EMERGENCY MEDICINE PRACTICE

AN EVIDENCE-BASED APPROACH TO EMERGENCY MEDICINE

Code Stroke: A State-Of-The-Art Strategy For Rapid Assessment And Treatment

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CME Objectives

Upon completing this article, you should be able to:

1. list common stroke presentations and major stroke syndromes;
2. describe blood pressure management guidelines for acute stroke patients;
3. discuss the controversies and level of evidence surrounding heparin and t-PA therapy for acute stroke; and
4. identify the components of a safe and effective t-PA screening and treatment protocol for acute ischemic stroke in your ED.

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MOST emergency physicians can probably remember a busy ED shift when a patient suffering from an obvious acute stroke was triaged to a hallway gurney. They shared the corridor with other patients for whom medicine had little to offer. Nearly all physicians viewed this ancient affliction with the same fatalism reserved for the terminally ill. In the not-so-distant past, stroke was a tragedy, but not an emergency. Today, effective therapies exist for treating some types of acute stroke. However, some therapies require tremendous alacrity, preparation, and teamwork by the hospital staff. Emergency physicians must take the lead in destroying the notion of stroke as an untreatable malady. We must transform therapeutic nihilism into a proactive strategy.

This issue of *Emergency Medicine Practice* provides a structured approach to evaluating patients with acute stroke symptoms. It describes a procedure for the expeditious, yet thorough, assessment of patients. While certain steps highlight thrombolysis, these protocols must not be viewed as "t-PA protocols." We discuss many interventions to improve the overall acute care of stroke patients.

Epidemiology, Etiology, Pathophysiology

The personal and societal impact of stroke is well-known to the emergency physician. From the paralyzed nursing home patient with infected decubiti, to the family who "can't take care of grandpa since his stroke," the ED is regularly confronted with the devastating sequelae. Stroke is the third most common cause of death in the U.S. and the leading cause of adult disability.[1,2] Next to Alzheimer's disease, it is the most common reason for being in a nursing home. Over the next three decades, as the proportion of the U.S. population over age 65 explodes, the public health impact of stroke will only escalate.

The term "stroke" represents mixed syndromes with heterogeneous causes that are traditionally lumped together. (See **Table 1**.) Anywhere from 80-85% of strokes are ischemic, with the majority of these being thrombotic.[3,4] Intracerebral hemorrhages account for most remaining cases.[5] Although subarachnoid hemorrhages (SAH) are frequently included as a subtype of stroke, this is not a

practical categorization. From a "problem-based" emergency medicine viewpoint, SAH is best considered in patients with headache. Headache is a prominent SAH symptom, while focal neurologic findings are not. Because SAH represents a distinctly different process, both from a pathophysiologic and ED evaluation perspective, it will not be discussed in depth in this article.

The target for most acute stroke interventions is the ischemic *penumbra*. This is the area of marginally perfused brain tissue surrounding a cerebral infarct or hemorrhage. It is likely to progress to complete injury as time increases. However, in some cases, prompt emergency treatment can salvage this area. Potential pharmacologic interventions include thrombolytic, antithrombotic, anticoagulant, and neuroprotective therapy. Neuroprotective agents represent a broad range of drugs that oppose the histochemical cascade leading to brain death. Pivotal steps in this process include the release of glutamate, a rise in intracellular calcium, and over-activation of enzymes that ultimately lead to the destruction of cellular membranes, proteins, and nucleic acids.[6] Although no neuroprotective drug has yet proven efficacious for acute stroke, dozens of these agents are currently in phase II and III clinical research trials. These agents are likely to be effective in both ischemic and hemorrhagic strokes.

Different pharmacologic agents have distinct therapeutic windows. A common factor is the need for early administration, usually within the first few hours of stroke onset. Extrapolation from animal studies, and current experience with intravenous thrombolysis, suggests this window is approximately three hours. After 3-4 hours, reperfusion is likely to have little or no benefit, and may even worsen outcome.[7-11] For this reason, emergency physicians must quickly evaluate all potential stroke patients.

Table 1. Stroke Subtypes And Major Etiologies.

Stroke Subtype	Percent of all S trokes
Ischemic	80-85%
Large artery atherosclerosis with thrombus	
Small vessel (lacunar) disease	
Cardioembolism	
Nonatherosclerotic vasculopathies	
Hypercoagulable states	
Hemorrhagic	10-15%
Hypertensive	
Arteriovenous malformation (AVM) related	
Oral anticoagulation related	
Subarachnoid H emorrhage	6-7%
Ruptured aneurysm	
Ruptured AVM	

Sources: Cerebral Embolism Task Force. Cardiogenic brain embolism: The second report of the cerebral embolism task force. *Arch Neurol* 1989;46:727-743; Mohr JP, Caplan LR, Melski, et al. The Harvard cooperative stroke registry: A prospective registry. *Neurology* 1978;28:754-762; Foulkes MA, Wolf PA, Price, et al. The stroke data bank: Design, methods, and baseline characteristics. *Stroke* 1988;19(5):547-554.

Table 2. "Stroke Mimics": The Differential Diagnosis Of Stroke.

Neurologic
Todd's paralysis (persistent neurologic signs post seizure)
Complicated migraine
Non-convulsive status epilepticus
Neuropathies:
Bell's palsy
Radial nerve palsy
Spinal cord disorders

Metabolic
Hypoglycemia
Hyperglycemia
Hyponatremia
Hypernatremia
Hepatic encephalopathy

Infectious
Meningitis
Encephalitis
Brain abscess
Cerebral malaria
Rocky Mountain Spotted Fever

Neoplastic
Tumor

Traumatic
Subdural hematoma
Epidural hematoma

Toxic
Drug overdose
Botulism
Paralytic shellfish poisoning

Vascular
Thoracic dissection
Vertebral artery dissection
Carotid artery dissection
Cerebral vasculitis

Other
Heat stroke
Sickle cell crisis—cerebral crisis

Differential Diagnosis

The "hallmark" of an acute stroke is the sudden onset of focal neurologic dysfunction, *corresponding to a distinct vascular territory*. Common neurologic conditions that mimic stroke include Todd's paralysis after a seizure or a complicated migraine with persistent focal deficits. Rapid identification of "stroke mimics" is not only essential in considering thrombolysis or other stroke interventions, but is also important because many of these conditions require specific treatment. Patients with profound hypoglycemia may present with focal neurologic signs, fooling even the most experienced practitioners. Other diagnoses that should be considered are listed in **Table 2**. Frequently, the details of the patient's history, a bedside determination of serum glucose, along with the performance of a rapid neurologic evaluation, will allow the emergency physician to determine stroke vs. an alternative diagnosis. While occasionally an acute stroke may pose a diagnostic dilemma, the emergency physician will correctly diagnose the majority of cases.[12,13] Interestingly, an initial evaluation of an abbreviated neurologic scale showed that any combination of facial palsy, motor dysfunction of the arm, or abnormal speech was 100% sensitive and 88% specific for stroke.[14] If this finding is confirmed by future testing, it may become an excellent prehospital and triage tool for identifying stroke patients.

Although the diagnosis or localization of stroke can be challenging, most patients present with one of three syndromes. (See **Table 3**.) Since the majority of cerebral blood flows through the "anterior circulation" (carotid vessels), most deficits localize to a single cerebral hemisphere. Rules of thumb for stroke localization include:

- Aphasia usually corresponds to a left hemispheric stroke.
- Neglect or "hemi-inattention" usually indicates a right hemispheric stroke.

- If a "gaze preference" (inability to look voluntarily to the contralateral side) exists due to a hemispheric stroke, the patient will "look to the lesion" (i.e., toward the ischemic site).
- "Crossed signs" (ipsilateral face and contralateral body) usually indicate brainstem involvement.

Two common stroke mimics include Bell's palsy (palsy of the peripheral VIIth nerve) and radial nerve palsy, conditions frequently seen by the emergency physician. A Bell's palsy is easily distinguished from a central nervous system lesion by the fact that patients with peripheral nerve compromise cannot wrinkle their forehead normally. Patients with a more serious central problem have normal motor function of the brows due to the bilateral innervation of the forehead from both facial nerves. Patients with radial nerve palsy complain of weakness in one hand. While the primary deficit is unilateral wrist drop, the grip seems weak on physical examination because a dropped wrist impairs the grip mechanics. When the emergency physician passively extends the patient's wrist, the patient's grip returns to normal. This condition usually occurs in the intoxicated patient, as a result of falling asleep in a chair with the involved arm hanging over the back of the seat. The chair compresses the radial nerve at the axilla and produces a "Saturday Night Palsy."

Table 3. Stroke Syndromes.

"Anterior Circulation"
Left (Dominant*) Cerebral Hemisphere
Right hemiparesis
Right-sided sensory loss
Right visual field deficit
Left gaze preference
Aphasia*

Right (Nondominant) Cerebral Hemisphere
Left hemiparesis
Left-sided sensory loss
Left visual field deficit
Right gaze preference
Left-sided neglect or hemi-attention**

"Posterior Circulation"
Brainstem And Cerebellum
(several of the following usually present)
Hemiparesis or quadriparesis (in the "locked-in" syndrome, movement of the upper lids may be the only clue to consciousness)
Hemisensory loss or sensory loss in all four extremities
"Crossed" deficits
Diplopia
Dysconjugate gaze
Gaze palsy
Nystagmus
Dysarthria with dysphagia
Vertigo
Decreased level of consciousness
Limb or gait ataxia
Intractable vomiting

* "Dominance" is determined by controlling language function. The left cerebral hemisphere is dominant in the majority of both right-handed and left-handed individuals.
** May be manifest by inability to identify objects in the patient's left hemispace, "extinguishing" of double simultaneous stimulation (acknowledgement of only right-sided stimulation in the presence of stimulation simultaneously to both sides of the body), or anosognosia (denial of illness).

Emergency Department Evaluation

Establishing a "Code Stroke" or "Brain Attack" protocol helps ensure prompt evaluation for all potential stroke patients presenting to the ED. This coordinated approach is essential both to meet the time demands of acute stroke therapy, and because many patients initially thought to have a stroke will have other, treatable conditions. In most EDs, the "stroke team" consists of the emergency physicians, nurses, and a radiologist. While most emergency physicians would welcome the addition of a neurologist, "stroke nurses," and other ancillary personnel, the luxury of such a grand squadron applies to few EDs. At most non-teaching hospitals, the same physicians and nurses comprising the "trauma team" will constitute the "stroke team."

The aims of emergent stroke evaluation are listed in **Table 4** (see also the Clinical Pathway "Acute Stroke Patient ED Evaluation" on page 9). Begin with basic supportive care to ensure optimal brain perfusion and oxygenation. If there is any question regarding cervical trauma, maintain appropriate C-spine precautions until the C-spine can be cleared. Airway management, including adequate ventilation and oxygenation, is essential. If the patient is obtunded and unable to control his or her tongue or secretions, perform rapid sequence intubation using neuroprotective agents (a minimum of lidocaine, an induction agent, and paralytic) and begin mechanical ventilation. Airway protection is crucial because potential stroke patients require emergent neuroimaging, which at most hospitals necessitates the patient leaving the ED. Proactive management of the airway will avoid a respiratory arrest in CT.

Because acute cardiac ischemia and arrhythmias can accompany acute stroke, place stroke patients on a cardiac monitor and treat malignant arrhythmias. While vascular access should be obtained in all stroke patients, administer IV fluid, such as normal saline or Ringer's lactate, only if the patient is hypotensive. Avoiding unnecessary fluids will minimize brain edema. The fluids should not include dextrose, since some data suggests that hyperglycemia is associated with worse neurologic outcomes.[15-17] (Class of Evidence: IIa-IIb) Whether the hyperglycemia causes the morbidity, or is simply a marker for bad outcome, is unknown.

Table 4. Aims Of ED Stroke Patient Evaluation And Treatment.

- Achievable with the resources routinely available
- Protocol flow consistent with the usual ED evaluation
- Ensure stable vital signs
- Confirm the presence of stroke vs. another diagnosis
- Identify the type, location, and severity of stroke
- Determine the duration/age of stroke and candidacy for pharmacologic therapy
- Predict the likelihood of immediate complications
- Begin appropriate treatment

All patients suspected of acute stroke require a stat measurement of their glucose; do *not* wait for the results of a routine chemistry panel. Few trips are as embarrassing or unnecessary as a race to the CT scanner with an amp of D50 in hand.

History

While a thorough history is usually the cornerstone of evaluation, several aspects of stroke undermine this tenet. Among the most problematic obstacles is the presence of aphasia. Nonetheless, if aphasia coexists with a left gaze preference and right-sided hemiparesis, initiate CT scanning and interview family members. The most important historical information to obtain is the precise time of symptom onset. This will not only determine candidacy for thrombolysis and dictate the feasibility of a three-hour t-PA treatment window, but it will also predict the likelihood of stroke-related complications in the ED. The best strategy for determining symptom onset is to ask the patient and/or family when the patient was last known to be without symptoms. If the time of onset remains ambiguous, avoid thrombolytics. A patient who awakens in the morning with a neurologic deficit is *not* a candidate for t-PA.

The presence of pain is an important finding. Headache is infrequent in ischemic stroke and raises the possibility of cerebral hemorrhage, subarachnoid bleed, or complex migraine. However, history alone is not sufficiently sensitive to distinguish an ischemic from a hemorrhagic stroke. Features suggesting a hemorrhagic stroke include a significant decrease in level of consciousness, headache, nausea, or vomiting; however, none of these findings is specific. Finally, always consider arterial dissection as the cause for stroke symptoms. If the patient had neck pain before the event, suspect an arterial dissection, since this diagnosis will profoundly affect thrombolytic, antithrombotic, or anticoagulant therapy decisions. The combination of chest pain and neurologic findings must always trigger suspicion of thoracic aortic dissection.

The emergency physician must also determine any contraindications to thrombolysis, such as recent trauma, surgery, intracranial malignancy, recent GI hemorrhage, and the like. (See **Tool 1** on page 13.)

