Guidelines for the Early Management of Adults with Ischemic Stroke:

I. Prehospital Management and Field Treatment

Conclusions and Recommendations: Public educational programs likely will increase the proportion of patients with stroke who will utilize EMS as their first contact with the healthcare system. This trend should be encouraged. In response, EMS should have protocols in place to rapidly assess, treat, and transport patients. The objectives of the EMS phase of stroke care are as follows: (1) rapid identification of stroke as the cause of the patient’s findings, (2) elimination of comorbid conditions that could mimic stroke, (3) stabilization, (4) rapid transportation of the patient to the closest appropriate ED, and (5) notification to the receiving institution about impending arrival of a patient with suspected stroke. Such steps are especially critical for the use of time-dependent therapies. Community and physician educational programs on acute stroke treatment appear to enhance the use of recombinant tPA (rtPA), and these programs should be encouraged. Strategies such as telemedicine or air medical transport (helicopter) may provide access to specialized stroke care when it is not available locally. Such approaches may increase the number of patients who can be treated, especially in rural or otherwise underserved areas. To maximize therapeutic options, treatment guidelines and transfer protocols should be established in advance to ensure orderly patient transition from a prehospital to a hospital environment.

Class I Recommendations:
1. Activation of the 9-1-1 system by patients or other members of the public is strongly supported because it speeds treatment of stroke (Class I, Level of Evidence B), 9-1-1 Dispatchers should make stroke a priority dispatch.
2. To increase the number of patients who can be seen and treated within the first few hours after stroke, educational programs to increase public awareness of stroke are recommended (Class I, Level of Evidence B).
3. To increase the number of patients who are treated, educational programs for physicians, hospital personnel, and EMS personnel are also recommended (Class I, Level of Evidence B).
4. Brief assessments by EMS personnel as outlined in Tables 3 and 5 are recommended (Class I, Level of Evidence B).
5. The use of a stroke identification algorithm such as the Los Angeles or Cincinnati screens is encouraged (Class I, Level of Evidence B).
6. The panel recommends the EMS personnel begin the initial management of stroke in the field, as outlined in Table 3 (Class I, Level of Evidence B). The development of stroke protocols to be used by EMS personnel is strongly encouraged.
7. Patients should be transported rapidly for evaluation and treatment to the closest institution that provides emergency stroke care as described in the statement (Class I, Level of Evidence B). In some instances, this may involve air evacuation. EMS personnel should notify receiving ED so that the appropriate resources may be mobilized.

Class IIa Recommendations:
1. Telemedicine can be an effective method to provide expert stroke care to patients located in rural areas (Class IIa, Level of Evidence B).

II. Emergency Evaluation and Diagnosis of Acute Ischemic Stroke

Conclusions and Recommendations: The evaluation and initial treatment of patients with stroke should be performed as a priority in the hospital ED. The development of an organized protocol and stroke team should speed the clinical assessment, the performance of diagnostic studies, and decisions for early management. The clinical assessment (history, general examination, and neurological examination) remains the cornerstone of the evaluation. This evaluation should be performed by the physicians in the ED. The goals are to determine whether the patient has had a stroke and to establish potential contraindications for emergency treatment with agents such as rtPA. A stroke rating scale, such as the NIHSS, provides important information about the severity of stroke. It provides prognostic information and the score may influence decisions about acute treatment. Some of the recommendations included in the present statement are influenced by the NIHSS. This scale can be performed with a reasonable degree of accuracy by practitioners in a broad range of specialties. Education in the nuances of NIHSS can improve the accuracy of this scale.

Because time is critical, a limited number of diagnostic tests are recommended. These tests should be available on a 24-hours-per-day, 7-days-per-week basis. These tests are used to screen for ischemic stroke, to exclude important alternative diagnoses (especially intracerebral hemorrhage), to assess for serious comorbid diseases, and to search for acute medical or neurological complication of the stroke. Examination of the cerebrospinal fluid has a limited role in the evaluation of patients with suspected stroke. Additional diagnostic studies, including cardiac and vascular imaging, often are time consuming and may delay emergency treatment. Thus, most of these tests are not done until after the acute treatment or after the patient is admitted to the hospital.

