3. CEREBROVASCULAR DISEASE

Beatrice A. Golomb, MD, PhD

The development of quality indicators for stroke prevention and
treatment began with a MEDLINE search of English language review
articles from 1992 to 1996. More targeted searches on carotid
endarterectomy, hypertension, antiplatelet therapy, anticoagulation, and
thrombolysis were then performed to supplement the original group of
articles. In addition, selected clinical studies referenced in review
articles were retrieved when relevant to the development of specific
preventive or therapeutic indicators.

IMPORTANCE

Stroke is a leading cause of death and disability in developed
countries (Feinberg, 1996). The incidence of stroke is estimated at one
to ten per 1000 persons aged 60 years and older (Brodedrick, Phillips et
al., 1989; Phillips and Whisnant, 1992). New or recurrent stroke
affects approximately 550,000 persons in the U.S. each year, for an
average of approximately one stroke each minute (Post-Stroke
Rehabilitation Guideline Panel, 1995; Brickner, 1996). Stroke is the
third leading cause of mortality in the U.S. (Brickner, 1996),
accounting for approximately 150,000 deaths each year (Taylor et al.,
1996). Stroke accounts for ten to 12 percent of all deaths in
industrialized countries (Bonita, 1992). Mortality among those who have
had a stroke is approximately 17 to 34 percent at one month, and 25 to
40 percent at one year (Post-Stroke Rehabilitation Guideline Panel,
1995). Eighty-eight percent of deaths attributed to stroke occur in
people over the age of 65 (Bonita, 1992). Stroke is also the leading
cause of serious disability in the U.S. with over three million people
living with disability from stroke (Post-stroke Rehabilitation Guideline
Panel. 1995). Of those who survive to one year after the incidence of
stroke, one-third will no longer be able to live independently
(Humphrey, 1995). The economic burden of stroke was estimated to be $30

billion in 1993, with $17 billion in direct medical costs and $13 billion in costs associated with lost earnings (Taylor et al., 1996).

"Stroke" is a generic term for a clinical syndrome that includes focal cerebral infarction (ischemic stroke), focal hemorrhage in the brain, and subarachnoid hemorrhage. "Infarction" refers to necrosis defined at microscopic examination and inferred from neuroimaging (Phillips, 1992). Transient ischemic attacks (TIAs) are arbitrarily distinguished from strokes, and refer to ischemic deficits (acute, focal neurologic symptoms resulting from vascular disease) that persist for less than 24 hours (Humphrey, 1995; Gress 1994). The majority of TIAs last from five to 15 minutes (Kelley et al., 1992). Some events designated as TIAs by this clinical definition will have infarction demonstrated by computed tomography (CT) or magnetic resonance imaging (MRI) studies (Gress, 1994). The incidence of TIAs is 0.5 per 1000 people (Humphrey, 1995). The risk of stroke after TIA is highest in the first year, and approximately 30 percent in five years (Humphrey, 1995). In patients with carotid stenosis of unspecified degree, the risk of stroke is approximately ten to 12 percent in the first year after TIA (Humphrey, 1995).

SCREENING

Screening for reversible risk factors for cerebrovascular disease (CVD), specifically hypertension and cigarette smoking, is widely advocated because it may lead to treatment that reduces the rates of stroke and death. Hypertension and smoking are risk factors not only for cerebrovascular but for cardiovascular and other diseases, which increases the utility of screening for these factors. Additional discussion of the benefits of intervention for these risk factors is discussed below in the section on Primary and Secondary Prevention.

The physical exam (auscultation) for carotid bruits is neither sensitive nor specific for carotid stenosis. In one evaluation, specificity was 70 percent and sensitivity was 57 percent for 70 to 99 percent of stenosis cases (Humphrey, 1995; Brown et al., 1994). Because data do not clearly support intervention (i.e., carotid endarterectomy) to reverse even tight stenosis in asymptomatic patients, the utility of

screening asymptomatic patients for CVD through auscultation of carotid bruits is currently limited (UPSTF, 1996).

Primary and Secondary Prevention

Hypertension

The most well-identified predictor of stroke, hypertension is a factor in nearly 70 percent of strokes (Bronner, 1995). Meta-analysis has shown a 10 to 12-fold increase in the risk of stroke for people in the high category of diastolic blood pressure (mean: 105 mm Hg) compared with the lowest category (mean: 76 mm Hg) (Bronner, 1995). Moreover, reduction in diastolic blood pressure has been shown to reduce the risk of cardiovascular events, particularly stroke, in persons aged 60 to 79 years (Phillips, 1992). Screening and treatment for hypertension are covered in another Chapter 5.

Smoking

Cigarette smoking is a major independent risk factor for both ischemic and hemorrhagic stroke. Smokers have a significant (50%) increased risk of stroke compared with nonsmokers, and the risk appears to increase in a dose-response manner (Bronner et al., 1995). The risk of stroke for former smokers is lower than that for current smokers, with reductions of 30 to 40 percent in the first two to five years after smoking cessation (Bronner et al., 1995). Screening for smoking, and smoking cessation, are covered in another chapter.

