The home study portion is designed to provide a comprehensive foundational knowledge to the participant so that they can engage in the subsequent didactic and interactive case-based program.

At the conclusion of the self study, participants should be better able to:

1. Describe and explain the basic aspects of the coagulation cascade.
2. Define thrombogenesis and hemostasis.
3. Describe hemostatic mechanisms and apply this knowledge to patient management.
4. Compare and contrast the pharmacology, pharmacokinetics and pharmacodynamics of anticoagulant agents:
   a. VKA
   b. DTI’s
   c. Heparin and heparin like agents
   d. Anti-Xa agents
5. Compare and contrast the pharmacology, pharmacokinetics and pharmacodynamics of the antiplatelet agents:
   a. Aspirin,
   b. P2Y12 inhibitors
   c. Cilostazol
   d. Dipyridamole/ASA
   e. IIB/IIIA inhibitors
6. Compare and contrast the pharmacology, pharmacokinetics and pharmacodynamics of the thrombolytic agents:
   a. Alteplase
   b. Tenecteplase
7. Describe the basics of warfarin dosing and monitoring.
8. Define the current recommendations for indication-specific intensity and duration of warfarin therapy.
9. Identify risk factors for thromboembolism.
10. Discuss therapeutic treatment strategies for the prevention and treatment of venous thromboembolism.
11. Identify the anticoagulation needs of atrial fibrillation patients.
12. List the drug therapies needed in different stroke stages; acute stroke, peri-stroke period and secondary prophylaxis.
13. Describe the pathophysiology of atherosclerosis and acute coronary syndromes and relate this back to the antithrombin and antiplatelet agents used to manage this disorder.
14. Identify the onset of heparin induced thrombocytopenia and develop treatment strategies.
15. Interpret strategies used to manage hemorrhagic complications associated with anticoagulant and antiplatelet agents.
16. Be able to determine a peri-procedural anticoagulant regimen for patients based upon indication for anticoagulation and risk factors.

Be advised, although the primary reference is the ACCP 2012 guidelines in Chest, there may be other readings the participant is referred to, these will be specifically indicated in each section. The materials are all provided in a PDF format for each section. These materials are to assist you in completing the home study guide and the examination. A copy of the participant’s completed self-study guide must be submitted on the 1st day of the live programming. After completing these sections, the participant will be required to complete the self-study open book test. The test must be completed by no later than October 11, 2013. The home study portion must be completed in order to participate in the live program. A passing score of 70% must be achieved on the self-study online exam. Those failing to achieve this score will be contacted prior to the program for discussion and remediation.

1. Describe and explain the basic aspects of the coagulation cascade.
2. Define thrombogenesis and hemostasis.
3. Describe hemostatic mechanisms and apply this knowledge to patient management.

Readings for the Home Study Guide (provided as pdf)
2. Refer to appendix A-C of this home study for review of coagulation cascade coordinated with mechanism of anticoagulant drug therapy

QUESTIONS:
Describe Virchow’s triade and its relationship to thrombosis.

Appreciate the differences in the pathophysiology of arterial and venous thrombosis

Define the aspects of clot initiation, propagation and amplification.

Identify the role of Factor VIIa in and tissue factor in clot formation

What are our body’s natural anticoagulants?
4. Compare and contrast the pharmacology, pharmacokinetics and pharmacodynamics of anticoagulant agents:
   a. VKA  b. DTI’s  c. Heparin and heparin like agents  d. Anti-Xa agents

5. Compare and contrast the pharmacology, pharmacokinetics and pharmacodynamics of the antiplatelet agents:
   b. Aspirin, b. P2Y12 inhibitors  c. Cilostazol  d. Dipyridamole/ASA  e. IIB/IIIA inhibitors

6. Compare and contrast the pharmacology, pharmacokinetics and pharmacodynamics of the thrombolytic agents:
   a. Alteplase  b. Tenecteplase

Readings for the Home Study Guide
1. New Antithrombotic Drugs CHEST ACCP guidelines, 9th ed. 2012;141(2_suppl):e120S-e151S
5. Refer to appendix D of this home study for review of warfarin metabolism

Recommended Readings  Anticoagulation Therapy: A Point-of-Care Guide  Chapter 2-7 and 9 and 18

<table>
<thead>
<tr>
<th>Agent</th>
<th>Classification</th>
<th>Site of action</th>
<th>Route</th>
<th>Tmax</th>
<th>T 1/2</th>
<th>Metabolism</th>
<th>Elimination</th>
<th>Dosing</th>
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<th>Food &amp; Drug Interactions</th>
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Questions:

List some of the advantages of low-molecular weight heparin (LMWH) over UFH.

