

Dartmouth-Hitchcock Medical Center

Practice Guidelines are intended to assist physicians and other health care providers in clinical decision-making by describing generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. These guidelines should not be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the same results. Final judgement regarding the care of an individual patient must be made by each physician. Parts of this guideline were taken with permission from the "Guideline for the Management of Adult Patients with Acute Ischemic Stroke" from Baystate Health System.

## Clinical Practice Guideline

# Guideline for the Management of Adult Patients with Acute Ischemic Stroke and Transient Ischemic Attack

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## ***Introduction***

The evaluation and treatment of the patient experiencing an acute stroke or transient ischemic attack (TIA) is a complex and rigorous process. This process requires coordinated and collaborative, multidisciplinary management that optimally begins with proper triage, characterization of the pathophysiology and etiology of symptoms, and concludes with the initiation of rehabilitation and secondary prevention. The following clinical practice guideline was developed by a task force at Dartmouth-Hitchcock Medical Center charged with improving the care of stroke patients. It is primarily based upon the American Heart Association's recently released update "Guidelines for the Early Management of Patients with Ischemic Stroke"<sup>1</sup> and the "Supplement to the Guidelines for the Management of Transient Ischemic Attacks"<sup>2</sup>. Much of it was taken, with permission, from the "Guideline for the Management of Adult Patients with Acute Ischemic Stroke" from Baystate Health System. It also includes recommendations based on the National Stroke Association's "Stroke: The First Hours, Guidelines for Acute Treatment",<sup>3</sup> the American College of Chest Physicians' "Antithrombotic and Thrombolytic Therapy for Ischemic Stroke",<sup>4</sup> the American Stroke Association/American Academy of Neurology Statement "Anticoagulants and Antiplatelet Agents in Acute Ischemic Stroke",<sup>5</sup> The Brain Attack Coalition's "Recommendations for the Establishment of Primary Stroke Centers",<sup>6</sup> and recent clinical trials, and relies upon the reviews published in the Cochrane Database of Systematic Reviews. This guideline also includes an order set. An on-line data collection tool, The "Stroke Patient Management Tool", from the American Stroke Association and quality improvement activities will re-enforce this guideline and be used to modify it in the future.

## **ACUTE ISCHEMIC STROKE**

### ***Decision to Admit***

It is recommended that all patients with the diagnosis of ischemic stroke be admitted under the inpatient designation to a dedicated stroke unit. Randomized controlled trials have demonstrated that stroke units reduce mortality, dependency and institutionalization and improve quality of life when compared to general medical wards.<sup>7,8</sup>

Essential features of stroke units are nurses who are trained to closely monitor a patient's neurologic status, physiatrists, rehabilitation therapists and physicians trained to diagnose and treat cerebrovascular disease. At Dartmouth-Hitchcock Medical Center, 5 West is organized as a dedicated stroke unit.

### ***Admission to the NSCU***

Admission to the Neuro Special Care Unit instead of a regular bed on 5 West is recommended for stroke patients with the following characteristics:

- Recent treatment with Alteplase (t-PA)
- Severe behavioral deficits (e.g., severe aphasia or agitation requiring continuous observation)
- Unstable neurologic signs/symptoms (e.g., frequent severe TIAs, deteriorating course)
- Significantly impaired level of consciousness (e.g., requires more than minor stimulation to respond or National Institutes of Health Stroke Scale (NIHSS) item 1a. score equals 2 or 3)
- Recent cardiac arrhythmia requiring cardiac monitoring but without hemodynamic instability. Patients thought to be at high risk of developing a life-threatening tachyarrhythmia or bradycardia are better managed in the ICU or ICCU.
- Frequent doses of intravenous antihypertensive medication is required

### ***Admission to the ICU***

Admission to the Intensive Care Unit is recommended for stroke patients with the following characteristics:

- Intubated or mechanically ventilated or at high risk of developing airway compromise or hypoventilation in the near future
- Severe hypertension or hypotension requiring the use of an arterial line or continuous intravenous infusions of antihypertensive (except Nicardipine) or pressor medications
- Patients thought to be at high risk of developing a life-threatening tachyarrhythmia or bradycardia
- Severe medical comorbidity (sepsis, recent cardiac ischemia)

## ***Inpatient Treatment Goals***

Inpatient treatment goals are:

1. To determine the etiology of stroke, treat the acute consequences of stroke and to initiate an appropriate treatment plan aimed at preventing recurrent stroke.
2. To determine the patient's clinical deficit and care needs and to establish a plan for rehabilitation.
3. To prevent and/or treat the subacute complications of stroke including deep venous thrombosis, aspiration, and urinary tract infection.
4. To educate the patient and caregivers.

