a greater response to IV methylprednisolone versus those with less severe relapses (based on the decrease in EDSS score from relapse to post-treatment),[37] other studies have found that greater severity of relapse predicts worse overall recovery[19] or residual disability.[18] Incomplete recovery from a prior relapse, increased age, and location (spinal cord) also may be predictors of worse recovery.[19] Therefore, managing patients' expectations is challenging and requires an understanding of patients' perceptions of their relapse symptoms and associated disability, as well as their expectations of treatment (or with respect to recovery if treatment is not initiated). As illustrated by the aforementioned NARCOMS Registry data,[10] follow-up evaluations of patients' assessment of their recovery and/or treatment response are important for ascertaining whether a given relapse has been managed successfully. Moreover, these assessments are helpful and informative for determining the optimal management of future relapses.

Development of the Assessing Relapse in Multiple Sclerosis (ARMS) Questionnaire

The group of MS expert nurses agreed that there is a need for a relapse assessment tool that can be used clinically to evaluate short-term, relevant changes in symptoms and disability, as well as to assess treatment response in a way that more closely mirrors patients' perceptions. In creating this assessment tool, the aim was to develop questions that are easy to understand and that help patients identify how they are feeling relative to baseline when they arrive for treatment and following their treatment. It is important to determine patients' capabilities with respect to ADLs and to identify those symptoms that are experienced on a regular basis or at baseline, in order to assess both the impact of relapse symptoms and the degree of treatment response/recovery. Other considerations were that the assessment tool include an organized, systematic evaluation, with fatigue and cognitive function specifically addressed; that the tool determine whether patients have experienced changes in function; that the assessment of response gauge patients' status relative to how they were feeling during the relapse and also relative to "normal" (ie, prior to relapse), and inquire into treatment tolerability; and that the instrument be adaptable to a variety of clinical settings.

The Assessing Relapse in Multiple Sclerosis (ARMS) Questionnaire is shown in Figure 1. There are two parts to this questionnaire, with information collected at two time points. Figure 1A includes seven questions to evaluate a patient's relapse symptoms and how these symptoms affect his or her ADLs and overall function. This section also assesses the patient's response to past treatments of prior relapses and is thus a means of guiding treatment selection. Figure 1B includes seven questions to evaluate treatment response in terms of symptom relief and function, as well as treatment tolerability; this section is intended to be used approximately 3 to 6 weeks after treatment. The questionnaire can be used in MS specialty centers, general neurology practices, or other practice settings, and was designed with enough flexibility to be administered by nurses, other clinicians, or patients themselves. It lends itself to use for telephone interviews and ultimately could be incorporated into electronic health records.

The assessment tool will be pilot-tested in the practices of the meeting participants in order to evaluate its utility in describing relapses and in evaluating how patients respond to relapse treatment. Following collection of data from the pilot program and feedback, the assessment tool will be further refined. There are plans to report on the findings, and future initiatives may be undertaken to develop algorithms that provide guidance on relapse assessment and management.

Summary and Conclusions

Diagnosis and treatment of MS relapses can be challenging because of the variable nature of the disease. Establishing long-term relationships with patients allows clinicians to more easily recognize and determine the appropriate course of treatment for those individuals experiencing relapses. Knowledge of an individual patient, his or her history, and the patient's life quality and satisfaction following treatment are key elements in evaluating relapses and treatment response, as well as selecting optimal treatment approaches for future relapses. The reality of clinical practice, however, is such that many clinicians are challenged to efficiently assess the nature, quality, and impact of relapses. The development of an easy-to-use MS relapse assessment tool that is adaptable to a variety of practice settings, facilitates communication with patients, and is reliable and valid would be of great value in the comprehensive management of MS. □

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PracticePoints

- MS relapses are common and may be debilitating. However, the variability in each clinical picture from one case to another, and even from one relapse to another within the same patient, may lead to clinicians' having difficulty in identifying and managing relapses.
- The MS professional community currently lacks a standardized assessment tool to assess symptoms of a relapse and their impact on daily functioning, response to and tolerability of prescribed treatments, and extent of resolution and functional recovery.
- Better definition of patients' and professionals' perceptions of the effects of relapses and potential treatment response would enhance relapse management in clinical practice.

