



Treatment of Blood Clots

Samuel Z. Goldhaber, MD; Nicole Grasso-Correnti, RN, BSN



This Cardiology Patient Page will focus on medical treatment of blood clots that can cause critical illness by blocking the blood supply to the heart, brain, lungs, or legs. Blood clots that develop in the arteries can cause heart attack, stroke, and severe leg pain and difficulty walking. Blood clots in the veins or venous system can cause deep venous thrombosis (DVT) in the pelvic, leg, and upper extremity veins. When these DVTs break off and travel through the bloodstream to the heart and then to the lung blood vessels, they cause acute pulmonary embolism (PE).¹

What Medications Will Be Used to Treat My Arterial Blood Clots?

Treatment of arterial clots may include aspirin and clopidogrel (oral antiplatelet agents), intravenous antiplatelet agents, heparin (a blood thinner and anticoagulant), and clot busters (thrombolytic agents). In addition to medications, special interventional catheters may be used to remove or compress these arterial clots.

Antiplatelet Agents

Chewing an adult-strength aspirin tablet (325 mg) at the onset of heart

attack symptoms can improve survival by 20%.² Consequently, health-care professional personnel administer aspirin to patients who may be experiencing a heart attack, thereby avoiding further injury to the heart muscle before the arrival of emergency medical services.³ The Clopidogrel in Unstable angina to prevent REcurrent events (CURE) Trial showed that clopidogrel, another oral antiplatelet agent, given in conjunction with aspirin, reduces the risk of death even further in the setting of certain types of heart attacks.⁴ Intravenous antiplatelet agents may also be used to treat impending or evolving heart attacks in combination with aspirin and clopidogrel. This triple antiplatelet therapy is highly potent and predisposes the patient to bruising. However, major bleeding complications, such as stomach ulcer bleeding, are rare.

Anticoagulants

Intravenous (IV) heparin, administered continuously, is the traditional anticoagulant prescribed to prevent growth of a blood clot. Achieving the most effective dose requires frequent blood test measurements with a laboratory clotting test that records the activated partial thromboplastin time

(aPTT). To treat heart attack patients, the heparin dose is adjusted to a target aPTT in the range of 50 to 70 seconds.

Low molecular weight heparin (LMWH) constitutes an important advance over traditional heparin. LMWH, administered once or twice daily by injection based on the patient's weight, ordinarily requires no dose adjustment and little or no blood test monitoring. The two Food and Drug Administration (FDA)-approved agents for treatment of certain types of established or impending heart attack are enoxaparin and dalteparin. Like traditional heparin, they may cause unintended bleeding as a side effect.

Thrombolytic Agents

These clot busters can dissolve arterial clots but cause more serious bleeding problems than antiplatelet agents or anticoagulants. The thrombolytics cannot differentiate a bad clot that is causing a heart attack from a good clot that has sealed over a stomach ulcer or weak brain artery. Consequently, the approximate 20% improvement in heart attack survival is complicated by a brain hemorrhage rate of about 1%.

From the Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Mass.
Correspondence to Samuel Z. Goldhaber, MD, Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115. E-mail sgoldhaber@partners.org
(*Circulation*. 2002;106:e138-e140.)
© 2002 American Heart Association, Inc.

TIPS ON SELF-INJECTION OF LOW MOLECULAR WEIGHT HEPARIN

- Select a site where you can “pinch an inch” of fat, usually the abdomen, thigh, or hip. Stay at least 3 fingerbreadths away from the belly button.
- Cleanse the injection site gently with an alcohol swab prior to injection, but do not rub or swab the site after injection.
- Inject with a rapid, purposeful movement. If using a prefilled syringe of enoxaparin, do not expel the air bubble prior to injection.
- Dispose of the needle and syringe in a box especially designed for this purpose (a sharps box). Bring the filled sharps box to your health care provider for proper disposal, or follow carefully your town or city’s regulations for proper disposal.

What Medications Will Be Used to Treat My Venous Blood Clots?

Anticoagulants prevent formation of additional clots and permit the body’s natural clot-dissolving activity to nibble away at the DVT or PE that has already formed. Venous blood clot treatment requires heparin for its rapid action as a blood thinner in conjunction with the oral blood thinner warfarin. Warfarin, administered once daily, usually requires at least 5 days to become fully effective.

Patients with a massive DVT or PE may receive thrombolytic agents in addition to heparin and warfarin. For the 5% or so of patients unable to

tolerate blood thinners or in whom blood thinners fail, a permanent metal filter may be inserted into the inferior vena cava, the largest vein below the heart. The filter prevents large blood clots from reaching the lungs after breaking off from the pelvic or deep leg veins. However, the filter does not halt the blood clotting process.⁵

LMWH

LMWHs have transformed acute uncomplicated DVT from a disease requiring at least a 5-day hospitalization to an illness that can usually be managed either on an outpatient basis or with an overnight hospital stay. The only FDA regimen specifically approved for outpatient treatment of DVT is the LMWH agent enoxaparin administered as 1 mg per kilogram of body weight twice daily. The dose is reduced in the presence of kidney disease or marked obesity. The blood-thinning action of LMWH is fully effective within several hours of administration, and patients or family members learn how to inject it.

