



## *Module 2. Stroke Risk Factors* **Preventing Strokes**

### Objectives for Module 2

#### **Knowledge**

- Name at least 6 treatable or controllable risk factors for stroke
- Name at least 4 populations (groups of individuals) that have an increased risk of stroke

#### **Clinical Applications and Reasoning**

- Relate the major “modifiable” stroke risk factors to stroke pathogenesis
- Develop a series of questions that would enable you to screen a patient for major stroke risk factors, and create a stroke risk profile for that individual
- Consider ways that individuals living in a community might be encouraged to learn more about stroke, and to take part in a screening for stroke risk factors

#### **Clinical Applications to Patient Education**

- Develop 3 points that you would use in explaining *to a patient or family member* how hypertension, atrial fibrillation, or carotid stenosis is related to the risk of having a stroke.

### **Overview**

**Risk factors reflect the pathology that is responsible for the major types of strokes.** Many risk factors have some role in *promoting or accelerating atherosclerotic plaque formation and ulceration*. This makes sense when you remember that 87% of all strokes are ischemic, and that atherosclerosis plays an important role in most ischemic strokes. However, it is usually thrombus that finishes the job – this is what completely occludes the vessel, and is the immediate cause of an ischemic stroke. Recall that a thrombus that threatens blood flow to the brain can form locally in a cerebral artery, in neck arteries, or in the heart. Therefore other important risk factors are conditions that *promote thrombus formation in locations from which it can embolize to affect the brain*.

**Some of the risk factors for stroke are potentially “modifiable.”** This means that they can be treated or controlled. In most cases, there is good evidence that treatment leads to significant reductions in the occurrence of stroke and in death from stroke. It has recently been estimated that if current prevention activities were uniformly performed at levels achieved by the best U.S. health care delivery systems, 20% of strokes would be prevented (*Circulation*. 2008; 118:576; also see module 6).

“Modifiable” risk factors for stroke are often separated into **medical conditions** which reflect the existence of underlying pathology or pathophysiology, and **lifestyle-related factors** which may be independent risk factors and/or contribute to one or more of these medical conditions.

<b>MEDICAL CONDITIONS</b>	<b>LIFESTYLE-RELATED FACTORS</b>
<b>High Blood Pressure</b>	<b>Cigarette Smoking</b> (or passive cigarette smoke)
<b>Myocardial Infarction</b>	<b>Physical Inactivity</b>
<b>Atrial Fibrillation</b>	<b>Excessive Alcohol Consumption</b> (including occasional binge drinking)
<b>Diabetes Mellitus</b>	<b>Obesity</b>
<b>Dyslipidemia</b> (high total cholesterol; low HDL and high LDL)	
<b>Carotid Artery Stenosis (asymptomatic)</b>	

**Peripheral Arterial Disease** also associated with increased risk

Other major risk factors for stroke are called “unmodifiable,” because they are things that neither you nor your patients can do anything about. You need to know the “unmodifiable” risk factors, because they help you to define high-risk individuals and groups for whom treating or controlling their “modifiable” risk factors is a priority.

<b>UNMODIFIABLE FACTORS – POPULATIONS AT SPECIAL RISK</b>	
<b>Age</b>	The risk of having a stroke increases with age, doubling every ten years after 55. The rate of death following a stroke also increases with age.
<b>Gender</b>	Men have a higher risk of stroke than women before the age of 75, but not at older ages. Overall, more women than men have strokes, due to the larger number of elderly women. Women also tend to have greater disability after stroke than men.
<b>Race/Ethnicity</b>	Black Americans have almost twice the risk of first-ever stroke than do whites, tend to suffer greater physical disability after a stroke, and have a 1.8 times higher rate of fatal strokes compared to whites. Hispanics and Mexican Americans may have a greater risk than non-Hispanic whites.
<b>Family History</b>	An individual's risk may increase if a maternal or paternal relative has had a stroke. Possible mechanisms include: genetic heritability of risk factors or susceptibility to their effects; shared environmental/lifestyle factors; interaction of genetic and environmental factors. Inherited defects in blood cells or the clotting mechanism can also increase risk.
<b>Previous Stroke or TIA</b>	These are the most significant risk factors, since both indicate the presence of significant vascular pathology. TIAs carry a substantial short-term risk of stroke. (One recent study indicates that after TIA the 90-day stroke risk is about 3-17%, and is higher within the first 30 days.)