Anticoagulation for Atrial Fibrillation

Atrial fibrillation affects about one percent of the general population, six percent of people over age 65, and ten percent of those over age 75. Nonvalvular atrial fibrillation is estimated to cause 75,000 strokes each year in the U.S., with an annual stroke risk of approximately three to eight percent (Gorelick, 1995). Warfarin reduces the risk of arterial thromboembolism by an average of 70 percent (Feinberg, 1996; MAST-I Group 1995; Gorelick, 1995). There is consensus that anticoagulation in selected patients should be used to reduce risk of stroke with atrial fibrillation (Indicator 3 and 4) (Dalen, 1994). Use of anticoagulation for atrial fibrillation is covered in another chapter.

Other Measures

Although glucose intolerance is associated with increased risk of stroke, the preventive role of strict glycemic control remains uncertain (Bronner, 1995). The population attributable risk of stroke associated with obesity is 15 to 25 percent (Bronner, 1995). Some of this effect is probably modified by hypertension, dyslipidemia, and glucose intolerance, although an independent association has also been observed (Bronner, 1995). However, the effect of obesity control on stroke is uncertain. Evidence of the relationship between serum cholesterol level and risk of stroke is mixed. If trials with clofibrate are excluded, no appreciable association has been found between cholesterol-lowering treatment and risk of fatal or nonfatal stroke, although some studies have shown a trend toward benefit (Scandinavian Simvastatin Survival Study Group, 1994; Shepherd et al., 1995). Trials have shown clofibrate to be associated with an increased risk of fatal stroke and a decreased risk of nonfatal stroke (Bronner, 1995).

Observational studies have shown physical activity to be inversely related to risk of ischemic and hemorrhagic stroke in men and women (Bronner, 1995); however, this relationship could be mediated in part by a reduced ability to exercise in those with preexisting atherosclerotic disease. Use of aspirin in primary prevention in middle-aged individuals failed to demonstrate a significant positive or negative effect on the incidence of all types of stroke in two large trials. Moreover, in the Physician's Health Study, a significant increase in hemorrhagic stroke and a trend to increase in all types of stroke was noted. In the British Doctor's Trial, a significant increase in disabling stroke was seen. A meta-analysis of observational studies found no apparent association between risk of stroke and post-menopausal estrogen replacement therapy (Bronner, 1995). The role of antioxidants in stroke remains to be clarified. Because each of these associations are either weak or inconclusive, we will not address them in the quality indicators.

DIAGNOSIS

Neurological Examination

Stroke and TIA are largely clinical diagnoses, often primarily based on history. Current review articles delineating the diagnostic process for stroke and TIA do not focus on -- indeed, often fail to mention -- the neurological examination (Poole, 1994; Pryse-Phillips 1994). Evidence from one study on the utility of clinical examination found that history and physical exam together allowed accurate diagnosis in 77 percent of cases (Chimowitz et al., 1990); however, the majority of this may be derived from history alone, and 77 percent may be too low a sensitivity to preclude the need for routine use of neuroimaging. Formal scored neurologic exams such as the National Institutes of Health Stroke Scale or the Canadian Neurological Scale have been found to: 1) correlate with infarct size (Brott et al., 1989); 2) predict prognosis; and 3) demonstrate utility in guiding treatment -- for example, by identifying patients at higher risk of hemorrhagic transformation if treated with heparin or tissue plasminogen activator (TPA) (Toni et al., 1996). Findings from a neurological examination may appear consistent with a nonstroke etiology and may direct evaluation toward other diagnoses. Furthermore, an initial neurological examination will permit ongoing assessment of subsequent recovery or deterioration. Nonetheless, there are no data to verify that the physical examination changes therapeutic management if neuroimaging is routinely performed. Moreover, the difficulty of rating the neurological physical examination retrospectively on chart review is formidable enough to warrant excluding it from the quality indicators.

CT Scan or MRI

After a presumed stroke, CT or MRI studies are commonly recommended to differentiate hemorrhagic from ischemic stroke, because management for the two types of stroke may differ (Humphrey, 1995; Brown et al., 1994). Debate remains on whether CT is indicated in all instances of presumed stroke or TIA. The American Heart Association (AHA), like many others (Wardlaw, 1994), advocates the use of CT or MRI in all patients acutely, as seen in its Guidelines for Management of Patients with Acute

Ischemic Stroke (AHA, 1994). Opponents of this position cite the costs of CT and the data indicating that CT does not affect the rate of misdiagnosis (Allison, 1994). For this reason, we do not propose an indicator for routine use of CT in patients presenting with stroke, although routine use of neuroimaging is probably appropriate. However, thrombolytic, anticoagulant, and antiplatelet therapy are clearly inappropriate in hemorrhagic stroke, and an estimated 24 percent of hemorrhagic strokes may have been misdiagnosed as infarcts in the pre-CT era (Phillips, 1992; Drury et al., 1984). Because of this, we have included an indicator requiring that CT or MRI be performed before initiation of each of these treatments (Indicators 1 and 2).

