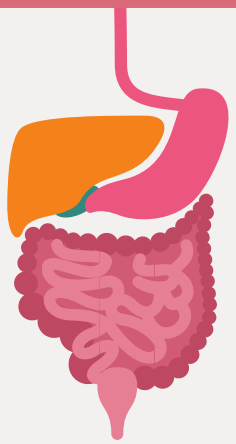
Anticoagulant drugs



Objectives:

- Introduction about coagulation cascade.
- Classify drugs acting as anticoagulants.
- Elaborate on their mechanism of action, correlating with that methods of monitoring.
- Contrast the limitations and benefits of injectable anticoagulants in clinical settings.
- Emphasis on the limitations of VKAs and on variable altering or modifying their response.

Done by:

- **A**bdulaziz Alhammad, **I**brahim AlAsoos, **Y**ousef Alsamil, **M**ohammed Abunayan, **S**ara Alkhalifah, **K**halid Aburas, **A**theer Alnashwan
- **Revision: J**waher Alharbi, **Q**usay Ajlan, **K**halid Aburas, **A**theer Alnashwan

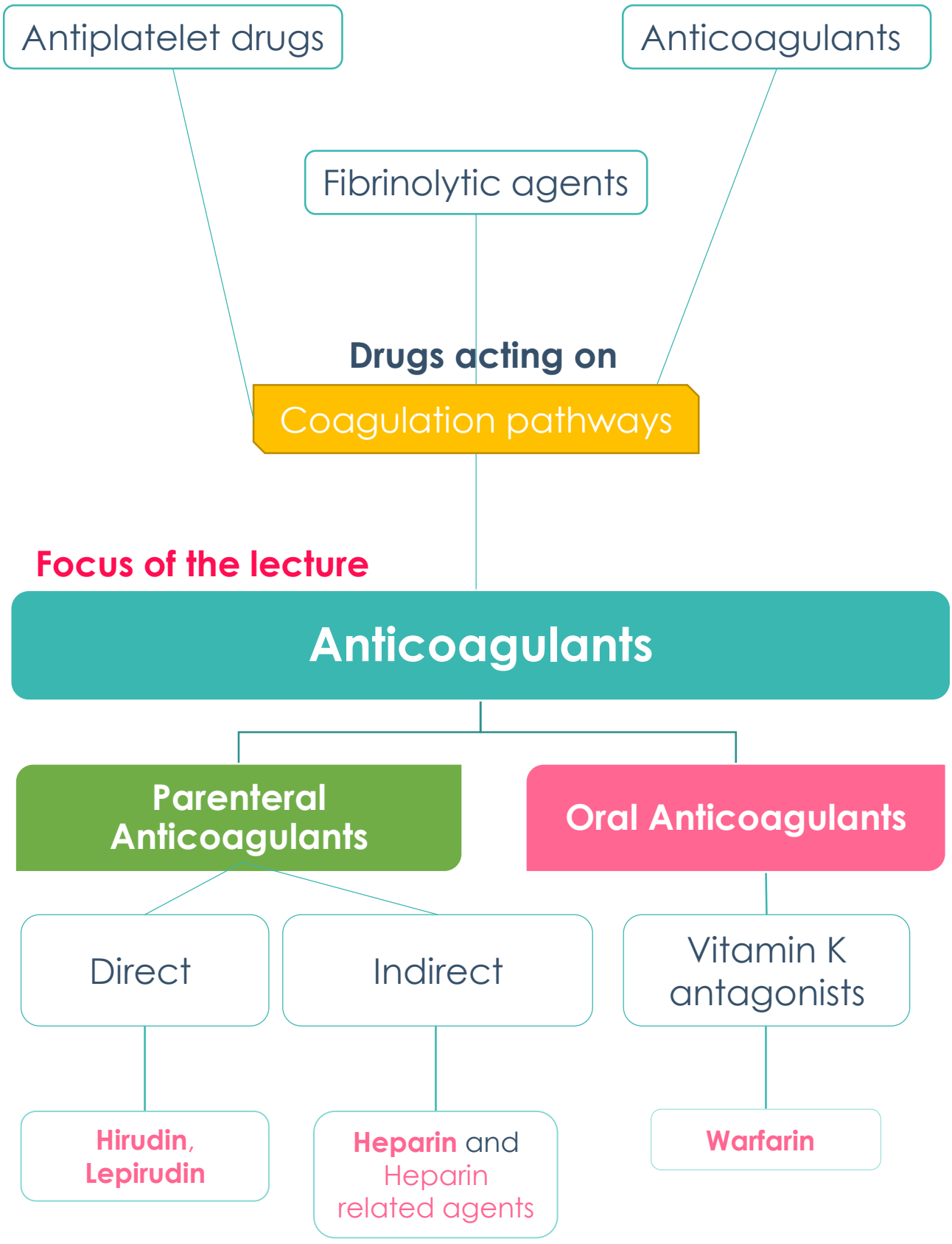
Editing file

Revised by
هشام الغفيلي & خولة العماري

Drugs names | Doctors notes | Important | Extra

« **باذلًا وسعي** في استنقاذها من الهلاك والمرض، والألم والقلق »

