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Dr Belagaje discusses the unlabeled/investigational use of fluoxetine for poststroke motor recovery treatment, cholinesterase inhibitors and memantine for the treatment of aphasia, and dopaminergic agents to aid in the treatment of poststroke depression.

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Stroke Rehabilitation

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ABSTRACT

Purpose of Review: Rehabilitation is an important aspect of the continuum of care in stroke. With advances in the acute treatment of stroke, more patients will survive stroke with varying degrees of disability. Research in the past decade has expanded our understanding of the mechanisms underlying stroke recovery and has led to the development of new treatment modalities. This article reviews and summarizes the key concepts related to poststroke recovery.

Recent Findings: Good data now exist by which one can predict recovery, especially motor recovery, very soon after stroke onset. Recent trials have not demonstrated a clear benefit associated with very early initiation of rehabilitative therapy after stroke in terms of improvement in poststroke outcomes. However, growing evidence suggests that shorter and more frequent sessions of therapy can be safely started in the first 24 to 48 hours after a stroke. The optimal amount or dose of therapy for stroke remains undetermined, as more intensive treatments have not been associated with better outcomes compared to standard intensities of therapy. Poststroke depression adversely affects recovery across a variety of measures and is an important target for therapy. Additionally, the use of selective serotonin reuptake inhibitors (SSRIs) appears to benefit motor recovery through pleiotropic mechanisms beyond their antidepressant effect. Other pharmacologic approaches also appear to have a benefit in stroke rehabilitation.

Summary: A comprehensive rehabilitation program is essential to optimize poststroke outcomes. Rehabilitation is a process that uses three major principles of recovery: adaptation, restitution, and neuroplasticity. Based on these principles, multiple different approaches, both pharmacologic and nonpharmacologic, exist to enhance rehabilitation. In addition to neurologists, a variety of health care professionals are involved in stroke rehabilitation. Successful rehabilitation involves understanding the natural history of stroke recovery and a multidisciplinary approach with judicious use of resources to identify and treat common poststroke sequelae.

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INTRODUCTION

Stroke is the fifth leading cause of death and a leading cause of long-term disability in the United States. The economic impact of a stroke is tremendous. By 2030, total direct annual stroke-related medical costs are expected to increase from \$71.55 billion in 2012 to \$184.13 billion, and indirect annual costs are expected to rise from \$33.65 billion in 2012 to \$56.54 billion.¹ Because of the recent advances in acute stroke treatment

and neurocritical care, more patients now survive stroke, with varying degrees of disability.

In general, neurologists are familiar with acute stroke treatments and prevention strategies but tend to be less familiar with aspects of stroke rehabilitation. Because neurologists are involved in the continuum of stroke care in both inpatient and outpatient settings, it is important to be knowledgeable in this important aspect of stroke. At the very least, this

knowledge will help neurologists to educate stroke survivors and their families on the prognosis and secondary complications of stroke, identify barriers to recovery, and develop individualized plans to help patients improve.

STROKE REHABILITATION VERSUS STROKE RECOVERY

It is important to differentiate between stroke recovery and stroke rehabilitation. These two terms are often used interchangeably in the clinical setting and literature but important differences exist. *Stroke rehabilitation* has been broadly defined as any aspect of stroke care that aims to reduce disability and promote participation in activities of daily living. Stroke rehabilitation is a process; its objectives are to prevent deterioration of function, improve function, and achieve the highest possible level of independence (physically, psychologically, socially, and financially) within the limits of the persistent stroke impairments. During this process, treatment and training are provided to stroke survivors to help them return to normal life. By regaining and relearning skills of everyday liv-

ing through rehabilitation, many stroke survivors obtain greater independence in activities of daily living and improved functional capacity.² **Table 11-1** lists the major rehabilitation approaches, the goals of each approach, and an example.³

On the other hand, *stroke recovery* may be best defined as improvement across a variety of outcomes, beginning with biological and neurologic changes that manifest as improvement on performance and activity-based behavioral measures. A variety of measures exist, and, depending on the definition of successful recovery, the proportion of patients classified as recovered in stroke outcome studies can vary markedly. For example, Duncan and colleagues⁴ compared patterns of recovery using different outcome measures and varying thresholds for defining successful recovery. The percentage of patients who achieved full recovery at 6 months differed based on the scale and how recovery was defined. Therefore, recovery may not necessarily reflect functional improvement either behaviorally or biologically. It is important to tailor the definition of recovery to the individual patient and

KEY POINT

- Rehabilitation is a process of stroke care that reduces disability and improves participation in therapy. Recovery is defined as improvements across a variety of outcomes.

TABLE 11-1 Rehabilitation Approaches and Goals

Approach	Goals	Example
Restoration	Retrain parts of the central nervous system to engage lost functions; restore the function of damaged brain tissue	Home exercise program to improve hemiparesis
Compensation	Adapt behavior to the loss of function without changing the impairments, or reorganization of partially spared brain pathways to relearn lost functions	Use of prisms in glasses to address poststroke diplopia
Modification	Altering environmental setting to promote function and activities of daily living	Adding rails in shower to assist with transfers and prevent falls

KEY POINTS

- The human brain recovers from a stroke through adaptation, regeneration, and neuroplasticity.
- Neuroplasticity is driven by principles of task specificity, repetition, and challenge.

develop a rehabilitation plan to reach the defined recovery goals.

A human brain recovers from stroke in three main ways: adaptation, regeneration, and neuroplasticity. Most successful rehabilitation techniques incorporate at least one of these processes. Adaptation is the reliance on alternative physical movements or devices to compensate for poststroke deficits. An example would be the use of the nondominant hand to feed oneself after hemiplegia affecting dominant hand function. Assistive devices include a walker for poststroke gait and balance dysfunction and prisms in glasses to compensate for visual field deficits. While adaptation is helpful, it may also be harmful to the recovery process because of learned disuse. This phenomenon occurs when individuals do not use their affected limb because they have developed habits to complete actions and tasks bypassing use of the limb, even though they have the capacity to use it. Limiting use of the limb can also limit its recovery.

Regeneration is the growth of neurons and associated cells and circuitry to replace those damaged from a stroke. This approach has historically been considered least useful in stroke rehabilitation as it was believed that central nervous system tissue did not have the capacity for regrowth after injury. However, regeneration has been the focus of attention in recent years because of research advances in stem cell and growth factor interventions. At this time, it is not considered a standard clinical aspect of stroke recovery. Questions still exist regarding the type of stem cell to use, how to deliver it (intravenously, via surgical resection, or endovascularly), dosing, and long-term safety effects. Nevertheless, ongoing clinical trials are attempting to answer these

questions, and regeneration holds hope for the future.

