

## Emotional Disorders in Multiple Sclerosis

*by Sarah Minden, MD  
Aaron Turner, PhD, ABPP(RP),  
Rosalind Kalb, PhD,  
Dominique Burke, MS*

### INTRODUCTION

Emotional disorders are common in people with MS, compounding the complexities of life with a chronic illness, worsening quality of life for patients and their families, and creating challenges for healthcare teams. This bulletin describes the types of emotional disorders that can occur and offers general information about diagnosis and treatment for clinicians who provide neurologic and medical care for individuals with MS. We will also discuss ways to improve patient and clinician communication about mental health issues.

During office visits, a patient's emotional well-being generally takes a back seat to discussions about disease-modifying therapies, medication side effects, and physical symptoms. Too often, both patient and clinician discount these symptoms: "Who wouldn't be depressed or anxious with a chronic illness like MS?" Depression and anxiety are never "normal" states, however. Clinicians, patients, family members, and friends need to be alert and respond to the first signs of an emotional disorder: undetected and untreated, it may increase functional impairment (Arnett et al., 1999), worsen quality of life (Wang et al., 2000; Gulick, 1997; Vickrey et al., 1995; McIvor et al., 1984; O'Brien, 1993), decrease adherence to treatment (Mohr et al., 1997) and lead to suicide (Stenager et al., 1992a; Stenager & Stenager, 1992b; Stenager et al., 1996; Brønnum-Hansen et al., 2005; Sadovnick et al., 1991; Feinstein, 1997; Feinstein, 2002). This component of the burden of MS can be reduced for patients and their families if clinicians promptly identify emotional disorders in their patients and refer them for diagnostic evaluation and treatment by mental health professionals in their practices or the community. In short, clinicians should inquire about the patient's and family's emotional wellbeing at every visit. And patients, families, and friends should become familiar with the symptoms and signs of emotional disorders and seek help promptly.

## Disorders of mood and affect

Individuals with MS may suffer from various types of emotional disorders (Goldman Consensus Group, 2005; Minden and Schiffer, 1990). We find it helpful to divide emotional disorders into disorders of mood (a “pervasive and sustained emotional ‘climate’”) and disorders of affect (“fluctuating changes in emotional ‘weather’”) (American Psychiatric Association, 2013). The affect disorders – euphoria, pseudobulbar affect (PBA), and apathy – result directly from the effects of MS on the brain. In contrast, mood disorders – depression, mania, and anxiety – arise from a complex interaction of MS pathological processes, a pre-existing or predisposition to a mental disorder, and normal grieving of the losses associated with the disease. This bulletin addresses mood disorders; detailed information about PBA is available in a separate bulletin (Minden, 2012). As Table 1 shows, mood disorders are more prevalent among individuals with MS than in the general population. Psychotic disorders may also be more common (Patten et al, 2005).

**Table 1. Prevalence rates of emotional disorders**

	MS	General population
<b>Mood Disorders</b> <sup>[1]</sup>		
Major Depressive Disorder	36%-54% <sup>[25,38,40,50,55,58]</sup>	16% <sup>[27]</sup>
Anxiety Disorders*	36% <sup>[29]</sup>	29% <sup>[28]</sup>
Persistent Depressive Disorder	NA**	NA**
Adjustment Disorder	22% <sup>[63]</sup>	0.2 – 2.3% <sup>[13,32]</sup>
Bipolar Disorder	13% <sup>[25,59]</sup>	1-5% <sup>[34]</sup>
<b>Affect disorders</b>		
Pseudobulbar Affect	7-10% <sup>[14,15]</sup>	NA**
Euphoria	0-63% <sup>[40,67]</sup>	NA**
Apathy	NA**	NA**

\*Generalized Anxiety Disorder, Panic Disorder, Social Anxiety Disorder, and others