Class I Recommendations:
1. An organized protocol for the emergency evaluation of patients with suspected stroke is recommended (Class I, Level of Evidence B). The goal is to complete an evaluation and to decide treatment within 60 minutes of the patient’s arrival in ED. Designation of an acute stroke team that includes physicians, nurses and laboratory/radiology personnel is encouraged. Patients with stroke should have a careful clinical assessment, including neurological examinations.
2. The use of a stroke rating scale, preferably the NIHSS, is recommended (Class I, Level of Evidence B). Hospitals (i.e., administration) must provide the necessary resources to use such a scale.
3. A limited number of hematologic, coagulation, and biochemistry tests are recommended during the initial emergency evaluation (Class I, Level of Evidence B).
4. Patients with clinical or other evidence of acute cardiac or pulmonary disease may warrant chest x-ray (Class I, Level of Evidence B).
5. An ECG is recommended because of the high incidence of heart disease in patients with stroke (Class I, Level of Evidence B).
Class III Recommendations:
1. Most patients with stroke do not need a chest x-ray as part of initial evaluation (Class III, Level of Evidence C).
2. Most patients with stroke do not need an examination of the cerebrospinal fluid (Class III, Level of Evidence B). The yield of brain imaging is very high for detection of intracranial hemorrhage. The clinical course of subarachnoid hemorrhage or acute central nervous system infections usually is distinct from that of ischemic stroke. Examination of the cerebrospinal fluid may be indicated for evaluation of a patient with a stroke that may be secondary to an infectious illness.

III. Early Diagnosis: Brain and Vascular Imaging

Conclusions and Recommendations: Brain imaging remains a required component of the emergency assessment of patients with suspected stroke. Both CT and MRI are options for imaging the brain, but for most cases and at most institutions, CT remains the most practical initial brain imaging test. A physician skilled in assessing CT or MRI studies should be available to examine the initial scan. In particular, the scan should be evaluated for evidence of early signs of infarction. Baseline CT findings, including the presence of ischemic changes involving more than one third of a hemisphere, have not been predictors of responses to treatment with rtPA when the agent is administered within the 3-hour treatment window. Information about multimodal CT and MRI of the brain suggests that these diagnostic studies may help in the diagnosis and treatment of patients with acute stroke. Imaging of the intracranial or extracranial vasculature in the emergency assessment of patients with suspected stroke is useful at institutions providing endovascular imaging for predicting responses to treatment before intravenous administration of thrombolytic agents has not been demonstrated.

Class I Recommendations:
1. Imaging of the brain is recommended before initiating any specific therapy to treat acute ischemic stroke (Class I, Level of Evidence A).
2. In most instances, CT will provide the information to make decisions about emergency management (Class I, Level of Evidence A).
3. The brain imaging study should be interpreted by a physician with expertise in reading CT or MRI studies of the brain (Class I, Level of Evidence C).
4. Some findings on CT, including the presence of a dense artery sign, are associated with poor outcomes after stroke (Class I, Level of Evidence A).
5. Multimodal CT and MRI may provide additional information that will improve diagnosis of ischemic stroke (Class I, Level of Evidence A).

Class II Recommendations:
1. Nevertheless, data are insufficient to state that, with the exception of hemorrhage, any specific CT finding (including evidence of ischemia affecting more than one third of a cerebral hemisphere) should preclude treatment with rtPA within 3 hours of onset of stroke (Class IIb, Level of Evidence A).
2. Vascular imaging is necessary as a preliminary step for intra-arterial administration of pharmacological agents, surgical procedures, or endovascular interventions (Class IIa, Level of Evidence B).

Class III Recommendations:
1. Emergency treatment of stroke should not be delayed in order to obtain multimodality imaging studies (Class III, Level of Evidence C).
2. Vascular imaging should not delay treatment of patients whose symptoms started <3 hours ago and who have acute ischemic stroke (Class III, Level of Evidence B).