Neuroplasticity, generally defined as changes or a rewiring in the neural network, is considered to be the main recovery process. Soon after a stroke, activation is decreased in cortical areas directly affected by the stroke. This reduced activity is associated with a change in the localization of certain tasks such as movement. As time progresses through the acute and subacute period, the neural networks that had been disrupted by the stroke reconnect in areas adjacent to the area of stroke and coincide with clinical recovery. For example, functional neuroimaging techniques show that as hand function improves, cortical representation that once subserved the hand moves toward the cortical face area (Figure 11-1⁵).⁶ This, in turn, causes an activation in the peris ischemic area/ischemic area with return of laterality to functions and alteration of representative cortical maps. Furthermore, the amount of recovery correlates with the degree of activation in the peri-infarct areas. In general, less functional poststroke recovery is seen in neural networks that have activation in areas more widely distributed beyond the peri-infarct territory.

Research studies have demonstrated that neuroplasticity is driven by several key principles. For plasticity to fully occur, rehabilitation interventions must be task specific and goal directed rather than general and nonspecific movements. Furthermore, the goal-directed tasks must be challenging and interesting enough to maintain an individual's attention, and the task should allow for repetition through multiple attempts.⁷⁻⁹

NATURAL HISTORY OF STROKE

Most stroke deficits will see the highest rate of recovery during the

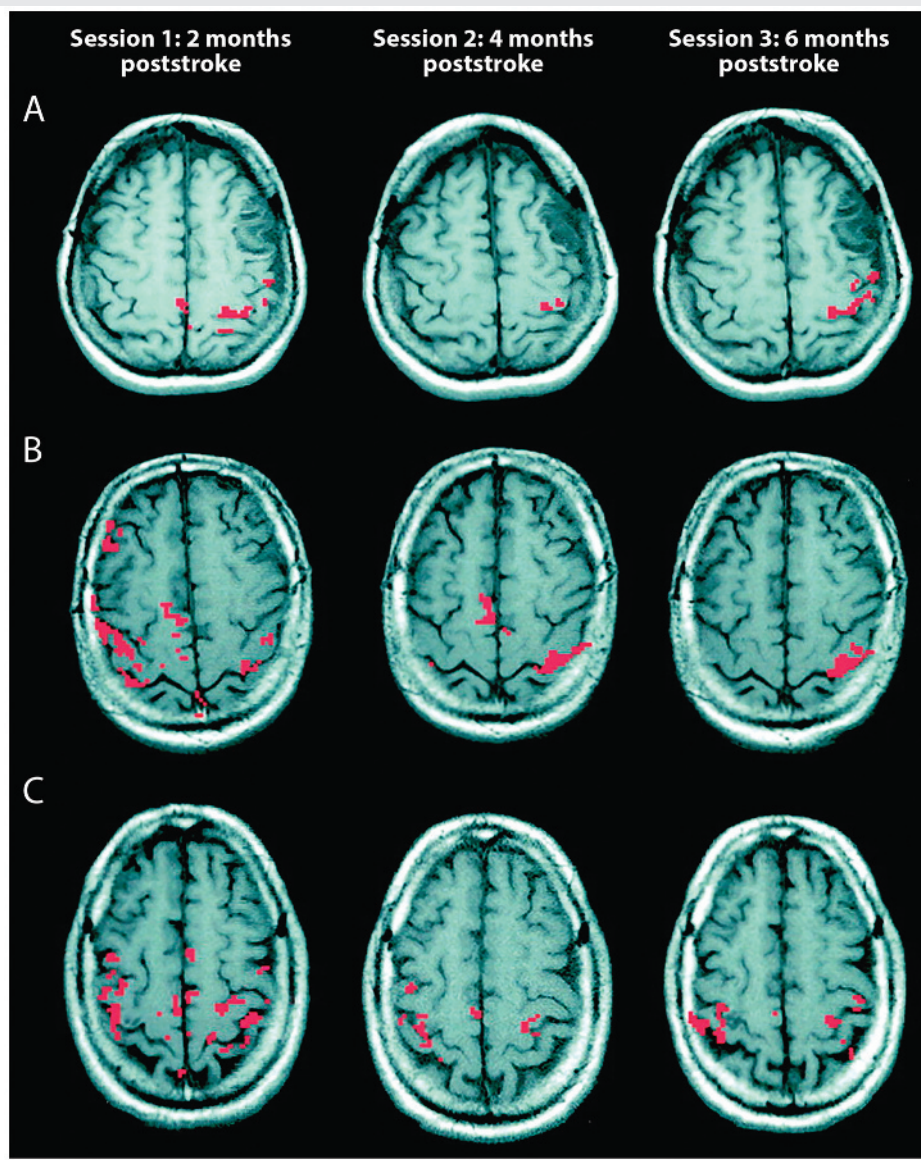


FIGURE 11-1 Three patterns of evolution of functional MRI (fMRI) activation after middle cerebral artery stroke and use of the affected hand for three different patients. As time progresses, the activated sites become more consolidated, lateralized, and smaller.

Modified with permission from Feydy A, et al, *Stroke*.⁵ © 2002 American Heart Association, Inc. stroke.ahajournals.org/content/33/6/1610.long.

first 3 to 6 months after stroke. After 6 months, recovery then reaches a plateau phase without additional significant improvement. However, exceptions exist, and improvement can continue for several years after stroke. Models to predict potential for recovery beyond 6 months and interventions

to facilitate continued recovery in the plateau phase remain an active area of clinical research.

Swallowing, facial movement, and gait tend to demonstrate better recovery than other deficits. One hypothesis to explain this observation is that these deficits have bihemispheric representation

KEY POINTS

- Different functions recover differently. Swallowing, facial movement, and gait tend to have better recovery than language and dominant hand function.
- Upper extremity motor recovery can be predicted very early at the bedside through the presence/absence of voluntary finger extension and shoulder abduction.

in the cortex as part of their normal functional anatomy.^{10,11} On the other hand, cortical functions, such as language and spatial attention as well as dominant hand movement, are more lateralized in functional anatomy and consequently recover more slowly.¹⁰

In addition to the limitations of spontaneous recovery, multiple factors play a role in the plateau of recovery. Limited therapy or absence of therapy often leads to learned disuse and hinders improvement.¹² Poststroke depression has been shown to impede recovery across a variety of measures such as cognitive deficits and mortality. Other factors that can hinder recovery include side effects of medications, such as excessive benzodiazepine use, and physical comorbidities, such as cervical spine disorders. Neurologists managing the patient with stroke in the acute, subacute, and chronic settings should attempt to ensure that patients are receiving appropriate therapy and are periodically screened for depression.