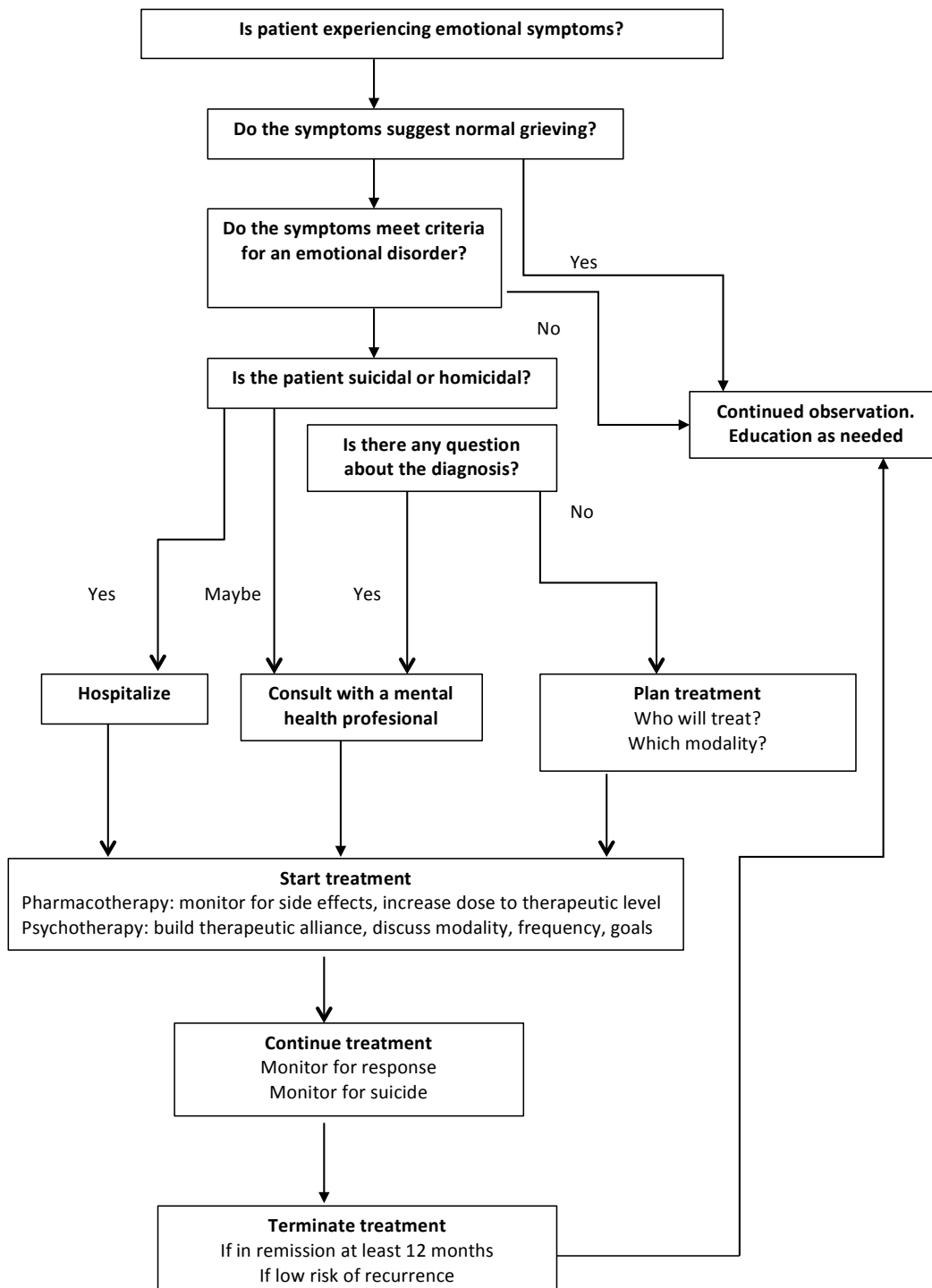
\*\*Not available

It is also helpful to distinguish emotional symptoms (e.g., depressed mood and anxiety) and emotional disorders (e.g., Major Depressive Disorder). Patients come to their clinicians with symptoms that are painful or disruptive. Whether an emotional disorder can be diagnosed depends on the duration and intensity of the symptoms, the extent to which they impair daily functioning, and the presence of other specified symptoms (American Psychiatric Association, 2013). It is important to remember, however, that symptoms of depression or anxiety that fail to meet the criteria for a diagnosable disorder are nevertheless a significant source of discomfort and distress.

## Assessment

As Figure 1 shows, the first step in assessment is to determine whether a patient is experiencing emotional symptoms. “How are you feeling?” is a simple, effective way to initiate the conversation, and most patients will tell you if they are feeling sad, down, blue, nervous, scared, worried – or any of the everyday terms we all use to describe our emotions. “How bad is it?” is equally useful for encouraging patients to talk about the severity of their symptoms.

Figure 1. Assessing and treating emotional disorders



Symptom severity rating scales and questionnaires are customary in research settings; in clinical settings, they are best used to initiate a conversation: as we emphasize repeatedly, the most important factor in helping patients with emotional disorders is open and ongoing communication. Even if a patient is not experiencing emotional symptoms, the question “How are you feeling?” creates an opportunity to talk about the prevalence of emotional disorders in MS, the importance of letting others know how one feels, and the effectiveness of treatment. This conversation itself helps remove the stigma from emotional disorders.

The second step in an assessment is to decide whether the symptoms suggest normal grieving or meet criteria for an emotional disorder, and which one.

## Diagnosis

As with any medical condition, diagnosis follows a systematic process of putting symptoms together into a coherent whole, a diagnostic category or a specific condition. After determining that the patient’s symptoms suggest a mood rather than an affective disorder, decide whether they signify grief or a diagnosable mental disorder (see Table 1 and Figure 1). For mental disorders, this determination depends on whether or not symptoms meet well-specified criteria, not on elucidating their cause (American Psychiatric Association, 2013).

**Grief.** In its early stages, grief looks a lot like depression: sadness, withdrawal, and trouble concentrating, sleeping, and eating. Time and intensity distinguish them: with grief, the symptoms resolve, and people re-engage with others and the pleasures of life. This may take months, but there is steady progress back to the way one was before the loss.

Grief is normal, whether due to losing a loved one, physical capacity, a job or a marriage. In MS, grief is common at the time of diagnosis, during relapses, with deterioration of functioning, and at major transition points – needing a cane or wheelchair, becoming unable to work or live at home. The natural healing process is so familiar and predictable that we generally “know” when grieving is too intense or too prolonged.

