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Emergency physicians deal with anticoagulation on a daily basis. We have all dealt with the bleeding patient on anticoagulants. What is relatively new for us is the initiation of anticoagulants. Once reserved for pulmonary embolism, anticoagulation now is initiated for a variety of disorders and likely will be used with greater frequency. Not only must the emergency physician decide when to initiate therapy, but now the choices of anticoagulant therapy are more numerous and complex.

The issues covered in this article and in Part II of this series are important. For those facing the Lifelong Learning and Self-Assessment for the American Board of Emergency Medicine, this article relates to the 2005 reading on stroke, the 2006 article on deep venous thrombosis, and the 2007 article on acute coronary syndrome.

—Sandra M. Schneider, MD, FACEP, Editor

Anticoagulation and Thrombolytic Therapy in the Emergency Department: Part I

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The Scope of the Problem

The number of patient visits to emergency departments (EDs) in the United States rose from 90 million in 1993 to 114 million in 2003. This increase in demand occurred while the number of EDs decreased from more than 6000 to about 4000 during the time period. Increased demand for ED access is in part due to the growth in the U.S. population, and in part due to growth in the population older than 45 years,

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a group with more acute medical and surgical problems than those 45 years and younger. In addition, as the population ages, and more elderly citizens survive conditions such as cancer, cardiovascular diseases, renal failure, and sepsis, the number of patients who have survived complicated medical illnesses has increased. A shortage of intensive care beds in many parts of the United States means that this population must be stabilized, diagnosed, and treated in the ED for several hours or days before being assigned an inpatient bed.

Randomized controlled clinical trials have demonstrated that rapid restoration of blood flow to a major vascular bed in the aftermath of an acute occlusion can dramatically reduce the morbidity and mortality associated with these events.[1] Since such patients are directed to EDs for their initial assessment and care, the initiation of anticoagulant or thrombolytic therapy for conditions such as venous thrombosis (VTE), acute coronary syndrome (ACS), and cerebrovascular accident and transient ischemic attack (CVA/TIA) now often occurs in the ED. In addition, when patients who are being treated with anticoagulants present to the ED with complications of anticoagulant therapy, or another condition that is associated with bleeding, they are more difficult to manage. Emergency medicine providers must therefore be prepared to initiate anticoagulation and treat the associated complications.

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Current treatment for acute vascular occlusion may involve pharmacotherapy, percutaneous intervention, surgery, or a combination of these approaches. Advances in our understanding of the conditions and events leading to acute occlusion permit the development of treatment strategies aimed at re-establishing flow and diminishing the likelihood of subsequent occlusive events. Research has demonstrated that the degree of benefit to the patient from revascularization is correlated with the time taken to re-establish flow in the affected vessel.[2] The methods available to re-establish circulation are associated with serious complications such as bleeding, immune reactions, and vascular rupture. Therefore, before initiating anticoagulant or thrombolytic treatment, clinicians must complete a risk/benefit analysis based on what is known about the patient's past medical history, presenting symptoms, and physical findings. The potential benefit from the treatment must exceed the risks associated with the particular treatment being considered. Since a combination of pharmacotherapy and invasive procedure may be used, the physician initiating treatment must be prepared to monitor the patient's progress and intervene when complications develop.

Patient outcomes improve when predetermined protocols for diagnosis and treatment of suspected ACS patients are followed.[3] Clinical pathways represent the collective wisdom of all health care providers involved in the management of a specific clinical condition within a medical system. Pathways provide a means to achieve the best outcome for a patient in a given clinical setting while helping to minimize the occurrence of errors in the delivery of care. The use of clinical pathways for ACS, VTE, and CVA/TIA can facilitate the use of anticoagulants and thrombolytic agents in the ED.

Epidemiology/Pathophysiology

Venous Thromboembolism. VTE is defined by two types of clinical presentations that share a common pathophysiology and involve partial or complete occlusion within the venous circulation. These clinical presentations are deep venous thrombosis (DVT) and pulmonary embolism (PE). Approximately 2 million cases of VTE are detected each year in the United States with approximately 600,000 having evidence of PE.[4] In patients with VTE, death occurs within 1 month in 6% of the patients found to have DVT, and 12% of patients with PE. The lifetime cumulative incidence of DVT is somewhere between 2-5% for the U.S. population. Once DVT has been diagnosed, the patient has a 17% likelihood of a recurrence within two years of their initial diagnosis and treatment.[5] Patients treated in an intensive care unit and the elderly are more likely to experience VTE.

Pathophysiologic changes that increase a patient's risk for VTE include: endothelial injury, stasis, and hypercoagulable states. Patients who are acutely immobile or will be immobile (such as patients who are acutely ill or injured) are at high risk in the initial weeks of immobilization. With time, that risk decreases so that patients who have been immobile for long periods of time have no increase in risk for VTE. Examples of clinical entities associated with these changes are listed in Table 1. Anticoagulation is started in the ED in patients with VTE and PE. In some

Table 1. Venous Thromboembolism Pathophysiology

UNDERLYING ETIOLOGY	CLINICAL EXAMPLES
Endothelial injury	• Acute infection • Acute coronary syndrome • Varicose veins
Stasis	• Major surgery • Stroke • Morbid obesity • Long-term indwelling catheters
Hypercoagulable states	• Pregnancy • Birth control medication • Inherited or acquired thrombophilia

CONDITIONS ASSOCIATED WITH INCREASED RISK FOR VTE

- Hypovolemic shock
- Sepsis
- Advanced heart failure (particularly NYHA Class IV)
- Complicated surgical procedures associated with periods of immobility
- Orthopedic procedures involving the hip or knee
- Inflammatory bowel disease
- Heparin-induced thrombocytopenia
- Patients who require mechanical ventilation
- Morbid obesity
- Stroke with physical impairment
- Extensive varicose veins or abnormalities of the venous circulation

cases, patients can be discharged from the ED or after a brief observation stay on anticoagulation started in the ED. In addition, patients admitted to the hospital who will be immobile (for example walking less than 30 feet in a day) may be started on prophylactic anticoagulation. As many of these patients now remain in the ED, anticoagulation and its management become the emergency physician's issue.