IV. General Supportive Care and Treatment of Acute Complications

Conclusions and Recommendations: Most of the recommendations about general acute management are based on limited data. Some of the aspects of acute management may never be tested in clinical trials, whereas other aspects of treatment, such as the best strategy for treatment of hyperglycemia or arterial hypertension, likely will be clarified by ongoing or future clinical research. Pending such trials, many of the suggestions that follow are based on consensus and thus are Grade C recommendations.

Class I Recommendations:
1. Airway support and ventilatory assistance are recommended for the treatment of patients with acute stroke who have decreased consciousness or who have bulbar dysfunction causing compromise of the airway (Class I, Level of Evidence C).
2. Hypoxic patients with stroke should receive supplemental oxygen (Class I, Level of Evidence C).
3. It is generally agreed that sources of fever should be treated and antipyretic medications should be administered to lower temperature in febrile patients with stroke (Class I, Level of Evidence C).
4. General agreement supports the use of cardiac monitoring to screen for atrial fibrillation and other potentially serious cardiac arrhythmias that would necessitate emergency cardiac interventions. It is generally agreed that cardiac monitoring should be performed during the first 24 hours after onset of ischemic stroke (Class I, Level of Evidence B).
5. The management of arterial hypertension remains controversial. Data to guide recommendations for treatment are inconclusive or conflicting. Many patients have spontaneous declines in blood pressure during the first 24 hours after onset of stroke. Until more definitive data are available, it is generally agreed that a cautious approach to the treatment of arterial hypertension should be recommended (Class I, Level of Evidence C). Patients who have other medical indications for aggressive treatment of blood pressure should be treated.
6. Patients who have elevated blood pressure and are otherwise eligible for treatment of rtPA may have their blood pressure lowered so that their systolic blood pressure is < 185 mm Hg and their diastolic blood pressure is < 110 mm Hg (Class I, Level of Evidence B) before lytic therapy is started. If medications are given to lower blood pressure, the clinician should be sure that the blood pressure is stabilized at the lower level before treating with rtPA and maintained below 180/105 mm Hg for at least the first 24 hours after intravenous rtPA treatment. Because the maximum interval from stroke onset until treatment with rtPA is short, many patients with sustained hypertension above recommended levels cannot be treated with intravenous rtPA.
7. Until other data become available, consensus exists that the previously described blood pressure recommendations should be followed in patients undergoing other acute interventions to recanalize occluded vessels, including intra-arterial thrombolysis (Class I, Level of Evidence C).

8. It is generally agreed that patients with markedly elevated blood pressure may have their blood pressure lowered. A reasonable goal would be to lower blood pressure by ≈ 15% during the first 24 hours after onset of stroke. The level of blood pressure that would mandate such treatment is not known, but consensus exists that medications should be withheld unless the systolic blood pressure is > 220 mm Hg or the diastolic blood pressure is > 120 mm Hg (Class I, Level of Evidence C).

9. It is generally agreed that the cause of arterial hypotension in the setting of acute stroke should be sought. Hypovolemia should be corrected with normal saline, and cardiac arrhythmias that might be reducing cardiac output should be corrected (Class I, Level of Evidence C).

10. It is generally agreed that hypoglycemia should be treated in patients with acute ischemic stroke (Class I, Level of Evidence C). The goal is to achieve normoglycemia. Marked elevation of blood glucose levels should be avoided.

Class II Recommendations:
1. No data are available to guide selection of medications for the lowering of blood pressure in the setting of acute ischemic stroke. The recommended medications and doses included in Table 10 are based on general consensus. (Class Ia, Level of Evidence C).

2. Evidence from one clinical trial indicates that initiation of antihypertensive therapy within 24 hours of stroke is relatively safe. Thus, it is generally agreed that antihypertensive medications should be restarted at ≈ 24 hours for patients who have preexisting hypertension and are neurologically stable unless a specific contraindication to restarting treatment is known (Class IIa, Level of Evidence B).

