



JOHNS HOPKINS  
M E D I C I N E

# Atrial Fibrillation

## The Latest Management Strategies



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## ABOUT JOHNS HOPKINS MEDICINE



**M**uch of what we take for granted in medicine today—from the rigorous training of physicians and nurses to the emphasis on research and the rapid application of that research to patient care—emerged from innovations made more than a century ago at a brand new medical center in Baltimore: Johns Hopkins.

Hopkins now uses one overarching name—Johns Hopkins Medicine—to identify its whole medical enterprise. This \$6.7 billion virtual organization unites the physicians and scientists of The Johns Hopkins University School of Medicine with the health professionals and facilities that make up the broad Johns Hopkins Health System.

A little history: Toward the end of the 19th century, American medical education was in chaos; most medical schools were little more than trade schools. Often, it was easier to gain admission to one of these than to a liberal arts college.

With the opening of The Johns Hopkins Hospital in 1889, followed four years later by The Johns Hopkins University School of Medicine, Johns Hopkins ushered in a new era marked by rigid entrance requirements for medical students, a vastly upgraded medical school curriculum with emphasis on the scientific method, the incorporation of bedside teaching and laboratory research as part of the instruction, and integration of the School of Medicine with the Hospital through joint appointments.





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## ATRIAL FIBRILLATION: THE LATEST MANAGEMENT STRATEGIES

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Hopkins medicine counts many “firsts” among its achievements during its early years: the first major medical school in the United States to admit women; the first to use rubber gloves during surgery; the first to develop renal dialysis and CPR.

Two of the most far-reaching advances in medicine during the past 25 years were made at Hopkins. The Nobel Prize-winning discovery of restriction enzymes gave birth to the genetic engineering industry and can be compared, some say, to the first splitting of an atom.

Also, the discovery of the brain’s natural opiates has triggered an explosion of interest in neurotransmitter pathways and functions. Other accomplishments include the identification of the three types of polio virus and the first “blue baby” operation, which opened the way to modern heart surgery. Hopkins also was the birthplace of many medical specialties, including neurosurgery, urology, endocrinology and pediatrics.

## ABOUT THE AUTHORS

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### **HUGH G. CALKINS, M.D.**

Dr. Calkins is the Nicholas J. Fortuin, M.D., Professor of Cardiology, Professor of Pediatrics, and Director of the Arrhythmia Service, the Electrophysiology Lab, and the Atrial Fibrillation Center at The Johns Hopkins Hospital. He has clinical and research interests in the treatment of cardiac arrhythmias with catheter ablation, the role of device therapy for treating ventricular arrhythmias, the evaluation and management of syncope, and the study of arrhythmogenic right ventricular dysplasia. Dr. Calkins has authored more than 500 manuscripts and chapters. He was lead author of the 2007 and 2012 HRS/EHRA/ECAS Consensus Document on Catheter and Surgical Ablation of Atrial Fibrillation and is also a member of the writing group for the 2013 ACC/AHA/HRS Atrial Fibrillation Guidelines. Dr. Calkins is a member of the editorial boards of five major cardiology journals.

### **RONALD BERGER, M.D., PH.D.**

A Professor of Medicine and Biomedical Engineering at Johns Hopkins, Dr. Berger is Director of the Electrophysiology Fellowship Program at The Johns Hopkins Hospital. He serves on the editorial boards of three major journals in the cardiovascular field, has authored more than 200 articles and book chapters, and holds over 20 patents on methods and devices used in electrophysiology diagnosis and treatment. Along with Dr. Hugh Calkins, Dr. Berger and his colleagues perform approximately 3,500 electrophysiology procedures and 500 atrial fibrillation ablation procedures each year.





## ATRIAL FIBRILLATION: THE MOST COMMON ARRHYTHMIA

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A racing heartbeat is familiar to anyone who has had to run up a flight of stairs or has been in a frightening situation. But for the estimated 2.6 million Americans who suffer from atrial fibrillation (AF or AFib), that sensation of a fast, irregular, and chaotic heartbeat all too often becomes a way of life. Moreover, for many, it severely impairs their quality of life and may put their health at risk. Recent studies have reported a link between AF and dementia.

AF is remarkably common. It is found in approximately 1% of the general population, and it's the most common cardiac arrhythmia seen by doctors today. Men and women over age 40 have a 1 in 4 lifetime risk of developing AF. The ailment becomes more likely with age. AF is rare prior to the age of 50 years, but by the age of 80, 10% of individuals will have AF. It's estimated that 70% of all AF patients are between the ages of 65 and 85. By the year 2050, some 12 million Americans are expected to have AF due to an aging population as well as the obesity epidemic, with more than half of people affected by AF expected to be over the age of 80.

### How AF Affects the Heart

The heart beats close to 100,000 times a day. That's about 70 beats per minute, every minute, every hour, every day, every year. However, for some people, the rhythmic lub-dub, lub-dub, lub-dub of the heart is not as precise as a Rolex. For some reason, the heart's electrical system goes haywire, leading to less efficient blood circulation and an irregular and chaotic pulse. That's because the heart's atria (upper chambers) quiver rather than contract forcefully, which then leads to an irregular—and often rapid—beating of the lower heart chambers, called the ventricles.

The *sinoatrial (SA) node* (also referred to as the sinus node), which is located in the upper right atrium, acts as a natural pacemaker that governs the heart's rate and rhythm. Special muscle fibers in the heart then conduct these electrical messages through the chambers. When a normally functioning SA node controls heart rhythm, it's called "normal sinus rhythm."

However, the specialized cells of the SA node are not the only ones capable of controlling electrical stimulation; the millions of heart muscle cells all have the ability to create their own electrical signals, disrupting the normal sinus rhythm in the process. If these cells misfire, the heart may race from a normal resting rate of 60 to 90 beats per minute (bpm) up to 200 bpm, then slow down after a few moments. *This irregularity may occur hundreds of times a day, or only in several short episodes a year.*

These misfirings can result in what are called premature or ectopic beats—that is, coming from a source other than the SA node. If there is a so-called “run” of premature beats in the atria, the heart rhythm can go into what’s called atrial fibrillation. This fibrillation—the multiple or rapid firing of electrical signals from different areas of the atria rather than the SA node—alters the movement of blood through the atria.

In cases where a person’s heartbeat is extremely fast—as high as 190 beats per minute after getting out of bed or rising from a chair—symptoms such as shortness of breath, dizziness, weakness, palpitation, or chest pain may occur, and can range from mild to severe. Some people complain that it feels as if “my heart is going to jump out of my chest.”

AF, by far the most common sustained arrhythmia, can last for minutes, hours, days, or weeks. While it’s not always possible—or even necessary—to restore the heart to normal rhythm, most physicians attempt to restore the normal tempo of a healthy heart for those who have symptoms and an impaired quality of life as a result of the heart rhythm abnormality.

## **AF and Stroke**

Contrary to popular belief, AF itself is not usually life threatening. However, the presence of AF increases the risk of blood clots (embolisms) forming in the heart, and if a clot travels to the brain, a stroke will result. The stroke risk in patients with AF is up to seven times that of the general public—and the incidence of stroke attributable to AF increases with age, dramatically so after age 80. Upwards of 24% of all ischemic strokes (strokes caused by a blood clot blocking a narrowed artery or a clot that travels to the brain from somewhere else in the body) are due to AF. Moreover, strokes related to AF are often major strokes that have worse outcomes than non-AF strokes, with a greater likelihood of significant disability or death.

## **Making Treatment Decisions**

A nuisance to some, a danger for others, AF runs the gamut of patient complaints and has many possible solutions—if, in fact, a solution is needed. In this special report, we will first review the symptoms and causes of AF and then discuss what is involved in diagnos-

## THE HEART'S ELECTRICAL SYSTEM

**E**ach heartbeat is initiated by an electrical signal. The signal originates in a group of cells in the right atrium called the sinoatrial (SA) node and travels throughout the atria toward a region in the center of the heart called the atrioventricular (AV) node. This causes the atria to contract, pushing blood into the ventricles. The signal then travels through a network of specialized fibers to all parts of the ventricles. The ventricles contract, and blood is sent into the aorta and other arteries in the body.

Arrhythmias are abnormalities in the heart's rhythm. They can occur if the SA node develops an abnormal rate or rhythm, if the electrical signal is interrupted along its route, or if another part of the heart beats faster than the SA node and produces its own electrical signal.

The end result is an irregular and sometimes fast heart rate. While a normal heart rate is between 60 and 100 beats per minute, heart rate in AF can jump between 100 and 180 beats per minute many times during a one-minute interval.

In arrhythmias called supraventricular tachycardias, the atria contract too rapidly.

AF is a type of supraventricular tachycardia in which the atria quiver and do not contract effectively. In ventricular tachycardia, the ventricles contract too rapidly, while in ventricular fibrillation, the ventricles quiver, and do not contract effectively. The term bradycardia is used to indicate that the heart is beating too slowly.

**Normal Heart Rhythm**—An electrical signal originates in the SA node, travels through the atria and the AV node, and continues into the ventricles. (Arrows denote pathway of electrical signal.)

**Atrial Fibrillation**—The electrical activity in the atria becomes chaotic and uncoordinated, so that the atria quiver rather than contract effectively.

**Ventricular Fibrillation**—Chaotic and uncoordinated electrical activity in the ventricles causes the ventricles to quiver rather than contract effectively.

**Heart Block**—A cause of bradycardia in which the AV node delays or prevents the electrical signal from traveling from the atria to the ventricles.

ing and treating AF. We address what we first ask about any patient: Do we need to do anything to reduce the risk of stroke? Many people are at low risk, and so we don't need to do anything. But for those who score high on a basic self-test evaluating their risk, anticoagulation therapy is strongly recommended. Anticoagulation therapy in these patients has been shown not only to dramatically reduce stroke risk, but it also lowers mortality by approximately 30%. AF treatment strategies, including rate and rhythm control (with medication or catheter or surgical ablation), are also discussed in detail.

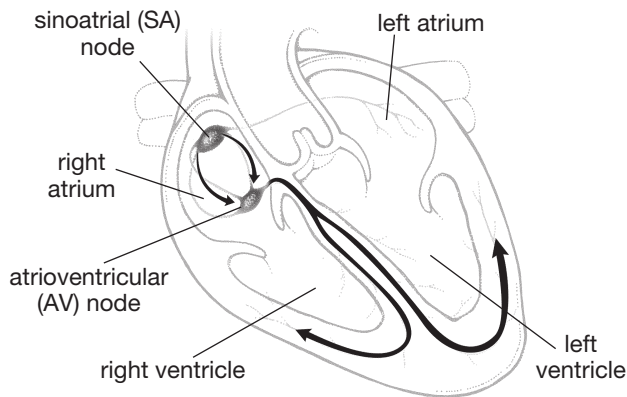




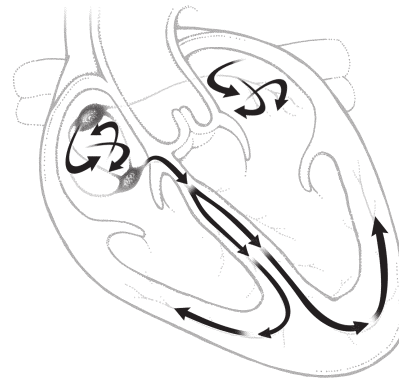
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ATRIAL FIBRILLATION: THE LATEST MANAGEMENT STRATEGIES

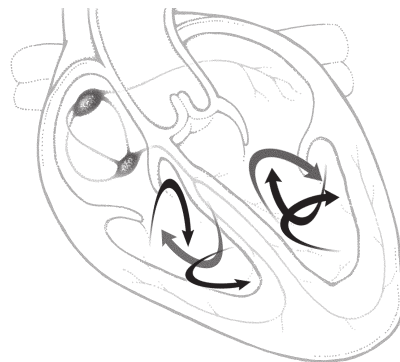
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**Normal Heart Rhythm**—An electrical signal originates in the SA node, travels through the atria and the AV node, and continues into the ventricles. (Arrows denote pathway of electrical signal.)



**Atrial Fibrillation**—The electrical activity of the atria becomes chaotic and uncoordinated, so that the atria quiver and the blood is pumped less effectively into the ventricles.



**Ventricular Fibrillation**—Chaotic and uncoordinated electrical activity in the ventricles causes them to quiver rather than pump blood to the rest of the body.

A point we make with our patients is that, unlike some arrhythmias, AF is generally not a life-threatening problem. For most people, it's just a darned nuisance. The reason to do something about AF, if something is done at all, is because of the bothersome symptoms that may adversely affect your quality of life.

We have three treatment goals when it comes to AF:

- Restoration and maintenance of sinus rhythm whenever possible
- Controlling heart rate

- Preventing clot formation (stroke prevention)

As you will read, the various approaches we can take to treat AF or prevent a recurrence of the ailment make use of some of the following:

### ■ Medications

Drug therapy is typically the first line of treatment for AF. Drugs can be used as a monotherapy or in combination as a way to control heart rate during AF, as a way to restore heart rhythm, or simply to reduce AF symptoms.

- A variety of antiarrhythmic drugs can be used to get the heart back to normal sinus rhythm.
- The rapid ventricular rate can be controlled with various medications, including beta-blockers, calcium channel blockers, and digoxin.
- Anticoagulants that include warfarin (Coumadin) and newer drugs such as dabigatran (Pradaxa), rivaroxaban (Xarelto), and apixaban (Eliquis) are used for the prevention of ischemic stroke for patients who are at risk.

### ■ Cardioversion

- Electrical cardioversion uses a powerful but brief electric shock delivered to the heart through paddles placed on the chest. This helps to restore normal heart rhythm when medication does not improve symptoms.
- Antiarrhythmia medications are also used to restore and maintain the heart's normal rhythm.

### ■ Radiofrequency catheter ablation

- Areas of the heart muscle that trigger abnormal rhythm are eliminated through an innovative minimally-invasive medical procedure called pulmonary vein antrum isolation (PVAI), which delivers concentrated radiofrequency energy waves that heat and destroy a ring of tissue surrounding each pulmonary vein. By achieving electrical isolation of the pulmonary vein, AF is prevented.

### ■ Cryoballoon catheter ablation

- Areas of the heart muscle that trigger abnormal rhythm are eliminated by positioning a balloon in each pulmonary vein antrum. Cryothermal energy (freezing) is then applied to the tissue through the balloon to electrically isolate the pulmonary vein, preventing AF.

### ■ Surgical ablation

- Appropriate candidates for surgical ablation of AF are patients undergoing other cardiac surgical procedures who have bothersome AF symptoms and asymptomatic patients who are undergoing cardiac surgery (and their ablation can be performed with minimal risk). The procedure can also be considered for AF patients who have failed one or more catheter ablation attempts, and also for patients who are not candidates for catheter ablation or prefer a surgical approach.

## New Therapies, New Guidelines

Any patient who experiences an episode of AF needs to be evaluated by a cardiologist, who can determine the best course of therapy. Making treatment decisions can be tricky.

Recently, there have been several important revisions to clinical practice guidelines for managing AF. In 2010, the European Society of Cardiology (ESC) revised their entire set of guidelines and issued an additional update in 2012. The American College of Cardiology/American Heart Association (ACC/AHA) published a substantial update to their guidelines in 2011 that incorporates new medications and research data. In addition, the Heart Rhythm Society (HRS) released an expert consensus statement in 2012 (with one of us, Hugh Calkins, as lead author) that describes the science and best practices for catheter ablation. The ACC, AHA, and HRS are currently preparing a complete rewrite of the 2006 and 2011 AF Guidelines.

This report makes use of these latest guidelines. It will familiarize you with AF and provide you with detailed information on all key topics, including the newest treatments—and it will provide you with the essential questions you'll want to discuss with your doctor.

## **SYMPTOMS, CAUSES, AND RISKS OF ATRIAL FIBRILLATION**

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**S**ymptoms of atrial fibrillation (AF) can vary from person to person. Some people with AF are fatigued by the ailment and it puts a crimp on everyday activities; others find themselves short of breath after a little physical exertion. Some people may also find that they have an inability to concentrate. We have a patient who swears his IQ drops 20 points when he goes into AF, leaving him somewhat disabled until the AF passes. Not everyone who develops AF will experience symptoms, and for those who do, symptoms can range from mild to severe. Symptoms of AF can include the following:

- Fatigue
- Palpitations (irregular, rapid, or a pounding sensation in the neck or chest)
- Shortness of breath
- Lightheadedness
- Dizziness
- Chest pain/discomfort
- Syncope (transient loss of consciousness, or fainting)

### **Causes of Atrial Fibrillation**

A long list of circumstances and conditions is associated with AF.