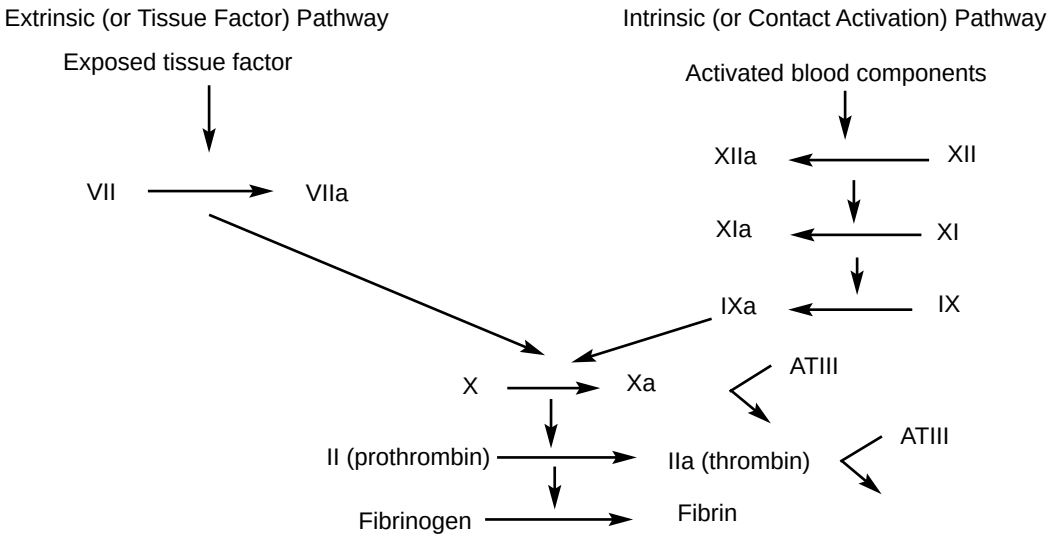
Acute Coronary Syndrome. The three clinical syndromes that are included under the definition of ACS are unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI), and ST segment elevation myocardial infarction (STEMI). These clinical presentations share a similar underlying pathophysiologic process, which is acute thrombosis superimposed on coronary artery atherosclerosis. Approximately 8 million patients visit EDs in the United States with symptoms that may represent a form of ACS. About 2 million of these individuals will be experiencing a partial or compete occlusive event involving the coronary vasculature. Current approaches to the diagnosis and treatment of ACS have dramatically reduced the mortality associated with ACS. For example, Furman, et al. demonstrated a reduction in mortality for acute myocardial infarction from 24% in 1975 to 14% in 1997.[6] Morbidity and mortality associated with ACS has continued to decline. STEMI is occurring today in an older population and more often in those who have had a prior major cardiovascular event or other complicated medical conditions.

Most atheromatous plaques develop over years. They are more likely to occur and progress rapidly in patients with diabetes mellitus, hyperlipidemia, uncontrolled hypertension, certain inflammatory conditions, and in families with a history of premature coronary artery disease. Acute thrombosis most often develops after the endothelial surface overlying a plaque ruptures, erodes, or fissures. Once the endothelial layer is disrupted, underlying tissue factor and collagen are exposed to blood components in the circulation. This stimulates prothrombotic events, such as platelet adhesion and activation leading to thrombus formation. If the endothelial injury is small and the subsequent thrombus is small, no significant interruption in flow through the coronary artery occurs, and the patient remains asymptomatic. If the thrombosis is more occlusive, the patient may experience ischemic symptoms such as angina or near syncope. Complete occlusion caused by the newly formed thrombus may result in acute myocardial infarction, sometimes immediately progressing to cardiac arrest. After sudden occlusion of a coronary artery, collateral circulation from nearby vessels may prevent some ischemic myocardium from progressing to necrosis. A minority of patients with ACS symptoms, particularly if induced by exercise, will have patent but underdeveloped coronary vessels or abnormalities of the cardiac architecture as the basis for their symptoms. Embolization of clot that has formed in the chambers of the left side of the heart into coronary arteries, and dissection involving the coronary arteries and thoracic aorta produce ACS symptoms in a small number of patients. Finally, any condition that impairs the delivery of oxygen to myocardial tissue or impairs cellular metabolism in myocytes can cause irreversible injury to the heart muscle. Prolonged hypotension, severe anemia, or carbon monoxide poisoning are examples of situations that may lead to ischemic symptoms. A careful medical history, including a discussion of the events leading up to the onset of acute symptoms, often helps determine the pathophysiologic process.

Since thrombus formation is pivotal to the development of ACS symptoms in most cases, antithrombotic and/or thrombolytic therapy play critical roles in the definitive management of patients with ACS. While in the ED, the goal should be to identify the cause of the symptoms, initiate therapy to lyse the culprit thrombus, and to take steps to prevent the formation of additional thrombi in the affected vessels. Anticoagulant drugs interfere with clot formation by blocking the coagulation cascade at various points. (*See Figure 1.*) These drugs should be administered with care in patients with congenital or acquired deficiencies of clotting factors, acquired factor inhibitors, and advanced liver disease (and therefore decreased clotting factor production). Examples of procoagulant states include antithrombin III deficiency, protein C or S deficiency, and increased plasma levels of Factor VII. Consultation with a coagulation specialist is advised for such patients.

Cerebrovascular Accident. Transient ischemic attacks (TIAs) are defined as periods of temporary neurological dys-

Figure 1. Coagulation Cascade



Drug	Principle Site of Action
Heparin	Thrombin (via ATIII)
LMWH	Factor Xa (via ATIII)
Warfarin	Factors II, VII, IX, X
DTIs	Thrombin
Fondaparinux	Factor Xa (via ATIII)
Fibrinolytics	Fibrin

function associated with diminished but not completely interrupted flow to portions of the central nervous system (CNS). TIAs represent temporary or partial occlusion in the cerebrovascular circulation just as UA represents a similar process involving the coronary circulation. Clinically, TIAs commonly present as transient aphasia, monocular blindness, or focal motor or sensor deficits. Traditionally, TIAs were defined as deficits that lasted less than 24 hours. However, recent MR studies demonstrated that many longer lasting TIAs actually are small, completed strokes.[8] Typically TIA-related deficits are short-lived, lasting for minutes to about one hour. The pathophysiologic processes that cause TIAs are similar to that for CVAs, and a significant number of patients with a TIA often experience a CVA with days or weeks of their initial TIA symptoms.

CVAs, also known as strokes, commonly are caused by a sudden disruption of blood flow to the brain or brainstem. Interruption of blood flow to the CNS causes an abrupt onset of a neurologic deficit.