Mind Map



The most important slides are: 5, 6, 7, 8, 10 & 11

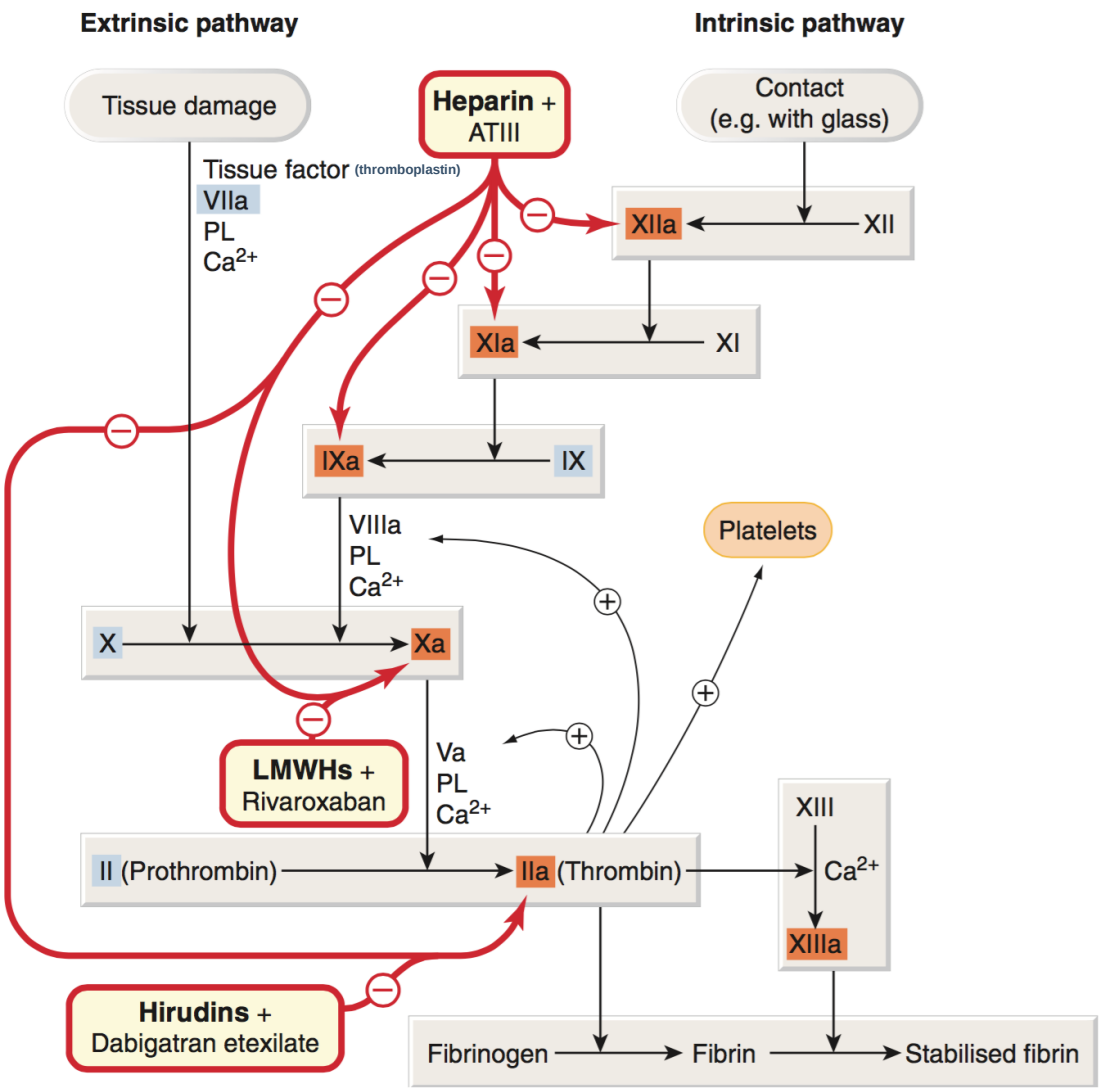
To understand better

Definitions we need to understand:

Anticoagulants	They **prevent thrombus formation** and extension by inhibiting clotting factors (e.g. heparin, low molecular weight heparin, coumarins (warfarin)
Antiplatelet drugs	They reduce the risk of clot formation by inhibiting platelet functions (e.g. aspirin and ticlopidine).
Fibrinolytic agents	They dissolve thrombi that is already formed (e.g. streptokinase)

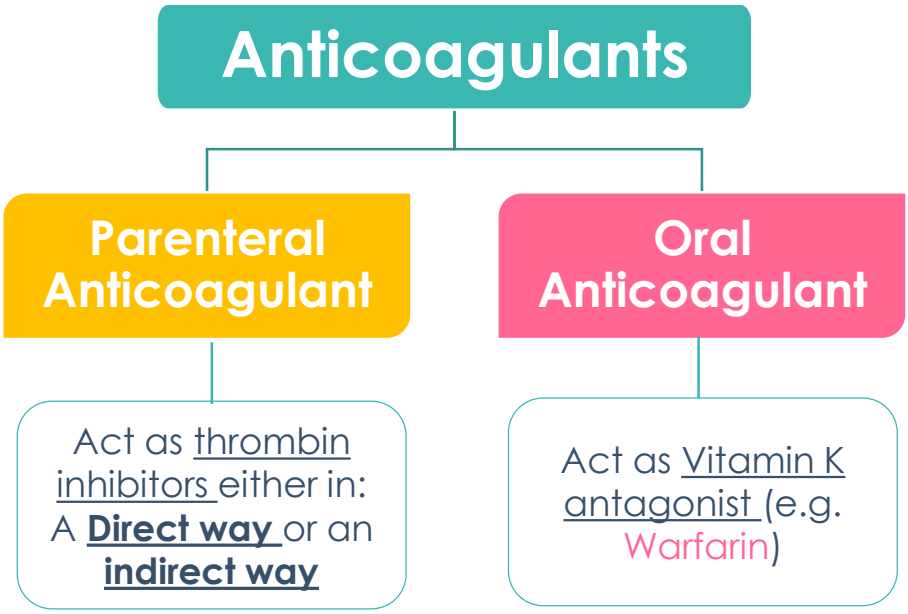
Coagulation pathways:

6:27min
7:43min



Endogenous inhibitors of coagulation:

Anti-thrombin III	It's a plasma protein that acts by **inhibiting the activated thrombin (factor IIa)** and **inhibits factor Xa**, it is the site of action of **heparin**.
Prostacyclin (prostaglandin I_2)	It is synthesized by endothelial cells and **inhibits platelet aggregation**.
Protein C and protein S	These are vitamin K dependent proteins that slow the coagulation cascade by inactivating factor Va and VIIIa. The site of action of warfarin



Anticoagulants indications:

- In **myocardial infarction**,
- **Deep venous thrombosis**.
- Peripheral arterial **emboli**, pulmonary **embolism** and many other conditions.
- Also used in **blood transfusions** and **dialysis procedures**.

Heparin

(Unfractionated Heparin –UFH-) overview

Origin	○ Normally occurs as a macromolecule in mast cells with Histamine with an unknown physiologic role. ○ Commercial preparations extracted from **beef** lung or **pig** intestine (can cause **hypersensitivity** reaction)
Function	○ It **stops the expansion of a thrombus** and prevents the formation of new thrombi, **but it does not dissolve an existing thrombus.** ○ **Indirect** thrombin inhibitor.
MOA (general)	○ It ↑ **the activity of the anticoagulant** "**Antithrombin III**" and consequently results in ⊗ **the activity of clotting factors.**
P.K	○ **Injectable** → rapidly acting anticoagulant. ○ It is strongly acidic. ○ Active **in vitro** (tested on blood within glass) and **in vivo** (tested on blood within living organisms) ○ **Low-Molecular Weight Heparin forms (LMWHs):** they are derived from the chemical or enzymatic degradation of UHF. They are 1/3 the size of UFH, used as well and have **many advantages over UFH**.

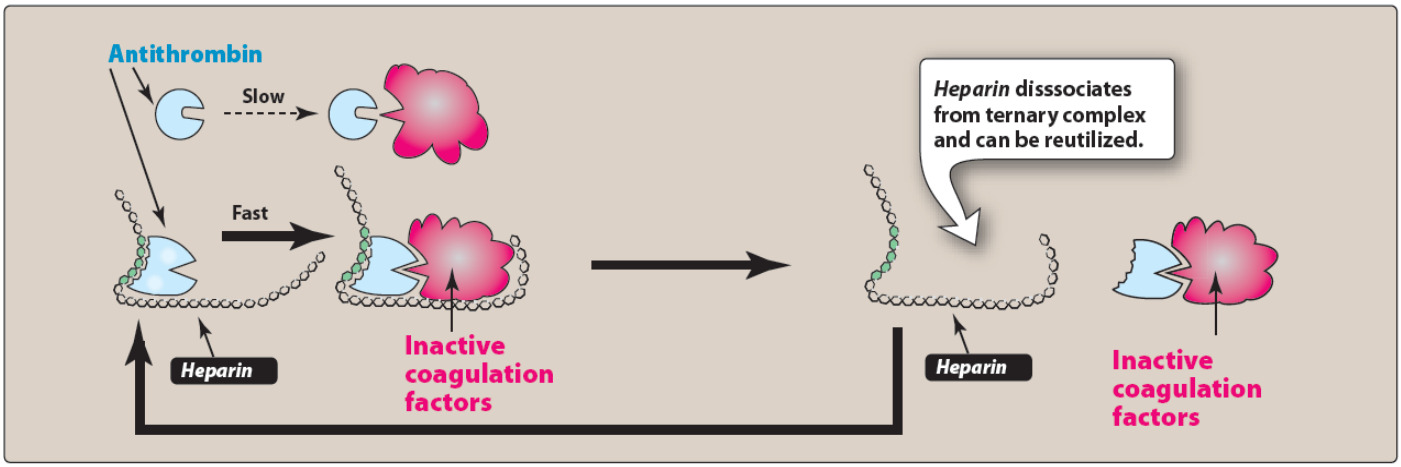


Figure 20.13
Heparin accelerates inactivation of coagulation factors by antithrombin.

Indirect Parenteral Anticoagulants

Drug	Heparin
Mech. of action	○ It acts **indirectly** by ↑ **the activity of the endogenous anticoagulant "Antithrombin III"** by **1000** folds → which **inhibits activated** clotting factors mainly **thrombin (factor IIa) and Xa.** ○ After binding to "Antithrombin III" → conformational changes that ↑ its rate of action by 1000 folds. ○ It binds to **both antithrombin III** and **thrombin** to form a **ternary complex.** ○ It dissociates **leaving the thrombin bound to its inhibitor** (see the previous figure) ○ Once dissociated, Heparin is **free to bind to another antithrombin** molecule and subsequently → **inhibits more thrombin**.
P.K	○ Heparin is **not absorbed from the GIT** → It should be administrated by **IV** or **SC** injection but **not IM as it causes haematomas at the injection site.** (bc muscles are rich in BV) ○ Once in the blood stream, **UFH binds to plasma proteins**, endothelial cells, macrophages & osteoblasts. → **Unpredictable pharmacological effect!** ○ Patients with renal impairment, the dose should be **reduced** to account for decreased renal function ,It undergoes depolymerization and desulfation to inactive products, Heparin has a **longer half-life** in patients with **hepatic cirrhosis**, Excreted into the urine (renal insufficiency prolongs the half-life), Half-life for heparin is 1.5-2 hours while LMWHs have 3-7 hour half-life. ○ Does **not** cross placenta, therefore, it is the **drug of choice as an anticoagulant during pregnancy.** ○ **Close monitoring of the activated partial thromboplastin time (aPTT) is necessary in patients receiving UFH**. UFH بالذات، لكن LMWH ما نحتاج
Therapeutic uses	○ Due to its **rapid onset of action**, it is used to **initiate immediate anticoagulation in thromboembolic disease** (PE, DVT, MI)[1] mainly as induction for **oral vitamin K antagonists** (warfarin) في البداية أبي الإفكت سريع؛ أستخدم الهيبارن، لكن لما تروح حالة الإمرجنسي، أستخدم غيره من الoral & slow onset of action ○ Prevention of **postoperative** DVT (in patient undergoing hip replacement) because their conditions leave them immobilized for long periods of time. ○ Prevention of coagulation during **renal dialysis** or **cardiac surgery**.