IV Heparin

Standard treatment of acute PE requires a continuous IV infusion of heparin, used in a higher intensity than for arterial blood clots, with the dose adjusted to a target aPTT of 60 to 80 seconds. IV heparin is administered throughout the hospitalization, which typically averages 5 to 7 days, until the oral blood thinner, warfarin, has become fully effective. There is an evolving trend toward using LMWH rather than IV heparin, especially after the first day or two of hospitalization, once clinical improvement has become apparent. Some low-risk patients with PE are being discharged after several days of using LMWH as a bridge to warfarin.⁶

Warfarin

Warfarin (also referred to by its brand name, Coumadin) functions as an oral anticoagulant by disrupting the body’s natural vitamin K-clotting system. Warfarin is the foundation for long-term treatment of DVT and PE and is

essential for the prevention of stroke from atrial fibrillation⁷ and for prevention of clotting in mechanical heart valves.

Warfarin poses a greater challenge in safe and effective administration, requires more patient-healthcare provider collaboration, and generates more questions than any other drug that we prescribe. Patients walk a tightrope: too little warfarin can lead to catastrophic clotting; too much warfarin can cause life-threatening major bleeding. Warfarin, like IV heparin but unlike most other drugs, cannot be prescribed in a fixed or weight-adjusted dose. Instead, the dose must be adjusted according to a laboratory blood test that measures the length of time it takes for clotting to begin, or prothrombin time (PT). The test is standardized to account for different laboratory processes and is called the International Normalized Ratio (INR). The INR of a healthy individual not taking warfarin is 1.0. The INR increases with increasing intensity of anticoagulation. For patients with DVT or PE, the usual target INR is 2.0 to 3.0. For the occasional patient requiring even more intensive anticoagulation, the target INR may be raised to levels as high as 4.0.

When warfarin is used, there are multiple drug-drug and drug-food interactions that affect the INR. Regular monitoring of the INR is therefore essential to provide optimal dosing. The INR is usually obtained several times weekly at the initiation of treatment with warfarin. Once a stable INR and warfarin dose are achieved, the INR frequency is gradually decreased to once monthly. More frequent monitoring is essential when other medications are started or discontinued, including over-the-counter medications, vitamins, and nontraditional natural herbs, minerals, or plants. For example, the commonly prescribed antiarrhythmic drug amiodarone and many antibiotics markedly increase the anticoagulant effect of warfarin, causing an excessive rise in the INR. Sudden binges or abstinence from vitamin

Frequently Asked Questions About Warfarin

Question	Answer
1. What time of day should I take warfarin?	1. We recommend 8:00 PM. Your blood will be drawn for testing in the morning, thus allowing your health care provider to obtain laboratory results and to inform you in the afternoon or early evening whether the dose should be changed.
2. What medicine can I take safely to treat minor aches or pains, including headache?	2. We recommend acetaminophen in as low a dose as possible to control pain adequately. Let your health care provider know you are taking acetaminophen, because high and prolonged doses increase the anticoagulant effect of warfarin and raise the INR.
3. May I drink alcohol while taking warfarin?	3. We recommend no more than one glass of wine, one beer, or one shot of whiskey daily.
4. May I eat green leafy vegetables while taking warfarin?	4. Yes. The guiding principle is to refrain from making sudden changes in your intake of these vitamin-K-containing foods.
5. What should I do if a doctor other than the one who regulates my warfarin prescribes a new medication or discontinues a medication that I was previously taking?	5. Within one business day, inform the nurse, pharmacist, or physician who regulates your warfarin about the medication change.
6. What happens if I have to discontinue warfarin temporarily for an operation or diagnostic procedure?	6. Inform the provider who regulates your warfarin. You may receive instructions to self-inject LMWH temporarily while warfarin is temporarily discontinued. This process is known as bridging.
7. If I am knocked unconscious and rushed to the hospital, how will emergency personnel know that I take warfarin?	7. Order and wear a medical alert bracelet.
8. How long will I have to take warfarin?	8. Lifelong if you have a mechanical heart valve, indefinitely if you have atrial fibrillation. For DVT and PE, the optimal duration is controversial, but probably for at least 6 months.

K-containing foods such as spinach, broccoli, and brussel sprouts will affect the INR. The combination of alcohol and warfarin will increase the likelihood of bleeding, even in situations when the INR does not rise markedly. Sometimes, important fluctuations can occur in the INR without an identifiable reason.

What Are the Alternatives to Warfarin?

Alternative strategies are very limited. For now, they include self-injected LMWH once or twice daily and self-injected traditional heparin twice or three times daily. In the future, other agents will become available and pro-

vide immediate anticoagulation with much less frequent blood test monitoring.

References

1. Goldhaber SZ, Morrison RM. Pulmonary embolism and deep vein thrombosis. *Circulation*. 2002;106:1436–1438.
2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet*. 1988;2:349–360.
3. Ornato JP, Hand MM. Warning signs of a heart attack. *Circulation*. 2001;104:1212–1213.
4. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med*. 2001; 345:494–502.
5. Gelfand EV, Piazza G, Goldhaber SZ. Venous thromboembolism guidebook. *Critical Pathways in Cardiology*. 2002;1: 26–43.
6. Well PS, Büller HR. Outpatient treatment of patients with pulmonary embolism. *Seminars in Vascular Medicine* 2001;1: 229–233.
7. Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation) Developed in Collaboration With the North American Society of Pacing and Electrophysiology. *Circulation*. 2001;104:2118–2150.