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Prevention of a First Stroke

A Review of Guidelines and a Multidisciplinary Consensus Statement From the National Stroke Association

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STROKE IS A LEADING CAUSE OF death and disability worldwide. In the United States, for example, there are an annual estimated 731 000 strokes and 4 million stroke survivors.^{1,2} Stroke also exacts an enormous financial burden. It is estimated that annual direct and indirect costs for stroke care total \$40 billion.³ Although stroke remains a leading cause of death, disability, and health care expenditures, it can be prevented.²

Several conditions and lifestyle factors have been identified as risk factors for

See also Patient Page.

Objective To establish, in a single resource, up-to-date recommendations for primary care physicians regarding prevention strategies for a first stroke.

Participants Members of the National Stroke Association's (NSA's) Stroke Prevention Advisory Board and Cedars-Sinai Health System Department of Health Services Research convened on April 9, 1998, in an open meeting. The conference attendees, selected to participate by the NSA, were recognized experts in neurology (9), cardiology (2), family practice (1), nursing (1), physician assistant practices (1), and health services research (2).

Evidence A literature review was carried out by the Department of Health Services Research, Cedars-Sinai Health System, Los Angeles, Calif, using the MEDLINE database search for 1990 through April 1998 and updated in November 1998. English-language guidelines, statements, meta-analyses, and overviews on prevention of a first stroke were reviewed.

Consensus Process At the meeting, members of the advisory board identified 6 important stroke risk factors (hypertension, myocardial infarction [MI], atrial fibrillation, diabetes mellitus, blood lipids, asymptomatic carotid artery stenosis), and 4 lifestyle factors (cigarette smoking, alcohol use, physical activity, diet).

Conclusions Several interventions that modify well-documented and treatable cardiovascular and cerebrovascular risk factors can reduce the risk of a first stroke. Good evidence for direct stroke reduction exists for hypertension treatment; using warfarin for patients after MI who have atrial fibrillation, decreased left ventricular ejection fraction, or left ventricular thrombus; using 3-hydroxy-3 methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors for patients after MI; using warfarin for patients with atrial fibrillation and specific risk factors; and performing carotid endarterectomy for patients with stenosis of at least 60%. Observational studies support the role of modifying lifestyle-related risk factors (eg, smoking, alcohol use, physical activity, diet) in stroke prevention. Measures to help patients improve adherence are an important component of a stroke prevention plan.

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stroke. These include hypertension, myocardial infarction (MI), atrial fibrillation, diabetes mellitus (DM), blood lipids,

asymptomatic carotid artery disease, smoking, and alcohol use (TABLE 1). Recognition of these risk factors is impor-

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 †Dr Raps died on December 9, 1998.

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tant to reduce the incidence of stroke, which has been increasing.⁸ This trend has been accompanied by an increase in the prevalence, or less adequate control, of key cerebrovascular risk factors.⁹

Preventing persons from having their first stroke will require a comprehensive multidisciplinary strategy to identify and manage major stroke risk factors and to promote adherence to preventive protocols.¹⁰ The objective of this consensus statement is to focus attention on prevention of a first stroke and to provide, in a single resource, up-to-date recommendations regarding preventive strategies.

METHODS

We carried out an evidence-based review to develop recommendations for prevention of a first stroke.^{11,12} We placed greatest emphasis on recommendations from randomized controlled trials and meta-analyses.¹³⁻¹⁷ As part of the process, National Stroke Association (NSA) Stroke Prevention Advisory Board members identified key stroke risk factors and strategies for prevention of a first stroke.

