## **STROKE RISK FACTORS**

Strokes tend to occur with equal frequency among both men and women; data from the 2002 Behavioral Risk Factor Surveillance System (BRFSS)<sup>1</sup> indicated that 3.1% of West Virginia adults, or an estimated 43,419 individuals, had been told by a doctor that they had suffered a stroke, 3.1% of women

In 2001, 1,262 West Virginians died of stroke; 62% were women. Among women, stroke was the third leading cause of death in the state.

and 3.2% of men. Women, however, are more likely than men to die from stroke. In 2001, women accounted for 61% of total stroke deaths in the United States. In West Virginia, a total of 1,262 people died of stroke in 2001, 780 or 62% of whom were women. Among women only, stroke was the third leading cause of death in the state.

The risk of stroke increases with age; in fact, age is the single most important risk factor for stroke. BRFSS data showed a range of reported stroke from 2.7% of respondents aged 45-54 to 5.1% of those aged 55-64 to a high of 9.1% among those aged 65 and older. In the United States in 2001, three-quarters (74.5%) of all stroke deaths occurred among people age 75 and older, while 88% occurred among those aged 65 and older. In West Virginia, 90% of all stroke deaths were among residents aged 65 and over.

Statistics show that the risk of stroke more than doubles in each successive decade after 55 years of age (30). Women are less likely than men to suffer a stroke before the age of 65, at which time the gap closes. While strokes are less common among younger people, they still occur.

In West Virginia, 12% of men and 18% of women who have had a stroke had their first stroke before the age of 55.

According to some sources, about 28% of all stroke victims are under the age of 65 (31); younger victims are more likely to survive a stroke, although they are often left disabled. In West Virginia, 11.9% of men and 18.2% of women who reported a stroke had their first stroke before the age of 55 (29). Strokes also

occur, although rarely, among children. Pediatric strokes happen more frequently among boys than girls and twice as often among African-American children as among white children (32). Boys are also more likely to die from a stroke than are girls.

<sup>&</sup>lt;sup>1</sup>The BRFSS is a monthly telephone survey established by the Centers for Disease Prevention and Control (CDC) that allows states to monitor health behaviors among their adult populations (18+). The BRFSS was begun in 1984 with 15 participating states, expanding to 54 states and territories in 2001. The prevalence of stroke occurrence was measured in West Virginia in 2000 and 2002. The West Virginia Bureau for Public Health publishes annual reports on the BRFSS survey results, which were used extensively in the preparation of this document (29).

The male-to-female mortality ratio differs by age and type of stroke. Mortality rates for both ischemic and hemorrhagic stroke are lower for women than for men under the age of 65 but higher for ischemic stroke among women aged 65 and older (33). Death rates for intracerebral hemorrhagic stroke are similar for men and women, but women have a higher risk of death from subarachnoid hemorrhage, a differential that increases with age. The survival ratio also differs by sex; because of their longer life expectancy, women make up more than half of the stroke survivors in the United States.

Stroke is a particularly serious problem among African-Americans, who have dramatically higher death rates from stroke than other racial and ethnic groups. In fact, of the three leading causes of death in the United States – heart disease, cancer, and stroke – the disparity is greatest for stroke (34). According to CDC's *Atlas of Stroke Mortality*, whose researchers examined 1991-1998 data for persons aged 35 and older, African-Americans had the highest rates of mortality, followed by whites, Asians and Pacific Islanders, Hispanics,



and American Indians and Alaska Natives (35) (Figure 2). A study published in the January 2003 *Neurology* reported that elderly blacks (aged 65+) were 6% more likely to die within three years after a stroke than were elderly whites (36). Premature stroke deaths are also more likely among African-Americans. Research published in the *Morbidity and Mortality Weekly* in 2000 found that the relative risk of stroke among African-Americans compared with non-Hispanic whites is *four times higher at ages* 35-54, three times higher at ages 55-64, and nearly twice as high at ages 65-74 (37).