Multiple factors can contribute to the development of AF and the abnormal functioning of the heart's upper chambers; these include high blood pressure, coronary heart disease, cardiomyopathy (progressive degeneration of the heart muscle), obesity, sleep apnea, and valvular disorders.

AF is also associated with diabetes, an overactive thyroid (hyperthyroidism), and pneumonia, and it commonly develops after cardiac surgery.

Age is a key factor—AF is rare before age 50, whereas 1 in 10 people age 80 have it. AF is also more common in men than in women, and it is more common in whites than blacks. It is also well established that AF can run in families. The presence of a first-degree relative with AF results in a doubling of the likelihood that other members of the family will

### WHAT HAPPENS WHEN YOU HAVE AF

**H**ere's a good way to visualize what goes on when you have AF: You're out in the middle of a placid lake in a canoe. You drop a stone overboard, causing the water to ripple out in gentle circles away from the boat. That stone represents your atrioventricular (AV) node and it controls the rhythmic water ripples, which are the heartbeats. When the water is calm again, toss a handful of smaller stones into the water. A chaotic pattern of uncoordinated water ripples develops. This represents your heartbeat in atrial fibrillation.

develop AF. Although some specific genetic abnormalities have been reported in some families with AF, this is very unusual and there is currently no clinical role for genetic testing in patients with AF.

### Alcohol and AF

Although some alcohol consumption may help protect against heart disease, your heart may pay a price if you drink excessively. According to a recent study in the journal *Circulation*, heavy alcohol intake increases the risk of AF in men. Researchers studied 16,415 men and women in Denmark, assessing their intake of beer, wine, and spirits with a questionnaire and performing ECGs to check for the presence of AF.

No association was found between moderate alcohol use and AF. But when alcohol intake reached a level of 35 or more drinks per week, men had a 45 to 63% increased risk of AF, compared to men who consumed less than one drink per week. An estimated 5% of the cases of AF in the men were attributed to heavy alcohol consumption. There was no association between alcohol consumption and AF in women, who rarely consumed the high levels of alcohol seen in some of the men.

The authors hypothesize that heavy alcohol intake may lead to AF by affecting the structure and size of the heart or by promoting irregular heart rhythms in people predisposed to AF. And some patients develop AF after consuming even small amounts of alcohol.

Of course, alcohol consumption, especially heavy consumption, carries other health risks in addition to AF—which is why experts recommend that, if you drink alcohol, you should have no more than 1 to 2 drinks a day. In our experience, AF in some patients is uniquely sensitive to alcohol and even one drink may trigger AF. However, this is rare, and for most patients moderate levels of alcohol do not trigger or impact their AF. It is for this reason that we do not routinely tell all patients with AF to stop drinking alcohol.



## Obesity, Sleep Apnea, and AF

AF is more common in obese patients. Part of the reason for this is that obese patients are more likely to develop obstructive sleep apnea, or OSA. And AF is very common in patients with OSA, which causes a person's breathing to be interrupted during sleep and is considered one of the most dangerous sleep disturbances. Obesity may also trigger AF by increasing inflammation in the body. An increasing body of research has demonstrated that weight loss can play an important role in improving AF control in many patients.

Sleep apnea is quite common, affecting an estimated 12 to 18 million Americans. About 4% of middle-aged men and 2% of middle-aged women have the condition, according to the National Heart, Lung, and Blood Institute.

Sleep apnea is caused by a blockage of the airway due to a collapse of the soft tissue at the back of the throat during sleep. People with sleep apnea snore and repeatedly experience brief interruptions of breathing (*apnea*) during sleep. This may occur hundreds of times during sleep, which deprives the brain and other vital organs of life-sustaining oxygen. These pauses in breathing can cause drastic changes in oxygen levels, putting an enormous strain on the heart that can lead to an increase in heart rate and risk for vascular disease.

One fact that has become evident is that there is now a clear link between sleep apnea and cardiovascular problems. It's possible that the constant fluctuation in blood oxygen levels caused by sleep apnea may contribute to arterial inflammation, blood flow obstruction, insulin resistance, and, eventually, increased hypertension and cardiovascular-related events such as AF.

A study in *The Lancet* reported that the risk of a cardiovascular event was three times higher in men with severe apnea. A study in *The New England Journal of Medicine* noted that sudden cardiac death in people with sleep apnea *peaks* between midnight and 6 A.M., unlike the general population, where the risk of death *sinks* to its lowest point during sleeping hours.

Sleep apnea is a grossly underdiagnosed disorder. However, it is easily detected with an at-home testing device or in a sleep laboratory, and there are effective treatments for it.

When left untreated, sleep apnea can have life-threatening cardiovascular consequences by causing abnormal heart rhythms, high blood pressure, and increased risk of heart attack and stroke. Sleep experts consider sleep apnea to be as great a risk factor for cardiovascular disease as cholesterol, smoking, hypertension, and diabetes. It is for these reasons that it is important to screen AF patients for sleep apnea—especially if they are obese or if they snore or their spouse reports they intermittently stop breathing while sleeping. Once diagnosed, treatment of sleep apnea helps control AF.

## Weighty Implications

Your risk of developing AF may rise in tandem with your weight. A recent article in the *American Heart Journal* analyzed 16 studies from two groups of people: 78,600 European adults and about 45,000 heart surgery patients. In the first group, overweight adults were 39% more likely, and obese adults 87% more likely, to develop AF than their normal-weight counterparts. But obesity didn't increase AF risk among those in the second group—the patients who'd had heart surgery. Although AF is a fairly common complication after certain heart procedures, such as bypass surgery, postsurgical AF may arise for reasons that differ from those in the general population.

In people who have not had heart surgery, excess pounds may contribute to AF by causing an enlargement of the left ventricle, the heart's main pumping chamber. This, in turn, may cause the atria to enlarge.

In addition, health problems linked to obesity—like high blood pressure and diabetes—can contribute to AF.

**The bottom line:** AF may be another addition to the list of reasons to control your weight with a heart-healthy diet and regular exercise. The most important step someone can take to reduce the risk of developing AF is to avoid becoming obese. More and more data has confirmed the link between obesity and AF, and there is also data showing that weight reduction can lower the risk of AF. It's also important to avoid hypertension—or, if you have it, to treat it aggressively. And anyone who is at risk should avoid drinking high levels of alcohol. Most patients can tolerate small amounts of alcohol and caffeine without triggering an episode of AF.

## Atrial Fibrillation and the Risks to Health

In addition to impacting quality of life, AF increases the risk of heart failure, stroke, dementia, and death. The mortality rate associated with AF is double that of patients with normal sinus rhythm. Moreover, in patients who already have heart failure, AF aggravates the condition. Conversely, heart failure also promotes AF.

**AF and stroke.** As we've already mentioned, there is a risk of stroke with AF. One in every five ischemic strokes (caused by a blood clot blocking a narrowed artery or a clot that travels to the brain from somewhere else in the body) occurs in patients with AF. That's because blood can pool in the fibrillating atria—typically the left atrium—making it more likely to clot. Clots can form after just two days, then eventually break off and move to the brain, where they can cause a stroke. In people over age 70, AF is the single most common risk factor associated with stroke. *(Text continues on page 18.)*

**A CLOSER LOOK AT STROKES**

**E**ach year approximately 795,000 Americans suffer strokes; just over 600,000 of these are first attacks. On average, someone in the United States has a stroke every 40 seconds. Although the incidence is highest among people over age 65, a stroke may afflict anyone at any age.

Most people survive a stroke. But about 20% of stroke victims die shortly after the stroke, and about 25% will have a second stroke within five years. A major consequence of stroke is disability: nearly half of stroke victims experience moderate to severe impairments requiring special care. After heart disease and cancer, stroke is the third leading cause of death and the leading cause of disability among Americans.

Thankfully, the death rate from strokes has dropped—by more than 34% between 1998 and 2008. This decline is probably the result of more aggressive treatment of stroke risk factors (such as hypertension and smoking), earlier diagnosis of strokes, and better treatments. Still, the best weapon against strokes is prevention. Stroke prevention is essential in controlling the devastating physical, emotional, and financial repercussions of cerebrovascular disease. *More than half of strokes could be avoided if people took the appropriate preventive steps by embracing and adhering to healthful habits.*

We should do all we can to prevent strokes, but Americans are much more worried about heart attacks than they are about strokes. A recent survey reported

that only 1% of those interviewed mentioned stroke as a leading health concern. By comparison, 13% listed heart disease and 33% mentioned cancer. Surprisingly, even among people who had experienced a stroke or who knew someone who had, only 2% said that strokes were a major health worry.

**What Is a Stroke?**

A stroke occurs when an artery that supplies blood to part of the brain becomes blocked or ruptures. As a result, blood flow to a portion of the brain is interrupted, and neurons (nerve cells) in the affected area are deprived of the oxygen and nutrients they need to function properly. These neurons can suffer damage in as little as four minutes; if the deprivation continues for a few hours, neurons cannot survive, and some brain function is lost.

The damage to brain cells caused by a stroke can produce lasting disabilities that may impair a person's senses, motor skills, behavior, language ability, memory, and thought processes. The specific deficits that occur depend on which portions of the brain are damaged, as well as the type and severity of the stroke. In addition to these deficits, a stroke may produce long-term problems—from erratic sleep patterns and emotional instability to poor judgment and depression.

Nerve cell damage due to a stroke is usually permanent, producing such impairments as difficulty walking, speaking, and thinking. Despite the death of neurons, however, people who have had a stroke



usually have some improvement in function over time, because other neurons gradually take over the functions of those that were lost.

There are two basic types of strokes: *ischemic* and *hemorrhagic*. Prompt and accurate diagnosis of the stroke type is essential for determining the best treatment; when a stroke has occurred, every minute counts.

**Ischemic strokes.** About 87% of all strokes are ischemic; these result from a blockage in a blood vessel providing blood to the brain. Deprived of oxygen and nutrients, neurons become damaged within minutes and start to die. Further damage is caused by the so-called ischemic (or glutamic) cascade, which leads to a buildup of toxins. Where the blockage occurs and how long it lasts determine whether the brain suffers only temporary impairment, irreversible damage to only a few highly vulnerable neurons, or extensive neurological damage.

There are two major types of ischemic strokes: *thrombotic* and *embolic*.

**Thrombotic stroke.** The most common type of ischemic stroke is a thrombotic stroke. It occurs when a thrombus (blood clot) forms along the wall of one of the major arteries supplying the brain and completely blocks blood flow. The affected artery may be one of the carotid or vertebral arteries or a smaller artery within the brain itself.

Blood clots are most likely to develop in arteries that are already narrowed by fatty deposits called plaques, which also cause coronary heart disease. The hard, rough, uneven surfaces of the plaques are ideal sites for the formation and growth of blood clots.

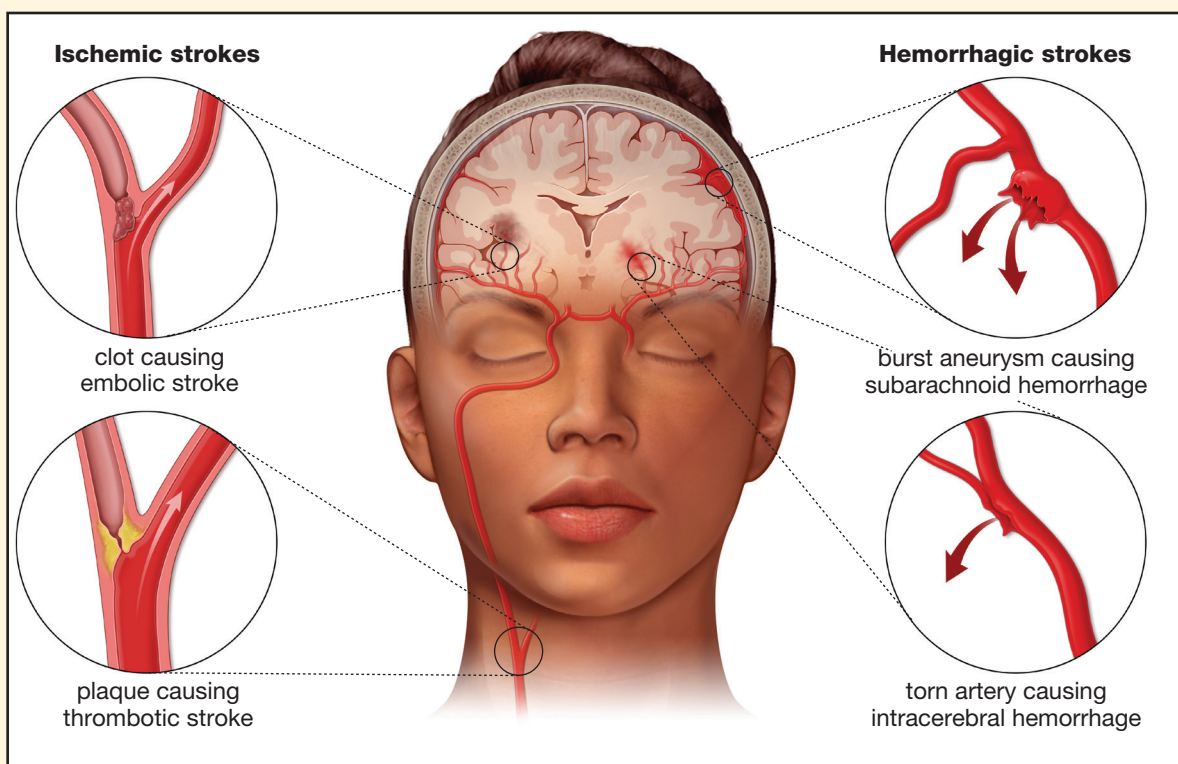
**Embolic stroke.** This type of ischemic stroke most often occurs when an embolus (part of a blood clot or a piece of atherosclerotic plaque) breaks off and travels through the bloodstream until it lodges in a smaller artery supplying the brain, thus blocking blood flow. Most of these emboli originate in the heart or in large arteries such as the carotid.

As discussed on page 5, one of the most common causes of emboli is atrial fibrillation (AF). Because of the abnormal heart rhythm that characterizes AF—in which the atria (the upper chambers of the heart) quiver chaotically instead of contracting in a rhythmic pattern—the atria do not empty completely of blood. The blood that remains behind can form clots that can escape and ultimately lodge in an artery (usually in the brain). One third of people with untreated atrial fibrillation suffer a stroke.

Other conditions that can increase the risk of an embolic stroke include a heart attack, heart failure (an impaired ability of the heart to pump blood), valvular heart disease (damage to one or more of the heart's valves), and plaque in the aorta (the body's main artery).

**Hemorrhagic Strokes.** Hemorrhagic (or bleeding) strokes account for about 13%

A CLOSER LOOK AT STROKES (CONTINUED)



of all strokes. These strokes occur when an artery in the brain tears or ruptures and blood leaks into the surrounding tissue. The bleeding can enter tissue deep within the brain itself (an intracerebral hemorrhage) or it can flow into the space between the brain and the skull (a subarachnoid hemorrhage).

Damage from a hemorrhagic stroke occurs in two ways: First, the blood supply is cut off to the parts of the brain beyond the site of the tear or rupture. Second—and posing greater danger—the escaped blood forms a mass that exerts excessive pressure on the brain. Blood continues to leak

from the torn or ruptured artery until the blood clots or the pressure inside the skull is equal to the pressure in the damaged artery.

An intracerebral hemorrhage is often caused by a tear in a small blood vessel in the brain; a subarachnoid hemorrhage is usually the result of a ruptured aneurysm in the brain. An aneurysm is a blood-filled pouch that balloons out from a weak spot in a blood vessel wall. While some aneurysms are congenital (present at birth), they may be made worse or even caused by hypertension. An intracerebral hemorrhagic stroke also can be caused by the





rupture of a congenital blood vessel defect known as an arteriovenous malformation (AVM, a tangled web of arteries and veins).