**Combination of Risk Factors for Stroke.** Each risk factor that has been described is associated with an increase in stroke risk, but to varying degrees. Although an increase in the number of risk factors corresponds directly with a further increase in stroke risk, the relationship is not linear.

# More on Medical Conditions that increase stroke risk

## High Blood Pressure

**High blood pressure (systolic  $\geq$  140 mm Hg or diastolic  $\geq$  90 mm Hg) for an extended period, is the most important modifiable risk factor for stroke.** Hypertension at least doubles the lifetime risk of stroke, independent of other risk factors. It is estimated that about 77% of individuals who have a first stroke have blood pressure higher than 140/90 mm Hg. Successful, *long-term* control of high blood pressure can reduce the incidence of stroke by as much as 35% to 44%.

Populations at special risk: It is estimated that more than 41% of adult *blacks* in the United States have hypertension, compared to about 28% of adult whites. The prevalence of high blood pressure among black women is 44%. Furthermore, black Americans develop high blood pressure earlier in life, and their average blood pressures are much higher compared to most other populations. Finally, regardless of race or gender, more than 60% of all *Seniors* over 65 years of age have high blood pressure.



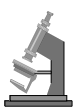
Relationship to stroke pathogenesis: Atherosclerotic plaque development in the carotid and vertebrobasilar system is a slowly progressive process that apparently begins in the teenage years. Arteries that are continuously subjected to high pressures are more likely to develop plaque, and it is more likely that the endothelial surface of the vessel will be damaged, promoting plaque rupture and the formation of thrombi. A thrombus can occlude the vessel locally or can break off and embolize the brain. Hypertension also increases the likelihood that small thin-walled penetrating vessels will rupture, producing an intracerebral hemorrhage.

A little about control/treatment: The cause of most cases of hypertension isn't known; however hypertension is easily detected, and usually controllable. Data from 2005-2008 show that about 80% of adults with hypertension are aware of their condition, and that about 48% have it under control, while 52% do not. This represents a significant improvement in both awareness and control rates that has taken place within the past 10 years.

**Recommended blood pressure is <140/90, or <130/80 if the patient has additional risk factors for stroke.** For a small number of patients, treatment of kidney, adrenal or thyroid disease can reverse hypertension. However for most patients, the physician's challenge is to create a management plan that will enable the patient to maintain the recommended blood pressure levels *over an extended time period*. This plan usually combines lifestyle changes (more fruits/vegetables and lower fat in diet, weight loss, increased physical activity, alcohol moderation, smoking cessation) and medications. Adhering to such a regimen is difficult for many patients. One troubling statistic suggests that only half of those who have prescribed medications take them consistently.

## Myocardial Infarction

At 45-64 years of age, 2% of men and 6% of women who have a first myocardial infarction (MI) will go on to have an stroke within 5 years. The risk of stroke is far greatest in the first month following an MI.



Relationship to stroke pathogenesis: Since atherosclerosis is the underlying pathology for both MI and most ischemic strokes, this relationship should not be a surprise. Furthermore,

an MI may produce damage to the heart wall or persistent atrial fibrillation, both of which promote thrombus formation. Bits of thrombus may break off and embolize the brain. Finally, the thrombolytic agents used to treat an MI by breaking up clot in the coronary vessels increase the risk of intracerebral hemorrhage.

A little about control/treatment: Many of the risk factors for stroke and MI are the same, therefore preventing a second MI or a stroke will involve many of the same considerations. These may include lifestyle changes such as increasing fruits/vegetables and reducing fat in the diet, moderation of alcohol consumption, smoking cessation, and increasing physical activity. Medical therapies that may be indicated include reducing blood pressure, antiplatelet agents, anticoagulation if cardiac problems that increase the risk of thrombus formation are present, lipid-lowering agents, and medical treatment of diabetes mellitus if it is present.

## **Atrial Fibrillation**

Atrial fibrillation is a powerful risk factor for stroke, independently increasing stroke risk about 5 times. It is the most common cardiac dysrhythmia, and its prevalence had been projected to about 2.7 million Americans in 2010. For reasons that are not fully understood, the two atria contract ineffectively, rather than in the normal forceful and regular manner. Beyond age 65, at least 6% of the population has atrial fibrillation.