TREATMENT

Treatment of Acute Stroke

There is no proven medical treatment for acute stroke. Dextran has not been shown to be beneficial, and trials of calcium antagonists, steroids, and glycerol are inconclusive (Humphrey, 1995). Heparin has been used for many years in the treatment of stroke, but the data supporting its use are inadequate (Wityk et al., 1994). Although many elect to treat mild stroke cases acutely with anticoagulation (Humphrey, 1995), there is currently no clear indication for heparin in acute stroke (Wityk et al., 1994; AHA, 1994). Therefore, we have not developed an indicator for the use of heparin. Thrombolytic therapy (which is discussed below) and neuroprotective agents may prove useful in selected patients, but investigation is ongoing to clarify the patient population for whom benefit most clearly exceeds risk. Data on aspirin have, until this year, been equivocal. However, results of the International Stroke Trial and the Chinese Aspirin Stroke Trial being reported this year will, it appears, give conclusive evidence in support of aspirin treatment (Dr. Jeff Saver, personal communication). Nonetheless, it would not be appropriate at present to include use of aspirin as a quality indicator.

Thrombolysis

Early studies failed to uniformly demonstrate benefit to stroke outcomes with thrombolytic therapy (Levine, 1992). Although instances

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of sustained and significant neurological improvement have been demonstrated with thrombolysis (Hund, 1995), identification of the patient subgroup most likely to benefit is difficult (e.g., those with moderate-to-severe neurologic deficit and without extended infarct signs on initial CT scan) (Hacke et al., 1995). Recent results have not entirely settled the matter. Four trials of early thrombolysis after stroke were identified in MEDLINE for the period 1995 to 1996. One trial found a nonsignificant trend toward worse outcomes (i.e., both death and disability) in those assigned to thrombolysis (Donnan, 1996). A second trial found an increase in mortality in the group assigned to thrombolysis at ten days (p < .002) and at six months (p < .06) (Europe Study Group, 1996). Another trial found a "marginal" nonsignificant reduction in both death and severe disability with thrombolysis (MAST-I, 1995). The fourth trial found that some functional measures and neurologic outcome were improved with thrombolysis in selected patients; however, the authors cautioned that identification of the appropriate subgroup was difficult and that "therefore, since treating ineligible patients is associated with an unacceptable increase of hemorrhagic complications and death, intravenous thrombolysis cannot currently be recommended for use in an unselected population of acute ischemic stroke patients" (Hacke, 1995). Data suggest that there is benefit in moderate-dose TPA given early. Indeed, national guidelines on TPA use have been published by the AHA (1994) and the American Academy of Neurology (1996). Continued efforts may clarify more effectively which patients are suitable candidates for thrombolytic treatment, and the use of TPA as thrombolytic therapy may be appropriate for a quality indicator in the future.

Treatment of Hypertension in Acute Stroke

High blood pressure after acute stroke is common and often resolves spontaneously. Reduction in blood pressure may worsen outcome (Reid, 1993). Because of concerns that ischemic brain damage may be worsened with efforts to control blood pressure after stroke (Powers, 1993), the AHA recommends that hypertension in the setting of acute ischemic stroke be treated rarely and cautiously (Emergency Cardiac Care Committee and

Subcommittees 1992; O'Connell, 1996). Treatment may be acceptable in the following circumstances:

1) systolic blood pressure exceeding 220 mm Hg, or diastolic blood pressure exceeding 130 mm Hg;

2) presumed hypertensive encephalopathy;

3) myocardial ischemia;

4) congestive heart failure;

5) worsening renal function;

6) aortic dissection;

7) proven cerebral hemorrhage (Humphrey, 1995; Wityk, 1994).

Some maintain that pre-stroke antihypertensive treatment should be continued in the post-stroke period (O'Connell, 1996), but there is agreement that no treatment should be added merely for management of acute elevations of blood pressure, barring exceptional circumstances. Because of the difficulties of retrospectively ascertaining by chart review an exceptional circumstance such as "presumed hypertensive encephalopathy," and because of the ongoing debate on the advisability of continuing prior antihypertensive treatment during the acute stroke period, no indicator on the use of antihypertensive treatment in acute stroke has been formulated.

Treatment of Known Cerebrovascular Disease: Secondary Prevention

The risk of stroke in patients with a carotid stenosis who have had a TIA is approximately ten percent per year (Humphrey, 1995). The risk of stroke in patients with a previous hemispheric stroke is five to 20 percent per year, with an average five-year recurrence rate of 50 percent. (Moore, 1993). Therefore, there is a need for interventions that reduce the high rates of stroke in those with prior symptomatic CVD.

