



# Understanding the Hazards of Heparin

**1 Contact Hours**

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## Acknowledgments

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**Note:** All dosages given are for adults unless otherwise stated. The information on medications contained in this course is not meant to be prescriptive or all-encompassing. You are encouraged to consult with physicians and pharmacists about all medication issues for your patients.

## Purpose

The purpose of this course is to inform healthcare workers about the risks related to the administration of heparin and strategies to reduce the volume of adverse drug reactions related to heparin administration.

Given the severity of the consequences of heparin errors, it is important that nurses adhere to standard medication safety procedures prior to administering heparin and other high alert drugs.

## Learning Objectives

**After successful completion of this course, you will be able to:**

- Discuss heparin's effect on the clotting cascade
- Differentiate unfractionated heparin and low molecular weight heparin
- Discuss the importance of heparin administration protocol use
- Identify adverse drug events related to heparin administration and treatment of the ADE

**Important Note:** In this course, the term "heparin" refers to both LMWH and UFH, unless otherwise specified.

## Introduction

One third of all hospitalized patients or 12 million individuals are exposed to heparin annually (Eke, 2018).

Intravenous heparin is considered one of the highest-risk medications used in the in-patient setting. Safe use of heparin requires a diligent approach:

- Weight-based dosing
- Frequent monitoring of the patient's blood clotting ability
- Lab-based adjustment of dosing
- Assessment for sources of bleeding
  - Internal
  - Puncture sites
  - Vascular access sites
  - Surgical sites

(Agency for Healthcare Research and Quality (AHRQ), 2017)

Adverse drug events caused by anticoagulants add approximately 45% to the cost of hospitalization. This equates to greater than 2.5 billion dollars annually (Spector, Limcangco, Furukawa, & Encinosa, 2017).

In this course, we will review the clotting cascade, heparin's effect on the clotting cascade, types of heparin, heparin administration, adverse drug events (ADE) related to heparin, and ADE treatment.

There are other types of anticoagulants in use today, Vitamin K antagonists, direct and indirect thrombin inhibitors, and factor Xa inhibitors; however, this module will not cover them.

## Accreditation Standards

The Joint Commission (TJC) established its National Patient Safety Goals to help accredited organizations identify and solve specific areas of concern. Each year, these goals are updated and/or changed based on the data TJC obtains from Sentinel Event Reporting. In 2018 the goals included

NPSG.03.05.01: Reduce the likelihood of patient harm associated with the use of anticoagulant therapy.

- Rationale: Anticoagulation medications are more likely than others to cause harm due to complex dosing, insufficient monitoring, and inconsistent patient compliance. The use of standardized practices for anticoagulation therapy that include patient involvement can reduce the risk of adverse drug events.
- Applies to hospital, ambulatory health care, critical access hospital (Fenner, 2018)

### **The Clotting Cascade**

The clotting cascade involves a series of events utilizing an intrinsic and extrinsic pathway. Both pathways result in the formation of a fibrin clot.

- Intrinsic pathway:
  - Slower responding pathway
  - Occurs when there is trauma within the vessel
    - Is activated by platelets, exposed endothelium, collagen, or chemicals
- Extrinsic pathway:
  - Faster responding pathway
  - Activated by external trauma allowing blood to escape from the vessel
- Common pathway:
  - The intrinsic pathway merges with the extrinsic pathway to finish the clot formation (Web.edu, ND)