Vital Signs

While blood pressure is typically the vital sign of most interest in acute stroke, other vital signs provide important diagnostic clues and may trigger therapeutic interventions. An irregularly irregular pulse suggests the presence of atrial fibrillation and a possible cardioembolic etiology. Ascertain the source of any fever, and consider a CNS infection or postictal state. While there are no clinical data regarding the usefulness of antipyretics in treating fever that accompanies stroke, fever worsens prognosis in acute stroke.[18,19] Current consensus recommends antipyretics for elevated body temperature occurring with stroke.[17] (Class of Evidence: IIb)

Obtaining blood pressure in both arms is important, since aortic dissections can present as an acute neurologic event. Any significant deviation in blood pressures between arms (usually more than 20 points in systolic pressure) should raise concern for an acute arterial dissection. This is especially true in the setting of marked hypertension. Initially verify blood pressure equivalence in both arms, then monitor blood pressure in one arm at least every 15 minutes.

Physical Exam

Important features of the physical exam include evidence of head or neck injury, carotid bruits, and cardiac murmur or rhythm abnormalities. Note any signs of respiratory distress and listen to the lungs for clues to aspiration, which may occur with acute stroke.

Beyond attending to the ABCs, performing and documenting an appropriate neurologic exam is of paramount importance. An "appropriate exam" for a thrombolytic candidate would encompass the NIH Stroke Scale. (See **Tool 3** on page 14.) Performing the National Institutes of Health Stroke Scale (NIHSS) on all stroke patients is worthwhile. It correlates with stroke severity and long-term outcome, and it helps assess the risk for symptomatic hemorrhage if t-PA is administered.[20] The NIHSS is comprised of six major areas: 1) level of consciousness; 2) assessment of gaze and visual fields; 3) motor function; 4) sensation and neglect; 5) language; and 6) cerebellar function.[21] Most of the specific components of the NIHSS are included as parts of a standard neurologic examination routinely performed by emergency physicians on stroke patients.

The emergency physician must recognize the limitations of this scale. The NIHSS does not evaluate gait, nystagmus, or all cranial nerves, which are important to assess in brainstem or cerebellar strokes. When these stroke locations are suspected, perform a neurologic exam beyond the NIHSS. While a complete neurologic exam is neither feasible nor necessary in every stroke patient, a cerebellar stroke can be missed by not testing gait. (Of course, the gait examination should not be attempted in the patient with an obvious hemiparesis.) Nebulous documentation like "cranial nerves grossly intact" is not appropriate in the ED record, especially in the chart of a stroke patient.

Some level of obtundation may accompany any stroke, but coma, papilledema, or fever must prompt consideration of other diagnoses, such as tumor, infection, or metabolic abnormalities. The finding of a significantly depressed level of consciousness is rare in ischemic stroke. It is usually a sign of brainstem or bilateral cerebral hemispheric involvement, stroke-related seizure, hypoglycemia, or hypoxia. A sudden onset of decreased consciousness suggests a vertebrobasilar occlusion or a large intracerebral or subarachnoid hemorrhage.

Diagnostic Studies

Limited ED testing helps ascertain that a patient is suffering from an acute stroke. The greatest value of emergent laboratory testing is identifying a diagnosis other than stroke. Obtain a bedside glucose test in all patients suspected of stroke.[17] (Class of Evidence IIa; see also **Table 5** on page 5.) However, postpone other diagnostic studies that will unnecessarily delay the diagnosis of stroke or timely

administration of t-PA. (Studies necessary to determine candidacy for t-PA are discussed later in the article.)

Obtain an electrocardiogram (EKG). Recent MI may result in mural thrombi that can embolize to produce stroke. Recognize that T wave inversions may have a cerebral, and not a primary cardiac, etiology. T wave inversions occur in a substantial number of acute stroke patients, especially those with hemorrhage.[22,23] Alternatively, atrial fibrillation suggests a cardioembolic etiology.

Other than immediate bedside testing of glucose, a non-contrast head CT is the most urgent emergency diagnostic test to perform. While no clinical features reliably differentiate intracranial hemorrhage from ischemic stroke, a non-contrast head CT is sensitive to blood. Careful head CT interpretation will identify hemorrhagic strokes and help determine eligibility for t-PA. While a magnetic resonance image (MRI) is more sensitive than CT for small infarctions or posterior fossa lesions, a "stat MRI" is an oxymoron at most institutions. However, in some institutions, emergent diffusion / perfusion MRIs and / or magnetic resonance angiograms (MRAs), which can identify a cerebrovascular occlusion, are becoming increasingly available on an emergent basis. If such studies are immediately available and question exists as to what neuroimaging study to perform, seek the advice of a neurologist or neuroradiologist.

Since the brainstem and posterior fossa are best imaged with MRI, this test (virtually always combined with an MRA) is the most sensitive neuroimaging modality for vertebrobasilar attacks. Nonetheless, because CT scanners are more readily available, most patients receive a CT as their first neuroimaging study.

As time allows, the various diagnostic possibilities will dictate additional testing. Such investigations might include ethanol levels or other toxicological screens (especially cocaine). If vasculitis is suspected, an erythrocyte sedimentation rate or serologic testing for syphilis may ultimately be helpful. However, because such tests rarely influence ED treatment, defer esoterica to the internist or neurologist.

Table 5. Recommended ED Testing For Suspected Stroke Patients (Class IIb).

Bedside blood glucose*
CT of the brain without contrast*
Electrocardiogram*
Complete blood count*
Prothrombin time*
Partial thromboplastin time*
Serum electrolytes*
Indices of renal function (BUN and creatinine)*
Liver function tests
Arterial blood gas levels (if hypercarbia or an acid-base disturbance is suspected)**
Chest x-ray (determine if patient has stigmata of thoracic dissection or has suffered aspiration)
Complete cervical spine x-ray series. Obtain if the patient is comatose and C-spine injury cannot be excluded or if the patient has cervical spine pain and tenderness in the setting of associated trauma.

* Must be completed to determine candidacy for t-PA
** Arterial punctures should be avoided if t-PA is being considered

Source: Adams H, Brott T, Crowell R, et al. Guidelines for the management of patients with acute ischemic stroke. *Circulation* 1994;90(3):1588-1601.

Treatment

Blood Pressure Management

Hypertension is common in both ischemic and hemorrhagic strokes. Especially since the approval of t-PA for treating stroke, high blood pressure management in stroke has received considerable attention. Nonetheless, it must be emphasized that no well-designed scientific trials demonstrate how or when to manage hypertension in acute stroke. The American College of Emergency Physicians (ACEP) chose to only "agree with reservations" to the AAN / AHA (American Academy of Neurology / American Heart Association) guidelines on the use of thrombolytics in the treatment of acute ischemic stroke. One of several reasons for this reluctance was that the blood pressure management recommendations in those guidelines are inadequately supported by the literature.[24] Nonetheless, the American Heart Association's Stroke Council has published consensus-based guidelines for blood pressure management.[17,25-27] (See the Clinical Pathways on high blood pressure management on pages 11-12.) Acute *hypotension*, while relatively uncommon in stroke, requires prompt treatment, since it limits cerebral perfusion pressure and cerebral blood flow.

A common error in stroke management is an overly aggressive response to mild-to-moderate hypertension. Mild-to-moderate hypertension during stroke is both *common and neuroprotective;* the elevated pressure is often a physiologic response to ensure adequate brain perfusion. The majority of patients with mild-to-moderate hypertension require only serial blood pressure measurements and therapeutic restraint. A policy of "benign neglect" is safer for most patients than aggressive pressure control. Although high blood pressure can increase hemorrhage risk and worsen brain edema, acutely lowering blood pressure may decrease cerebral perfusion, especially if intracranial pressure is elevated.[28] (If the emergency physician feels compelled to give medications for mild hypertension, benzodiazepines are indicated—for the physician!) In patients with hemorrhagic strokes, however, the degree of hypertension does correlate with poor outcome.[29]

If patients with stroke have *severe* hypertension, therapy is required. The numeric definition of severe hypertension depends upon the type of stroke (ischemic vs. hemorrhagic) and upon whether thrombolytics are being considered. (See the Clinical Pathways on blood pressure on pages 11-12.) The management guidelines for high blood pressure consistently mention several agents. Labetalol is acclaimed as a superior agent for blood pressure control in acute stroke because it is easily titratable. Nonetheless, while intravenous labetalol is fast-acting, it has an elimination half-life of 5.5 hours after intravenous administration; therefore, administer it cautiously and consider initial dosing at 5 mg.[30,31] Sodium nitroprusside is often recom-

mended as a second-line agent for treating blood pressure in acute stroke. Like labetalol, it is fast-acting, but it is more easily titratable due to its short duration. Because sodium nitroprusside may precipitously lower blood pressure, it usually requires concurrent arterial pressure monitoring. Sublingual nifedipine should *not* be used, since it can cause unpredictable abrupt drops in blood pressure and worsen the stroke.[32,33]

Cerebral Edema

With the exception of cerebellar strokes, brain edema producing *early* clinical deterioration in stroke patients is an unusual phenomenon. When clinically significant edema of the cerebral hemispheres does occur, it is usually a complication of major intracranial artery occlusions or large multilobar infarction.[34] However, even in these situations edema peaks several days after stroke onset.

Several interventions are useful should acute treatment of edema be necessary. Treat any factors that can increase ICP, such as hypoxia, hypercarbia, and hyperthermia. If a spinal injury is not suspected, elevate the head of the bed about 30 degrees. While hyperventilation and osmotic diuretics are sometimes used for patients who are deteriorating, there are no trials demonstrating their efficacy in stroke. Hyperventilation, which reduces the pCO_2 by 5-10 mmHg, will promptly lower ICP by 25-30%.[35] Recent literature regarding severe head injury points out the dangers of hyperventilation. Hyperventilation can lead to vasoconstriction and worsen ischemia. Therefore, routine hyperventilation in severe head trauma, once recommended, is now condemned.[36]

Although furosemide and / or mannitol are often administered to control cerebral edema after stroke, no randomized trials support this indication. Finally, neither conventional nor large doses of corticosteroids improve outcome, but instead increase the rate of infections.[37-40]

Seizures

Seizures certainly occur after strokes, but the exact incidence is unknown.[17] Since there are no data about the value of prophylactic anticonvulsants after stroke, their routine use is not recommended. However, anticonvulsants are strongly recommended to prevent *recurrent* seizures after stroke.[17] (Class of Evidence: I) When seizures occur acutely after stroke, status epilepticus is rare, and anticonvulsant management parallels that for other conditions.

Anticoagulant Therapy

Unfractionated Heparin

The use of heparin in acute stroke is supported more by myth and anecdote than scientific study. Acute anticoagulant therapy, like thrombolytic therapy, is a double-edged sword. The risk of heparin-related hemorrhage must be weighed against any theoretical benefit. Heparin is *theoretically* beneficial—it *possibly* limits stroke progression in patients with an acute thrombotic infarction or *may* prevent acute, recurrent embolism in patients with a stroke of cardioembolic etiology.[41,42] However, the true efficacy of heparin for any of these conditions remains unproven. Some authorities argue that it should not be used even in cases of stroke due to atrial fibrillation because of the high risk of recurrent hemorrhagic stroke.[43]

The largest trial involving unfractionated heparin in acute stroke is methodologically flawed and primarily addressed the efficacy of aspirin in ischemic stroke patients.[44,45] In this study, heparin did not benefit victims of stroke. However, the trial involved subcutaneous heparin, which is not the typical route of administration in the United States. Therefore, it is difficult to draw any meaningful conclusions about intravenous heparin. However, when researchers pooled data from 16 randomized, controlled trials on stroke involving more than 22,000 patients, heparin showed no significant benefit in eventual outcome.[46]

Once the physician recognizes the lack of proven efficacy, other questions arise. In considering heparin therapy for a stroke patient without blood on the CT, the astute emergency physician must ask, "Can I predict whether or not this patient is likely to bleed if I start heparin?" Unfortunately, our ability to predict this is severely limited. Patient factors such as advanced age, elevated blood pressure, embolic etiology, and stroke size all affect hemorrhagic transformation of ischemic strokes. Heparin-related factors include the use of a bolus dose or the extent of coagulation based on the PTT.[47-50] While the presence of these features raises concern for hemorrhagic transformation, their predictive value remains unknown.

Despite the paucity of scientific evidence, emergency physicians and neurologists traditionally consider acute heparin therapy for several scenarios. Heparin is frequently initiated after cardioembolic strokes in the hope of preventing early recurrent strokes—despite the absence of data and even conflicting evidence.[51-53] "Stroke in evolution" or "progressing stroke" is an imprecise term that many emergency physicians view as the "unstable angina of the brain."[54,55] Based on small, flawed, and inconclusive studies, many emergency physicians and neurologists perceive this to be an appropriate indication for heparin, once intracerebral hemorrhage has been excluded on a CT.[56-59] However, the scientific data are unconvincing, and the decision to use heparin in this clinical situation is actually a matter of personal preference or local tradition.[60-63] Vertebrobasilar thrombosis is another area in which physicians consider heparin, despite the lack of studies supporting this indication. Heparin is anecdotally favored for patients suffering from carotid and vertebral artery dissection. In keeping with this theme of hopeful conjecture, heparin is sometimes administered for lacunar strokes, although there is no scientific support for this practice.[64]

Based on the uncertainty regarding the benefit of heparin for any given stroke scenario, start heparin only after discussion with the neurological consultant or the admitting physician. Also, recognize that they know no more about this matter than you do. If you do choose to give heparin to stroke patients, carefully assess them for contraindications to anticoagulation. Many physicians begin a heparin drip without a bolus dose in patients with stroke.[65]

In contradistinction to t-PA therapy for AMI, heparin is contraindicated within the first 24 hours following throm-

bolysis for acute ischemic stroke.

Low Molecular Weight Heparin (LMWH)

While the first published study evaluating LMWH in stroke was promising, subsequent studies have failed to show a benefit.[66,67] Based on the cumulative data, there is currently no indication for LMWH in acute stroke treatment. Beyond establishing clinical benefit, unanswered questions regarding LMWH include the safest and most efficacious route of administration, dose, duration of therapy, and level of anticoagulation.