Numerous studies have shown an inverse relationship between stroke mortality and socioeconomic status, especially among African-Americans (38, 39). A 1998 study examined the frequent assumption that these differences are in fact due to the increased likelihood of unhealthy behaviors among lower SES groups. Lantz et al., using a nationally representative sample of 3,617 adults in the Americans' Changing Lives survey, investigated the degree to which cigarette smoking, alcohol use, sedentary lifestyle, and obesity (all risk factors for stroke) affected the association between all-cause mortality and low-income status. Their findings showed that these behaviors explained no more than 12 to 13% of the effect of income on mortality (40), indicating the need for further examination of the impact of lower socioeconomic status on stroke morbidity and mortality.

There is much evidence to support the hypothesis that the chance of stroke is greater among persons who have a **family history** of stroke, suggesting a genetic predisposition. A Danish study of twins with long-term follow-up found an increased risk of stroke among monozygotic pairs of twins (41). Researchers with the Family Heart Study (supported by the National Heart, Lung, and Blood Institute) assessed the personal and familial histories of stroke in 3,168 individuals. Their findings

showed a significant association of increased risk of stroke with parental history, especially on the father's side (42). Stroke among younger persons (aged 65 or less) was found to significantly correlate with familial history by British scientists, both for large vessel disease (odds ratio [OR]=2.93, 95% CI:1.68 to 5.13) and small-vessel disease (OR=3.15, 95% CI:1.81 to 5.50) (43); however, no correlation with cardioembolic stroke was found.

Researchers worldwide are studying the genetic basis for stroke, in agreement that it is likely to be multigenic and influenced by environmental factors. In 2003, Icelandic researchers with the company deCode Genetics identified a specific gene (PDE4D) associated with ischemic stroke, finding that those who have the stroke-susceptibility gene have a three to five times greater chance of having an ischemic stoke (44). The preliminary results of a population-based study conducted by researchers in the United States suggest a significant association between the presence of an apolipoprotein E4 or E2 allele and the risk of hemorrhagic stroke (45). A genetic abnormality that affects the body's processing of cholesterol has recently been found to increase the risk of stroke among adults younger than 45. The abnormality in the PON1 gene was found in a study at the Whitaker Cardiovascular Institute at the Boston University School of Medicine; overall in the study population, the presence of the genetic abnormality was the second most potent risk factor for stroke, following hypertension (46).

## **OTHER STROKE RISK FACTORS**

While an individual's sex, age, racial/ethnic group, family history, and socioeconomic status are viewed as nonmodifiable risks for stroke, there are numerous other risk factors that are amenable to change. There are also risk factors, such as heart disease and certain blood disorders, for which the potential risk can be decreased through careful monitoring and changes in one's lifestyle. The most widely recognized of these risk factors for stroke are discussed below. Where possible, state and national prevalence data from the BRFSS have been included.

**Hypertension**, or high blood pressure, is the **leading** cause of both ischemic and hemorrhagic strokes. Normal blood pressure is defined as a persistent reading below the levels of 120 mm Hg for systolic pressure (the amount of force exerted when the heart beats) and 80 mm Hg for diastolic

pressure (the force exerted when the heart is at rest). High normal blood pressure, or prehypertension, includes readings of 120-139 mm Hg for systolic and 80-89 mm Hg for diastolic pressure. Hypertension refers to consistent readings of equal to or higher than 140 mm Hg for systolic pressure and/or 90 mm Hg for diastolic pressure. A recent study published in *Diabetes This Week* indicated that

In 2001, West Virginians reported higher rates of hypertension than their national counterparts regardless of sex, age, or income. Nearly onethird of adults in the state have been told they have high blood pressure.

"nondipping" blood pressure, i.e., blood pressure that decreases less than 10% when a person is asleep, is an additional risk factor (47).