**Depression and anxiety.** When sadness is unrelenting and accompanied by loss of interest, feelings of worthlessness, helplessness, and hopelessness, patients, families, and clinicians should be thinking in terms of depression (American Psychiatric Association, 2013). (See footnotes for illustrative comments by patients about their symptoms.) With a depressed mood, life seems not worth living, and thoughts of death and suicide may be unrelenting. Appetite and sleep diminish or increase, it becomes hard to concentrate and think clearly, energy is sapped, and nothing is interesting or pleasurable. Some people suffer from guilt and shame, or become preoccupied with physical symptoms and aches and pains. Difficulty adhering to treatment, moodiness and irritability, , are not uncommon, nor are social isolation, withdrawal, and self-medication with alcohol and drugs.

Anxiety, whether expressed as apprehension and fear, tension, or worry and rumination, may co-exist with a depressed mood or be a separate disorder. Indeed, many believe that depression and anxiety are on a continuum, and that this explains the efficacy of antidepressant medication in both conditions. Just as grief differs from depression, reasonable concern about the unpredictability of MS and uncertainty about the future differ from anxiety. Persistent worry,

panicky feelings, and preoccupation with physical sensations suggest an anxiety disorder. Like depression, anxiety may occur at diagnosis, with relapses, when disability increases, and with job loss or strain in a marriage or family. To distinguish between the depressive and anxiety disorders, and among the various types of each, clinicians should consult the criteria specified in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth edition (American Psychiatric Association, 2013).

There are other diagnostic considerations. It is possible to mistake the symptoms of a depressed mood for those of MS. For example, cognitive impairment may be so prominent and severe in a depressed individual that neuropsychological testing is necessary to determine whether it represents the enduring cognitive impairments due to MS (Benedict, 2004) or the "pseudodementia" of depression – problems with memory, concentration, and processing speed that will resolve with effective treatment (Caine, 1981; Brown, 2005). This distinction is particularly difficult in patients with known cognitive impairment which is likely to worsen during a depressive episode. Fatigue occurs in both MS and emotional disorders, but is more likely a symptom of depression if it occurs early in the day. Depression-related psychomotor slowing and the muscle tension of generalized anxiety disorder do not produce abnormal findings on a neurologic exam. Symptoms of depression and anxiety may also result from a medical condition (e.g., hypo- and hyperthyroidism, respectively) or from medications and other substances. Research suggests that high doses of corticosteroids, commonly used to treat MS relapses, may lead to depressive and manic or hypomanic symptoms, and that these may be prevented by prophylactic treatment with lithium carbonate (Minden et al, 1988). Although predictors include personal and family histories of these disorders, they can occur spontaneously. The relationship between depressed mood and the disease modifying therapy, interferon beta, remains unclear and further research is needed (Feinstein, 2000).

Two questions have been shown to correlate highly with major depressive disorder, and should become routine for all MS clinicians (Mohr et al, 2007; Kroenke et al, 2003): "During the past 2 weeks, have you often been bothered by ...

... feeling down, depressed, or hopeless?

... little interest or pleasure in doing things?"

As with MS itself, a definitive diagnosis usually depends on the expertise and experience of a specialist, and MS clinicians should have a low threshold for consulting with and referring their patients to mental health professionals. This is discussed in detail below.

## **Suicide**

The rate of suicide among MS patients is unacceptably high – in large part because depression is underdiagnosed and inadequately treated (see above). In addition to depressed mood, the risk factors for suicide by individuals with MS include social isolation, low income, progressive course, and greater disability (Turner et al, 2006). Accompanying anxiety and substance abuse also increase the risk of suicide. Asking whether a person has been thinking about suicide does not cause it. Rather, talking about suicide is essential for prevention, and usually brings great relief to the patient and family. With any indication of a depressed mood or

anxiety, clinicians should ask: “Are you feeling hopeless about the present or the future?” “Have you had thoughts about taking your life?” A clinician who has any concern at all that a patient has suicidal ideas should immediately ensure the patient’s safety and obtain a full psychiatric assessment. Although much less common, some patients direct their despair and anger outward and think about harming others.

## Treatment Overview

Once symptoms have been identified, a physiological cause ruled out, and at least a preliminary diagnosis of a mood disorder made, the focus shifts to planning and implementing treatment. As with all treatments, a systematic approach is essential, and should begin with answering two critical questions:

- Is the patient suicidal or homicidal? If yes, hospitalize.
- Is there any question about the diagnosis? If yes, consult with a mental health professional.

Subsequent issues involve deciding who will provide the mental health treatment (a mental health professional, the patient’s neurologist, or the patient’s primary care physician); determining the optimal treatment (pharmacotherapy, psychotherapy, complementary and alternative approaches, or all of these); and ensuring coordinated ongoing care (the clinician[s] who will monitor the patient’s response to treatment). MS clinicians must obtain from their patients written permission to talk to family members and other clinicians (who, in turn, need permission to talk to the MS clinician).

**Safety first.** Patients need to be evaluated for hospitalization if they have suicidal or homicidal ideas or other behaviors that could harm themselves or others. Significant weight loss, dehydration, agitation, insomnia, psychosis, delirium, and mania may warrant hospitalization, as will inability to care for themselves or others for whom they are responsible. Clinicians who are unfamiliar with psychiatric hospitalization, should call their mental health colleagues or the nearest emergency room for guidance.

**Consultation.** MS clinicians who are uncertain about their patient’s safety or diagnosis should consult immediately with a mental health professional. Less urgent but timely consultation is advised to discuss whether to refer or treat the patient and the best treatment options. Throughout the course of treatment, MS clinicians (whether or not they are providing mental health care), will benefit from talking to a mental health professional when treatment response is suboptimal or it is time to consider terminating treatment (see below). Mental health professionals can also suggest ways to talk to a patient who is reluctant to accept a diagnosis or treatment of a mental condition.