## ***Stroke Treatment***

### *General Measures*

Rapid evaluation and treatment of those eligible for thrombolysis is encouraged (refer to DHMC's t-PA for Acute Ischemic Stroke Guideline for details).

There is general agreement to recommend airway support and ventilatory assistance for patients with a depressed level of consciousness, oxygen supplementation to correct hypoxemia, assessment and treatment of hypoglycemia, hyperglycemia and fever as these measures may reduce the degree and volume of infarction.<sup>1</sup>

### *Blood Pressure Management*

Arterial hypertension is common in the setting of acute stroke and there is no evidence that the use of agents to artificially lower or raise blood pressure improves outcome. Many authors have expressed concerns about the use of antihypertensive agents, which may deleteriously effect the ischemic penumbra or cause recurrent ischemia in patients with large artery stenoses.

There is general consensus that blood pressure treatment should be considered when the systolic blood pressure remains consistently above 220 mm Hg, the diastolic blood pressure remains consistently above 120 mm Hg and the mean arterial pressure (MAP) remains above 130 mm Hg or in the setting of emergencies such as myocardial infarction or aortic dissection. <sup>1</sup>

In situations where blood pressure needs to be reduced it should be done gradually in 10-20% decrements in the MAP while observing the patient for clinical deterioration.

Recommended agents include intravenous labetalol, nicardipine, hydralazine, and enalaprilat with appropriate intensity of physiological monitoring if used. (For blood pressure management after Alteplase [ t-PA] is used, please refer to the Alteplase [ t-PA] Practice Guideline).

Persistent arterial hypotension can be managed with volume replacement with normal saline, correction of arrhythmias, and vasopressor agents including dopamine (Adams 2003).

### *Anticoagulation*

There is a growing consensus against the *routine* use of anticoagulants in the management of acute ischemic stroke.<sup>1,4,5</sup> Unfractionated and low molecular weight heparins in lower doses are effective agents for the prophylaxis and treatment of DVT following stroke. Nonpharmacologic treatments for preventing DVT including early mobilization, anti-embolic stockings, and intermittent compression boots should also be considered

In recent large randomized trials evaluating unfractionated heparin (International Stroke Trial, 1997), low-molecular weight heparins (FISS, FISS bis, Heparin in Acute Embolic Stroke Trial, and TAIST)<sup>8-10, 12, 13</sup> and a heparinoid (Trial of ORG 10172 in Acute Stroke Treatment),<sup>14</sup> these agents were not helpful in patients with acute ischemic stroke. Subgroup analysis of the TOAST study showed a benefit at 3 months

among patients with large artery atherosclerotic stroke and severe stenosis or occlusion of the internal carotid artery after treatment with a heparinoid (Adams 1999).<sup>15</sup>

At this time, anticoagulation in specific stroke subtypes has received inadequate attention.<sup>1,5</sup> Experts suggest that anticoagulation should be considered ONLY for patients who have an unstable course consisting of recent recurrent episodes of brain ischemia and in patients believed to be at high risk of recurrent embolism or thrombus extension. These patients include those with a high risk cardiac source of embolism (i.e., atrial fibrillation, recent anterior wall myocardial infarction, dilated cardiomyopathy, or valvular heart disease), noninfectious cerebral vein thrombosis, or severe stenosis or recent occlusion of a large extracranial or intracranial artery.<sup>16</sup>

A modified protocol for intravenous unfractionated heparin is included in addition to the standard DHMC protocol. This modified protocol is also weight-based and allows one to avoid all boluses which may reduce the risk of hemorrhagic complications.<sup>17</sup> A protocol for enoxaparin is also provided. Low molecular weight heparins including enoxaparin have not been shown to be superior to unfractionated heparin in the prevention of early stroke recurrence or progression, but potential advantages include the ease of administration and the avoidance of boluses, and may allow certain patients to be discharged to home as they start Coumadin. Low molecular weight heparins have been accepted as first-line therapy for patients with unstable angina/non-ST-elevation myocardial infarction and have several pharmacological advantages over unfractionated heparin.<sup>18</sup> Low molecular weight heparins are not recommended in patients with prosthetic heart valves because cases of valve thrombosis have been reported. Unfractionated heparin is preferred over low-molecular weight heparins in the setting of renal failure and if surgery or invasive procedures are expected in the near future.