Good data exist to predict recovery very soon after stroke onset. Motor recovery tends to begin in the proximal musculature of the upper and lower extremities and progresses. The Early Prediction of Functional Outcome After Stroke (EPOS) study found that recovery of upper extremity function at 6 months could be accurately predicted if voluntary finger extension and shoulder abduction were present at 48 hours poststroke.¹³ In fact, if these movements were present, the probability of a good outcome was 98%; if finger extension was not present within 48 hours, the probability of a good outcome was 25%. If the movements did not improve by day 9 poststroke, the likelihood of complete upper extremity recovery decreased to 14%.¹³ Similar predictive models are being developed for recovery of lower extremity deficits.¹⁴

TIMING AND INTENSITY OF REHABILITATION

Uncertainty remains as to the optimal timing and intensity of rehabilitation. In a study examining differences in outcomes for patients for whom therapy was initiated 20 days apart, a strong inverse relationship between the start date and functional outcome was observed, albeit with wide confidence intervals.¹⁵ In other words, those who initiated therapy soon after stroke onset exhibited significantly higher effectiveness of treatment than did the medium- or late-initiating groups. Treatment initiated within the first 20 days was associated with a significantly higher probability of excellent therapeutic response compared to treatment beginning at 20 or 40 days. These findings should not be surprising given the natural history of stroke recovery as previously discussed.

Consensus is lacking as to when to start rehabilitation after stroke as specific guidelines for early mobilization do not exist. Patients with stroke who receive thrombolytic therapy are often immobilized for at least 24 hours to minimize complications from recombinant tissue plasminogen activator. One reason is that strict blood pressure guidelines are placed on patients after thrombolysis to reduce the risk of hemorrhage. Therefore, clinicians may be hesitant to increase physical activity in these patients for fear that an elevation in blood pressure may result. In addition, patients treated with endovascular arterial reperfusion are often confined to bedrest to minimize the risk of complications related to femoral access. However, prolonged bedrest increases the risk of complications related to immobility, including pressure sores, aspiration pneumonia, and deep vein thrombosis.

In the A Very Early Rehabilitation Trial (AVERT), 2104 patients who were

hospitalized with either ischemic or hemorrhagic strokes were randomly assigned to receive customary therapy or a very early intervention. In the intervention arm, the first mobilization was aimed to begin within 24 hours following stroke onset, with the additional goals of the patient being upright and out of bed at least twice daily. This intervention continued for the first 14 days poststroke or until discharge from the acute stroke unit and was delivered by a physical therapy team, including a trained nurse. Those who were mobilized had a worse outcome, defined as a modified Rankin Score of less than 3, compared to standard care (46% versus 50%; adjusted odds ratio = 0.73, $P = .004$).¹⁶ However, in a prespecified dose-response analysis of the trial, it appears that shorter but more frequent sessions of early mobilization improved patients' chances of regaining independence.¹⁷ Similarly, early rehabilitation starting within 48 hours demonstrated benefit in 6-month survival and functional outcomes in patients with intracerebral hemorrhage.¹⁸

Once therapy is initiated, unanswered questions exist regarding the "dose" of rehabilitation. Analogous to medications prescribed for stroke, variations in the duration and intensity of rehabilitation therapy affect recovery outcomes. However, the exact nature of this relationship is unclear. Data from the Very Early Constraint-Induced Movement During Stroke Rehabilitation (VECTORS) trial, a study of the amount of therapy and motor improvement after stroke, suggest that more therapy does not always result in significantly better outcomes. This single-blind phase 2 randomized trial compared traditional upper extremity therapy with dose-matched and high-intensity constraint-induced movement therapy protocols administered over

the course of 2 weeks in 52 patients with upper extremity weakness from either ischemic or hemorrhagic strokes. The therapy was started in the first 28 days after a stroke. Improvement, as measured by the Action Research Arm Test (ARAT) score, was demonstrated in all groups; the high-intensity constraint-induced movement therapy group had significantly less improvement at day 90 compared to the dose-matched constraint-induced movement therapy and control groups at day 90.¹⁹ Similarly, animal models have demonstrated enlargement in areas of ischemia correlating with poor function when constraint therapy is applied early after a stroke.²⁰ It is not clear why early use of constraint therapy impairs early recovery; however, as this therapy is more intense than conventional therapies, greater ischemic demand exists, which can cause neurologic injury. Based on these results, it appears that more data are needed before any definite conclusions can be made about the early application of intense therapy such as constraint-induced movement therapy.

In the 2016 Interdisciplinary Comprehensive Arm Rehabilitation Evaluation (ICARE) trial, 361 subjects were given rehabilitation in one of three arms: an Accelerated Skill Acquisition Program, dose-equivalent usual and customary occupational therapy, or usual and customary occupational therapy. Motor outcomes were not significantly different between the three groups.²¹

Based on the results of these studies, answers to the dosing question remain elusive. Generally accepted practice at this time includes consulting therapists to first evaluate patients within the first 48 hours, using less intense therapy practices as determined by the rehabilitation teams and tolerated by patient, and,

KEY POINT

- The generally accepted practice for stroke rehabilitation at this time involves using less intense therapy in the acute/hyperacute setting and increasing the intensity for those who can tolerate it in the rehabilitation/outpatient setting.

KEY POINT

■ Based on current guidelines, inpatient rehabilitation facilities are appropriate posthospital discharge locations for patients who are able to actively participate in two disciplines of therapy for 3 hours per day, have medical issues requiring physician supervision, and have a reasonable expectation of resuming community living.

for those who can tolerate it, increasing the intensity of rehabilitation in the rehabilitation/outpatient setting.