Aspirin (ASA)

Surprisingly, the value of aspirin in the acute treatment of stroke had not been evaluated until recently. Two major clinical trials involving more than 40,000 patients investigated the effect of ASA given within 48 hours after ischemic stroke.[44,68] The ASA dose studied was 160-300 mg daily. The combined studies showed that ASA produces a small net benefit by reducing early recurrent strokes and the likelihood of death or dependency weeks or months later. To put the actual numbers in perspective, if early ASA treatment were given to 1 million new stroke patients a year—a fraction of the worldwide total with acute ischemic stroke—about 10,000 early deaths would be avoided without increase in disability.[68] Aspirin is inexpensive, *relatively* safe for most people, and there is no narrow time window to administration. However, because ASA is contraindicated within the first 24 hours after t-PA treatment, defer aspirin administration while t-PA use is being considered.

Other Interventions

Neuroprotective Agents

For several years, the pharmaceutical industry has been developing agents that interfere with virtually every step in the histochemical cascade leading to brain injury. Unfortunately, no agent has yet shown sufficient benefit to be approved for treatment of acute stroke. While a "stroke cocktail" is often foreseen, the ingredients of this potion are yet unknown.

Acute Surgical Treatment For Intracerebral Hemorrhage And Cerebellar Hemorrhage And Infarction

Intracerebral and cerebellar hemorrhages have higher morbidity and mortality rates than ischemic stroke.[69] The efficacy of emergency surgical treatment for intracerebral hemorrhages remains controversial, but the hematoma size and level of consciousness appear critical. Awake patients with small hematomas (<3 cm diameter) usually recover without surgery, while comatose patients with large hemorrhages (>6 cm diameter) usually do poorly, regardless of management.[27]

Cerebellar hemorrhage and infarction can rapidly compress the brainstem and halt respiratory function. Immediate neurosurgical consultation is especially important for patients with moderate-to-large hematomas in the posterior fossa. As with intracerebral hemorrhages, the size of the hemorrhage or infarction is crucial. While patients with small cerebellar hemorrhage or infarction (≤ 3 cm) can often be managed with observation, strongly consider surgical intervention for patients with large infarctions or hemorrhages, even if the patient is comatose.[27,70] This is common practice despite the fact that there are no data proving the value of early evacuation of deep intracranial hematomas.

Controversies/Cutting Edge

t-PA Treatment

The U.S. is the only country in which intravenous t-PA is approved for stroke treatment.[25,26] The majority of studies on the use of thrombolytics in stroke have demonstrated poor outcomes.[71-73] Despite approval by the Food and Drug Administration (FDA) almost three years ago, the treatment of ischemic stroke with t-PA remains highly controversial, within both emergency medicine and neurological circles.[74-80] Nonetheless, based on the available data, for select patients, t-PA treatment can be beneficial.[81] Even when a patient comes immediately to an ED after a stroke, the best-prepared system is challenged to accomplish all interventions before the three-hour mark.[82] One thing, however, is certain: Without some pre-established protocol for systematically and expeditiously evaluating a stroke patient for t-PA treatment, meeting the time and safety constraints of t-PA administration will be almost impossible.

The essential features of a t-PA treatment protocol are listed in **Table 6**, while the NIH time goals for phases of t-PA treatment are listed in **Table 7**. Following the sequence listed in the Clinical Pathway "Assessing Candidacy for t-PA Therapy" on page 10 and using the corresponding Tools cited therein can help ensure that all potential t-PA

Table 6. Essential Features Of An ED t-PA Stroke Treatment Protocol.

Rapid triage. Paramedics and nurses need guidelines to quickly identify a stroke patient.
Rapid alert—a "Code Stroke." The team response must be easily triggered when any potential stroke patient presents to the ED. May include an overhead page, a beeper system, or both.
A "stroke packet" that includes:
- Inclusion and exclusion criteria
- Standing orders—a checklist of needed studies and interventions
- The National Institutes of Health Stroke Scale (NIHSS)

t-PA stored in the ED
Prompt availability of a head CT
Prompt expert interpretation of a head CT

Table 7. National Institutes Of Health t-PA Treatment-Related Time Goals.

Door to emergency physician evaluation	10 minutes
Door to CT scanner	25 minutes
Door to expert CT interpretation	45 minutes
Door to t-PA	60 minutes
Door to ICU bed	2 to 3 hours

Source: Proceedings of a National Symposium on Rapid Identification and Treatment of Acute Stroke. The National Institute of Neurological Disorders and Stroke. Marler J, Winters P, Emr M, eds. 1997.

candidates get appropriate care. Nonetheless, even with an established protocol, some clinicians will be reluctant to consider t-PA therapy. Debate in this area persists for several reasons, including:

1) A perception by many "experts" of insufficient Level I data supporting t-PA's effectiveness.
2) Multiple negative international experiences with thrombolytics in stroke.
3) A therapeutic profile that pits an excellent neurologic outcome against lethal intracranial hemorrhage.
4) Persistent battles in the professional literature and at scientific meetings regarding the use of t-PA in stroke.
5) ACEP's stand to only "Agree with Reservations" to t-PA therapy.[24]
6) A pharmaceutical company with a history of aggressive marketing.

While a thorough review of all issues regarding this controversy is beyond the scope of this article, some points must be emphasized. Although the approval of t-PA treatment for stroke was based largely (some say solely) on the NINDS Stroke Study, two other randomized, placebo-controlled trials of t-PA have been performed: the ECASS and ECASS II trials.[81,83,84]

The NINDS trial treated patients within three hours of symptom onset with a dose of 0.9 mg/kg. It found a 15-20% absolute difference in normal or near normal neurologic function at three months in t-PA treated patients compared with placebo-treated patients.[79,83] However, symptomatic intracerebral hemorrhage during the first 36 hours after t-PA treatment was 10 times as likely: 6.4% compared to 0.6% in placebo-treated patients. Importantly, symptomatic hemorrhage correlated to both the presenting CT scan and the NIHSS. Hemorrhage was increased in several groups. Patients who showed edema or infarct on the initial CT scan had a symptomatic hemorrhage rate of 31%; for those with an NIHSS score greater than 20, the symptomatic hemorrhage rate was 17%.[20] Nonetheless, there was no statistical difference in three-month mortality rate between t-PA and placebo-treated patients. While small vessel strokes responded as well as large vessel strokes, and cardioembolic strokes tended to do better, this was not statistically significant.

Results of the other two t-PA studies did not show such sanguine results. The ECASS trial used a larger window for treatment (6 hours) and a larger t-PA dose (1.1 mg/kg) than the NINDS trial.[83] This trial emphasized the expertise needed for CT interpretation. Eight percent of patients given t-PA should have been excluded based on large areas of hypodensity on CT. When considering only patients who *should* have been enrolled in this study, there was significant improvement in global function at three months. Even so, parenchymal hematomas were significantly more common in t-PA treated patients, including those who did not violate protocol.[83]

The ECASS II trial included 800 patients and used the same dose of t-PA (0.9 mg/kg) used in NINDS, but kept the six-hour treatment window used in the first ECASS trial. While the study did show a significant improvement in the t-PA treatment group in functional independence at three months, many considered this to be a negative study because the primary outcome measurement did not show a significant difference between the treatment and control groups.[84] ECASS II emphasized the importance of early signs of infarction on the CT, particularly when they involved more than 33% of the middle cerebral artery (MCA) territory. Adverse results were frequent among patients with these CT changes.[84]

What of the subgroup who were treated in the same three-hour window used in the NINDS study? Only 20% of the patients in each of the alteplase and placebo groups in ECASS II were treated in 0-3 hours. Because of these small numbers, the authors could not draw any statistically meaningful conclusions based on a subgroup analysis.

Key Points

Although each major t-PA trial differed in design, all three trials reinforced three points:

1) t-PA should be administered within three hours of symptom onset.
2) The presence of CT signs of infarction is a crucial aspect in considering thrombolysis.
3) A lack of any early ischemic changes on CT carries the least risk for hemorrhagic transformation after t-PA administration.

A crucial issue regarding thrombolytic eligibility concerns not the patient, but the physician who reads the CT scan. The scan must be read by someone with "expertise" in interpreting head CTs. This is no time to obtain a "wet reading" from a radiologist most experienced at reading mammograms. Moreover, the average neurologist can sensitively interpret early infarct signs on head CTs in only 44% of patients with stroke, and few emergency physicians possess this skill.[85] In one study, researchers asked a variety of physicians to identify the presence of intracranial hemorrhage on a series of CT scans; only 16% of emergency physicians identified every hemorrhage.[85]

It is clearly optimal to have a neuroradiologist interpret the CT. While this standard may at first seem unattainable, recent technology allows transmission of high-resolution CT scans across the country. This "teleradiology" could provide high-level consultation to small EDs. The "expert" reader must unequivocally document that the CT "demonstrates no early changes of a recent major infarction, such as sulcal effacement, mass effect, edema, or possible hemorrhage."

Who Gets t-PA?

The emergency physician must screen for contraindications for thrombolysis. Chief among these are stroke onset greater than three hours and high-risk CT criteria associated with post-thrombolytic hemorrhage. An absence of any early ischemic changes carries the least risk for hemorrhagic transformation after t-PA administration,[20,86] while those with major infarctions are more likely to bleed. Most experts define a major infarction as a hypodensity in more than a third of the middle cerebral artery territory. In one study, patients with small areas of parenchymal hypoattenuation on the baseline CT (less than one-third of the middle

Continued on page 17

Clinical Pathway: Acute Stroke Patient ED Evaluation

Triage screen: Sudden onset of neurologic dysfunction referable to the brain?* — No → Triage as per standard operating procedure (Class IIb)

↓ Yes

Immediate triage to a monitored bed and physician/nurse evaluation:
- Ensure adequacy of airway, breathing, and ventilation
- Elevate HOB 30 degrees unless spinal injury is suspected
- Obtain VS and ensure BP readings at least every 15 minutes
- Measure glucose level at bedside
- Obtain CBC, PT, PTT, electrolytes, BUN, creatinine, and 12-lead EKG

(Class IIb)

↓

History and physical exam consistent with possible acute stroke? — No → Continue evaluation as indicated (Class IIb)

↓ Yes

Patient last known to be without symptoms 2 hours ago or less? — No → Continue stroke patient evaluation and treatment as feasible/indicated. Do not initiate Clinical Pathway: Assessing Candidacy For t-PA Therapy unless all resources available to deliver t-PA within one hour. (Class IIb)

↓ Yes

CT scanner, physician with expertise in stroke diagnosis, and physician with expertise in head CT interpretation promptly available? — No → Continue stroke patient evaluation and treatment as feasible/indicated. Do not initiate thrombolysis. (Class IIb)

↓ Yes

Go to Clinical Pathway: Assessing Candidacy For t-PA Therapy

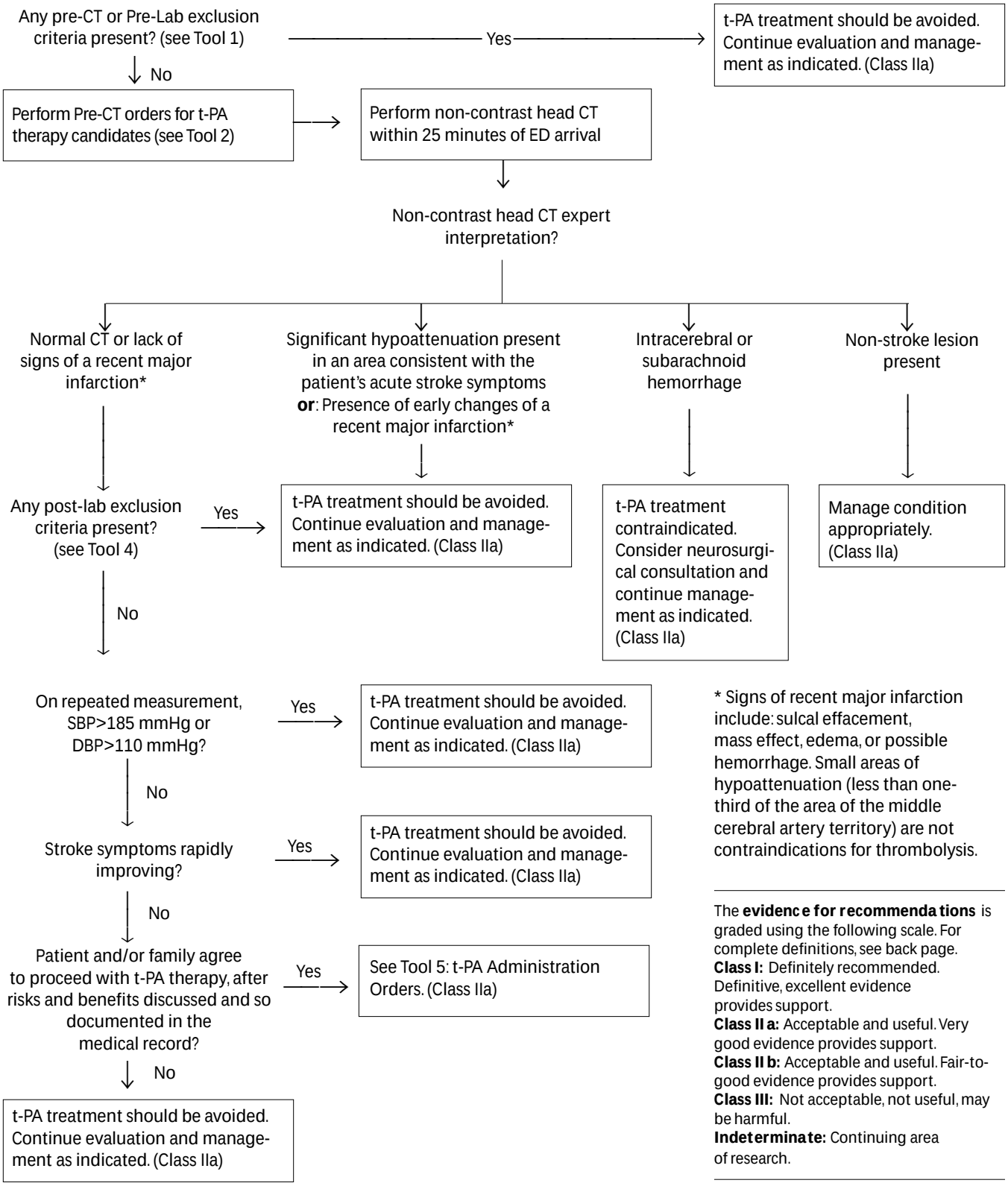
*Includes symptoms such as: weakness/paralysis/sensory loss or incoordination of one or more limbs, facial weakness/asymmetry, dysarthria, aphasia, ataxia/poor balance/clumsiness or difficulty walking, monocular/binocular visual field loss, double vision, vertigo, or alteration in consciousness.