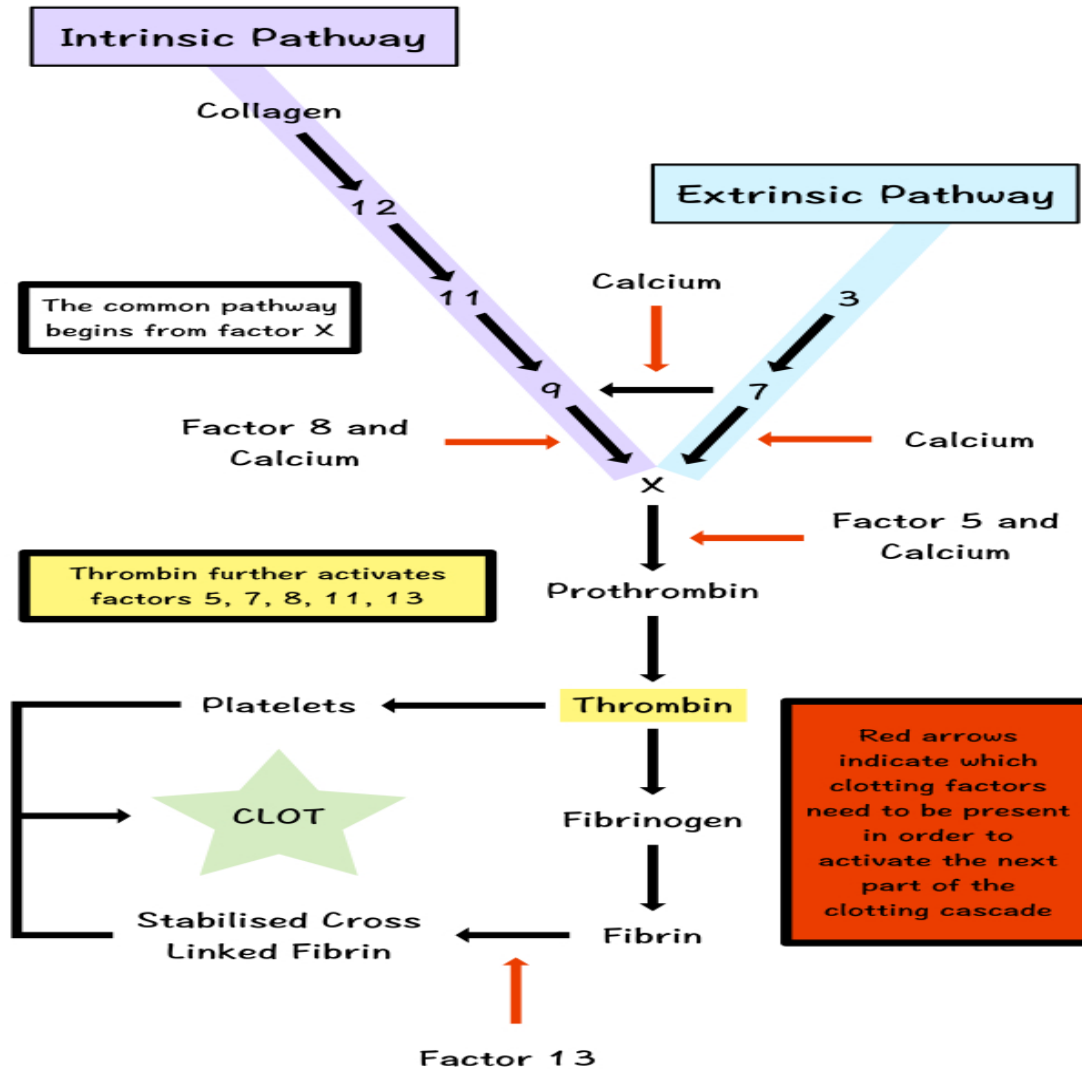
### **Test Your Knowledge**

How many patients who are hospitalized receive heparin therapy:

- A. 10%
- B. 20%
- C. 30%**
- D. 40%

Rationale: 12 million individuals or 1/3 of all hospitalized patients are exposed to heparin annually. (Eke, 2018)

# To Clot or Not to Clot: The Coagulation Cascade Made Easy



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## Heparin

Heparin sodium is the drug of choice to prevent and reduce blood clot formation. There are two types of heparin that are used, low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH). Institutions have policies in place to prevent deep vein thrombosis (DVT) in hospitalized patients and protocols for heparin administration, monitoring, and transitioning to oral anticoagulants. Be sure to know and use the policies and protocols in place at your institution.

Heparin sodium is used in many situations to:

- Diminish the clotting ability of blood – post operative clot prophylaxis, heart attack
- Prevent existing clots from getting bigger – deep vein thrombosis, heart attack, pulmonary embolism
- Prevent clot formation – post operative clot prophylaxis

Heparin **does not**:

- Dissolve blood clots that have already formed
- Usually affects platelet count, unless HIT occurs

## Effects on the Clotting Cascade

Heparin works on the intrinsic and common pathway to inhibit reactions that lead to coagulation and development of fibrin clots.

Heparin:

- Inhibits thrombosis by inactivating factor X
- Inhibits conversion of prothrombin to thrombin
- Inactivates thrombin and prevents the conversion of fibrinogen to fibrin
- Inhibits the fibrin stabilizing factor prevention stable clot formation

## Laboratory Testing

### Unfractionated Heparin:

- Peak plasma levels are achieved 2-4 hours post administration

The body's ability to ability to form clots is measured by a partial thromboplastin time (aPTT).