### **The Warning Signals of a Stroke**

- Sudden weakness or numbness of the face, arm, or leg on one side of the body.
- Sudden dimness or loss of vision, particularly in only one eye.
- Loss of speech, or trouble talking or understanding speech.
- Sudden severe, unexplained headaches.
- Unexplained dizziness, unsteadiness, or sudden falls, especially along with any of the previous symptoms.

*If you notice one or more of these signs, don't wait. See a doctor right away!*

About 10% of strokes are preceded by “mini-strokes,” or transient ischemic attacks (TIAs). TIAs can occur days, weeks, or even months before a major stroke. A person who's had one or more TIAs is 9.5 times more likely to have a stroke than someone of the same age and sex who hasn't. Thus, TIAs—which occur when a blood clot temporarily clogs an artery—are extremely important warning signs.

TIA symptoms occur rapidly and last a relatively short time. More than 75% of TIAs last less than five minutes. The average is about a minute, although some last several hours. By definition, TIAs can last up to—but not over—24 hours, although this is very unusual. Unlike a stroke, a TIA leaves no lasting disability.

TIA symptoms are very similar to those of stroke; their short duration and lack of permanent damage is the main distinction between TIA and stroke.

Although TIAs signal only about 10% of strokes, they're very strong predictors of stroke risk. Don't ignore them! *Get medical attention immediately.* A doctor should determine if a TIA or stroke has occurred, or if it's another medical problem with similar symptoms (seizure, fainting, migraine, or general medical or cardiac condition). Prompt medical or surgical attention to these symptoms could prevent a fatal or disabling stroke from occurring.

### **Preventing a Stroke**

It's estimated that more than half of all strokes could be averted if more people took the appropriate preventive steps. Most of the steps for reducing stroke risk are identical to those for preventing a heart attack. These include controlling high blood pressure (the single most important risk factor for stroke); not smoking; losing weight if your body weight is excessive; drinking alcohol moderately (if you drink at all); keeping your cholesterol levels in check; getting regular exercise; and controlling diabetes.

Low daily doses of aspirin or other antiplatelet drugs may be prescribed if you have had a TIA or are otherwise at high risk of stroke. If you have AF, your doctor will determine if you should be treated with anticoagulant therapy. (See pages 24-35 for more information.)

**AF and dementia.** Evidence of a link between AF and dementia comes from the Intermountain Heart Collaborative Study, which used data on 37,000 people, average age 60, who were treated in a large hospital system in Utah, Idaho, and Wyoming. Researchers evaluated the subjects for signs of AF and Alzheimer's disease or vascular, senile, or non-specific dementia. During an average of five years' follow-up, 4% of the subjects developed dementia and 27% developed AF. AF was associated with each of the four types of dementia, independent of other cardiovascular disease. The youngest group with AF (under age 70) had the highest incremental risk of dementia: those with AF were 130% more likely to develop Alzheimer's disease. Dementia is linked to older age, so this finding suggests the relationship between AF and dementia is particularly strong.

## Classification of Atrial Fibrillation

Based on a patient's most frequent complaints, AF is classified as paroxysmal, persistent, or longstanding persistent. Here is how we define the three types:

- **Paroxysmal AF** is a recurrent condition where the rapid heart rate and abnormal electrical signals spontaneously begin, typically last for a day or two, sometimes as long as a week, and then suddenly disappear as mysteriously as it began. Symptoms can range from barely noticeable to severe.
- **Persistent AF** lasts longer than a week, or lasts less than a week but symptoms are stopped following cardioversion (medical or electrical).
- **Longstanding persistent AF** is continuous AF that lasts longer than a year and a rhythm control strategy is pursued.

At first, patients may have brief episodes of AF, then revert to normal sinus rhythm for extended periods—and this pattern may persist for some time. But ultimately, episodes of both paroxysmal and persistent AF may become more frequent and bothersome and eventually may result in longstanding persistent AF.

One additional term that is sometimes used is “permanent AF”—and it's less a description of a patient's AF than it is of a therapeutic strategy whereby the patient and physician together have decided not to pursue rhythm control. If a patient is asymptomatic, he can decide to take anticoagulant medication and stay in AF “permanently.” If subsequently the patient undergoes cardioversion, that would take away the permanent AF status and is followed by efforts to get the patient back to normal sinus rhythm. The patient's status is redesignated as longstanding persistent AF.



## DIAGNOSING ATRIAL FIBRILLATION

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Symptoms of atrial fibrillation (AF) vary from person to person. Many people with AF have no symptoms—and in such people, AF may be detected as an incidental finding during a physical examination or test that has been ordered for some other reason. Palpitations are a common symptom of AF, and if you experience palpitations—or any of the other symptoms associated with AF (see page 10)—you should make an appointment with your family doctor. If AF is present on your electrocardiogram or if your history suggests atrial fibrillation, your doctor may then refer you to an electrophysiologist for further testing and/or treatment.

Electrophysiologists are cardiologists who specialize in the heart's electrical system. These arrhythmia specialists (cardiac electrophysiologists) utilize a patient's medical history plus the results of various procedures to diagnose heart rhythm abnormalities. When an electrical disorder is diagnosed, the electrophysiologist works with your doctor to determine the risk it poses and makes recommendations about possible treatment options. Along with your primary care doctor (or general cardiologist), you and the arrhythmia specialist decide on the best course of action for you.

Your doctor will probably ask many of the following questions, so in order to prepare for your visit, write down your answers beforehand.

- What particular symptoms are bothering you?
- When did you first begin to experience these symptoms?
- Did you start taking any new vitamins, supplements, or prescription drugs before the onset of symptoms?
- Are these symptoms *paroxysmal* (occasional or intermittent, beginning and stopping on their own), or *persistent* (present all the time, or lasting at least a week at a time continuously)?
- On a scale of 1 to 5, with 1 being little or no bother and 5 being severely bothersome, how would you rate your symptoms?
- Is there anything that appears to worsen your symptoms?
- Is there anything that appears to lessen your symptoms?

Whenever an abnormal heart rhythm is suspected, your doctor may recommend one or more tests to diagnose the arrhythmia and determine if it is causing your symptoms. These tests may include one or more of the following (*text continues on page 22*):



## GETTING A SECOND OPINION

**T**he last time you bought a car or other big-ticket item, you probably spent days or weeks doing research and shopping around before making a final decision. So why would you do anything less when making important decisions about the health of your heart?

One way to ensure that your health decisions are informed ones is to seek a second medical opinion. For example, let's say your cardiologist recommends a major procedure—perhaps a pulmonary vein antrum isolation for your atrial fibrillation. You might feel more comfortable about undergoing the procedure if another doctor confirms that the treatment is necessary.

As medicine grows more complex and the number of treatment options continues to multiply, getting a second opinion is becoming more commonplace and helpful. Yes, your own cardiologist will probably continue to manage your care. But because some doctors are more cautious or conservative in their treatment recommendations, and others are more aggressive, patients may want a different perspective on the same set of medical facts.

You might be concerned that your own doctor will be offended if you seek another opinion. That's rarely the case. Today's physicians are quite accustomed to and comfortable with their patients consulting with another doctor to get a second point of view. In fact, with certain types of medical conditions or procedures, most physicians expect their patients to seek another assessment of their disease and the best way to treat it.

### When To Seek Another Opinion

In general, second opinions aren't necessary for everyday medical decisions. If your doctor adjusts the dosage of your antiarrhythmic medication or puts you on a new blood pressure drug, for example, there's usually no need to open the Yellow Pages to look for another doctor's opinion. But when the issue is a procedure for atrial fibrillation or another major decision about your heart, that's the time to consider whether or not you should consult another physician.

Here are some situations when you might want to consider a second opinion:

- You've been diagnosed with a heart condition by your family doctor or internist, and you want the opinion of a specialist like a cardiologist or electrophysiologist.
- Your doctor recommends cardiac ablation or another procedure that poses considerable risk or is costly, and you want to make sure the procedure is really necessary. You might also want to seek a second opinion for relatively minor procedures (like the insertion of an implantable pacemaker) if it would make you feel more comfortable before going ahead with the procedure.
- You have several treatment options to choose from, and you want to make sure that your doctor is recommending the one that most other doctors would recommend as well. Even though cardiologists have gone through similar training, they can have different points of view on managing various heart conditions, including atrial fibrillation.
- You feel pressured to agree to a particular treatment and are unsure the treatment is the right one for you.



- You live in a small community or rural area where your doctor does not manage many patients with your particular heart condition, and you'd like to hear the advice of a doctor affiliated with a major medical center or medical school.

Interestingly, your insurance company may insist that you get a second opinion, particularly if your doctor has recommended a major (and perhaps expensive) procedure.

In other cases, if you belong to an HMO (health maintenance organization), you might be interested in getting the perspective of a doctor outside of the health organization. You'll probably have to pay for the second opinion out of pocket, but many people believe that it's worth the price for the peace of mind that you have received the best advice on your treatment options.

### **Finding a Doctor**

Once you've reached the decision to seek a second opinion, let your physician know and ask him or her for advice on how to proceed. Your primary care doctor should be able to refer you to a cardiologist. And your cardiologist should have the name of another cardiologist in your community who can provide an opinion from a different vantage point. You can also ask family members and friends for the name of a physician who has treated them for the same or similar health problem.

If you prefer, call your local medical society, or a nearby medical center or medical school, and request the names of appropriate specialists. If you want to check the credentials of a particular doctor, reference books in the library (such as The Official

American Board of Medical Specialists [ABMS] Directory of Board Certified Medical Specialists) can provide the name of the medical school the doctor attended, and where he or she received residency and specialty training. You can also scan the book *America's Top Doctors*, which compiles lists of leading physicians based on surveys that ask doctors who they themselves would go to for treatment in their own specialty.

Before you meet with this new doctor, have your physician send your relevant medical records, including the results of any tests already conducted. You might have to sign a release form for these records to be sent to the new doctor.

### **When Doctors Disagree**

Sometimes the doctor you choose for a second opinion makes a recommendation different from your own physician. What should you do? In a case like this, don't hesitate to get a third opinion. In fact, many insurance companies will pay for a third opinion when the first two doctors you've consulted have opposing viewpoints.

Here's another option to consider. After getting a second opinion, let both your own doctor and the one you've consulted know that they've disagreed about your diagnosis or the best course of action. Suggest that the two physicians confer with one another to discuss your case and to try to reach a consensus. Once each of them has described how and why he or she reached their conclusion, they may find common ground on which they can both agree and make a joint recommendation on what you should do.



**Electrocardiogram (ECG).** An electrocardiogram (ECG) is a simple test that traces the electrical activity of your heart. During an ECG, you lie flat on a table, connected to an ECG machine with wires taped to your chest, arms, and legs. The test is painless and takes only a few minutes. The ECG produces a printout that doctors can examine to diagnose arrhythmias or other types of heart disease. When you have AF, the atria produce a signature set of wiggles in the tracing, and the ventricular rate is typically irregular.

**Holter Monitoring.** Holter monitoring is a continuous ECG recording—usually for 24 to 48 hours—while you go about your normal daily activities. It is useful to detect arrhythmias that may not occur during a resting ECG.

During Holter monitoring, wires are connected to your chest and attached to a small recording device that you carry with you. If you experience any symptoms, you are asked to push a button and record your symptoms so that your heart rhythm at the time of your symptoms can be determined.

An arrhythmia specialist will later analyze the electrical recordings to determine what your actual heart rhythm was at the time that you were experiencing your symptoms and also whether any asymptomatic abnormal heart rhythms occurred while you were wearing the Holter monitor.

**Event Monitor.** An event monitor is similar to a Holter monitor but it does not record the heart rhythm continuously. Event monitors only record the heart rhythm when an abnormally fast or slow heartbeat occurs or when you activate them. An event monitor is used for one or two months, during which you are instructed to trigger the device and record your symptoms if symptoms occur. Once a recording is obtained, the ECG tracing can be transmitted over the phone to a monitoring station that will analyze the ECG recording and send it to your arrhythmia specialist for interpretation.

**Implantable Monitor.** The implantable monitor is a small device that is inserted under the skin (similar to a pacemaker) and functions like an event monitor. This device is typically recommended for patients who have passing-out spells every three to 12 months and in whom other tests have not determined a cause. One of the advantages of these devices is that they note the amount of time a patient is in atrial fibrillation.

The technique involved with inserting this monitor is similar to a pacemaker insertion. However, the incision is smaller, no wires need to be placed in the heart, and the procedure is usually performed on an outpatient basis.

**Exercise Stress Test.** Some arrhythmias only occur while a patient is exercising. Because of this, your doctor may recommend an exercise stress test. During this test, you briskly walk or jog on a treadmill while hooked up to an ECG machine. This allows your arrhythmia specialist to determine if you are experiencing any arrhythmias while exercising and also determine if you have evidence of a blocked heart artery.

**Echocardiogram and Transesophageal Echocardiogram.** An echocardiogram is a non-invasive, painless test that allows cardiologists to see if your heart is functioning normally or if it is enlarged or weakened or has a damaged valve. Ultrasound waves are directed through the chest to the heart. The echoes of the sound waves are processed and used to produce images of the heart.

Additionally, a transesophageal echocardiogram (TEE) may be performed by having you swallow the ultrasound probe (following numbing medication to the throat and appropriate sedation). The TEE provides close-up images of the heart from the esophagus. This technique is an excellent way to search for blood clots in the atria. Your physician may request that you have a TEE prior to an electrical cardioversion or catheter ablation. Most patients tolerate this test quite well.

**CT Scan.** Computed tomography (CT) scanning is performed by taking high-resolution X-ray images using a multislice scanner. This advanced imaging can detect coronary artery disease, evaluate congenital heart disease, and may be used to evaluate a patient's heart prior to a complex catheter ablation procedure.

**Magnetic Resonance Imaging.** Cardiac magnetic resonance imaging (MRI) is a painless means of evaluating the heart's structure and function. It can sometimes detect rare heart conditions (such as arrhythmogenic right ventricular dysplasia and cardiac sarcoidosis) and involves no radiation. MRI scans are sometimes obtained prior to complex catheter ablations. MRI of other parts of the body is also a useful diagnostic test for patients with various kinds of medical problems. In the past, MRI was not allowed in patients with implanted cardiac pacemakers and defibrillators. Thanks to the research efforts of several physicians and researchers, including those at The Johns Hopkins Hospital, MRI can now be safely performed in many patients with implanted cardiac devices.

**Electrophysiology Study.** Some arrhythmias are difficult to diagnose and may require an electrophysiology (EP) study. An EP study is often used to evaluate patients who have "fainted" or have experienced an abnormal rapid heart rhythm. This test may be recommended for patients who have impaired heart function and intermittent extra heartbeats, even if they are not experiencing symptoms. In other circumstances, patients with an inherited cardiac condition may undergo an EP study as part of their risk assessment. In these cases, the EP study may identify patients who are at high risk of developing a serious arrhythmia indicating the need for preventive treatment.

In an EP study, an electrophysiologist inserts several intravenous (IV) lines into large veins. The electrophysiologist then passes several electrical catheters through the IVs and guides them into the heart using X-ray imaging. This allows the electrophysiologist to examine the electrical activity inside your heart to determine if and why the rhythm is abnormal. Once that is known, your physician can prescribe the most effective treatment.

## ANTICOAGULATION THERAPY FOR ATRIAL FIBRILLATION

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**A**s we indicated earlier, in treating atrial fibrillation (AF) there are three objectives to consider: rhythm control, rate control, and stroke prevention. With every patient, you have to think about all three—but first and foremost is stroke prevention. Those people at risk of stroke due to their AF need anticoagulation therapy to “thin the blood.” This entails the use of a prescription anticoagulant. For many years, that anticoagulant was warfarin, also known by its brand name Coumadin. But over a span of two years, the U.S. Food and Drug Administration (FDA) has approved new medications that offer patients alternatives to warfarin—and that have some significant advantages over warfarin, as we explain on page 29. Although warfarin and the newer drugs are sometimes referred to as blood thinners, they don’t actually thin the blood. Instead, they prevent the formation of unwanted and dangerous blood clots. And although they don’t act to break up existing blood clots, they can keep those clots from getting bigger.

