1. The most recent ACC/AHA/HRS guidelines recommend which scoring system(s) to determine whether a patient would benefit from anticoagulation/antiplatelet therapy?

A. CHADS\textsuperscript{2}  
B. CHA\textsubscript{2}DS\textsubscript{2}VASc  
C. CHADS\textsuperscript{2} and CHA\textsubscript{2}DS\textsubscript{2}VASc  
D. HAS-BLED  

For many years, the CHADS\textsuperscript{2} scoring system was used to determine whether a patient would benefit from anticoagulation/antiplatelet therapy. More recently, it was found that the CHADS\textsuperscript{2} scoring system missed a number of patients who were at risk for stroke. The newer CHA\textsubscript{2}DS\textsubscript{2}VASc scoring system incorporates additional parameters. The CHA\textsubscript{2}DS\textsubscript{2}VASc scoring system is recommended in place of CHADS\textsuperscript{2} in the most recent American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) guidelines for the treatment of patients with AF. [Fuster V 2006]

2. Warfarin is an agent of which drug class?

A. Vitamin K antagonist  
B. Direct thrombin inhibitor  
C. Factor Xa inhibitor  
D. Antiplatelet  

Pharmacologic treatment options for the prevention include antiplatelet agents— aspirin with or without concomitant clopidogrel—and anticoagulant agents—the vitamin K antagonist warfarin, direct thrombin inhibitors, and factor Xa inhibitors. [Odum LE 2012]

3. The ACTIVE-W trial compared ________________.

A. Apixaban with warfarin  
B. Apixaban with rivaroxaban  
C. Aspirin and clopidogrel with warfarin  
D. Aspirin and clopidogrel with apixaban  

The ACTIVE-W trial compared aspirin plus clopidogrel with warfarin. It showed a 40% risk reduction in stroke with warfarin with no significant difference in bleeding. [Connelly SJ 2009]

4. When treating patients with warfarin, it is important to know that_____________________.

A. When the INR rises to 3.6, the risk of a thrombotic event increases.  
B. When the INR rises to 3.6, the risk of intracranial hemorrhage increases.  
C. When the INR falls to 2.0, the risk of a thrombotic event increases.  
D. When the INR falls to 2.0, the risk of an intracranial hemorrhage increases.  

When the INR rises above 3.5, the risk of intracranial hemorrhage increases 3-fold. Conversely, an INR below 1.8 increases the risk of a thrombotic event. [Singer DE 2009]
5. The most recent ACC/AHA/HRS guidelines recommend which anticoagulant(s) as an alternative to warfarin in some patients?

A. Rivaroxaban  
B. Apixaban  
C. Dabigatran  
D. All  

The most recent ACC/AHA/HRS guidelines include recommendations for the use of non-warfarin (novel oral anticoagulant [NOAC]) anticoagulant therapy depending on the patient’s CHA$_2$DS$_2$VASc score. The inclusion of all NOAC therapies is a notable change to the guidelines. [January CT 2014]

6. In the Miller 2012 meta-analysis of pooled outcomes data from the RE-LY, ROCKET AF, and ARISTOTLE trials, ________________.  

A. NOACs were found to be either noninferior or superior compared with warfarin for the prevention of stroke and systemic embolism.  
B. NOACs were found to be superior compared with warfarin for the prevention of stroke and systemic embolism.  
C. Rivaroxaban was found to be either noninferior or superior compared with dabigatran for the prevention of stroke and systemic embolism.  
D. Dabigatran was found to be either noninferior or superior compared with apixaban for the prevention of stroke and systemic embolism.  

In a meta-analysis of pooled outcomes data from the RE-LY, ROCKET AF, and ARISTOTLE trials, NOACs were more efficacious compared with warfarin for the prevention of stroke and systemic embolism, with a decrease in instances of ischemic and unidentified stroke. Specifically, dabigatran 150 mg twice daily and apixaban 5 mg twice daily were superior to warfarin; dabigatran 110 mg twice daily (not an approved dose) and rivaroxaban 20 mg once daily were noninferior to warfarin. [Miller CS 2012]

7. Which anticoagulant has the lowest risk for GI bleeding specifically?  

A. Apixaban  
B. Rivaroxaban  
C. Dabigatran  
D. Warfarin  

In a meta-analysis of NOAC randomized trials, there was a 19% relative risk reduction for stroke and systemic embolism compared with warfarin, with a 14% relative risk reduction in major bleeding ($P = 0.06$, NS). Importantly, however, all NOACs showed a higher risk of GI bleeding compared with warfarin. [Riff CT 2014]
8. The AVERROES trial found _________________.

A. A 50% relative risk reduction in stroke and systemic embolism for apixaban compared with warfarin.
B. A 50% relative risk reduction in stroke and systemic embolism for apixaban compared with aspirin.
C. A relative risk reduction in stroke and systemic embolism for apixaban compared with warfarin.
D. A 25% relative risk reduction in stroke and systemic embolism for apixaban compared with aspirin.

Apixaban is the only NOAC that was compared with aspirin for reducing risk of stroke and systemic embolism. The AVERROES trial found a 50% relative risk reduction in stroke and systemic embolism compared with aspirin. The trial was stopped early because of efficacy. [Connolly SJ 2011]

9. Please indicate which statement is INCORRECT with regard to NOACs:

A. NOACs are dosed 3 times daily.
B. NOACs do not require routine INR testing.
C. NOACs have predictable pharmacokinetic profiles.
D. NOACs have rapid onset of action.

NOACs offer the benefits of no routine INR testing and fixed dosing. Rivaroxaban is dosed once daily, and apixaban and dabigatran are dosed twice daily; this may be a consideration with some patients. Also, NOACs have predictable pharmacokinetic profiles, with rapid onset and termination of action.