Know each products FDA approved indication and corresponding dosing.

Know the impact of obesity and renal dysfunction on each of the agents.

What are the recommendations for validating a therapeutic range for Unfractionated Heparin (UFH) for an institution?
7. Describe the basics of warfarin dosing and monitoring.
8. Define the current recommendations for indication-specific intensity and duration of warfarin therapy.

<table>
<thead>
<tr>
<th>Readings for the Home Study Guide (provided as pdf)</th>
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<tbody>
<tr>
<td>1. Oral Anticoagulants  CHEST. 2012;141(2_suppl):e44S-e88S</td>
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<tr>
<td>2. Evidenced Based Medicine of Anticoagulant Therapy, CHEST. 2012;141(2_suppl):e152S-e184S</td>
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<tr>
<td>3. Refer to appendix D of this home study for review of warfarin metabolism</td>
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<th>Recommended Readings</th>
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<th>QUESTIONS:</th>
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<tr>
<td>List the vitamin K dependent clotting factors that warfarin interferes with and their respective half-lives.</td>
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<tr>
<th>Describe how warfarin exerts it’s pharmacologic effect. (focus on the difference between anticoagulant and antithrombotic effect)</th>
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<th>What two reasons do we overlap UFH/LMWH/fondaprinux with warfarin for?</th>
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<th>How do we monitor warfarin for efficacy?</th>
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<th>What is the most common target range for warfarin?</th>
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<th>Describe the metabolism of warfarin and indicate the rationale behind the stereo-specific drug interactions.</th>
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<th>Indicate factors that are associated with an increased a bleeding while on warfarin.</th>
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<th>What is the recommended INR monitoring for VKA?</th>
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<th>What is the typical % dosage change that is made to warfarin (either up or down)?</th>
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</table>
Discuss the genetic polymorphisms of the cytochrome P450 2C9 and VKOR1 and their resultant effects on response to warfarin.

What is the pathology behind the following side effects of warfarin and how would you manage each episode?:
   a. purple toe syndrome
   b. warfarin induced skin necrosis (WISN or CISN (for Coumadin induced skin necrosis))

Discuss the teratogenicity of warfarin and utility/safety in any stage of pregnancy.

9. Identify risk factors for thromboembolism.
10. Discuss therapeutic treatment strategies for the prevention and treatment of venous thromboembolism.

Readings for the Home Study Guide (provided as pdf)
3. Prevention of VTE orthopedic. CHEST. 2012;141(2_suppl):e278S-e325S
4. Antithrombotic Therapy for VTE Disease CHEST. 2012;141(2_suppl):e419S-e494S
5. Evidenced Based Medicine of Anticoagulant Therapy, CHEST. 2012;141(2_suppl):e152S-e184S

Recommended Readings

QUESTIONS:

Use the following case to answer questions 1-6:

RT is a 67 yo male patients admitted to hospital for community acquired pneumonia (CAP) and chronic obstructive pulmonary disease (COPD) exacerbation and hypertension. His medications upon admission include: spiriva 1 capsule inhaled qday, Advair 50-250 1 puff BID, MVI 1 qday, lisinopril/HCTZ 20/25 1tab qday and calcium 500 elemental qday. He has varicose veins, weight is 287 lbs, HT=5’10”, history of phlebitis.

1. What is the PADUA score?

2. List RT’s risk factors for developing a deep vein thrombosis while in hospital.
3. Is RT a candidate for DVT prevention and if so list all available options and expected efficacy of each.

4. RT develops a DVT and PE while in hospital, provide therapeutic recommendations to manage this event, one using UFH and the other using LMWH and when and what dose to begin warfarin with and recommendation for how long to overlap therapy.

5. The recommended duration of warfarin therapy for RT would be, justify your answer:

6. The recommended target INR would be:
   a. 1-2
   b. 1.5-2
   c. 2-3
   d. 2.5-3.5

Be able to determine if patients who are candidates for outpatient therapy.

What is the role of thrombolytics for treatment of acute PE? What about DVT?

What is the role of IVC filters in the management of VTE?
11. Identify the anticoagulation needs of atrial fibrillation patients.

**Readings for the Home Study Guide (provided as pdf)**

5. Pradaxa (dabigatran), Xarelto (rivaroxaban), Eliquis (apixaban) Prescribing Information (Access via [www.fda.gov/cder](http://www.fda.gov/cder), or [www.pradaxa.com](http://www.pradaxa.com), [www.xarelto.com](http://www.xarelto.com) & [www.eliquis.com](http://www.eliquis.com)).