[1]PE: pulmonary embolism, DVT: deep vein thrombosis, MI: myocardial infraction.

Heparin (cont.)

Disadvantages

- The inconvenience of administration by injection.
- **The need for regular monitoring (aPTT)**
- UFH carries a risk of **heparin-induced thrombocytopenia (HIT)**, a ↓ in the platelet count and risk of **thrombosis** due to binding to platelets (chronic use due ↓ antithrombin III activity) (Venous thrombosis occurs most commonly)
- Generally, ↓ platelets → bleeding, ↑ platelets → thrombosis , however, HIT → ↓ platelets that cause **thrombosis instead of bleeding.** → Emergency situation!

ADRs

- Bleeding (major adverse effect of Heparin)
- **Allergic reactions** (chills, fever, urticarial "Rash that itches intensely sometimes with swelling") as heparin is of **animal origin** and should be used cautiously in patients with allergy.
- Long-term heparin therapy is associated with **osteoporosis.** → bc it binds to osteoblast.
- **Heparin-induced thrombocytopenia (HIT)** → in 4% pts. on heparin, latency 5-10 dys. after 1st exposure or 2-3 dys. after re-exposures → Venous > Arterial thrombosis.

C.I

- Bleeding disorders, **hemophilia**.
- Patients with **hypersensitivity** to the drug.
- **Recent surgery of the brain, eye or spinal cord.**
- **Threatened abortion** → blood into the placenta → losing of pregnancy.
- Alcoholics.

Reversal of Heparin Action

- Discontinuation (stopping) of the drug → No packed platelets → **More thrombosis**. → give **DTI** (direct thrombin inhibitors)
- **Heparin** is strongly **acidic &** -ve charge and is neutralized by **I.V. Protamine Sulfate** (a strongly **basic &** +ve charge protein). **It combines with heparin to form a stable complex devoid of anticoagulant activity.** **Completely block the effect of heparin, while Protamine incompletely blocks LMWH effect! (imp).** It is very imp to treat this condition!

lower molecular weight heparin (LMWH)

Heparin fragments (Enoxaparin, Dalteparin) **&** **Synthetic pentasaccharide** (Fondaparinux)

Drug	Enoxaparin	Dalteparin	Fondaparinux

MOA

- Increase the action of anti-thrombin III on factor **Xa** (inhibit factor X) but there's **no action on thrombin**, (because the molecules are **too small to bind** to both enzyme & inhibitor). UFH inhibit both IIa & Xa

الفرق بين UFH و LMWH مهمة مرة، احتمال SAQs

Advantages

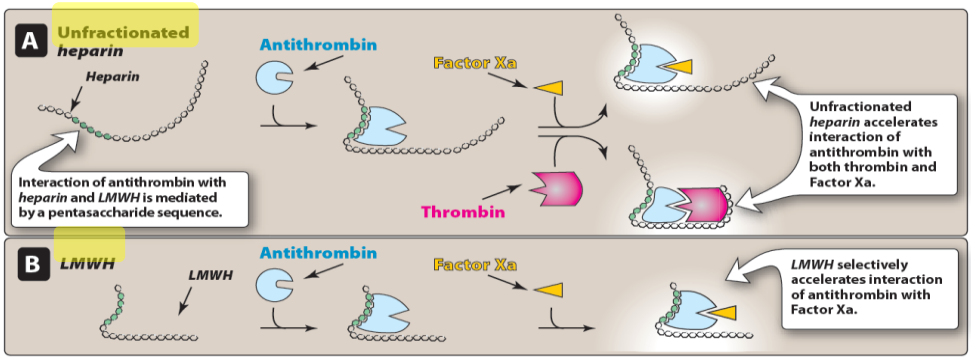
Advantages may come in SAQs if not in MCQs ☺

- ✓ Are used increasingly in place of unfractionated heparin UFH.
- ✓ The convenience of once or twice daily subcutaneous injection.
- ✓ Have equal efficacy.
- ✓ **Without frequent laboratory monitoring (outpatient therapy)**
- ✓ Have **more predictable** anticoagulant response because of **reduced** binding to plasma protein, platelets & osteoblasts.
- ✓ Better bioavailability & **longer $t_{1/2}$**.
- ✓ Less platelet activation and Lower risk of **re-thrombosis** & **thrombocytopenia**

Synthetic Heparin Derivatives

Drug	**Fondaparinux**
MOA	○ Synthetic compound that inhibits factor **Xa** by anti-thrombin but **does not inhibit thrombin**.
Advantages	✓ Less likely to trigger **HIT** than UFH & LMWH. ✓ Can be given **once** a day **without** **coagulation monitoring**.