Approximately 700,000 patients per year are found to have suffered a new CVA in the United States. CVAs account for about 160,000 deaths annually, making CVA the third leading cause of death. CVA is the leading cause of long-term disability, and it has been noted that only 10% of CVA victims return to their baseline neurologic function after an acute event.[9]

Acute ischemic strokes most often are caused by acute thrombosis forming over an atherosclerotic plaque in an intracranial artery or by emboli from the heart or great vessels. Eighty-five percent of CVAs are the result of an acute ischemic event; most of the remaining 15% are a result of hemorrhage. Approximately 80% of acute ischemic strokes involve cerebral vessels that are supplied by the carotids, while 20% involve vessels supplied by the vertebro-basilar system. CVAs also may be precipitated by emboli released from the left atrium ascending aorta, or from atherosclerotic plaques in the carotid arteries. Atrial fibrillation has been shown to be a major risk factor for embolic stroke with 15% of strokes occurring in people with a history of atrial fibrillation.[10]

It has been estimated that 2.3 million Americans experience persistent or episodic atrial fibrillation, and that 5% of the population older than 70 years will develop atrial fibrillation. Overall, people with atrial fibrillation have a 5-fold increase in the incidence of CVA as compared to those with sinus rhythm. A small number of CVAs will occur in individuals who have a patent foramen ovale (PFO). PFO is found in up to one-third of otherwise normal hearts. In patients with PFO or other atrial or ventricular septal defects, venous thromboemboli may pass from the right side of the heart to the left without entering the pulmonary circulation.

CVA also can be caused by rupture of cerebral arterial aneurysm or penetrating cerebral artery, particularly in patients with uncontrolled systemic hypertension, congenital or acquired cerebrovascular defects. In addition, dissection of the cerebral arteries can cause a stroke; this commonly is seen after high-speed

Figure 2A. VTE Clinical Practice Guidelines (sample)

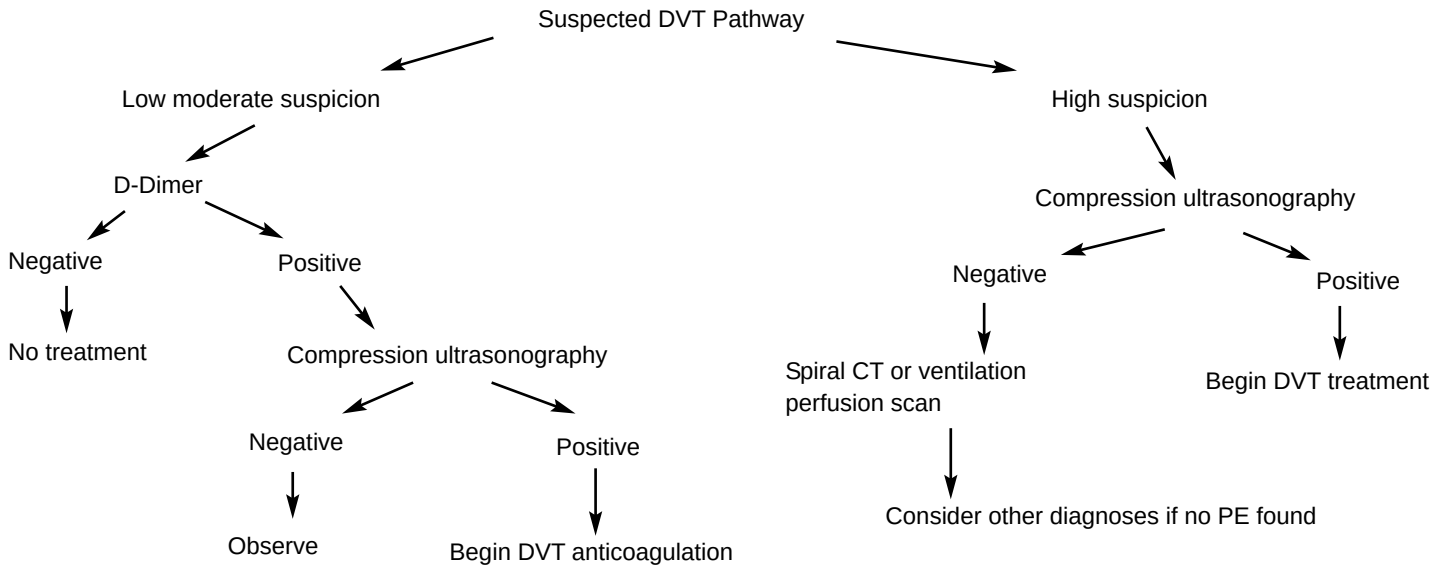
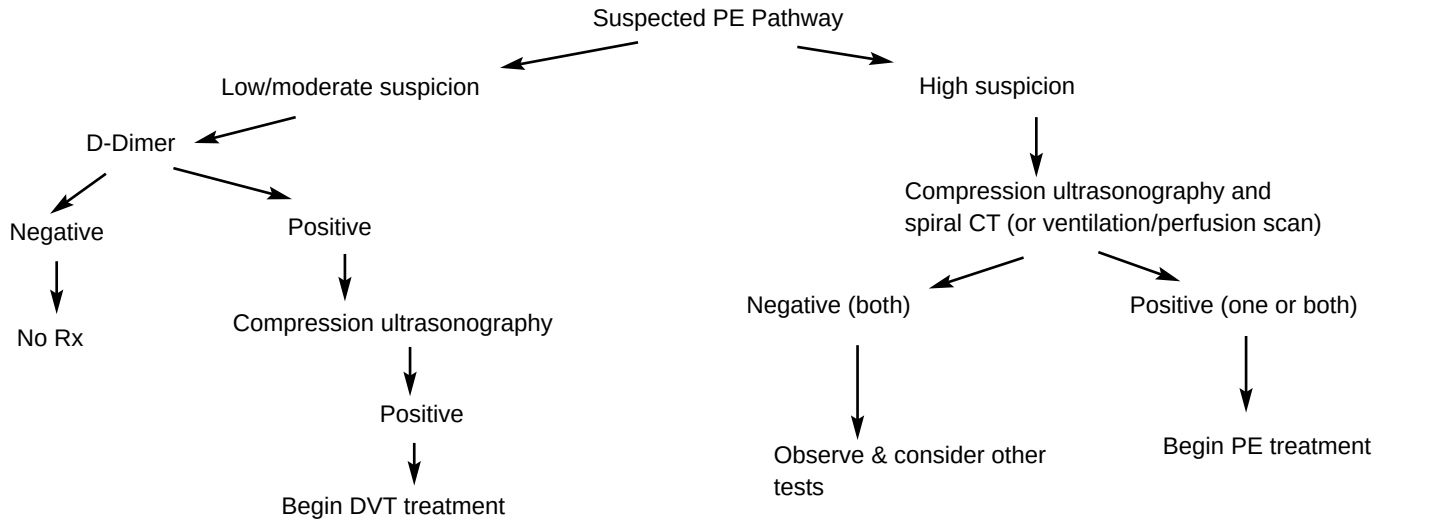


Figure 2B. VTE Clinical Practice Guidelines (sample)



injuries such as those from a motor vehicle accident associated with craniofacial injuries. The extent of the CVA is determined by the amount of intracranial hemorrhage, associated ischemic injury, and the subsequent distortion of CNS anatomy. Cerebral venous thrombosis also can cause CVA; it usually is seen in individuals with congenital or acquired thrombophilia (risk for thrombosis). Finally CVAs may be caused by tumors (benign or malignant), abscesses, by expanding aneurysms, or processes that lead to hydrocephalus. Since CVA may be precipitated by a wide variety of pathophysiologic events, a thorough diagnostic evaluation and a risk/benefit assessment must be completed prior to selection of a therapeutic intervention for a particular patient.