Figure 1A. Assessing Relapse in Multiple Sclerosis (ARMS) Questionnaire – New relapse

MS Relapse Evaluation—New Relapse

Patient's age in years: _____

Patient's sex (circle one): **Male**   **Female**

1) What are the **new or worsening** symptoms that you are currently experiencing? (*Check all that apply*)

☐ Vision changes   ☐ Speech changes   ☐ Dizziness/poor balance
☐ Chewing/swallowing   ☐ Numbness/tingling   ☐ Pain, burning, itching
☐ Hand/arm weakness*   ☐ Leg/foot weakness*   ☐ Bladder problems
☐ Bowel problems   ☐ Sexual problems   ☐ Memory problems
☐ Fatigue   ☐ Muscle tightness or stiffness ☐ Thinking problems
☐ Difficulty walking   ☐ Coordination (tripping, dropping things)
☐ Other:_____

*Indicate left, right, or bilateral

2) When did these symptoms begin? (*Check one*)

☐ Within the last 3 days   ☐ 4 -7 days ago   ☐ 8 -15 days ago   ☐ 16+ days ago

3) How much have these symptoms affected your daily activities or overall function? *(Mark one)*

Not at all   A Little   Somewhat   Very Much   Severely
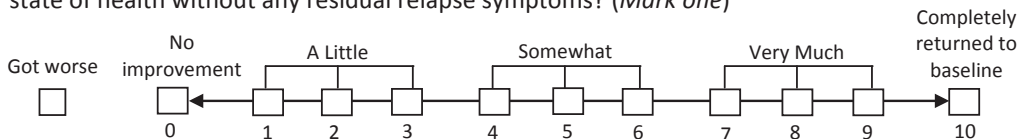0   1   2   3   4   5   6   7   8   9   10
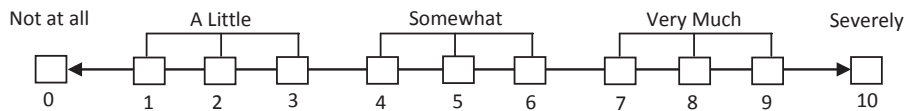
4) How many days/months ago was your last relapse (attack, exacerbation) prior to this current episode?

_____

5) What treatment did you receive for your last relapse (attack, exacerbation)? (*Check all that apply*)

☐ IV steroid infusion   ☐ Oral steroid tablets (only)   ☐ Oral steroid tablets (after IV steroids)
☐ Acthar/ACTH injections ☐ Plasma exchange   ☐ No treatment (*skip questions 6 and 7*)
☐ Not sure   ☐ Other:_____

6) After treatment for your last relapse (attack, exacerbation), how much did you return to your baseline state of health without any residual relapse symptoms? (*Mark one*)

Got worse   No improvement   A Little   Somewhat   Very Much   Completely returned to baseline
0   1   2   3   4   5   6   7   8   9   10

7) Have you had any side effects from treatments for previous MS relapses (attacks, exacerbations)?
(*Check all that apply*)

☐ Mood changes/depression/anxiety   ☐ Weight gain   ☐ Nausea and/or vomiting
☐ Sleep disturbance   ☐ Increased blood pressure   ☐ Low blood pressure
☐ Stomach upset or heartburn   ☐ Headache   ☐ Faintness (light headedness)
☐ High blood sugar   ☐ Increased fatigue   ☐ Dizziness
☐ Increased appetite   ☐ Fever   ☐ Muscle cramps
☐ Chills   ☐ Infection   ☐ Other:_____

If you have any questions, please ask your MS Nurse

For office use only

Date:_____
Patient initials: _____   _____   _____
Type of MS (circle one): RRMS   PPMS   SPMS
Type of visit (circle one):   Phone   Office
Questionnaire completed by (circle one):   Patient   Office Staff
Site Identifier

