Suicide in Neurologic Illness

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Opinion statement

The risk of attempted or completed suicide is increased in patients with migraine with aura, epilepsy, stroke, multiple sclerosis, traumatic brain injury, and Huntington's disease. Contrary to the general perception that the risk of suicide among patients with Alzheimer's disease and other dementing conditions is low, several reports suggest that the risk of suicide in these patients increases relative to the general population. Some patients at risk for neurologic disorders are also at increased risk for suicide; in particular, the risk of suicide is increased among persons at risk for Huntington's disease, independent of the presence or absence of the Huntington's gene mutation. The risk of attempted or completed suicide in neurologic illness is strongly associated with depression, feelings of hopelessness or helplessness, and social isolation. Additional suicide risk factors in persons with neurologic illness include cognitive impairment, relatively younger age (under 60 years), moderate physical disability, recent onset or change in illness, a lack of future plans or perceived meaning in life, recent losses (personal, occupational, or financial), and prior history of psychiatric illness or suicidal behavior. Substance dependence, psychotic disorders, anxiety disorders, and some personality disorders (*eg*, borderline personality disorder) may also contribute to increased risk of suicide among persons with neurologic illnesses. Identification and aggressive treatment of psychiatric problems, especially depression, as well as reduction of modifiable suicide risk factors among patients with neurologic illness is needed to reduce the risk of attempted and completed suicide in this population.

Introduction

Suicide is generally defined as intentional self-inflicted death [1], and is the result of either a deliberate action or inaction directed toward that end. The rate of suicide is estimated at 11.3 per 100,000 persons, and accounts for more than 30,000 deaths per year in the United States [2]. The death rate from suicide is more than 1.5 times that of homicide, and it is the eighth leading cause of death in the United States. Although many suicides occur in the context of primary psychiatric disorders, suicidal ideation, suicide attempts, and completed suicide are also associated with serious medical and neurologic illnesses.

For example, Kishi *et al.* [3] reported that in a series of 496 patients hospitalized with stroke, traumatic brain injury (TBI), myocardial infarction, and acute spinal cord injury, 36 (7.3%) patients experienced clinically significant suicidal ideation with a plan. Twenty-six of these patients (or 72% of those with suicidal ideation) suffered from major depression, two (6%) had minor depression, and eight (22%) had no clinically significant mood disorder. Patients with suicidal ideation were more likely to be younger, not married, and had a greater frequency of prior psychiatric illness or alcohol abuse. Patients with and without suicidal ideation in the context of these medical and neurologic illnesses did not differ in terms of sex, race, education, or family history of psychiatric illness. The majority of patients responded to treatment for depression, and suicidal ideation resolved as the patients responded to antidepressant treatment. These observations demonstrate that suicidal ideation may develop after the onset of serious medical or neurologic illness, particularly

when the onset of such is complicated by major depression or social isolation.

Among persons who commit suicide, well over 90% suffer from a diagnosable psychiatric illness and in particular depression [4]. Individuals who attempt or complete suicide in the midst of a depressive episode may regard the act of suicide as the best or only remaining solution to a problem (*eg*, neurologic illness or disability, social isolation, or some combination of these and other problems) that is experienced as *interminable*, *inescapable*, and *intolerable*. Overwhelmed by such experiences, suicide may be viewed by the patient as a reasonable solution to an unreasonable circumstance. Such ideas may—and often do—arise in the setting severe and persistent depression during which (and because of) the individual no longer maintains hope of relief. Depression, particularly in the context of cognitive impairment, negatively affects the ability to realistically self-observe, apply reason, and problem-solve. All of these abilities (executive functions) are needed to flexibly and adaptively cope with neurologic illness and the problems such illnesses create, leading to cognitive distortions that can include viewing of suicide as the best and only solution to those problems.

Similarly, debilitating pain, cancer, and progressive and incurable medical or neurologic conditions may so adversely affect the patient's perceived quality of life that suicide begins to be viewed as a reasonable solution to an unreasonable quality of life. Impaired executive function may negatively affect perceived quality of life [5]. When perceptions about quality of life are accompanied by impaired executive function, patients are less able to reframe their experiences and circumstances in a fashion that permits the development of a new or renewed sense of purpose or meaning in life. Importantly, with support and assistance, the patient may reframe his or her experience such that quality of life is improved, and suicide is no longer viewed as a solution at all.