Literature Search

We first searched the MEDLINE database for articles from 1990 through April 1998 and updated in November 1998 using keyword or publication type for the exploded topics: *guideline*, *consensus*, *cerebrovascular disorders*, and *risk factors*. Also, we searched the subcategory *primary prevention* for cerebrovascular disorders, hypercholesterolemia, and hyperlipidemia. We then hand searched for all "Guidelines" and "Consensus" articles through 1998 in the following journals: *Stroke*, *Hypertension*, *Circulation*, *Diabetes Care*, *Diabetes*, and *Neurology*. We reviewed the selected articles (guidelines, statements, meta-analyses, and overviews) and identified additional articles from accompanying text and bibliographies. The spectrum of evidence-based recommendations was assessed critically and the highest rank was given to randomized controlled trials and meta-analyses. The second component of the search involved reviewing nonjournal sources (ie, textbooks, reference guides, other nonjournal publications, Internet Web sites).

Consensus Process

The compilation of guidelines from the medical literature, addressing the prevention of a first stroke, was reviewed initially at a meeting of NSA's Stroke Prevention Advisory Board on April 9, 1998. The conference attendees included recognized experts in neurology, cardiology, family practice, nursing, physician assistant practices, and health services research. From the information presented at the meeting and subsequent literature searches that were performed, areas in which the current literature differed from previously published guidelines were identified and recommendations were updated. The following risk factors for first stroke were selected by the board for review: hypertension, MI (with special attention to blood lipid levels), atrial fibrillation, DM, asymptomatic carotid artery stenosis, and lifestyle factors (cigarette smoking, alcohol use, physical activity, diet). Advisory board members then wrote summary statements for each of these topics. The Cedars-Sinai Health System Department of Health Services Research, Los Angeles, Calif, collated the summary statements as a first draft. After several rounds of feedback and revisions, consensus was achieved regarding the contents of the statement.

HYPERTENSION

Hypertension affects approximately 43 million men and women in the United States,¹⁸ but less than 30% of those being treated have blood pressure lower than 140/90 mm Hg.⁹ Hypertension is the most prevalent and modifiable risk factor for stroke, and its treatment substantially reduces the risk of stroke. A systematic overview of 14 prospective randomized controlled trials indicates that a decrease in diastolic blood pressure of 5 to 6 mm Hg reduces the risk for stroke by 42%.¹⁹ The Systolic Hypertension in the Elderly Program (SHEP) study shows that treatment of isolated systolic hypertension in the elderly decreases the risk for stroke by 36%.²⁰

Previously Published Guidelines

We identified 2 evidence-based guidelines^{9,21} that provide detailed recommendations for managing patients with hypertension. The more comprehensive of the 2 documents was the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI).⁹ This report includes recommendations for lifestyle modifications (eg, weight reduction, physical activity), pharmacologic treatment, and strategies to improve adherence.

Table 1. Stroke Risk Factors, Relative Risk, Attributable Risk, and Status of Prevention of First Stroke*

Risk Factor	Relative Risk		Estimated Population-Attributable Risk§	Prevention of First Stroke Proved by Clinical Trial?
	Framingham Study†	Rochester, Minn, Study‡		
Hypertension	1.16	4.0	High	Yes
Coronary heart disease	2.0¶	2.2	Medium	Yes#
Atrial fibrillation	1.82	2.9**	Low	Yes
Diabetes mellitus	1.41	1.7	Low	No
Blood lipids	Medium††	Yes#
Cigarette smoking	1.69	...	Low	No‡‡
Heavy alcohol consumption	Low	No‡‡
Asymptomatic carotid artery stenosis (60%-99%)	Low-medium††	Yes

*Data are from Gorelick.⁴ Ellipses indicate no data were provided.

†From Cox proportional hazards regressions. Data are from D'Agostino et al.⁵

‡From proportional hazards model (time-dependent covariate). Data are from Davis et al.⁶

§Low indicates population-attribution risk (PAR) is less than 15%; medium, PAR from at least 15% to less than 40%; and high, PAR at least 40%. PAR = (1 + A), where A = prevalence × (relative risk - 1). Data are from Gorelick.⁷

||Relative risk is computed for an increase of systolic blood pressure in mm Hg of 10 units.

¶Relative risk is for persons aged 60 to 69 years.

#With use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors.

**Relative risk is from univariate screen.

††Estimates uncertain.

