

**Anticoagulants**

1. Which of the following agents are considered as anticoagulants?

- a) Warfarin
- b) Heparin
- c) Clopidogrel
- d) Streptokinase
- e) Dabigatran

# Drugs in thrombosis



```
graph TD; A[Drugs in thrombosis] --> B[Antiplatelet drugs]; A --> C[Thrombolytic]; A --> D[Anticoagulants]; B --> E["Aspirin<br/>Dipyridamole<br/>Clopidogrel<br/>Prasugrel<br/>Ticagrelor<br/>Glycoprotein IIb/IIIa receptor antagonists<br/>Epoprostenol<br/>Terutroban"]; C --> F["Streptokinase<br/>Plasminogen activators"]; D --> G["Direct acting-Heparins<br/>UFH<br/>LMW(Enoxaparin)<br/>(Fundoparinux)"]; D --> H["Indirect acting-Coumarins/Warfarin"];
```

The diagram is a hierarchical flowchart. At the top is a box labeled 'Drugs in thrombosis'. A line from this box branches into three boxes: 'Antiplatelet drugs', 'Thrombolytic', and 'Anticoagulants'. From 'Antiplatelet drugs', a line leads down to a box containing a list of drugs: Aspirin, Dipyridamole, Clopidogrel, Prasugrel, Ticagrelor, Glycoprotein IIb/IIIa receptor antagonists, Epoprostenol, and Terutroban. From 'Thrombolytic', a line leads down to a box containing 'Streptokinase' and 'Plasminogen activators'. From 'Anticoagulants', a line branches into two boxes: 'Direct acting-Heparins' (listing UFH, LMW(Enoxaparin), and (Fundoparinux)) and 'Indirect acting-Coumarins/Warfarin'.

## Antiplatelet drugs

Aspirin  
Dipyridamole  
Clopidogrel  
Prasugrel  
Ticagrelor  
Glycoprotein IIb/IIIa receptor antagonists  
Epoprostenol  
Terutroban

## Thrombolytic

Streptokinase  
Plasminogen  
activators

## Anticoagulants

Direct acting-Heparins  
UFH  
LMW(Enoxaparin)  
(Fundoparinux)

Indirect acting-  
Coumarins/Warfarin

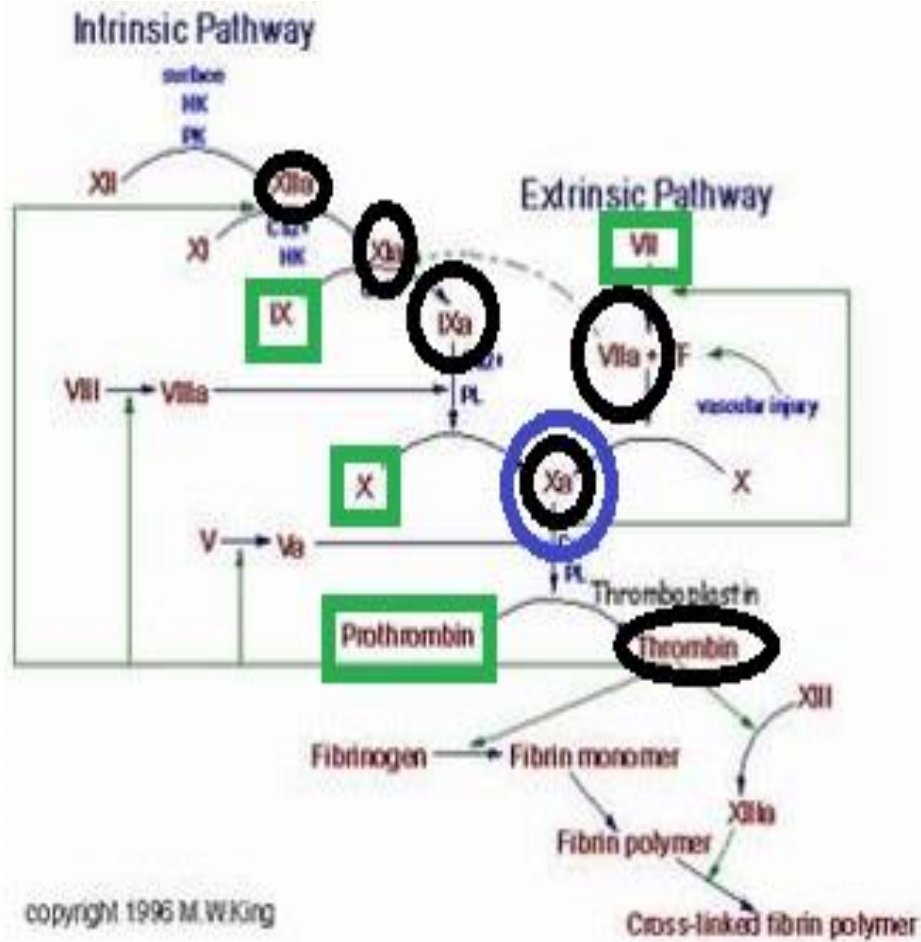
# Anticoagulants

- heparinoids – unfractionated heparin (UFH), low-molecular-weight heparin (LMWH) and fondaparinux
- vitamin K antagonists (VKA) – warfarin
- new oral agents – dabigatran, rivaroxaban, apixaban