Clinical Presentation of Thrombosis

The development of venous thrombosis is encouraged by situations where flow within the venous circulation is mechanically impeded or fluctuates widely during periods of hemodynamic instability. Shock is associated with diminished venous flow whether caused by massive bleeding, severe burns, or cardiac compromise. These situations increase the risk for thrombosis in the venous system. Prolonged periods of immobility following an orthopedic procedure, major trauma, disabling stroke, exacerbation of an arthritic condition, disabling heart failure, or damage to veins (varicosities) are associated with increased risk for VTE.[7] Some patients with heart failure, inflammatory bowel dis-

Table 2. Evaluation of Patients Prior to Initiating Anticoagulation

1. History
2. Physical examination
3. PT/INR, aPTT
4. Platelet count
5. Uncommonly performed tests:
   a. Antithrombin, protein C, protein S levels and activity
   b. Factor VIII, IX levels
   c. Factor VIII or IX inhibitors (warm and cold antibodies)
   d. Lupus anticoagulant, antiphospholipid levels
   e. Factor V Leiden
   f. Prothrombin 20210A mutation
   g. Individual factor levels (eg, VII, XIII)

ease, or cancer may have a combination of diminished venous flow and immobility increasing their risk for VTE. Some patients have an increased propensity to venous thrombosis because of congenital thrombophilia or an acquired (most often drug-induced) disturbance of normal clotting mechanisms in the body. In some instances it is appropriate to initiate anticoagulation in the ED when certain sedentary patients with complex medical conditions are transported to the ED for treatment of acute exacerbations of the chronic conditions. (*See Insert.*)

When a large clot breaks off from its site of origin in the proximal venous system, it likely will lodge in the pulmonary arterial tree. Sudden occlusion in the pulmonary artery bed by a large embolism produces right ventricular (RV) strain. RV strain leads to RV dilatation. Dilatation of the RV causes alteration in the heart's chambers and valves, making the heart much less efficient as a pumping organ. Decreased blood flow from the right to the left of the heart through the pulmonary circulation causes a decrease in the left ventricular output which, in turn, results in the release of compensatory catecholamines to increase blood pressure. In previously damaged hearts or in normal hearts suddenly confronted with a large clot burden, the increase in demand on the heart muscle may cause the heart to fail and arrest. In addition, blockage of pulmonary artery flow causes a ventilation perfusion mismatch that may cause hypoxia and reflex hypocapnia due to a compensatory increase of the respiratory rate. The clinical result often is sudden shortness of breath and cardiovascular instability. Embolization of a large thrombosis may progress rapidly to cardiovascular collapse and death. Sudden death precipitated by a massive and lethal PE often goes unrecognized during resuscitation or in the immediate post resuscitation phase of patient management. Therefore, death precipitated by a massive PE may be inappropriately attributed to acute coronary occlusion, aortic dissection, or a lethal arrhythmia if an autopsy is not performed.

Pathways for ED Anticoagulation

Pathways (or patient care guidelines) are useful in maintaining the "continuum of care" for the VTE, ACS, and CVA/TIA patients. In ACS, for example, pathways permit the expedious transfer of patient care responsibilities from EMTs to ED personnel and to cardiologists or primary care physicians who manage the patient on the inpatient service and after discharge. Pathways should take into consideration the resources and personnel available at the point of care. The development of pathways should be multidisciplinary with all specialties equally involved. This not only results in pathways that are more likely to be followed but also builds relationships and mutual respect. This article give sample guidelines that can be used to start the conversation among disciplines. When pathways are employed, physicians can deviate from the pathway to customize therapy to a particular patient's needs, providing written justification is included in the medical record. The figures on the Insert and Figures 2A and 2B represent examples of ACS, VTE, and stroke pathways. (*See Figures 2A, 2B and Insert*).

Assessing the Patient in the ED

Patients presenting to the ED with an indication for any type of anticoagulant should have a detailed history and physical examination oriented toward eliciting prior bleeding problems and exposure to anticoagulants and antiplatelets. Any recent admission for ACS, VTE, or CVA should raise the suspicion that the patient has been exposed to heparin, another anticoagulant, and/or antiplatelet agents. Such a history may indicate the patient is at increased risk for thrombosis, or is experiencing a complication of anticoagulation. The presence of bruising, ecchymosis, and easy bleeding should lead to a comprehensive evaluation prior to the administration of any anticoagulants.

Along with the history and exam, a panel of coagulation-oriented blood tests should be performed to establish a normal baseline before the introduction of therapy. (*See Table 2.*) Establishing a normal baseline is important to avoid iatrogenically inducing a hemorrhagic state in patients with hereditary or acquired defects in coagulation. Although hereditary coagulopathies such as hemophilia and Von Willebrand's disease are relatively uncommon and usually apparent from the patient's history, a few patients may present with undiagnosed coagulopathies that can be detected on a screening evaluation. More commonly, patients will have an acquired coagulopathy due to the administration of antiplatelet agents (physician-prescribed or self-prescribed) or warfarin. Less commonly, patients may be on chronic outpatient parenteral anticoagulation with a low molecular weight heparin (LMWH). Rarely, patients may have an acquired inhibitor of coagulation associated with disorders such as lymphoproliferative diseases or lupus.

The most commonly performed tests to assess the state of the coagulation system are the prothrombin time (PT)/international normalized ratio (INR), activated partial thromboplastin time (aPTT), and a platelet count. The PT/INR is used to evaluate the extrinsic system while the aPTT is used to evaluate the intrinsic coagulation system. (*See Figure 1.*) The extrinsic system initiates thrombosis through the release of tissue factor, which complexes with factor VII; the tissue factor:FVII complex sets off the clotting cascade through activation of factor X, ultimately generating thrombin, which in turn catalyzes the generation of fibrin from

fibrinogen. This currently is believed to be the predominant pathway for thrombosis. Hepatic disease and warfarin are the most common conditions causing an isolated prolongation of the PT/INR, although severe liver disease and warfarin excess can prolong both the PT/INR and aPTT. The PT/INR may be "falsely" prolonged by a lupus anticoagulant, a condition paradoxically associated with thrombotic complications.[11]

The aPTT evaluates the intrinsic system and generally is used to detect hemophilia A and B, which are due to deficiencies of factors VIII and IX, respectively. It also is used to evaluate the effects of many of the rapid-onset anticoagulants including heparin and the direct thrombin inhibitors, although the generalized use of a fixed aPTT range for guiding heparin therapy is recommended against.[12] Each hospital should have its own guideline. In the ED, the aPTT rarely is prolonged, but it may be the first indication of an undiagnosed coagulopathy. It is minimally affected by LMWHs and so is not useful for monitoring their effect.