‡‡Observational studies suggest beneficial effect for risk factor control.

NSA Commentary

To help decrease the risk for a first stroke, we recommend 3 of the following approaches for lowering blood pressure: (1) blood pressure should be controlled in patients with hypertension who are most likely to develop stroke, (2) physicians should check the blood pressure of all their patients at every visit, and (3) patients with hypertension should monitor their blood pressure at home.

In general, hypertension occurs earlier, more frequently, and is more severe in black people.^{9,18,22} Community-based efforts such as church-based screening programs, health fairs, and public service announcements may increase awareness of hypertension and help identify those at risk for hypertension. Treatment with antihypertensive medications, and diuretics in particular, is useful to decrease stroke morbidity and mortality in black people and others.

Elderly persons represent another group in which hypertension and stroke are prevalent. In the Third National Health and Nutrition Examination Survey (NHANES III), hypertension was present in 60% to 71% of persons 60 years or older.¹⁸ A study of men and women in Rochester, Minn, demonstrated that 55% of strokes occurred in those 75 years or older.²³ A recent overview of clinical trials suggests that diuretics are associated with a 39% odds reduction (odds ratio [OR], 0.61; 95% confidence interval [CI], 0.51-0.72) and β -blockers a 25% odds reduction (OR, 0.75; 95% CI, 0.57-0.98) for stroke events in older persons with hypertension.²⁴

Finally, because hypertension is often a "silent" condition, it may go undetected. To promote detection of hypertension, blood pressure measurement should be an essential component of regular health care visits.⁹ The JNC VI advocates self-monitoring; electronic or manual sphygmomanometers are recommended for home use.

MYOCARDIAL INFARCTION

The incidence of ischemic stroke is approximately 1% to 2% per year after MI.²⁵ This risk is greatest in the first month after MI (31%).²⁶ Treatment to prevent

stroke after MI may include oral anticoagulants, antiplatelet agents, and lipid-lowering agents.

Previously Published Guidelines

Oral Anticoagulants. To reduce the risk for a first stroke in patients with MI by using oral anticoagulant agents, recommendations include the following: (1) use of warfarin (international normalized ratio [INR] of 2.0-3.0) is indicated for patients with MI plus one or more of the following conditions: persistent atrial fibrillation, decreased left ventricular function (eg, ejection fraction \leq 28%),²⁷ or when left ventricular thrombi are detected within several months after MI; (2) but because the evidence is less substantial for use of warfarin in patients who have only wall motion abnormalities or paroxysmal atrial fibrillation, warfarin cannot be recommended as a means to prevent stroke in patients with MI unless there are known risk factors for stroke (eg, persistent atrial fibrillation, decreased left ventricular function, left ventricular thrombi) as the absolute risk reduction per year is small (\approx 1% per year). These recommendations for the use of oral anticoagulation agents in patients with MI are similar to conclusions reached by the Fifth Annual American College of Chest Physicians Conference on Antithrombotic Therapy in 1998,^{28,29} the American College of Physicians (ACP) in 1994,¹⁴ the American College of Cardiology/American Heart Association in 1996,³⁰ and the North of England Aspirin Guidelines Development Group¹⁷ in 1998.

Antiplatelet Agents. The same guidelines^{14,17,27-29} suggest that aspirin reduces the relative risk for stroke after MI by approximately 30%. However, because there is only a small absolute risk reduction ($<$ 0.5% per year), aspirin is not recommended for preventing stroke in patients with MI, but it is recommended for prevention of subsequent MI.

NSA Commentary

Oral Anticoagulants. Several studies³¹⁻³³ have demonstrated reduction of stroke risk with warfarin after MI. An overview of these trials has shown that

INR values of 2.5 to 4.8 may be associated with a 10-fold increase in hemorrhagic stroke,²⁵ whereas INR values below 2.0 may not be effective for prevention of ischemic stroke.³⁴ An INR range of 2.0 to 3.0 with a target goal of 2.5 is recommended.