**Anticoagulants are contraindicated for 24 hours after intravenous ALTEPLASE (t-PA) is used. Anticoagulants are also contraindicated for large cerebral infarcts, small or medium sized infarcts with significant hemorrhagic transformation (with the exception of venous thrombosis), uncontrolled severe hypertension, bacterial endocarditis, and sepsis.**

#### Antiplatelet agents

Aspirin started within 48 hours of cerebral infarction modestly lowers the risk of death and recurrent stroke at 6 months.<sup>19,20</sup> On the basis of the International Stroke Trial<sup>8</sup> and the Chinese Acute Stroke Trial,<sup>21</sup> aspirin can prevent an estimated 9 fewer deaths or nonfatal stroke per 1000 patients treated. Based on these studies, Aspirin 160-325 mg/day is recommended on admission for patients able to take aspirin.

Dipyridamole with aspirin (available as Aggrenox®) and Clopidogrel (Plavix®) have been shown to be effective in the secondary prevention of stroke,<sup>22,23</sup> but their role in acute ischemic stroke is undefined. Clopidogrel is the drug of choice in patients who are unable to take aspirin. Dipyridamole with aspirin (available as Aggrenox®) is currently not on the formulary at DHMC. Glycoprotein IIb/IIIa agents have not been studied sufficiently after acute ischemic stroke and are not recommended.

**Antiplatelet agents are contraindicated for 24 hours after ALTEPLASE (t-PA) is used.**

#### Seizures

The reported frequency of seizures following acute ischemic stroke has most consistently been estimated to be from 5% to 10%, and occur less often than following acute hemorrhagic stroke. Most often, seizures complicating brain infarction occur after the acute period.<sup>24</sup> Most are partial and the incidence of status epilepticus is very rare. Recurrent seizures are observed in only a minority of patients who experience a first seizure. Phenytoin, fosphenytoin, and carbamazepine are appropriate anticonvulsants for patients with post-stroke seizures. There is no data to support the prophylactic use of anticonvulsants following ischemic stroke.

#### Elevated Intracranial Pressure

Clinical deterioration as a result of focal “compartmentalized” or generalized elevated intracranial pressure occurs in 10-20% of patients, usually as a complication of large hemispheric infarction associated with

extensive cerebral edema. Large cerebellar infarctions can also lead to hydrocephalus and increased intracranial pressure. Edema usually peaks at 3-5 days following the initial stroke.

Conservative measures include elevating the head, avoiding neck rotation and compression of jugular vein flow, avoiding hypo-osmolar intravenous fluids and treating conditions such as hypoxia and hyperthermia that may increase intracranial pressure. Hypotension can further decrease cerebral perfusion and can be treated with intravenous fluids and, if associated with clinical deterioration, pressors such as phenylephrine (2-10 micrograms/kg/min) or dopamine (2-20 micrograms/kg/min).<sup>1</sup> Therapies that can be used to reduce intracranial pressure in patients whose condition is deteriorating include osmotherapy (e.g., mannitol, glycerol, and hypertonic saline), hyperventilation and ventriculostomy. Mannitol 20% is most commonly used and is given as 0.25-0.50 grams/kg over 20 minutes and is often given with furosemide 10 mg intravenous push to encourage diuresis and avoid volume overload. Doses are repeated up to every 6 hours based on the response but serum osmolality should remain less than 310 mOsm/L. Craniotomy with partial temporal lobectomy and hemicraniectomy are sometimes considered in massive hemispheric infarction with deterioration and hemicraniectomy is currently under investigation.<sup>1</sup> There are currently no trials to assess the efficacy of these treatments in patients with acute stroke.<sup>25</sup> Corticosteroids have been shown to be ineffective.<sup>1</sup>

Surgical decompression and evacuation can be effective in the management of large cerebellar infarctions that compress the brain stem if extensive brainstem infarction has not already occurred.<sup>1</sup>

### *Dysphagia*

It has been estimated that up to 45% of all strokes are complicated by dysphagia. More than half of patients with dysphagia improve by the end of the first week.<sup>26</sup> Improvement, however, may still not mean that they are able to eat a non-modified diet, or consume enough to maintain their caloric needs.

Our recommendation is to keep stroke patients NPO until they have had a preliminary bedside swallowing evaluation by a Speech Language Pathologist if any of the following are present: lethargy; dysarthria; gurgling vocal quality; hypophonia; aphasia; severe neglect; obvious weakness of face, tongue or palate; confusion; significant apraxia; difficulty handling secretions; or drooling.