The American Heart Association estimates that as many as 50 million Americans age 6 and older have high blood pressure (48). Overall, one in four adults suffers from hypertension, but this statistic increases to one in three among African-Americans. Of persons with high blood pressure, nearly one-third (32%) are not aware they have it; the Heart Association also estimates that only 27% of people with high blood pressure are receiving adequate treatment (diet or drugs). A higher percentage of men than women have hypertension, up to the age of 55; following age 55, more women have high blood pressure. Even though hypertension risk increases with age, it can also occur in children; it is estimated that 1% to 2% of school-aged children have high blood pressure (49).



For nine out of ten persons with hypertension, the cause is unknown (50). Known risk factors for primary or essential hypertension include a family history of high blood pressure, aging, being African-American, obesity, excessive alcohol consumption, and high sodium intake (in those individuals with a susceptibility). Other possible risk factors include physical inactivity, low potassium, calcium, and magnesium intake, sleep apnea, and insulin resistance. Among men, long-term exposure to lead may contribute to hypertension

(51); in women, high blood pressure is two to three times more likely among those taking oral contraceptives, especially if they are older or obese (52). Secondary hypertension is caused by such conditions as pregnancy or narrowing of the kidney arteries or by certain medications.

The Behavioral Risk Factor Surveillance System measures adult hypertension prevalence biennially by asking survey respondents the question "Have you ever been told by a doctor, nurse, or other health professional that you have high blood pressure?" Nationally, 25.6% (national median) of respondents answered yes to this question in 2001; however, 32.5% of West Virginia adults reported having been told they have high blood pressure (hypertension awareness), a statistically

significant difference, and the continuation of an upward trend since 1992. In 2001, West Virginians reported higher rates of hypertension than their national counterparts regardless of sex, age, or income level, as noted in Figures 3 and 4. Five years of BRFSS data were combined in order to produce an adequate sample size to analyze responses among West Virginia's African-American population. The 1998-2002 prevalence of hypertension among African-American adults was 44.1%, compared with 30.8% for whites over the same time period.



📓 West Virginia 🗖 United States

Certain **cardiac disorders** increase the risk of having a stroke; in fact, heart disease is the second most important risk factor for stroke (53). According to data from the National Stroke Association (NSA), approximately 15% of all stroke sufferers have a heart condition called atrial fibrillation (AF) (54). AF occurs when the two upper chambers of the heart, the atria, beat rapidly and irregularly, allowing blood to pool in the heart. This can lead to the formation of blood clots that can then travel to the brain, causing a cerebral embolism. The risk of AF increases with age and hypertension. The NSA estimates that AF is associated with 7% of all strokes among people aged 50 to 59; by ages 80 to 89 this percentage has increased to 36% (54). Other heart disorders that contribute to stroke risk include heart valve disease, dilated cardiomyopathy, and myxoma (a benign heart tumor that can embolize, with fragments entering the circulatory system).

An individual who has had one or more **TIAs** has nearly 10 times the risk of a stroke as someone who has not had a TIA (55). The chance of a subsequent full ischemic stroke is greatest within the first month following a TIA. It is estimated that 50% of strokes occurring following a TIA will occur within the first year; after that, the risk diminishes.

**Cigarette smoking** doubles an individual's chance of having a stroke (56). The carbon monoxide and nicotine in tobacco smoke damage blood vessel walls, which leads to an increased likelihood of clot formation. A meta-analysis of 32 studies showed that smoking independently contributes to the risk

In 2002, West Virginia adults smoked at rate of 28.4%; however, recent data show that youth smoking in the state declined by 20% between 1999 and 2002.

of stroke (57); the greatest risk was of subarachnoid hemorrhage, followed by ischemic stroke and cerebral hemorrhage. A 2003 study of the incidence of SAH among young adults aged 18-49 found that two-thirds of those who had suffered a SAH were current cigarette smokers (58). According to one of the researchers, "If you're a smoker in this age group, you are about 3.7 times more likely to have this type of stroke than if you're not a smoker" (59).