Because many people, including physicians, project their own anxieties about disability and progressive neurologic illness when considering the "reasonableness" of suicide in neurologic illness, there is often resistance to identifying suicidal ideation among these patients or regarding such ideation as pathologic when it is identified. Even when patients experience harm of their own doing, there remains a tendency among clinicians to discount the possibility that an act or event represents a suicide attempt, and to overlook suicide as a possible cause of death [6•].

A minority of individuals may attempt suicide as an expression of anger towards themselves or others, or as a means of bringing to attention the need for assistance with a problem they are unable to resolve independently [7]. Even where suicide attempts are accurately understood as gestures that call attention to the need for psychiatric assistance, clinicians should not dismiss the seriousness of the event simply for having understood it; repeated suicide attempts are predictive of future suicide attempts, one of which may eventually end in completed suicide. Any suicidal behavior bespeaks the need for identification and treatment of either a psychiatric condition or other suicide risk factors.

In this article, the authors will review the general risk factors for suicide and the literature describing suicidal ideation, suicide attempts, and completed suicide among persons with several of the most common neurologic illnesses. The authors will also review basic strategies for the identification of persons at risk for suicide. The approach recommended herein suggests identifying suicidal ideation, evaluating and reducing associated suicide risk factors, treating the suicidal patient's depressive disorder, and facilitating the patient's construction of new sources of hope, optimism, and meaning in the context of his or her neurologic condition.

SUICIDE RISK FACTORS

Risk factors for suicide in the general population include age over 45 years (or, worse, 65 years) [8], alcohol dependence, agitation or other violent behavior, prior suicide attempt, male gender, recent marital loss (widowed, divorced, or separated), living alone, unemployment or recent retirement, financial problems, and other recent adverse psychosocial events [9–11]. Although depression, physical illness, and relatively greater social isolation influence suicide risk among the elderly, the increased rate of completed suicides in the elderly population appears to reflect their greater use of highly lethal methods [2]. Although the absolute risk of suicide is lower in younger individuals, suicide is the second leading cause of death (after accidents) among people aged 15 to 24 years [2].

Gender and ethnicity also appear to influence suicide risk. Although women are more likely than men to attempt suicide, men are four times more likely to die by suicide than women [12]. The increased rate of completed suicide among men appears to reflect their tendency to use methods of greater lethality (*ie*, firearms, hanging, jumping from high places) than those used by women (*ie*, overdose on psychoactive medications or toxic substances). Almost three quarters of suicides occur among white men, and white men and women combined account for over 90% of all completed suicides [2].

Almost 60% of suicides are committed with a firearm, and these weapons remain the most common means of completing suicide in older men (78%) and women (approximately 35%) [2]. Cummings and Koepsell [13] and Miller and Hemenway [14] offer evidence that the availability of a firearm increases substantially the risk of suicide. In light of these figures, access to firearms of patients with risk factors for suicide or with frank suicidal ideation should be assessed carefully.

EPIDEMIOLOGY OF SUICIDE IN NEUROLOGIC ILLNESSES

Interpretation of epidemiologic studies that estimate suicide in patients with neurologic illness is limited by virtue of the highly selected populations in which such studies are conducted, the criteria used for establishing the presence of neurologic illness, the method by which control groups are selected, the choice of statistical methods, and the reliability of establishing suicide as the cause of death [6]. Nonetheless, the risk of suicide is increased among patients with a variety of neurologic illnesses. In the context of these illnesses, associated factors such as pain, therapies for the primary illness of only limited benefit, discouraging and uncertain prognosis, and comorbid neuropsychiatric illnesses appear to contribute to the increased risk of attempted or completed suicide.

Stroke The risk of suicide is increased among patients with stroke. This risk appears to vary with stroke severity, age at time of stroke, physical disability, and associated psychiatric problems such as depression. Kishi *et al.* [15] observed suicidal ideation in 20 of 301 (6.6%) patients following acute stroke. The development of such did not appear to be strongly associated with the severity of post-stroke physical impairment. In a subsequent study of this cohort of patients, an additional 11.3% developed suicidal ideation 3 to 24 months after illness-onset [16]. In both groups the development of suicidal ideation remained strongly associated with major depression and relative social isolation, and additional risks included sensory deficits, and impaired cognitive function. Similar findings are reported by Pohjasvaara *et al.* [17], who observed suicidal ideation in 10% of the stroke patients at 3 months follow-up, and in 14% at 15 months follow-up. In this study, patients with suicidal ideation were more likely to have a history of prior stroke, right hemispheric stroke, more severe physical disability, and greater dependence on others for issues in daily living.