3. Evidence indicates that persistent hyperglycemia (>140 mg/dL) during the first 24 hours after stroke is associated with poor outcomes, and thus it is generally agreed that hyperglycemia should be treated in patients with acute ischemic stroke (Class IIa, Level of Evidence C). Close monitoring of glucose concentrations with adjustment of insulin dose to avoid hypoglycemia is recommended. Simultaneous administration of glucose and potassium also may be appropriate.

Class III Recommendations:
1. Nonhypoxic patients with acute ischemic stroke do not need supplemental oxygen therapy (Class III, Level of Evidence B).

2. Data on the utility of hyperbaric oxygen are inconclusive, and some data imply that the intervention may be harmful. Thus, with the exception of stroke secondary to air embolization, the utility of induced hypothermia for the treatment of patients with ischemic stroke is not established. At the present time, insufficient evidence exists to recommend hypothermia for treatment of patients with acute stroke (Class III, Level of Evidence B).

V. Intravenous Thrombolysis

Conclusions and Recommendations: Intravenous administration of rtPA is the only FDA-approved medical therapy for treatment of patients with acute ischemic stroke. Its use is associated with improved outcomes for a broad spectrum of patients who can be treated within 3 hours of stroke onset. Earlier treatment (i.e., within 90 minutes) may be more likely to result in a favorable outcome. Later treatment, at 90 to 180 minutes, also is beneficial. Patients with major strokes (NIHSS score >22) have a very poor prognosis, but some positive treatment effect with rtPA has been documented. Because the risk of hemorrhage is considerable among patients with severe deficits, the decision to treat with rtPA should be made with caution. Treatment with rtPA is associated with symptomatic intracranial hemorrhage, which may be fatal. In the original NINDS trials, the risk of symptomatic bleeding was ≈ 6%. Recent community-based studies and registries report lower rates of hemorrhage. Recommendations for the management of intracranial hemorrhage after treatment with rtPA are provided in the AHA Stroke Council’s updated guidelines statement on management of intracerebral hemorrhage, which is being issued contemporaneously with this statement. The best methods for preventing bleeding complications are careful selection of patients and scrupulous ancillary care, especially close observation, and monitoring of the patient with early treatment of arterial hypertension. Case series have suggested that thrombolysis may be used in patients with seizures at the time of presentation when evidence suggests that residual deficits are due to ischemia rather than the postictal state. The use of anticoagulants and antiplatelet agents should be delayed for 24 hours after treatment.

Although written consent is not necessary before administration of rtPA for treatment of stroke, a full discussion of the potential risks and benefits of treatment with rtPA with the family and the patient, if possible, is recommended.

Although other thrombolytic agents, including defibrinogenating drugs, are being tested, none has been established as effective or as a replacement for rtPA.

Class I Recommendations:
1. Intravenous rtPA (0.9 mg/kg, maximum dose 90 mg) is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke (Class I, Level of Evidence A).

2. Besides bleeding complications, physicians should be aware of the potential side effect of angioedema that may cause partial airway obstruction (Class I, Level of Evidence C).

Class II Recommendations:
1. A patient whose blood pressure can be lowered safely with antihypertensive agents may be eligible for treatment, and the physician should assess the stability of the blood pressure before starting rtPA (Class IIa, Level of Evidence B). An elevated blood pressure that requires a continuous infusion of sodium nitroprusside may not be sufficiently stable for the patient to receive rtPA. However, because time is limited, most patients with markedly elevated blood pressures cannot be managed adequately and still meet the 3-hour requirement.
2. A patient with a seizure at the time of onset of stroke may be eligible for treatment as long as the physician is convinced that residual impairments are secondary to stroke and not a postictal phenomenon (Class IIa, Level of Evidence C).

Class III Recommendations:
1. The intravenous administration of streptokinase for treatment of stroke is not recommended (Class III, Level of Evidence A).
2. The intravenous administration of ancond, tenecteplase, reteplase, desmoteplase, urokinase, or other thrombolytic agents outside the setting of a clinical trial is not recommended (Class III, Level of Evidence C).