### Who Can Benefit from Anticoagulation Therapy?

Currently the best way to determine whether or not you need daily anticoagulation is a risk scoring system known as CHA<sub>2</sub>DS<sub>2</sub>-VASc—which is an acronym for a set of risk factors. This score is a refinement of a risk score in use for many years called the CHADS<sub>2</sub> Score. CHADS<sub>2</sub> is a mnemonic that helps physicians remember the following risk factors for stroke:

- C:** congestive heart failure
- H:** hypertension (above 140/90 mmHg)
- A:** age (75 or older)
- D:** diabetes
- S:** stroke (prior stroke or TIA)

Scores range from 0 to 6—with 1 point for each risk factor except Stroke/TIA, which is 2 points. The advantage of CHADS<sub>2</sub> is that it’s simple to use. However, it doesn’t include a number of common stroke risk factors, and some recent studies have highlighted its limitations—most importantly, that about 40 to 50% of patients were assessed as low risk with the CHADS<sub>2</sub> score and so weren’t receiving anticoagulants. Yet these patients turned

**USING CHA2DS2-VASC TO DETERMINE WHO NEEDS  
ANTICOAGULATION THERAPY**

<b>Condition</b>	<b>Score</b>
<b>C</b> Congestive Heart Failure	1
<b>H</b> Hypertension (or Treated Hypertension)	1
<b>A2</b> Age 75 years or more	2
<b>D</b> Diabetes Mellitus	1
<b>S2</b> Prior Stroke, TIA, or Thromboembolism	2
<b>V</b> Vascular Disease (e.g., heart attack, PAD, aortic plaque)	1
<b>A</b> Age 65-74 years	1
<b>Sc</b> Sex Category (female gender)	1

**Maximum Score 9**

TIA = transient ischemic attack; TE = thromboembolism; vascular disease = priormyocardial infarction, peripheral artery disease, or aortic plaque

Source: ESC Guidelines: *European Heart Journal*, October 2010, page 2382

The CHA2DS2-VASc score, a refinement of the CHADS2 score, includes eight risk factors that can yield a maximum score of 9. For each point increase in score, stroke risk increases. Based on recent guidelines from the European Society of Cardiology (ESC), anticoagulation with warfarin or one of the newer oral anticoagulants is recommended for patients who have one or more risk factors (that is, a score of 1 or greater).

If you have a score of 0, you are considered at “truly low risk” and will not benefit from anticoagulant therapy. If you have a score of 1, you can discuss with your doctor the option of taking a daily aspirin, but oral anticoagulation is the preferred prevention strategy.

out to have a significant rate of stroke, so they weren’t all truly low risk—and some of them would have benefited from anticoagulant therapy. Therefore, the latest ESC guidelines for managing AF use the categories of CHADS2, but have added vascular disease, the age range of 64-74, and female gender as additional factors to arrive at CHA2DS2-VASc (see box, above).

By introducing these other risk factors, the new scoring system allows a doctor to subdivide the lowest scores of CHADS2 and identify “truly low risk” patients and seemingly low risk patients who in fact are at risk. Studies have shown that CHA2DS2-VASc also better

predicts stroke in high-risk patients with AF. Because of this superior risk stratification, CHA2DS2-VASc is superseding CHADS2.

By the way, your particular AF symptoms and complaints don't enter into this scoring system. It's strictly based on your stroke risk factors. AF is just one more risk factor for stroke. That is how we look at it. In fact, in and of itself, AF is not much of a risk. Combine it with these other risk factors, however, and you have increased risk.

The recent guidelines also stress a simple means of targeting patients for anticoagulant therapy. Instead of focusing on the varying tiers in the risk score or singling out high-risk patients, the CHA2DS2-VASc tool is used to identify patients who are at truly low risk (a score of "0"). These patients don't need any anticoagulant therapy. This means that if a patient is young (under 64) and healthy, with no high blood pressure or diabetes or other risk factors and a structurally normal heart, then very likely no anticoagulation is going to be needed. That patient can ignore his AF or just focus on treatment for AF symptoms.

For everyone else, anticoagulant therapy is recommended.

Earlier guidelines recommended aspirin or a combination of aspirin and antiplatelet therapy for individuals at low risk of stroke and the option of either aspirin or warfarin for those at moderate risk. But with research data validating risk assessment with CHA2DS2-VASc—accompanied by the approval of new oral anticoagulants that have a net benefit even for lower risk patients—effective stroke prevention is essentially anticoagulant therapy for everyone other than individuals who are at the very lowest level of risk.

It is important to recognize that aspirin is not a true anticoagulant and that there is little evidence that it significantly reduces stroke risk; at the same time, it increases the risk of bleeding. It is for this reason that the ESC guidelines now suggest that aspirin only be used for patients who "refuse" anticoagulation therapy with warfarin or with one of the new anticoagulant drugs.

Patients with coronary artery disease may need to take aspirin and other platelet inhibitors to prevent recurrent coronary artery blockages. When patients have AF and coronary artery disease, it may be necessary to take both aspirin and an anticoagulant, although it is important to recognize that this increases bleeding risk.

## **Warfarin: An Effective But Problematic Therapy**

Until recently, patients with AF relied on one drug—warfarin (Coumadin)—to reduce the risk of blood clots. In use for more than 60 years, warfarin is a vitamin K antagonist—it inhibits the action of vitamin K, which promotes the formation of blood-clotting proteins.



**A BETTER TOOL TO ASSESS BLEEDING RISK**

A risk of bleeding is the major complication associated with oral anticoagulants, and concern about bleeding risk is a key reason why oral anticoagulants are underused for stroke reduction among at-risk AF patients. Therefore, assessment of a patient's bleeding risk is integral to the decision about prescribing oral anticoagulants. Another tool incorporated into the latest AF guidelines is the HAS-BLED bleeding risk score, which can be used with CHA2DS2-VASc to better guide decision-making for anticoagulant therapy. HAS-BLED provides an indication of the risk of major bleeding in a patient taking an anticoagulant—using risk factors that include hypertension, abnormal liver or renal function, stroke, history of GI bleeding, age (over 65), and drug or alcohol use. HAS-BLED is not intended by itself to recommend for or against anticoagulant therapy; instead, it allows a doctor to identify patients for whom extra precautions are warranted to minimize the risk of bleeding, including monitoring drug therapy and correcting risk factors that can be modified, such as controlling blood pressure and reducing excessive alcohol intake.

	<b>Clinical characteristic</b>	<b>Points if present</b>
<b>H</b>	Hypertension (systolic $\geq$ 160 mm Hg)	1
<b>A</b>	Abnormal liver or renal function	1 for each
<b>S</b>	Stroke (previous history)	1
<b>B</b>	Bleeding (major bleeding history)	1
<b>L</b>	Labile INR (see below)	1
<b>H</b>	Elderly (age 65 or older)	1
<b>D</b>	Drugs or alcohol	1 for each

A score of 3 or more indicates an increased risk of bleeding within one year on oral anticoagulation sufficient to justify caution or more regular review. The risk is for intracranial bleed, bleed requiring hospitalization, or a drop in hemoglobin that requires transfusion.

"Labile INR" refers to a high or unstable International Normalized Ratio, a measure of the time it takes blood to clot. Drugs or alcohol refers to concomitant use of certain drugs (such as antiplatelets and NSAIDs) or alcohol abuse.

Source: ESC Guidelines: *European Heart Journal*, October 2010, page 2385

Oral anticoagulation with warfarin is very effective at preventing strokes in AF patients, reducing stroke by about 68% compared with a placebo and lowering mortality by 26%. But warfarin often poses problems for patients who faithfully take the drug daily. While the

drug has proven to reduce the risk of stroke, its efficacy depends on maintaining an often-delicate balance between causing excessive clots and preventing excessive bleeding. This is monitored by means of a test called the International Normalized Ratio (INR), a measure of the time it takes blood to clot. In order for warfarin to produce the desired effect, the INR must be within a designated (and narrow) target range—typically 2.0-3.0. For patients with mechanical heart valves, the range could be between 2.5 and 3.5 and higher.

Due to its narrow therapeutic range and great variation in the way people respond to the drug, which can change day to day, warfarin requires regular and frequent monitoring. However, we know from studies that, even with monitoring under the best of circumstances, it is difficult to maintain the necessary INR. We have evidence from tightly controlled clinical trials that were strictly managed in anticoagulation clinics that only 60% of patients were able to accomplish this.

Warfarin dosages can vary widely in terms of how much is needed by each individual to inhibit vitamin K, and it can take weeks before a safe and effective dose of warfarin is determined. There is a high risk of bleeding when the INR goes out of range.

People taking warfarin must also watch their consumption of vitamin K (from both food and dietary supplements), since higher or lower intakes than usual can alter the drug's effectiveness. Foods rich in vitamin K include broccoli, spinach, cabbage, kale, Brussels sprouts, canola oil, and soybean oil. (This doesn't mean that warfarin users should exclude these foods from their diet—leafy green vegetables are very healthful and we encourage you to eat them. But you need to let your doctor know if you are consuming leafy green vegetables or other vitamin K-rich foods in larger amounts than you are accustomed to.)

Many prescription and over-the-counter medications can also alter warfarin's effects. Examples include NSAIDs (non-steroidal anti-inflammatory drugs) such as ibuprofen and naproxen; Tagamet (cimetidine) for heartburn; and medications to treat thyroid problems. Actually, there is a long list of drugs that interfere with warfarin's effects, so be sure to discuss all medications you are taking—be they prescription, over-the-counter, or vitamins and herbal supplements—with your physician.

It's estimated that more than 40,000 patients are treated at local hospital emergency departments for adverse reactions to warfarin. The most common adverse reaction to warfarin therapy is bleeding. Warfarin and two other drugs—insulin and digoxin, which also carry a high risk for overdosing and toxicity—are responsible for 1 in 3 adverse drug reactions in this country and for more than 40% of all hospitalizations in people over age 65.

## **The New Choices in Anticoagulants**

Three new oral anticoagulant medications are now available to reduce the risk of stroke and blood clots in patients with AF. These so-called “novel agents” are the result of 15 or more years of research and development. In clinical trials, they have proven to be as effective or more effective than warfarin in reducing the risk of embolic strokes—but they have a much easier regimen to follow than warfarin. The new drugs don’t have the narrow therapeutic index that warfarin has, food does not affect the way they are metabolized, and their anticoagulant effect is so predictable that they can be given in fixed doses. So there is no need for careful and frequent monitoring or dosage adjustments to make sure treatment goals are achieved. The new drugs don’t require dietary restrictions, and they have fewer drug-drug interactions than warfarin. They also have a rapid onset of action: whereas it can take four to five days for warfarin to reach the target therapeutic range, the new drugs accomplish this in only a few hours.

Safety is also a significant advantage of the new anticoagulants: they are less likely to cause serious, life-threatening or intracranial bleeding when compared to comparable dosage levels of warfarin. In fact, intracranial hemorrhage—the most feared complication of anticoagulant therapy—is reduced by more than half compared with warfarin, which is a very comforting message to share with patients.

*The new oral anticoagulants have features in common, but there are some key differences as well—and some disadvantages they have in comparison with warfarin.*

**Dabigatran (Pradaxa)**, the first of the new drugs to receive FDA approval for stroke prevention (in 2010), acts as an anticoagulant by directly inhibiting the enzyme thrombin, a protein involved in the formation of blood clots. A large clinical trial of 18,000 patients comparing dabigatran with warfarin showed that at the standard dose—150 mg twice a day—dabigatran was more effective than warfarin at stroke prevention, with 34% fewer strokes occurring among patients taking dabigatran. Rates of major bleeding were similar for both drugs—but the rate of gastrointestinal bleeding was higher with dabigatran (mostly in patients over age 75), while intracranial hemorrhages were significantly lower. A 75 mg twice-daily dosage of dabigatran is approved for people with kidney impairment. (Dabigatran and the other new anticoagulants are primarily excreted from the body by the kidneys.)

**Rivaroxaban (Xarelto)** is the first in a new class of blood thinners that work by blocking a clotting protein called factor Xa; it was approved by the FDA in November 2011. A trial of 14,000 patients showed that it was as effective as warfarin in terms of stroke prevention. The trial found no significant difference in major bleeding between the two drugs, but intracranial or fatal bleeding events are less frequent with rivaroxaban. The standard dose is 20 mg taken once a day. A lower dose (15 mg once a day) is available for patients with less than normal kidney function. *(Text continues on page 32.)*

**ATRIAL FIBRILLATION: THE LATEST MANAGEMENT STRATEGIES**

**Antiplatelet and Anticoagulant Drugs for Stroke Prevention**

**Drug type:  
Brand (generic)**

**Typical daily  
dosages\***

**How to take†**

**Antiplatelets**

Bayer, Bufferin, Ecotrin,  
St. Joseph, etc. (aspirin)

81-325 mg

One 81-mg tablet 1-2x/day or one 325-mg tablet 1x/day. Take with a full glass of water. Take with food to minimize stomach upset.

Plavix (clopidogrel)

75 mg

One 75-mg tablet 1x/day at the same time each day with or without food.

**Anticoagulant**

Coumadin, Jantoven  
(warfarin)

2-10 mg

One or two 1-, 2-, 2.5-, 3-, 4-, 5-, 6-, 7.5-, or 10-mg tablets 1x/day at the same time each day with or without food.

Pradaxa (dabigatran)

300 mg

One 150-mg tablet 2x/day at the same time each day with or without food.

Eliquis (apixaban)

10 mg

One 5-mg tablet 2x/day.

Xarelto (rivaroxaban)

20 mg

One 20 mg tablet 1 x/day with the evening meal.

\* These dosages represent the usual daily dosages for most patients for the prevention of ischemic strokes. The precise effective dosage varies from person to person and depends on many factors. Do not make any changes to your medication without consulting your doctor. Discontinuing an anticoagulant drug in the absence of adequate alternative anticoagulation may increase the risk of thrombotic events.

† These instructions represent the typical way to take the medication. Your doctor's instructions may differ. Always follow your doctor's recommendations.



ATRIAL FIBRILLATION: THE LATEST MANAGEMENT STRATEGIES

**Precautions**

Because you may bleed more easily: 1) use with extreme caution if you have a stomach ulcer or other condition that causes bleeding; 2) tell your doctor you are taking aspirin before scheduling a surgical procedure; and 3) limit your alcohol intake (no more than one or two drinks a day).

Same as for aspirin (see above). In addition, do not take Plavix in combination with aspirin, unless recommended by your doctor.

Same as for aspirin (see above). In addition, you'll need periodic prothrombin tests to make sure you are not receiving too much or too little of the drug. Vitamin K in food can affect warfarin. Eat a consistent amount of vitamin K each day. Foods high in vitamin K include green, leafy vegetables, liver, broccoli, cauliflower, and Brussels sprouts. Avoid cranberry juice and other cranberry products, because they can make warfarin stronger.

Same as for aspirin (see above). Do not take Pradaxa if you currently have abnormal bleeding or unusual bleeding. Discuss with your doctor whether it is safe to take Pradaxa if you are over age 75, have kidney problems, have stomach or intestinal bleeding that keeps coming back, have a stomach ulcer, or take other medications that increase your risk of bleeding.

Same as for aspirin (see above). Do not take Eliquis if you currently have abnormal or unusual bleeding. Before taking Eliquis, tell your doctor if you have ever had bleeding problems, if you have kidney or liver problems, and about all the medications and dietary and herbal supplements you take.

Same as for Eliquis (see above).

**Most common side effects**

Abdominal pain with cramps, heartburn, nausea, vomiting.

Stomach upset or pain, diarrhea, constipation, headache, dizziness, rash, flu-like symptoms, back or joint pain.

Abdominal pain with cramps, hair loss, diarrhea, nausea, vomiting.

Upset stomach, nausea, abdominal pain/discomfort, GERD, bleeding.

Bleeding.

Bleeding.

**Call your doctor if...**

You experience signs of gastrointestinal bleeding: black stools, severe stomach or abdominal pain, vomit that resembles coffee grounds.

You experience signs of serious bleeding: unusual or easy bleeding or bruising, black stools, vomit that resembles coffee grounds. Signs of infection: fever, chills, persistent sore throat.

You experience signs of unusual bleeding: prolonged bleeding from cuts; nosebleeds; bleeding of gums when you brush your teeth; easy bruising or blood blisters; red or dark brown urine; red, dark brown, or black stools; headache; dizziness; weakness.

Same as for warfarin (see above).

Same as for warfarin (see above).

Same as for warfarin (see above).