Stenager *et al.* [18] reported on a registry of all stroke patients admitted to hospitals in one county in Denmark over a 16-year period ending in 1989. The study included 37,869 stroke patients, and identified 140 suicides during the study period; this represents a significant increase in suicide rate compared with the general population. Importantly, time of suicide did not bear a clear relationship to time of stroke, suggesting the need for ongoing monitoring of suicidal ideation and risk throughout the post-stroke period. Teasdale *et al.* [19] performed a similar study among 114,098 patients with stroke in Denmark over the study period of 1979 to 1993. They identified 359 suicides in this population, an annual rate twice that of the general population. As with the study of Stenager *et al.* [18], the time of suicide did not bear a clear relationship to the time of stroke, although the risk for suicide appeared to be greatest in the first 5 years post-stroke.

The present evidence suggests a need for careful monitoring of stroke patients for suicidality both in the acute and late post-stroke periods, and particularly among patients with post-stroke depression, moderate to severe post-stroke physical disabilities, and post-stroke cognitive impairments, and suggests a need for clinicians to undertake aggressive treatment of patients developing such problems.

Huntington's disease Huntington [20] himself noted the association of mental illness and suicide in his patients. The suicide risk is increased among patients with either a definite or a probable diagnosis of Huntington's disease, and is estimated to be four to five times that of the general population [21]. Di Maio *et al.* [22] evaluated suicide risk in the families of 2793 subjects registered with the National Huntington's Disease Research Roster. Suicide was reported in 205 (7.3%) subjects, including affected and possibly affected subjects, subjects at 50% and 25% risk, possibly at risk subjects, and normal relatives. In all of these categories, suicide rates were higher than in the general population.

Sorensen *et al.* [23] examined the cause of death among 395 Danish subjects with Huntington's disease and 282 of their unaffected siblings, and compared their findings with the causes of death in the general Danish population. Suicide accounted for 5.6% of deaths among the Huntington's disease subjects, and 5.3% of deaths among their unaffected sibs. Both frequencies of suicide were significantly higher than the corresponding frequency in the general Danish population (2.7%). The authors also speculate that some of the deaths of unaffected siblings recorded as accidents may have been overlooked (or hidden) suicides. Age did not appear to strongly influence the rate of suicide in this study. However, other groups have reported that completed suicide is rare or that the risk is increased in patients with Huntington's disease over 50 years of age but not in younger patients [24,25].

In an effort to identify psychosocial factors associated with completed suicide in families with Huntington's disease, Lipe *et al.* [26] reviewed the clinical and social characteristics of 11 such families. Eight men and one woman affected with Huntington's, one woman at risk for Huntington's, and one unaffected woman, ranging in age from 24 to 65 years, were identified as having completed suicide. Of the nine individuals with Huntington who committed suicide, six (66%) were single or divorced. There was no clear relationship with duration of symptoms, which ranged from 1 to 14 years. However, there was a strong association between suicide and social isolation, and was particularly increased among patients without offspring. Modest risk factors for suicide in this group included a history of other suicides in the family, being unmarried, living alone, contact with others affected with Huntington's

Disease, and depression. However, methodologic problems in each of these studies make it difficult to draw firm conclusions about suicide risk among patients with Huntington's disease more generally.