VI. Intra-Arterial Thrombolysis

Conclusions and Recommendations: Since the publication of the last guidelines, no new Class I evidence has been published. Intra-arterial administration of at least one specific thrombolytic agent appears to be of benefit in the treatment of carefully selected patients with acute ischemic stroke secondary to occlusion of the MCA. New evidence about the use of intra-arterial urokinase in patients with vertebral or basilar artery occlusion treated within 24 hours of symptom onset and patients with embolic stroke involving the anterior circulation within 4.5 hours of symptom onset suggests that intra-arterial therapy may be used. Patients who are evaluated within 6 hours of symptoms but who are ineligible to receive intravenous thrombolysis because of recent surgery or other procedures may be candidates for intra-arterial thrombolysis.

New criteria have been established to determine the qualifications of physicians who can perform intra-arterial thrombolysis on the basis of recent statements from professional organizations and clinical trials.

Class I Recommendations:
1. Intra-arterial thrombolysis is an option for treatment of selected patients who have major stroke of <6 hours’ duration due to occlusions of the MCA and who are not otherwise candidates for intravenous rtPA (Class I, Level of Evidence B).
2. Treatment requires the patient to be at an experienced stroke center with immediate access to cerebral angiography and qualified interventionalists. Facilities are encouraged to define criteria to credential individuals who can perform intra-arterial thrombolysis (Class I, Level of Evidence C).

Class II Recommendations:
1. Intra-arterial thrombolysis is reasonable in patients who have contraindications to use of intravenous thrombolysis such as recent surgery (Class IIa, Level of Evidence C).

Class III Recommendations:
1. The availability of intra-arterial thrombolysis should generally not preclude the intravenous administration of rtPA in otherwise eligible patients (Class III, Level of Evidence C).

VII. Anticoagulants

Conclusions and Recommendations: The results of the recent trials show that early administration of either heparin or a LMW heparin/danaparoid is associated with an increased risk of bleeding complications. These medications increase the risk of symptomatic hemorrhagic transformation of ischemic strokes, especially among persons with severe events. These medications are also associated with a risk of serious bleeding on other parts of the body. Although the likelihood of bleeding appears to be lower than that associated with the administration of thrombolytic agents, it is sufficiently high to require convincing evidence of efficacy to justify urgent anticoagulation. The risk of bleeding appears not to be greatly affected by the use of a bolus dose to start treatment or by the route of administration (intravenous or subcutaneous). Monitoring of the level of anticoagulation and adjustment of the dosages in response to levels probably increase the safety of treatment.

Present data indicate that early administration of heparin or the LMW heparins/danaparoid does not lower the risk of early recurrent stroke, including among patients with cardio-embolic stroke. Early administration of anticoagulants does not lessen the risk of early neurological worsening. Data are not sufficient to indicate whether anticoagulants might have efficacy among some potentially high-risk groups, such as persons with intracardiac or intra-arterial thrombi. The efficacy of urgent anticoagulation is not established for treatment of patients with vertebrobasilar disease or an arterial dissection.

Most trials have not demonstrated the efficacy of anticoagulation in improving outcomes after acute ischemic stroke. One relatively small trial found that intravenous heparin, when administered within 3 hours of onset of stroke to patients with nonlacunar stroke, may improve outcomes. In light of the generally negative data, the results of this trial may not need to be replicated.

Class III Recommendations:
1. Urgent anticoagulation with the goal of preventing early recurrent stroke, halting neurological worsening, or improving outcomes after acute ischemic stroke is not recommended for treatment of patients with acute ischemic stroke (Class III, Level of Evidence A). This recommendation may change if additional data demonstrate the usefulness of very early intravenous administration of anticoagulants for treatment of patients with infarctions secondary to large-artery thrombosis or cardioembolism. Urgent anticoagulation should not be used in lieu of intravenous thrombolysis for treatment of otherwise eligible patients (Class III, Level of Evidence A).
2. Urgent anticoagulation is not recommended for patients with moderate to severe strokes because of an increased risk of serious intracranial hemorrhagic complications (Class III, Level of Evidence A).
3. Initiation of anticoagulant therapy within 24 hours of treatment with intravenously administered rtPA is not recommended (Class III, Level of Evidence B).
VIII. Antiplatelet Agents