Carotid Doppler/Duplex Ultrasound to Detect Carotid Stenosis

The North American Symptomatic Carotid Endarterectomy Trial (NASCET, 1991) and the European Carotid Surgery Trial (ECST, 1991) found that patients with a TIA or nondisabling stroke involving carotid symptoms, and with 70 to 99 percent internal carotid stenosis on the appropriate side, had 75 percent fewer strokes after carotid

endarterecomy than with antiplatelet medication alone over a two to three year follow-up period. The risk of post-TIA stroke was reduced to two to three percent per year (Humphrey, 1995; North American Symptomatic Carotid Endarterectomy Trial Collaborators, 1991; European Carotid Surgery Trialists' Collaborative Group 1991) with an absolute risk reduction in ipsilateral stroke of 17 percent in NASCET (North American Symptomatic Carotid Endarterectomy Trial Collaborators, 1991). For this reason, it is recommended that patients who have suffered a TIA or stroke with recovery and who have a tight symptomatic stenosis should be offered surgery, with an explanation of the risks and benefits (Humphrey, 1995; Ad Hoc Committee, 1995). The reported benefits depended on a perioperative (30 day) complication rate of stroke or death of no more than six percent, and a perioperative rate of major stroke or death of less than two percent (Barnett, 1995). Surgical risk of carotid endarterectomy varies from one to 25 percent (Humphrey, 1995) and is institution- and surgeon-specific. Benefit is greatest if surgery is performed soon after TIA or stroke with recovery, because the risk of a recurrent event is highest in the first six months after an initial event. Therefore, it has been recommended that patients be assessed within a few days of symptoms and prepared for surgery, if appropriate, within two weeks after TIA and six to eight weeks after strokes with recovery (Indicator 6) (Humphrey, 1995).

In a European trial of carotid surgery, the surgical risk was found to outweigh the benefit if there was symptomatic carotid stenosis of 29 percent or less (European Carotid Surgery Trialists' Collaborative Group, 1991). The AHA has issued guidelines that identify carotid endarterectomy as inappropriate in patients with the following conditions:

1) moderate stroke with stenosis of less than 50 percent, not on aspirin;

2) single TIA with stenosis of less than 50 percent, not on aspirin;

3) high-risk patient with multiple TIAs and stenosis of less than 50 percent, not on aspirin;

4) high-risk patient with mild or moderate stroke and stenosis of less than 50 percent, not on aspirin;

5) global ischemic symptoms with stenosis of less than 50 percent; or,

6) acute dissection, asymptomatic on heparin (Ad Hoc Committee AHA, 1995).

The relative harm or benefit associated with carotid endarterectomy in patients with intermediate degrees of stenosis remains to be clarified.

Experts agree that the results of Doppler/duplex ultrasound are highly operator-dependent. Nonetheless, patients with carotid-distribution TIAs, small stroke, or stroke with recovery merit evaluation with Doppler/duplex ultrasound to detect severe carotid stenosis, so that candidacy for carotid endarterectomy can be determined (Indicator 5) (Humphrey, 1995; Wityk, 1994). There is no consensus that routine arteriography is needed before carotid endarterectomy (Dawson, 1993). Because morbidity and mortality from carotid endarterectomy is operator-dependent, the surgeon's skill must be taken into account in the final decision to perform carotid endarterectomy; however, referral for endarterectomy is clearly appropriate. Because of the potential difficulties of operationalizing "small stroke" and "stroke with recovery," we have confined our quality indicator to referral for carotid endarterectomy in persons diagnosed with TIA.

Antiplatelet Agents

Patients with TIA or stroke with recovery merit antiplatelet treatment, usually with aspirin. Patients with monocular or hemispheric TIAs have a stroke risk of ten to 30 percent within one year of symptom onset, which continues at six percent per year thereafter, and an overall stroke risk of 35 to 50 percent within five years of symptom onset (Moore, 1993). In multiple studies (The Canadian Cooperative Study Group, 1978; Bousser et al., 1983; UK-TIA Study Group, 1991; ESPS, 1987; ATC, 1994) and one meta-analysis (Sze et al., 1988), aspirin has been shown to reduce the combined risk of stroke and death in patients with TIA by 15 to 42 percent. Data are inconclusive on the optimal dose of aspirin. Ticlopidine may be more effective than aspirin but may cause skin rash, diarrhea, and reversible neutropenia or, occasionally,

irreversible bone marrow failure (Humphrey, 1995). Therefore, it is usually reserved for patients who are allergic to aspirin or who have had cerebrovascular events while taking aspirin. Some studies have shown little or no effect of aspirin on stroke risk in women (The Canadian Cooperative Study Group, 1978; Sherman, 1992; UK-TIA Study Group, 1988), which is akin to the finding by some of no benefit from aspirin for secondary prevention of myocardial infarction in women (Breddin et al., 1980). However, other trials, such as the French "AICLA" studies, have found aspirin to provide a magnitude of stroke risk reduction in women comparable with that seen in men (Bousser et al., 1983).