There also appears to be an increased risk of suicidal ideation among patients at risk for Huntington's disease undergoing presymptomatic Huntington's disease gene testing [27]. Eleven percent of patients awaiting testing stated they considered suicide as an option should the test result prove to be positive. There does not appear to be a difference between gene carriers and noncarriers in pretest attitudes, suicidal ideation, self-injurious behavior, and other psychiatric dysfunction. Almqvist *et al.* [28••] investigated the frequency of catastrophic events among 4527 persons undergoing testing (including predictive testing) for Huntington's disease through questionnaires sent to predictive-testing centers worldwide. Forty-four individuals (0.97%) were reported to have suffered a severe psychiatric event following receipt of testing results, including five successful suicides, 21 suicide attempts, and 18 psychiatric hospitalizations. All of those reported to have committed suicide, 11 of 21 (52%) of those attempting suicide, and eight of 18 (44%) of those hospitalized psychiatrically had symptoms of Huntington's disease. Among the asymptomatic patients experiencing a catastrophic event in the first year following testing, 11 of 13 (84.6%) received a gene testing result indicated an increased risk for developing the disease. The presence of psychiatric problems within 5 years prior to testing and employment status was associated with the occurrence of catastrophic events following gene testing. Robins *et al.* [29] report elevated frequencies of psychiatric illnesses, suicidal ideation, attempted suicide and completed suicide in family members of persons with Huntington's disease independent of their genetic status. Collectively, these observations support the importance of assessing suicide risk in the setting of confirmatory or at-risk Huntington's gene testing programs and the need for adequate psychiatric support and counseling in these contexts.

Multiple sclerosis The risk of suicide appears to be higher among patients with multiple sclerosis (MS) than in the general population. The best evidence regarding the increased risk of suicide among persons with MS comes from data derived from the Danish MS registry [30,31]. Of the 5525 patients identified with MS and who died between 1953 and 1985, suicide was judged to be the cause of death in 9.5%. The standardized mortality ratio for suicide was 1.83 in this group of patients. The risk was higher among men, and among patients diagnosed with MS before age 40. Men committing suicide tended to be 40 to 49 years old, had moderate disability, had a recent deterioration, and had a previous mental disorder. Sadovnick *et al.* [32] reported a suicide risk 7.5 times that of the age-matched general population for over 3000 patients attending an MS clinic. Although other groups have reported no increase in the suicide risk in patients with MS, the relatively small numbers of persons included therein and methodologic problems in suicide estimation limit the generalizability of these negative studies [6•]. The relationship between suicide, depression, and MS remains uncertain; although MS patients are at increased risk for depression, not all suicides among patients with MS occur in the context of a clearly diagnosed depressive episode or disorder [32].

Epilepsy The risk of attempted suicide is higher among patients with epilepsy than in the general population. Hawton *et al.* [33] found the number of attempted suicides to be five times the rate in the general population based a 2-year study of patients admitted to the hospital following a suicide attempt. Epilepsy patients attempting suicide were more likely to have attempted suicide in the past and to have had prior psychiatric treatment. Nilsson *et al.* [34] reported 26 patients with completed suicide, and 23 patients with suspected but not proved suicide. Suspected or completed suicide was associated with the presence of mental illness, the use of antipsychotic drugs, higher seizure frequency, need for multiple antiepileptic drugs, and age of onset of epilepsy at younger than 18 years. There was no association between suicide risk and any particular anticonvulsant medication, epilepsy type, or localization of epileptogenic focus. Barraclough *et al.* [35] reported an increased rate of suicide among patients with temporal lobe epilepsy relative to other epilepsy types. The risk was much higher among patients with difficult-to-treat temporal lobe epilepsy. The association between suicide and temporal lobe epileptogenic foci was also reported by Mendez *et al.* [36].

Batzel and Dodrill [37] observed increased rates of suicide attempts among patients with anxiety, other emotional problems, and lower intelligence. The authors of this study suggested that availability of substantial quantities of antiepileptic medications with which a suicide attempt may be undertaken increased risk for suicide among these patients.

It is also possible that some anticonvulsants, especially phenobarbital, may contribute to the risk of depression or suicide in persons with epilepsy. Brent *et al.* [38] observed higher rates of major depressive disorder (40% vs 4%) and suicidal ideation (47% vs 4%) among patients treated with phenobarbital than with carbamazepine. Although this finding remains controversial, it suggests that clinicians should remain vigilant for the development of depression and suicidal ideation among persons with epilepsy.

Migraine Breslau *et al.* [39,40] studied patients with migraine based on a structured interview, and report an increased odds ratio (3.0) for attempted suicide among patients with migraine with aura (adjusted for coexisting major depression). Among those included in their

studies, the risk for suicidal ideation and attempted suicide was much higher in patients with both major depression and migraine with aura. Interestingly, there was no association of suicide attempts and suicidal ideation with migraine without aura. The explanation for the association of migraine with aura (with or without depression) and suicide remains open to speculation. However, this observation suggests the need to be vigilant for suicidality among patients with this condition independent of the presence of depression.