Special Populations: The percentage of stroke attributable to atrial fibrillation increases from 1.5% at 50-59 years of age to 23.5% in *Seniors* aged 80-89. (NOTE: These numbers may be a significant underestimate, as atrial fibrillation is often asymptomatic and may not be detected clinically.)



Relationship to stroke pathogenesis: Patients with atrial fibrillation have a greatly increased risk of embolic strokes. Ineffective contraction of the atrium allows blood to pool along its walls and increases thrombus formation. Bits of these thrombi can travel through the left ventricle, enter the systemic circulation and embolize the brain.

A little about control/treatment: In some patients, atrial fibrillation resolves spontaneously. Cardioversion, ablation, or drug therapy may be used to restore a normal cardiac rhythm. However none of these approaches has been shown to reduce stroke risk. However, anticoagulation with warfarin reduces stroke risk by about 60% compared with untreated patients. For patients who have a low overall stroke risk or for whom warfarin therapy is not an option, an antiplatelet agent like aspirin or clopidogrel is an appropriate alternative. Clinical decisions concerning the use of these therapies must be balanced by the risk of hemorrhagic complications.

## **Diabetes Mellitus**

Impaired glucose tolerance nearly doubles stroke risk as compared to patients with normal glucose levels. In patients with diabetes mellitus, stroke risk is tripled. Diabetes mellitus is defined as a fasting plasma glucose  $\geq 126$  mg/dL measured on 2 occasions, and reflects the inability of the body to produce or respond properly to insulin. At least 10% of the U.S. population has diagnosed or undiagnosed diabetes. *Even when glucose levels are considered "well controlled," diabetes increases the risk of stroke 1 to 3 times in adults.* Identifying and treating diabetic patients will significantly reduce their risk of many other vascular complications of diabetes. However, since diabetes puts these patients at high risk for stroke, it is particularly important to control any additional risk factors for stroke such as hypertension that they may have.

Populations at special risk: WWA *Adult non-Hispanic blacks and Hispanics* have a disproportionately high prevalence of diabetes compared to non-Hispanic whites.



Relationship to stroke pathogenesis: Diabetes increases the risk of ischemic strokes through several interrelated mechanisms that favor (and accelerate) the formation of atherosclerotic plaque. In patients with diabetes, plaque is much more common in the smaller branches of cerebral arteries than in nondiabetics. The narrowing of these smaller vessels can directly increase the risk of stroke.

## **Dyslipidemia**

Higher levels of mean total blood cholesterol ( $\geq 240$  mg/dL), LDL cholesterol ( $\geq 160$  mg/dL), and triglycerides ( $> 150$  mg/dL) and lower levels of HDL cholesterol levels ( $< 40$  mg/dL) are all associated with an increased risk for ischemic stroke in adults.

Populations at special risk: Overall, total cholesterol levels are slightly higher and HDL levels slightly lower in *non-Hispanic whites* and *Mexican Americans* than in the US overall population.



Relationship to pathogenesis: Concerning *cerebrovascular* disease specifically, what is known is that elevated total cholesterol and LDL is associated with increased degree and progression of carotid atherosclerosis, while elevated HDL levels have the opposite effect.

A little about control/treatment: To reduce the risk of both stroke and myocardial infarction, recommended levels are total cholesterol  $< 200$  mg/dL and HDL  $\geq 40$  mg/dL (men) and  $\geq 50$  mg/dL (women). An individual's LDL goal depends on how many additional risk factors they have. The recommended levels may be achieved by diet (daily recommendation:  $\leq 30\%$  of calories from total fat,  $\leq 10\%$  of calories from saturated fat,  $< 300$  mg cholesterol), increased physical activity, and/or cholesterol-lowering agents (statins or other pharmacological agents). The statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) may have important effects on atherosclerotic disease in addition to their lipid-lowering properties, and recent studies show that they reduce stroke risk.

## **Carotid Artery Stenosis**



Relationship to stroke pathogenesis: When a carotid artery is narrowed by atherosclerotic plaque so that its cross-sectional area is reduced by 70% or more, the patient has a significantly increased risk of stroke. Narrowing of the carotid can be symptomatic, producing a stroke or transient ischemic attack (TIA), or asymptomatic. This depends on factors like whether the plaque surface is disrupted, increasing the likelihood of thrombus formation (a source of emboli) or whether there is an effective collateral circulation that supplements the blood supply to brain regions in the jurisdiction of the partially occluded carotid.