Comparison between UFH & LMWH



DRUG CHARACTERISTIC	*HEPARIN*	*LMWHs*
Intravenous half-life	2 hours	4 hours
Anticoagulant response	Variable	Predicable
	HIT & osteoprosis	Less ADRs
Bioavailability:	20%	90%
Major adverse effect	Frequent bleeding	Less frequent bleeding
Setting for therapy	Hospital	Hospital and outpatient
Specific antagonist	Protamine sulphate (complete)	Incomplete

Direct thrombin inhibitors (DTIs)

Drug	**Hirudin** was isolated from the saliva of the leech علقة	**Lepirudin** polypeptide that binds directly to the active site of thrombin
MOA	○ Exert their effect by direct binding to **thrombin**.	
Advantages	✓ This direct effect is **rapid & potent**. ✓ **Not associated with thrombocytopenia.** ✓ **Recombinant hirudin "Lepirudin" is used as IV anticoagulant in patients with HIT** (Heparin-induced thrombocytopenia) ✓ Lepirudin, like heparin, it must be administered parenterally and is **monitored by the aPTT.**	

Oral Anticoagulants "Vitamin K antagonists"

Vitamin K (Fat soluble vitamin)

It is from the coumarin anticoagulants, which include commonly used warfarin and rarely used dicumarol.

Sources of vitamin K

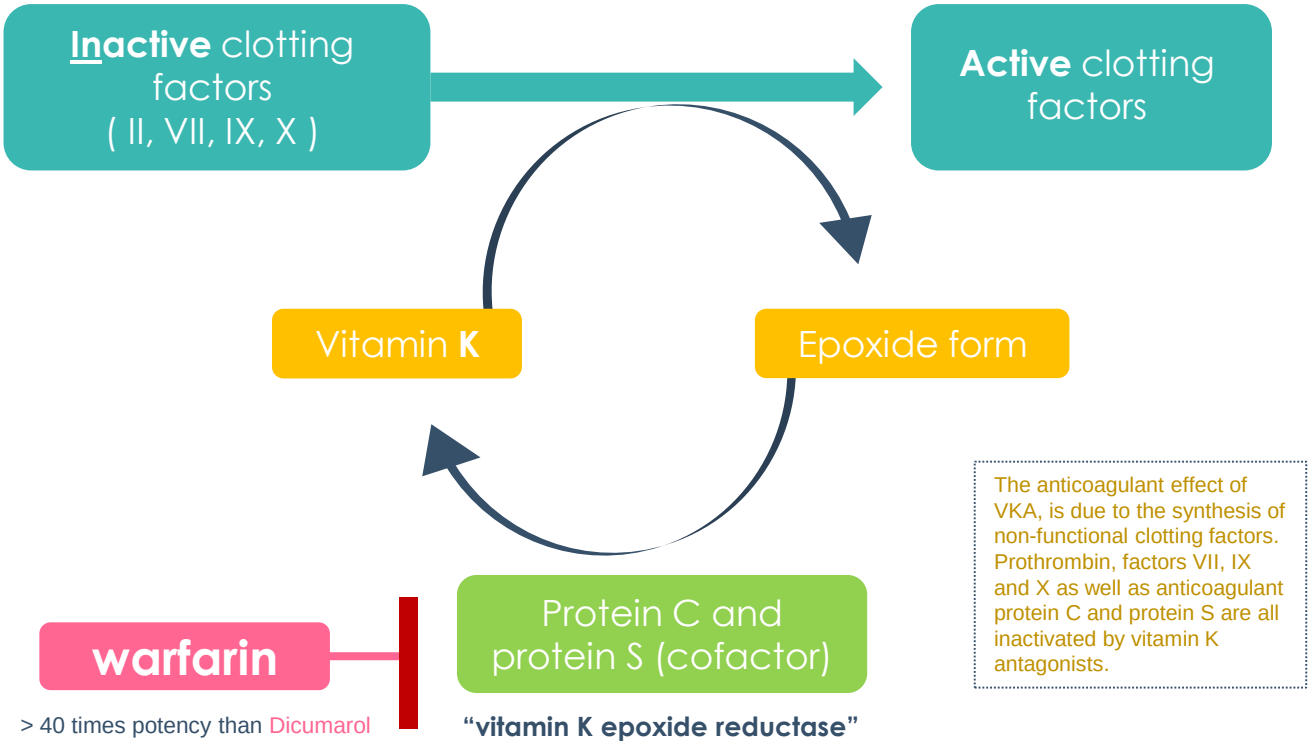
1) Green vegetables
2) Synthesized by intestinal flora

Vitamin k Required for

1) Synthesis of Factors **II**, **VII**, **IX** , **X** → 27910 ☺ سبع وعشرين ألف وتسمع مية وعشرة
2) Protein **C** and **S** (endogenous anticoagulants)

Causes of vitamin k deficiency

1) Malnutrition
2) Malabsorption
3) Antibiotic therapy



The anticoagulant effect of VKA, is due to the synthesis of non-functional clotting factors. Prothrombin, factors VII, IX and X as well as anticoagulant protein C and protein S are all inactivated by vitamin K antagonists.

After the peptide chains in clotting factors II, VII, IX and X have been synthesised, reduced vitamin K (the hydroquinone) acts as a **co-factor in the conversion of glutamic acid to γ-carboxyglutamic acid**. During this reaction, the reduced form of vitamin K is converted to the **epoxide**, which in turn is reduced to the hydroquinone by **vitamin K epoxide reductase**, the **site of action of warfarin**.