Conclusions and Recommendations: No new data are available about the utility of oral antiplatelet agents (used singly or in combination) for treatment of patients with acute ischemic stroke. Currently available data demonstrate a small but statistically significant decline in risk of mortality and morbidity when aspirin is started within 48 hours after onset of stroke. It appears that the primary effects of the aspirin are due to reduction of early recurrent stroke rather than limitation of the neurological consequences of the stroke. No data are available on the utility of other antiplatelet agents, including clopidogrel, given as monotherapy or in combination with aspirin for treatment of patients with acute ischemic stroke. The relative indications for the long-term administration of antiplatelet agents to prevent recurrent stroke are beyond the scope of this statement. However, the panel recommends the administration of such agents as part of management after acute stroke.

Class I Recommendations:
1. The oral administration of aspirin [initial dose is 325 mg] within 24 to 48 hours after stroke onset is recommended for treatment of most patients [Class I, Level of Evidence A].

Class III Recommendations:
1. Aspirin should not be considered a substitute for other acute interventions for treatment of stroke, including the intravenous administration of rtPA [Class III, Level of Evidence B].
2. The administration of aspirin as an adjunctive therapy within 24 hours of thrombolytic therapy is not recommended [Class III, Level of Evidence A].
3. The administration of clopidogrel alone or in combination with aspirin is not recommended for the treatment of acute ischemic stroke [Class III, Level of Evidence C].
4. Outside the setting of clinical trials, the intravenous administration of antiplatelet agents that inhibit the glycoprotein IIb/IIIa receptor is not recommended [Class III, Level of Evidence B].

IX. Volume Expansion, Vasodilators, and Induced Hypertension

A. Hemodilution in Acute Ischemic Stroke

Conclusions and Recommendations: The present data indicate that intentional Hemodilution, with or without venesection in clinical practice, does not reduce case fatality or improve functional outcome in survivors. The data do not support the use of hypervolemia and isovolumic Hemodilution protocols, including dextran, albumin, and hydroxyethyl starch. The only possible exception for the use of Hemodilution is in stroke patients with severe polycythemia. Maintenance of a normal circulating blood volume with regulation of metabolic parameters within physiological ranges is desirable.

Class III Recommendations:
1. Hemodilution with or without venesection and volume expansion is not recommended for treatment of patients with acute ischemic stroke [Class III, Level of Evidence A].

B. Vasodilators in Acute Ischemic Stroke

Conclusions and Recommendations: On the basis of current data, neither pentoxifylline nor pentofylline has been shown to improve outcomes after stroke.

Class III Recommendations:
1. The administration of medications such as pentoxifylline is not recommended for treatment of patients with acute ischemic stroke [Class III, Level of Evidence A]. This recommendation has not changed since the previous guideline was published.

C. Induced Hypertension for the Management of Acute Ischemic Stroke

Conclusions and Recommendations: Preliminary and small clinical studies suggest that drug-induced hypertension could be used in the management of some patients with acute ischemic stroke. However, data from large clinical trials are not available. Thus, the efficacy of this treatment strategy has not been established. The administration of vasopressors may be complicated by side effects, including myocardial ischemia, in some patients with stroke. Some patients may not be able to be treated with this therapy. The safety of drug-induced hypertension for treatment of stroke in a broad spectrum of patients has not been established.

Class I Recommendations:
1. In exceptional cases, a physician may prescribe vasopressors to improve cerebral blood flow. If drug-induced hypertension is used, close neurological and cardiac monitoring is recommended [Class I, Level of Evidence C].

Class III Recommendations:
1. Drug-induced hypertension, outside the setting of clinical trials, is not recommended for treatment of most patients with acute ischemic stroke [Class III, Level of Evidence B].