Figure 1B. Assessing Relapse in Multiple Sclerosis (ARMS) Questionnaire – After relapse treatment

MS Relapse Evaluation—After Relapse Treatment (1 month [± 1 week] follow-up)
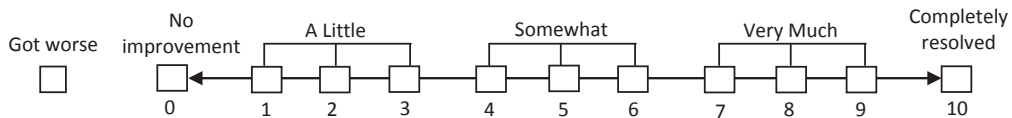
Patient's age in years: _____

Patient's sex (circle one):   Male   Female

1) What treatment was prescribed for this most recent relapse (attack, exacerbation)? (*Check all that apply*)
   ☐ IV steroid infusion   ☐ Oral steroid tablets (only)   ☐ Oral steroid tablets (after IV steroids)
   ☐ Acthar/ACTH injections   ☐ Plasma exchange   ☐ No treatment
   ☐ I'm not sure   ☐ Other: _____

2) Did you complete the prescribed relapse treatment?
   ☐ Yes
   ☐ No   If not, why? _____

3) How many days/months has it been since you completed treatment for this most recent relapse (attack, exacerbation)? _____
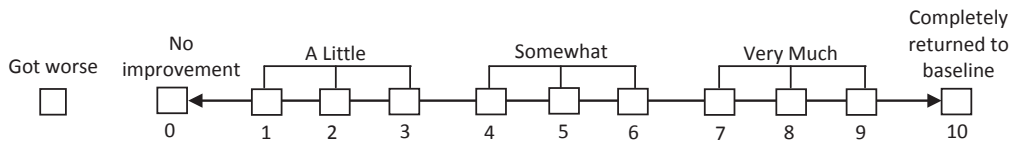
4) Do you think that the treatment for this most recent relapse (attack, exacerbation) resulted in improvement of your relapse symptoms? (*Mark one*)

Got worse | No improvement | A Little | Somewhat | Very Much | Completely resolved
0   1   2   3   4   5   6   7   8   9   10

5) Following treatment for this most recent relapse (attack, exacerbation), how much are your relapse symptoms continuing to affect your daily activities or overall function? (*Mark one*)

Not at all | A Little | Somewhat | Very Much | Severely
0   1   2   3   4   5   6   7   8   9   10
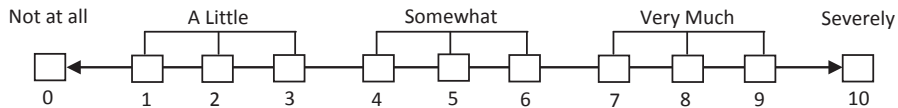
6) Following treatment for this most recent relapse (attack, exacerbation), how much do you feel that you have returned to your baseline state of health without any residual relapse symptoms? (*Mark one*)

Got worse | No improvement | A Little | Somewhat | Very Much | Completely returned to baseline
0   1   2   3   4   5   6   7   8   9   10

7) Did you have any side effects from the treatment you received for this relapse (attack, exacerbation)? (*Check all that apply*)
   ☐ Mood changes/depression/anxiety   ☐ Weight gain   ☐ Nausea and/or vomiting
   ☐ Sleep disturbance   ☐ Increased blood pressure   ☐ Low blood pressure
   ☐ Stomach upset or heartburn   ☐ Headache   ☐ Faintness (light headedness)
   ☐ High blood sugar   ☐ increased fatigue   ☐ Dizziness
   ☐ Increased appetite   ☐ Fever   ☐ Muscle cramps
   ☐ Chills   ☐ Infection   ☐ Other: _____

If you have any questions, please ask your MS Nurse

For office use only

Date: _____
Patient initials: _____
Type of MS (circle one): RRMS   PPMS   SPMS
Type of visit (circle one):   Phone   Office
Questionnaire completed by (circle one):   Patient   Office Staff
                        Site Identifier

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