A little about control/treatment: When a carotid artery is narrowed  $\geq 70\%$ , carotid endarterectomy (surgical removal of fatty deposits) is often recommended. This procedure has been shown to significantly reduce stroke risk for both symptomatic and asymptomatic patients. Carotid stenting is also available, and a clinical trial comparing it to endarterectomy showed similar outcomes in individuals under 70 years of age; however endarterectomy appeared superior with advancing age. Blockages  $\leq 30\%$  are often treated using lipid-lowering agents (statins) and antiplatelet therapy, with the combined goals of slowing atherosclerotic disease and reducing the risk of thrombus formation.

# More on Lifestyle Factors that increase Stroke Risk

## **Cigarette Smoking**

In 2009, about 20% of the U.S. population age 18 and over were currently cigarette smokers. Current smoking approximately doubles the risk of ischemic stroke, after controlling for other risk factors. It is also associated with a 2-4-fold increased risk of hemorrhagic stroke. The risk in heavy smokers is greater than in light smokers, and is somewhat greater for women than for men. Passive exposure to cigarette smoke also increases stroke risk. When an individual quits smoking, stroke risk begins decreasing almost immediately, and after 5 years drops to nearly that of a nonsmoker.

Populations at special risk: Cigarette smoking increases the stroke risk of women using low-estrogen oral contraception, however even in nonsmoking, normotensive women there is a slightly increased stroke risk associated with these oral contraceptives.



Relationship to stroke pathogenesis: Cigarette smoke contains carbon monoxide and nicotine as well as numerous additional toxic compounds. Cigarette smoking has a role in promoting the atherosclerotic process particularly in the carotid arteries. (It is thought that carbon monoxide may play a role in damaging the arterial endothelium). Smoking also causes several changes in the blood. They include increased adhesiveness and clustering of platelets, shortened platelet survival, faster clotting time, and increased viscosity of the blood, which can affect flow velocity. Smokers have an increased risk of both ischemic and hemorrhagic stroke. Many of these same changes in the blood can also be caused by short exposures to secondhand smoke; their effects are not known.

## **Physical Inactivity**

Higher levels of physical activity are related to lower stroke risk across all racial/ethnic groups, ages, and in both men and women. Moderate-to-vigorous exercise for at least 30 minutes daily is associated with lower risk of both ischemic and hemorrhagic stroke. Exercise helps control obesity and diabetes, increases levels of HDL cholesterol, and may lower blood pressure in some people.

Populations at special risk: Physical inactivity is more prevalent among *women* than men, among *black and Hispanic* adults than white adults, among *seniors* than younger adults, and among *those reporting lower educational attainment*.

## **Excessive Alcohol Consumption**

The incidence of ischemic stroke in those who consume *small* amounts of alcohol (an average of 1-2 drinks per day for men and 1 for women) is *lower* than in nondrinkers. The reasons may involve a reduction in coronary artery disease. However, chronically drinking too much alcohol (an average of  $\geq 5$  drinks per day) and/or acute binge drinking are significant risk factors for stroke.



Relationship to stroke pathogenesis: The exact pathogenic mechanism is unknown, but alcohol can contribute to high levels of triglycerides, produce cardiac arrhythmias, and cause heart failure.

A little about control/treatment: In the case of alcohol abuse, counseling and support groups.

## **Obesity**

Obesity, defined as a body mass index (BMI) of 30.0 kg/m<sup>2</sup> or greater, approximately doubles the risk of stroke. Abdominal body fat is an independent risk factor for ischemic stroke in all race/ethnic groups. Obesity strains the heart, and predisposes people to other risk factors like high blood cholesterol and triglyceride levels, hypertension, low HDL cholesterol levels, and diabetes.

Populations at special risk: In 2007-8 it was reported that 34% of all U.S. adults were obese.

## **Depression**

Although not yet widely studied, two recent reports suggest that risk of stroke/TIA is about 4 times greater in individuals less than 65 years old with symptoms of depression.