Finally, thrombocytopenia of less than 150,000/L is present in 7%[13] to 10.4%[14] of ED patients. It is important to document the platelet count, since thrombocytopenia usually precludes the administration of an anticoagulant or antiplatelet agent. Thrombocytopenia may reflect an isolated case of idiopathic thrombocytopenic purpura (ITP) or thrombotic thrombocytopenic purpura (TTP) or may be the manifestation of some systemic disorder such as DIC or sepsis. Thrombocytopenia also may be the only clue to the presence of heparin-induced thrombocytopenia (HIT). (*This will be covered in detail in Part II of this article.*) Aspirin, adenosine diphosphate receptor antagonists such as clopidogrel, and the non-steroidal anti-inflammatory agents inhibit platelet function; this will not be detected by the platelet count. Although assays of platelet function are not part of a routine screen in the ED, history of exposure to an antiplatelet agent in a patient suffering a life-threatening hemorrhage is sufficient to justify platelet transfusions and the administration of desmopressin (DDAVP) in an attempt to restore normal formation of a thrombus.

Some patients presenting to the ED with ACS, VTE, or some other thrombotic event may on history be noted to have a strong family history of thromboses or the patient may have had multiple thrombotic events. Although not routinely part of the ED evaluation, several screening tests can be obtained to expedite the patient's definitive evaluation prior to the initiation of anticoagulant therapy, which can interfere with and delay the diagnosis of several clotting disorders. (These less commonly performed tests include antithrombin, protein C and protein S levels and activity, as well as tests for the factor V Leiden mutation and prothrombin 20210A gene mutation.)[15] When indicated, lupus anticoagulant tests as well as determination of antiphospholipid antibody levels may be an important part of the workup.

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Physician CME Questions

41. Thrombosis over an atherosclerotic plaque in proximal coronary artery may lead to:
    A. STEMI.
    B. NSTEMI.
    C. U/A.
    D. no discernable symptoms.
    E. all of the above.

42. Activation of both the extrinsic pathway and the intrinsic pathway lead to thrombin formation through the conversion of factor X to factor Xa.
    A. True
    B. False

43. Approximately 2 million cases of pulmonary embolism are diagnosed each year.
    A. True
    B. False

44. Adults with atrial fibrillation are:
    A. twice as likely to experience a CVA as those in sinus rhythm.
    B. are prone to develop a clot in the right atrium of the heart.
    C. may develop atrial or ventricular septal defects.
    D. All of the above
    E. None of the above

45. A panel of coagulation-oriented tests to establish a normal baseline before the introduction of anticoagulant therapy in the ED would commonly include:
    A. PT/INR and aPTT.
    B. Factor V Leiden.
    C. platelet count.
    D. A and C.
    E. A, B, and C.

46. Which of the following patients is at risk for VTE?
    A. Patient with a radial head fracture
    B. Patient with a massive CVA and hemiplegia, decreased level of consciousness
    C. Patient who has been paraplegic for 5 years
    D. All of the above

47. This paper discusses the role of clot formation in the development of cardiac ischemia. Cardiac ischemia can also occur with:
    A. carbon monoxide poisoning.
    B. prolonged hypotension.
    C. severe anemia.
    D. all of the above.

48. Several examples of treatment pathways are given in this article. Pathways:
    A. provide strict rules for physicians who are uncertain how to properly treat patients.
    B. are best created by the specialty that knows the subject matter best (e.g., cardiology for patients with chest pain).
    C. provide an example for physicians but generally are not followed, and deviation requires no justification or documentation.
    D. provide a continuum of care between disciplines.

49. A patient presents with bleeding, yet PT/INR, aPTT, and platelet count are all normal. Which of the following may explain this?
    A. TTP
    B. ITP
    C. Use of clopidogrel
    D. All of the above

50. A 17-year-old patient presents 5 days after a motor vehicle accident. He suffered significant facial trauma but has been at home ambulatory for the past 3 days. He complains of persistent headache and neck pain. For the past two hours he has been unable to move his right arm or leg. The most likely diagnosis in this patient is:
    A. carotid dissection.
    B. cervical spine fracture.
    C. central cord syndrome.
    D. malingering.

CME Answer Key

41. E; 42. A; 43. B; 44. E; 45. D; 46. B; 47. D; 48. D; 49. C; 50. A

In Future Issues: **Anticoagulation Part II**

Emergency Medicine Reports CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- apply state-of-the-art diagnostic and therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur.

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to evaluate their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. *After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a certificate of completion.* When your evaluation is received, a certificate will be mailed to you.