X. Surgical Interventions

Conclusions and Recommendations: Data on the safety and effectiveness of carotid endarterectomy and other operations for treatment of patients with acute ischemic stroke are not sufficient to permit a recommendation. Surgical procedures may have serious risks and may not favorably alter the outcome of the patient.

XI. Endovascular Interventions

Conclusions and Recommendations: The area of endovascular treatment of patients with acute ischemic stroke shows great promise. A number of techniques and devices are being studied. Already, the FDA has approved devices to extract a thrombus from an occluded intracranial artery. Emergency angioplasty also may achieve a role in management. As with the intra-arterial administration of thrombolytics, the use of these devices will be limited to those comprehensive stroke centers that have the resources and physician expertise to perform these procedures safely.
Conclusions and Recommendations:

1. Although the MERCI device is a reasonable intervention for extraction of intra-arterial thrombi in carefully selected patients, the panel also recognizes that the utility of the device in improving outcomes after stroke is unclear (Class IIb, Level of Evidence B).

2. The usefulness of other mechanical endovascular treatments is not established (Class IIb, Level of Evidence B). These devices should be used in the setting of clinical trials.

XII. Combination Reperfusion Therapy

Conclusions and Recommendations: The potential for combination interventions to restore perfusion to the brain given with or without neuroprotective therapies has great appeal. However, currently available data do not provide conclusive evidence for either the safety or efficacy of combinations of medications to improve cerebral perfusion. Data are limited with regard to the usefulness of mechanical devices to augment the effects of pharmacological thrombolysis to treat acute ischemic stroke.

Class III Recommendations:

1. At present, combinations of interventions to restore perfusion cannot be recommended outside the setting of clinical trials (Class III, Level of Evidence B).

XIII. Neuroprotective Agents

Conclusions and Recommendations: Considerable experimental and clinical research is required before an intervention with identified neuroprotective effects can be recommended for treatment of patients with acute ischemic stroke. Several steps to improve research have been recommended. It is hoped that ongoing studies of neuroprotective interventions, including hypothermia, potentially tested alone or in combination with measures to restore perfusion, will demonstrate safety and efficacy.

Class III Recommendations:

1. At present, no intervention with putative neuroprotective actions has been established as effective in improving outcomes after stroke, and therefore none currently can be recommended (Class III, Level of Evidence B).

XIV. Admission to the Hospital and General Acute Treatment (After Hospitalization)

Conclusions and Recommendations: The management of patients after admission to the hospital remains a key component of overall treatment, and it is as important as the acutely administered therapies. The components of this aspect of treatment dovetail with the acute interventions to restore perfusion. In addition, these components of management can be given to the large number of patients who are not eligible for treatment with the acutely administered interventions. These therapies can improve outcomes by lessening complications and speeding recovery from stroke.

Class I Recommendations:

1. The use of comprehensive specialized stroke care (stroke units) incorporating rehabilitation is recommended (Class I, Level of Evidence A).

2. The use of standardized stroke care order sets is recommended to improve general management (Class I, Level of Evidence B).

3. Early mobilization of less severely affected patients and measures to prevent subacute complications of stroke are recommended (Class I, Level of Evidence C).

4. Assessment of swallowing before starting eating or drinking is recommended (Class I, Level of Evidence B).

5. Patients with suspected pneumonia or urinary tract infections should be treated with antibiotics (Class I, Level of Evidence B).

6. Subcutaneous administration of anticoagulants is recommended for treatment of immobilized patients to prevent deep vein thrombosis (Class I, Level of Evidence A). The ideal timing for starting these medications is not known.

7. Treatment of concomitant medical diseases is recommended (Class I, Level of Evidence C).

8. Early institution of interventions to prevent recurrent stroke is recommended (Class I, Level of Evidence C).

Class II Recommendations:

1. Patients who cannot take food and fluids orally should receive nasogastric, nasoduodenal, or PEG feedings to maintain hydration and nutrition while undergoing efforts to restore swallowing (Class IIa, Level of Evidence B). The timing of placement of a PEG is uncertain.