THERAPY APPROACHES TO REHABILITATION

A goal of stroke rehabilitation should be to facilitate relearning of skills that were possible before the stroke, but in some cases the focus of rehabilitation must be adaptation and compensation for deficits. This process begins while the patient is hospitalized for stroke and involves motor skill retraining, preventing complications, and teaching adaptive techniques using a comprehensive approach. In the US health care system, stroke survivors in need of further rehabilitation following the acute hospitalization have three possible posthospital dispositions: (1) home with outpatient therapy, (2) home with home health therapy, or (3) inpatient rehabilitation facility or skilled nursing facility placement. The disposition is based on the nature and severity of deficits, comorbidities, and insurance/reimbursement. For example, inpatient rehabilitation facilities are available to patients who are able to actively participate in at least two disciplines of therapy (physical therapy, occupational therapy, or speech and language therapy) for 3 hours per day, have medical issues requiring physician supervision, and have a reasonable expectation of resuming community living. The length of stay in these settings is dependent on a variety of factors, including the severity of neurologic deficits, medical comorbidities, and rehabilitation progress; on average, the length of stay is about 2 weeks. It is important to note that in many areas of the United States, the presence and type of third-party insurance will determine where patients continue rehabilitation following acute hospital discharge. Consequently,

unfortunately, many stroke survivors who are uninsured or underinsured, despite being good candidates for inpatient rehabilitation facilities, are discharged to a skilled nursing facility. The importance of posthospital discharge disposition on outcomes is discussed later in this article.

Rehabilitation is often provided in a team-based approach and involves various disciplines, such as physical therapy, occupational therapy, and speech and language therapy. The role of the team involves setting goals, reevaluating these goals on a regular basis, and making adjustments to the rehabilitation plan as needed. In addition to improving the function of the patient, caregiver training is an important aspect of rehabilitation.

Physical therapists perform evaluations to detect problems with movement and balance. They work with the patient and the rehabilitation team to perform exercises to strengthen muscles for walking, standing, and other activities. Occupational therapists help stroke survivors learn strategies to manage daily activities such as eating, bathing, dressing, writing, and cooking. One simple way to differentiate between physical and occupational therapy is that the focus of physical therapy is on the lower extremities, while occupational therapy focuses on upper extremity impairments, but it is important to note that this is a generalization and there are exceptions and nuances in this difference.

Speech and language pathologists (ie, speech therapists) help stroke survivors learn strategies to overcome swallowing and language deficits. In the acute setting, they are involved with dysphagia and swallowing evaluations and may make recommendations for alternative methods of oral intake, such as nasogastric tubes or percutaneous endoscopic gastrostomy

tubes. In the subacute and outpatient settings, aphasia tends to be the focus of speech and language therapy.

Following the initial evaluation, therapists develop a program and provide exercises that use the principles of neuroplasticity mentioned previously (task specificity, repetition, challenging). Teaching of compensatory and adaptive techniques is another important goal. Therapists train the patient and family in activities such as safe transfers, assisted ambulation, proper feeding, and provision of appropriate adaptive techniques. Device-based and adjunctive therapies, such as robotic arms and body-weight support treadmills, have been proposed; however, studies have failed to demonstrate their superiority over currently used therapies and evidence to support regular clinical use is lacking.^{22,23}

Several nontraditional strategies have demonstrated improved efficacy compared to traditional therapy. Constraint-induced movement therapy is a motor rehabilitation therapy technique in which the unaffected extremity is constrained with a mitt, thereby forcing use of the affected hand. This approach, even in a modified dose using a decreased frequency of constraint-induced movement therapy, has been shown to be more effective than standard therapy in the 3- to 9-month poststroke window.^{24,25}

Melodic intonation therapy has been shown to enhance recovery of poststroke aphasia.²⁶ Melodic intonation therapy uses musical elements, including melody and rhythm, to improve language production. The theoretical basis of this approach is that language is localized in the dominant hemisphere, but singing and melody localize to the nondominant hemisphere. Consequently, advocates of this therapy take advantage of

preserved singing abilities in the unaffected hemisphere and engage language-capable regions in the non-dominant (usually right) hemisphere. While robust evidence for this approach is lacking, it appears that this therapy is most beneficial in stroke survivors with expressive (Broca) aphasia but with some retained expressive abilities as well as absent bi-hemispheric damage.

Functional electrostimulation is another technique that can be used to enhance motor recovery in patients with stroke.^{27,28} This technique involves applying electrical stimulation to muscles of interest. Functional electrostimulation devices are commercially available, and improving these types of devices is an area of active research interest. An example of a functional electrostimulation device is shown in **Figure 11-2**.

Following a stroke, it is important that the rehabilitation setting is appropriate and optimized for the individual patient. Patients who receive their posthospital rehabilitation in an

KEY POINTS

- Constraint-induced movement therapy is an alternative motor rehabilitation therapy technique for the upper extremity in which the unaffected extremity is constrained with a mitt, thereby forcing use of the affected hand.
- Melodic intonation therapy is an alternative therapy technique that has been shown to enhance recovery of poststroke aphasia. It involves the use of musical elements, including melody and rhythm, to improve language production.



FIGURE 11-2

An example of a functional electrostimulation device that provides electrical stimulation to muscles of the forearm and hand to enable a stroke survivor to extend the wrist and flex fingers. The stimulation intensity can be adjusted depending on the level of the patient's weakness and progress with therapy. It is portable and can be used at home.

Courtesy of Bioness Inc.

KEY POINT

- When patients with stroke are unable to return home following their acute hospitalization, discharge to an inpatient rehabilitation facility will likely result in a better outcome.

inpatient rehabilitation facility have improved outcomes following endovascular therapy compared to those in a subacute or skilled nursing facility.²⁹ In a cohort with no significant differences in age, comorbidities, infarct volume, or recanalization rates, patients who went to a skilled nursing facility had significantly worse outcomes than those patients who went to an inpatient rehabilitation facility.³⁰ These points are important for clinicians to remember when deciding on appropriate postacute care and discharge disposition for patients with stroke as there may be confounders and the appropriate destination may not be immediately clear. These points are illustrated in **Case 11-1**.