Vitamin K (Fat soluble vitamins) Antagonist

Drug	Coumarin (Warfarin)
MOA	○ It inhibits the synthesis of biologically **active forms of vitamin K**-dependent clotting factors II, VII, IX and X as well as **anticoagulant proteins C & S**. ○ 3-4 days until effect is seen. → Because it **does not have any effect on already-synthesized coagulation factors**; therefore, the therapeutic effects are not seen until these factors are depleted
P.D	○ Act only **in vivo**. (heparin act in vivo & in vitro) ○ Bioavailability 100% (taken orally) ○ 98% bound to plasma proteins (albumin) ○ Monitoring anticoagulant effect of warfarin by measuring **PT** (prothrombin time → the rate at which prothrombin is converted to thrombin in citrated blood with added calcium; used to assess the extrinsic coagulation system of the blood), which is expressed as an **International Normalized Ratio (INR)**. مهم تعرفون الاسم ○ Their effect takes **several days** (3-4) to develop because of the time taken for degradation of circulating functional clotting factors, therefore the onset of action **starts when these factors have been eliminated.** ○ It has a **slow offset of action** due to the time required for synthesis of new, functional coagulation factors.
Uses	○ Warfarin is used to **prevent the progression or recurrence of acute deep vein thrombosis or pulmonary embolism** after initial heparin treatment. ○ It is also used for the **prevention of venous thromboembolism during orthopedic or gynecologic surgery**.
Disadvantages	○ Variable, unpredictable effect necessitating **regular INR monitoring** and dose adjustment. ○ **Narrow therapeutic window** leading to increased risk of severe bleeding. ○ **Slow onset and offset of action**. ○ **Numerous interactions** with foods containing vitamin K and drugs. ○ Polymorphisms in CYT P450 **(2C9)** isoforms that metabolizes **warfarin** → adds to its non predictable response → liability to toxicities or under use. ○ Cutaneous necrosis with reduced activity of protein C sometimes occurs during the first weeks of therapy
C.I	○ **Pregnancy** → as it can **cross the placental barrier** and cause **Teratogenicity abortion** (1st months), **hemorrhagic disorder** (later stages) in the fetus and birth defects.
Factors altering response	From boys' slides, read it 1. Vitamin K deficiency • **Inadequate diet**; malnutrition, dieting, decreased GI absorption. 2. Impaired synthesis of clotting factors • In **hepatocellular disorders**; (hepatitis; infective or chronic alcoholism) 3. Increased catabolism (degradation) of clotting factors → augment warfarin's effect • In **hypermetabolic states**; as in fever, **thyrotoxicosis** 4. Decreased plasma protein binding → increase elimination of free drug & shortening of its t1/2. as pts with nephrotic syndrome (**proteinuria**) 5. Decreased catabolism of clotting factors → **Hypothyroidism** 6. Hereditary resistance to oral anticoagulants.

Drug interactions with oral anticoagulants

Potentiate anticoagulation through inhibition of warfarin metabolism

1. Inhibition of Vit. K synthesis by intestinal flora; **oral antibiotics**
2. Inhibition of Vit K **absorption**; liquid **paraffin**. (laxative)
3. Decrease in drug metabolism by **microsomal enzyme inhibitors**; **chloramphenicol** (antibiotic) & **cimetidine**.
4. **Displacment** of the drug from protein binding sites; **phenylbutazone** & **salicylates**. The most serious interactions
   When the drug bind to albumin, its effect is low.
   Once it dissociate from it → potentiate its action
5. Co-administration of drugs that **increase bleeding tendency** by; inhibiting platelet function; **NSAIDs**, **heparin**.

Attenuation (weakness) of anticoagulant through stimulation of warfarin metabolism

1. **Inhibition of drug absorption** from GIT; **cholystyramine**, **colestipol**.→ lipid lowering agents, they bind warfarin in the **intestine and reduce its absorption and bioavailability**.
2. **Increase in synthesis of clotting factors**; VitK, oral **contraceptives**. السنّات اللي بياخذوا oral contraceptive regularly بيبؤوا عرضة لل**DVT**
3. Increase in drug metabolism by **microsomal enzyme inducers**; **Carbamazepine**, **barbiturates**, **rifampicin**.

What do you do in case of warfarin associated bleeding?

- If we have bleeding due to warfarin
- **Stop** the drug
- IV injection of **vitamin K** (vitamin K1 → phytonadione) (the antidote of warfarin)
- Fresh frozen blood

Cases – From Dr's slides.

An old, peptic ulcer patient, sustained on cimetidine, has been bed ridden since a month following a major orthopedic surgery for pelvic fracture. The last week he began to complain of pain, tenderness, warmth & swelling of his left leg. He was diagnosed as deep vein thrombosis. His treating physician put him first on heparin that was replaced after three days by VKAs. Today he began to show bleeding of gums.

- **What is the expected explanation of his finding?** Warfarin toxicity → Cimetidine inhibits its metabolism
- **Will the treating physician 1st of all, consider giving an antidote to stop bleeding (if so then state) or will he probably ask for lab investigation (if so then state)?** bleeding of gums → not emergency situation, so we have time to do lab investigations.
- **Once lab findings are there, is the physician expected first to withdraw or to adjust the existing therapy?** Give him another anti-peptic ulcer drug.

A young rheumatic artheritic patient has underwent valve replacement and is sustained on warfarin therapy for the last three years. When she married, last summer, she did not want to get pregnant, so she has taken since then, oral contraceptive pills.
Her regular lab monitoring today showed a decrease in INR this time.

- **What is the expected explanation of her lab result?** Contraceptive pills induces the coagulation factors → ↓ INR → increase tendency of thrombus.
- **What will the treating physician consider doing?**

A. Giving heparin on top
B. Adjusting warfarin dose → 1st step
C. Stopping the OC → Better
D. Stopping warfarin

A 53 years old patient had an aortic valve replacement since 5 years and he is sustained on warfarin. A week ago, he developed low grade fever, diarrhea and was diagnosed as having typhoid. He was given rehydration fluid and a course of chloramphenicol.
Today he is complaining from haematuria.