Table. Chest Pain Clinical Practice Guideline

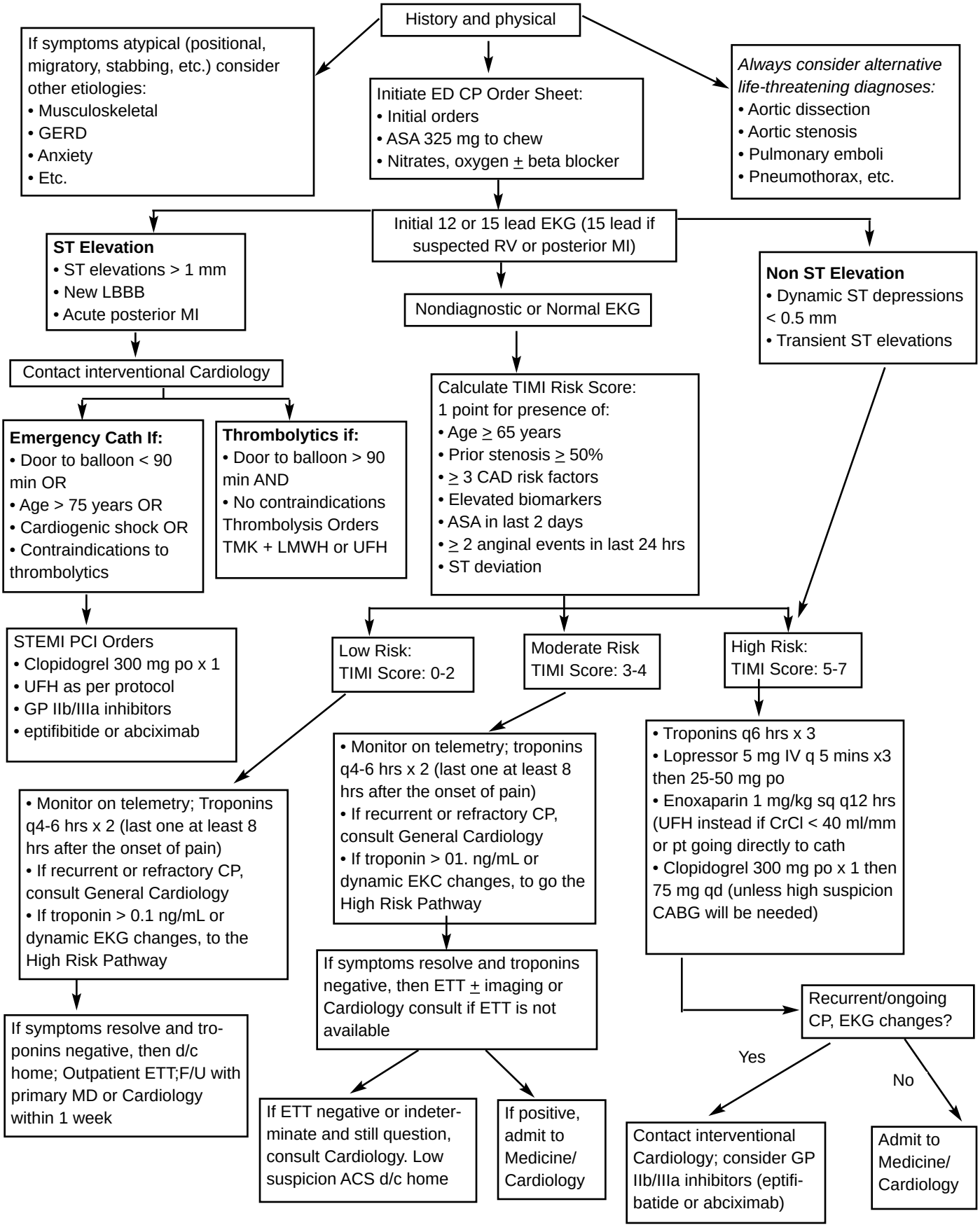

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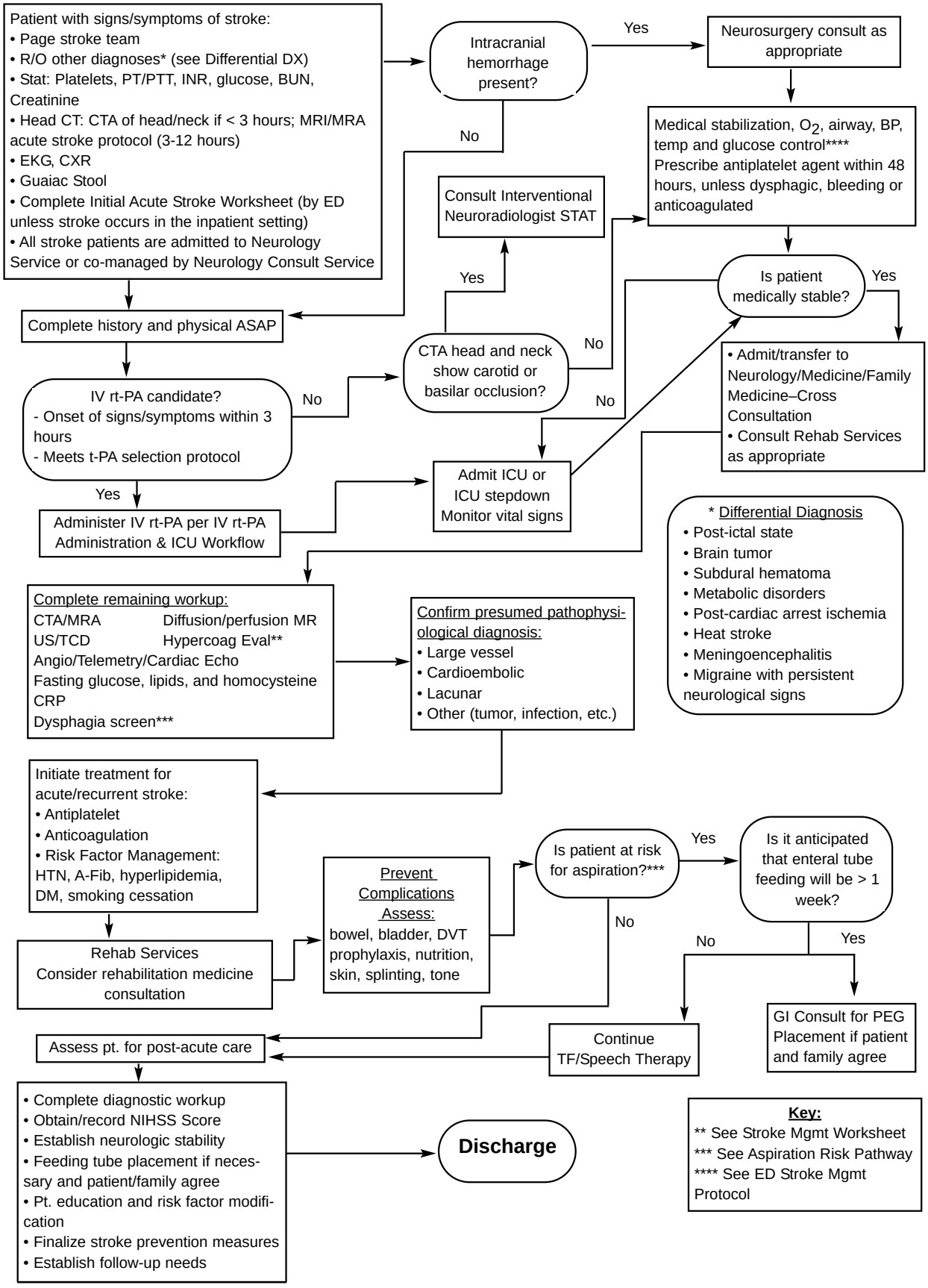
Table. CVA/TIA Clinical Practice Guideline