A prospective study on cessation of smoking and the risk of stroke in middle-aged men over a 13-year period showed that, after adjustment for other risk factors, current smokers had nearly four



times the risk of stroke compared with never smokers (60). Ex-smokers had a lower risk than current smokers but a higher risk than never smokers. Switching to a pipe or cigars conferred no benefit. Cessation was most beneficial to hypertensive men.

Secondhand, or passive, smoke has also been found to increase stroke risk. An Australian study published in the *American Journal of Public Health* reported that the risk of ischemic stroke



was doubled for persons whose spouses smoked when compared with those whose spouses did not smoke, even after adjusting for the subject's own smoking, high blood pressure, heart disease, diabetes, and educational level (61).

BRFSS data for 2002 show West Virginia adults smoke at a significantly higher rate than the national average (28.4% vs. 23.0%). Both males and females in the state are significantly more likely to be smokers than their

counterparts nationally; in addition, higher rates of smoking were reported by state respondents in every age and income category (see Figures 5 and 6). The 1998-2002 rate of smoking among African-Americans was 31.8%; the five-year white rate was 27.1%.

The 2002 West Virginia Youth Tobacco Survey, published in 2003, reported that high school students showed a significant decrease in current smoking from 1999, when the rate was 42.2%, to 2002, when the rate was 33.7% (62). These declines may be reflected in the BRFSS prevalences among adults in coming years.

The relationship between **obesity** and stroke has only recently become more clearly defined. While it has been recognized that excess weight increases the risk of stroke, this increased risk was often attributed to the link between obesity and hypertension, diabetes, and high cholesterol levels. Several new studies,

In 2002, only 28.5% of men and 43.8% of women in West Virginia were of a healthy weight, i.e., not overweight or obese.

however, have documented that obesity, abdominal obesity in particular, is an independent risk factor for stroke. The Northern Manhattan Stroke Study, funded by NINDS, found abdominal obesity to be an independent risk factor for ischemic stroke among all racial and ethnic groups, with a greater effect noted among younger (aged <65) study subjects, especially African-Americans and Hispanics (63).

Research published in the *Archives of Internal Medicine* analyzed data from the Physicians' Health Study, confirming an independent relationship between obesity and stroke risk in men (64). Men having a body mass index (BMI) of 30 or greater were twice as likely to suffer a stroke as men with a BMI of less than 23. In fact, gaining only six or seven pounds can increase stroke risk by 6%. A similar study by Harvard researchers looked at women in the Nurses' Health Study. Their findings showed that obesity significantly raised the risk of ischemic stroke among women (65).

Scientists at the University of Michigan Medical School published research findings in *Journal of the American Medical Association* (*JAMA*) in 2002 that suggested that the link between obesity and stroke might be explained by high levels of the hormone **leptin** (66). Leptin is released by fat cells and normally acts to signal the brain to suppress appetite when a person is full. In grossly overweight people, however, this process breaks down and obese persons become resistant to leptin's signal. Researchers suggest



that there is an interaction between high levels of leptin and the leptin receptor on platelets, resulting in an increased tendency for blood clotting and thus an increased risk for stroke. In subsequent studies, both ischemic and hemorrhagic stroke have been associated with high leptin levels (67, 68).

In 2002, West Virginia ranked highest among the 54 participants of the BRFSS with an obesity (BMI=30+) prevalence of 27.6% (significantly higher than the U.S. rate of 22.2%). Nearly three out of every ten adult males (29.4%) in the state were obese in that year; 25.8% of adult females were obese. West Virginians were more likely than their national counterparts to be obese in every income category and in all but the youngest age group (Figures 7 and 8). Another 42.1% of men and 30.4% of women were overweight (BMI=25.0-29.9) in that year. In other words, only 28.5% of men and



43.8% of women were of a healthy weight in 2002. Among the state's African-American population, the 1998-2002 prevalence of obesity was 40.5%, compared with a five-year rate of 23.7% among whites.