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page.
Class I: Definitely recommended. Definitive, excellent evidence provides support.
Class IIa: Acceptable and useful. Very good evidence provides support.
Class IIb: Acceptable and useful. Fair-to-good evidence provides support.
Class III: Not acceptable, not useful, may be harmful.
Indeterminate: Continuing area of research.

Adapted from: Adams H, Brott T, Crowell R, et al. Guidelines for the management of patients with acute ischemic stroke. *Circulation* 1994;90(3):1588-1601; Adams HP, Brott TG, Furlan AJ, et al. Guidelines for thrombolytic therapy for acute stroke: A supplement to the guidelines for the management of patients with acute ischemic stroke. A statement for healthcare professionals from a special writing group of the stroke council, American Heart Association. *Circulation* 1996;94:1167-1174; Quality Standards Subcommittee of the American Academy of Neurology: Practice Advisory: Thrombolytic therapy for acute ischemic stroke—Summary Statement. *Neurology* 1996;47:835-839.

This clinical pathway is intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: Assessing Candidacy For t-PA Therapy

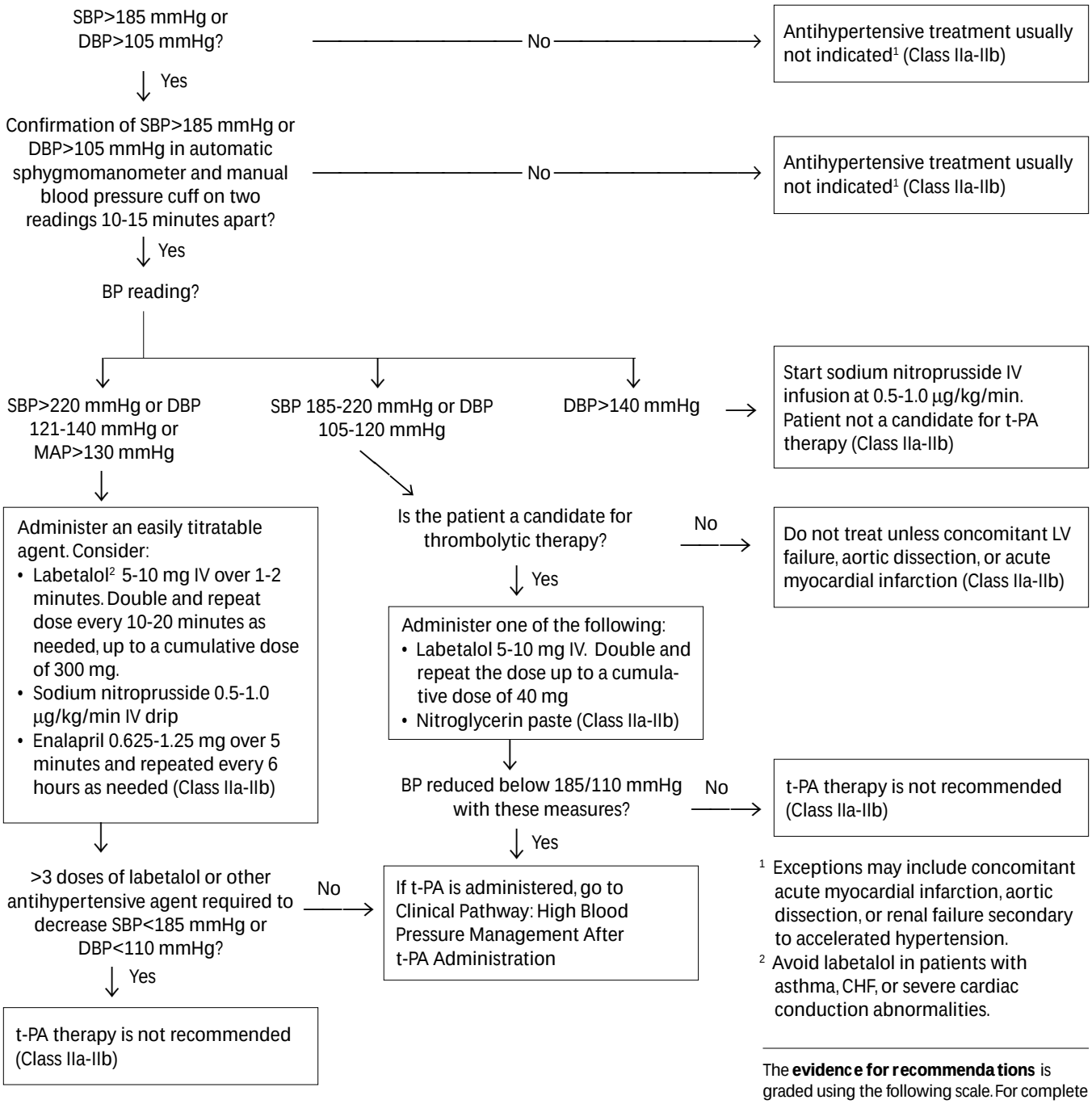


* Signs of recent major infarction include: sulcal effacement, mass effect, edema, or possible hemorrhage. Small areas of hypoattenuation (less than one-third of the area of the middle cerebral artery territory) are not contraindications for thrombolysis.

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page.
Class I: Definitely recommended. Definitive, excellent evidence provides support.
Class II a: Acceptable and useful. Very good evidence provides support.
Class II b: Acceptable and useful. Fair-to-good evidence provides support.
Class III: Not acceptable, not useful, may be harmful.
Indeterminate: Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: High Blood Pressure Management In Acute Stroke



[1] Exceptions may include concomitant acute myocardial infarction, aortic dissection, or renal failure secondary to accelerated hypertension.

[2] Avoid labetalol in patients with asthma, CHF, or severe cardiac conduction abnormalities.

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II a:** Acceptable and useful. Very good evidence provides support. **Class II b:** Acceptable and useful. Fair-to-good evidence provides support. **Class III:** Not acceptable, not useful, may be harmful. **Indeterminate:** Continuing area of research.

Adapted from: Adams H, Brott T, Crowell R, et al. Guidelines for the management of patients with acute ischemic stroke. *Circulation* 1994;90(3):1588-1601; Adams HP, Brott TG, Furlan AJ, et al. Guidelines for thrombolytic therapy for acute stroke: A supplement to the guidelines for the management of patients with acute ischemic stroke. A statement for healthcare professionals from a special writing group of the stroke council, American Heart Association. *Circulation* 1996;94:1167-1174; Quality Standards Subcommittee of the American Academy of Neurology: Practice Advisory: Thrombolytic therapy for acute ischemic stroke—Summary Statement. *Neurology* 1996;47:835-839; Consensus Panel of the National Stroke Association. Stroke: The first hours: Emergency evaluation and treatment. *Stroke Clinical Updates* 1997;1-14.

This clinical pathway is intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: High Blood Pressure Management After t-PA Administration

Monitor BP after starting t-PA treatment:
- Every 15 minutes for 2 hours, then
- Every 30 minutes for 6 hours

↓

BP reading?

DBP >140 mmHg	SBP > 230 mmHg and/or DBP 121-140 mmHg	SBP 180-230 mmHg and/or DBP 105-120 mmHg on two readings 5-10 minutes apart
↓	↓	↓
Start an IV infusion of sodium nitroprusside (begin drip at 0.25-0.5 meq/kg/minute and titrate. Usual dose ranges from 0.5-10 μg/kg/min) (Class IIb)	• Labetalol 10 mg IV over 1-2 minutes. The dose may be repeated and/or doubled every 10 minutes up to 150 mg. Alternatively, following the first IV bolus, an IV infusion of 2-8 mg/min may be initiated and continued until the desired BP is reached. • If satisfactory response is not achieved, use sodium nitroprusside (Class IIb)	

Clinical Pathway: Management Of Suspected Intracranial Hemorrhage After t-PA Administration

Suspicion of intracranial hemorrhage symptoms, such as neurological deterioration, new headache[1], acute hypertension, nausea, or vomiting?

No → Continue monitoring BP, level of consciousness, and motor function of the arms and legs every 15 minutes x 2 hours, then every 30 minutes x 6 hours following t-PA administration (Class IIb)

↓ Yes

- Discontinue t-PA infusion if intracranial hemorrhage is the presumed diagnosis[2]
- Immediate head CT scan
- Draw blood and measure CBC, PT, PTT, and fibrinogen
- Prepare to give 6-8u cryoprecipitate[3,4]
- Prepare to give 6-8u platelets if platelets are low or if the patient has been on antiplatelet therapy[4] (Class IIb)

↓

Intracranial hemorrhage present on CT scan?

No → Resume t-PA if t-PA has been halted <15 minutes and no other contraindications to t-PA therapy exist (Class IIb)

↓ Yes

- Evaluate laboratory results: fibrinogen, platelets, PT, PTT
- Consider alerting/consulting a neurosurgeon[5]
- Consider alerting/consulting a hematologist[5]
- Consider obtaining a delayed CT scan to assess size change of bleed
- Plan surgical and/or medical therapy based on a consensus decision

(Class IIb)

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II a:** Acceptable and useful. Very good evidence provides support. **Class II b:** Acceptable and useful. Fair-to-good evidence provides support. **Class III:** Not acceptable, not useful, may be harmful. **Indeterminate:** Continuing area of research.

[1] A mild headache following t-PA administration is not unusual.
[2] t-PA can be resumed only if halted for <15 minutes.
[3] FFP with fibrinogen is an alternative if cryoprecipitate is not available.
[4] Preparations for giving platelets and fibrinogen can be initiated at the first suspicion of hemorrhage so that they will be ready if needed.
[5] A plan for obtaining hematological and neurosurgical advice is highly recommended.

Adapted from: Adams HP, Brott TG, Furlan AJ, et al. *Circulation* 1996;94:1167-1174; Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 1996;47:835-839.

These clinical pathways are intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with these pathways does not represent a breach of the standard of care.

Tool 1. Pre-CT And Pre-Laboratory t-PA *Exclusion* Criteria Checklist

Any "Yes" answer excludes t-PA

Age < 18	( ) Yes	( ) No
Time of stroke symptom onset greater than 2 hours prior to triage	( ) Yes	( ) No
Patient has only minor stroke symptoms (ataxia alone, sensory loss alone, dysarthria alone, minimal weakness)	( ) Yes	( ) No
Patient has a clinical presentation that suggests subarachnoid hemorrhage	( ) Yes	( ) No
Patient had a seizure at the onset of the stroke	( ) Yes	( ) No
Patient is a female known or suspected to be pregnant	( ) Yes	( ) No
Patient has the presence of open wounds, active internal bleeding, or potential bleeding sites that may not be easily controlled should t-PA be administered	( ) Yes	( ) No
Patient has a clinical presentation consistent with pericarditis	( ) Yes	( ) No
Patient has a history of subacute bacterial endocarditis	( ) Yes	( ) No
Patient has history of an intracranial hemorrhage	( ) Yes	( ) No
Patient has a known intracranial aneurysm, neoplasm, or AVM	( ) Yes	( ) No
Within the past three months, the patient has had:		
Intracranial surgery	( ) Yes	( ) No
Previous stroke	( ) Yes	( ) No
Head trauma	( ) Yes	( ) No
Within the past three weeks, the patient has had:		
Gastrointestinal hemorrhage	( ) Yes	( ) No
Urinary hemorrhage	( ) Yes	( ) No
Within the past 14 days, the patient has had surgery or major trauma excluding head trauma	( ) Yes	( ) No
Within the past seven days, the patient has had a:		
Lumbar puncture	( ) Yes	( ) No
Arterial puncture at non-compressible site	( ) Yes	( ) No
Patient requires aggressive blood pressure treatment to maintain systolic ≤ 185 mmHg and diastolic ≤ 110 mmHg	( ) Yes	( ) No

Adapted from: Adams HP, Brott TG, Furlan AJ, et al. Guidelines for thrombolytic therapy for acute stroke: A supplement to the guidelines for the management of patients with acute ischemic stroke. A statement for healthcare professionals from a special writing group of the stroke council, American Heart Association. *Circulation* 1996;94:1167-1174; Quality Standards Subcommittee of the American Academy of Neurology. Practice Advisory: Thrombolytic therapy for acute ischemic stroke—Summary Statement. *Neurology* 1996;47:835-839; The NINDS rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333(24):1581-1587.

Tool 2. Pre-CT Orders For t-PA Therapy Candidates

1. Document and verify time consistency of stroke symptom time onset
2. Verify no pre-CT and pre-lab t-PA *exclusion* criteria noted on checklist (see Tool 1)
3. Notify CT scanning area that acute stroke patient is in the ED and will require prompt performance of non-contrast head CT and prompt expert interpretation
4. Notify hospital laboratory that patient's CBC, PT/PTT, electrolytes, and urinalysis will need to be immediately processed
5. Notify appropriate ICU that an t-PA therapy candidate is in the ED
6. Consult on-call neurologist
7. Verify BP concordance initially in both arms, then check blood pressure at least every 15 minutes. Immediately notify physician for BP >185 mmHg systolic or BP >110 mmHg diastolic.
8. Immediately obtain and process CBC, PT/PTT, electrolytes, and urinalysis
9. Immediately perform 12-lead EKG
10. No aspirin or heparin administration in the ED
11. Insert IV with NS at 50cc per hour in one arm and 18g prn adaptor in opposite arm
12. Continuous pulse oximetry
13. Perform and document NIH Stroke Scale (see Tool 3)
14. Determine patient's weight by asking the patient or a family member. If accurate patient weight is unknown and estimated weight is less than 220 pounds, weigh the patient if feasible.
15. Immediately perform a non-contrast head CT when all of the above are completed.
16. Check level of consciousness, motor function of arms and legs, and speech every 15 minutes while in the ED. Immediately notify physician if any change in neurological status.
17. Identify and contact the patient's primary care physician to inform him or her of the patient's condition and the consideration for administering t-PA.