Dementia Suicidal ideation or "a wish to die" is reported by 4% of patients with dementia visiting a memory disorders clinic [41]. In this series, the presence of such thoughts was strongly associated with comorbid depressive symptoms, but unrelated to the presence of insight into memory loss. Rao *et al.* [42] reported that suicidal ideation was associated higher depression scores, but not with awareness of cognitive impairment in a group of nursing home dementia patients over the age of 81. Interestingly, all patients with suicidal ideation in this series had evidence of significant cerebrovascular disease, suggesting the possibility that suicidal ideation may be increased among patients with dementia of cerebrovascular etiology. However, Rubio *et al.* [43] reported that among a series of elderly patients who completed suicide, Alzheimer's pathology at autopsy was over-represented among the suicide completers. This observation suggests that, contrary to clinical lore, the development of Alzheimer's type dementia is associated with increased risk of suicide. Depression is common among patients with dementia including Alzheimer's disease [44], and feelings of hopelessness are present in 10% of patients with Alzheimer's disease and are more frequent among patients with greater awareness of their deficits [45]. These observations suggest that assessment of suicide risk, including such predictors as depression or feelings of hopelessness, and also overt suicidal ideation should part of the care of patients with dementia. Although there is no literature regarding the effectiveness of modifications of suicide risk (including aggressive treatment of depression) in this population, it is hoped that such modifications may reduce the likelihood of attempted or completed suicide in this population.

Parkinson's disease Depression affects 40% to 50% of patients with Parkinson's disease [46]. Given the combination of significant neurologic disability and depression in this generally older-aged population, it seems reasonable to hypothesize that Parkinson's patients are at higher risk for suicide. However, this hypothesis is not at present well supported by the available evidence. Earlier and relatively small observational series reported a modest increase [47] or no increase [48] in suicide risk among persons with Parkinson's disease. The largest epidemiologic study of suicide risk among persons with Parkinson's disease, conducted by Myslobodsky *et al.* [49], describes a decrease in such risk in this population. The authors identified 144,364 patients over the age of 40 with a primary diagnosis of Parkinson's disease using the National Center of Health Statistic's mortality database. Among those so identified, 122 died by suicide. The rate of suicide in this population was 10 times less than that of an age-matched cohort in the general population. This reduction in suicide risk may reflect the effects of bradykinesia, akinesia, bradyphrenia, apathy, and executive dysfunction on the planning or attempting of suicide. In this study, the suicide rate for persons with Parkinson's disease was *higher* among those who were married than among those who were single, divorced or widowed, an observation contrary to the epidemiologic observations on suicide in the general population and without satisfactory explanation to-date.

Traumatic brain injury Suicide appears to occur more often among patients with a history of traumatic brain injury (TBI). Silver *et al.* [50] reviewed standardized and validated structured interviews of 5034 adults from the New Haven portion of the National Institute of Mental Health Epidemiologic Catchment Area program. Among those interviewed, 361 reported a history of injury producing either loss of consciousness or confusion and on this basis were categorized as having experienced a TBI of at least mild severity. Those reporting a TBI experienced a poorer quality of life than those not reporting such an event did. Even after controlling for socioeconomic and demographic factors, quality of life indicators, and alcohol use, persons reporting a TBI were at increased risk for major depression, dysthymia, panic disorder, obsessive-compulsive disorders, phobic disorder, and drug abuse or dependence. The lifetime risk of suicide attempt was elevated among those who experienced a TBI than among the comparison subjects in the study sample.

Teasdale *et al.* [51••] reported on a Danish registry of 145,000 patients with concussion, cranial fracture, or traumatic intracranial hemorrhage admitted to the hospital. The suicide risk was increased among all patients with TBI compared with the general population, and highest among those with traumatic intracranial hemorrhage. Women, patients with a history of substance abuse, and patients injured between the ages of 21 and 60 also appeared to be at increased risk for suicide compared with both younger and older aged individuals. Increased rates of suicide were also increased among patients suffering mild traumatic brain injuries, although the authors suggest that this increased risk may be attributable to concomitant risk factors such as psychiatric conditions and psychosocial disadvantage. The authors of this study suggest that the higher rate of suicide following severe TBI suggests that the combination of physical, psychologic, and social consequences of TBI interact to increase suicide risk, and that there is a need for ongoing assessment of suicidality following TBI at all levels of severity.