**Refer or treat?** MS clinicians generally refer their patients with emotional disorders to mental health professionals for treatment, but some neurologists prefer to treat their patients’ emotional disorders (Schiffer, 1987). Some patients want a familiar clinician or the convenience of co-located care (Minden et al., 2013; Rintell et al., 2012). Mental illness still carries stigma and some patients will accept treatment only from their medical providers. Many health plans have limited mental health care coverage and deductibles and copayments may be very high for out-of-network mental health providers. Mental health care provided by a neurologist or primary care physician is fine when the clinician is experienced and the diagnosis and treatment are

straightforward (e.g., a recurrent depressive episode that previously responded well to antidepressant medication and support). However, when this is a new type of arrangement for the clinician or there are concerns about safety, diagnosis, or treatment response, the MS clinician should consult with a mental health professional.

When referring a patient to a mental health professional, it is important to explain whether this will be for a one-time consultation or ongoing treatment; tell the patient what to expect; and answer questions. Of course, it is essential to discuss the patient with the mental health professional before they meet and continue the communication throughout the treatment. Patients need and appreciate clear and explicit explanations of their mental illness and its treatment just as they do for their MS. When there are treatment options, patients and families should be fully informed and participate as equal partners in making decisions.

**How to find a mental health professional.** Consulting with or referring to a mental health professional is not always easy. Rural communities have few mental health providers; even in large urban centers the number of mental health professionals with experience in treating individuals with MS may be small. Patients can contact the National MS Society (1-800-344-4867) for referrals to mental health professionals in their area. Mental health professional societies may also be a source of referrals. Once connected, many MS clinicians establish ongoing collegial collaborations with one or more mental health professionals in their communities. Some MS centers can afford to hire a mental health provider; others provide office space and the mental health clinician sees the center's patients on a fee-for-service basis. Another successful model involves regular in-person or telephone meetings to discuss how to manage challenging clinical situations.

There are many types of mental health professionals: psychiatrists, psychologists, social workers, and psychiatric nurses. Which type is most appropriate depends on the patient's mental and medical conditions and his or her community's resources. All mental health professionals conduct diagnostic evaluations and provide psychotherapy, but may differ in approach, technique, and personal style. Psychiatrists, as physicians, are most appropriate for patients who are likely to require medication and who have complex medical problems.

**Treatment planning.** The planning phase is critical to a successful treatment outcome: this is where the therapeutic alliance between patient and clinician begins. Simply by asking "How are you feeling?", a clinician conveys concern and empathy, and sets the stage for a relationship built on mutual respect and trust. A collaborative approach to treatment planning, attentive listening, and open and frank discussion (Minden, 2009) solidify the partnership. Remember that even as health care takes a more patient-oriented approach, individuals vary in how much they want to know; their use of internet and other information sources; and their preferences for and styles of decision-making: some will want to share in treatment decisions, others will want unequivocal recommendations. Conversations about these issues contribute to building rapport, as do discussions about the patient's attitude to family involvement in their treatment.

Treatment planning involves striking a balance between optimism and realism. Patients should be told that treatment of emotional disorders is almost always effective and they can expect to return to their usual emotional state. It is equally important to say that this will take some time. Psychotherapy is a process that cannot be rushed. A full 8-12 weeks may pass before an antidepressant becomes effective; and different medications may need to be tried before

finding the right one. Side effects may be uncomfortable at first, but they usually pass relatively quickly. Patients can manage these challenges if they know what to expect, see the clinician weekly during the initiation phase of treatment, and have as-needed phone contact for support and to discuss medication side effects.

**Treatment options.** Research and clinical experience indicate that for emotional disorders, a combination of psychotherapy and pharmacotherapy are better than either one alone. Below we discuss a general approach to treatment. Specifics must be determined by the treating clinician and patient based on: diagnosis; personal and family psychiatric history, including treatments and their effectiveness; co-morbid medical conditions and medications; community resources; patient preferences; and clinician expertise.

*Psychotherapy* is a general term for treatment by a trained mental health professional that involves talking and interacting with an individual, couple, family, or group. There are many different techniques, each based on a particular philosophy or model of human behavior, thinking, and feeling. The most common are insight-oriented, supportive, and cognitive-behavioral therapy (although they may go by different names such as psychodynamic, psychoanalytic, interpersonal, behavioral, etc.) (Minden, 1992; Minden et al., 2014). Experienced mental health professionals typically tailor their approach to the individual and are pleased to explain their particular ways of working with patients.

*Pharmacotherapy* may be provided by a general psychiatrist, a psychopharmacologist, another type of physician, and, in some states, advanced practice registered nurses. Although psychotropic medications are so widely used as to seem commonplace, they are powerful agents that can do harm as well as good. The decision to use a psychotropic agent is as serious as that concerning use of a disease modifying therapy (DMT): benzodiazepine anxiolytics have an addiction potential (Lader, 2009); antidepressants involve a commitment of at least one year and a willingness to try a second, or even third, drug if the first is not effective. To inexperienced prescribers and patients, the number of seemingly different anxiolytics and antidepressants can be overwhelming. In actuality, within-class differences are minimal, leading to the term “me too” drugs (Angell, 2004; Light and Lexchin, 2012). Selecting a particular medication to treat depression or anxiety can be as challenging as choosing among the injectable DMTs: there is no way to predict with any certainty which agent will be effective for which patient.