Anticoagulation

In patients with TIA, nonhemorrhagic small stroke, or stroke with recovery, warfarin is indicated for persons with definite cardiac emboli or atrial fibrillation (Humphrey, 1995). In these persons, warfarin has been found to reduce the risk of subsequent stroke by 60 to 70 percent compared with placebo (Antiplatelet Trialists' Collaboration, 1994). The risk of serious bleeding was three percent per year, with 1.2 percent intracranial bleeds. This compares with a non-significant, 17 percent reduction in stroke with 300 mg/day of aspirin. Anticoagulation for atrial fibrillation is addressed in another chapter. Difficulty in identifying the presence or absence of a definite cardiac source from chart abstraction precludes development of a quality indicator for anticoagulation for embolic disease. Moreover, while some recommend immediate anticoagulation for mild defects, with an 11 day delay in initiation for more severe defects (Humphrey, 1995), timing will not be included in the quality indicators because of the potential difficulties in quantifying severity of stroke from medical record abstraction.

FOLLOW-UP

Antihypertensive Treatment

Data on the treatment of hypertension after stroke are mixed. Some evidence suggests that there is benefit in blood pressure reduction. Other studies have found a J-shaped relationship between post-stroke diastolic blood pressure and stroke recurrence, with an optimal

diastolic pressure of 80 to 85 mm Hg. One study found no reduction in recurrence with antihypertensive treatment (O'Connell, 1996). Current evidence does not demonstrate that benefits of blood pressure reduction after stroke clearly exceed risks. For this reason, no indicator has been generated regarding blood pressure reduction as a secondary prevention measure.

Rehabilitation

It is widely agreed that efforts to restore function through post-stroke rehabilitation are important, and guidelines such as those by the Agency for Health Care Policy and Research have been issued (DHHS, 1995). Most gains occur within the first six months, although minimal additional improvement may occur for an additional six months. Patients are viewed as unsuitable for rehabilitation if their functional loss is minimal, or if their "rehabilitation potential" is low due to loss of cognitive skills or other severe deficits in which meaningful recovery is unlikely. Unfortunately, assessment of the potential for rehabilitation is an inexact science (Post-stroke Rehabilitation Guideline Panel, 1995; Brummel-Smith, 1995) and would be difficult to ascertain from medical record review. Therefore, no indicators have been developed on the use of post-stroke rehabilitation.

Smoking Cessation

Smoking promotes atherosclerosis and is a leading risk factor for CVD (DHHS, 1989). General counseling of smokers is covered in another chapter. Although no studies exist to demonstrate the benefit of smoking cessation in known CVD, smoking has been shown to be related to the likelihood of first stroke in a dose-dependent manner (Bronner et al., 1995). Additionally, there is general consensus that patients at risk for stroke should not smoke. Our indicators specify the need for smoking cessation counseling in patients who have presented with TIA (Futrell and Millikan, 1996) (Indicators 7 and 8). Although it is appropriate to provide smoking cessation counseling to patients who have had a small stroke and who remain functional, the difficulty of estimating the stroke size and of understanding patients post-stroke functional status from a retrospective review of the medical record

makes it complicated to write a counseling indicator for all post-stroke patients.

REFERENCES

Ad Hoc Committee American Heart Association. 1995. Guidelines for
    carotid endarterectomy. *Stroke* 26: 188-201.

Allison S. 1994. Is routine computed tomography in strokes unnecessary?
    Costs outweight benefits. *British Medical Journal* 309: 1498-1500.

Antiplatelet Trialists' Collaboration. 1994. Collaborative overview of
    randomised trials of antiplatelet therapy--I: Prevention of death,
    myocardial infarction, and stroke by prolonged antiplatelet
    therpay in various categories of patients. *British Medical Journal*
    308: 81-106.

Barnett H, and Meldrum H. 1995. Update on carotid endarterectomy.
    Current Opinion in Cardiology 10: 511-516.

Bonita R. 1992. Epidemiology of stroke. *The Lancet* 339: 342-344.

Bousser M, Eschwege E, Haguenau M, et al. 1983. "AICLA" controlled trial
    of aspirin and dipyridamole in the secondary prevention of
    atherothrombotic cerebral ischemia. *Stroke* 14: 5-14.

Breddin K, Loew D, Lechner K, et al. 1980. The German-Austrian Aspirin
    trial: a comparison of acetylsalicylic acid, placebo and
    phenprocoumon in secondary prevention of myocardial infarction.
    Circulation 62 (suppl V): V63-71.

Brickner M. 1996. Cardioembolic stroke. *American Journal of Medicine*
    100: 465-74.

Brodedrick J, Phillips S, et al. *Stroke* 1611-1626.

Bronner L, Kanter D, and Manson J. 1995. Primary prevention of stroke.
    The New England Journal of Medicine 333: 1392-1400.

Brott T, Adams H,et al. 1989. Developing measurements of acute cerebral
    infarction: a clinical examination scale. *Stroke* 20: 864-870.