For patients for whom the decision has been made to provide supplemental enteral nutrition, initial feeding is usually through a soft, small bore nasogastric feeding tube until the degree of, and or, resolution of dysphagia is determined.<sup>26</sup> Because initial recovery from dysphagia may occur spontaneously, decision making regarding percutaneous gastrostomy (PEG) placement is generally best delayed for 2-4 weeks except in special patient populations. These include those with brainstem infarction or large hemispheric infarction and severe bulbar dysfunction with little clinical improvement.

Serial evaluations by a Speech and Language Pathologist and, as recommended by Speech Pathology, a modified barium swallow examination are helpful when making clinical decisions related to non-oral or modified oral means of nutrition. Decisions regarding the management of dysphagia will be based on the clinical presentation of the patient, the length or time the dysphagia is expected to persist and the caloric intake required.

### ***Initial Diagnostic Evaluation***

In addition to a thorough neurological examination, the initial evaluation of the patient with an acute stroke should include a comprehensive history and physical examination. Special attention should be paid to identifying any prior history of brain ischemia and physical evidence of cardiac murmurs, rhythm disturbances and carotid bruits.<sup>1</sup>

Initial imaging should be carried out by non-contrast head CT to determine whether the stroke is ischemic or hemorrhagic since this carries immediate implications for further treatment.

Initial laboratory testing should include an ECG, chest x-ray, complete blood count including platelets, PT, PTT, serum electrolytes, glucose, BUN, and creatinine. For patients with known or suspected diabetes, a glycosylated hemoglobin (HbA1C) is recommended. A fasting lipid panel should be ordered on admission if a recent one is not available.

Extracranial Doppler ultrasonography should be considered in all cases to screen for internal carotid and proximal vertebral artery disease. Transcranial Doppler ultrasonography can be used to evaluate patients for intracranial stenosis and abnormal blood flow patterns related to extracranial disease.

MRI and MRA of the brain are recommended when causes of symptoms other than stroke are being considered or when the cause of stroke is not evident after the above tests are obtained. MRI may provide useful information on possible mechanism of stroke and prognosis. MRA of the cervical arteries can be useful when ultrasonographic evaluation is limited, not available, or needs corroboration, or if disease of the extracranial vertebral or common carotid arteries is suspected.

The use of hyperacute multi-modal MRI with diffusion-weighted imaging (DWI), perfusion-weighted imaging, and gradient-recalled echo (GRE) or susceptibility-weighted MRI sequences is currently under investigation and, at this time, is not recommended for most patients. These techniques may allow one to distinguish tissue with potentially reversible ischemia from tissue with irreversible infarction while having adequate sensitivity for detecting hemorrhage.<sup>1</sup> Axial T1-weighted images with fat suppression of the neck and brain can detect changes of arterial dissection.

CT angiography can provide information on the intracranial and extracranial vasculature and should be considered when MRI is contraindicated, technically limited or not tolerable. CT angiography of the intracranial vasculature can be obtained on admission, when decisions regarding intravenous and intra-arterial thrombolysis and anticoagulation need to be made rapidly.

Echocardiography should be ordered on admission if a cardiac or aortic source is strongly suspected, and in other cases, after the above investigations fail to identify the probable cause of stroke and a cardiac or aortic source is suspected. For patients with recent anterior wall myocardial infarction or a known cardiomyopathy, transthoracic echocardiography (TTE) is the appropriate initial study to order. Transesophageal echocardiography (TEE) is indicated when TTE results are technically inadequate.

We suggest that TEE be performed BEFORE TTE in patients less than 50 years of age and when sources of embolism usually not adequately detected by TTE are strongly suspected. These sources include: left atrial enlargement and thrombus, atrial septal aneurysms, patent foramen ovale, aortic arch atherosclerosis, and valvular vegetations from endocarditis. For stroke patients with brain embolism attributed to atrial fibrillation, echocardiography is not always required unless the results would assist decision making about anticoagulation or cardioversion.

Telemetry or 24-hour Holter monitoring should be considered if the history or cardiac examination suggests increased risk of arrhythmia or cardiac ischemia.