The prevalence of obesity in West Virginia has, with few exceptions, shown a consistent upward trend since 1987. Given the relationship between obesity and stroke, this would indicate that a corresponding increase in stroke incidence and mortality is a potential problem.

High levels of both **cholesterol and triglycerides** have been shown to have independent effects on the risk of stroke. A study published in *Archives of Internal Medicine* in 2002 reported that ageadjusted rates of ischemic stroke and TIA were found to increase with increasing total cholesterol and low-density cholesterol and decreasing high-density cholesterol levels (69). A 2001 study demonstrated conclusively, for the first time, that having a high triglyceride level is a strong independent predictor of an individual's risk for stroke or TIA (70). After adjusting for other risk factors, the researchers found a nearly 30% higher risk among persons with high triglycerides. In 2001, West Virginia ranked first among BRFSS participants in the rate of adults who had been told they had high cholesterol.

When there is an excess of cholesterol in the blood, especially low-density lipoprotein cholesterol, it becomes deposited in artery walls. These fatty deposits, or plaques, are called atheromas and occur in large and medium-sized arteries, including the carotid and vertebral arteries. The narrowing of these

arteries can result in blood clots or reduced blood flow to the brain and increase the risk of ischemic stroke or TIA.

The BRFSS monitors the prevalence of adults who have been told by a doctor or other health professional that their blood cholesterol is high. In 2001, West Virginia ranked 1<sup>st</sup> among the 54 participants in respondents that reported having high cholesterol levels. The state prevalence of cholesterol awareness of 37.7% was significantly higher than the national rate of 30.2%. Both men and women had significantly higher rates than men and women in the nation as a whole. As Figures 9 and 10 show, state respondents were more likely to have been told their cholesterol was high than other respondents



in every age group but one and in every income category. Aggregating 1998-2002 data, the African-American rate of high cholesterol was 26.0%, the white rate 37.2%.



**Diabetes** has long been recognized as an independent risk factor for vascular disease; because circulatory problems and blood clotting are major factors in diabetes, the risk for ischemic stroke and TIA is increased two- to threefold (71, 72). Increased glucose in the blood causes damage to artery walls; when combined with high levels of cholesterol, this even more significantly increases the risk of developing atherosclerosis. Diabetes combined with hypertension also raises the odds of having a stroke, again from the increased damage to vessel walls. In particular,

the risk of brain lesions called "silent strokes" is increased, according to an article published in 2003 in *Stroke* (73). Japanese researchers found that silent strokes, which occur when the smaller blood vessels in the brain become blocked, were significantly more likely to occur if patients, particularly males, had diabetes and had suffered hypertension for 10 years or more. Silent strokes are markers for future, more serious strokes. A Danish study of diabetic and nondiabetic acute stroke patients

found that the patients with diabetes were on average 3.2 years younger at the time of their stroke, were more likely to be hypertensive, recovered more slowly, and had higher mortality rates than nondiabetic stroke sufferers (74).



West Virginians are more likely to have diabetes than people in the rest of the country regardless of sex, age, or educational level.

In 2002, West Virginia ranked  $2^{nd}$  to Puerto Rico in diabetes prevalence among the 54 BRFSS participants. The state's rate of 10.2% was significantly higher than the national median of 6.7%. As shown in Figure 11, both sexes reported significantly higher rates than men and women nationwide, as did each age group from 45 and older; sample sizes were too small among younger respondents for valid comparisons. Sample sizes were also too small in certain income categories for comparison, but large enough by educational level to show that West

Virginians were more likely than others to report having diabetes in each level (Figure 12). African-Americans in West Virginia reported a

prevalence of diabetes of 10.5% from 1998-2002, compared with 7.0% for the white population.