Date: _____

Time: _____

Signature: _____

Tool 3. NIH Stroke Scale

1a. Level of Consciousness:
The physician must choose a response, even if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, or orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.

- **0 =** Alert; keenly responsive
- **1 =** Not alert, but arousable by minor stimulation to obey, answer, or respond
- **2 =** Not alert, requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped)
- **3 =** Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, areflexic

Score: ☐

1b. LOC Question:
The patient is asked the *month* and his or her *age*. The answer must be correct—there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the question will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or nonverbal cues.

- **0 =** Answers both questions correctly
- **1 =** Answers one question correctly
- **2 =** Answers neither question correctly

Score: ☐

1c. LOC Commands:
The patient is asked to *open and close the eyes* and then to *grip and release the nonparetic hand*. Substitute another one-step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him (pantomime) and score the result (i.e., follows none, one, or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.

- **0 =** Performs both tasks correctly
- **1 =** Performs one task correctly
- **2 =** Performs neither task correctly

Score: ☐

2. Best Gaze:
Only horizontal eye movements are tested. Voluntary or reflexive (oculocephalic) eye movements will score but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV, or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements and choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.

- **0 =** Normal
- **1 =** Partial gaze palsy. This score is given when gaze is abnormal in one or both eyes, but where forced deviation or total gaze paresis are not present
- **2 =** Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver

Score: ☐

3. Visual
Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat as appropriate. Patient must be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1 and the results are used to answer question 11.

- **0 =** No visual loss
- **1 =** Partial hemianopia
- **2 =** Complete hemianopia
- **3 =** Bilateral hemianopia (blind including cortical blindness)

Score: ☐

4. Facial Palsy:
Ask, or use pantomime to encourage the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape, or other physical barrier obscures the face, these should be removed to the extent possible.

- **0 =** Normal symmetrical movement
- **1 =** Minor paralysis (flattened nasolabial fold, asymmetry on smiling)
- **2 =** Partial paralysis (total or near total paralysis of lower face)
- **3 =** Complete paralysis of one or both sides (absent of facial movement in the upper and lower face)

Score: ☐

5 and 6. Motor Arm and Leg:
The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine) and the leg 30 degrees (always tested supine). Drift is scored if the arm falls before 10 seconds or the leg before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime but no noxious stimulation. Each limb is tested in turn, beginning with the nonparetic arm. Only in the case of amputation or joint fusion at the shoulder or hip is no score assigned, and the examiner must clearly write the explanation for not scoring.

- **0 =** No drift, limb holds 90 (or 45) degrees for full 10 seconds
- **1 =** Drift; limb holds 90 (or 45) degrees but drifts down before full 10 seconds; does not hit bed or other support
- **2 =** Some effort against gravity, limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity
- **3 =** No effort against gravity, limb falls
- **4 =** No movement
- **or** Amputation, joint fusion—explain:

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5a. Left Arm **Score:** ☐

5b. Right Arm **Score:** ☐

0 = No drift, leg holds 30 degrees position for full 5 seconds
1 = Drift, leg falls by the end of the 5-second period but does not hit bed
2 = Some effort against gravity; leg falls to bed by 5 seconds, but has some effort against gravity
3 = No effort against gravity, leg falls to bed immediately
4 = No movement
or Amputation, joint fusion—explain:
_____

6a. Left Leg **Score:** ☐

6b. Right Leg **Score:** ☐

7. Limb Ataxia:
This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion is no score assigned, and the examiner must clearly write an explanation for not scoring. In case of blindness, test by touching nose from extended arm position.
0 = Absent
1 = Present in one limb
2 = Present in two limbs

Score: ☐

If present, is ataxia in [*circle number(s)*]:*
Right arm
1 = Yes
2 = No
or Amputation, joint fusion—explain:
_____
Left arm
1 = Yes
2 = No
or Amputation, joint fusion—explain:
_____
Right leg
1 = Yes
2 = No
or Amputation, joint fusion—explain:
_____
Left leg
1 = Yes
2 = No
or Amputation, joint fusion—explain:
_____

8. Sensory
Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal, and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss. A score of 2, "severe or total," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will therefore probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in coma (item 1a = 3) are arbitrarily given a 2 on this item.
0 = Normal; no sensory loss
1 = Mild-to-moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick but patient is aware that he or she is being touched
2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg

Score: ☐

9. Best Language:
A great deal of information about comprehension will be obtained during the preceding sections of the examination. The patient is asked to describe what is happening in a drawing, to name items such as a pen or a watch, and to read from a list of simple sentences. Comprehension is judged from responses here as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in coma (question 1a = 3) will arbitrarily score 3 on this item. The examiner must choose a score in the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one step commands.
0 = No aphasia, normal
1 = Mild-to-moderate aphasia; some obvious loss of fluency or facility of comprehension, however, makes conversation about provided material difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card from patient's response.
2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response.
3 = Mute, global aphasia; no usable speech or auditory comprehension.

Score: ☐

10. Dysarthria:
If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from a list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barrier to producing speech is no score assigned, and the examiner must clearly write an explanation for not scoring. Do not tell the patient why he or she is being tested.
0 = Normal
1 = Mild to moderate; patient slurs at least some words and, at worst, can be understood with some difficulty
2 = Severe; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric
or Intubated or other physical barrier
Explain:_____

Score: ☐

11. Extinction and Inattention (formerly Neglect):
Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosognosia may also be taken as evidence of neglect. Since the abnormality is scored only if present, the item is never untestable.
0 = No abnormality
1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities

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2 = Profound hemi-inattention or hemi-inattention to more than one modality. Does not recognize own hand or orients to only one side of space.

Score: ☐

Examiner's Signature: _____

Time: _____

Date: _____

TOTAL SCORE:

_____

*For limb ataxia (#7), codes for affected limbs should not be added to the total.

Adapted from and reprinted in part with permission: National Institute of Neurologic Disorders and Stroke t-PA Study Group; Lyden P, Brott T, Tilley B, et al. Improved reliability of the NIH Stroke Scale using video training. *Stroke* 1994;25:2220-2226.

Tool 4. Post-Laboratory And Post-CT *Exclusion* Criteria

Any "Yes" answer is a contraindication to t-PA

Patient has abnormal blood glucose (<50 or >400 mg/dl)	( ) Yes	( ) No
Platelet count <100,000	( ) Yes	( ) No
Prothrombin time >15 or INR > 1.7	( ) Yes	( ) No
Patient has received heparin within 48 hours and has an elevated partial thromboplastin time (greater than upper limit of normal for laboratory)	( ) Yes	( ) No
Presence of early changes of a recent major infarction on CT (signs of recent major infarction include: sulcal effacement, mass effect, edema, or possible hemorrhage)	( ) Yes	( ) No

Adapted from: Adams HP, Brott TG, Furlan AJ, et al. Guidelines for thrombolytic therapy for acute stroke: A supplement to the guidelines for the management of patients with acute ischemic stroke. A statement for healthcare professionals from a special writing group of the stroke council, American Heart Association. *Circulation* 1996;94:1167-1174; Quality Standards Subcommittee of the American Academy of Neurology. Practice Advisory: Thrombolytic therapy for acute ischemic stroke—Summary Statement. *Neurology* 1996;47:835-839; The NINDS rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333(24):1581-1587.

Tool 5. t-PA Administration Orders

1. Review all exclusion criteria (see Tools 1 and 4 as well as the Clinical Pathway "Assessing Candidacy For t-PA Therapy"). If patient meets t-PA eligibility criteria, proceed with the following orders.
2. No aspirin or heparin to be administered in the ED.
3. Begin administration of t-PA no longer than three hours after the onset of symptoms, to be administered at 0.9 mg/kg dosage in 1:1 dilution, with a maximum dose limitation of 90 mg. Administer as a 10% initial bolus over 1-2 minutes, followed by the remainder infused over 60 minutes.
4. Monitor blood pressure every 15 minutes for two hours after starting the infusion.

   *If for two readings 5-10 minutes apart, the systolic blood pressure is between 180-230 mmHg **or** the diastolic pressure is in the range 105-120 mmHg:*
   - Give labetalol 10 mg intravenously over 1-2 minutes. The dose may be repeated and/or doubled every 10-20 minutes up to 150 mg. Monitor blood pressure at least every 15 minutes during treatment. Observe for hypotension.

   *If the systolic blood pressure is greater than 230 mmHg **or** the diastolic pressure is in the range 121-140 mmHg:*
   - Give labetalol 10 mg intravenously over 1-2 minutes. The dose may be repeated and/or doubled every 10 minutes up to 150 mg. If satisfactory response is not obtained, use nitroprusside. Monitor blood pressure at least every 15 minutes during treatment. Observe for hypotension. If no satisfactory response, infuse sodium nitroprusside (0.5 to 10 mcg/kg/minute).

   If the diastolic blood pressure is greater than 140 mmHg:
   - Infuse sodium nitroprusside (0.5 to 10 mcg/kg/minute). Monitor blood pressure at least every 15 minutes during treatment. Observe for hypotension.

Date: _____ **Time:** _____ **Signature:** _____

Adapted from: Adams HP, Brott TG, Furlan AJ, et al. Guidelines for thrombolytic therapy for acute stroke: A supplement to the guidelines for the management of patients with acute ischemic stroke. A statement for healthcare professionals from a special writing group of the stroke council, American Heart Association. *Circulation* 1996;94:1167-1174; Quality Standards Subcommittee of the American Academy of Neurology. Practice Advisory: Thrombolytic therapy for acute ischemic stroke—Summary Statement. *Neurology* 1996;47:835-839.

Continued from page 8

cerebral artery territory) had the greatest benefit of all subgroups that received t-PA.[87]

Based on the NINDS data, both the treating physician and the patient need to understand the risks and benefits of treatment in context.[81] Measuring the NIHSS score is essential, since it will not only aid in quantifying the neurologic exam, but will also help assess the risk of symptomatic intracranial hemorrhage. In the NINDS t-PA trial, patients with an NIHSS score less than 10 had a symptomatic hemorrhage rate of 3%. Those with an NIHSS score 20 or greater suffered a symptomatic hemorrhage rate of 17%.[20]

The correlation of stroke scores and ultimate outcomes, regardless of thrombolytics, raises some important concerns. Patients with minor strokes (<6 on the NIHSS) generally do well with conservative therapy, and the risk of t-PA-associated bleeding, even at 3%, may be unacceptably high to some patients.

On the other hand, nearly one-fifth of patients with major strokes (>20 on the NIHSS) may sustain severe intracranial hemorrhage with t-PA. An NIHSS of 22 is not an absolute contraindication for lytic therapy. In NINDS, although an NIHSS greater than 20 was associated with an increased risk of intracranial hemorrhage, as a population, patients with an NIHSS greater than 20 treated with t-PA had a better overall outcome at three months compared to patients with an NIHSS greater than 20 who received placebo.[81,88] If a patient and his or her family understand the increased risk of bleeding, but still want aggressive treatment, the physician may elect to give thrombolytics (although the consent form should clearly emphasize the likelihood of death or permanent disability).

While patients with moderate to severe disability (6-20) would seem to be the best candidates for thrombolysis, the decision to use lytics must involve the patient and / or family. The decision to ultimately offer t-PA therapy to any given patient must combine a clinical decision by the physician and a personal choice by the patient or legal surrogate.

Patients who develop a stroke while taking warfarin may still receive t-PA under certain circumstances. While thrombolytics are contraindicated if the PT is greater than 15 or INR greater than 1.7, some patients taking warfarin may have sub-therapeutic levels, thus making them candidates for lysis. If a patient is on warfarin, wait for the results of the coagulation profile before deciding to use thrombolytics. In patients not on anticoagulants, and without known liver disease, it is probably safe to treat with thrombolytics if the three-hour window is approaching and the lab has not yet completed the tests.

Finally, do not employ t-PA therapy unless facilities or arrangements to manage complications are in place. While an on-call neurosurgeon is not imperative, the stroke protocol should provide options for neurosurgical assistance in case of an intracerebral hemorrhage.

External Validity

There is a big difference between efficacy and effectiveness. Efficacy of a particular therapy is measured by performance in carefully controlled clinical trial, often at a large research institution. Effectiveness is performance in actual practice, often in a community ED located in Anywhere, USA. At least one study shows that t-PA therapy can be effective in a community hospital with outcomes and complications comparable to those of multicenter trials.[89] However, success depends upon preparedness and teamwork throughout the prehospital and hospital system.

Intra-arterial Thrombolysis

No data yet proves that intra-arterial thrombolytic therapy can improve outcome in stroke patients. However, the results of a randomized, double-blind, placebo-controlled trial of pro-urokinase in stroke is forthcoming. Its publication should provide some Level I evidence in this area.[90] Although intra-arterial thrombolysis remains investigational, it has been used successfully up to 13 hours after symptom onset, particularly for patients with acute vertebrobasilar artery occlusion.[91-94] This expanded time window may become an important consideration in patients who present hours after stroke onset. Other cutting-edge intra-arterial techniques include catheter-based mechanical clot disruption combined with a lytic agent.