When routine testing or clinical factors fail to establish a likely etiology of stroke, additional laboratory tests (e.g., thrombosis screen, urine drug screen, RPR), and occasionally, conventional angiography, and cerebrospinal fluid analysis, may be helpful in select cases. At DHMC, the thrombosis screen tests to be performed are usually determined by a clinical pathologist after reviewing the available clinical data. If venous thrombosis is in the differential diagnosis (e.g., cerebral vein thrombosis, patent foramen ovale), this should be included in CIS clinical notes. The clinical pathologist can be contacted (extension 5-7171 or 5-8604) regarding the content of this screen. An excellent review of selection and performance of tests for thrombosis risk assessment in ischemic stroke patients is available at: <http://stroke.ahajournals.org/cgi/content/full/31/12/3067><sup>27</sup>

## **Preventive Measures**

### Early mobilization and return to self care

Early mobilization should be encouraged as soon as possible after admission, if medically and neurologically feasible, as this can prevent the complications discussed below. Patients should also be encouraged to resume self-care activities including eating, toileting, dressing, and grooming and participate in mental and social activities as soon as possible after admission as this enhances recovery and the patient's sense of control and well-being.<sup>28</sup>

### Deep Vein Thrombosis

Stroke patients are at high risk of developing deep vein thrombosis (DVT) and non-ambulatory patients should receive an effective regimen for DVT prevention. Acceptable measures include intermittent pneumatic compression sleeves, low dose unfractionated heparin, and low-molecular weight heparin.<sup>1</sup>

### Aspiration

Aspiration is one of the most common complications following stroke. Effective measures for preventing aspiration include keeping the head of bed elevated to 30 degrees, avoiding sedative and anticholinergic drugs which can impair swallowing, and the careful screening and subsequent feeding of patients (see above section, Dysphagia). There is no data that clearly demonstrate that nasogastric or PEG tubes independently prevent or reduce the incidence of aspiration in patients with impaired swallowing.<sup>26</sup> However, it appears that dysphagia specific management likely reduces the risk of pneumonia and improves nutritional support.<sup>26</sup>

### Urinary tract infection

Urinary tract infection is a common complication of stroke and often relates to the use of indwelling urinary catheters. The use of catheters should be avoided if possible. Bladder ultrasonography is available on 5 West and can be helpful in assessing a patient's post-void residual and need for catheterization. For patient's unable to void independently, intermittent catheterization is an alternative to indwelling catheterization that is associated with a lower risk of infection.

### Constipation/obstipation

Daily bowel programs should be started from admission to allow appropriate regulation of bowels. Bowel movements slow as a result of immobility, illness, and change in routine. Maintaining rectal vault evacuation daily will assist in avoiding obstipation which can delay recovery. Symptoms of obstipation include anorexia, fatigue, nausea, progressing to abdominal pain and vomiting. A bowel regimen is included in the order set.

### Skin breakdown:

Attention to early changes of skin breakdown is important following stroke. Correct positioning can prevent skin breakdown and joint contractures. Frequent repositioning, the use of specialized pressure-reducing mattresses and chairs, splints, range of motion exercises, elbow and heel protection, and local wound care are recommended in immobilized patients. Physical and occupational therapists should be consulted regarding these treatments.

## **Prevention of Recurrent Stroke**

Initiation of measures to prevent recurrent stroke, with the exception of aggressive lowering of blood pressure in the acute phase, are encouraged during the hospitalization following ischemic stroke. See "Risk Factor Management" below. The timing of anticoagulation for prevention of stroke from atrial fibrillation and endarterectomy for symptomatic carotid artery disease is controversial and is based on many factors including the size of infarction, neurologic status, medical comorbidities, and the estimated risk of recurrent stroke.

## **Multidisciplinary Care**

Effective management of patients with stroke requires a coordinated multidisciplinary approach to care. We recommend, on admission, consultation with Rehabilitation Medicine Department staff (in the form of

Physical Therapy, Occupational Therapy, Speech/Language Pathology). Clinical Resource Coordinators and Social Workers on 5 West are an integral part of stroke patient care.

### Assessment of Stroke Severity

A number of valid instruments have been developed to assess stroke severity and predict prognosis. These scales can also be used to measure the impact of medical interventions on stroke outcomes. As part of the management of patients admitted to the Stroke Unit, we plan on training the staff to administer the National Institutes of Health Stroke Scale (NIHSS) on admission and recorded in the medical record.