PHARMACOLOGIC APPROACHES TO STROKE REHABILITATION

Medications can also play a role in promoting stroke recovery. The Flu-

oxetine for Motor Recovery After Acute Ischaemic Stroke (FLAME) trial was a randomized double-blind placebo-controlled trial comparing fluoxetine 20 mg/d and placebo beginning 5 to 10 days after stroke onset in patients with hemiplegia or hemiparesis.³¹ In the intervention group, the change in motor function, as measured by the Fugl-Meyer Assessment of Sensorimotor Recovery After Stroke score, was significantly higher than in the placebo group.³¹ The study results suggest that, rather than just treating poststroke depression (which was addressed in the trial), selective serotonin reuptake inhibitors (SSRIs) may also impact motor recovery, likely through neuroplastic mechanisms. Other antidepressant or neuro-modulating agents have also been examined with positive benefits. For example, clinical trials using cholinesterase inhibitors and

Case 11-1

An 80-year-old woman presented with a right middle cerebral artery distribution acute ischemic stroke. She received both IV recombinant tissue plasminogen activator and mechanical thrombectomy. She was admitted to the hospital for further testing and close monitoring. Despite the acute therapy she still had deficits from her stroke. On hospital day 3, she was evaluated by the therapy team and found to be lethargic and participating poorly in therapy. Because of her lethargy, the therapy team determined that she was unable to participate in her 3 hours of therapy per day and recommended skilled nursing facility placement. Evaluation by the primary team revealed that she had a low-grade fever and leukocytosis and a urinalysis suggestive of a urinary tract infection. Antibiotics were started, and she improved over the next 2 days. Her ability to participate in therapy sessions improved, and the discharge recommendation was upgraded to an inpatient rehabilitation facility.

Comment. This case is an example of how neurologic status can be confounded by infection-induced encephalopathy, a condition that is reversible with appropriate treatment, and illustrates the potential mutability of posthospital discharge recommendations in a short period of time. Had the primary team just proceeded with the initial discharge recommendations and not addressed and treated her confounders to participation in therapy, and had not pursued a repeat evaluation by the therapy team, it is likely that her poststroke recovery would have been compromised.

glutamatergic agents suggest improvements in aphasia rehabilitation.^{32–34} Similarly, it appears that dopaminergic medications may help address post-stroke depression and attention.^{35,36} The trials are limited by their small numbers, heterogeneity of stroke size, and locations. Given these limitations, insufficient evidence exists to implement the medications in routine clinical practice. However, as the safety profile of these interventions is reasonably demonstrated, in certain situations it would be reasonable to consider these pharmacologic agents as part of the rehabilitation plan of patients after discussion with patients and care teams.

Certain medications can impair poststroke recovery, in particular when used in the acute period. Based on their mechanistic effect on neurotransmitters, older antiepileptic agents, such as phenobarbital, diazepam, and phenytoin, can impede synaptic formation in animal models.³⁷ To avoid such detrimental effects on poststroke recovery, newer-generation antiepileptic drugs should be considered as the first-line treatment for poststroke seizures.

H2 blockers (such as famotidine or ranitidine) are a type of antihistamine used during hospitalizations to reduce the risk of gastric reflux and counter the potential gastrointestinal side effects of antithrombotic medications such as aspirin. Since antithrombotics are an evidence-based intervention for secondary stroke prevention, the use of H2 blockers is widespread. However, antihistamines can cause sedation in patients who are elderly and compromise attention vital for effective performance of motor and cognitive tasks. Evidence suggests that these medications can impede plasticity through inhibition of long-term potentiation.³⁸ Given this potential risk of treatment,

proton pump inhibitors are preferable to H2 blockers in this setting.

SPECIFIC ISSUES IN STROKE REHABILITATION

While each stroke presents its own individual issues in rehabilitation due to factors such as stroke size, stroke location, and patient comorbid factors, several common themes or issues often present. This section reviews the most common sequelae and issues impeding overall recovery and quality of life.

Shoulder Syndrome

Loss of arm function is a common poststroke outcome and results in shoulder pain in up to 70% of patients with upper extremity dysfunction.³⁹ Shoulder pain delays recovery as the painful joint limits participation in rehabilitation and may mask improvements in motor function. Shoulder pain can result from multiple causes, including subluxation, impingement, complex regional pain syndrome, thalamic pain syndrome, spasticity, or other conditions such as radiculopathies. To discern between the various causes of shoulder pain, careful assessments of both normal and affected shoulders and ranges of motion (passive and active) are required. A palpable fingerbreadth gap between the acromion and humeral head suggests joint subluxation. A restricted range of movement without pain at rest but present on limited movement suggests adhesive capsulitis as the primary pathology.

Treatment for shoulder pain should begin early by recognizing patients at risk for shoulder syndromes. Patients with flaccid upper extremity paresis are prone to shoulder subluxation and traction in the glenohumeral capsule, which lead to damage of surrounding

KEY POINTS

- Caution and careful consideration must be used when prescribing antiepileptic medications and antihistaminergic medications as they may adversely affect stroke recovery.
- Shoulder pain is a common sequela after a stroke and may be caused by a variety of conditions.

KEY POINT

■ Depression is a common sequela after a stroke and adversely affects outcomes. Medications such as selective serotonin reuptake inhibitors can be effectively used in the treatment of poststroke depression.

soft tissues. Proper positioning that includes supporting the distal forearm from the elbow down to reduce strain at the shoulder reduces the tension on the shoulder; slings can be used to provide additional support. Strapping or taping of the upper arm to the shoulder and clavicle has been used routinely in the management of subluxation. An intraarticular cortisone injection (1 mg to 5 mg) into the glenohumeral joint can be used to treat pain in patients with adhesive capsulitis. Functional electrostimulation can be used for muscle contraction and pain relief. The management of spasticity is discussed later in this article.

Depression

Poststroke depression is increasingly recognized as a common sequela of stroke. The prevalence of clinically diagnosed poststroke depression ranges from 20% to 40%, and it is likely underdiagnosed.⁴⁰⁻⁴² The interaction between depression and stroke recovery is complex, but when depression is untreated or undertreated in patients, poststroke recovery is not optimized. Depression symptoms (eg, fatigue, reduced motivation, loss of confidence, and attention and concentration difficulties) limit the benefits of rehabilitation and can even

counteract them. Studies show that higher rates of mortality and morbidity are seen in stroke patients diagnosed with poststroke depression,^{43,44} while treatment of depression leads to improved functional recovery after stroke. Moreover, by restoring the balance of central neurotransmitters, improving motivation to work with rehabilitation therapists, and increasing compliance with medications, treatment of depression leads to improved functional recovery after stroke.

SSRIs are the most studied agents for the treatment of poststroke depression. Evidence exists for the use of citalopram (20 mg/d), sertraline (50 mg/d to 100 mg/d), and fluoxetine (20 mg/d), which are superior to placebo in treating poststroke depression and producing improvement in quality-of-life measures.⁴⁵⁻⁴⁷ Evidence also supports the efficacy of tricyclic antidepressants for the treatment of poststroke depression.⁴⁸ **Case 11-2** is a clinical example of how poststroke depression affects recovery and its treatment.