**Apixaban (Eliquis)**, the newest oral anticoagulant (it was approved in December 2012), is also a factor Xa inhibitor. In a trial of 18,000 patients with AF and at least one additional risk factor for stroke, apixaban was more effective than warfarin for stroke prevention, preventing 21% more strokes. It was also better than warfarin at lowering overall mortality, and, in contrast to the results with rivaroxaban, apixaban had a lower rate of bleeding—though the differences in bleeding rates may have to do with differences in the patient populations and study design. Another study compared apixaban to aspirin in AF patients who didn't want to take warfarin, and apixaban was far superior. The standard dosage for apixaban is 5 mg twice a day. Half that dosage is recommended for patients who are 80 years of age or older or who have impaired kidney function.

These three new drugs promise to make the management of AF safer and more effective—and because of their greater convenience, more patients will be willing to stay on anticoagulation therapy, which will prevent more strokes. In the near future, moreover, there will very likely be additional options for oral anticoagulation: Two other factor Xa inhibitors—edoxaban and betrixaban—are in phase 3 testing.

*Here are the questions we typically discuss with a patient in making a decision about medications for anticoagulant therapy.*

**Q. How do you decide between warfarin and one of the newer oral anticoagulants in newly diagnosed patients?**

**A.** Assuming that anticoagulation is warranted, based on a score of one or higher on the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, the first thing we ask a patient is: Do you have a prosthetic valve or do you have rheumatic heart disease? If so, you should get warfarin, since none of the new agents have been shown to be safe and effective in this population of patients.

Another circumstance that can mandate warfarin is when a patient has severe kidney disease, since the newer drugs are cleared from the body to some extent by the kidneys. Otherwise, we have a preference for one of the newer agents because they really are more effective and safer than warfarin. In addition, we have observed improved patient compliance and more consistent anticoagulation with these drugs.

**Q. What about patients who have longstanding persistent AF and have been taking warfarin? Under what circumstances should they consider switching to a newer drug?**

**A.** We first explain that the novel anticoagulation agents are available and they appear to be more effective and safer than warfarin. Second, we inquire as to whether the patient's INR levels are usually in a therapeutic range of 2 to 3.5. The efficacy of warfarin is directly linked to the time in therapeutic range. If the time in therapeutic range is low (< 65%) we strongly encourage that the patient switch to a novel anticoagulation agent. And we also



ask those patients about their experience with warfarin. If you've been on warfarin for many years and you've had a stable experience with it—you can maintain a regular diet, you don't mind the monitoring—then you may want to stay on warfarin. Testing is typically done at a doctor's office or at an anticoagulation center, and there are patients who like that routine.

Home testing is also an option—Medicare has expanded coverage of home testing so that it now includes patients on warfarin therapy for the treatment of chronic AF. Self-testing is more convenient—it's done with a small drop of blood from a fingerstick as opposed to having blood drawn from a vein at your doctor's office, and you can do it when you need to, wherever you are. Frequent testing at home makes it easier for your doctor to adjust your warfarin therapy on a timely basis, which may result in more time in the therapeutic range for you and reduced risk of complications, such as bleeding.

Cost can be a factor, too. Warfarin, a generic drug, can cost as little as \$50 a year—but to that must be added monitoring costs, which can be an additional \$500. The new drugs can cost up to \$3,000 a year—so what you pay depends on your insurance coverage. Most patients can count on part of the cost being covered by health insurers or Medicare. There are also manufacturers' coupons that can significantly limit copays for the new drugs, resulting in an out-of-pocket cost that is little different than warfarin.

**Q. And for patients who don't like warfarin?**

**A.** There are definitely many patients who say they can't stand warfarin and want to get started on a new drug. In that case, we encourage switching. And certainly if you have trouble maintaining the necessary therapeutic range on warfarin, then switching to a newer drug only makes sense. That's also true for patients who have a history of intracranial hemorrhage, since the rate of bleeding is significantly lower with any of the newer drugs compared with warfarin.

**Q. Do the newer drugs have any downsides in comparison with warfarin?**

**A.** Each of the three drugs has a shorter half-life than warfarin, which means it's important to follow the regimen for taking them. If you miss a dose, the anticoagulant effect wears off quickly, increasing the risk of an embolic event. So you need to take your medication on schedule and to order refills before you run out.

A short half-life has this advantage: the drugs can easily be stopped 24 to 48 hours before any elective surgery to prevent bleeding risks. At the same time, if a patient has a serious bleeding incident or needs emergency surgery, the blood-thinning effects of these drugs can't be reversed easily or quickly. Warfarin, by contrast, can be reversed with oral or intravenous vitamin K or other medications that are accessible and inexpensive. Researchers are working on antidotes to reverse the blood-thinning effects of the new drugs.

We don't think the lack of reversal agents is a sufficient reason not to use the drugs—and if a serious bleed occurs, there are other supportive measures that can be taken while waiting for the anticoagulant effect to wear off. But it's also critical to evaluate bleeding risk in a patient and to exercise appropriate caution in prescribing these drugs.

**Q. What are the signs that an anticoagulant is causing bleeding?**

**A.** You may bleed more easily after brushing your teeth or shaving once you have started anticoagulant therapy. But these signs are not ordinarily cause for concern. However, if any unusual bleeding occurs for no apparent reason—blood in your urine or bowel movements, coughing up blood, bruising that doesn't heal, uncontrollable bleeding from a cut or nosebleed—you should contact your doctor. You may require a change in your dosage or in your medication.

Also contact your doctor if you are involved in a car accident or suffer a fall or injury to the head, even if you are not bleeding. And ask your doctor if you should wear a medical alert bracelet or carry a card that indicates you take an anticoagulant. Be sure to inform all of your healthcare providers and your dentist that you are taking an anticoagulant.

**Q. How do you decide which of the new anticoagulants a patient should use?**

**A.** The choice of a drug is based on a few differences among the drugs that we've seen in the clinical trials and on patient preference and medical history. There have been no trials directly comparing the drugs to one another, so we can't say that one drug is "better" than another. With every patient, we have a discussion about the pros and cons of each drug, including what the cost is likely to be.

For example, dabigatran is more likely to cause gastrointestinal (GI) symptoms, especially stomach upset, so if a patient has GI problems, we tend to avoid dabigatran. Dabigatran is also not suitable for someone with severe kidney impairment, because there is a potential for the drug to accumulate in the blood. So rivaroxaban or apixaban, used cautiously, are better choices. All three drugs can be dose adjusted for patients with mild or moderate kidney impairment.

For older patients with a recent history of GI bleeding, apixaban may be the first choice, since dabigatran and rivaroxaban have shown more bleeding compared with warfarin, especially in patients over age 75.

Compliance is also a consideration. If you always take your drugs on schedule, then dabigatran and apixaban, which are taken twice a day, have the advantage of being more effective than warfarin. But if you are less likely to be compliant, then we're comfortable with rivaroxaban, which you take only once a day—and with less of a chance of GI side effects than dabigatran.

**Q. Is there still a role for antiplatelet therapy in AF-related stroke prevention?**

**A.** There are a few patients who cannot or will not take an anticoagulant, and for them a combination of aspirin and the antiplatelet drug clopidogrel (Plavix) does offer an alternative. Patients taking this combination were, in one major study, 28% less likely to suffer a stroke compared with those taking aspirin alone.

In fact, the efficacy of stroke prevention with aspirin alone is weak, while the risk of bleeding is not much lower than with warfarin or one of the newer anticoagulants. The combination of aspirin and Plavix is more effective, but the addition of Plavix also increases bleeding risk compared with aspirin alone. Therefore, aspirin plus Plavix only makes sense if your risk of suffering a stroke outweighs the added risk of bleeding associated with the combination. It's clear that, even for patients at low or moderate risk of stroke, anticoagulant therapy is preferable.

As noted earlier, platelet inhibitors still play an important role in preventing coronary artery blockages, particularly in patients who have received coronary stents. Therefore, patients with a history of both AF and coronary artery disease may need to take both an anticoagulant and platelet inhibitors, although this combination increases the risk of bleeding.

**Q. Is there a point when a patient can stop anticoagulant therapy?**

**A.** Not really, unless you can't tolerate the medication or for some other reason are non-compliant in taking it. The latest guidelines state that even with patients who opt for ablation or are cardioverted to regain sinus rhythm, the decision about continuing anticoagulant therapy should be based on their stroke risk profile. If you are deemed to be at risk, you should be treated with anticoagulants long term.

## SUPPRESSING AF SYMPTOMS: RATE CONTROL

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**A**s we've already mentioned, atrial fibrillation (AF) has a range of possible adverse consequences due to the reduction in synchronized cardiac output. These include stroke and obstructive sleep apnea to an exacerbation of heart failure. When reviewing your particular case with your cardiologist, a major discussion will entail whether or not to restore normal sinus rhythm and maintain it, or simply allow AF to persist but control it with medication to maintain adequate ventricular rate and anticoagulation medication (warfarin) to prevent stroke.

The preferred and most frequently used initial therapy for AF is a strategy to restore and maintain a normal heart rhythm. This is especially the case in young and middle aged patients as well as those with symptoms that persistent after initial attempts at slowing down the rate of AF.

Although a rhythm control strategy is attempted in many patients, it is often difficult to achieve heart rhythm and maintain it for long periods. Older patients, especially those with underlying structural heart issues (prior heart attack, left ventricular hypertrophy, marked left atrial dilation, or depressed ejection fraction), have less chance to remain in rhythm. Older patients are also more likely to have side effects (bradycardia, dizziness, fatigue, nausea, ventricular arrhythmia) from the antiarrhythmic medications they need to take daily.

Furthermore, in patients with long-standing persistent AF, the likelihood of restoring and maintaining normal sinus rhythm is low. For this reason, the focus for these patients is not aimed at efforts at establishing rhythm control but rather at maintaining long-term rate control. This will improve quality of life by reducing or eliminating such bothersome symptoms as palpitations, lightheadedness, and reduced exercise capacity.

The primary goal of rate control therapy is to slow the heart rate with drugs that slow conduction through the atrioventricular (AV) node during activities of daily living and exercise so that the average heart rate over a 24-hour period is less than 100 beats per minute.

## **The Reasons for Rate Control**

The AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study was the largest and most comprehensive clinical trial ever conducted on the treatment of AF. Researchers enrolled more than 4,000 patients with AF that was likely to be recurrent. Study results reported in *The New England Journal of Medicine* in 2002 noted that rate control is at least as good as rhythm control and, in some respects, may be even better since there was an almost significant trend toward lower mortality with rate control.

Moreover, the researchers found that the rhythm approach did not result in a lower risk of stroke, improved quality of life, or improved cognitive function—all of which had been *presumed* to be benefits over the heart rate strategy.

Although the AFFIRM study has implications for the management of AF, it is important not to overinterpret the results of this study. In particular, it is important to recognize that only minimally symptomatic elderly patients were enrolled in this clinical trial. Thus, the results cannot be extrapolated to patients with highly symptomatic AF and also to younger patients. It is also important to recognize that these patients were only followed for three to four years. It remains unknown what the lifetime implications of AF are, especially for younger patients.

In our experience, rate control is a good approach for minimally symptomatic or asymptomatic elderly patients, and especially for those elderly patients whose clinical profile and AF history suggests a low chance of long-term success with a rhythm control strategy.

It is important to have a discussion with your physician about whether a rate or rhythm control strategy is right for you.

## **The Goals of Long-Term Rate Control**

When we see a patient in the clinic, we ideally want the resting heart rate to be less than about 80 beats per minute (bpm). But a better way to assess rate control is to have a patient wear a Holter monitor for 24 hours and to know that, over 24 hours, the average heart rate is less than 100 bpm. There have been studies suggesting that more lenient control—a resting heart rate under 110 bpm—is adequate as a therapeutic target. But the subjects actually had better rate control than the methods that were used suggested. Also, in the AFFIRM study mentioned above, heart rates over 100 bpm in patients with permanent AF were associated with significantly increased risk of heart attack and mortality. So we aim for an average rate of less than 100 bpm that is best assessed with a Holter monitor.

Heart rate control can be achieved in two ways, with medication or through catheter ablation of the AV node. Let's review these strategies.

### CARDIAC PACEMAKERS

A pacemaker is used primarily to correct some types of bradycardia, or slow heart rhythms. The pacemaker is implanted in the body, usually below the collarbone, where it monitors the heart rhythm and triggers an electrical impulse if the heart is beating too slowly. The pacemaker is composed of a small, titanium-encased pulse generator that contains a lithium battery and electrical circuitry attached to one, two or three leads (wires) that are inserted into the heart. Pacemaker pulse generators are checked two to three times a year and must be replaced every five to 10 years.

Pacemaker implantation takes place in the electrophysiology lab. A 1- to 2-inch incision is made beneath the collarbone and a small “pocket” is created for the pulse generator under the skin. The leads are inserted into the heart through a large vein that runs under the collarbone. Once the leads are positioned in the heart, they are attached to the pulse generator.

You will receive detailed follow-up instructions before you leave the hospital. It is important that you follow these instructions and call your doctor or nurse with any questions. You will also need to carry a pacemaker ID card with you. It contains useful, manufacturer-specific details regarding your device for medical personnel.

### Medications for Rate Control

Beta-blockers and calcium channel blockers are the mainstay of rate control therapy. Adequate rate control with these drugs is oftentimes achievable and sustainable, but unfortunately, while many of these drugs provide rapid rate control and are effective in reducing heart rate in many patients with AF, the drugs have some bothersome side effects. The patient, therefore, along with counseling from his or her physician, has to decide what is worse: The fatigue and other symptoms caused by the AF or the fatigue and other symptoms from all the medications that are being used to bring the heart rate down and maintain it below 100 bpm.

Medications used for rate control include calcium-channel blockers such as diltiazem (Cardizem, Tilazem, Cartia XT) and verapamil (Calan, Isoptin). What calcium-channel blockers do so well is prevent or slow the flow of calcium ions into smooth muscle cells of the heart and blood vessels. They help decrease the number of electrical impulses that go to the ventricles. Calcium-blockers are typically recommended if you have heart or lung disease in addition to AF.



Beta-blockers can also be used as a rate control strategy. Beta-blockers block the action of adrenaline on beta-receptors in the cells of heart muscle, slow down conduction through the heart, and make the AV node less sensitive to erratic AF signals.

Beta-blockers include atenolol (Tenormin), metoprolol (Lopressor, Toprol-XL), esmolol HCl (Brevibloc), propranolol (Inderal), timolol (Blocadren), pindolol (Visken), carvedilol (Coreg), and nebivolol (Bystolic).

In addition to the beta-blockers and calcium channel blockers, there is digoxin (Lanoxin, Digitek). Digoxin slows down and controls the heart rate by blocking the electrical conduction between the atria and ventricles. While digoxin is prescribed for rate control, it is the least effective medication and is reserved for patients with heart failure.

Amiodarone is a powerful antiarrhythmic drug that also has important rate controlling properties. Despite its efficacy as a rate control agent, we rarely prescribe it for this use because it is associated with a high risk of complications, including damage to the lungs, thyroid, and liver. Dronedarone also has important rate controlling properties. Dronedarone should not be prescribed for rate control alone, however, since the recent PALLAS trial revealed that treatment of patients with dronedarone increases the risk of adverse outcomes. (See pages 45-46 for more detailed information about dronedarone and the PALLAS study.)

## **Catheter Ablation of the AV Node**

If a patient's heart rate is in a reasonable range at rest, then we don't do anything, and it wouldn't help even if we did. However, for those people who are not able to achieve and maintain adequate rate control with medication and are still bothered by persistent symptoms—and for those who have AF persistently and an elevated heart rate (130 to 140 bpm) that goes even higher with exercise because they have poor exertional tolerance—catheter ablation of the AV node is a reasonable next step to consider.

This approach, which attempts to disconnect triggers that cause AF by selectively destroying tissue (ablation) with low-voltage, high frequency electricity, is also recommended for patients older than 80 and patients with heart failure.

The goal of destroying the AV node—the pathway that connects the upper and lower chambers of the heart—is to correct heart rhythm disturbances by preventing the atria from sending faulty electrical signals to the ventricles, thereby maintaining optimal heart rate.