- This test measures the amount of time it takes a blood sample to clot after being exposed to the chemical found in the laboratory test tube.
- Timing and the correct amount of blood placed in the specialized tube is crucial for a correct reading that heparin administration adjustments can be made from.

### Low molecular weight heparin:

- Does not require routine aPTT monitoring
- In obese, pregnant, or renal dysfunction patients, monitoring anti-factor Xa may be helpful

## Complications

Complications of heparin administration are bleeding, allergic episodes, and immunologically-induced complications.

- Episodes of bleeding may occur during and after heparin administration
- Allergic episodes are medical emergencies
- Immunologically-induced complications, such as heparin-induced thrombocytopenia may be

life-threatening

## **Heparin-Induced Thrombocytopenia (HIT)**

Heparin-induced thrombocytopenia (HIT) is a potentially lethal, immunologically-induced complication to unfractionated heparin therapy and to a smaller degree, low molecular weight heparin (Salter, 2016).

HIT occurs when the body's immune system identifies platelet factor 4 (PF4) and heparin as foreign bodies and develops antibodies that bind to the complexes of PF4 and heparin. This binding action activates platelet production promoting a hyper-thrombotic state. Under these conditions, the platelets clump, reducing the number available in the circulation and become clots which may wedge in veins and arteries.

HIT can manifest as a complication of heparin therapy in two ways.

- HIT Type I (Non-immune HIT):
  - Occurs: within the first two days of heparin exposure
  - Platelet count normalizes with continued heparin therapy
- HIT Type II (Immune-mediated HIT):
  - Occurs: 4-10 days of heparin treatment
  - Life & Limb threatening thrombotic complications

(Coutre & Crowther, 2018; Eke, 2018; & Salter, 2016)

## **Did You Know?**

The difference between thrombocytopenia and HIT, is that there is NO bleeding associated with HIT (Coutre & Crowther, 2018; Eke, 2018; & Salter, 2016).

For more information regarding HIT, refer to RN.com's course: Heparin Induced Thrombocytopenia

## **Risk Factors**

There are factors that increase the risk of bleeding with heparin administration. The most common are:

- Women over the age of 60 years
- Medications (prescription, over-the-counter)
  - NSAIDS (aspirin, ibuprofen, naprosyn, celecoxib, diclofenac, among others)
  - Fish oils
  - Vitamin K supplements may decrease the effectiveness of heparin

## **Types of Heparin**

There are three types of heparin that are commonly used in the in-patient and out-patient populations. UFH and Heparinoids are interchangeable, but neither are interchangeable with LMWH.

### **Unfractionated Heparin (UFH)**

- Used for the prevention and treatment of thrombosis
- Heparin is mainly obtained from porcine intestine
- Administered parenterally
  - Continuous dosing
  - Intermittent dosing
- Has a highly variable anticoagulant response

- Inactivates several coagulation enzymes, including Factors IIa (thrombin), Xa, IXa, XIa, and XIIa, by binding to the cofactor AT<sup>2</sup> (Thrombosis Advisor, 2018)

### Heparin Treatment

- Therapeutic Infusion:
  - 80 units/kg IV bolus; then 18 units/kg/hr IV infusion
  - Check aPTT 6 hours after bolus
    - Adjust infusion to maintain aPTT within the therapeutic range
    - It is recommended to use an algorithm-based dosing protocol based on the laboratory values of your institution
- Prophylaxis:
  - 5000 units subcutaneously every 12 hours for patients 120 kg or less
  - 5000 units subcutaneously every 8 hours for patients over 120 kg
  - There are no dose adjustments required for renal failure
- Reversal:
  - 1 mg IV per 100 units (if heparin administered within previous 30 minutes)
  - 0.5 mg IV per 100 units (if 30-60 minutes have elapsed since heparin administration)
  - 0.25 mg IV per 100 units (if more than 2 hours have elapsed since heparin administration)

(Kearon, Aki, Ornelas, Blaivas, Jimenez, Bounameaux, H.....& Moores,,2016)

### Low Molecular Weight Heparins (LMWH)

- Are derived from UFH by depolymerization
- Each product has a specific molecular weight distribution that determines its anticoagulant activity and duration of action, so one product cannot always be substituted for another
- Administered subcutaneously
- Inactivate several coagulation enzymes by binding to AT50
- Associated with a predictable dose–response and have fewer non-hemorrhagic side effects
- Is cleared by the kidneys; therefore, may not be useful in end stage renal patients
- Do not require frequent monitoring (Thrombosis Advisor, 2018)