**Physical activity** has an impact on the risk of stroke in numerous ways. It has an independent effect and it can help reduce or eliminate several other risk factors associated with stroke:

- high blood pressure
- cigarette smoking (smokers who exercise on a regular basis are more likely to stop smoking)
- diabetes (exercise may reduce insulin requirements)
- obesity/overweight
- high triglycerides
- high cholesterol

A meta-analysis published in *Stroke* in 2003 reviewed 23 studies examining physical activity and stroke (75). Lee et al. found that both moderately and highly active people had lower risks of stroke than low-activity people; moderately active people were 20% less likely to suffer a stroke than low-activity people, and high-activity people were 27% less likely to have a stroke. Both ischemic and



Since 1994, the prevalence of adults reporting physical inactivity in West Virginia has decreased by 37%, following a national trend toward adding more leisure-time exercise to our lives.

hemorrhagic strokes were less frequent in moderately and highly active individuals. Researchers in the Northern Manhattan Stroke Study also found benefits to physical activity in lowering stroke risk (76). In that study, leisuretime activity was found to be significantly protective for stroke, even after adjusting for hypertension, diabetes, smoking, alcohol use,

obesity, heart disease, and peripheral vascular disease. Both moderate and heavy physical activity were associated with a decrease in stroke occurrence in a dose-response relationship among both men and women, in younger and older age groups, and among whites, African-Americans, and Hispanics.



In 2002, West Virginians were more likely to report physical inactivity in every age group except young adults aged 18-24 (Figure 13). Both statewide and nationally, women were more likely than men to report being inactive (Figure 14). The state also showed higher rates in every income category but one (\$25,000-\$34,999). Physical inactivity was reported by 39.6% of African-Americans and 38.8% of whites from 1998-2002. The BRFSS survey asks the question "During the past month, did you participate in any physical activities?" In 2002, West Virginia ranked 10<sup>th</sup> among the 54 BRFSS participants in the rate of respondents who answered no to this question. The state's prevalence of 28.4% was significantly higher than the national median of 24.4% but shows a marked decrease from a high of 45.3% reported in 1994 and continues a promising trend among state residents.

Figure 14. Prevalence of Physical Inactivity by Sex and Incor BRFSS, West Virginia and United States, 2002



Studies on **alcohol use** and stroke have produced mixed results. A meta-analysis performed by Reynolds et al. and published in *JAMA* in 2003 reviewed 35 studies on the effects of alcohol consumption on stroke (77). Their results indicated that heavy alcohol consumption (>60 g per day) increased the relative risk of total stroke, ischemic stroke, and hemorrhagic stroke, while light or moderate consumption (<24 g per day) decreased the risk of total and ischemic stroke when compared with abstainers.

Binge drinking increases blood pressure, thereby increasing the risk of stroke. In 2002, 11.4% of adult West Virginians reported binge drinking.

Researchers using data from the Stroke Prevention in Young Women study found that moderate alcohol consumption (defined for this study as two or fewer drinks per day) was associated with a decreased risk of ischemic stroke among women aged 15-44 (78). These results persisted even after controlling for age, race, education, and smoking status. Data from

the Northern Manhattan Stroke Study showed a protective effect of moderate alcohol consumption (defined as not exceeding one drink per day for women and two per day for men), which persisted after adjusting for other stroke factors and was found among men and women, all age groups, and whites, blacks, and Hispanics (79). The same study showed an association between heavy alcohol use (seven or more drinks per day) and increased risk of ischemic stroke; another study by Kissela et al. confirmed the association between heavy alcohol consumption and subarachnoid hemorrhage (80). A more recent study, however, conducted by researchers at Johns Hopkins University found no evidence that low to moderate alcohol use lowered stroke risk (81).