Medicolegal Issues

The public may have unrealistic expectations of these "clot busters." The lay press emphasizes the benefits and downplays the risks of thrombolytics in stroke. The FDA approval of t-PA created not just a new treatment option, but also new malpractice liability. Stroke patients often suffer catastrophic neurologic injury, against the expectations of a family who has read about "the new miracle drug." Add the complexities and time constraints of t-PA treatment to a bad outcome, and what emerges is the substance of a plaintiff lawyer's dream.

Establishing good patient and family rapport and mentally preparing patients and families for a poor outcome are important steps in avoiding lawsuits. In case of a bad outcome, patients and families will be less likely to sue if they fully understood the risks of t-PA therapy. Documentation that they understood these risks will bolster the physician's defense in case of litigation.

Ultimately, emergency physicians and neurologists who profess expertise in stroke will determine the legal standard of care regarding t-PA in stroke. Proponents of t-PA will espouse the findings of the NINDS trial and the FDA's, AHA's, and AAN's endorsements. Those against t-PA use will rely on the findings of ECASS, and perhaps ECASS II, and will be sure to reference ACEP's "Agree with Reservations" stand on t-PA therapy as evidence that t-PA clearly should not be the standard of care. Finally, as the literature already demonstrates, failure to follow reasonable treatment protocols increases liability.[95,96] For this reason, any protocol established for an individual ED must be routinely achievable. The policy should include few "standards" for care, but many "guidelines." Recognize that in the case of a lawsuit, every ED action and delay will be scrutinized.

Disposition

Many physicians believe that any patient diagnosed with an acute stroke should be admitted to a bed with continuous cardiac monitoring. Creation of a dedicated "stroke unit" is a recent trend of larger hospitals that have a sufficient volume of stroke admissions to justify such a specialized unit. These specialized care units may foster the multidisciplinary interventions required by stroke patients and can ultimately decrease the length of hospital stay.[14,97,98] Standard consultants may include neurology, occupational therapy, physical therapy, and speech pathology. By using clinical pathways or other forms of structured care, stroke units can reduce mortality and disability.[99]

Some experts envision and advocate the creation of "stroke centers," which are hospitals identified as having particular expertise and resources for the treatment of stroke.[100] Selection of such centers would occur through a verification process analogous to trauma center designation, and local government might direct paramedics to transport possible stroke victims to these centers. The theoretical benefit of this hierarchical structure includes a referral network that would provide optimal care. Telemedicine or teleradiography could augment this expertise.[101] It is not clear, however, that the designation of stroke centers would accomplish these stated goals. The massive bureaucracy this system would demand might squander resources better spent on educating healthcare providers on the optimal treatment of stroke.

Transient Ischemic Attacks

One of the great challenges in emergency medicine regards the proper disposition of patients presumed to have a transient ischemic attack (TIA). The ED management of such patients remains controversial, primarily due to the lack of well-designed, prospective studies. There is limited scientific evidence to determine either the need for hospitalization or the pace of diagnostic evaluation.

The overall estimated risk of stroke for patients with TIA is 4-8% by one month, 12-13% by one year, and 24-29% by five years.[102] However, the emergency physician is most concerned with the incidence of stroke within several days

Ten Excuses That Won't Work In Court

1. "But the 'wet reading' of the CT was 'normal.'"
The wet reading may certainly be the "final reading" as far as the patient is concerned. Whoever is responsible for reading the CT must be an expert in detecting contraindications to thrombolysis in stroke. If it is any consolation, the "wet" radiologist will be your co-defendant.

2. "The patient thought his symptoms started 'about' two hours before coming to the hospital."
The patient or family must be "sure" the symptoms began less than two hours before presentation. If t-PA is given more than three hours after onset, a bad outcome is likely.

3. "I always tell the paramedics and nurses to give everyone with a systolic blood pressure greater than 160 mmHg 10 mg of nifedipine."
Change your practice. There are numerous articles warning against this intervention. Although the numerator is unknown (how many patients get nifedipine without developing problems), acute treatment of mild-to-moderate hypertension serves no useful purpose and can worsen the stroke by decreasing cerebral perfusion pressure. Only patients with hemorrhagic stroke need strict attention to blood pressure control, and Procardia is *not* the drug to use.

4. "But I always write 'grossly intact' and 'WNL' on my charts."
"Grossly" in this case implies "grossly negligent," while "WNL" stands for "We Never Looked." Document a careful neurologic exam, and if anticipating thrombolysis, use the NIHSS.

5. "I start all patients who aren't candidates for t-PA on heparin."
You must subscribe to JAME (*Journal of Absent Medical Evidence*). Pooled data from 16 randomized controlled trials on stroke involving more than 22,000 patients show no benefit to heparin and clear risk.

6. "In the European studies, they also gave t-PA up to six hours after symptom onset."
True. But the patients did worse with the lytics than they did with placebo.

7. "When I see edema on the head CT, I always give steroids."
Neither conventional nor large doses of corticosteroids improve outcome, but instead increase the rate of infections.

8. "The radiologist said he had just a small cerebellar stroke on his CT."
Then why didn't you consult a neurosurgeon? Patients with cerebellar strokes can decompensate quickly because of the limited space in the posterior fossa and the proximity of the brainstem. While a neurosurgeon will not always operate on patients with cerebellar stroke, allow them the opportunity to decline.

9. "When we called the time from door to CT of 15 minutes on our clinical pathway a 'standard,' we really meant it to be a 'guideline.'"
Juries and experts expect a standard to be followed. Make sure that policies are reasonable and that the goals can be routinely achieved. Failure to meet one's own rules results in being hoisted by your own petard in court—always a painful experience.

10. "But no one ever told me he was a diabetic!"
The chair of neurology at Harvard cannot tell the difference between an ischemic stroke and hemiplegia from a low glucose—unless he orders a bedside glucose test. Avoid the frantic foot-race to CT scan prompted by a low blood sugar on the chemistry panel; measure the glucose at the beside in all stroke patients.

of a TIA and whether or not hospitalization will decrease this risk. These numbers remain obscure.

Studies comparing carotid endarterectomy with medical therapy show that surgery will benefit patients with recent hemispheric strokes or amaurosis fugax if they have an ipsilateral high-grade stenosis (70-99%) of the internal carotid artery. Carotid endarterectomy reduces risk of future strokes in these patients by about 10% over *a two-year period*.[103] Those with less significant stenosis experience a correspondingly lower benefit to the procedure, and those with stenosis of less than 50% do not benefit at all.[104]

These data do not argue for "emergency" endarterectomy. More to the point, if a patient is admitted for TIA on a Monday, and has a positive carotid ultrasound on Tuesday, what is the likelihood they will undergo carotid surgery by Wednesday? Answer: little, if any. While an expeditious work-up and surgical intervention may be indicated for a select population, the appropriate time frame for this intervention has never been established.

The best argument for hospitalization for TIAs rests with the potential for immediate thrombolysis in case of a subsequent stroke. To make this argument, we must determine the risk of stroke during the expected hospitalization for a TIA. If the risk of stroke following TIA is highest in the first month, should the patient anticipate a 30-day stay?

No firm data support either the efficacy of hospitalization or acute anticoagulation of patients with a TIA. However, from a risk-management standpoint, several specific clinical scenarios are considered high-risk for recurrence of TIA or early stroke. These include:

1) Patients known to have a high-grade stenosis in the vascular territory corresponding to the symptoms
2) Patients already on antiplatelet therapy
3) A cardioembolic cause of the TIA
4) Attacks occurring with increasing frequency
5) Patients with more than four TIAs within a two-week period
6) TIAs associated with a severe transient deficit

Pooled analyses from several large, randomized trials show that warfarin reduces stroke occurrence by 68% (95% CI, 50-79%) in patients with nonvalvular atrial fibrillation.[105,106] However, this literature did not examine the need for acute hospitalization and heparinization before achieving therapeutic levels of warfarin.

If heparinization and hospitalization are not undertaken, consider starting the patient on an agent that inhibits platelet aggregation, such as aspirin, ticlopidine, or clopidogrel. Nonetheless, while these medications abate recurrent TIA and stroke when taken *chronically*, there is no proof that these agents influence short-term outcomes.[107-110]

Investigators have studied a broad range of ASA doses, but a dose of 325 mg / day is likely to produce an almost immediate effect on platelets, depending on the rate of absorption.[111,112] Ticlopidine's full effect on inhibiting platelet aggregation may take several days, but dosed at 250-mg bid, it is as effective as ASA in reducing stroke. Clopidogrel, given at 75 mg / day, is sometimes favored over ticlopidine because it does not cause neutropenia, thrombotic thrombocytopenic purpura, and diarrhea sometimes associated with ticlopidine.[31]

If a patient with a TIA is sent home, clearly document and verbally emphasize the most essential discharge instruction—*return immediately* for any weakness, slurred speech, or other stroke symptom. The patient and family

Cost-Effective Strategies For Stroke Management

1. Patients with a sensory deficit only (by history or physical examination) may not require urgent CT scanning.
   Risk Management Caveat: Patients at high risk for stroke need a detailed history, a careful neurologic examination, and follow-up.

2. Not all patients with a resolved TIA require admission. Early follow-up and an expedited outpatient evaluation may suffice.
   Risk Management Caveat: Patients who are sent home must be told to return *immediately* for any stroke-like symptoms. Screen for high-risk TIAs (see the section on page 18). Warn the patient and their family that it is possible to have a stroke shortly after discharge but that hospitalization will not prevent its occurrence. Before discharging the patient, discuss outpatient evaluation with the patient's physician and document scrupulously. Some hospitals have established an ED-based "stroke center" similar in concept to a chest pain center. Here patients receive an expedited work-up for TIAs, including carotid Dopplers and echocardiography.

3. Not all patients with stroke require admission. Surprisingly, patients may present to the ED days after an acute stroke at the urging of their family. Hospitalization may offer little in this case.
   Risk Management Caveat: Determine beyond any reasonable doubt that the stroke is complete and the time from onset is measured in days and not hours. See the preceding caveats regarding TIA and discharge home.

4. Aspirin is inexpensive, relatively safe, and may be used in many patients with stroke or TIA without regard to a narrow time window.
   Risk Management Caveat: Do not give aspirin to patients who are candidates for t-PA. Always screen for contraindications such as allergy, a history of prior GI bleeds, and concurrent medications that can produce significant drug interactions (such as Coumadin).

5. Not all patients with altered mental status require CT. Patients with confusion and a non-focal neurologic examination may suffer from a metabolic or infectious problem. A bedside test for glucose and rapid assessment of serum sodium is more cost-effective (and useful) in some patients than a CT.
   Risk Management Caveat: Patients who have fever, headache, or stiff neck in conjunction with altered mental status may suffer a life threat from meningitis or a CNS bleed. Such patients may require intravenous antibiotics or emergent neuroimaging.

must realize that if the patient develops a subsequent stroke, rapid treatment in the ED may improve outcome. For patients with a resolved TIA who are not admitted to the hospital, performing the first phase of a stepwise TIA evaluation is reasonable.[103,113] (See **Table 8**.)

Conclusion

Despite controversy surrounding particular issues, in general, emergency physicians should embrace the paradigm shift in acute stroke care. If patients quickly seek

Table 8. Stepwise Diagnostic Evaluation For Patients With A Transient Ischemic Attack.

Initial evaluation—initiated by ED physician
The National Institutes of Health Stroke Scale (NIHSS)
Non-contrast head CT
Prothrombin time, activated partial thromboplastin time
CBC
Bedside glucose
Chemistry profile
Electrocardiogram

Second Step—usually initiated by consultant
Transthoracic or transesophageal echocardiography
Transcranial and carotid doppler ultrasound
Magnetic resonance angiography (MRA)
Cerebral arteriography
Antiphospholipid antibodies

Other options for consultants
Ambulatory electrocardiographic monitoring
Noninvasive arterial imaging (ultrasound, MRA)
Further screening for pro-thrombotic states (e.g. protein C, antithrombin III, thrombin time, hemoglobin electrophoresis, serum protein electrophoresis)
Cerebrospinal fluid examination
Erythrocyte sedimentation rate, syphilis serology (not significant for emergency management)
Testing for silent myocardial ischemia (exercise electrocardiogram and/or thallium perfusion)

Adapted from: Feinberg WM, Albers GW, Barnett, et al. Guidelines for the management of transient ischemic attacks. *Stroke* 1994;25(6):1320-1335.

Table 9. Common Pitfalls And Key Points For Stroke Management.

History
History alone cannot distinguish ischemic from hemorrhagic stroke
Consider an arterial dissection in patients with neck or chest pain and focal neurologic findings
Be a "bulldog" regarding the time of stroke onset. A patient who awakens in the morning with a neurological deficit is not a candidate for thrombolytics

Physical exam
Perform and document a neurological exam that is easily interpretable. Never use the phrase "grossly intact" to describe any part of a neurological exam
While performing the NIHSS is recommended, this scale should not supplant a neurological exam
Evaluate aphasia, visual field defects, and left-sided neglect in all alert patients suspected of stroke
Any of facial palsy, loss of arm strength, or abnormal speech appears accurate for detecting stroke

Initial ED management
Manage the airway. Obtunded patients may arrest in CT
Never miss hypoglycemia. Perform a bedside glucose, *before* sending the patient to CT

Neuroimaging
The CT may help confirm the stroke onset time given by the patient or family. If obvious hypoattenuation is present, the likelihood of onset within the past few hours is low
If considering t-PA therapy, the head CT must be read by someone with *expertise* in interpreting head CTs
While MRI is more sensitive than CT for small cortical or subcortical infarctions, or posterior fossa lesions, it is less sensitive for acute blood

Blood pressure management
Recommended thresholds for treating blood pressure are relatively high in patients with ischemic stroke
More harm than good comes from routine and aggressive control of BP in stroke
Thresholds for treatment depend upon whether the stroke is ischemic or hemorrhagic and whether or not lytics are planned
Patients with hemorrhagic stroke are less tolerant of high pressures
Nifedipine should never be used for blood pressure reduction in a stroke patient

Heparin
The literature regarding the value of heparin in stroke and TIA is weak
The vast majority of studies on heparin and stroke show no indication for its use
Do not start heparin unless a neurological consultant or the admitting physician agrees with the decision
Many physicians who use heparin in stoke give only a drip and not a bolus

Aspirin
For patients with ischemic stroke who do not receive t-PA therapy, administer 160-325 mg of aspirin if the patient is within 48 hours of their stroke onset
Wait for the CT scan results before giving aspirin

t-PA
Without a pre-established protocol, the time and safety constraints of t-PA therapy will not be consistently achieved
Advanced age, severe neurologic deficit, and early signs of infarction on the CT increase the risk of parenchymal hemorrhage
Small areas of hypo-attenuation do not prevent thrombolysis. However, patients with hypo-attenuation of greater than one-third of the area of the middle cerebral artery are more likely to bleed if given t-PA

Other interventions
Consult a neurosurgeon in case of hemorrhagic stroke and cerebellar strokes.

emergency care, and the ED is prepared to treat stroke with the alacrity it deserves, we can improve outcome. (See **Table 9** on page 20 for common pitfalls and key points concerning stroke patient management.)