Antiplatelet Agents. The Antiplatelet Trialists' Collaboration concluded in 1994 that in patients with previous MI, antiplatelet agents reduce the odds of nonfatal stroke by 39%, nonfatal MI by 31%, and vascular death by 15%.³⁵ A pooled analysis of 11 trials performed by the North of England Aspirin Guideline Development Group¹⁷ demonstrated that aspirin use in patients with previous MI results in a risk difference of 3.2% for the combined end point of MI, stroke, or vascular death. However, the ACP¹⁴ reports that aspirin use in patients with previous MI results in only a small absolute stroke risk reduction of -2% (95% CI, -4% to 0%), and this is not substantial enough evidence to conclude that antiplatelet agents are useful in preventing a first stroke after MI.

Lipid-Lowering Agents. Current evidence suggests that cholesterol-lowering agents, in particular the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statin agents), decrease the risk of stroke after MI.³⁶⁻³⁸ The Cholesterol and Recurrent Events (CARE) Trial (n = 4159) showed that in patients with previous MI and average cholesterol levels ($<$ 6.2 mmol/L [$<$ 240 mg/dL]), pravastatin sodium is associated with a 31% risk reduction (95% CI, 3%-52%) for stroke compared with placebo.³⁶ The antistroke effects of the statin agents may be separate from the lipid-lowering properties (eg, nonlipid mechanisms that modify endothelial function, inflammatory responses, plaque stability, and thrombus formation).³⁹ The Scandinavian Simvastatin Survival Study (4S) (n = 4444) assessed patients with coronary heart disease and high cholesterol levels from 5.5 to 8.0 mmol/L (213-309 mg/dL); post hoc analysis demonstrates a reduction in stroke and transient ischemic attack for patients taking simvastatin (relative risk, 0.70; $P = .02$).³⁷ However, reduction in stroke alone was

not shown to be statistically significant. In a larger study, the Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID) trial (n = 9014), patients with coronary heart disease and normal to high cholesterol levels, from 4.0 to 6.9 mmol/L (155-270 mg/dL)³⁸ who took pravastatin experienced a 20% risk reduction for stroke.

The US Food and Drug Administration recently has approved pravastatin for patients who have had MI and have average cholesterol levels of less than 6.2 mmol/L (<240 mg/dL), and simvastatin for patients with coronary heart disease and high cholesterol for prevention of stroke or transient ischemic attack. The NSA supports these recommendations for patients with MI. For patients without coronary heart disease or MI but who have had a stroke or other atherosclerotic disease, the NSA recommends following the National Cholesterol Education Program II (NCEP II) guidelines for initiating dietary or drug treatment.⁴⁰⁻⁴³

ATRIAL FIBRILLATION

Nonvalvular atrial fibrillation (NVAF) is an important risk factor for stroke. It increases the risk of stroke by about 6 times.^{44,45} More than 2 million adults in the United States have NVAF, and about 36% of strokes in patients between the ages of 80 and 89 years are attributed to this condition.⁴⁴

Previously Published Guidelines

We identified 4 guidelines and consensus statements on prevention of a first stroke in patients with NVAF. The statements were developed by the American College of Chest Physicians in 1998,^{29,46} the ACP in 1994,¹⁴ the American Academy of Neurology in 1998,^{47,48} and the American Heart Association in 1996.⁴⁹

These recommendations were in general agreement that oral anticoagulation with warfarin is indicated for patients with NVAF who have specific risk factors for stroke, including age, previous transient ischemic attack or stroke, hypertension, heart failure, and DM. However, not all sources identified the same age cutoffs (eg, ACP considered patients <60 years,

whereas American College of Chest Physicians considered patients <65 years). They also did not identify the identical risk factors (although there was considerable overlap in definitions). However, most of these authorities recommended that patients with NVAF who do not have specific risk factors be treated with aspirin (325 mg/d).^{29,46-49}