*Complementary and alternative therapies* and self-management strategies – including mindfulness and meditation (Grossman et al., 2010); journaling; yoga; self-help groups; and others -- can also promote healing and recovery from an emotional disorder when used in conjunction with psychotherapy and pharmacotherapy (Moss-Morris, 2012). Exercise tailored to a person’s abilities and limitations has also been shown to improve mood and quality of life (Motl & Pilutti, 2012; Petajan et al., 1996; Bombardier 2013). Many patients do not tell their clinicians that they are using alternative therapies because they fear disapproval. It is important for clinicians to ask about herbs and supplements not only to show support and acceptance, but because they may interact with traditional medications (Bowling, 2010).



## Starting, continuing, and terminating treatment

**Starting.** Some general principles and clinical “pearls” follow to help MS clinicians become familiar with commonly used treatments for depression and anxiety. Those who treat their own patients should refer to standard sources and readily consult with a mental health professional as needed. Our focus here is on pharmacotherapy since that is the most common form of treatment provided by MS clinicians. Although MS clinicians who spend time listening to and talking with their patients are enormously helpful to them, they are not, technically, providing psychotherapy.

*Depressed mood.* Selective serotonin (and norepinephrine) reuptake inhibitors (SSRIs, SSNRIs) are the most commonly used antidepressants because of their efficacy and minimal adverse effects. In choosing among them, a medication that was effective for a patient previously, or for a biological relative, has a higher chance than others of being helpful. An important strategy for minimizing side effects and preventing discontinuation of a drug that might have been useful, is to “start low” and “go slow” when increasing doses to therapeutic levels. In addition, although side effects are mild and resolve quickly, seeing patients weekly for the first month or so, and being available by telephone, helps them through the early phases of treatment. Sexual side effects – difficulty with arousal and orgasm – occur in about 70% of SSRI and SNRI users in the general population; rates are probably higher among individuals with MS because of the effects of the disease on sexual functioning (Foley, 2008; Foley, 2009). Sexual side effects should be discussed during treatment planning and with patients already on these medications. Some pharmacologic remedies are available but they are variably effective. Tricyclic antidepressants (TCAs) may be useful for some patients, but strongly anticholinergic preparations can precipitate urinary retention in individuals with MS and overdoses may be lethal. All antidepressants have potential interactions with other drugs and some have age-related adverse effects; prescribers should refer to standard sources for pharmacologic information.

*Bipolar disorder.* Lithium carbonate, anticonvulsant mood stabilizers, and some atypical antipsychotics are the standard treatments, but should be initiated by a psychiatrist or psychopharmacologist. Antidepressants may precipitate mania or hypomania in patients with bipolar disorder. If the patient or a family member has a history of bipolar disorder, a mood stabilizer is typically used in conjunction with an antidepressant; if there is no known history, clinicians should alert their patients to the symptoms of hypomania and mania, and monitor them closely.

*Anxiety.* All benzodiazepines produce tolerance, physical dependence, and withdrawal. They are most useful for time-limited anxiety associated with diagnosis, relapse, and life events, and while waiting for an antidepressant to take effect. Benzodiazepines are often effective at doses that are one-quarter to one-half of what many practitioners prescribe: low doses “take the edge off” of the anxiety without causing drowsiness, leave room for dose increases, and reduce the risk of addiction. Clinicians should prescribe benzodiazepines only in small amounts (e.g., a 10-14 day supply) with no refills and see the patient frequently during the situation that necessitated their use. In this way, the patient receives a consistent message: ‘This is a short-term treatment for anxiety due to a particular set of circumstances. We will monitor how you are feeling and discontinue the medication as soon as possible because it can be addictive.’ Anxiety is painful, however, and no one should be deprived of relief because of an exaggerated fear of addiction: thoughtful prescribing and close follow-up are the solution to this dilemma.

For generalized anxiety, social anxiety, and panic disorder, antidepressants are the treatment of choice.

**Continuing.** Medication can improve physical symptoms in a few weeks and mood in a couple of months, but improvement in the interpersonal, occupational, and social difficulties associated with depression and anxiety generally take much longer. In contrast with MS, the end-point of treatment for mood disorders is full return to usual or “normal” functioning: symptoms should completely remit. Continuing distress generally indicates the presence of issues that require ongoing psychotherapy.

Short-term monitoring for the adverse and positive effects of medication involves as-needed telephone calls and weekly visits until the clinician and patient feel that the medication is stable and the treatment plan is proceeding well. If a patient does not respond to treatment at the maximum dose after several weeks, or if adverse effects are intolerable, the first option is to try another drug. If there is still no response, the clinician should consult with or refer the patient to a psychiatrist or psychopharmacologist who will re-evaluate the diagnosis and suggest additional treatment options. These may include another trial of an antidepressant, augmentation with other medications, or electroconvulsive therapy.

Once symptoms resolve, medication visits can be decreased to monthly, then bimonthly, and in some cases less often. Some patients do well, but then plateau after a few months of treatment or begin to slip backwards. Increasing the dose slightly usually restores the drug’s effectiveness. The frequency of psychotherapy visits depends on the type of therapy but treatment should also be goal-oriented and periodically reassessed.

