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 88% 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 can form locally in a cerebral vessel, or a piece can break off and travel from the heart to the brain (as an embolus). Therefore other important risk factors are conditions that promote thrombus formation in locations where it can 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.

These “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.

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.
<table>
<thead>
<tr>
<th>MEDICAL CONDITIONS</th>
<th>LIFESTYLE-RELATED FACTORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Cigarette Smoking (or passive cigarette smoke)</td>
</tr>
<tr>
<td>Heart Disease</td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>Physical Inactivity</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>Excessive Alcohol Consumption</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>Obesity</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
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<td>(high total cholesterol; low HDL cholesterol)</td>
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<tr>
<td>Carotid Artery Stenosis (asymptomatic)</td>
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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.

### UNMODIFIABLE FACTORS – POPULATIONS AT SPECIAL RISK

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>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.</td>
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<tr>
<td>Gender</td>
<td>Overall, men and women have about the same number of strokes, but women tend to be older when they have a first stroke, and are more likely to die. Before the age of 65, men have about a 20% higher risk of stroke.</td>
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<td>Race/Ethnicity</td>
<td>Black Americans have a 60% greater likelihood of having a stroke, suffer greater physical disability after a stroke, and are nearly twice as likely to die from a stroke than other groups studied in the US. Some Hispanic Americans are also at greater risk than European Americans.</td>
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<td>Family History</td>
<td>An individuals’ risk may increase 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 the clotting mechanism can also increase risk.</td>
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<tr>
<td>Previous Stroke or TIA</td>
<td>These are the most significant risk factors, since both indicate the presence of significant vascular pathology. 1 in 6 individuals who survive a first stroke or TIA will have another one within 1 year. TIAs carry a substantial short-term risk of stroke. (One recent study indicates about 10% of TIA patients have strokes within 90 days, with nearly half occurring in the first 2 days.)</td>
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**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

Hypertension

Hypertension, defined as having blood pressure 140/90 mm Hg or higher for an extended period, is the most important modifiable risk factor for stroke. Hypertension increases the risk of stroke by 2 to more than 4 times, independent of other risk factors. Elevation of either systolic or diastolic pressure is associated with greater risk. Successful, long-term treatment of hypertension can reduce the incidence of stroke by as much as 35% to 44%.

Populations at special risk: It is estimated that more than 40% of adult blacks in the United States have hypertension, compared to about 20% of adult non-Hispanic whites. The prevalence of high blood pressure among black women is 44%. Furthermore, black Americans develop hypertension 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 60 years of age are hypertensive.

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. Vessels 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 90-95% of cases of hypertension isn’t known; however hypertension is easily detected, and usually controllable. In most cases, hypertension is a silent disease; recent data suggest that 30% of those with hypertension are unaware they even have it.

Recommended blood pressure is <140/90, or <135/85 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 about half of those who have prescribed medications actually take them consistently.

Heart Disease: Myocardial Infarction

About 3-4% of people who have a myocardial infarction (MI) will go on to have an embolic stroke. The risk of stroke is far greater 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.

### Heart Disease: Atrial Fibrillation

Atrial fibrillation is the most common cardiac dysrhythmia, affecting about 2.3 million Americans. For reasons that are not fully understood, the atria quiver erratically instead of contracting forcefully and regularly. By age 70, more than 5% of the population has atrial fibrillation and the prevalence continues to increase with age. Atrial fibrillation is associated with about 60,000 strokes annually. A patient with atrial fibrillation has a 5 times increased risk of stroke, and these strokes are especially large and disabling.

**Special Populations:** In Seniors aged 65-85, the majority of all strokes are attributed to atrial fibrillation.

**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 break free, 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. Electrical cardioversion also may be used to restore a normal cardiac rhythm. Anticoagulation with warfarin in patients with atrial fibrillation reduces their 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

Diabetes mellitus, defined as a fasting plasma glucose of 126 mg/dL or greater measured on 2 occasions, reflects the inability of the body to produce or respond properly to insulin. *Even when glucose levels are considered to be “well controlled,” diabetes increases the risk of stroke 1 to 3 times above that of people without the disease.* It is important to identify patients who are diabetic and to treat their diabetes (which 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:** The risk of diabetes for Mexican Americans and African Americans is almost twice that for non-Hispanic whites. The risk for American Indians is even higher.
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 total blood cholesterol (above 240 to 270 mg/dL) seem to be associated with an increased risk for ischemic stroke in both men and women. It appears that low HDL is a risk factor for ischemic stroke in men; more data are needed to verify its effect in women.