# **Populations at Special Risk for Stroke**

## **Some Introductory Thoughts**

When considering populations of individuals who are at special risk for stroke and stroke death, there are numerous complicated and interrelated factors to think about:

- culture-based (or population-determined) social or lifestyle factors
- extent of knowledge (and belief) that there are ways to decrease the risk of having a stroke
- health care disparities: economic and other factors governing access to preventive care and monitoring, as well as to high quality in-hospital acute emergency care and therapy at discharge (longer-term rehabilitation and follow-up care)
- potential of following medical management plans (economic and social issues, support, etc.)
- genetic factors or “pathology” especially prevalent in that population

While studies that are now underway attempt to tease apart these variables so that they can be separately identified and addressed, the results to date remain limited. Therefore what we present here about several populations at special risk for stroke is incomplete. However we hope that this information will encourage you to think about some of these issues as you continue learning about stroke and stroke prevention.

## **Non Hispanic Black Americans**

Blacks have almost twice the risk of first-ever stroke compared with whites. Blacks under 55 years old have particularly high stroke/TIA risk (2-5 times higher than age-matched white subjects). Risk is increased for both ischemic and hemorrhagic strokes. The age-adjusted stroke incidence rates in people ages 45-84 are higher overall for blacks than whites, and for black men than for black women. This racial disparity in stroke incidence does not seem to be changing over time. Additionally, black stroke survivors have greater activity limitations than do white stroke survivors.

In 2008, the prevalence of hypertension in black adults in the US was about 44%. It was somewhat greater among black women than black men. Rates vary substantially within the black community. Compared to whites, blacks develop high blood pressure earlier in life and their average blood pressures are much higher.

In 2008, the prevalence of physician-diagnosed diabetes in non-Hispanic black adults age 20 and older was 14.3% for men and 14.7% for women (in non-Hispanic whites the prevalence was 6.8% for men and 6.5% for women).

In at least one study, the relative risk of stroke among blacks was found to be higher than among whites, even when the statistics were adjusted for age, hypertension, and diabetes.

Rates of stroke mortality are highest in a region of the southeastern US which is known as the 'Stroke Belt.' This area is variably defined, but usually includes the states of North Carolina, South Carolina, Georgia, Tennessee, Mississippi, Alabama, Louisiana, and Arkansas. In this region average stroke mortality is about 20% higher than in the rest of the US. This geographic disparity has existed more or less unchanged for the past 70 years. Even more striking, within this 'Stroke Belt' the coastal regions of North Carolina, South Carolina, and Georgia have average stroke mortality that is 40% higher than the rest of the nation. Black Americans who live in the so-called 'Stroke Belt' have sharply increased stroke mortality rates; whites also have somewhat increased rates. Increased stroke mortality continues despite a recent trend toward better hypertension management in the 'Stroke Belt.'

In the US, most people with sickle cell disease are non-Hispanic blacks. Sickle cell disease is strongly associated with stroke, especially in children. In these individuals, the vascular endothelium may be damaged by repeated episodes of red cell sickling, making it prone to thrombus formation. Long-term exchange transfusion or bone marrow transplants can prevent the vascular pathology from progressing, and therefore decrease the risk of stroke. If a child with sickle cell disease has a stroke, he or she often recovers quite well, thanks perhaps to the increased plasticity of the young nervous system. However without therapy, these children remain at high risk for additional strokes that may produce a lifetime of disability.

## **Mexican Americans**

Stroke is one of the most common causes of death and disability among Mexican Americans. Incidence of hemorrhagic strokes and of ischemic stroke at younger ages is increased, compared with non-Hispanic whites.

## **Seniors**

Atrial fibrillation becomes increasingly common in the very elderly, and this may contribute to their increased incidence of stroke. Amyloid angiopathy (and the lobar hemorrhages that appear to be associated with this small vessel pathology) is also most common in the elderly. However accumulation and destabilization of atherosclerotic plaques with accompanying thrombus formation remains the pathology underlying the majority of strokes, regardless of age.

## **Patients with TIAs and Stroke Survivors**

Of those who survive a stroke, at least 10% will have another stroke within the year. After 5 years more than 30% will have had another stroke if untreated. However it has been shown that these individuals can decrease their risk of a second stroke by up to 50% by surgical and medical treatments (for example, relieving severe carotid artery stenosis and/or anticoagulation therapy) and addressing any risk factors, particularly hypertension, atrial fibrillation or smoking. For those who have had a TIA, the outlook is even more favorable. Many of these same therapies can now significantly reduce the risk that they will go on to have a stroke.