Monitoring for suicidal ideas must be ongoing: symptom relief is no guarantee that a patient considers life to be worth living. Sadly, some individuals become more despairing about the future when the veil of a depressed mood is lifted. With more energy and clearer thinking, some patients plan and carry out suicide; discharge from hospital is a particularly high-risk time.

**Terminating.** Antidepressants (whether for depression or anxiety) should be continued at the remission dose for about one year and then reevaluated. If the patient has returned to normal, it is appropriate to consider discontinuing the medication, tapering gradually to avoid uncomfortable serotonin withdrawal symptoms. Relapse rates are significant with discontinuation before six months and a history of previous depressive episodes. For patients with frequently recurring depression, ongoing treatment may be indicated.

## Epilogue

We have come a long way since the time when emotional disorders were seen as something anyone with a disease like MS would have and something which the right attitude and determination would overcome. We now know that emotional disorders arise from a complex set of biopsychosocial factors and are not “fixed” by efforts of will. We have highly effective treatments, stigma is decreasing, and patients, families, and clinicians are increasingly accepting and benefiting from treatment.

Partners, children, and parents of individuals with MS may also suffer from depression, anxiety, and other emotional disorders. Family members who provide care are particularly at risk, often neglecting their own physical and mental health to provide care for the person they love. Although many care partners find great satisfaction and joy in their caregiving activities, the responsibilities can feel overwhelming. Caregivers are “invisible patients” (Andolesk et al, 1988): they, too, are at higher risk of depression and reduced quality of life (Aronson, 1997; Buchanan and Huang, 2013). MS clinicians should routinely ask their patients about their families, and, as needed, meet with family members to discuss their health, mental health, and wellbeing.

In some cases, spouses and partners may feel so drained and helpless that they become verbally, emotionally, or physically abusive. Depression and anxiety in the individual with MS may be an indicator of this type of abuse, or of financial and sexual abuse by a paid caregiver. Neglect and omission, which may manifest as poor hygiene, malnutrition, dehydration, debilitation, and recurrent urinary tract infections and decubitus ulcers in severely disabled individuals, are also forms of abuse (Minden et al, 1999). MS clinicians must be alert to signs of abuse and prepared to intervene. Questions such as these may be helpful: “Does anyone make it hard for you to see your friends and family?” “Do you ever feel afraid or unsafe?” “Does anyone ever use your money without permission?” All states have protective service agencies that will advise clinicians on how to manage these difficult situations. They will evaluate the home situation and provide services as needed. MS clinicians are mandated reporters: if concerned, even when patient and family deny a problem, they are required to arrange for protective services.

### Illustrative Comments

“I feel worthless to myself and everyone else – I just don’t know if I can keep going.”

“I must have done something terribly wrong to deserve this.”

“I don’t even know who I am at this point; none of the things that made me who I am seem to work any more.”

“I just don’t care about anything any more, nothing interests me, not even getting better -- that’s why I stopped taking my medication.”

“Everything rubs me the wrong way – I jump down people’s throats for no good reason.”

“My husband is so moody -- one moment he’s ok and the next he’s losing his temper and yelling and then he just wants us all to get away and leave him alone.”

“My wife seems so sad all the time. She won’t go out and do anything, and has isolated herself from her friends. She is drinks a lot -- as if she is trying to numb herself from pain.”

“If I see or even think about a wheelchair, I get this awful feeling in the pit of my stomach.”

“I know life can change in a second. The minute I start to have a funny feeling somewhere I panic.”

“I’m always so tense and on edge.”

“I get scared when I have relapses. What’s next? Can I keep working? How will I support my wife & kids?”

## References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (Fifth ed.). Arlington, VA: American Psychiatric Publishing, 2013.
2. Andolsek K, Clapp-Channing N, Gehlbach S, Moore I, Proffitt V, Sigmon A, et al. Caregiving in elderly relatives: The prevalence of caregiving in a family practice. *Archives of Internal Medicine* 1988; 148, 2177–2180.
3. Angell M. The truth about the drug companies: how they deceive us and what to do about it. New York: Random House, 2004.
4. Arnett PA, Higginson CI, Voss WD, Wright B, Bender WI, Wurst JM. Depressed mood in multiple sclerosis: Relationship to capacity-demanding memory and attentional functioning. *Neuropsychology* 1999;13:434-446.
5. Aronson, K. Quality of life among persons with multiple sclerosis and their caregivers. *Neurology* 1997, 48, 74–80
6. Benedict RH, Cox D, Thompson LL, Foley F, Weinstock-Guttman B, Munschauer F. Reliable screening for neuropsychological impairment in multiple sclerosis. *Multiple Sclerosis* 2004;10:675-678.
7. Bombardier CH, Ehde DM, Gibbons LE, Wadhvani R, Sullivan MD, Rosenberg DE, Kraft GH. Telephone-based physical activity counseling for major depression in people with multiple sclerosis. *Journal of Consulting and Clinical Psychology* 2013;81 :89-99.
8. Bowling AC. Complementary and Alternative Medicine in MS. *Clinical Bulletin, National Multiple Sclerosis Society*, 2010. [http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ClinBull\\_CompAltMed\\_2010.pdf](http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ClinBull_CompAltMed_2010.pdf). Accessed April 2014
9. Brønnum-Hansen H, Stenager E, Stenager EN, Koch-Henriksen N. Suicide among Danes with multiple sclerosis. *Journal of Neurology, Neurosurgery and Psychiatry* 2005;76:1457-1459.
10. Brown, W. Pseudodementia: Issues in Diagnosis. *Psychiatric Times*. April 9, 2005. <http://www.psychiatrytimes.com/dementia/pseudodementia-issues-diagnosis>. Accessed April, 2014.
11. Buchanan RJ, Huang C. The Need for Mental Health Care Among Informal Caregivers Assisting People with Multiple Sclerosis' *Int J MS Care* 2013;15:56–64.
12. Caine, ED. Pseudodementia. Current concepts and future directions. *Archives of General Psychiatry* 1981;38: 1359–64.
13. Casey P, Maracy M, Kelly BD, et al. Can adjustment disorder and depressive episode be distinguished? Results from ODIN. *Journal of Affective Disorders* 2006;92:291- 297.