NSA Commentary

Pooled analyses from several large, randomized trials show that warfarin reduces stroke occurrence by 68% (95% CI, 50%-79%) and aspirin by 21%.⁵⁰ Serious bleeding complications with warfarin occur at a rate of 1.3% per year, a rate that is slightly higher than that observed with aspirin (1.0%).^{51,52} The evidence supports the use of warfarin in patients with NVAF who are at highest risk for stroke⁵³ (eg, >75 years or with specific risk factors). Warfarin, however, continues to remain underused for older persons.⁵⁴⁻⁵⁷ Underuse may be due to in part lack of

physician and patient awareness about the risk-benefit profile of warfarin, logistical challenges of monitoring anticoagulation, concerns about patient adherence, and financial considerations.^{56,57}

Decisions regarding the use of anti-thrombotic and antiplatelet therapy in patients with NVAF should be based on careful assessment of patients individually, weighing the risk of stroke against the risk of hemorrhage. A recent overview of studies on this topic identifies criteria for administering warfarin and aspirin, based on specific risk factors.⁴⁶ Summary recommendations are presented in TABLE 2.

DIABETES MELLITUS

Diabetes mellitus is the most prevalent endocrinologic problem in primary care practice and is a well-established risk factor for stroke.^{72,73} Diabetes mellitus may increase the risk of thromboembolic stroke through multiple and potentially synergistic mechanisms. These include accel-

Table 2. National Stroke Association Summary Recommendations for Prevention of a First Stroke

Condition	Recommendation
Hypertension	The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure ⁹ recommendations for lifestyle modification, initiation of specific therapy, and multidisciplinary management strategies
Myocardial infarction	Aspirin therapy if previous myocardial infarction (MI) ^{14,17,28-30} or warfarin at an international normalized ratio of 2-3 in patients with atrial fibrillation, left ventricular thrombus, or significant left ventricular dysfunction, ^{14,17,28-30} and statin agents after MI in patients with normal to high lipid levels ⁵⁸⁻⁶²
Atrial fibrillation*	Patients >75 years with or without risk factors should be treated with warfarin; patients aged 65-75 years with risk factors should be treated with warfarin and those without risk factors should be treated with warfarin or aspirin; patients <65 years with risk factors should be treated with warfarin, those without risk factors should be treated with aspirin
Diabetes mellitus	American Diabetes Association recommendations ⁶³ for control of diabetes to reduce microvascular complications ⁶⁴ (further studies are needed to determine if aggressive glycemic control lowers the risk of stroke)
Lipid levels	Statin agents in patients with high cholesterol and coronary heart disease ⁵⁸⁻⁶² and National Cholesterol Education Program guideline principles for dietary and pharmacologic management of patients with hyperlipidemia or atherosclerotic disease ⁴³
Asymptomatic carotid artery disease†	Carotid endarterectomy for asymptomatic carotid stenosis ≥60% (but <100%) When surgical morbidity and mortality is <3% ^{12,17,65-69}
Lifestyle factors	Modification of smoking, alcohol consumption, physical activity, and diet according to published guidelines ^{16,21,70,71}

*Adapted from Laupacis et al.⁴⁶ Risk factors include previous transient ischemic attack, systemic embolism or stroke, hypertension, and left ventricular dysfunction. Efforts to improve patient and practitioner awareness regarding the benefits and risks of warfarin will serve as a first step toward increasing appropriate usage. The warfarin international normalized ratio goal is ranged 2.0 to 3.0 with a target value of 2.5.

†The at least 60% asymptomatic carotid artery stenosis cut point should be replicated in other studies.

eration of large artery atherosclerosis via glycosylation-induced injury, adverse effects on both low-density lipoprotein and high-density lipoprotein cholesterol levels, and promotion of plaque formation through hyperinsulinemia.⁷⁴

Previously Published Guidelines

Previously published guidelines addressing the management of DM include recommendations by the Scottish Intercollegiate Guidelines Network in 1997⁷⁵ and by the American Diabetes Association in 1998.⁶³ The guidelines published by the American Diabetes Association are more comprehensive and detailed.