Which one of the following best explains the haematuria?

A. Inhibition of Vit K synthesis by chloramphenicol
B. Displacement of warfarin from protein binding site by rehydration
C. Decrease in warfarin metabolism induced by chloramphenicol
D. Inhibition of Vit K absorption caused by the diarrhea

Which is the right decision to do in such a case?

A. Give a urinary antiseptic for fear of infection
B. Stop administering the regular intake of warfarin
C. Adjust the dose of warfarin after monitoring the situation.
D. Stop the course of chloramphenicol intended for typhoid therapy

Summary-1

Drug	Heparin	Lower molecular weight heparin (LMWH)	
		Enoxaparin	Dalteparin
Mech. of action	indirectly by increasing the activity of the endogenous anticoagulant "antithrombin III" which inhibits activated clotting factors mainly **thrombin (factor IIa) and Xa**	LMWHs increase the action of antithrombin III on factor Xa but not its action on thrombin, because the molecules are too small to bind to both enzyme and inhibitor	
P.K	**I.V or S.C** Not I.M → hematoma	advantage over UFH	• it works on factor Xa and it don't work on thrombin IIa The convenience of once- or twice- daily subcutaneous injections without regular coagulation monitoring. • More predictable response • Long plasma half-life and improved bioavailability • Less plasma protein binding • Less platelet activation and lower risk of re-thrombosis and thrombocytopenia
Indications	- initiate immediate anticoagulation in (PE, DVT, MI) mainly as induction for oral vitamin K antagonists (VKAs) - Prevention of postoperative DVT - Prevention of coagulation during renal dialysis or cardiac surgery - Drug of choice in pregnancy	Mech. Of action	Fondaparinux: a synthetic heparin compound that inhibits factor Xa by antithrombin but does not inhibit thrombin Hirudin, Lepirudin: • DTIs exert their anticoagulant effect by direct binding to thrombin • This direct effect is rapid and potent
Antidote	Protamine sulfate	Advantages	-can be given once a day at a fixed dose without coagulation monitoring -Less likely than UFH or LMWHs to trigger HIT DTIs are not associated with the development of thrombocytopenia
ADRs	-bleeding -Allergic reactions (chills, fever, urticaria) -Longterm heparin therapy →osteoporosis -heparin induced thrombocytopenia		
C.I	-Bleeding disorders, -Hypersensitivity -Recent surgery		

Summary-2

Drug	Warfarin
Mech. of action	• Inhibits synthesis of Vitamin K-dependent coagulation factors II, VII, IX, & X as well as anticoagulant proteins C & S • Does not have an effect on already-synthesized coagulation factors; therefore, the therapeutic effects are not seen until these factors are depleted • 3-4 days until effect is seen
Limitations	Has narrow therapeutic window, So any change in that level can be hazardous. Slow onset of action Polymorphisms in CYT P450 Numerous food- & drug-drug interactions liability to toxicities or under use.
C.I	**Pregnancy** → give heparin or LMWH instead
Factors altering response	1-Inadequate diet 2-Impaired synthesis of clotting factors: a- In hepatocellular disorders b- In hepatic congestion 3-Increased catabolism of clotting factors: In hypermetabolic states Decrease response: 1-Decreased plasma protein binding: elimination of free drug & shortening of its t1/2 as pts with nephrotic syndrome (proteinuria). 2-Decreased catabolism of clotting factors: Hypothyroidism. 3-Hereditary resistance to oral anticoagulants
Drugs modulating response	1- Inhibition of Vit. K synthesis by intestinal flora; oral antibiotics 2. Inhibition of Vit K absorption; liquid paraffin 3. Decrease in drug metabolism by microsomal enzyme inhibitors (chloramphenicol, & cimetidine) 4. Displacement of the drug from protein binding sites; (phenylbutazone & salicylates) 5. Co-administration of drugs that increase bleeding tendency by; - inhibiting platelet function; NSAIDs - inhibiting coagulation factors; heparin

IF not clear, click here

Drugs affecting blood coagulation

Procoagulant drugs: vitamin K

- Reduced vitamin K is a co-factor in the post-translational γ-carboxylation of glutamic acid (Glu) residues in factors II, VII, IX and X. The γ-carboxylated glutamic acid (Gla) residues are essential for the interaction of these factors with Ca^{2}+ and negatively charged phospholipid.

Injectable anticoagulants (e.g. heparin, low-molecular-weight heparins)

- Potentiate antithrombin III, a natural inhibitor that inactivates Xa and thrombin.
- Act both in vivo and in vitro.
- Anticoagulant activity results from a unique pentasaccharide sequence with high affinity for antithrombin III.
- Heparin therapy is monitored via activated partial thromboplastin time (APTT), and dose individualised. Unfractionated heparin (UFH) is used for patients with impaired renal function.
- Low-molecular-weight heparins (LMWHs) have the same effect on factor X as heparin but less effect on thrombin; therapeutic efficacy is similar to heparin but monitoring and dose individualisation are not needed. Patients can administer them subcutaneously at home. They are preferred over UFH except for patients with impaired renal function.

Oral anticoagulants (e.g. warfarin)

- Act on vitamin K epoxide reductase component 1 (VKORC1) to inhibit the reduction of vitamin K epoxide, thus inhibiting the γ-carboxylation of Glu in II, VII, IX and X.
- Act only in vivo, and their effect is delayed until preformed clotting factors are depleted.
- Many factors modify their action; genetic factors (polymorphisms of CYP2C6 and VKORC1) and drug interactions are especially important.
- There is wide variation in response; their effect is monitored by measuring the international normalised ratio (INR) and the dose individualised accordingly.
- Orally active direct thrombin inhibitors (e.g. dabigatran etexilate) or factor Xa inhibitors (e.g. rivaroxaban) are used increasingly and do not require monitoring/dose individualisation.