Treatment

General assessment

- The prevention of suicide among patients with neurologic illness first and foremost begins with the clinician's inquiry about suicidal ideation. Simple questions that may be life saving include the following: do you ever feel that life is no longer worth living? Do you have thoughts of wanting to hurt yourself or to end your own life? Have you every tried to hurt yourself or end your own life?
- When patients offer or affirm the presence of suicidal ideation, the clinician should further assess the nature of the patient's suicidal thoughts (passive wish for some other circumstance vs active violent ideation regarding self-harm or death), intent to carry forward with a suicide attempt, access to the means (*ie,* firearms, potentially lethal medications), and a history of making previous suicide attempts.
- Major risk factors for suicide among persons with neurologic illness should then be assessed, and concern should be very high among patients with depression, other major psychiatric conditions, feelings of hopelessness or helplessness, and social isolation. Other issues that should raise concern for suicide in a person with neurologic illness include the following, alone or in combination: cognitive impairment, relatively younger age (often under 60 years), relatively moderate physical disability, recent onset or change in illness, a lack of future plans or perceived meaning in life, and recent losses (personal, occupational, functional, or financial).
- The decision to hospitalize a suicidal patient is ultimately at the discretion of the clinician assessing the patient. However, the constellation of active suicidal ideation with intent, a plan, and access to means to commit suicide should prompt immediate psychiatric evaluation or hospitalization. If the patient refuses to be psychiatrically evaluated or hospitalized, physicians should consult with a psychiatrist in the state in which the patient resides to determine whether involuntary psychiatric hospitalization is an available therapeutic option.
- In cases in which the patient is judged not to be imminently suicidal, but in which the quality or intensity of suicidal ideation is still concerning to the clinician, the decision regarding hospitalization becomes more challenging. In such circumstances, consultation with a psychiatrist may clarify whether hospitalization for acute crisis management and psychiatric stabilization is an available and reasonable therapeutic option. For some patients, outpatient management may be appropriate.
- When the attending neurologist or medical physician becomes by default (*eg,* psychiatric care is refused or is not immediately available) the primary provider of outpatient psychiatric care to the patient, the patient's ability to engage in developing a safety plan should be assessed. Such plans typically include a commitment by the patient to contact the physician in the event that the patient is no longer able to guarantee his or her own safety and impulse control. In return for the patient's commitment to his or her own safety, the clinician must be able to provide a return commitment of 24 hour-per-day availability (either personally or through willing and similarly minded colleagues) until the period of acute suicidality is over. This process is often referred to as the development of a "safety contract" between the patient and the physician. The patient's work and home phone numbers should be obtained and shared with colleagues providing coverage, because some patients may be unwilling to provide such information in the midst of a crisis, and because this information may be needed in order to direct police or paramedic services to the patient.

- Although safety contracts are often made in the service of suicide risk reduction, clinicians should be aware that such contracts do not by themselves reliably prevent suicide; suicidal patients may break the contract impulsively. Consequently, family members, significant others, or friends of the patient should also be engaged to take responsibility for monitoring and supporting the patient 24 hours a day during the period of active suicidal ideation if the suicidal patient is to be managed as an outpatient.
- The physician must also work with the patient to reduce modifiable factors contributing to the patient's suicidal ideation (*ie,* depression, pain, substance abuse, physical and cognitive disability, social isolation). Treatment for depression should be undertaken using a medication appropriate to the patient's neurologic or medical condition(s). Counseling of not only the patient but also involved family members or caregivers should be provided and referral to support groups related to the illness from which the patient is suffering should be made. Additionally, the physician should assist the patient's development of realistic short-term goals; this process may help patient establish sufficient meaning and purpose in their lives that they become able to accept such goals as alternatives to suicide.