Spasticity

Spasticity is a motor disorder generally defined as a velocity-dependent increase in tonic stretch reflexes leading to increased tone. It is often identified

Case 11-2

A 45-year-old man was admitted to the hospital with a basal ganglia lacunar stroke. Despite having a small stroke with minimal comorbidities and mild to moderate deficits, the patient was not improving. His therapists reported decreased participation and minimal functional gains in therapy sessions. The patient reported increased fatigue and somnolence, and his family noted poor engagement and a change in personality. Poststroke depression was diagnosed. He was started on citalopram 20 mg/d, with gradual improvement in his mood and other symptoms.

Comment. This case illustrates the importance of screening for poststroke depression and having a low threshold to treat it. It is important to note that the effect of selective serotonin reuptake inhibitors (SSRIs) may not be seen for 1 to 2 weeks.

during the chronic phase of post-stroke recovery. At 12 months, patients without spasticity have shown significantly better motor and activity scores, have lower Barthel Index scores, and are less likely to receive institutional care ($P < .0001$) compared to those with spasticity.⁴⁹ Likewise, another study demonstrated that modified Rankin Scale and Barthel Index scores were greater for patients with spasticity than for patients without spasticity.⁵⁰ These studies show that spasticity adversely affects functional outcomes in the chronic phase of stroke; therefore, management of spasticity is an essential part of stroke rehabilitation.

Historically, treatment of spasticity has involved oral medications such as baclofen, nerve blocks, and serial casting, but these interventions are limited because of side effects. Alternatively, botulinum toxin and intrathecal baclofen are now widely accepted in the management of spasticity in patients with chronic stroke. Compared to the oral route, intrathecal baclofen achieves muscle-relaxing properties at significantly lower doses, thus limiting systemic side effects. In studies of intrathecal baclofen in patients who were poststroke with spasticity, improvement was seen in mobility, activities of daily living, and quality of life.⁵¹ Botulinum toxin is beneficial for poststroke spasticity, demonstrating improvement in upper limb musculature tone. In studies supporting its use, botulinum toxin was administered into muscles of interest in the hand, wrist, and upper arm at least 6 weeks post-stroke. Study participants had a Modified Ashworth Scale score of 2 to 3 in upper extremity muscles of interest and were followed for at least 10 weeks.⁵²

Return to Work

A common concern of stroke survivors regards return to employment. In

addition to financial independence and full integration into society, patients enjoy subtle benefits from employment, such as improvement in self-esteem and confidence. Clinicians often concentrate on the severity of physical and cognitive impairments when considering a patient's ability to return to work; however, studies have demonstrated that other factors, such as younger age, educational level, level of skill, and prestroke professional status, appear to be strong influencers of a patient's ability to return to work.^{53,54} Vocational rehabilitation programs are available for patients, and often neuropsychological testing can help assess a patient's cognitive ability to return to work. For patients who are deemed unable to return to work, health care teams should assist patients with completing temporary disability forms or long-term disability forms, if needed.

Return to Driving

The ability to drive plays an important role in routine activities and frequently serves as the key to independence. Stroke survivors are often restricted in their driving ability because of hemiparesis; visual field, cognitive, and coordination deficits; and poststroke seizures. The ability to return to driving is often viewed by patients as their metric for return to normalcy and independence, and inability to return to driving can affect their ability to return to work. Consequently, patients often ask for clearance to return to driving or ask when they can anticipate this clearance. A clearance to return to driving should involve both a medical clearance and a functional assessment clearance. The medical clearance evaluation can be performed by a health care professional; it should ensure that visual field, cognitive, and motor deficits are not severe enough to impact

KEY POINTS

- Spasticity adversely affects poststroke outcomes.
- Botulinum toxin and intrathecal baclofen are the preferred treatments of spasticity in patients with chronic stroke.
- Studies show that the severity of physical and cognitive impairments is not associated with a stroke survivor's ability to return to work. More important factors include age, educational level, and prestroke professional status.

KEY POINT

- A formal driving assessment is helpful in determining a stroke survivor's ability to drive.

driving ability and that seizure control is compliant with local laws. The medical clearance evaluation should also assess other medical comorbidities, such as cardiac conditions, that could potentially affect the patient's driving and lead to harm for the patient or others on the road. However, more complex aspects of driving, such as planning, motor coordination, and reaction times, are difficult to ascertain in the office. A formal driving assessment can be helpful to evaluate these skills and can be conducted on a driving simulator or by in-car evaluation by a specialist assessor.

EMERGING TECHNIQUES IN STROKE REHABILITATION

Further advances in stroke recovery and rehabilitation will likely occur in the next decade. On a systems of care level, telemedicine is currently playing a role in the acute management of stroke but will likely expand to the recovery phase of stroke (telerehabilitation). Telemedicine networks can be applied to assess and evaluate the rehabilitation needs of patients at home or in rural areas where rehabilitation resources and expertise may not be readily available. For patients with residual deficits who have exhausted insurance, telemedicine avenues may be developed to focus on wellness and self-training. In a health care system that stresses evidence-based medicine, quality metrics, and cost-containment, rehabilitation strategies that are not only more clinically effective but also more cost-effective and efficient are needed.

Research studies are ongoing to test the viability of interventions such as novel pharmacologic agents, stem cells, brain stimulation, and virtual reality. To better identify candidates for specific rehabilitation interventions and tailor treatments to the individual, biomarkers must be developed.

CONCLUSION

Stroke rehabilitation is a complex process that involves multiple health care specialties and multiple approaches, depending on the nature of the patient's deficits. While the timing and dosing of therapy and novel approaches have not been fully validated and established, it is clear that successful rehabilitation can make a positive impact on the outcome of stroke survivors. Neurologists can play a role in rehabilitation by advising patients on the natural history of stroke, ensuring that the appropriate therapy and therapy location are provided, screening for poststroke depression, and recognizing and managing specific issues in stroke rehabilitation. Stroke rehabilitation is the next frontier in stroke care, and physicians involved in this field will have more knowledge and many more tools at their disposal in the coming years.