Extra helpful summaries!

Component or Factor	Common Synonym	Target for the Action of:
I	Fibrinogen	
II	Prothrombin	Heparin (IIa); warfarin (synthesis)
III	Tissue thromboplastin	
IV	Calcium	
V	Proaccelerin	
VII	Proconvertin	Warfarin (synthesis)
VIII	Antihemophilic factor (AHF)	
IX	Christmas factor, plasma thromboplastin component (PTC)	Warfarin (synthesis)
X	Stuart-Prower factor	Heparin (Xa); warfarin (synthesis)
XI	Plasma thromboplastin antecedent (PTA)	
XII	Hageman factor	
XIII	Fibrin-stabilizing factor	
Proteins C and S		Warfarin (synthesis)
Plasminogen		Thrombolytic enzymes, amino-caproic acid

Table summary of warfarin interaction

Clinical uses of anticoagulants

Heparin (often as low-molecular-weight heparin) is used acutely. **Warfarin** or a direct thrombin or Xa inhibitor is used for prolonged therapy. Anticoagulants are used to prevent:

- deep vein thrombosis (e.g. perioperatively)
- extension of established deep vein thrombosis
- pulmonary embolus
- thrombosis and embolisation in patients with atrial fibrillation (Ch. 21)
- thrombosis on prosthetic heart valves
- clotting in extracorporeal circulations (e.g. during haemodialysis)
- myocardial infarction in patients with unstable angina.

MCQs

1- Which of the following is a major adverse effect of Heparin?
A- Renal failure
B- Hepatic cirrhosis
C- Bleeding
D- Dependance

2- Which of the following is a therapeutic use of Heparin?
A- Thrombocytopenia
B- Post-operative deep vein thrombosis
C- Allergic reactions
D- Osteoporosis

3- Which of these drugs is used as anticoagulant in patient with Heparin induced thrombocytopenia?
A- Lepirudin
B- Fondaparinux
C- Enoxaparin

4- Which of these drugs is a direct thrombin inhibitor?
A- Enoxaparin
B- Lepirudin
C- Dalteparin

5- 54-year-old male with a prosthetic aortic valve replacement complained to his family physician of black and tarry stools. Physical examination and vital signs were unremarkable except for subconjunctival hemorrhages and bleeding gums. Stools tested positive for heme, and hematuria was observed. The patient has been receiving oral warfarin since his valve replacement 1 year earlier. Prothrombin time was found to be significantly elevated. Which one of the following therapies would provide the most rapid recovery from the observed bleeding second- ary to warfarin treatment?
A- Intravenous vitamin K
B- Transfusion of fresh frozen plasma
C- Intravenous protamine sulfate
D- Immediate withdrawl of warfarin treatment

6- A 33-year-old woman who is 20 weeks pregnant with a porcine heart valve is at risk for thromboembolism. Which of the following is the best agent to use in this situation?
A- Heparin
B- Streptokinase
C- Warfarin

7- Which one of the following is NOT an indication for anticoagulants:
A- Myocardial infarction
B- Pulmonary embolism
C- Blood transfusion
D- Bleeding diatheses

Answers: 1-C 2-B 3-A 4-B 5-B 6-A 7-D

MCQs

8- Which one of the following acts by inhibiting factor IIa:
A- Protein C
B- PG I2
C- Anti-thrombin III
D- Protein S

9- The primary mechanism by which heparin prevents coagulation of blood is:
A- Direct inhibition of prothrombin to thrombin conversion
B- Facilitation of antithrombin III mediated inhibition of factor Xa and thrombin
C- Activation of antithrombin III to inhibit factors IX and XI
D- Inhibition of factors XIIa and XIIIa

10- The following can be used to antagonise the action of heparin in case of overdose:
A- Heparan sulfate
B- Dextran sulfate
C- Protamine sulfate
D- Ancrod

11- The most clear cut beneficial results are obtained in the use of anticoagulants for the following purpose:
A- Prevention of recurrences of myocardial infarction
B- Prevention of venous thrombosis and pulmonary embolism
C- Cerebrovascular
D- Retinal artery thrombosis

12- The following is a proven human teratogen:
A- Heparin
B- Warfarin
C- Fondaparinux

13- A 61-year-old female is hospitalized for COPD exacer- bation. She is obese and not able to ambulate very far on her own. Upon discharge, the physician wants to send her home on heparin to reduce the risk of deep vein thrombosis. Why would the physician choose a low-molecular-weight heparin (LMWH) instead of unfractionated heparin (UFH)?
A- LMWH is a better inhibitor of thrombin
B- LMWH carries no risk of bleeding
C- LMWH does not cause HIT
D- LMWH is easier to manage for outpatients

14- Anticoagulation is needed immediately in a patient with pulmonary embolism. Since there is some concern about a possible drug-induced thrombocytopenia, the most appropriate drug for parenteral administration in this patient is:
A- Clopidogrel
B- Heparin
C- Warfarin
D- Enoxaparin

Answers: 8-C 9-B 10-C 11-B 12-B 13-D 14-D

Thank you for checking our team!

Pharmacology 435

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Sources:

1. 435's slides.
2. Pharmacology (Lippincotts Illustrated Reviews Series), chapter 20, 5th edition.
3. Rang & Dale's pharmacology, chapter 24, 7th edition.
4. Basic & Clinical Pharmacology by Katzung, chapter 34, 12th edition.