2. Aspirin is a potential intervention to prevent deep vein thrombosis but is less effective than anticoagulants (Class IIa, Level of Evidence A).

3. The use of intermittent external compression devices is recommended for treatment of patients who can not receive anticoagulants (Class IIa, Level of Evidence B).

Class III Recommendations:

1. Nutritional supplements are not needed (Class III, Level of Evidence B).

2. Prophylactic administration of antibiotics is not recommended (Class III, Level of Evidence B).

3. If possible, the placement of indwelling bladder catheters should be avoided because of the associated risk of urinary tract infections (Class III, Level of Evidence C). Some patients may need prolonged catheter drainage of the bladder, and measures to lower risk of infection should be taken.

XV. Treatment of Acute Neurological Complications

Conclusions and Recommendations: Considerable research is needed on the prevention and treatment of neurological complications of acute ischemic stroke, including seizures, hemorrhagic transformation of the infarction, and brain edema. The latter, which is a leading cause of death after a major ischemic stroke, is a pressing issue. At present, neither medical nor surgical interventions have been established as effective in controlling brain edema, preventing the neurological consequences of increased intracranial pressure or...
herniation, or improving outcomes after stroke. Although several medical interventions are used traditionally to control edema and although surgical procedures may be a life-saving measure, it appears that earlier interventions may be associated with better clinical outcomes than waiting for the patient to have signs of profound neurological dysfunction, such as herniation. Until additional data are available, the recommendations that follow are based on general consensus or limited information.

**Class I Recommendations:**
1. Patients with major infarctions affecting the cerebral hemisphere or cerebellum are at high risk for complicating brain edema and increased intracranial pressure. Measures to lessen the risk of edema and close monitoring of the patient for signs of neurological worsening during the first days after stroke are recommended (Class I, Level of Evidence B). Because many hospitals may not have neurosurgical expertise, transfer of patients at risk for malignant brain edema to an institution that has such expertise should be considered.
2. Patients with acute hydrocephalus secondary to an ischemic stroke most commonly affecting the cerebellum can be treated with placement of a ventricular drain (Class I, Level of Evidence B).
3. Decompressive surgical evacuation of a space-occupying cerebellar infarction is a potentially life-saving measure, and clinical recovery may be very good (Class I, Level of Evidence B). Although data from clinical trials are not available, it is recommended for patients with major cerebellar infarction.
4. Recurrent seizures after stroke should be treated in a manner similar to other acute neurological conditions (Class I, Level of Evidence B).

**Class II Recommendations:**
1. Although aggressive medical measures, including osmotherapy, have been recommended for treatment of deteriorating patients with malignant brain edema after large cerebral infarction, these measures are unproven (Class IIa, Level of Evidence C). Hyperventilation is a short-lived intervention. Medical measures may delay decompressive surgery.
2. Decompressive surgery for malignant edema of the cerebral hemisphere may be life-saving, but the impact of morbidity is unknown. Both the age of the patient and the side of the infarction (dominant versus non-dominant hemisphere) may affect decisions about surgery. Although the surgery may be recommended for treatment of seriously affected patients, the physician should advise the patient’s family about the potential outcomes, including survival with severe disability (Class IIa, Level of Evidence B).
3. No specific recommendation is made for treatment of patients with asymptomatic hemorrhagic transformation after ischemic stroke (Class IIb, Level of Evidence C). Measures to lessen the likelihood of hemorrhagic complications of thrombolytic agents or other interventions to restore or improve perfusion such as careful control of arterial blood pressure are recommended.

**Class III Recommendations:**
1. Because of lack of evidence of efficacy and the potential to increase the risk of infections complications, corticosteroids (in conventional or large doses) are not recommended for treatment of cerebral edema and increased intracranial pressure complicating ischemic stroke (Class III, Level of Evidence A).
2. Prophylactic administration of anticonvulsants to patients with stroke but who have not had seizures is not recommended (Class III, Level of Evidence C).