10. Patients with AF who may be eligible for treatment with NOACs include:

A. Patients with a history of unstable INRs
B. Patients with severe renal impairment
C. Both
D. Neither

Dialysis patients and those with severe renal impairment (CrCl <15 mL/min) should not be prescribed NOACs.

11. Anticoagulation antidotes are currently in development for which NOAC(s)?

A. Apixaban
B. Dabigatran
C. Rivaroxaban
D. All of the above

Specific NOAC antidotes are in phase 3 clinical trials. Idarucizumab, a fully humanized antibody fragment, is being studied as a specific antidote to dabigatran. Andexanet α, a recombinant, modified factor Xa molecule, may be effective as an antidote for rivaroxaban. Aripazine (PER977) is a synthetic small molecule with broad reversal activity against factor Xa inhibitors.
12. According to the Romero-Ortuno decision analysis tool for weighing the risk of bleeding versus the risk of stroke in patients with AF, _________________ therapy is favored in patients at a high risk of both stroke and bleeding.

A. Aspirin  
B. Warfarin  
C. NOAC  
D. Aspirin + warfarin  

A decision analysis tool has been developed to help determine whether anticoagulant therapy is warranted by balancing the patient’s risk of bleeding versus the risk for stroke. Using this decision analysis, a patient with a low CHA₂DS₂VASc score and a high HAS-BLED score may not be a good candidate for anticoagulant therapy, because the risk of bleeding outweighs the risk of stroke. However, a high CHA₂DS₂VASc score and a low HAS-BLED score would favor anticoagulation therapy. Patients with both a high risk of stroke and bleeding are challenging with regard to anticoagulation strategies. The decision analysis favors aspirin therapy in this patient group. [Romero-Ortuno]

13. Approximately _____ of patients who are eligible for warfarin therapy receive treatment.

A. 10%  
B. 25%  
C. 40%  
D. 50%  

In a cross-sectional study within a large health maintenance organization, of 11082 patients with nonvalvular atrial fibrillation and no known contraindications, 55% received warfarin. [Go AS 1999]

14. Rivaroxaban and apixaban are both _________________.

A. Direct thrombin inhibitors  
B. Antiplatelets  
C. Factor Xa inhibitors  
D. Vitamin K antagonists  

The vitamin K antagonist warfarin acts at factors II, VII, IX, and X. Rivaroxaban and apixaban are factor Xa inhibitors. Dabigatran affects factor II and is a direct thrombin inhibitor.

15. Which medication is 80% renally excreted?

A. Dabigatran  
B. Rivaroxaban  
C. Apixaban  
D. Warfarin  

Renal excretion is an important factor for some patients—dabigatran is the most highly renally excreted of the 3 medications (80%), compared with rivaroxaban (36%) and apixaban (25%).
16. Please select the TRUE statement below:

A. Of the NOACs, only dabigatran and rivaroxaban have been compared in head-to-head studies.
B. Of the NOACs, only dabigatran and apixaban have been compared in head-to-head studies.
C. All 3 NOACs were compared in a head-to-head study.
D. None of the NOACs have been compared in a head-to-head study.

There are no head-to-head studies that compare NOACs to each other.

17. Which treatment option is NOT effective in emergency anticoagulant reversal when using rivaroxaban?

A. aPCC
B. Dialysis
C. PCC
D. Packed red blood cells

Goals for the patient taking NOACs who experiences bleeding complications or requires emergency surgery are to establish clinical stability and hemostasis. The anticoagulant should be stopped, as well as other medications that can increase the risk of bleeding, such as antiplatelets. Patients having symptoms of hypotension or syncope should be transfused with fluids or packed red blood cells. Next steps for emergency anticoagulation depend on the type of NOAC the patient was taking. With dabigatran, because it has a low protein-binding percentage, it could potentially be dialyzed off if the patient is continually having bleeding after transfusion. Activated charcoal can be administered if the last dose was within 2 hours. Prolonged hemodialysis may be needed. Activated prothrombin complex concentrates (aPCCs) may then be used as reversal agents. Because rivaroxaban and apixaban have high percentages of protein binding, we would expect that hemodialysis would not be effective. Prothrombin complex concentrates (PCCs) or aPCCs may be used as reversal agents.

18. In the ACC/AHA/ARS guidelines, for the reduction of stroke risk in patients with AF, warfarin was given a 1A recommendation; NOACs were given a 1B recommendation because

A. NOACs have been shown to be less effective than warfarin at preventing stroke in patients with AF.
B. NOACs have less clinical data available.
C. NOACs are not indicated for the prevention of stroke in patients with AF.
D. NOACs are indicated for use for only a short period of time.

The NOAC therapies dabigatran, rivaroxaban, and apixaban are given a IB level of recommendation based on a lesser amount of available data.
19. NOACs are contraindicated in patients with _________________.

A. Prosthetic heart valves  
B. End-stage renal disease  
C. Both  
D. Neither

Patients with prosthetic heart valves, mitral valve repair, or mitral stenosis should not use a NOAC, nor should patients with end-stage renal disease; they should be prescribed warfarin if anticoagulant therapy is indicated.

20. Patients with AF who are on dialysis may be a candidate for ________________ treatment.

A. Rivaroxaban  
B. Apixaban  
C. Dabigatran  
D. All of the above

Rivaroxaban is not recommended in patients with a creatinine clearance (CrCl) <15 mL/min or on dialysis. Apixaban can be given at the usual dosage for patients with end-stand renal disease if they are on dialysis, but reduced dosing is recommended if they are ≥80 years old or if body weight is ≤60 kg. Dabigatran is not recommended in patients with CrCl <15 mL/min or on dialysis and should be avoided in patients with CrCl 15-30 mL/min taking concomitant P-gp inhibitors. [package inserts]