Having a persistently elevated heart rate can weaken the heart in some people over a period of months or years. In this case, we perform the AV node ablation to try and keep the heart rate from going too fast. Once this is done, none of the fibrillatory impulses get through to the ventricles. When this procedure is successful, it prevents arrhythmias from being

generated, thereby curing the patient. However, the ventricles continue to beat on their own at a very low rate, so we have to implant a pacemaker—a small electrical device that remains in the body connected to the heart with wires and stimulates the heart to contract regularly—to maintain a steady rate.

During a catheter ablation procedure (no surgical incisions are required), long flexible tubes known as catheters are passed to the heart through the blood vessels located in the groin. It's with these catheters that we are able to identify and then ablate the AV node.

Since ablation of the AV node does nothing to alter the fibrillatory activity in the atria, patients will still need anticoagulation therapy after this procedure is done.



## SUPPRESSING AF SYMPTOMS: RHYTHM CONTROL

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**R**hythm control, which consists of trying to get the heart in normal rhythm with medication or electrical cardioversion and then maintaining it with antiarrhythmic medication, is the preferred treatment approach for many patients with AF, and especially those who have persistent symptoms despite achieving adequate rate control.

After converting to normal sinus rhythm, only about 30% of patients are still in sinus rhythm a year later, so another antiarrhythmic drug may be added to the daily regimen, which may boost chances of remaining in sinus rhythm to between 40 and 80%. However, while rhythm control will most likely reduce the frequency of AF, in many cases it will *not* eliminate it entirely. Therefore, most people will continue with their regimen of anticoagulant therapy indefinitely.

The major benefit of rhythm control is improved cardiac function, but what patients typically notice the most are reduced symptoms, which greatly enhances their quality of life.

Finally, when all of these options fail to restore heart rhythm, patients can then think about a special procedure called catheter ablation of atrial fibrillation.

### **Cardioversion to Restore Normal Sinus Rhythm**

Getting the heart back into normal rhythm with medication or an electric shock is a process called cardioversion. This should be pursued as soon as possible following a positive AF diagnosis. However, it's now recommended that if a patient has had AF longer than 48 hours—or if it's not clear when the AF started and so its duration is unknown—the patient should receive anticoagulation therapy for three weeks before undergoing cardioversion.

For recent-onset AF (less than 48 hours), especially when there is unstable blood pressure, cardioversion should be performed as soon as possible, without anticoagulation.

Cardioversion can be attempted with medication, although it often requires the use of an electrical shock from a defibrillator. Most patients can safely undergo either method. Success with cardioversion appears to be related to how long you have had AF; generally, it is less successful

### WHEN RHYTHM CONTROL IS PREFERABLE

**W**e think, fundamentally, that control of sinus rhythm is more important than rate control, especially for younger patients (40 to 70 years of age). In our experience, if a patient in his 50s is showing even mild symptoms, we would discuss with him taking steps to achieve sinus rhythm. If he doesn't do something, he's going to spend years—and possibly the rest of his life—in atrial fibrillation.

It is important to recognize that the length of time a patient remains in continuous AF adversely impacts the chance of ever restoring and maintaining sinus rhythm. So a decision to not attempt a rhythm control strategy when AF is first diagnosed may result in a lifetime of AF. Therefore, our strategy would be to get him on anticoagulants and have him undergo cardioversion and return to sinus rhythm—and see how he feels.

Remember that the most common symptom of AF is fatigue. Typically, a patient comes in and complains of feeling tired all the time, of being a little more out of breath or having less tolerance for exercise, and often it's attributed to something else, like getting older. In fact, it's AF with these subtle symptoms—and we err on the side of getting that patient back to sinus rhythm.

if you have had AF for more than a year. Moreover, maintaining sinus rhythm for extended periods often proves to be the more difficult task, and so cardioversion is typically followed by daily maintenance with antiarrhythmic drug therapy.

Chemical cardioversion occurs after taking antiarrhythmia medication to restore the heart's rhythm. In about 40% of patients with AF, the medication will get the job done. This is a lower conversion rate than with electrical cardioversion, but conversion with medication doesn't require sedation or anesthesia.

### Electrical Cardioversion for AF

Electrical cardioversion—also referred to as direct current cardioversion—is successful at least 90% of the time, depending on underlying causes. It is an outpatient elective procedure performed in the hospital under brief but heavy sedation, since the quick but powerful electrical shock that is delivered can be painful, and as many electrophysiologists admit, it's one that you never want to remember having received.

Special cardioversion pads or paddles are placed on the chest and back, or just on the chest. If the first shock doesn't restore rhythm, another shock at a higher energy level is quickly delivered.

Patients awaken after the procedure with no memory of the shocks. Since the medication used for the procedure will make you drowsy, be sure to have someone at the hospital with you to bring you home. You will not be able to drive for the rest of the day.

In the past, it was thought that a return to normal sinus rhythm was enough to prevent strokes from occurring, and anticoagulant therapy was typically discontinued in the month following successful restoration of normal rhythm. But recent guidelines specify that even for patients who choose catheter ablation or are cardioverted to sinus rhythm, the decision to continue therapy should be based on their risk profile for stroke—and if they are deemed at risk, they should be treated with anticoagulation for the long term, even if they revert back to sinus rhythm.

### **Maintaining Normal Sinus Rhythm Following Cardioversion**

Successful cardioversion may last for years, but in some cases, it can last just minutes, hours, or days before AF returns. Despite treatment, about 50 to 70% of patients continue to have AF episodes. The chance of a recurrence of AF is increased the longer you've had AF before cardioversion, by being older, and if you've had previous recurrences.

While no medication is particularly effective at converting fibrillation, a variety of antiarrhythmic medications are helpful at maintaining sinus rhythm once a patient has undergone cardioversion. In the event of a relapse or if AF symptoms are unacceptable, electrical cardioversion can also be repeated—and pretreatment with an antiarrhythmic drug can help enhance the effectiveness of electrical cardioversion. There is no lifetime limit on the number of times a patient can undergo cardioversion. Some patients experience AF one to four times each year that does not stop on its own and arrange to get cardioverted with each AF recurrence. Other patients have more frequent recurrences of AF or find even infrequent cardioversion procedures to be disruptive to their life style. These patients may elect to proceed with catheter ablation of AF in hopes of preventing all AF recurrences.

### **Using Antiarrhythmic Drugs to Restore and Maintain Sinus Rhythm**

When it's necessary to return the heart to normal sinus rhythm and to maintain rhythm after it's been achieved after successful cardioversion, there are a variety of medications that can be used.

All of these antiarrhythmic medications work by affecting the ion channels of the heart. It's these electrically charged molecules of potassium, magnesium, sodium, and calcium stimulate the contractions of the heart.

## Antiarrhythmic Drug Side Effects

While antiarrhythmic medications are often effective in treating AF, they may also cause what is known as a proarrhythmia (ventricular tachycardia or ventricular fibrillation) in some patients, which is a more dangerous (and potentially deadly) problem for some patients. It's well understood that close monitoring of these drugs is essential.

In addition to proarrhythmia, antiarrhythmic drugs have other side effects, which can include:

- Slow heartbeat
- Palpitations
- Fatigue
- Dizziness
- Nausea
- Vomiting
- Stomach pain
- Constipation
- Diarrhea
- Rash
- Vision problems
- Urinary retention (men)

More specifically, the FDA has issued warnings about the antiarrhythmic drug amiodarone (see below) because it may cause serious side effects ranging from lung and liver damage to severe heartbeat difficulties and death.

## The Most Commonly Used Antiarrhythmic Medications

There are many drugs that can be used to suppress the bothersome arrhythmias caused by AF. Here are the most popular:

- **Amiodarone (Cordarone).** This drug is most commonly used for AF because it is one of the most effective drugs for suppressing arrhythmias. Unfortunately, it has a high side effect profile. The short-term side effects are few, but longer term—three to five years down the road—about 40% of patients will stop using it because of some side effect. The side effects can include nausea, constipation, hyperthyroidism or hypothyroidism, liver failure, respiratory failure, neuropathy, and sensitivity of the skin to sunlight. When the drug is used long term, having visual difficulties is another possible problem.

Most side effects are reversible and so will get better when the drug is stopped. And if you take amiodarone in a low dose, that significantly reduces the chance of side effects for many patients. But it shouldn't be used as a first-line drug, except in patients with heart failure



or severe left ventricular hypertrophy—who are at high risk of proarrhythmia. Otherwise, it should be a second-line therapy in patients who don't want catheter ablation and are highly symptomatic. It will control their AF, very possibly for up to five years before any side effects appear.

- **Flecainide (Tambocor).** For people with healthy hearts, this is an excellent medication for maintenance of sinus rhythm and is sometimes effective in converting fibrillation. The drug has been shown to be effective in preventing recurrences of AF in 40 to 60% of healthy patients. However, there is one major caution: People who have coronary artery disease, especially those who have had a heart attack, are not candidates for flecainide because it can trigger a lethal proarrhythmia.

- **Propafenone (Rythmol).** Similar to flecainide (see below), this drug is effective in maintaining sinus rhythm, but like flecainide, it can produce proarrhythmia in patients with coronary artery disease, especially those who have had a prior heart attack. In addition, the drug has some heart-rate-slowng effects.

- **Sotalol (Betapace).** This drug is also used for maintenance of heart rhythm. Sotalol has an efficacy similar to propafenone, but has a different side effect profile. A proportion of patients on sotalol will complain of severe fatigue. Sotalol should not be used in patients with severe heart failure or those with a long QT interval, because the drug may trigger a lethal cardiac arrhythmia in these patients. The term “long QT” refers to an abnormal pattern seen on an electrocardiogram (ECG). The QT interval, recorded on the ECG, corresponds to the time during which the lower chambers of the heart are triggered to contract and then build the potential to contract again.

- **Dofetilide (Tikosyn).** Tikosyn has an efficacy and side effect profile similar to sotalol, but unlike sotalol, Tikosyn does not slow the heart rate. Tikosyn is also less likely to result in fatigue. One of the major disadvantages of Tikosyn is that the FDA has mandated that all patients who start this medication be admitted to the hospital for three days for monitoring when the drug is started.

- **Dronedarone (Multaq).** This drug, chemically similar to amiodarone, was approved in 2009 and is another great option to have. While not as effective as amiodarone, it doesn't have amiodarone's toxicity. For patients for whom amiodarone is effective but the side effects are bothersome, dronedarone is an excellent choice. It's well tolerated and fairly good at rate control, and so we feel comfortable using it on an out-patient basis. And since the drug does not cause fatigue, it is a good drug to take the place of sotalol. Some patients experience some gastrointestinal side effects from dronedarone, however, and have to stop using the drug.

Results from the landmark ATHENA (A Trial with Dronedarone to Prevent Hospitalization or Death in Patients With Atrial Fibrillation) study of more than 4,600 patients in 37 countries

reported in *The New England Journal of Medicine* noted that dronedarone is the first drug approved in the United States that reduces the combined endpoint of hospitalization and cardiovascular mortality when compared to placebo. There is also some evidence that dronedarone may reduce stroke risk as well. One of the major advantages of dronedarone is that it does not require hospitalization for initiation of the drug.

Another trial, PALLAS (Permanent Atrial fibrillation Study), looked at patients (average age 75) with permanent AF. The researchers were hoping that dronedarone would have additional benefits for these patients. But in fact, patients in the PALLAS trial who took dronedarone had a significantly higher incidence of cardiovascular events—including stroke, heart attack, heart failure, and sudden death from cardiac arrhythmias—than patients taking a placebo. As a result of these adverse outcomes, the trial was stopped early.

Many of the PALLAS patients had heart failure, and so we've learned from this trial that if a patient ends up in continuous AF, you don't want to leave them on dronedarone. It also means that anyone taking dronedarone should be monitored regularly to make sure they haven't progressed to permanent AF or to new or worsening heart failure.

Dronedarone comes with a boxed warning, the FDA's strongest warning, cautioning that the drug should not be used for patients with severe heart failure (NYHA Class IV) or NYHA Class II-III patients requiring hospitalization or referral to a specialized heart failure clinic.

## **Antiarrhythmia Drug Treatment Guidelines**

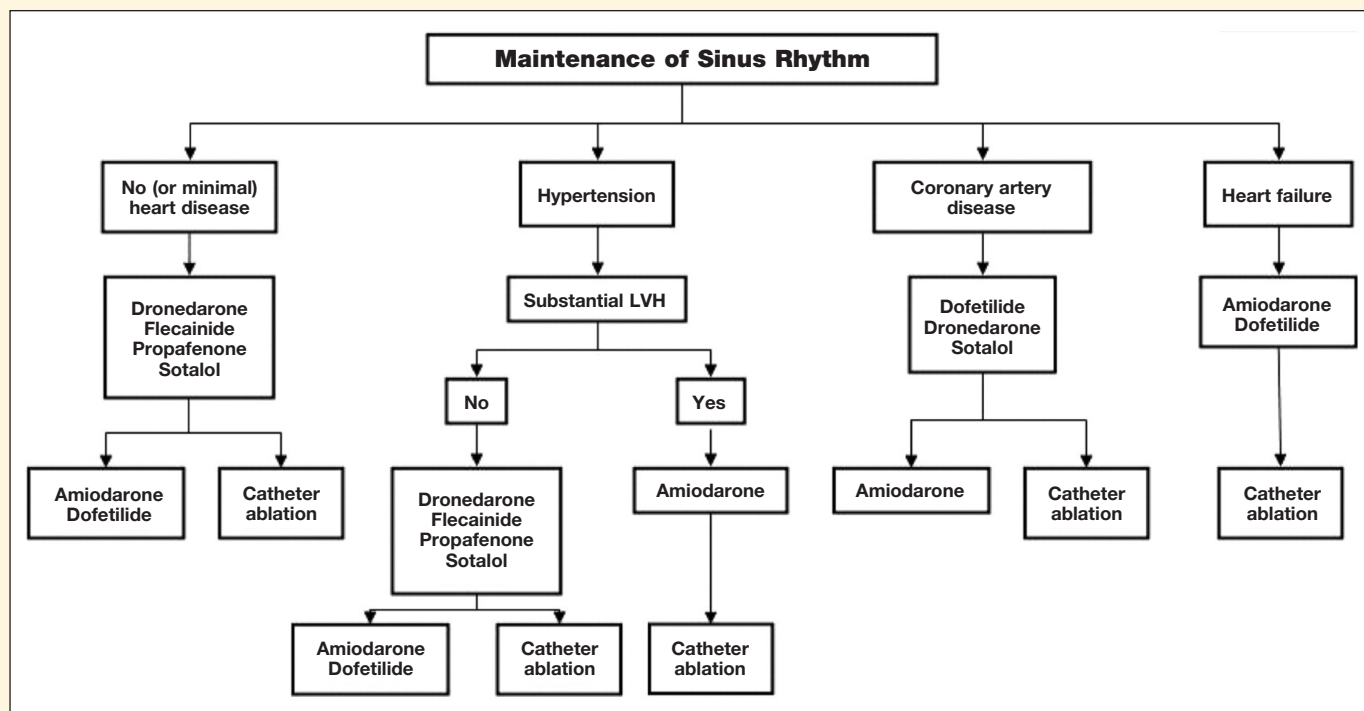
The majority of patients with AF have underlying heart disease. The choice of antiarrhythmic drug, therefore, is first based on whether or not the patient has significant underlying heart disease, especially coronary artery disease. Since the drugs that will be used have side effects, safety and efficacy are important considerations in choosing an antiarrhythmic drug for rhythm control.

Side effects can include drug-induced proarrhythmia, organ toxicity, bradyarrhythmia (heart rate under 60 beats per minute), negative inotropy (a weakening of heart contractions), and death. Other considerations in choosing an antiarrhythmic drug include convenience of dosing, drug metabolism, drug-drug interactions, and cost of the medications.

Based on safety information from a variety of clinical trials, the American College of Cardiology has issued the following treatment guidelines for long-term use of antiarrhythmic drugs for maintaining sinus rhythm.

- **Dronedarone, flecainide, propafenone, and sotalol:** Recommended for patients with no evidence of structural heart disease. Amiodarone or dofetilide can be used as alternatives.

## ANTIARRHYTHMIC DRUG THERAPY TO MAINTAIN SINUS RHYTHM



The chart above summarizes drug therapy strategies to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation. Drugs are listed alphabetically and not in order of suggested use. The selection of therapy in patients with multiple conditions depends on the most serious condition present (which in the chart progresses from left to right). LVH indicates left ventricular hypertrophy.