In a recent analysis by the TOAST investigators, the baseline NIHSS score strongly predicted outcome with one additional point on the NIHSS decreasing the likelihood of an excellent outcome at 3 months by 17%.<sup>29</sup> At 3 months, excellent outcomes were noted in 46% of patients with scores of 7 to 10 and in 23% with scores of 11 to 15. A score of greater than or equal to 16 predicts a high probability of death or severe disability whereas as score of 6 or less predicts a good recovery.<sup>29</sup> In another recent series, the initial NIHSS score predicted hospital disposition. A score of <5 was associated with discharge home, 6-13 with rehabilitation, and >13 with long-term nursing facility.<sup>30</sup> An admission score of >7 has been associated with a higher risk of deterioration.<sup>31</sup>

Table 1  
Ischemic Stroke Outcomes at 3 months based on admission NIHSS

NIHSS	Outcomes at 3 months	
	Good or excellent	Excellent
0-3	95%	80%
4-6	87%	64%
7-10	78%	45%
11-15	56%	23%
16-22	41%	18%
23+	19%	5%

### Discharge Timing and Planning and the Risk of Early Deterioration

Stroke severity, risk of deterioration, and the degree of long-term disability can be estimated within the first 48 hours after stroke onset. However, stroke is a very complex disease with an extremely variable presentation and course so early deterioration, recurrent stroke, and life-threatening complications can occur unpredictably. We therefore generally recommend close observation and neurological monitoring in an inpatient setting for a minimum of 3 days for patients with a significant functional deficit.

Neurological deterioration, either focal or global, has been reported to occur in 20-40% of patients within the first week of ischemic stroke<sup>32</sup> and can occur despite initial improvement. Of 92 patients presenting with a severe motor deficit, 24% had worsening of motor function during the first 5 days after stroke onset, and interestingly, these worsening patients tended to have small “lacunar” infarctions.<sup>33</sup> Predictors of deterioration include large hemispheric or cerebellar infarctions, severe large artery occlusive disease, pure motor stroke from lacunar infarction, chronic hypertension and diabetes. The admission NIHSS score has been shown to predict early deterioration. In one study, 66% of patients with a score > 7 worsened within 48 hours versus 15% of those with score < or equal to 7.<sup>31</sup>



Deterioration can be due to recurrent infarction or enlargement of infarction, hemorrhagic transformation, delayed cerebral edema, brainstem compression, hydrocephalus, seizures, medical complications (e.g., infection, myocardial infarction, pulmonary embolism, hyperglycemia, hypoglycemia, hyponatremia, withdrawal states) and medications (e.g., benzodiazepines, opioids, and neuroleptics).

This deterioration may be amenable to specific therapies if initiated early. Blood pressure elevation and hydration, and urgent revascularization may improve cerebral perfusion; osmotherapy, hyperventilation and sedation can decrease intracranial pressure; more aggressive antithrombotic agents may lessen the chance of thrombus propagation and recurrent embolism; ventriculostomy relieves hydrocephalus; and cerebellar and partial temporal lobe resection or hemicraniectomy can be lifesaving in select cases. Also, treatment of fever and hyperglycemia may lessen ischemic damage and improve outcome.

Discharge should be considered when the patient is judged to be clinically stable after a reasonable period of close observation has passed. A minimum hospitalization of 3 days is recommended for most patients with ischemic stroke and a longer period should be considered for patients at higher risk for deterioration and those with an unstable course or complications. In some cases, discharge needs to be delayed until diagnostic studies are completed so that high risk sources of stroke recurrence can be identified or excluded and the most appropriate therapy can be initiated (e.g., angiography to assess for severe stenosis of the internal carotid, basilar or middle cerebral artery). Discharge should not occur until functional status has been assessed, a stroke prevention and rehabilitation plan has been established and the patient and the family have been educated.

Follow-up in our Stroke Assessment and Prevention Clinic is appropriate for most patients and can be arranged by calling extension 3-1875.

## **TRANSIENT ISCHEMIC ATTACKS**

Over 50,000 Americans suffer a transient ischemic attack (TIA) each year and these symptoms are important warning signs of future stroke. Our recommendations for patients with TIA are based on the American Heart Association's "Guidelines for the Management of Transient Ischemic Attacks" published in 1994,<sup>34</sup> and the "Supplement to the Guidelines for the Management of Transient Ischemic Attacks" published in 1999.<sup>2</sup>

### ***Decision to Admit***

In general, we recommend hospitalization under observation status and an expeditious evaluation following recent TIA. Factors that should be weighed when making a decision about hospitalization include the nature and frequency of the symptoms, duration of time since symptoms occurred, medical comorbidity, the need for parenteral medications including anticoagulation, and the patient's ability and desire to complete the evaluation promptly as an outpatient.

The risk of early stroke following a TIA may be higher than previously estimated. In a recent study of patients presenting with their first TIA, the risk of stroke at 7 and 30 days was 8.6% and 12% respectively.<sup>35</sup>

A recent review of patients presenting to emergency departments with TIA found that certain clinical characteristics increased the risk of stroke in the next 90 days. These included: diabetes mellitus, age > 60 years, symptoms lasting more than 10 minutes, speech disturbance, and weakness.<sup>36</sup> Approximately 10% of TIA patients suffered a stroke within 90 days and half of those occurred in the first 48 hours after TIA.