As emergency medicine enters the 21st century, the historic lassitude regarding cerebrovascular emergencies must end. We must now approach stroke as one of many opportunities that dramatically justify our specialty. ▲

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, each reference will note (in bold type following the reference) pertinent information about the study, such as the type of study and the number of patients in the study. In addition, the most informative references cited in the paper, as determined by the author, will be noted by an asterisk (*) next to the number of the reference.

1. American Heart Association. Heart and Stroke Facts. Dallas, TX: 1992.
2. Rosenberg HM, Ventura SJ, Maurer JD, et al. Births and Deaths: United States, 1995. Monthly Vital Statistics Report 1996;45(3, Suppl 2):1-40.
3. Cerebral Embolism Task Force. Cardiogenic brain embolism: The second report of the cerebral embolism task force. *Arch Neurol* 1989;46:727-743. **(Review)**
4. Mohr JP, Caplan LR, Melski, et al. The Harvard cooperative stroke registry: A prospective registry. *Neurology* 1978;28:754-762. **(Prospective questionnaire; 694 patients)**
5. Foulkes MA, Wolf PA, Price, et al. The stroke data bank: Design, methods, and baseline characteristics. *Stroke* 1988;19(5):547-554. **(Prospective; 1,805 patients)**
6. Farooqui AA, Haun SE, Horrocks LA. Ischemia and hypoxia. In: Siegel GJ, Agranoff BW, Albers RW, Molinoff PB, eds. *Basic Neurochemistry* New York: Raven Press; 1994:867-883. **(Textbook)**
7. Kaplan B, Brint S, Tanabe J, et al. Temporal thresholds for neocortical infarction in rats subjected to reversible focal cerebral ischemia. *Stroke* 1991;22(8):1032-1039. **(Animal)**
8. Yang G, Betz L. Reperfusion-induced injury to the blood-brain barrier after middle cerebral artery occlusion in rats. *Stroke* 1994;25(8):1658-1665. **(Animal)**
9. Jones T, Morawetz R, Crowell R, et al. Thresholds of focal cerebral ischemia in awake monkeys. *J Neurosurg* 1981;54:773-782. **(Animal)**
10. Memezawa H, Smith ML, Siesjo BK. Penumbral tissue salvaged by reperfusion following middle cerebral artery occlusion in rats. *Stroke* 1992;23:552-559. **(Animal)**
11. Park CK, Nehis DG, Graham D, et al. Focal cerebral ischemia in the cat: Treatment with the glutamate antagonist MK-801 after the induction of ischemia. *J Cereb Blood Flow Metab* 1988;8:757-762. **(Animal)**
12. Ferro JM, Pinto AN, Falcao, et al. Diagnosis of stroke by the nonneurologist: A validation study. *Stroke* 1998;29:1106-1109. **(Retrospective; 241 patients)**
13. Kothari R, Brott T, Broderick J, et al. Accuracy in the diagnosis of stroke. *Stroke* 1995;26(12):2238-2241. **(Retrospective; 76 patients)**
14. Kothari R, Hall K, Brott, et al. Early stroke recognition: Developing an out-of-hospital NIH Stroke Scale. *Acad Emerg Med* 1997;4:986-990. **(74 patients)**
15. Pulsinelli, et al. Moderate hyperglycemia augments ischemic brain damage. *Neurology* 1982;32:1239-1246. **(Animal)**
16. Candelise L, Landi G, Orazio EN, et al. Prognostic significance of hyperglycemia in acute stroke. *Arch Neurol* 1985;42:661-663. **(Observational; 72 patients)**
17.* Adams H, Brott T, Crowell R, et al. Guidelines for the management of patients with acute ischemic stroke. *Circulation* 1994;90(3):1588-1601. **(Consensus statement based on graded levels of evidence)**
18. Reith J, Jorgensen HS, Pedersen, et al. Body temperature in acute stroke: Relation to stroke severity, infarct size, mortality, and outcome. *Lancet* 1996;347:422-425. **(Prospective, Observational; 390 patients)**
19. Castillo J, Davalos A, Noya M. Progression of ischemic stroke and excitotoxic amino acids. *Lancet* 1997;349:79-83. **(Prospective, Observational; 128 patients)**
20. The NINDS rt-PA Stroke Study Group. Intracerebral hemorrhage after intravenous t-PA therapy for ischemic stroke. *Stroke* 1997;28(11):2109-2118. **(Subgroup analysis of a randomized, double-blind, placebo-controlled trial; 22 patients)**
21. Brott T, Adams HP, Olinger, et al. Measurements of acute cerebral infarction: A clinical examination scale. *Stroke* 1989;20(7):864-870. **(Prospective; 24 patients)**
22. Manninen P, Ayra B, Gelb A, et al. Association between electrocardiographic abnormalities and intracranial blood in patients following acute subarachnoid hemorrhage. *J Neurosurg Anesthesiol* 1995;7:12-16. **(Retrospective; 70 patients)**
23. Ramani A, Shetty U, Kundaje GN. Electrocardiographic abnormalities in cerebrovascular accidents. *Angiology* 1990;41:681-686. **(Retrospective; 100 patients)**
24. ACEP "agrees with reservations" to new stroke guidelines. *ACEP News* October 1996, p.3.
25.* Adams HP, Brott TG, Furlan AJ, et al. Guidelines for thrombolytic therapy for acute stroke: A supplement to the guidelines for the management of patients with acute ischemic stroke. A statement for healthcare professionals from a special writing group of the stroke council, American Heart Association. *Circulation* 1996;94:1167-1174. **(Consensus statement based on graded levels of evidence)**
26. Quality Standards Subcommittee of the American Academy of Neurology. Practice Advisory: Thrombolytic therapy for acute ischemic stroke—Summary Statement. *Neurology* 1996;47:835-839. **(Consensus statement based on graded levels of evidence)**
27. Consensus Panel of the National Stroke Association. Stroke: The first hours: Emergency evaluation and treatment. *Stroke Clin Upd* 1997;1-14. **(Consensus statement)**
28. Powers WJ. Acute hypertension after stroke: The scientific basis for treatment decisions. *Neurology* 1993;43:461-467. **(Editorial)**
29. Dandapani BK, Suzuki S, Kelley, et al. Relation between blood pressure and outcome in intracerebral hemorrhage. *Stroke* 1995;26(1):21-24. **(Retrospective; 87 patients)**
30. Kirsten R, Nelson K, Kirsten D, et al. Clinical pharmacokinetics of vasodilators. *Clin Pharmacokin Part II* 1998;35(1):9-36. **(Review)**
31. *Physicians' Desk Reference.* (52 ed) 1997.
32. Opie LH. Calcium channel blockers for hypertension: Dissecting the evidence for adverse effects. *Am J Hypertens* 1997;10:565-577. **(Review)**
33. Dougall H, McLay J. A comparative review of the adverse effects of calcium antagonists. *Drug Saf* 1996;15:91-106. **(Review)**
34. Stroke Unit Trialists Collaboration. How do stroke units improve patient outcomes? A collaborative systematic review of the randomized trials. *Stroke* 1997;28(11):2139-2144. **(Review of randomized trials; 755 patients)**
35. Crockard HA, Coppel DL, Morrow WFK. Evaluation of hyperventilation in treatment of head injuries. *BMJ* 1973;4:634-640. **(Prospective; 31 patients)**
36. Bullock R, Chesnut R. Guidelines for the management of severe head injury. *Brain Trauma Foundation*. New York, NY 1995. **(Review)**
37. Bauer RB, Tellez H. Dexamethascone as treatment in cerebrovascular disease. A controlled study in acute cerebral infarction. *Stroke* 1973;4:547-555. **(Prospective, Double-blind, Controlled; 21 patients)**
38. Norris JW. Steroid therapy in acute cerebral infarction. *Arch Neurol* 1976;33:69-71. **(Double-blind, Placebo-controlled; 53 patients)**
39. Norris JW, Hachinski VC. High dose steroid treatment in cerebral infarction. *BMJ* 1986;292:21-23. **(Randomized, Double-blind, Placebo-controlled; 113 patients)**
40. Mulley G, Wilcox RG, Mitchell JRA. Dexamethasone in acute stroke. *BMJ* 1978;2:994-996. **(Randomized, Placebo-controlled; 118 patients)**
41. Phillips SJ. An alternative view of heparin anticoagulation in acute focal brain ischemia. *Stroke* 1989;20(2):295-298. **(Opinion and Review; 137 patients)**
42. Miller VT, Hart RG. Heparin anticoagulation in acute brain ischemia. *Stroke* 1988;19(3):403-406. **(Review; 28 patients)**
43. Lindley R. Drug therapy for acute ischaemic stroke: Risks versus benefits. *Drug Saf* 1998;19(5):373-382. **(Review)**
44.* International Stroke Trial Collaborative Group. The International Stroke Trial (IST): A randomised trial of aspirin, subcutaneous heparin, both, or neither among 19,435 patients with acute ischaemic stroke. *Lancet* 1997;349:1569-1581. **(Prospective,**