14. Feinstein A, Feinstein K, Gray T, O'Connor P. Prevalence and neurobehavioral correlates of pathological laughing and crying in multiple sclerosis. *Archives of Neurology* 1997;54:1116–1121.
15. Feinstein A, Feinstein K. Depression associated with multiple sclerosis. Looking beyond diagnosis to symptom expression. *Journal of Affective Disorders* 2001;66:193–198.
16. Feinstein A. An examination of suicidal intent in patients with multiple sclerosis. *Neurology* 2002;59:674-678.
17. Feinstein A. Multiple sclerosis, depression, and suicide. *British Medical Journal* 1997;315:691-692.
18. Feinstein A. Multiple sclerosis, disease modifying treatments, and depression: a critical methodological review. *Multiple Sclerosis* 2000;6:343–348.
19. Finger S. A happy state of mind: A history of mild elation, denial of disability, optimism, and laughing in multiple sclerosis. *Archives of Neurology* 1998;55:241-250.
20. Foley F. Assessment and Treatment of Sexual Dysfunction in Multiple Sclerosis. Clinical Bulletin, National Multiple Sclerosis Society, 2008. [http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ClinBull\\_Sexuality.pdf](http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ClinBull_Sexuality.pdf). Accessed April 2014.
21. Foley F. Talking about sexual dysfunction. Talking with Your MS Patients about Difficult Topics, National Multiple Sclerosis Society, 2009 [http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/4TwP\\_Sexual.pdf](http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/4TwP_Sexual.pdf). Accessed April 2014.
22. Goldman Consensus Group. The Goldman Consensus statement on depression in multiple sclerosis. *Multiple Sclerosis* 2005;11:328–337.
23. Grossman P, Kappos L, Gensicke H, et al. MS quality of life, depression, and fatigue improve after mindfulness training: a randomized trial. *Neurology*. 2010;75:1141-1149.
24. Gulick EE. Correlates of quality of life among persons with multiple sclerosis. *Nursing Research* 1997;46:305-311. <http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Depression-and-Other-Emotional-Changes.pdf>. Accessed April 2014.
25. Joffe RT, Lippert GP, Gray TA, Sawa G, Horvath Z. Mood disorders and multiple sclerosis. *Archives of Neurology* 1987;44:376-8.
26. Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2: Validity of a two-item depression screener. *Medical Care* 2003;41:1284-1292.
27. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA* 2003;289:3095-3105.

28. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry* 2005;62:593-602.
29. Korostil M, Feinstein A. Anxiety disorders and their clinical correlates in multiple sclerosis patients. *Multiple Sclerosis* 2007;13:67-72.
30. Lader M, Tylee A, Donoghue J. Withdrawing benzodiazepines in primary care. *CNS Drugs* 2009, 23 (1): 19–34.
31. Light DW, Lexchin JR. Pharmaceutical research and development: what do we get for all that money? *BMJ* 2012;344:e4348.
32. Maercker A, Forstmeier S, Enzler-Donatsch A. Adjustment disorders as stress-related disorders: prevalences from a representative community survey [Abstract P333]. *European Psychiatry* 2007;22(suppl):S321.
33. McIvor GP, Riklan M, Reznikoff M. Depression in multiple sclerosis as a function of length and severity of illness, age, remissions, and perceived social support. *Journal of Clinical Psychology* 1984;40:1028-1033.
34. Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RMA, Petukhova M, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey Replication. *Archives of General Psychiatry* 2007;64:543-552.
35. Minden S. Pseudobulbar Affect (Uncontrollable Laughing and/or Crying). *Clinical Bulletin. National Multiple Sclerosis Society*, 2012. [http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ClinBull\\_Pseudobulbar.pdf](http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ClinBull_Pseudobulbar.pdf). Accessed April 2014.
36. Minden S, Ding L, Cleary PD, Frankel D, Glanz BI, Healy BC, Rintell DJ. Improving the quality of mental health care in Multiple Sclerosis. *Journal of the Neurological Sciences* 2013;335:42-47.
37. Minden SL, Feinstein A, Kalb RC, Miller D, Mohr DC, Patten SB, Bever Jr. C, Schiffer RB, Gronseth GS, Pushpa Narayanaswami P. Evidence-based Guideline: Assessment and management of psychiatric disorders in individuals with multiple sclerosis. Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology* 2014;82:174–181.
38. Minden SL, Orav J, Reich P. Depression in multiple sclerosis. *General Hospital Psychiatry* 1987;9:426-434.
39. Minden SL, Orav J, Schildkraut JJ. Hypomanic reactions to ACTH and prednisone treatment for multiple sclerosis. *Neurology* 1988; 38:1631-1634.