Source: 2011 ACCF/AHA/HRS Focused Update (*Circulation*, January 4, 2011, p.111)

—Also recommended for patients with hypertension but *without* left ventricular hypertrophy.

—Flecainide and propafenone are commonly used as first line antiarrhythmic medications, especially in patients without evidence of heart disease. Flecainide and propafenone should not be used in patients who have experienced a heart attack or have coronary artery disease, due to an increased risk of serious complications in this setting.

- **Amiodarone:** Recommended for patients with hypertension and substantial left ventricular hypertrophy. Amiodarone is also the preferred first line antiarrhythmic medications in patients with heart failure or a significant decrease in their heart function.

—Recommended as a second-line choice for patients with hypertension but *without* left ventricular hypertrophy.

—Recommended as a second-line agent for patients with coronary artery disease.

- **Dofetilide and sotalol:** Recommended as first line therapy for patients with coronary artery disease.
- **Dronedarone:** Should be considered as first line therapy in patients with paroxysmal or persistent (non-permanent) AF and minimal or no structural heart disease. Dronedarone should not be used in patients with moderate or severe heart failure, and should be avoided in patients with less severe heart failure if appropriate alternatives exist.

## Should You Start Antiarrhythmic Drug Therapy for Your AF?

After completing your AF evaluation, your doctor will decide if you would benefit from treatment with an antiarrhythmic medication. The risks and benefits of these medications will be discussed with you. A patient with little or no underlying cardiovascular disease has multiple options, while the presence of coronary artery disease or heart failure mandates narrower choices. Your doctor will also discuss with you whether antiarrhythmic therapy is your only treatment option or whether other treatment options such as catheter ablation or device therapy are feasible.

For most AF patients, we recommend trying antiarrhythmic drugs first. If the first drug you try doesn't work, we will then recommend either trying a second drug, or else going directly to catheter ablation therapy (see page 49).

When you are considering antiarrhythmic therapy, it's important to think about what your end point is and to be realistic. Take a patient who is in AF much of the time and feeling miserable. If that patient is cardioverted and starts an antiarrhythmic drug and then goes from experiencing symptoms daily to only five minutes a month, that's very good. You don't necessarily need total elimination of symptoms for a therapy regimen to be considered successful.

We also know from a variety of studies that anywhere from 42% to more than 65% of patients go back to AF after starting long-term drug maintenance with antiarrhythmic medication. So there is roughly a 50% chance that a drug will work. If it doesn't, we have other options. In a prospective randomized multicenter clinical trial, catheter ablation of AF was shown to be effective in preventing AF in 64% of patients, as compared with a success rate of 23% for antiarrhythmic medications..



## CATHETER ABLATION OF ATRIAL FIBRILLATION: THE PVAI APPROACH

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If a patient experiences recurrent episodes of paroxysmal or persistent atrial fibrillation (AF) despite medications for rate and rhythm control, then ablation therapy may help prevent further episodes. The 2012 HRS/ERHA/ECAS Consensus Document on Atrial Fibrillation Ablation provides indications for AF ablation. For selected patients with symptomatic, paroxysmal AF who have failed treatment with at least one antiarrhythmic medication, catheter ablation performed in an experienced center is recommended with a Class 1A recommendation—meaning there is sufficient evidence from multiple randomized trials that the treatment is effective. (An experienced center is defined as one performing more than 50 AF catheter ablations a year.) This recommendation reflects the fact that there have been more than seven head to head comparisons of AF ablation with drug therapy in this patient population. All seven studies demonstrated that AF ablation had superior efficacy.

The Fibrillation and Atrial Tachyarrhythmia Center at The Johns Hopkins Hospital is focused on the evaluation and treatment of patients with AF and also patients with complex atrial tachyarrhythmia such as atrial flutter or atrial tachycardia. Much of our current emphasis is on catheter ablation of AF, which entails inserting a catheter, or thin tube, into the body so that tissue helping to cause the arrhythmia can be selectively damaged (ablated).

In patients with persistent AF, catheter ablation is considered an alternative to second-line drug therapy with amiodarone. We generally don't perform catheter ablation as a first-line therapy for AF. We try an antiarrhythmic drug, and if it doesn't work, then we discuss the choice between amiodarone as second-line therapy and catheter ablation. Some patients don't want to take amiodarone because of the side effects, while others don't want to undertake a serious procedure. It's very important to discuss the benefits and risks of each treatment—with the goal of getting the patient back to sinus rhythm. Catheter ablation eliminates symptoms in many patients, it improves their quality of life, and it's more effective than drug therapy in maintaining sinus rhythm. But there is also a moderate risk of complications that can be serious, as we'll discuss in a moment.

## **What Is Catheter Ablation of Atrial Fibrillation?**

Catheter ablation is performed in an electrophysiology laboratory. The most commonly used approach for catheter ablation of AF involves the creation of continuous circumferential lesions around the two right and the two left pulmonary veins in the left atrium. The end point for this type of ablation procedure is the electrical isolation of the pulmonary veins. This technique, which is called *pulmonary vein antrum isolation* (PVAI), is used most widely at Johns Hopkins. PVAI can be performed either with radiofrequency energy or with cryothermal energy. Your doctor can discuss the advantages and disadvantages of each of these ablation strategies.

Electrophysiologists have determined that much of the electrical activity that initiates and sustains AF often comes from the pulmonary veins of the heart. These are the vessels that carry oxygenated blood from the lungs to the left atrium.

We now know that during the gestation period, the pulmonary veins often push outward as the heart is developing. These veins will sometimes pull tiny pieces of atrial muscle with them. Problems can develop later in life when this area of tissue from the pulmonary vein and tissue from the atrial muscle begin to send out wayward electrical signals. Why this happens in some people and not others is still not known.

Now that we know that these veins are often the cause of AF, we have found a way to stop them affecting the heart's rhythm—with PVAI. This innovative procedure is also called pulmonary vein ablation and pulmonary vein isolation.

## **What Happens During an AF Ablation Procedure?**

No matter what it's called, here's how the two-step pulmonary vein ablation procedure works: In step one, we start by taking a computed tomography (CT) or magnetic resonance (MR) scan of the patient's heart. Later on in the procedure, we use a special system that allows information from the CT or MR scan to be imported into the procedure to allow for precise 3-D mapping.

After administering anesthesia to the patient, we begin step two by snaking several thin catheters up the patient's groin through the femoral vein and into the right atrium of the heart. We are able to navigate this journey to the heart by images created by a fluoroscope, an x-ray-like machine that provides continuous "live" images of the catheter and tissue. The septum (wall) between the right and left atria is then punctured, and two catheters are advanced into the left atrium.

One of the catheters has a circular tip that measures electrical activity in and around each pulmonary vein. Another delivers electrical current from a special machine that heats the



tissue targeted for ablation. At the side of the operating table are several video monitors that show the catheters, electrical activity throughout the patient's heart, and all other vital signs.

Once we have mapped the electrical activity in the patient's heart, we start the actual ablation (damage by heat) procedure. We touch the heating catheter to the inner wall of the left atrium, just outside the opening of the pulmonary veins. The current briefly heats the tissue, killing a small focus of cells.

We then repeat the process dozens of times, forming a ring of scar tissue around the opening to the veins from the left lung. We then repeat the process around the veins entering the left atrium from the right lung.

The goal of PVAI is to create continuous rings of burns; one around the upper and lower left pulmonary veins and another around the upper and lower right pulmonary veins. Once this is accomplished, the electrical signals generated in and around the pulmonary veins can no longer pass through the scar tissue, so they can no longer affect the heart rhythm. For some patients, we may also have to ablate other areas in the left or right atrium.

When we first started performing PVAI, the procedure used to take seven or more hours to complete. We are now down to three to four hours from beginning to end. If everything goes as planned, the patient goes home after one night in the hospital.

The procedure in the electrophysiology lab is finished when we are sure that we have electrically isolated all four pulmonary veins. It will actually take up to three months for scar tissue to form, and once it does, it will effectively prevent any electrical impulses coming from the pulmonary veins. In essence, what this procedure does so well is "isolate" the wayward impulses from the heart, allowing the sinoatrial node to regain and maintain control of heart rhythm, undisturbed by any abnormal signals.

Catheter ablation of AF can also be performed using a cryoablation system. The procedure is similar to the procedure described above with the exception that the ablation is performed by positioning a balloon catheter into each PV. Cryothermal energy is then delivered to each vein for 3 to 4 minutes to freeze the tissue surrounding the PV and in doing so achieve PV isolation.

For about three months after the procedure, an oral anticoagulant is taken daily to prevent blood clot formation. Antiarrhythmia medication will also be taken for about two months. Arrhythmias may persist for about a month, but after that, most patients will be AF free and able to stop taking the antiarrhythmia drugs. Current guidelines advise that anticoagulation therapy be continued indefinitely in patients who are at high risk of stroke based on their CHA<sub>2</sub>DS<sub>2</sub>-VASc risk profile.

*The following questions about catheter ablation for AF are the ones we're most often asked by patients and interested doctors.*

**Q. Who are the best candidates for AF ablation?**

**A.** This procedure works best for people who are comparatively young and healthy—that is, a patient under age 70 with paroxysmal AF or recently persistent AF, a structurally normal heart, and no coexisting disease. It's also a patient who has failed on one or more antiarrhythmic drugs and is highly symptomatic. At the other extreme would be a patient in his 80s who has been in AF for five years, has other co-morbidities, hasn't been on a drug, and has only mild symptoms. We would consider that man or woman a very poor candidate for the procedure.

If a patient is, say, 83 but healthy, and has tried other therapies and failed, we wouldn't rule him or her out as a candidate—but that is when you need to have a careful discussion about risks and benefits of catheter ablation. The younger the patient is, the higher the success rate—and the more symptomatic the patient is after failed drug therapy, the more justified you are in doing an ablation..

**Q. What is the success rate for AF ablation?**

**A.** Following ablation, most patients are free of recurrent, paroxysmal AF for one year or more. Still, even for the best candidates, AF ablation isn't always completely effective. Data we have from a worldwide survey show that the success rate for a single procedure is about 57% after an average follow-up of 14 months; the success rate was even higher—72%—in patients who continued taking antiarrhythmic drugs. For patients undergoing multiple ablation procedures, the success rate without or with drugs is 71% and 77%, respectively. These are very respectable results.

At the same time, AF ablation has real risks, including stroke, damage to the heart, damage to the nerves that control the diaphragm, and obstruction of blood flow from the lungs to the heart (pulmonary vein stenosis). The overall incidence of complications is about 1 to 4%. This is why we generally do not offer catheter ablation as a first-line therapy for AF.

What's important to understand, however, is that the risks of catheter ablation have improved dramatically when the procedure is performed by experienced practitioners. Data from our center show that whereas 10 years ago the complication rate was in the 11% range, now it's less than 2%. Experience really does count, and the technique is getting better.

Even with a good outcome after your procedure, you're not necessarily free from AF the rest of your life. There is research showing that one in four patients will have a recurrence about five years out. And there is no evidence so far that successful AF ablation results in reduced mortality.

Less optimal candidates fare less well with ablation therapy. For them, the success rate for a single procedure one year out is 50 to 70% and for candidates with poor health factors (obesity, hypertension, sleep apnea, heart failure or other cardiac disease), the rate is less than 40 percent. But it's clear that in optimal patients, where the success rate is 60 to 80% for a single procedure one year out, catheter ablation has high efficacy and reasonable safety.

**Q. What happens after the AF ablation procedure is performed?**

**A.** The procedure itself can provoke AF. We tell patients that they should expect their AF might be worse, not better, in the first month following the procedure. That shouldn't discourage them. We liken the procedure to stirring up sand at the bottom of a lake. We are causing inflammation in the atrium, triggering heart cells that normally would not provoke AF to go into a pro-fibrillatory state. After a few weeks, the inflammation subsides and the antiarrhythmic benefit of the procedure is then realized.

You should have a follow-up visit at three months, then at six-month intervals for at least two years to monitor for any recurrence of AF.

The primary goal of PVAI therapy is the elimination of AF symptoms. We also want to eliminate all arrhythmias, as well as the use of antiarrhythmic drugs. What we often find, however, is that there are patients who have a very good response to AF ablation in the weeks after the procedure, a time when they are also taking antiarrhythmic drugs. But there are some who are so happy with how they now feel that they are often reluctant to stop taking the drugs to see how they will do without them.

On the other hand, AF ablation may prove not to be totally effective for some patients who had previously been unable to prevent their AF with drug therapy. However, some surprisingly discover that antiarrhythmia drugs now work for them. In cases such as this—especially for patients who don't want to have another AF ablation procedure—drug therapy will be recommended as a long-term management strategy for their AF.

**Q. What can be done if AF ablation isn't successful?**

Not infrequently, a patient will require a repeat of the ablation procedure to achieve successful arrhythmia suppression. However, we don't even discuss the possibility of a repeat procedure—if one is needed—until we see how things are going three months after the initial ablation. If a repeat is needed because the AF returned, most patients will have the procedure done six months later. And some patients require a repeat AF ablation because the initial procedure had no affect whatsoever. Among the 20 to 30% of patients for whom the AF ablation doesn't work the first time, about half will come back for a repeat procedure.

However, we think there is a point of diminishing returns with the PVAI after a second attempt. At that point, we may be dealing with a different type of AF, and we are going after the wrong target in the heart.

**Q. How many AF ablation procedures are feasible?**

**A.** There are patients who have had three, four, even five procedures. When we repeat a procedure, we often find that the pulmonary veins recovered from the previous procedure, but there are gaps. We can fill those gaps, which has significant benefit. There is data showing that until you get to a fourth procedure, there are always some gaps. We are working on achieving better pulmonary vein isolation with the first procedure. But until we are able to do that, we are faced with repeat procedures, and it's reasonable to do them. There is an incremental amount of radiation exposure, but in our experience, the repeat procedure is easier and quicker because there are usually only small gaps remaining to ablate. Much of the work has already been done.

## **SURGICAL ABLATION OF ATRIAL FIBRILLATION**

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**A**nother option available at Johns Hopkins and other leading medical centers is the surgical ablation of AF. This procedure can be performed through small incisions in the chest wall. Surgical ablation of AF requires three or four days in the hospital.

The “mini-Maze” ablation procedures used in this surgery are derived from the original Cox-Maze operations developed in the 1980s and early 1990s. Performed through a standard sternotomy (an incision made through the breastbone) and using the heart-lung bypass machine, these operations were designed to surgically interrupt the “reentrant” electrical pathways found in atrial wall tissue that cause AF. The most refined of these operations achieved high success rates, but the surgery quickly fell out of favor and is not performed much anymore due to its invasiveness and surgical complexity.

However, new surgical technology now permits cardiac surgeons to perform procedures based on the Cox-Maze principles through much smaller incisions made between the ribs on each side of the chest without using the heart-lung machine. This has made what used to be a technically difficult and time-consuming surgery much easier for all cardiac surgeons to perform.

Using a fiber optic camera to visualize the heart through these small incisions, the surgeon makes a series of lesions on the outside of the heart using various types of energy such as radiofrequency, freezing, or ultrasonic energy.

Success rates of these newer mini-Maze procedures are as good as, and often better than, those achieved with catheter ablation. But the risks are higher and the recovery is longer.

Often, the left atrial appendage is also removed during these procedures, because it is widely believed that this is where blood clots tend to form in patients suffering from AF. Removing this source of clots is intended to significantly reduce the risk of stroke and, in many cases, reduce or eliminate the need for long-term anticoagulant therapy.

Most mini-Maze operations take three to four hours and, as mentioned, minimally invasive approaches used usually result in a relatively short postoperative hospital stay averaging three to four days. Most patients are able to resume normal activities two to four weeks after

surgery. Since it often takes several months for the procedure to take full effect, patients are generally placed on a short course of antiarrhythmic drugs and an oral anticoagulant.

It is our belief that all patients with AF who have to undergo other cardiac surgery should be considered for AF ablation if the risk for doing the procedure is low. The good news is that when an experienced surgeon performs the surgery, the chance for success is extremely high.

### **The Best Candidates for Surgical Ablation of AF**

As with catheter-based interventions, patients with recent-onset paroxysmal (episodic) AF enjoy greater success rates than patients with longstanding continuous AF. These patients are undergoing another cardiac surgical procedure and then have the surgical ablation performed at the same time.