REFERENCES

1. Ovbiagele B, Goldstein LB, Higashida RT, et al. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. *Stroke* 2013;44(8):2361–2375. doi:10.1161/STR.0b013e31829734f2.
2. Dewey HM, Sherry LJ, Collier JM. Stroke rehabilitation 2007: what should it be? *Int J Stroke* 2007;2(3):191–200. doi:10.1111/j.1747-4949.2007.00146.x.
3. Cumberland Consensus Working Group, Cheeran B, Cohen L, et al. The future of restorative neurosciences in stroke: driving the translational research pipeline from basic science to rehabilitation of people after stroke. *Neurorehabil Neural Repair* 2009;23(2):97–107. doi:10.1177/1545968308326636.
4. Duncan PW, Lai SM, Keighley J. Defining post-stroke recovery: implications for design and interpretation of drug trials. *Neuropharmacology* 2000;39(5):835–841. doi:10.1016/S0028-3908(00)00003-4.
5. Feydy A, Carlier R, Roby-Brami A, et al. Longitudinal study of motor recovery after stroke: recruitment and focusing of brain activation. *Stroke* 2002;33(6):1610–1617. doi:10.1161/01.STR.0000017100.68294.52.

6. Willer C, Ramsay SC, Wise RJ, et al. Individual patterns of functional reorganization in the human cerebral cortex after capsular infraction. *Ann Neurol* 1993;33(2):181–189. doi:10.1002/ana.410330208.
7. Kleim JA, Barbay S, Nudo RJ. Functional reorganization of the rat motor cortex following motor skill learning. *J Neurophysiol* 1998;80(6):3321–3325.
8. Nudo RJ. Functional and structural plasticity in motor cortex: implications for stroke recovery. *Phys Med Rehabil Clin N Am* 2003;14(1 suppl):S57–S76.
9. Nudo RJ, Milliken GW, Jenkins WM, Merzenich MM. Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. *J Neurosci* 1996;16(2):785–807.
10. Cramer SC, Crafton KR. Somatotopy and movement representation sites following cortical stroke. *Exp Brain Res* 2006;168(1–2): 25–32. doi:10.1007/s00221-005-0082-2.
11. Hamdy S, Aziz Q, Rothwell JC, et al. Recovery of swallowing after dysphagic stroke relates to functional reorganization in the intact motor cortex. *Gastroenterology* 1998;115(5):1104–1112. doi:10.1016/S0016-5085(98)70081-2.
12. Wolf SL, Blanton S, Baer H, et al. Repetitive task practice: a critical review of constraint-induced movement therapy in stroke. *Neurologist* 2002;8(6):325–338. doi:10.1097/01.nrl.0000031014.85777.76.
13. Nijland RH, van Wegen EE, Harmeling-van der Wel BC, et al. Presence of finger extension and shoulder abduction within 72 hours after stroke predicts functional recovery: early prediction of functional outcome after stroke: the EPOS cohort study. *Stroke* 41(4):745–750. doi:10.1161/STROKEAHA.109.572065.
14. Stinear CM, Byblow WD, Ward SH. An update on predicting motor recovery after stroke. *Ann Phys Rehabil Med* 2014;57(8):489–498. doi:10.1016/j.rehab.2014.08.006.
15. Paolucci S, Antonucci G, Grasso MG, et al. Early versus delayed inpatient stroke rehabilitation: a matched comparison conducted in Italy. *Arch Phys Med Rehabil* 2000;81(6):695–700. doi:10.1016/S0003-9993(00)90095-9.
16. Carlsson GE, Möller A, Blomstrand C. A qualitative study of the consequences of ‘hidden dysfunctions’ one year after a mild stroke in persons <75 years. *Disabil Rehabil* 2004;26(23):1373–1380. doi:10.1080/0963828040000211.
17. Bernhardt J, Churilov L, Ellery F, et al. Prespecified dose-response analysis for A Very Early Rehabilitation Trial (AVERT). *Neurology* 2016;86(23):138–145. doi:10.1212/WNL.0000000000002459.
18. Liu N, Cadilhac DA, Andrew NE, et al. Randomized controlled trial of early rehabilitation after intracerebral hemorrhage stroke: difference in outcomes within 6 months of stroke. *Stroke* 2014;45(12):3502–3507. doi:10.1161/STROKEAHA.114.005661.
19. Dromerick AW, Lang CE, Birkenmeier RL, et al. Very Early Constraint-Induced Movement during Stroke Rehabilitation (VECTORS): a single-center RCT. *Neurology* 2009;73(3):195–201. doi:10.1212/WNL.0b013e3181ab2b27.
20. Kozlowski DA, James DC, Schallert T. Use-dependent exaggeration of neuronal injury after unilateral sensorimotor cortex lesions. *J Neurosci* 1996;16(15):4776–4786.
21. Winstein CJ, Wolf SL, Dromerick AW, et al. Effect of a task-oriented rehabilitation program on upper extremity recovery following motor stroke: The ICARE randomized clinical trial. *JAMA* 2016;315(6):571–581. doi:10.1001/jama.2016.0276.
22. Duncan PW, Sullivan KJ, Behrman AL, et al. Body-weight-supported treadmill rehabilitation after stroke. *N Engl J Med* 2011;364(21): 2026–2036. doi:10.1056/NEJMoa1010790.
23. Lo AC, Guarino PD, Richards LG, et al. Robot-assisted therapy for long-term upper-limb impairment after stroke. *N Engl J Med* 2010;362(19):1772–1783. doi:10.1056/NEJMoa0911341.
24. Wolf SL, Winstein CJ, Miller JP, et al. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. *JAMA* 2006;296(17):2095–2104. doi:10.1001/jama.296.17.2095.
25. Page SJ, Levine P, Leonard A, et al. Modified constraint-induced therapy in chronic stroke: results of a single-blinded randomized controlled trial. *Phys Ther* 2008;88(3):333–340. doi:10.2522/ptj.20060029.
26. van der Meulen I, van de Sandt-Koenderman ME, Ribbers GM. Melodic Intonation Therapy: present controversies and future opportunities. *Arch Phys Med Rehabil* 2012;93(1 suppl): S46–S52. doi:10.1016/j.apmr.2011.05.029.
27. Xu B, Yan T, Yang Y, et al. Effect of normal-walking-pattern-based functional electrical stimulation on gait of the lower extremity in subjects with ischemic stroke: a self-controlled study. *NeuroRehabilitation* 2016;38(2):163–169. doi:10.3233/NRE-161306.