Binge drinking, i.e., having five or more drinks on one occasion, is known to raise blood pressure, increasing stroke risk (82). The BRFSS monitors the prevalence of binge drinking on a biennial basis, most recently in 2002. In that year, West Virginia was 49<sup>th</sup> among 54 participants in percentage of adults who reported having had five or more drinks on one occasion at least once during the month prior to their interview. Eleven percent (11.4%) of state respondents reported binge drinking, compared with the national median of 16.1%.

Diets high in **fruit and vegetable consumption** have been found to be associated with a lower risk of stroke. Data from the allfemale Nurses' Health Study and the all-male Health Professionals' Follow-up Study were analyzed to evaluate the relationship between fruit and vegetable intake and ischemic stroke

Only about one-fifth of West Virginia adults eat the recommended five or more servings of fruits and vegetables each day.

(83). Results pointed to a inverse relationship between the consumption of fruits and vegetables, especially cruciferous and green leafy vegetables and citrus fruits. The Hiroshima/Nagasaki Life Span Study examined fruit and vegetable intake and its association with both ischemic and hemorrhagic stroke (84). Daily consumption of green and yellow vegetables and fruits was found to be associated with a lower risk of ischemic stroke and intracerebral hemorrhage in both men and women.

The BRFSS monitors the average daily consumption of fruits and vegetables among West Virginia's adult population. In 2002, only about one in five (21.3%) West Virginians reported eating the recommended five or more servings of fruits and vegetables each day, compared with 22.6% of adults nationwide (Figure 15). State women were more likely to meet the recommendation (26.4%) than were men (15.7%).



Figure 15. Average Fruit and Vegetable Consumption per Day BRFSS, West Virginia and United States, 2002

The consumption of **fish** and **omega-3 polyunsaturated fatty acids** has also been linked to a significantly reduced risk of ischemic stroke among both men and women (85, 86), as has a higher intake of **whole-grain foods** (87, 88).

There are several **blood disorders** that can increase the risk of stroke. Both an excess and a deficiency of red blood cells can lead to stroke. Polycythemia refers to a moderate or marked increase in the number of red blood cells in circulation. This thickens the blood, increasing the possibility of a blood clot forming. Anemia is an abnormally low number of red blood cells. Red blood cells carry hemoglobin, which provide oxygen to the body. When

this mechanism is compromised, it can result in a lack of oxygen to the brain, causing stroke.

**Sickle cell anemia** is a genetic disorder in which the red blood cells are hard and shaped like little sickles instead being soft and round like normal cells. Because of this, sickle cells move through the blood vessels with greater difficulty and are more likely to clog the smaller vessels. When this happens, there can be a lack of oxygen to the brain. While sickle cell anemia is found among many nationalities and ethnic groups, it is most common among African-Americans; it is estimated that approximately 9% of African-Americans carry the sickle-cell trait (89). A recent study published in *Radiology* found that African-American children with siblings with sickle cell anemia are more likely to have "twisted" arteries in the brain, which are commonly seen in elderly hypertensive persons but rarely in children. The researchers hypothesize that this finding might help to explain why young to middle-aged African-American men are three to four times more likely to suffer a stroke than white American men of the same age (90).

**Sleep apnea**, a disorder that causes its sufferers to stop breathing briefly but repeatedly during their sleep, has been linked to a higher risk of hypertension and stroke. The American Stroke Association recently published findings showing that sleeping more than eight hours a night, snoring, and daytime drowsiness were associated with an increased risk for stroke (91). The disrupted sleep of a person with sleep apnea can result in all of these risks.

Numerous studies have found an independent association between high levels of **homocysteine** (tHcy), an amino acid found in the blood, and an increased risk of stroke (92). Data from the Framingham Heart Study showed nonfasting total homocysteine levels to be a risk factor for incident stroke in elderly persons (93). Finnish researchers examined the relationship between tHcy levels and cerebral infarction among Finnish male smokers; after adjusting for traditional stroke risk factors, they

found an increase in the risk of stroke per quartile increase in tHcy (94). A Danish study found elevated total tHcy to be an independent explanatory variable of recurrent stroke within 15 months after an initial stroke (95).