### ***Inpatient Treatment Goals***

1. Clarify if the patient has a high-risk source of acute ischemic stroke and begin appropriate therapy if identified.
2. Begin antithrombotic therapy aimed at the presumed mechanism of TIA and other medical therapies and behavioral changes that are aimed at minimizing cardiovascular risk factors (see below).

### ***Initial Evaluation***

The recommended diagnostic evaluation of TIA symptoms is very similar to that recommended for ischemic stroke (see the above section for acute ischemic stroke). Despite the resolution of symptoms, TIA patients often have abnormalities on MRI (DWI) sequences. These changes can be useful in confirming the vascular nature of the symptoms and providing useful clues that can help establish the potential pathogenic mechanism.

### ***Risk Factor Management***

The following recommendations are based on the American Heart Association's "Supplement to the Guidelines for the Management of Transient Ischemic Attacks" published in 1999.<sup>2</sup>

*Hypertension* should be treated to maintain systolic blood pressure below 140 mm Hg and diastolic blood pressure below 90 mm Hg. For persons with diabetes, blood pressure levels <130/85 mm Hg are recommended.<sup>2</sup> The most recent guideline from The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) recommends that individuals with a systolic BP of 120 to 139 mm Hg or a diastolic BP of 80 to 89 mm Hg should be considered as prehypertensive and require health-promoting lifestyle modifications to prevent CVD, including dietary changes and regular physical exercise. JNC-7 also recommends the use of thiazide-type diuretics and ACE-I to treat hypertension following stroke.<sup>37</sup> Adjustment of these blood pressure goals may be necessary in some patient subgroups (e.g., those with severe carotid stenosis and possible hemodynamic impairment).

*Cigarette smoking* should be discontinued. Counseling, nicotine replacement therapies, bupropion, and formal smoking cessation programs should be made available.<sup>2</sup>

*Excessive use of alcohol* should be eliminated. Formal alcohol cessation programs are recommended. Mild to moderate use of alcohol (1 to 2 drinks per day) has been associated with a reduction in stroke rates.

*Treatment of hyperlipidemia* is recommended. The AHA dietary guidelines for those with elevated LDL or pre-existing cardiovascular disease (formerly known as the Step II diet) are recommended. These consists of <30% of calories derived from fat, <7% from saturated fat, and <200 mg/d cholesterol consumed is recommended along with maintenance of ideal body weight and engagement in regular physical activity. If lipid levels remain elevated (LDL >130 mg/dL), use of a lipid-lowering agent, preferably a statin, is recommended. The goal of therapy should be an LDL level <100 mg/dL.<sup>38,39</sup> Recent studies have found that these medications reduce the risk of stroke in patients with systemic vascular disease, diabetes, or hypertension (absolute risk reduction 1.4%) and the risk of major vascular events but not stroke alone in patients with cerebrovascular disease with low LDL levels.<sup>40</sup>

*Additional dietary changes* including increased intake of fruits and vegetables and fish should be encouraged as they have been associated with improvement in vascular disease risk factors and a decreased risk of stroke.<sup>36</sup>

*Fasting blood glucose* levels <126 mg/dL are recommended. Diet and oral hypoglycemics or insulin should be prescribed as needed to control diabetes.<sup>2</sup>

*Physical activity* (at least 30 minutes per day, most days of the week) is recommended.

### ***Antithrombotic Therapy***

#### ***Atherothrombotic TIAs***

We recommend the following based on the American Heart Association's "Supplement to the Guidelines for the Management of Transient Ischemic Attacks" published in 1999.<sup>2</sup>

In general, aspirin at a dosage range of 50 to 325 mg/d is recommended as initial therapy for patients who are not allergic or intolerant to aspirin. Clopidogrel and the combination of aspirin and extended-release

dipyridamole are acceptable options for initial therapy following an atherothrombotic TIA, although their cost-effectiveness has been questioned.<sup>22,23</sup> Aspirin with extended-release dipyridamole (available as Aggrenox®) is not currently on the inpatient formulary at DHMC.