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 ≥40 mg/dL (men) and ≥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: ≤ 30% of calories from total fat, ≤ 10% of calories from saturated fat, < 300 mg cholesterol), increased physical activity, and/or cholesterol-lowering agents (statins). 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 70% or more, 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 angioplasty with stenting is also available, and clinical trials comparing it to carotid endarterectomy are ongoing. Less severe blockages (30% or less) 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
Smoking 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. Smokers who also use oral contraceptives have an increased stroke risk. When an individual quits smoking, their stroke risk begins to decrease almost immediately. After 5 years, ex-smokers have nearly the same stroke risk as nonsmokers.

Populations at special risk: In the US, about 21% of the total population age 18 and over smoke. The early forms of oral contraceptives, with higher doses (>50 micrograms) of estrogen and progestin, increased a woman’s risk of stroke. However the lower-dose oral contraceptives now being prescribed carry a much lower risk of stroke, except for women who smoke or have hypertension.

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. Smokers have an increased risk of both ischemic and hemorrhagic stroke.

Physical Inactivity
Lack of physical activity is an independent risk factor for both stroke and heart disease. Increasing levels of moderate-to-vigorous exercise (such as brisk walking, gardening, swimming, aerobics, etc.) to an average of at least 30 minutes daily can reduce stroke risk. 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 blacks and Hispanics than whites, among seniors than younger adults, and among those of lower socioeconomic status.

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 for this protective effect are currently under study, and may involve a reduction in coronary artery disease. However, chronically drinking too much alcohol (an average of ≥ 5 drinks per day) and/or acute binge drinking are significant risk factors for both ischemic and hemorrhagic 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 or greater, approximately doubles the risk of stroke. Increased weight is associated with an increased risk of stroke in a dose-dependent fashion. Abdominal body fat tends to be a stronger predictor of stroke risk than BMI. 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 2004 the prevalence of obesity was over 30% for the overall US population. It approached 40% or more for black and Mexican-American women.

**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
- economic and other factors governing access to preventive care and monitoring, as well as to acute emergency care and longer-term rehabilitation
- 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.

**African Americans**

Blacks have almost twice the risk of first-ever stroke compared with whites. They suffer greater physical disability after a stroke, and adults are far more likely to die from a stroke than are whites. Risk is increased for both ischemic and hemorrhagic strokes. The age-adjusted stroke incidence rates are higher for black men than black women.

The prevalence of hypertension in black adults in the US is 41.4% and it is increasing; it is particularly high among black women. Compared to whites, blacks develop high blood pressure earlier in life and their average blood pressures are much higher.

In 2004 the prevalence of physician-diagnosed diabetes in black adults age 20 and older was 10.7% of men and 13.2% of women (in non-Hispanic whites the prevalence was 6.7% of men and 5.6% of women).
However, in at least one study, the relative risk of stroke among African Americans was higher, even when the statistics were adjusted for age, hypertension, and diabetes.

In African Americans, atherosclerotic plaque tends to deposit more often in the intracranial branches of the major arteries, especially the carotid, while extracranial lesions occur more frequently in whites. The significance of this difference is unclear at present.

Black Americans who live in the so-called Stroke Belt in the southeast US have the highest death rates from stroke in the US. The Stroke Belt includes Alabama, Arkansas, Georgia, Indiana, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia. Although not a state, Washington DC has also been identified as part of the Stroke Belt. Black Americans living in these regions also have the greatest prevalence of high blood pressure. Whites who live in the Stroke Belt also have somewhat increased incidence of hypertension and stroke.

In the US, most people with sickle cell disease are African American. 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. The prevalence of stroke is somewhat higher for Mexican American men, but somewhat lower for Mexican American women compared to non-Hispanic whites. Statistical data are currently being collected in an effort to discover which risk factors may be most important.

**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 may 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. However it has been shown that these individuals can decrease their risk of a second stroke 50% by addressing their risk factors – especially hypertension, atrial fibrillation and cigarette smoking – and anticoagulation therapy. For those who have had a TIA, their outlook is even more favorable. Many of these same medical and surgical treatments can now significantly reduce the risk that they will go on to have a stroke.