Brown R, Evans B, and Wiebers D et al. 1994. Transient ischemic attack
    and minor ischemic stroke: An algorithm for evaluation and
    treatment. *Mayo Clinic Proceedings* 1027-39.

Brummel-Smith K. 15 February. Management of the poststroke patient.
    Hospital Practice 42-52.

Chimowitz, M, E Logigian, et al. 1990. The accuracy of bedside
    neurological diagnosis. *Annals of Neurology* 28: 78-85.

Dalen J. 1994. Atrial fibrillation: reducing stroke risk with low-dose anticoagulation. *Geriatrics* 49: 24-32.

Dawson D, Zierler E, Strandness E, Clowes A, and Kohler T. The role of duplex scanning and arteriography before carotid endarterectomy: A prospective study. *Journal of Vascular Surgery* 193 (18): 673-83.

Donnan G, Davis S, Chambers B, et al. 1996. Streptokinase for acute ischemic stroke with relationship to time of administration: Australian Streptokinase (ASK) Trial Study Group. *Journal of the American Medical Association* 276: 961-6.

Drury I, Whisnant J, and Garraway W. 1984. Primary intracerebral hemorrhage: impact of CT on incidence. *Neurology* 34: 653-657.

Emergency Cardiac Care Committee and Subcommittees AHA. 1992. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Part IV. Special resuscitation situations: stroke. *Journal of the American Medical Association* 268: 2242-4.

Europe Study Group. 1996. Thrombolytic therapy with streptokinase in acute ischemic stroke.The Multicenter Acute Stroke Trial--Europe Study Group. *New England Journal of Medicine* 335: 145-5.

European Carotid Surgery Trialists' Collaborative Group. 1991. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. *The Lancet* 337: 1235-1243.

European Stroke Prevention Study Group. 1987. ESPS: principal end points. *The Lancet* 2: 1351-54.

Feinberg W. 1996. Primary and secondary stroke prevention. *Current Opinion in Neurology* 9: 46-52.

Gorelick P. 1995. Stroke prevention. *Archives of Neurology* 52: 347-355.

Gress D. 1994. Stroke: Revolution in therapy. *Western Journal of Medicine* 161: 288-291.

Hacke W, Kaste M, Fieschi C, et al. 1995. Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke. The European Cooperative Acute Stroke Study (ECASS). *Journal of the American Medical Association* 274: 1017-25.

Humphrey P. 1995. Management of transient ischaemic attacks and stroke. *Postgraduate Medical Journal* 71: 577-84.

Hund E, Grau A, and Hacke W. 1995. Neurocritical care for acute ischemic stroke. *Neurol Clin* 13: 511-527.

Kelley R, and Berger J. 1992. TIA and minor stroke. *Postgraduate Medicine* 91: 197-202.

Levine S, and Brott T. 1992. Thrombolytic therapy in cerebrovascular disorders. *Progress in Cardiovascular Diseases* 34: 235-262.

Meissner I, and Meyer F. 1994. Carotid stenosis and carotid endarterectomy. *Cerebrovascular and Brain Metabolism Review* 6: 163-179.

Moore W. 1993. Carotid endarterectomy for prevention of stroke. *Western Journal of Medicine* 159: 37-43.

Multicentre Acute Stroke Trial--Italy (MAST-I) Group. 1995. Randomised controlled trial of streptokinase, aspirin, and combination of both in treatment of acute ischaemic stroke. *Lancet* 346: 1509-14.

North American Symptomatic Carotid Endarterectomy Trial Collaborators. 1991. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade stensosis. *New England Journal of Medicine* 325: 445-453.

O'Connell J, and Gray C. 1996. Treatment of post-stroke hypertension: A practical guide. *Drugs and Aging* 8: 408-415.

Phillips S, and Whisnant J. 1992. Hypertension and the brain. *Archives of Internal Medicine* 152: 938-945.

Poole R, and Chimowitz M. 1994. Ischemic stroke and TIA: Clinical clues to common causes. *Geriatrics* 49: 37-42.

Post-stroke Rehabilitation Guideline Panel. 1995. Post-stroke rehabilitation: Assessment, referral and patient management. *American Family Physician* 52: 461-470.

Powers W. 1993. Acute hypertension after stroke. *Neurology* 43: 461-7.

Pryse-Phillips W, and Yegappan M. 1994. Management of acute stroke. *Postgraduate Medicine* 96: 75-85.

Quality Standards Subcommittee of the American Academy of Neurology. 1996. Practice advisory -- throbolytic therapy for acute ischemic stroke. *Neurology* 47: 835-839.

Reid J. 1993. Hypertension and stroke: opportunities for prevention and prospects for protection. *Journal of Hypertension* 11: S2-S6.

Scandinavian Simvastatin Survival Study Group. 1994. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S). *Lancet* 344: 1383-9.