Randomized, Non-blinded; 19,435 patients)
45. Bousser MG. Aspirin or heparin immediately after a stroke. *Lancet* 1997;349:1564-1565. **(Commentary)**
46.* Hankey G. Heparin in acute ischaemic stroke. The T wave is negative and it's time to stop. *Med J Aust* 1998;169:534-536. **(Review of 16 Randomized, Controlled Trials)**
47. Chamorro A, Vila N, Saiz A, et al. Early anticoagulation after large cerebral embolic infarction: A safety study. *Neurology* 1995;45:861-865. **(Prospective, Observational; 171 patients)**
48. Shields RW, Laureno R, Lachman T, et al. Anticoagulant-related hemorrhage in acute cerebral embolism. *Stroke* 1984;15(3):426-437. **(Retrospective; 5 patients)**
49. Babikian VL, Kase CS, Pessin MS, et al. Intracerebral hemorrhage in stroke patients anticoagulated with heparin. *Stroke* 1989;20(11):1500-1503. **(Retrospective; 10 patients)**
50. Cerebral Embolism Study Group. Cardioembolic stroke, early anticoagulation, and brain hemorrhage. *Arch Intern Med* 1987;147:636-640. **(Retrospective; 18 patients)**
51. Cerebral Embolism Study Group. Immediate anticoagulation of embolic stroke: A randomized trial. *Stroke* 1983;14(5):668-676. **(Randomized, Non-blinded; 19 patients)**
52. Cerebral Embolism Study Group. Immediate anticoagulation of embolic stroke. Brain hemorrhage and management options. *Stroke* 1984;15:779-789. **(Retrospective; 63 patients)**
53. Broderick JP, Phillips SJ, O'Fallon M, et al. Relationship of cardiac disease to stroke occurrence, recurrence, and mortality. *Stroke* 1992;23(9):1250-1256. **(Population-based, Retrospective; 1,382 patients)**
54. Irino T, Watanabe M, Nishide M, et al. Angiographical analysis of acute cerebral infarction followed by "cascade"-like deterioration of minor neurological deficits. What is progressing stroke? *Stroke* 1983;14(3):363-368. **(Retrospective; 212 patients)**
55. Gautier JC. Stroke-in-progression. *Stroke* 1985;16(4):729-733. **(Review)**
56. Carter AB. Anticoagulant treatment in progressing stroke. *BMJ* 1961:70-73. **(76 patients)**
57. Millikan CH, McDowell FH. Treatment of progressing stroke. *Stroke* 1981;12(4):397-409. **(Review)**
58. Fisher CM. Anticoagulant therapy in cerebral thrombosis and cerebral embolism: A national cooperative study, interim report. *Neurology* 1961;11:119-131. **(Prospective, Randomized; 182 patients)**
59. Ramirez-Lassepas M, Quinones MR, Nino HH. Treatment of acute ischemic stroke. *Arch Neurol* 1986;43:386-390. **(Prospective, Open; 150 patients)**
60. Putman SF, Adams HP. Usefulness of heparin in initial management of patients with recent transient ischemic attacks. *Arch Neurol* 1985;42:960-962. **(Prospective, Non-controlled; 74 patients)**
61. Duke RJ, Bloch RF, Turpie AG, et al. Intravenous heparin for the prevention of stroke progression in acute partial stable stroke: A randomized controlled trial. *Ann Intern Med* 1986;105(6):825-828. **(Prospective, Randomized, Blinded, Placebo-controlled; 225 patients)**
62. Haley EC, Kassell NF, Torner JC. Failure of heparin to prevent progression in progressing ischemic infarction. *Stroke* 1988;19(1):10-14. **(Prospective, Non-controlled; 36 patients)**
63. Biller J, Bruno A, Adams HP, et al. A randomized trial of aspirin or heparin in hospitalized patients with recent transient ischemic attacks: A pilot study. *Stroke* 1989;20(4):441-447. **(Prospective, Randomized, Non-blinded; 55 patients)**
64. Dobkin BH. Heparin for lacunar stroke in progression. *Stroke* 1983;14(3):421-423. **(Prospective, Non-controlled; 120 patients)**
65. Alberts M, Dawson D, Massey E. A follow-up survey of clinical practices for the use of heparin, warfarin, and aspirin. *Neurology* 1994;44:618-621. **(Survey)**
66. Kay R, Wong K, Yu Y, et al. Low-molecular-weight heparin for the treatment of acute ischemic stroke. *N Engl J Med* 1995;333(24):1588-1593. **(Randomized, Double-blinded, Placebo-controlled; 312 patients)**
67. The Publications Committee for TOAST Investigators. Low molecular weight heparinoid, ORG 10172 (Danaproid), and outcome after acute ischemic stroke. *JAMA* 1998;279:1265-1272. **(Randomized, Double-blinded, Placebo-controlled; 1,281 patients)**
68.* CAST (Chinese Acute Stroke Trial) Collaborative Group. CAST: Randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. *Lancet* 1997;349:1641-1649. **(Randomized, Placebo-controlled; 21,106 patients)**
69. Macdonell RAL, Kalnins RM, Donnan GA. Cerebellar infarction: Natural history, prognosis, and pathology. *Stroke* 1987;18(5):849-855. **(Retrospective; 30 patients)**
70. Heros RC. Surgical treatment of cerebellar infarction. *Stroke* 1992;23(7):937-938. **(Editorial)**
71. Multicentre Acute Stroke Trial—Italy (MAST-I) Group. Randomized controlled trial of streptokinase, aspirin, and combination of both in treatment of acute ischemic stroke. *Lancet* 1995;346:1509-1515. **(Randomized, Controlled; 622 patients)**
72. The Multicenter Acute Stroke Trial—Europe Study Group. Thrombolytic therapy with streptokinase in acute ischemic stroke. *N Engl J Med* 1996;335(3):145-150. **(Prospective, Randomized, Placebo-controlled; 310 patients)**
73. Donnan G, Davis S, Chambers B, et al. Streptokinase for acute ischemic stroke with relationship to time of administration. *JAMA* 1996;276(12):961-966. **(Randomized, Double-blinded, Placebo-controlled; 340 patients)**
74. Caplan LR, Mohr JP, Kistler JP, et al. Thrombolysis—not a panacea for ischemic stroke. *N Engl J Med* 1997;337(18):1309-1310. **(Opinion)**
75. Grotta J. t-PA—The best current option for most patients. *N Engl J Med* 1997;337(18):1310-1313. **(Opinion)**
76. Villar-Cordova C, Morgenstern LB, Barnholtz JS, et al. Neurologists' attitudes regarding rt-PA for acute ischemic stroke. *Neurology* 1998;50:1491-1494. **(Survey)**
77. Furlan A, Kanoti G. When is thrombolysis justified in patients with acute ischemic stroke? *Stroke* 1997;28(1):214-218. **(Bioethical)**
78. Wardlaw JM, Warlow CP, Counsell C. Systematic review of evidence on thrombolytic therapy for acute ischaemic stroke. *Lancet* 1997;350:607-614. **(Review of Randomized Trials; 3,435 patients)**
79. Haley EC Jr, Lewandowski C, Tilley BC. Myths regarding the NINDS rt-PA stroke trial: Setting the record straight. *Ann Emerg Med* 1997;30(5):676-682. **(Editorial)**
80. Horowitz SH. Thrombolytic therapy in acute stroke. *Arch Neurol* 1998;55:155-157. **(Opinion)**
81.* The NINDS rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333(24):1581-1587. **(Randomized, Double-blinded, Placebo-controlled; 624 patients)**
82. Lyden P, Rapp K, Babcock T, et al. Ultra-rapid identification, triage, and enrollment of stroke patients into clinical trials. *J Stroke Cerebrovasc Dis* 1994;4:106-113. **(Retrospective; 1,127 patients)**
83.* Hacke W, Kaste M, Fieschi C, et al. Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke. *JAMA* 1995;274(13):1017-1025. **(Prospective, Randomized, Double-blinded, Placebo-controlled; 620 patients)**
84.* Hacke W, Kaste M, Fieschi C, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). *Lancet* 1998;35:1245-1251. **(Randomized, Double-blinded, Placebo-controlled; 800 patients)**
85. Schriger DL, Kalafut M, Starkman S, et al. Cranial computed tomography interpretation in acute stroke. *JAMA* 1998;279:1293-1297. **(Convenience sample study of 103 physicians, 569 CT readings)**
86. Larrue V, von Kummer R, del Zoppo G, et al. Hemorrhagic transformation in acute ischemic stroke. *Stroke* 1997;28(5):957-960. **(Subgroup analysis of a randomized, double-blind, placebo-controlled trial)**
87. von Kummer R, Allen K, Holle R, et al. Acute stroke: Usefulness of early CT findings before thrombolytic therapy. *Radiology* 1997;205:327-333. **(Prospective; 620 CT scans)**
88. The NINDS rt-PA Stroke Study Group. Symptomatic intracerebral hemorrhage after t-PA for stroke. *Stroke* 1997;January:272. **(Subgroup analysis of a randomized, double-blinded, placebo-controlled trial; 30 patients)**
89. Grond M, Stenzel C, Schmulling S, et al. Early intravenous thrombolysis for acute ischemic stroke in a community-based approach. *Stroke* 1998;29:1544-1549. **(Prospective, open-label; 100 patients)**
90. del Zoppo GJ, Higashida RT, Furlan AJ, et al. PROACT: A phase II randomized trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke. *Stroke* 1998;29:4-11. **(Randomized, Placebo-controlled; 105 patients)**
91. Wijdicks E, Nichols DA, Thielen KR, et al. Intra-arterial thrombolysis in acute basilar artery thromboembolism: The initial Mayo Clinic experience. *Mayo Clin Proc* 1997;72:1005-1013. **(Retrospective; 9 patients)**
92. Grond M, Rudolf J, Schmulling S, et al. Early intravenous thrombolysis with recombinant tissue-type plasminogen activator in vertebrobasilar ischemic stroke. *Ann Neurol* 1998;55:466-469. **(Prospective, Observational; 12 patients)**
93. Hacke W, Zeumer H, Ferbert A, et al. Intra-arterial thrombolytic therapy improves outcome in patients with acute vertebrobasilar occlusive disease. *Stroke* 1988;19(10):1216-1222. **(Retrospective; 65 patients)**
94. Brandt T, von Kummer R, Muller-Kuppers M, et al. Thrombolytic therapy of acute basilar artery occlusion: Variables affecting recanalization and outcome. *Stroke* 1996;27(5):875-881. **(Retrospective; 51 patients)**
95. National Health Lawyers Association. Colloquium report on legal

issues related to clinical practice guidelines. National Health Lawyers Association. 1995. **(Review)**
96. Hyams AL, Brandenburg JA, Lipsitz, et al. Practice guidelines and malpractice litigation: A two-way street. *Ann Intern Med* 1995; 122(6):450-455. **(Retrospective; 259 malpractice claims reviewed)**
97. Indredavik B, Bakke F, Solberg R, et al. Stroke unit treatment improves long-term quality of life: A randomized controlled trial. *Stroke* 1998;29(5):895-899. **(Randomized, Controlled; 110 patients)**
98. Ronning OM, Guldvog B. Stroke units versus general medical wards. *Stroke* 1998;29(1):58-62. **(Randomized, Controlled; 802 patients)**
99. Indredavik B. Treatment in the stroke unit reduces mortality, disability, and need for institutional care. *Nordisk Medicin* 1997;112:313-316. **(Review)**
100. Proceedings of a National Symposium on Rapid Identification and Treatment of Acute Stroke. The National Institute of Neurological Disorders and Stroke. Marler J, Winters P, Emr M, eds. 1997. **(Review)**
101. Levine S, Gorman M. "Telestroke": The application of telemedicine for stroke. *Stroke* 1999;30:464-469. **(Review)**
102. Feinberg WM, Albers GW, Barnett, et al. Guidelines for the management of transient ischemic attacks. *Stroke* 1994;25(6):1320-1335. (**Consensus Statement Based on Graded Levels of Evidence)**
103. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high grade stenosis. *N Engl J Med* 1991;325(7):445-453. **(Prospective, Randomized; 659 patients)**
104. Barnett H, Taylor D, Eliaziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med* 1998;339:415-425. **(Prospective, Randomized; 2,226 patients)**
105. Gorelick P, Sacco R, Smith D, et al. Prevention of a first stroke: A review of guidelines and a multidisciplinary consensus statement from the National Stroke Association. *JAMA* 1999;281:1112-1120. **(Consensus Statement)**
106. Hart R, Sherman D, Easton JD, et al. Prevention of stroke in patients with nonvalvular atrial fibrillation. *Neurology* 1999;51:674-681. **(Review)**
107. Antiplatelet Trialists' Collaboration. Secondary prevention of vascular disease by prolonged antiplatelet treatment. *BMJ* 1988;296: 320-331. **(Meta-analysis of Randomized Trials; 29,000 patients)**
108. The Dutch TIA Trial Study Group. A comparison of two doses of aspirin (30 mg vs 283 mg a day) in patients after a transient ischemic attack or minor ischemic stroke. *N Engl J Med* 1991;325(18):1261-1265. **(Double-blinded, Randomized, Controlled; 3,131 patients)**
109. Hass WK, Easton JD, Adams HP, et al. A randomized trial comparing ticlopidine hydrochloride with aspirin for the prevention of stroke in high-risk patients. *N Engl J Med* 1989;321(8):501-507. **(Randomized, Double-blind; 3,069 patients)**
110. CAPRIE Steering Committee. A randomized, blinded trial of clopidogrel versus aspirin in patients at risk of ischemic events (CAPRIE). *Lancet* 1996;348:1329-1339. **(Randomized, Double-blinded; 19,185 patients)**
111. Barnett HJM, Kaste M, Meldrum H, et al. Aspirin dose in stroke prevention: Beautiful hypotheses slain by ugly facts. *Stroke* 1996;27:588-592. **(Review; 2,435 patients)**
112. Hart RG, Harrison MJH. Aspirin wars: The optimal dose of aspirin to prevent stroke. *Stroke* 1996;27(4):585-587. **(Editorial)**
113. Brown RD, Evans BA, Wiebers DO, et al. Transient ischemic attack and minor ischemic stroke: An algorithm for evaluation and treatment. *Mayo Clin Proc* 1994;69:1027-1122. **(Evidence-Based Consensus Panel Statement)**

Physician CME Questions

6. Based on the AHA's guidelines, what is the maximum permissible time interval from stroke symptom onset to t-PA treatment?
a. 2 hours
b. 3 hours
c. 4 hours
d. 5 hours
e. 6 hours

7. Regarding anticoagulant and antithrombotic treatment for stroke, which of the following is *true*?
a. LMWH is an approved therapy for certain stroke subtypes.
b. Aspirin is beneficial by reducing early recurrent strokes and the likelihood of death some weeks to months after stroke.
c. Acute heparin therapy has been demonstrated to be beneficial for lacunar strokes.
d. Heparin should be given to stroke patients immediately after the t-PA bolus is finished.
e. The risk of bleeding from heparin therapy after stroke is 6%.

8. All of the following are true regarding edema associated with stroke *except*:
a. Steroids should be administered when intracranial swelling is suspected.
b. Furosemide and mannitol may help control cerebral edema.
c. Hyperventilation can lower the ICP.
d. Life-threatening edema from a cerebellar hemorrhage or infarction may develop while the patient is still in the ED.
e. With hemispheric strokes, edema peaks several days after stroke onset.

9. According to AHA guidelines, a patient's blood pressure must be below what threshold to be eligible for t-PA therapy?
a. DBP < 140 mmHg
b. SBP < 230 mmHg and DBP < 120 mmHg
c. MAP < 130 mmHg
d. SBP < 185 mmHg and DBP < 110 mmHg
e. SBP < 145 mmHg and DBP < 95 mmHg

10. Which of the following is *not* tested as part of the NIHSS?
a. Best horizontal gaze
b. Facial palsy
c. Limb ataxia
d. Language
e. Gait

11. For ischemic stroke patients, which of the following is among the NIH t-PA treatment-related time goals?
a. Door to emergency physician evaluation—25 minutes
b. Door to CT scanner— 45 minutes
c. Door to t-PA—3 hours
d. Door to expert CT interpretation—45 minutes

12. Which of the following is *true*?
a. A hemorrhagic stroke can be reliably distinguished from an ischemic stroke based on the history.
b. Aphasia is usually a sign of a right hemispheric stroke.
c. Hypotension is frequently associated acutely with stroke.
d. Sublingual nifedipine is an acceptable agent for treating hypertension associated with acute stroke.
e. Anticonvulsant therapy is not recommended unless an acute stroke patient experiences a seizure.

13. **The most important diagnostic test to perform in a potential stroke patient is the:**
    a. EKG
    b. CBC
    c. Electrolyte panel
    d. Erythrocyte sedimentation rate
    e. Head CT without contrast
14. **The correct t-PA dose for stroke is:**
    a. 1.1 mg/kg, with a maximum dose of 90 mg
    b. 1.1 mg/kg, with a maximum dose of 110 mg
    c. 0.9 mg/kg, with a maximum dose of 90 mg
    d. 0.9 mg/kg, with a maximum dose of 110 mg
15. **Signs of a posterior circulation stroke include all of the following *except:***
    a. Ataxia
    b. Aphasia
    c. Vertigo
    d. Diplopia
    e. Quadriparesis

Class Of Evidence Definitions

Each action in the clinical pathways section (see pages 9-12) of *Emergency Medicine Practice* receives an alpha-numerical score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness
- Must be used in the intended manner for proper clinical indications

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- Study results consistently positive and compelling

Class IIa
- Safe, acceptable
- Clinically useful
- Considered treatments of choice

Level of Evidence:
- Generally higher levels of evidence
- Results are consistently positive

Class IIb
- Safe, acceptable
- Clinically useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Generally, but not consistently, positive results

Class III:
- Unacceptable
- Not useful clinically
- May be harmful

Level of Evidence:
- No positive high-level data
- Some studies suggest or confirm harm

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Adapted from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA* 1992;268(16):2289-2295.

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