**Recommended Readings**

1. Anticoagulation Therapy: A Point-of- Care Guide Chapter 9 & Chapter 12 Available from [www.ashp.org/bookstore](http://www.ashp.org/bookstore)

**QUESTIONS**

What are the differences/commonalities for the following types of atrial fibrillation: paroxysmal, persistent, permanent, lone or postoperative?

What is the difference between rhythm control and rate control?

What is the primary purpose of anticoagulation therapy for atrial fibrillation patients?

What is the CHADS2 score and how is it calculated?

What is the most significant risk of anticoagulation therapy for atrial fibrillation patients? List additional risks of anticoagulation therapy.

What is the HAS-BLED score and how is it calculated?

When warfarin is selected, what is the dose/administration, goal INR and adverse effects/risk?

When dabigatran is selected, what is the dose/administration, monitoring and adverse effect/risk?

When rivaroxaban is selected, what is the dose/administration, monitoring and adverse effect/risk?

When apixaban is selected, what is the dose/administration, monitoring and adverse effect/risk?
12. List the drug therapies needed in different stroke stages; acute, peri-stroke period & 2nd prophylaxis.

Readings for the Home Study Guide (provided as pdf)

Recommended Readings
Anticoagulation Therapy: A Point-of-Care Guide Chapter 6 Available from www.ashp.org/bookstore
Cardiovascular Pharmacotherapy: A Point-of-Care Guide Chapter 13 Available from www.ashp.org/bookstore

QUESTIONS:
Describe the difference between an ischemic stroke, transient ischemic attack and intracerebral or subarachnoid hemorrhage.

When alteplase is selected for acute ischemic stroke, understand patient selection criteria and intravenous dose and administration.

Explain the bleeding risks associated with thrombolytics, including intracranial bleeding/hemorrhagic transformation.

List the dose, administration, contraindications/major warnings and common ADRs of the antiplatelet agents:
   a. Aspirin
      b. Ticlopidine
      c. Clopidogrel
      d. ASA/dipyridamole
      e. Cilostazol
13. Describe the pathophysiology of atherosclerosis and acute coronary syndromes and relate this back to the antithrombin and antiplatelet agents used to manage this disorder.

Readings for the Home Study Guide (provided as pdf)

1. Antiplatelet Drugs CHEST ACCP Guidelines, 9th ed. 2012: e89S-e1195

ACC/AHA Guidelines and statements pertinent to ACS/CAD also found at: http://my.americanheart.org/professional/StatementsGuidelines/ByTopic/TopicsA-C/ACCAHA-Joint-Guidelines_UCM_321694_Article.jsp


Recommended Readings


Describe the pathophysiology of acute coronary syndromes and the role pharmacologic therapy has on the outcomes of the disease.
What is the onset and duration of action of aspirin, clopidogrel, prasugrel and ticagrelor?

Compare and contrast the safety and efficacy of clopidogrel, prasugrel and ticagrelor.

How do drug interactions, genetic polymorphisms and other factors affect clopidogrel responsiveness?

List the risk factors for bleeding in patients receiving anti-thrombotic therapy for coronary artery disease.

What is the current role of thrombolitics in the management of ST-segment elevation MI?

Identify ACS high risk features and differentiate recommended therapy for low and high risk patients.

Compare and contrast the safety and efficacy of heparin, LMWH, bivalirudin, fondaparinux and IIbIIIa inhibitors in the management of ACS.

**14.Identify the onset of heparin induced thrombocytopenia and develop treatment strategies.**

**Readings for the Home Study Guide (provided as pdf)**
1. Treatment and Prevention of Heparin Induced Thrombocytopenia CHEST. 2012;141(2_suppl):e495S-e530S

**Recommended Readings**

**QUESTIONS:**
Describe the pathophysiology of heparin induced thrombocytopenia.
What is the role of the Elisa PF4 and serotonin release assays? What are the limitations of each?

Discuss the time of onset, expected impact on platelets, risk of thrombosis. Understand how to use this data in Warkentin’s 4T prediction model.

Develop a therapeutic recommendation for a patient with suspected HIT with thrombosis. List pros and cons of available treatment options, doses and monitoring.

15. Interpret strategies used to manage hemorrhagic complications associated with anticoagulant and antiplatelet agents

**Readings for the Home Study Guide (provided as pdf)**
1. Anticoagulation Therapy: A Point-of-Care Guide Chapter 7
2. Evidence Based Medicine of Anticoagulant Therapy. CHEST. 2012;141(2_suppl):e152S-e184S

**Recommended Readings**

**QUESTIONS:**
List the risk factors for increased anticoagulant bleeding. (Table 7-1; Anticoagulation Therapy: A Point-of-Care Guide)

a. Anticoagulation-

b. Patient-
**c. Procedures-**

List 4 different approaches to reversing anticoagulation effects. (Table 7-2; Anticoagulation Therapy: A Point-of- Care Guide)

a. 

b. 

c. 

d. 