Schneider L, Libman R, and Kanner R. 1996. Utility of repeat brain
     imaging in stroke. *American Journal of Neuroradiology* 17: 1259-
     1263.

Shepherd J, Cobbe S,et al. 1995. Prevention of coronary heart disease
     with pravastatin in men with hypercholesterolemia. *New England
     Journal of Medicine* 333 (20): 1301-7.

Sherman DG, Dyken ML, Fisher M, Gent M, Harrison M, and Hart RG. 1992.
     Antithrombotic therapy for cerebrovascular disorders. *Chest* 102:
     529S-537S.

Special Writing Group of the Stroke Council: American Heart Association
     (1994) "Guidelines for the management of patients with acute
     ischemic stroke" Stroke 25: 1901-1914.

Special Writing Group of the Stroke Council: American Heart Association
     (1994) "Guidelines for thrombolytic therapy for acute stroke"
     Stroke 27: 1711-1718.

Sze P, Reitman D, Pincus M, Sacks H, and Chalmers T. 1988. Antiplatelet
     agents in the secondary prevention of stroke: Meta-analysis of the
     randomized controlled trials. *Stroke* 19: 436-442.

Taylor T, Davids P, Torner J, Holmes J, Meyer J, and Jacobson M. 1996.
     Lifetime cost of stroke in the United States. *Stroke* 27: 1459-
     1466.

The Canadian Cooperative Study Group. 1978. A randomized trial of
     aspirin and sulfinpyrazone in threatened stroke. *New England
     Journal of Medicine* 9: 309-18.

Toni, D, M Fiorelli,et al. 1996. Hemorrhagic transformation of brain
     infarct; predictability in the first 5 hours from stroke onset and
     influence on clinical outcome. *Neurology* 46: 341-345.

UK-TIA Study Group. 1991. The United Kingdom transient ischaemic attack
     (UK-TIA) aspirin trial: final results. *J Neurol Neurosurg
     Psychiatry* 54: 1044-54.

UK-TIA Study Group. 1988. United Kingdom transient ischaemic attack (UK-
     TIA) aspirin trial: interim results. *British Medical Journal* 296:
     315-20.

US Department of Health and Human Services. Clinical practice guideline
     #16: Post-stroke rehabilitation. *AHCPR*

US Preventative Services Task Force. 1996. *Guide to Clinical
     Preventative Services, 2nd ed*. Baltimore: Williams & Wilkins.

Wardlaw J. 1994. Is routine computed tomography in strokes unnecessary.
     British Medical Journal 309: 1498-500.

Wityk R, and Stern B. 1994. Ischemic stroke: today and tomorrow. *Critical Care Medicine* 22: 1278-1293.

RECOMMENDED QUALITY INDICATORS FOR CEREBROVASCULAR DISEASE

These indicators apply to men and women age 18 and older.

Indicator	Quality of Evidence	Literature	Benefits	Comments
Diagnosis				
1. Patients who receive thrombolytic therapy[4] for treatment of acute stroke should receive a head CT or MRI after presenting with stroke and before initiation of thrombolytic treatment.	III	Phillips, 1992	Reduce complications of treatment.	CT or MRI is needed to reliably distinguish hemorrhagic from thrombotic stroke. Thrombolysis is contraindicated in the presence of hemorrhagic stroke.
2. Patients who receive anticoagulant or antiplatelet therapy[2] for treatment of acute stroke within 7 days of presentation should receive a head CT or MRI prior to the initiation of anticoagulant or antiplatelet treatment.	III	Phillips, 1992	Reduce complications of treatment.	CT or MRI is needed to reliably distinguish hemorrhagic from thrombotic stroke. Anticoagulation is contraindicated in the presence of hemorrhagic stroke.
Treatment				
3. Patients newly diagnosed with a stroke or TIA who are not already on antiplatelet[2] or antithrombotic[3] treatment should be started on antiplatelet therapy or antithrombotic therapy within 1 month of the diagnosis unless a contraindication is documented.[6,7]	I	Sze, 1988; Antiplatelet Trialists' Collaboration, 1994	Reduce risk of second stroke. Reduce risk of death from stroke.	Aspirin has been shown to reduce risk of second stroke. Ticlid is used in some patients who are sensitive to aspirin or have had a cerebrovascular event while taking aspirin. If patients are placed on antithrombotic treatment (e.g., for atrial fibrillation), additional antiplatelet treatment is not needed.
4. Patients with a documented history of stroke or TIA should be on daily antiplatelet[2] or antithrombotic[3] treatment, unless a contraindication to antithrombotic treatment is documented.[7]	I	Sze, 1988; Antiplatelet Trialists' Collaboration, 1994	Reduce risk of second stroke. Reduce risk of death from stroke.	Aspirin reduces risk of second stroke. Anticoagulants (e.g., coumadin) reduce stroke incidence in patients with atrial fibrillation and other conditions. Antiplatelet agents are not needed in patients receiving anticoagulation.