According to the AHA, “for patients who have an atherothrombotic TIA while taking aspirin, there is no compelling evidence that increasing the dose of aspirin provides additional benefit. Alternative antiplatelet agents and combination antiplatelet regimens are typically considered for these patients, although they have not been specifically evaluated in patients who have failed aspirin”.<sup>2</sup>

According to the AHA guidelines, “anticoagulant therapy is not routinely recommended for patients with atherothrombotic TIAs, as either short- or long-term therapy”.<sup>2</sup> As stated above for acute ischemic stroke, anticoagulation in specific stroke and TIA subtypes has received inadequate attention. Experts suggest that anticoagulation should be considered only for those with “crescendo TIAs” and those believed to be at high risk of recurrent embolism or thrombus extension. These patients include those with severe stenosis or recent occlusion of the ICA, MCA, vertebral or basilar artery.<sup>16</sup>

With intense anticoagulation with INR 3.0 to 4.5, the risk of brain hemorrhage outweighs the potential benefits (grade A-1). **Therefore, if oral anticoagulants are used for atherothrombotic TIA patients, a target INR <3.0 should be chosen.**

The standard DHMC protocol for intravenous unfractionated heparin is provided. A protocol for enoxaparin is also provided.

### **Cardioembolic TIAs**

In accordance with the American Heart Association’s “Supplement to the Guidelines for the Management of Transient Ischemic Attacks” published in 1999,<sup>2</sup>:

“Long-term oral anticoagulation is recommended for patients with atrial fibrillation who have a TIA. For these patients, a target INR of 2.5 (range 2.0 to 3.0) is recommended. Oral anticoagulation is also beneficial for prevention of stroke in patients with other high-risk cardiac sources of embolism. These include mechanical prosthetic valves, left ventricular thrombus, and recent anterior wall myocardial infarction. The role of anticoagulation for patent foramen ovale, atrial septal aneurysms, and mobile aortic arch atheromata is less clear. Aspirin is recommended for patients with contraindications to oral anticoagulation”.<sup>2</sup>

### ***Surgical/endovascular Therapies***

#### **Extracranial Carotid Artery Disease**

In accordance with the AHA guidelines, we have the following recommendations:<sup>2</sup>

##### *Stenosis of 70% to 99%\**

“Carotid endarterectomy is indicated for patients who are good surgical candidates and who have experienced TIA or minor stroke within the last 2 years, regardless of the response to antiplatelet drugs .

##### *Stenosis of 50% to 69%\**

Patients with a recent TIA or minor stroke have a reduced stroke rate with endarterectomy versus medical treatment and should be considered for endarterectomy . The absolute benefit of surgery is less than that for patients with higher degrees of stenosis and among women and patients with retinal TIAs. Consideration should be given to clinical features that influence stroke risk and surgical morbidity.<sup>41,42</sup>

##### *Stenosis <50%\**

Patients with <50% stenosis with recent symptoms of cerebral ischemia do not benefit from carotid endarterectomy. Antiplatelet therapy is recommended for these patients”.<sup>2</sup>

##### *Endovascular Treatment*

“Prospective trials evaluating the results of angioplasty and stent placement in comparison with carotid endarterectomy are now in progress. The use of endovascular treatment is not routinely recommended for treatment of carotid bifurcation stenosis”.<sup>2,43</sup>

Patients that may be appropriately treated with endovascular therapy rather than endarterectomy include those with surgically inaccessible bifurcations, restenosis following endarterectomy, radiation-induced atherosclerosis, and severe stenosis due to arterial dissection and fibromuscular dysplasia.<sup>44,45</sup>

### **Bypass Surgery**

According to the AHA Guidelines, “extracranial-intracranial bypass is not recommended for patients with TIAs. A subgroup of patients with anterior circulation ischemia unresponsive to medical therapy with hemodynamic disturbances may benefit from bypass surgery. Additional studies are required to determine the role of surgery in these patients. Patients with moyamoya disease may benefit from extracranial-intracranial bypass”.<sup>2</sup>

### **Therapy for Vertebrobasilar Ischemia**

According to the AHA Guidelines, “surgical or endovascular therapy may be appropriate for patients with significant vertebrobasilar stenosis who have continued symptoms referable to the posterior circulation despite medical therapy. For significant stenosis at the origin of the vertebral artery, vertebral artery transposition to the common carotid artery or angioplasty and stenting are treatment options. For significant stenosis at the distal vertebral artery, endarterectomy, bypass, or endovascular procedures are treatment options. For midvertebral lesions with fixed stenosis or positional obstruction with ischemic symptoms, surgical reconstruction or decompression can be effective in relieving symptoms”.<sup>2</sup>

### **Closure of Patent Foramen Ovale**

The role of surgical and transcatheter closure of patent foramen ovale is unclear and is currently under investigation in clinical trials.

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