Pharmacologic treatment

- A complete review of all pharmacologic treatments relevant to the treatment of psychiatric problems associated with increased risk of suicide among persons with neurologic illnesses is well beyond the scope of the present work. Because attempted and completed suicide in neurologic illness is strongly associated with depression, a brief review of recent studies of pharmacotherapy for depression in neurologic disorders is included herein.
- Most patients will not experience significant relief with antidepressant medications for several weeks following their initiation. Consequently, there is no clear antidepressant effect to be gained by increasing medication doses during the first weeks of treatment. Emphasis should instead be placed on supportive interventions, counseling, and reduction of other modifiable suicide risk factors during the early weeks of treatment.
- Neurologists should be aware that patients with psychotic depression demonstrate a very low rate of spontaneous recovery. The response of this type of depression to psychotherapy is almost nil [52, Class IIIc]. Effective treatment of this condition can be achieved in 70% to 80% of patient using a combination of antipsychotic and antidepressant medications [52, Class IIIc; 53, Class I] or, in some cases, electroconvulsive therapy [53, Class I]. Neurologists treating patients with this form of depression are strongly encouraged to obtain psychiatric assistance with the care of patients with psychotic depression and suicidal ideation, as these patient may require hospitalization in order maintain safety and to provide effective treatment.
- Tricyclic agents such as nortriptyline [54, Class I; 55, Class I], desipramine [56, Class IIa], and amitriptyline [57, Class IIIc] may be effective treatments for depression in some neurologic illnesses. However, Cole *et al.*[58, Class I] concluded, through a meta-analysis of the available literature, that as many as 83% of patients with post-stroke depression carry at least one medical contraindication to treatment with heterocyclic antidepressants, whereas only 11% of patients with post-stroke depression carry medical contraindications to treatment with selective serotonin reuptake inhibitor. The selective serotonin reuptake inhibitors (SSRIs) also carry a relatively lower risk of lethality when taken in overdose. Consequently, the authors recommend SSRIs as first-line therapies for use by neurologists treating depressed and suicidal patients with neurologic illness.

Fluoxetine, sertraline, paroxetine, and citalopram

Standard dosage	Fluoxetine 10 to 40 mg per day; doses should not exceed 80 mg per day. Sertraline 25 to 200 mg per day. Paroxetine 10 to 40 mg per day. Citalopram 10 to 40 mg per day.
Contraindications	Concomitant use of a monamine oxidase inhibitor; this combination can produce a fatal serotonin syndrome.
Main drug interactions	Fluoxetine inhibits cytochrome P (CYP) 450 isoenzyme 2D6, resulting in increased levels of cimetidine, warfarin, tolbutamide, tricyclic antidepressants, clozapine, benzodiazepines, theophylline, digoxin, or other 2D6 substrates. Sertraline and citalopram are relatively weaker inhibitors of CYP450-2D6 than fluoxetine, whereas paroxetine is a more potent inhibitor of this isoenzyme. Consideration of these effects is particularly important during concomitant prescription of clozapine or tricyclic antidepressants given the potential life-threatening complications of toxicity with these agents; concurrent use of these medications requires close monitoring of serum drug levels. Fluoxetine may also increase the risk of sedation with diazepam, neurotoxicity when used with phenytoin, carbamazepine, or lithium. Citalopram is primarily metabolized by CYP3A4 and 2C19, and inhibitors of these isoenzymes (ketoconazole, itraconazole, macrolide antibiotics, and omeprazole) may decrease the clearance of citalopram.
Main side effects	Headache, nausea, vomiting, diarrhea or constipation, dry mouth, insomnia or sedation, abnormal dreams, anxiety or anhedonia, tremor, dizziness, fatigue, impaired concentration, agitation, anorexia or weight gain, rash, decreased libido, and delayed ejaculation and anorgasmia.
Special points	Seizures occur at SSRIs therapeutic doses, with a 0.1% to 4% incidence [59, Class IIIc]. Although animal studies claimed an anticonvulsant action of fluoxetine, the human literature offers no support for this claim. Adverse events may occur during co-administration of fluoxetine and sumatriptan [60, Class IIIc].
Cost/cost effectiveness	Fluoxetine—30-day supply of 10-mg capsules costs $75.72; 20-mg capsules cost $77.67. Sertraline—30-day supply of 25-mg tablets cost $56.16; 50-mg tablets cost $57.99; 100-mg tablets costs $57.99. Paroxetine—30-day supply of 10-mg tablets cost $72.75; 20-mg tablets cost $75.93; 30-mg tablets cost $78.20; 40-mg tablets cost $82.60. Citalopram—30-day supply of 20-mg tablets cost $64.81; 40-mg tablets cost $68.99.