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Emergency Medicine Reports
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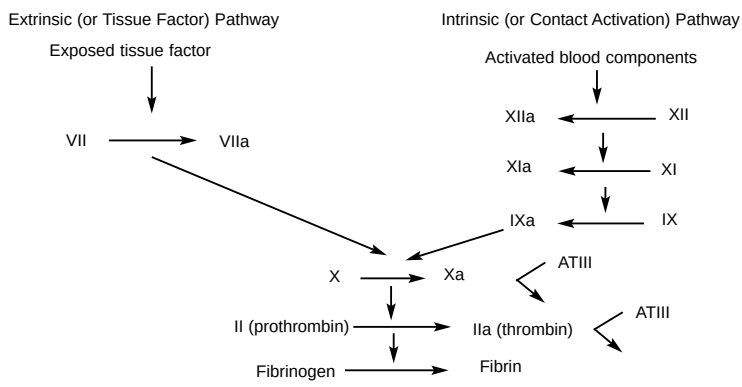
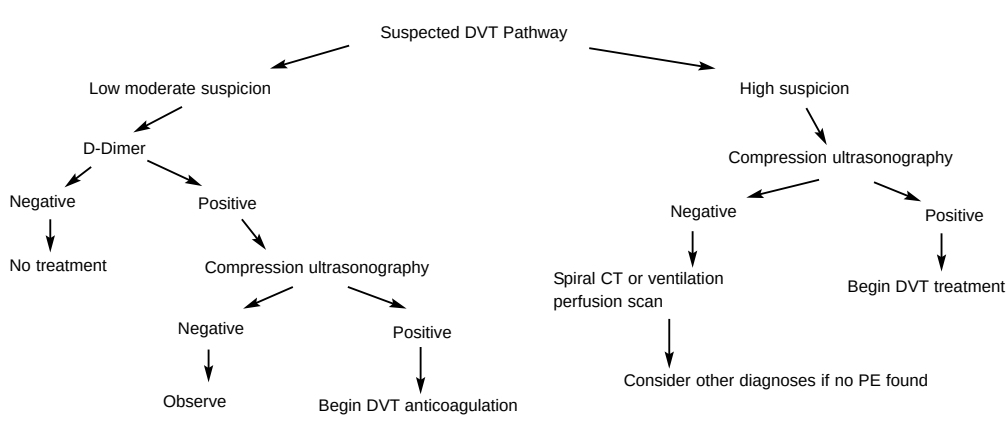
Anticoagulation and Thrombolytic Therapy, Part I

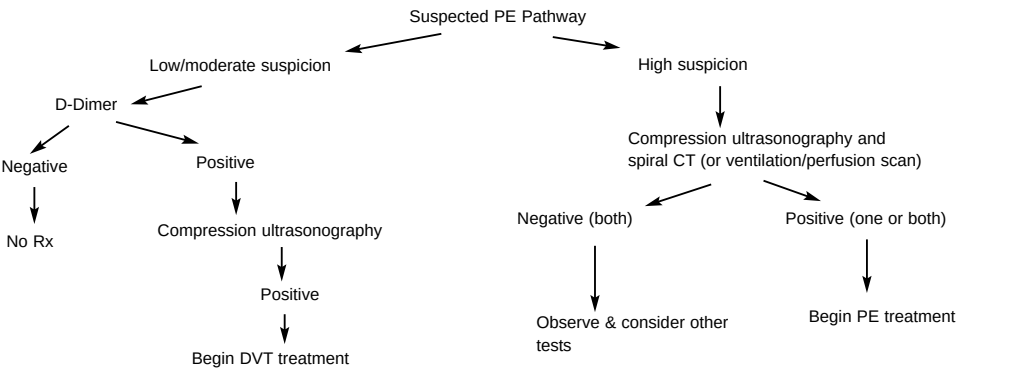
Coagulation Cascade



Drug	Principle Site of Action
Heparin	Thrombin (via ATIII)
LMWH	Factor Xa (via ATIII)
Warfarin	Factors II, VII, IX, X
DTIs	Thrombin
Fondaparinux	Factor Xa (via ATIII)
Fibrinolytics	Fibrin

VTE Clinical Practice Guidelines (sample)





Venous Thromboembolism Pathophysiology

UNDERLYING ETIOLOGY	CLINICAL EXAMPLES
Endothelial injury	• Acute infection • Acute coronary syndrome • Varicose veins
Stasis	• Major surgery • Stroke • Morbid obesity • Long-term indwelling catheters
Hypercoagulable states	• Pregnancy • Birth control medication • Inherited or acquired thrombophilia

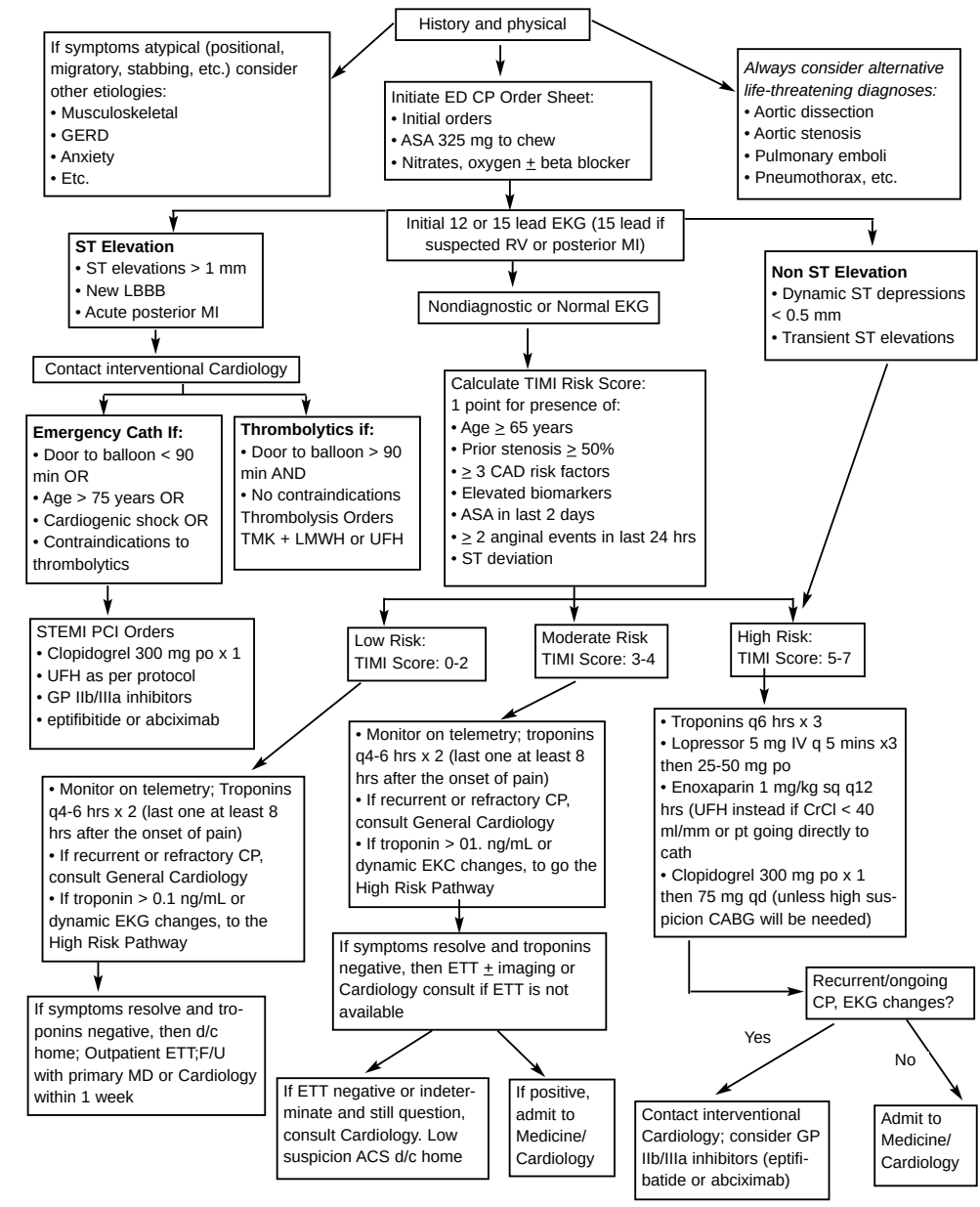
CONDITIONS ASSOCIATED WITH INCREASED RISK FOR VTE