NSA Commentary

Despite epidemiologic and basic science evidence that links DM to stroke, studies have not conclusively shown that tight control of serum glucose levels reduces the risk for stroke.⁷⁶ Two large, multicenter, randomized controlled trials have demonstrated that tight control of blood sugars with intensive insulin therapy in patients with type 1 DM⁷⁷ and intensive sulfonylurea and/or insulin therapy in patients with type 2 DM⁷⁸ results in a reduction in the number of microvascular complications (retinopathy, nephropathy, neuropathy)⁶⁴ but not macrovascular complications such as stroke. However, tight control of blood pressure (<150/85 mm Hg) in patients with hypertension and type 2 DM reduces the risk of fatal and nonfatal stroke by 44% compared with the group with less tight control ($P = .01$).⁷⁹ The NSA recommends rigorous comprehensive control of blood sugar levels for adherent patients with type 1 DM and type 2 DM to prevent microvascular complications, as we await more information on possible reduction in events from stroke and cardiovascular diseases.⁸⁰

ASYMPTOMATIC CAROTID ARTERY DISEASE

Atherosclerotic carotid artery disease is an important stroke risk factor. The risk of clinical symptoms increases with the degree of stenosis.^{42,81} At present, however, mass screening for high-grade asymptomatic carotid artery stenosis is not cost-effective.^{16,65}

Previously Published Guidelines

We identified 14 guidelines and consensus statements on the prevention of a first stroke in patients with asymptomatic carotid artery disease. Seven of these statements used evidence-based methods.^{16,21,65-69} The statements presuppose that patients have a reasonable life expectancy (typically ≥ 5 years) and that surgery can be performed with acceptable risks (perioperative morbidity and mortality of <3%).

NSA Commentary

In all of the recommendations, degree of carotid artery stenosis is the key determinant when considering carotid endarterectomy (CE). No guideline supports CE for asymptomatic lesions with less than 60% stenosis or for complete occlusion of the carotid artery. Conventional cerebral angiography in accordance with the North American Symptomatic Carotid Endarterectomy Trial (NASCET) is the generally accepted measure to determine the degree of stenosis.⁸² The use of noninvasive blood flow measures to supplant angiography has been vigorously debated and remains unsettled.^{83,84}

In the Asymptomatic Carotid Atherosclerosis Surgery (ACAS) trial, patients with 60% to 99% asymptomatic stenosis show an absolute risk reduction for stroke or death of 5.9% over 5 years with CE compared with medical treatment alone.⁸⁵ Several guidelines published between 1995 and 1997, however, do not uniformly support CE for asymptomatic carotid artery disease. Reasons given for this include concern about reproducibility of the low surgical morbidity rate of ACAS (1.1%) and the observation that CE may not significantly reduce the risk of major disabling stroke. The most recent American Heart Association guideline²¹ recommends CE for asymptomatic lesions of at least 60% stenosis.²¹ Without assurance that the local surgical risk is acceptable (<3%), CE cannot be recommended.

In the ACAS trial, the relative risk reduction for stroke and death in men treated with CE was 66%, but for women

it was only 17%.⁸⁵ This sex difference is not statistically significant, however, and may be related to a relatively small number of women enrolled in the trial.

LIFESTYLE FACTORS

Cigarette Smoking

Both case-control and prospective studies have shown cigarette smoking to be an independent risk factor for ischemic stroke.⁸⁶⁻⁸⁹ In a meta-analysis of 32 studies the summary relative risk of stroke for smokers is 1.5 (95% CI, 1.4-1.6).⁹⁰ Stroke risk increases 2-fold among heavy smokers compared with light smokers. In middle-aged British men, stroke incidence rises with increasing number of cigarettes smoked and among smokers with hypertension. Even passive exposure to cigarette smoke increases the risk of progression of atherosclerosis.⁹¹ Cigarette smoking is an independent determinant of carotid artery plaque thickness, a substantial predictor of severe extracranial carotid artery atherosclerosis,⁹²⁻⁹⁷ may increase coagulability, blood viscosity, and fibrinogen levels, enhance platelet aggregation, and elevate blood pressure.⁹⁶