Indicator	Quality of Evidence	Literature	Benefits	Comments
5. Patients presenting for care with carotid artery symptoms[1] who are diagnosed with TIA or stroke should have a carotid artery imaging study within 6 months before or 1 month after the event, unless the medical record documents, in the same time period, that the patient is not a candidate for carotid surgery.	I	NACET, 1991; ECST, 1991; Humphrey, 1995	Reduce recurrent stroke.	Carotid endarterectomy benefits patients with symptoms of a carotid with 70-99% stenosis, if the surgeon's perioperative complication rate is < 6%. The more promptly endarterectomy is carried out, the greater the benefit.
6. Patients presenting for care with carotid artery symptoms,[1] who are diagnosed with TIA and have carotid imaging evidence of >=70% stenosis on the side corresponding to the symptoms, should receive endarterectomy or referral for endarterectomy within 2 weeks of the diagnostic study.	I	NACET, 1991; ECST, 1991; Humphrey, 1995	Reduce recurrent stroke.	Carotid endarterectomy benefits patients with symptoms of a carotid with 70-99% stenosis, if the surgeon's perioperative complication rate is < 6%. The more promptly endarterectomy is carried out, the greater the benefit.
Follow-Up				
7. Patients who smoke and present with TIA but are not hospitalized should be counseled to stop smoking at the time they present with TIA.	III	Futrell & Millikan, 1996	Reduce mortality. Reduce stroke recurrence.	Smoking cessation reduces overall and cardiovascular mortality. To our knowledge, no data explicitly shows that smoking cessation reduces risk of second cerebrovascular event. However, there is no evidence that TIA and stroke patients are resistant to the mortality benefits of smoking cessation. Some stroke patients may not have adequate mental faculties to receive information regarding smoking cessation; thus, the indicator is confined to those with TIA.
8. Patients who smoke and are admitted to the hospital with a TIA should be counseled to stop smoking before hospital discharge.	III	Futrell & Millikan, 1996	Reduce mortality. Reduce stroke recurrence.	As above.

Definitions and Examples

[1] Carotid artery symptoms: From Humphrey (1995), common symptoms of carotid TIA and stroke include hemiparesis (complete or partial); hemisensory loss (complete or partial); dysphasia; and loss of vision in one eye (amaurosis fugax). Apraxia and visuospatial problems may also occur, and severe deficits may be accompanied by homonymous hemianopia and gaze palsy.

[2] Antiplatelet therapy: Aspirin or ticlopidine (ticlid).

[3] Antithrombotic therapy: coumadin or, less commonly, heparin.

[4] Thrombolytic therapy: Tissue plasminogen activator, streptokinase, urokinase.

[5] Carotid Artery Imagining Study: carotid duplex or angiography.

[6] Contraindications to aspirin/ antiplatelet agents:
   a. Hypersensitivity/ allergy to salicylates (rare).
   b. Bleeding within the past 4 weeks. This includes gastrointestinal bleeding, melena, epistaxis, any bleeding requiring transfusion; excluding occult hemoglobin in stools, or menses.

[7] Potential contraindications to heparin:
   a. Previous hemorrhagic stroke at any time or non-hemorrhagic stroke within 1 month.
   b. Known intracranial neoplasm, mass, or other intracerebral pathology (e.g. aneurysm, abscess).
   c. Bleeding within the past 4 weeks. This includes gastrointestinal bleeding, melena, epistaxis, any bleeding requiring transfusion; this does not include occult hemoglobin in stools, or menses.
   d. Suspected aortic dissection.
   e. Current use of anticoagulants in therapeutic doses.
   f. Bleeding diathesis (e.g., dysfunctional platelets, von Willebrand's disease, thrombocytopenia, clotting factor deficiency, hemophilia).
   g. Received streptokinase, APSAC, or urokinase during the current admission.

[8] Potential contraindications to thrombolytics:
   a. Previous hemorrhagic stroke at any time or non-hemorrhagic stroke within 1 month.
   b. Known intracranial neoplasm, mass, or other intracerebral pathology (e.g., aneurysm, abscess).
   c. Bleeding within the past 4 weeks. This includes gastrointestinal bleeding, melena, epistaxis, any bleeding requiring transfusion; this does not include occult hemoglobin in stools, or menses.
   d. Suspected aortic dissection.
   e. Current use of anticoagulants in therapeutic doses (e.g. coumadin with INR).
   f. Bleeding diathesis (e.g., dysfunctional platelets, von Willebrand's disease, thrombocytopenia, clotting factor deficiency, hemophilia).
   g. Blood pressure > 180/110.
   h. Trauma within 4 weeks (head trauma, concussion, bone fracture).
   i. CPR within 4 weeks.
   j. Surgery within 4 weeks (excluding cataract surgery).
   k. Pregnancy.

Quality of Evidence Codes
I   RCT
II-1   Nonrandomized controlled trials
II-2   Cohort or case analysis
II-3   Multiple time series
III   Opinions or descriptive studies