- Hypovolemic shock
- Sepsis
- Advanced heart failure (particularly NYHA Class IV)
- Complicated surgical procedures associated with periods of immobility
- Orthopedic procedures involving the hip or knee
- Inflammatory bowel disease
- Heparin-induced thrombocytopenia
- Patients who require mechanical ventilation
- Morbid obesity
- Stroke with physical impairment
- Extensive varicose veins or abnormalities of the venous circulation

Evaluation of Patients Prior to Initiating Anticoagulation

1. History
2. Physical examination
3. PT/INR, aPTT
4. Platelet count
5. Uncommonly performed tests:
   a. Antithrombin, protein C, protein S levels and activity
   b. Factor VIII, IX levels
   c. Factor VIII or IX inhibitors (warm and cold antibodies)
   d. Lupus anticoagulant, antiphospholipid levels
   e. Factor V Leiden
   f. Prothrombin 20210A mutation
   g. Individual factor levels (eg, VII, XIII)

Chest Pain Clinical Practice Guideline



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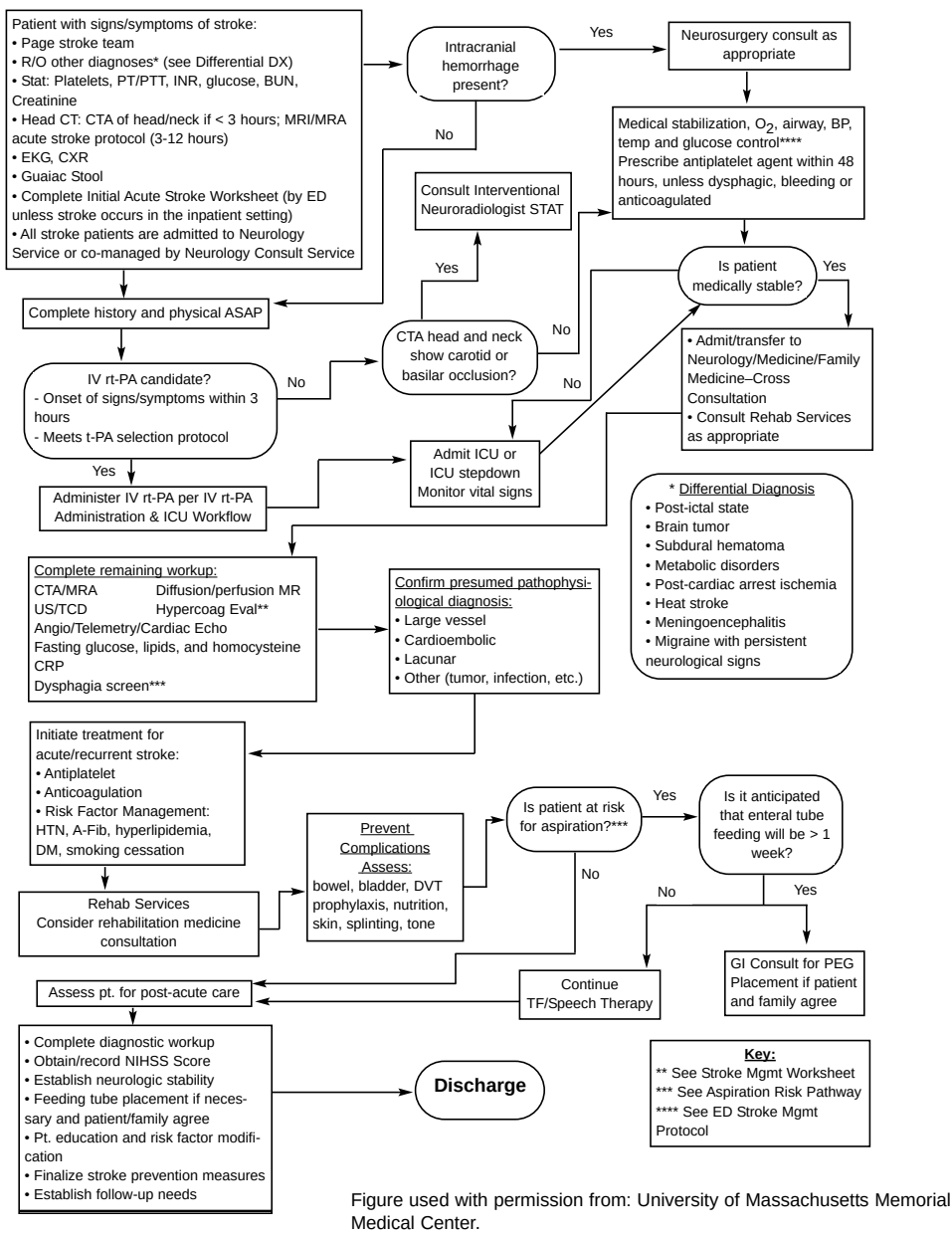
CVA/TIA Clinical Practice Guideline



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Supplement to *Emergency Medicine Reports*, February 19, 2007: "Anticoagulation and Thrombolytic Therapy in the Emergency Department: Part I." *Authors:* **Richard V. Aghababian, MD**, Professor and Chair, Department of Emergency Medicine, University of Massachusetts Medical School, Worcester; **Robert L. Levine, MD**, Associate Professor of Neurosurgery and Emergency Medicine, Chief, Division of Neurointensive Care, The University of Texas School of Medicine at Houston; and **Marcie J. Hursting, PhD, DABCC**, Director, Clinical Science Consulting, Austin, TX.