Researchers have always questioned why some individuals without conventional stroke risk factors such as high blood pressure, smoking, high cholesterol levels, etc., still suffer from cerebrovascular disease. **Inflammation** could be one answer. Inflammation is the body's response to an injury and is designed to kill germs and repair tissue damage. The plaque produced by cholesterol contains many of the inflammatory elements used by the body to fight infection and is drawn to injured and infected arteries. While designed to be helpful in the short term, this process is damaging when long-term inflammation continually draws plaque to artery walls. The buildup of plaque within arteries results in atherosclerosis, which sets the stage for ischemic stroke.

C-reactive protein (CRP) is a protein found in the blood whose level indicates the presence of inflammation in the body; researchers have found that high levels of CRP are present for many years (six to eight) preceding a first cardiovascular or cerebrovascular event. The American Heart Association estimates that persons with high levels of CRP have a doubled risk of stroke compared with those with lower levels of the protein (96). Physical activity, statins, and aspirin have all been shown to reduce CRP levels (97). Other studies have found additional markers in the blood (e.g., interleukin-6) that can predict cerebrovascular disease risk (98).

International attention is now being given to the possible role of **infection** in predicting stroke risk. Low-grade infections can be caused by either bacteria (e.g., chlamydia pneumoniae) or viruses (e.g., herpes simplex) (99). A German study of carotid plaque found in patients undergoing carotid endarterectomy supported the "infectious burden" hypothesis, i.e., there is an association between the number of infections a person has experienced and the risk for developing atherosclerosis (97). The German researchers were especially interested in the relationship between oral infection and atherosclerotic plaques, which was supported by their findings. Preliminary findings from the Oral Infections and Vascular Disease Epidemiology Study (INVEST) published in 2003 in *Stroke* suggest a link between tooth loss caused by **gum disease** and cerebrovascular disease (100). INVEST researchers found that the prevalence of carotid plaque increased with the number of missing teeth in study participants.

Recent research has linked the risk for stroke with **migraine**, especially migraine with aura, among young women. Findings presented at a 1999 symposium of the American Association for the Study of Headache showed that women who suffered from migraine were two to three times more likely to have a stroke than women without migraine; migraine with aura increased the risk to six times that of women without migraine (101). Smoking and/or taking oral contraceptives further increased the risk.

Stroke among young people is increasing due to the use of **illicit drugs**, in particular cocaine and amphetamines (102). Both of these drugs raise blood pressure and can cause an irregular heart beat, both risk factors for stroke. In addition, cocaine constricts blood vessels at the same time blood

pressure is increasing; this constriction can result in reduced or blocked blood flow to the brain (103). Cocaine use also promotes inflammation and clotting changes, which lead to cerebrovascular disease (104). While both ischemic and hemorrhagic strokes can occur due to illicit drug use, hemorrhagic strokes are much more common in stroke patients with recent drug use (105).

Several studies have examined the association between **stress and anger** and stroke. Everson et al. analyzed data from a population-based study of Finnish men, the Kuopio Ischemic Heart Disease Study, to evaluate the role of anger expression and hostility in cerebrovascular disease (106). Men who reported the highest level of expressed anger had twice the risk of stroke compared with men reporting the lowest level of expressed anger. These results were limited to men with a history of ischemic heart disease; however, the findings persisted even after adjustments for age, resting blood pressure, BMI, high cholesterol levels, smoking, alcohol consumption, fibrinogen, socioeconomic status, antihypertensive medication, and diabetes. Self-reported stress intensity and the risk of stroke were analyzed in the Copenhagen City Heart Study (107). Researchers found that persons who reported high stress intensity had nearly twice the risk of fatal stroke compared with persons with no stress (relative risk [RR] 1.89; 95% C.I. 1.11 to 3.21), but no significant differences were found among subjects who had nonfatal strokes.