ALCOHOL USE

Alcohol consumption has a direct dose-dependent effect on the risk of hemorrhagic stroke.⁹⁷ For cerebral infarction, results have ranged from a definite independent effect in both men and women, an effect only in men, and no effect after controlling for other confounding risk factors such as cigarette smoking.⁹⁸ A J-shaped relationship between alcohol use and ischemic stroke has been proposed with a protective effect in light or moderate drinkers and an elevated stroke risk with heavy alcohol consumption.⁹⁹ Alcohol may increase the risk of stroke through various mechanisms that include induction of hypertension, hypercoagulable states, cardiac arrhythmias, and cerebral blood flow reductions. There is evidence that light to moderate drinking may have beneficial effects by increasing high-density lipoprotein cholesterol levels and decreasing platelet aggregation and fibrinogen levels.^{100,101}

PHYSICAL ACTIVITY

Regular exercise has well-established benefits for reducing the risk of premature death and other cardiovascular disease. The beneficial effect of lowering the risk of stroke¹⁰² has been described predominantly among whites and is more apparent for men than women and younger rather than older adults. A dose-response relationship between increasing amounts of physical activity and the reduction in the risk of stroke has not been shown consistently. The protective effect of physical activity may be partly mediated through its role in controlling various risk factors for stroke (eg, hypertension, DM, obesity),¹⁰³⁻¹⁰⁵ by accompanying reductions in plasma fibrinogen levels and platelet activity, and elevations in plasma tissue plasminogen activator activity and high-density lipoprotein concentrations.¹⁰⁶⁻¹⁰⁹

Diet

Dietary factors may be risk factors for stroke. For example, increased sodium intake is associated with hypertension, and reduction in salt consumption may significantly lower blood pressure and may reduce stroke mortality.¹¹⁰ Homocysteine may be associated with stroke and is associated with deficiency of dietary intake of folate, vitamin B₆, and vitamin B₁₂.¹¹¹ Case-control studies have shown an association between moderately elevated homocysteine levels and stroke,^{112,113} but the evidence corroborating this relationship is less robust in prospective studies. Finally, the role of fat intake as a stroke risk factor remains uncertain, whereas fruits and vegetables may contribute to prevention of stroke through antioxidant mechanisms^{114,115} or through the elevation of potassium levels.¹¹⁶

Previously Published Guidelines

Smoking. In 1996, the Agency for Health Care Policy and Research published smoking cessation guidelines,¹⁶ which addressed various topics that included screening for tobacco use, advice to quit, interventions, smoking cessation pharmacotherapy, motivation to quit, and preventing relapse.

Alcohol Use. In 1998, the American Heart Association published recommendations for alcohol consumption.²¹ Moderate consumption of alcohol may prevent atherosclerotic heart disease, but heavy use of alcohol should be avoided.²¹

Physical Activity. Counseling to promote regular physical activity is recommended for all children and adults.¹⁶ This recommendation is based on evidence that regular physical activity reduces the risk for coronary heart disease, hypertension, obesity, and DM. Clinicians should determine each patient's current activity level, ascertain barriers specific to an individual, and provide information on the role of physical activity in disease prevention. Current guidelines recommend exercise at a moderately intense level (eg, brisk walking) for at least 30 minutes on most, and preferably all, days of the week.^{70,71} Sporadic exercise, especially if extremely vigorous in an otherwise sedentary individual, should be avoided in favor of moderate-level activities performed consistently.