40. Minden SL, Schiffer RB. Affective disorders in multiple sclerosis: Review and recommendations for clinical research. *Archives of Neurology* 1990;47:98-104.
41. Minden SL. Psychotherapy for people with multiple sclerosis. *The Journal of Neuropsychiatry and Clinical Neurosciences* 1992;4:198-213.
42. Minden SL. Talking about depression and other emotional changes. *Talking with Your MS Patients about Difficult Topics*. National Multiple Sclerosis Society, 2009.
43. Minden SL, Frankel D, Smith C, Newberger E. Abuse of people with multiple sclerosis. Report to the National Multiple Sclerosis Society, 1999.
44. Mohr D, Hart S, Julian L, Tasch E. Screening for depression among patients with multiple sclerosis: two questions may be enough. *Multiple Sclerosis* 2007;13:215-219.
45. Mohr DC, Goodkin DE, Likosky W, Gatto N, Baumann KA, Rudick RA. Treatment of depression improves adherence to interferon beta-1b therapy for multiple sclerosis. *Archives of Neurology* 1997;54:531-533.
46. Mojtabai R. Clinician-identified depression in community settings: concordance with structured-interview diagnoses. *Psychotherapy and Psychosomatic* 2013;82:161-9.
47. Moss-Morris R, McCrone P, Yardley L, van Kessel K, Wills G, Dennison L. A pilot randomised controlled trial of an Internet-based cognitive behavioural therapy self-management programme (MS Invigor8) for multiple sclerosis fatigue. *Behaviour Research and Therapy* 2012;50:415-421.
48. Motl RW, Pilutti LA. The benefits of exercise training in multiple sclerosis. *Nature Reviews Neurology* 2012;8:487-97.
49. O'Brien MT. Multiple Sclerosis: The relationship among self-esteem, social support, and coping behavior. *Applied Nursing Research* 1993;6:54-63.
50. Patten SB, Beck CA, Williams JVA, Barbui C, Metz L. Major depression in multiple sclerosis: a population-based perspective. *Neurology* 2003;61:1524-1527.
51. Patten SB, Newman S, Becker M, et al. Disease management for depression in an MS clinic. *International Journal of Psychiatry in Medicine* 2007;37:459-473.
52. Patten SB, Svenson W, Metz L. Psychotic disorders in MS: population-based evidence of an association. *Neurology* 2005;65:1123-1125.
53. Petajan JH, Gappmaier E, White AT, Spencer MK, Mino L, Hicks RW. Impact of aerobic training on fitness and quality of life in multiple sclerosis. *Annals of Neurology* 1996 Apr;39(4):432-41.

54. Rintell DJ, Frankel D, Minden SL, Glanz BI. Patients' perspectives on quality of mental health care for people with MS. *Gen Hosp Psychiatry* 2012;34:604-610.
55. Sadovnick AD, Eisen K, Ebers GC, Paty DW. Cause of death in patients attending multiple sclerosis clinics. *Neurology* 1991;41:1193-1196.
56. Sadovnick AD, Remick RA, Allen J, Swartz E, Yee IML, Eisen K, et al. Depression and multiple sclerosis. *Neurology* 1996;46:628-632.
57. Schiffer R. The spectrum of depression in multiple sclerosis. An approach for clinical management. *Archives of Neurology* 1987;44:596-599.
58. Schiffer RB, Caine ED, Bamford KA, Levy S. Depressive episodes in patients with multiple sclerosis. *American Journal of Psychiatry* 1983;140:1498-1500.
59. Schiffer RB, Wineman NM, Weitkamp LR. Association between bipolar affective disorder and multiple sclerosis. *American Journal of Psychiatry* 1986;143:94-95.
60. Stenager EN, Koch-Henriksen N, Stenager E. Risk factors for suicide in multiple sclerosis. *Psychotherapy and Psychosomatics* 1996;65:86-90.
61. Stenager EN, Stenager E, Koch-Henriksen N, Bronnum-Hansen H, Hyllested K, Jensen K. Suicide and multiple sclerosis: an epidemiological investigation. *Journal of Neurology, Neurosurgery and Psychiatry* 1992a;55:542-545.
62. Stenager EN, Stenager E. Suicide and patients with neurologic disease. Methodologic problems. *Archives of Neurology* 1992b;49:1296-1303.
63. Sullivan MJL, Weinschenker B, Mikail S, Bishop SR. Screening for major depression in the early stages of multiple sclerosis. *Canadian Journal of Neurological Sciences* 1995;22:228-231.
64. Turner AP, Williams RM, Bowen JD, Kivlahan DR, Haselkorn JK. Suicidal ideation in multiple sclerosis. *Archives of Physical Medicine and Rehabilitation* 2006;87:1073-8
65. Vickrey BG, Hays RD, Harooni R, Myers LW, Ellison GW. A health-related quality of life measure for multiple sclerosis. *Quality of Life Research* 1995;4:187-206.
66. Wang JL, Reimer MA, Metz LM, Patten SB. Major depression and quality of life in individuals with multiple sclerosis. *International Journal of Psychiatry in Medicine* 2000;30:309-317.
67. Work SS, Colamonico JA, Bradley WG, Kaye RE. Pseudobulbar affect: an under-recognized and under-treated neurological disorder. *Advances in Therapy* 2011;28:586-601.