What are the main characteristics of urgent, semi-urgent, non-urgent reversal and “rebound risk” for each? (Table 7-3, 7-4, 7-5, 7-6, figure 7-1; Anticoagulation Therapy: A Point-of- Care Guide)

a. Urgent-

b. Semiurgent-

c. Nonurgent-

List the factors impacting extent and speed of reversal. (Table 7-8; Anticoagulation Therapy: A Point-of- Care Guide)

a. Thrombosis risk-

b. Bridge therapy requirements-

c. Patient risk factors-

d. Intensity of current anticoagulation-

e. Dose of anticoagulant-

f. Ability of patient to eliminate anticoagulant-

g. Predictability of reversal agent effects

Using the FDA approved prescribing information for each of the following agents, list the following information points:

**Agents:** Aqua Mephyton IV, Protamine, Novoseven RT, FEIBA, Profilnine, Kcentra

**Points:** Active ingredient, recommended dose, route, frequency, onset of action, FDA approved indication, contraindications, black box warning and
Briefly list some of the considerations for reversal of each of the following agents-

- a. Unfractionated heparin
- b. Low Molecular Weight heparin
- c. AntiXa agents-
- d. DTI’s
- e. Warfarin

List usual protamine dose(s) for reversal of heparin and low-molecular-weight heparin associated bleeding. (Table 7-11; Anticoagulation Therapy: A Point-of-Care Guide)

16. Be able to determine peri-procedural anticoagulant regimen for patients based upon indication for anticoagulation and risk factors

Readings for the Home Study Guide (provided as pdf)
1. Chest supplement, 9th edition, 326S-350S - Appendix Table 3.1 and 3.2

Recommended Readings

QUESTIONS:

1. List those procedures that are of low risk and may not require interruption of anticoagulation.

2. List the questions that must be answered prior to determining periprocedural anticoagulation regimen.
3. List those procedures that place patients at high risk of bleed.

4. Describe the risk categories (i.e. high, moderate, low) of thromboembolism based on patient’s past medical history of a mechanical heart valve, or atrial fibrillation, or venous thromboembolism.

5. Describe the optimal level of anticoagulation based upon risk categories described in #4.

**Patient Case**
69 year old patient is planning to have knee replacement surgery

- **Medications:** Warfarin 3mg, metoprolol 12.5mg BID, Lisinopril 10mg daily
- **PMH:** paroxysmal atrial fibrillation, congestive heart failure, chronic kidney disease
- **Labs:** Calcium 8.7 mg/dL, Sodium 136 mmol/L, Potassium 4.3 mmol/L, WBC 13.3 K/ul, Hg9 G/dL, Platelets 397 K/UL, Creatinine 1.8 mg/dL, INR-2.1

1. What is this patient’s TE risk category?

2. What is this patient’s risk of bleed and procedural risk?

3. Should warfarin be discontinued prior to procedure and if so, at what time should that occur?
Regulation of the Cascade

Key:
- Inhibits
+ Activates

Vessel or Tissue Injury
Factor VII
Tissue Factor
Factor VIIa-Tissue Factor complex
TFPI

Protein C & Protein S
Factor VIIIa
Factor IX
Factor X
Factor IXa
Factor VIII
Factor Xa
Factor Va
Factor VII

Antithrombin III

Prothrombin
Thrombin

Thrombomodulin

Fibrinogen

Fibrin
Fibrin crosslinked
Plasmin
Plasminogen
Fibrin split products

The Fibrinolytic System

http://www.chelationtherapyonline.com/GarryGordon/images/regulate.gif
APPENDIX D

http://images.google.com/imgres?imgurl=http://www.nature.com/clpt/journal/v80/n1/images/clpt2006377f1.jpg&imgrefurl=http://www.nature.com/clpt/journal/v80/n1/fig_tab/clpt2006377f1.html&usg=__KKTc9kQ_T1gonv1A0EEdNc8GpBQ=&h=568&w=605&sz=48&hl=en&start=2&um=1&tbnid=1q8Wkp5ctTDqUM:&tbnh=127&tbnw=135&prev=/images%3Fq%3Dwarfarin%2Bmetabolism%26hl%3Den%26rlz%3D1W1DLUS_en%26sa%3DN%26um%3D1