28. Alon G, Levitt AF, McCarthy PA. Functional electrical stimulation enhancement of upper extremity functional recovery during stroke rehabilitation: a pilot study. *Neurorehabil Neural Repair* 2007;21(3):207–215. doi:10.1177/1545968306297871.
29. Deutsch A, Granger CV, Heinemann AW, et al. Poststroke rehabilitation: outcomes and reimbursement of inpatient rehabilitation facilities and subacute rehabilitation programs. *Stroke* 2006;37(6):1477–1482. doi:10.1161/01.STR.0000221172.99375.5a.
30. Belagaje SR, Sun CH, Nogueira RG, et al. Discharge disposition to skilled nursing facility after endovascular reperfusion therapy predicts a poor prognosis. *J Neurointerv Surg* 2015;7(2):99–103. doi:10.1136/neurintsurg-2013-011045.
31. Chollet F, Tardy J, Albucher JF, et al. Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. *Lancet Neurol* 2011;10(2):123–130. doi:10.1016/S1474-4422(10)70314-8.
32. Hong JM, Shin DH, Lim TS, et al. Galantamine administration in chronic post-stroke aphasia. *J Neurol Neurosurg Psychiatry* 2012;83(7):675–680. doi:10.1136/jnnp-2012-302268.
33. Berthier M, Green C, Higuera C, et al. A randomized, placebo-controlled study of donepezil in poststroke aphasia. *Neurology* 2006;67(9):1687–1689. doi:10.1212/01.wnl.0000242626.69666.e2.
34. Berthier ML, Green C, Lara JP, et al. Memantine and constraint-induced aphasia therapy in chronic poststroke aphasia. *Ann Neurol* 2009;65(5):577–585. doi:10.1002/ana.21597.
35. Gorgoraptis N, Mah YH, Machner B, et al. The effects of the dopamine agonist rotigotine on hemispatial neglect following stroke. *Brain* 2012;135(pt 8):2478–2491. doi:10.1093/brain/aws154.
36. Kohno N, Abe S, Toyoda G, et al. Successful treatment of post-stroke apathy by the dopamine receptor agonist ropinirole. *J Clin Neurosci* 2010;17(6):804–806. doi:10.1016/j.jocn.2009.09.043.
37. Goldstein LB. Potential effects of common drugs on stroke recovery. *Arch Neurol* 1998;55(4):454–456. doi:10.1001/archneur.55.4.454.
38. Chang M, Saito H, Abe K. Cimetidine inhibits the induction of long-term potentiation in the dentate gyrus of rats in vivo. *Jpn J Pharmacol* 1997;74(3):281–283. doi:10.1254/jip.74.281.
39. Dromerick AW, Edwards DF, Kumar A. Hemiplegic shoulder pain syndrome: frequency and characteristics during inpatient stroke rehabilitation. *Arch Phys Med Rehabil* 2008;89(8):1589–1593. doi:10.1016/j.apmr.2007.10.051.
40. Robinson RG. Poststroke depression: prevalence, diagnosis, treatment, and disease progression. *Biol Psychiatry* 2003;54(3):376–387. doi:10.1016/S0006-3223(03)00423-2.
41. Hackett ML, Yapa C, Parag V, Anderson CS. Frequency of depression after stroke: a systematic review of observational studies. *Stroke* 2005;36(6):1330–1340. doi:10.1161/01.STR.0000165928.19135.35.
42. de Man-van Ginkel JM, Gooskens F, Schuurmans MJ, et al. A systematic review of therapeutic interventions for poststroke depression and the role of nurses. *J Clin Nurs* 19(23–24):3274–3290. doi:10.1111/j.1365-2702.2010.03402.x.
43. Robinson RG, Bolduc PL, Price TR. Two-year longitudinal study of poststroke mood disorders: diagnosis and outcome at one and two years. *Stroke* 1987;18(5):837–843. doi:10.1161/01.STR.18.5.837.
44. Herrmann N, Black SE, Lawrence J, et al. The Sunnybrook Stroke Study: a prospective study of depressive symptoms and functional outcome. *Stroke* 1998;29(3):618–624. doi:10.1161/01.STR.29.3.618.
45. Andersen G, Vestergaard K, Lauritzen L. Effective treatment of poststroke depression with the selective serotonin reuptake inhibitor citalopram. *Stroke* 1994;25(6):1099–1104. doi:10.1161/01.STR.25.6.1099.
46. Rasmussen A, Lunde M, Poulsen DL, et al. A double-blind, placebo-controlled study of sertraline in the prevention of depression in stroke patients. *Psychosomatics* 2003;44(3):216–221. doi:10.1176/appi.psy.44.3.216.
47. Fruehwald S, Gatterbauer E, Rehak P, Baumhackl U. Early fluoxetine treatment of post-stroke depression—a three-month double-blind placebo-controlled study with an open-label long-term follow up. *J Neurol* 2003;250(3):347–351. doi:10.1007/s00415-003-1014-3.
48. Lauritzen L, Bendtsen BB, Vilmar T, et al. Post-stroke depression: combined treatment with imipramine or desipramine and mianserin. A controlled clinical study. *Psychopharmacology (Berl)* 1994;114(1):119–122. doi:10.1007/BF02245452.
49. Welmer AK, von Arbin M, Widén Holmqvist L, Sommerfeld DK. Spasticity and its association with functioning and health-related quality of life 18 months after stroke. *Cerebrovasc Dis* 2006;21(4):247–253. doi:10.1159/000091222.

-
50. Lundström E, Terént A, Borg J. Prevalence of disabling spasticity 1 year after first-ever stroke. *Eur J Neurol* 2008;15(6):533–539. doi:10.1111/j.1468-1331.2008.02114.x.
51. Dvorak EM, Ketchum NC, McGuire JR. The underutilization of intrathecal baclofen in poststroke spasticity. *Top Stroke Rehabil* 18(3):195–202. doi:10.1310/tsr1803-195.
52. BOTOX (onabotulinumtoxinA). FDA approved labeling text. www.accessdata.fda.gov/drugsatfda_docs/label/2011/103000s5232lbl.pdf.
- Revised August 2011. Accessed December 13, 2016.
53. Vestling M, Tufvesson B, Iwarsson S. Indicators for return to work after stroke and the importance of work for subjective well-being and life satisfaction. *J Rehabil Med* 2003;35(3):127–131. doi:10.1080/16501970310010475.
54. Wozniak MA, Kittner SJ, Price TR, et al. Stroke location is not associated with return to work after first ischemic stroke. *Stroke* 1999; 30(12):2568–2573. doi:10.1161/01.STR.30.12.2568.