### Enoxaparin (Lovenox)

- Available in prefilled syringes 30mg, 40mg, 60mg, 80mg, 100mg, 120mg, 150mg
- Therapeutic enoxaparin = 1.5-2mg/kg/day or 1mg/kg/bid
- Prophylactic enoxaparin = 30-40mg/day
- Dose adjustment required/precaution advised for CrCl < 30mL/min
- Routine monitoring usually not required
- Anti-Factor Xa level monitoring recommended in specific patient populations
  - Weight greater than 100 kg
  - Pregnant patients receiving treatment
  - Prolonged therapy (greater than 2 weeks)
  - Unstable kidney function
- Reversal: stop enoxaparin
  - Protamine has NOT been shown to completely reverse the effects on anti-factor Xa activity

(Thrombosis Advisor, 2018)

### Dalteparin (Fragmin)

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- Available in prefilled syringes 2500units, 5000units, 7500units, 10,000units, 12,500units, 15,000units, 18,000units, 25,000units
  - Therapeutic dalteparin = 200units/kg/day
  - Prophylactic dalteparin = 2500-5000units/day
  - Dose adjustment required/precaution advised for CrCl < 30mL/min
    - 5000 units/day may be reasonable for patients undergoing dialysis
- (Thrombosis Advisor, 2018)

## Heparinoids

- An alternative to heparin for patients suffering from HIT
  - Drug of choice during emergencies such as stroke, heart attack, pulmonary embolism
  - Used prophylactically after long surgical procedures such as orthopedic or cardiovascular surgeries
- IV administration
  - Continuous infusion
  - Intermittent dosing
- Utilized for patients who have a history of HIT, clotting, or atrial fibrillation
- Requires regular monitoring  
(Thrombosis Advisor, 2018)

## Danaparoid

- Prophylactic:
    - 75 kg or less: 750 units/every 12 hours
    - 75-90 kg: 750 units every 8 hours
    - Greater than 90 kg: 1500 units every 8 hours
  - Therapeutic:
    - 150-200 units/hour to maintain anti-Xa levels between 0.5 to 0.8 units/mL
- (Thrombosis Advisor, 2018)

## Transitioning

Transitioning to a different form of heparin requires stopping the current heparin and waiting a prerequisite time before starting the different form of heparin. Be sure to follow your institution's protocol for transitioning. General guidelines include:

- LMWH to unfractionated heparin
  - Wait 4 hours from the enoxaparin dose to begin heparin infusion
- Unfractionated heparin to LMWH
  - Stop the heparin infusion, wait one hour to administer enoxaparin

## Patient Education

### In-patient:

Patients who are receiving continuous heparin administrations should understand the following:

- Why they are receiving heparin
- Side effects and possible complications
- What to report to the nurse
  - Bleeding
  - Headaches, neurological changes, blurry vision
- Frequency of blood draws

- When to expect heparin to be discontinued

### **Out-patient/Discharge:**

Many patients are discharged on low dose molecular weight heparin. When these individuals are discharged from your care, it is critical that they understand the following:

- Administration techniques (including first dose demonstration)
- Length and frequency of treatment
- Syringe disposal
- Side effects and possible complications
- Injection site selection and monitoring
- Food and Drug interactions
- Handling missed doses
  - Take missed dose as soon as possible
  - If it is closer to the next dosing time than the missed time, do not take missed dose, resume regular dosing schedule
    - Do not double next dose
- Store LMWH at room temperature in a dry area
  - Do not store in bathroom
  - Keep away from children

For an example of a patient education format visit:

<http://www.med.umich.edu/1libr/AntiCoag/Enoxaparin.pdf>

### **Avoiding Adverse Drug Reactions**

The Institute for Safe Medication Practices (ISMP) has identified drugs that have a high-risk for causing significant patient harm when an error is made in administration, ordering, or preparing. Drug errors may not be more common with these drugs, but the consequences of these errors are significantly more devastating to the patient. The ISMP regularly publishes lists of the high-risk drugs and strategies to help reduce the risk of errors, such as:

- Standardizing the ordering, storage, preparation, and administration of these medications
  - Improving access to information about these drugs
  - Limiting access to high-alert medications
  - Using auxiliary labels and automated alerts
  - Employing redundancies
- (Institute for Safe Medication Practices, 2014)

View the complete list of ISMP (2018) High-Alert Medications at:

<http://www.ismp.org/Tools/highalertmedications.pdf>.

In addition to the ISMP recommendations, your institution will have policies and procedures to guide safe medication administration practices. Be sure to know and follow these policies and procedures.