Diet. Dietary guidelines include¹⁶ (1) limit the intake of dietary fat (especially saturated fat) to less than 30% of total energy, (2) limit the intake of dietary cholesterol to less than 10% of total energy, (3) emphasize the intake of fruits and vegetables (at least 5 servings per day) and products containing fiber (at least 6 servings per day), (4) maintain energy balance through diet and exercise, (5) maintain adequate intake of dietary calcium (eg, 1200-1500 mg/d for adolescents and young adults, 1000 mg/d for adults aged 25-50 years, 1000-1500 mg/d for postmenopausal women, 1200-1500 mg/d for pregnant and nursing women), (6) reduce the intake of dietary sodium, and (7) increase the intake of beta carotene and other antioxidants.

NSA Commentary

Observational epidemiologic studies indicate that modification of lifestyle-related risk factors can decrease the risk for stroke. The Framingham Study¹¹⁷ and the Nurses' Health Study¹¹⁸ both showed that the risk of ischemic stroke reverts to that of nonsmokers after 2 to 5 years following cessation of smoking. The

Agency for Health Care Policy and Research¹¹⁹ guideline for smoking cessation is cost-effective, and recent studies suggest nicotine replacement therapy and bupropion hydrochloride as adjuncts to smoking cessation strategies.¹²⁰ Since some ingestion of alcohol, perhaps up to 2 drinks per day, may actually help reduce the risk of stroke, drinking in moderation should be recommended for those who drink alcohol and have no health contraindications to alcohol use. However, those who do not customarily drink should not be encouraged to do so. The benefits of exercise for stroke reduction have been observed for even light to moderate physical activities, such as walking, and some data support additional benefits from increasing the level and duration of recreational activity (eg, 8400-12 595 kJ/wk). The deleterious consequences of extreme exercise, such as alterations in hormonal levels in women, musculoskeletal injuries, and risk of acute MI, should be considered when advising sedentary patients to exercise. Finally, it remains unclear whether dietary changes result in a decrease in stroke risk. Until additional data are available, it seems prudent to limit excess saturated fat and sodium intake, to replace vitamin B₁₂, vitamin B₆, and folate when such deficiencies are identified, and to maintain a diet that is rich in fruits and vegetables for stroke prevention.

ADHERENCE

Despite recognition of modifiable risk factors for a first stroke and the availability of well-known treatments, suboptimal control of risk factors continues to contribute to more than 700 000 strokes in the United States each year.¹ For example, only 29% of Americans with hypertension have blood pressure lower than 140/90 mm Hg,¹²¹ and up to 50% demonstrate poor or only partial adherence to medication regimens.¹²²

Innovative strategies to improve patient adherence have been described.¹⁰ Two meta-analyses^{123,124} have shown methods to improve attendance at follow-up visits. Effective strategies include providing reminders, clinic orientations, education about medications, and

forming an agreement with the patient to return for subsequent visits. Follow-up visits are important for improving patient outcomes.¹²⁵ Self-monitoring is an effective method to help promote nutrition and weight loss and to decrease smoking and alcohol abuse.¹²⁶ Interventions that promote patient participation contribute to improved patient outcomes in those with chronic disease.¹²⁷

Meta-analyses and systematic reviews support the need for a multilevel approach.¹⁰ Methods to reduce smoking and alcohol abuse and promote nutrition and weight control are most effective when patients are exposed to recommendations from the media in addition to personal communication with the physician.¹²⁵ Comprehensive interventions¹²⁷ that involved nurses, patient-specific dosing schemes, self-monitoring of blood pressure and pill taking, and rewards for adherence and lower blood pressure¹²⁸ have been associated with improved adherence and process measures (eg, lower blood pressure). Recognizing and using strategies that have demonstrated efficacy in encouraging patient adherence to treatment plans are important steps in preventing a first stroke and are major goals of NSA.

The NSA recommendations for prevention of a first stroke are summarized in Table 2. These recommendations should be applied and tailored to the individual patient by the treating physician.

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Science can never be a closed book. It is like a tree, ever growing, ever reaching new heights. Occasionally the lower branches, no longer giving nourishment to the tree, slough off. We should not be ashamed to change our methods; rather we should be ashamed never to do so.
—Charles V. Chapin (1856-1941)