Interventional procedures

Electroconvulsive therapy

	Electroconvulsive therapy (ECT) may be of benefit in the treatment of depression in several neurologic illnesses, including stroke [61,62, Class IIIa2; 63, Class IIIb], Huntington's disease [64, Class IIIa2; 65, Class IIIb], multiple sclerosis [66, Class IIIa2], epilepsy [67–69, Class IIIb], dementia [70, Class IIIb], Parkinson's disease [71, Class IIb], and TBI [72, Class IIIa2]. Electroconvulsive therapy is often regarded as a treatment of last resort, but may be the treatment of choice among patients with severe depression and suicidality or psychosis. Additionally, this may be the best treatment for patients that have failed treatment with antidepressant medications due to lack of efficacy or intolerable side effects.
Standard procedure	A course of treatment may consist of six to 20 treatments, usually offered three times per week (*ie,* Monday-Wednesday-Friday).
Contraindications	There are no absolute medical contraindications to ECT, although risk-benefit analysis is prudent in all depressed patients being considered for such treatment and especially for those with significant comorbid neurologic and medical illnesses. The presence of space-occupying lesions in the central nervous system is generally considered a relative contraindication to ECT. Severe hypertension and cardiac disease (including recent myocardial infarction) may be contraindications if the patient's cardiovascular status is considered too fragile to tolerate the stress of induced seizures.
Complications	Headache (including migraine and tension-type) are common sequelae of ECT, and may be effectively treated with typical headache abortive agents. Nausea and myalgia are also common side effects of ECT. Acute delirium and acute-to-subacute memory impairments are not uncommon following ECT; both are generally transient although memory impairments may sometimes linger for weeks to months following a course of treatment.

Special points Electroconvulsive therapy may be of benefit to motor symptoms in Parkinson's disease and may reduce seizure frequency in patients with epilepsy.

Cost/cost effectiveness $350 to $1000 per treatment session, including psychiatric, anesthesiology, post-procedure recovery room, and monitoring cost. Total cost varies with the number of treatments required.

Other treatments

- Suicide in neurologic illness, and in general, is associated with social isolation and relatively impoverished social supports. Encouraging patients to participate in support groups focused on coping with the neurologic illness that they are suffering with may be a useful suicide risk factor reduction strategy, although there is no evidence at present to evaluate this hypothesis.
- Some organizations in the United States offering local support groups that may be of use to persons with neurologic illnesses include the following:
  - National Stroke Association (http://www.stroke.org/supportsearch.cfm)
  - American Stroke Association (http://strokeassociation.org/strokegroup)
  - Huntington's Disease Society of America (http://www.hdsa.org)
  - National Multiple Sclerosis Society (http://www.nationalmssociety.org/mycommunity/index.asp)
  - Epilepsy Foundation (http://www.efa.org/services/ps_services.html)
  - MAGNUM, The National Migraine Association (http://www.migraines.org/help/helpsprt.htm)
  - Alzheimer's Association (http://www.alz.org/findchapter.asp)
  - National Parkinson Foundation, Inc. (http://www.parkinson.org/support.htm)
  - Brain Injury Association, Inc. (http://www.biausa.org/States.htm)
- When suicide prevention is not successful, surviving family members may require assistance coping with the loss of a loved one. Professional counseling or psychiatric care may be of use among those willing to accept it and when such care is accessible. The American Foundation for Suicide Prevention also hosts support groups in many communities in the United States that may be of assistance to surviving family members (http://www.afsp.org/index-1.htm).

Psychotherapy

- As discussed earlier, supportive interventions for the suicidal patient are a requisite element of any treatment plan. For patients with depression in neurologic disease, additional therapies may be of benefit although much work is needed to clarify the best methods of therapy as well as the cost-benefit of the provision of these treatments.
- For example, and as noted, Mohr *et al.* [73, Class IIa] demonstrate that cognitive behavioral therapy for major depression in MS is of comparable efficacy to sertraline, and that both of these treatments are superior to supportive-expressive group therapy. Whether such therapies may be of similar benefit to patients with other neurologic conditions and depression, and whether such therapies effectively reduce suicide risk in those patients, remains uncertain. Nonetheless, patients willing to undertake

such treatment should be encouraged to do so pending evidence with which to evaluate their effectiveness. The reduction of social isolation alone afforded by such therapies may be of use in the effort to reduce suicide risk.

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