The same goes for an asymptomatic AF patient who is undergoing cardiac surgery. The ablation procedure can be performed with minimal risk with great expectations of success with the elimination of AF. Finally, stand-alone AF surgery can also be an option for the symptomatic AF patient who truly wants surgical ablation, the patient who has already failed one or more attempts with PVAI, or the patient who is not a candidate for AF catheter ablation.





## DECIDING ON APPROPRIATE TREATMENT FOR ATRIAL FIBRILLATION

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**W**hen we counsel a patient who has been diagnosed with AF, we typically divide our talk into two distinct halves. The first half is about the potential health threat posed by AF, which is the possibility of an ischemic stroke. Because of this risk, there are some patients who should be taking an anticoagulant such as warfarin to prevent clot formation. Some people with lower risk can take a baby (81 mg) aspirin daily. And then there are some people with a stroke risk that is so low that they don't need to take anything.

The second part of our conversation is about AF symptoms. There are many patients with AF who have no substantial increase in stroke risk, and for those people, AF is just a nuisance. Some of these people have no symptoms at all from their AF or, if they have any, their symptoms are so mild that they don't want to do anything about them.

On the other hand, many patients have permanent AF. They have been in AF (knowingly or unknowingly) for months, sometimes years, and they have learned to live with their symptoms. If they have a stroke risk because of AF and it is then dealt with by taking an oral anticoagulant, there is often really no compelling reason to do anything else about the AF.

But then there are the patients who are extremely symptomatic, whose lives are made miserable by this heart irregularity, and they deserve everything we can do to eliminate those symptoms, whether by suppressing AF or taming it in a way so it's less symptomatic.

*Once your doctor has diagnosed AF, you need to have an informed dialogue about the next steps. Not every case of AF needs to be treated. We are often asked a variety of questions by patients and doctors alike about AF treatment, who needs it, and how successful the therapy is. To follow are our answers to the most frequently asked questions that we receive about AF treatment possibilities.*

**Q.** Is the AF experienced by an otherwise healthy person different from that of a person with underlying heart disease or other health issues?

**A.** There are people with diseased hearts who develop AF. Compared to the person with AF and a structurally sound heart, AF in a diseased heart may have different implications.

The AF may not be originating from areas of the heart where we typically expect to find the sources of the errant electrical signals in a person with a healthy heart. In addition, these people may be the ones particularly prone to forming blood clots and having strokes. That may be the reason why the combination of AF and structural heart disease is a well-recognized set of risk factors for stroke—and why those people usually need to be on oral anticoagulant therapy to “thin” their blood and prevent stroke.

**Q. Is every person who has AF at risk for a stroke?**

**A.** No, not at all. When we think about AF, we see an enormous spectrum of symptoms, from benign to disabling. We want to separate out symptoms from threat to health. A threat to health from AF would be stroke. *One important fact to realize is that not everyone with AF has increased risk of stroke.* However, along with AF, there are certain co-factors that have been shown to be associated with an increased risk of stroke, including the following:

- Age over 65
- Hypertension
- Diabetes
- Congestive heart failure
- Prior stroke or TIA (Transient Ischemia Attack)
- Vascular disease
- Being female

In addition, some patients with valvular disease, especially rheumatic heart disease, are at increased risk of stroke.

**Q. What would you recommend to the older patient—75 and older—who has AF but no symptoms that are bothersome?**

**A.** These patients are typically prescribed anticoagulant therapy and probably nothing else.

**Q. What would you typically recommend to a patient with paroxysmal AF who is younger than 75?**

**A.** We will present them with the following options:

- **Do nothing at all.** Depending on how symptomatic they are, however, this may not be a viable course of action. Some patients may want to pursue some sort of therapy.
- **Take daily medicine to prevent or terminate AF episodes.** There are antiarrhythmic medications taken daily that work well for many patients.
- **Follow the “pill-in-the-pocket” approach.** A popular strategy that many doctors have

used for years for patients with infrequent AF to convert the heart back to normal sinus rhythm is what is known as the “pill-in-the-pocket approach.”

Patients will carry an antiarrhythmic drug such as flecainide or propafenone with them. These drugs are often effective at terminating an episode of AF of very recent onset (less than an hour), have few side effects, and are inexpensive.

Whenever a person goes into AF, they simply take a pill from their pocket and swallow it. Within an hour or so, the AF episode is over. If AF is not gone within eight hours, they are usually instructed to take another pill.

Compare this approach to the 6 to 12 hours it might take to terminate the episode without the medication. If patients get AF once or twice a month, this is a nice strategy to offer. For patients prone to AF episodes once or more a week, they will take medication daily as a prophylactic measure.

**Q. What do you recommend for the patient who has more frequent episodes of AF?**

**A.** If the patient is prone to AF a couple of times a week, every week, we would recommend prophylactic drug therapy. Flecainide, propafenone, or dronedarone twice a day may work nicely, as long as the patient has not had a previous heart attack and does not have structural heart disease. If the patient has an occasional AF episode while on this therapy, an additional pill is taken.

**Q. What if antiarrhythmic medication fails to suppress the episodes?**

**A.** If the patient continues to have frequent symptomatic episodes of AF despite initial antiarrhythmic drug therapy, then we discuss second-line therapy with either the antiarrhythmic drug amiodarone or catheter ablation of AF with pulmonary vein antrum isolation. As we explain on page 50, this involves advancing a catheter from the vein in the groin up to the heart and into the left atrium, and ablating (cauterizing) tissue where the pulmonary veins join the left atrium, where the cells responsible for initiating AF are usually located.

**Q. What do you recommend for the person with longstanding persistent AF?**

**A.** In longstanding persistent AF, it is more difficult to restore and maintain sinus rhythm. The atria have changed over time and normal rhythm probably is more difficult to restore. Many of these patients are older and should be on anticoagulant therapy. If the patient is bothered by the AF symptoms, we can control the heart rate with medication or we can attempt to restore and maintain sinus rhythm with medications or catheter ablation. Another option is to ablate the atrioventricular (AV) node, which is the electrical connection between the atria and ventricles. A pacemaker would then be implanted to control the heart rate.

**Q.** A recent study examined a convergent procedure that combines surgical ablation and catheter ablation for treating patients with longstanding persistent AF. Is this likely to become a viable option for such patients?

**A.** The procedure involves both cardiac surgeons and electrophysiologists working together. Some centers perform this as one very lengthy procedure, whereas others perform it in stages. The patient has a surgical AF ablation procedure and then, a month later, a catheter ablation procedure is performed to optimize the outcome. The initial results of this procedure are encouraging. But they are very preliminary, and more research is needed in order to be able to better define the risks and benefits of this combined approach.



## ARRHYTHMIA GLOSSARY

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Here you will find the key terms most often used by electrophysiologists and cardiologists in describing fibrillation disorders.

**Accessory pathway.** An abnormal muscular connection between the upper and lower chambers of the heart. Patients with accessory pathways may develop supraventricular tachycardias. Some patients with accessory pathways also have Wolff-Parkinson-White syndrome.

**Arrhythmia.** An irregular heart rhythm, or an abnormality in the timing or pattern of the heartbeat, which causes the heart to beat too rapidly, too slowly, or irregularly.

**Arrhythmogenic right ventricular dysplasia (ARVD).** A familial disorder that may cause ventricular arrhythmias.

**Atrial fibrillation, rapid.** Uncoordinated firing of electrical impulses from multiple sites in the upper chambers, which causes ineffective contractions. A type of supraventricular tachycardia.

**Atrial flutter.** A single “short circuit” in the atria that causes the atria to beat at about 300 beats per minute while the lower chambers of the heart (the ventricles) beat at a slower rate (often 75-150 beats per minute). A type of supraventricular tachycardia.

**Atrial tachycardia.** A sustained, irregular heart rhythm that occurs in the upper chamber of the heart and causes it to beat too rapidly.

**Atrium, (plural: atria).** The two upper chambers of the heart, which receive blood after it has circulated through the body.

**AV nodal re-entrant tachycardia (AVNRT).** An abrupt, rapid heartbeat that occurs when electrical impulses mistakenly enter an extra pathway in or near the AV node. A type of paroxysmal supraventricular tachycardia.

**AV node.** The normal electrical connection between the atria and the ventricles where electrical impulses are delayed for a fraction of a second to allow the lower chambers to fill completely with blood.

**Bradycardia.** A slow heart rate (less than 60 beats per minute).

**Cardioversion.** A procedure used to shock the heart back into rhythm. Most often used with patients who have either atrial fibrillation or atrial flutter.

**Catheter ablation.** A procedure used to destroy (ablate) areas of the heart that are causing arrhythmias. In a radiofrequency (RF) ablation, electrophysiologists pinpoint the area and then use radio wave energy to “cauterize” the tiny part of the heart muscle causing the heart rhythm abnormality.

**Echocardiogram.** A non-invasive test in which sound waves are used to produce an image of the heart.

**Electrocardiogram (ECG).** A simple test that traces the electrical activity of the heart. Also known as an EKG.

**Electrophysiology.** The study of electrical activity in the heart.

**Electrophysiologist.** A cardiologist (heart doctor) who specializes in the electrical system of the heart.

**Electrophysiology study.** A test that allows the electrophysiologist to examine the electrical activity inside the heart and evaluate any abnormalities.

**Event monitor.** A wearable monitor that records the heart rhythm only when activated. It is typically used for one month, during which the patient is instructed to trigger the device if symptoms occur.

**Exercise stress test.** A test that determines irregular heart rhythms while a person is exercising on a stationary bike or treadmill. Also known as a treadmill test.

**Heart block.** A complete or partial interruption of the electrical impulses on their way to the ventricles that results in a slow, unreliable heartbeat. A type of bradycardia.

**Holter monitor.** A wearable monitor used to obtain a continuous ECG recording, usually for 24-48 hours. The recording is useful for detecting abnormalities that may not occur during a resting ECG.

**Implantable cardiac defibrillator (ICD).** Device commonly used to treat patients who have experienced a potentially dangerous ventricular arrhythmia. These devices continuously monitor the heartbeat and automatically deliver a small electrical shock to the heart if a sustained rapid heart rhythm occurs.



**Pacemaker.** A device used primarily to correct some types of bradycardia, or slow heart rhythms. The pacemaker is implanted in the body, usually below the collarbone, where it monitors the heart rhythm and supplies electrical triggers if the heart is beating too slowly.

**Paroxysmal supraventricular tachycardia (PSVT).** A “short circuit” arrhythmia that causes the heart to beat too rapidly. PSVT may be misdiagnosed as a panic attack.

**Pulmonary vein antrum isolation (PVAI).** An electrophysiological medical procedure in which electrical signals from the pulmonary veins are permanently blocked off, preventing them from affecting the heart’s rhythm.

**Rate control.** AF treatment in which drugs (beta blockers, calcium-channel blockers, and digoxin) are used to buffer electrical activity that passes through the atrioventricular node. The drugs keep the ventricles contracting at a rate of 70 bpm even when the atria are contracting much faster.

**Rhythm control.** AF treatment in which drugs (amiodarone, disopyramide, dofetilide, flecainide, procainamide, propafenone, or sotalol) are taken to restore normal heart rhythm by affecting the heart’s electrical activity. This may also be done with a jolt of electricity applied directly to the chest to shock the heart back into rhythm.

**Sick sinus syndrome.** A disorder in which the sinus node (the heart’s own pacemaker) fails and does not trigger enough heartbeats. A type of bradycardia.

**Signal-averaged electrocardiogram (SAECG).** A type of ECG recording that can determine if scarred tissue, which may predispose one to a heart arrhythmia, is present in the heart.

**Sinus node.** A group of specialized cells in the right atrium that is the place where the electrical impulse in the heart normally begins. It functions as the heart’s pacemaker.

**Supraventricular tachycardia.** A series of rapid heartbeats arising from the upper chambers of the heart that can cause the heart to beat very rapidly or erratically and may lead to inadequate blood supply to the body.

**Tilt table test.** Test used to diagnose an abnormality of blood pressure regulation, which may cause lightheadedness or a fainting spell.

**Ventricles.** The two major pumping chambers of the heart.

**Ventricular tachycardia.** A series of rapid heartbeats that originate in the lower chambers of the heart (the ventricles), which may cause the heart to beat inefficiently.

**Wolff-Parkinson-White Syndrome.** A specific type of heart rhythm abnormality. Patients with WPW syndrome have an accessory pathway connecting the upper and lower chamber of the heart. These patients may develop a rapid heartbeat caused by a “short circuit” heart arrhythmia. WPW syndrome also may cause dangerous heart arrhythmias.



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## Heart Attack Prevention White Paper

Heart attack remains the leading cause of death in America, but Johns Hopkins specialists have identified a number of steps that can dramatically lower your risk. The *Heart Attack Prevention White Paper* contains potentially lifesaving strategies for the millions of people with high cholesterol, hypertension (high blood pressure), weight control issues, a sedentary lifestyle, and other known risk factors for heart attack.

## The Johns Hopkins Memory Disorders Bulletin

Edited by Dr. Peter V. Rabins, Professor of Psychiatry at the Johns Hopkins University School of Medicine and co-author of *The 36-Hour Day*, the best-selling guide for caregivers. The *Johns Hopkins Memory Disorders Bulletin* brings timely information for anyone facing Alzheimer's disease, dementia, or another memory problem. In each quarterly issue,

you'll read about the latest scientific breakthroughs and research findings from the foremost medical journals and conferences—on diagnosis, medications, caregiver support and relief, how to safeguard your brain against memory loss, and many other issues. Subscribe today at the special web-only discount and get 4 FREE special reports.

## Coronary Heart Disease White Paper

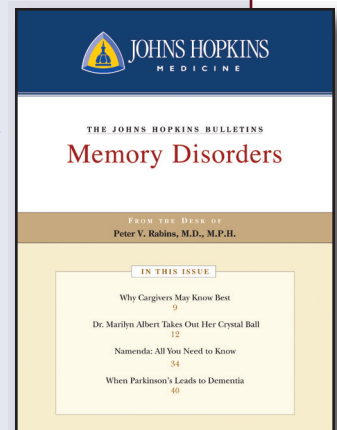
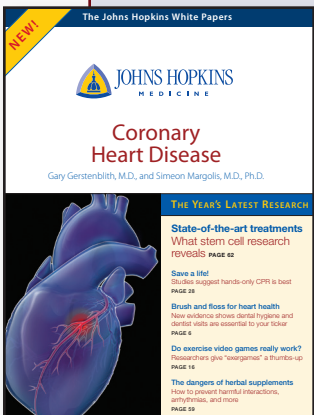
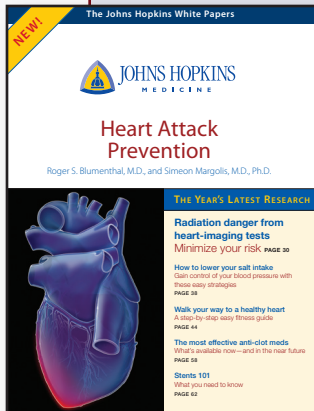
Johns Hopkins experts present the latest advances for your heart health in this report aimed at helping you prevent or treat coronary heart disease (CHD). Topics include angina and other symptoms of CHD; diagnostic testing; lifestyle measures and medications used in prevention and treatment; angioplasty, bypass surgery, and other revascularization procedures; diagnosis and treatment of cardiac arrhythmias, congestive heart failure, and other complications of CHD.

## The Johns Hopkins Medical Letter: Health After 50

Since 1989 this acclaimed monthly newsletter has delivered cutting-edge information on treating the major medical conditions affecting those over 50. Each eight-page issue delivers important news and research on women's health, men's health, nutrition, weight control, arthritis, COPD, colon cancer, dementia and much more. Friendly, easy-to-read, and written in plain English (without any advertising), *Health After 50* speaks directly to your personal health concerns.

For more information, or to order, go to:

[www.JohnsHopkinsHealthAlerts.com/bookstore/index.html](http://www.JohnsHopkinsHealthAlerts.com/bookstore/index.html)





The information contained in **Atrial Fibrillation: The Latest Management Strategies** is not intended as a substitute for the advice of a physician. Readers who suspect they may have specific medical problems should consult a physician about any suggestions made.

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