These practices might include:

- Use of unit dosing
- Bar coding
- Independent double checks
  - Two nurses will:
    - Review the order
    - Calculate the dose

- Compare results with unit dose
- Double signatures in medical record
- Use of smart pump technology
  - Drug libraries
  - Drug limits

## Sentinel Event: Case Review

Dr. Lee ordered a heparin infusion for Janet Williams with directions to follow weight-based protocol orders for lab monitoring and dosage changes.

Later that day, the protocol orders indicated that a bolus dose of heparin 1,400 units IV should be administered based upon Mrs. William's aPTT level.

Jackie, the patient's nurse, removed a 10-mL vial of heparin (1,000 units/mL) from an automated dispensing cabinet to prepare the dose. However, she miscalculated the volume that was needed as 14 mL, not 1.4 mL. The nurse, concerned that she would be using a second vial of heparin to prepare the bolus, quickly asked another nurse to "double check the math." The other nurse looked over the calculations but did not actually re-calculate the math herself. She told Jackie that it seemed right to her.

The result was that Mrs. Williams received 14,000 units of heparin. A medical student discovered the error after the patient began bleeding profusely from an abdominal incision that was previously healing.

### Test Your Knowledge

What might have prevented this error?

- A. Use of unit dosing**
- B. Bar coding**
- C. Independent double checks**
- D. Double signatures**

If you selected all the answers you are correct!

Rationale: In addition to the ISMP recommendations, your institution will have policies and procedures to guide safe medication administration practices. Be sure to know and follow these policies and procedures. These practices might include:

- Use of unit dosing
- Bar coding
- Independent double checks
  - Two nurses will:
    - Review the order
    - Calculate the dose
    - Compare results with unit dose
- Double signatures in medical record

A review of safe medication practices is available at RN.com: Medication Safety Course

## Case Study: A Review of Weight Based Heparin Calculations

Your 59-year-old patient is being treated on a medical surgical unit for pulmonary embolus following a

diagnosis of neck and mouth cancer. He weighs 150 lbs. or 68 kg.

**The physician orders the following:**

- Heparin Bolus 80 units/kg IV followed by Heparin Infusion 25,000 units/250 mL of D5W with an initial infusion rate 18 units/kg/hour.
- Draw a STAT aPTT six hours following initial bolus and any change in therapy
  - Once aPTT is between 46 - 70, two consecutive times in a row, then draw aPTT every 24 hours and a CBC every other day until discontinued
- Adjust heparin infusion based on sliding scale below:
  - If aPTT is < 35 sec, bolus with 80 units/kg IV and increase rate by 4 units/kg/hour
  - If aPTT is 36 - 45 sec, bolus with 40 units/kg IV and increase rate by 2 units/kg/hour
  - If aPTT is 46 - 70 sec, no change in therapy, then redraw APTT at next AM lab draw
  - If aPTT is 71 - 90 sec, decrease rate by 2 units/kg/hour
  - If aPTT is > 90 seconds, hold infusion for 1 hour, then decrease rate by 4 units/kg/hour

**Test Your Knowledge**

How many units of heparin will the bolus be?

- A. 5,440**
- B. 6,200
- C. 4,800
- D. 7,600

Rationale:  $(80 \text{ units}) \times (68 \text{ kg}) = 5,440 \text{ units}$

The pharmacy provides you with a unit dose syringe containing 1.1 mL of heparin with a concentration of 5000 units/mL.

**Test Your Knowledge**

What is your next step?

- A. Give the dose as the pharmacist drew it up
- B. Double check the dose based on the concentration
- C. Complete an independent double check**
- D. Call pharmacy for a multidose vial and draw up the medication yourself

Rationale: Your institution will have policies and procedures to guide safe medication administration practices. Be sure to know and follow these policies and procedures. These practices might include:

- Use of unit dosing
- Bar coding
- Independent double checks
  - Two nurses will:
    - Review the order
    - Calculate the dose
    - Compare results with unit dose

**Do you remember how to perform these calculations? If not or if you want more practice, review the RN.com courses on Calculations.**

**Conclusion**

Safe administration of heparin does not occur without the diligence of all involved in the patient's care. It is critical that orders are written clearly, unit dosing and other safe practices are utilized by the pharmacy to deliver the correct medication, and the nurse still needs to know how to calculate doses and amounts. There are many government agencies that can help your organization write policies, procedures, and protocols to help ensure that you are following the best practices.

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At the time this course was constructed all URL's in the reference list were current and accessible. RN.COM. is committed to providing healthcare professionals with the most up to date information available.

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