???Mechanisms of action

???Monitoring

# Coagulation pathways



Home work-READ ABOUT  
PT, INR & APTT

- ❖ Standard or UFH
  - ↓
  - Facilitation of Antithrombin III
  - Monitored by APTT
- ❖ LMW
  - ↓
  - Inhibition of Xa>IIa
  - Monitored by Xa level
- ❖ Warfarin
  - ↓
  - Interfere with Vit K metabolism
  - Monitored by PT(INR)

# Heparin

2. Which of the following statements are true regarding heparin
- a) Unfractionated heparin has a short half life compared to Low molecular weight heparin
  - b) Low molecular weight heparin is usually administered as an IV infusion
  - c) Unfractionated heparin is known to cause thrombocytopenia in some patients
  - d) Low molecular weight heparin is contraindicated during pregnancy
  - e) Low molecular weight heparin is monitored by APTT

UFH	LMWH
MW—13,000	MW-2000-8000 (Bioavailability is higher)
Unpredictable pharmacokinetics and a short elimination half-life	more predictable pharmacokinetics, a longer half-life
Facilitation of Antithrombin III & Inhibition of serine protease dependant coagulation factors	Binds to antithrombin but Inhibition of Xa>IIa
intravenous (IV) infusion or subcutaneous (SC) injection	Easier mode of administration (SC injection) than UFH.
Needs infusion followed by bolus	Bolus doses
SE- heparin-induced thrombocytopenia (HIT) and osteopenia	Less compared to UFH
No dose adjustment in RF	Reduce dose in RF
Monitoring - APTT	Factor Xa levels

# Warfarin

3.T/F regarding warfarin

- a) prevents gamma carboxylation of vitamin K-dependent clotting factors
- b) Monitored by APTT
- c) Safe during 1<sup>st</sup> trimester of pregnancy
- d) Is used to treat patients with acute myocardial infarction
- e) Should be combined with heparin or enoxaparin always when initiating therapy



# Mechanism of action

Prevents gamma carboxylation of vitamin K-dependent clotting factors (II, VII, IX and X), producing an anticoagulant effect by reducing their concentrations

# INR

4. You are seeing a 50 year old female who is on warfarin at the clinic. Her recent investigations show an INR value of 2.5. She is otherwise clinically well. The patient asks you whether the investigation result is satisfactory. What further information will you require to answer that question ?

# INR

- Reagent used to test PT is Thromboplastin
- When these reagents are derived from various sources they give rise to different PT results for the same sample.
- Therefore each thromboplastin is being compared with an international reference preparation so that it can be assigned an International Sensitivity Index (ISI)

INR is the “Ratio of patient’s PT to a Normal control when using the International reference preparation”

$$\text{INR} = (\text{prothrombin}_{\text{test}} / \text{prothrombin}_{\text{control}})^{\text{ISI}}$$

# INR targets with warfarin

Indication	Target INR
Pulmonary embolism	2.5
Proximal deep vein thrombosis	
Calf vein thrombosis	
Non-rheumatic atrial fibrillation (CHADS <sub>2</sub> score >1)	
Mural thrombus	
Cardiomyopathy	
Mechanical prosthetic aortic heart valve	3.5
Bioprosthetic valve	
Mechanical prosthetic mitral heart valve	
Recurrent venous thrombosis on warfarin therapy	

5. 60 year old male on warfarin for non valvular AF presents with gross hematuria. His INR is 7. What is the most appropriate immediate step in management?

- a) Stop warfarin and administer Prothombin factor concentrate
- b) Continue warfarin and give FFP
- c) Vitamin K and FFP
- d) FFP only
- e) Give IV tranexamic acid

INR/Bleeding	Action
When target is 2.5 & pt's INR is >3<6	?
When target is 3.5 & pt's INR is >4 <5	?
INR >5<8, No bleeding	?
INR >8 , no or minor bleeding	?
Major bleeding	Stop warfarin Give 4-factor prothrombin complex concentrate (FFP if PCC is not available) Give IV Vit k

PCC?

It contains sufficient concentrations of factors II, VII, IX and X to allow reversal of the anticoagulant effects of warfarin

6. What advice will you give a patient on commencing therapy with warfarin?

☐ **Introduce your self**

☐ **Introduce the name of the drug**

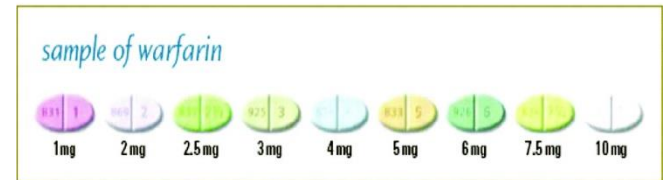
- Avoid getting warfarin from different sources

☐ **How Does Warfarin Work?**

By decreasing the clotting tendency of blood

☐ **Warfarin must be taken exactly as prescribed.**

- Take it at a constant time everyday
- Don't take meals 2hrs before & after the consumption of the drug
- If you miss the pill and remember it within the same day take it.
- But never take a double dose the next day
- Never increase or decrease your dose unless instructed to do so by your healthcare provider.





## ❑ **Monitoring and Dosing Tips**

- The goal of warfarin therapy is to decrease the clotting tendency, not to prevent clotting completely.
- Therefore, the effect of warfarin must be monitored by blood tests.
- On the basis of the results daily dose of warfarin will be adjusted to keep clotting time within a target range.
- PT/INR is the test used. It's measured 3days after a changing a dose & monthly thereafter.

## ❑ **Side Effects**

- Clotting due to underdosing or bleeding due to excessive anticoagulation.
- Most serious bleeding is gastrointestinal or intracerebral.

## ❑ Side Effects ctd

- Signs of unusual bleeding include:
- Skin bleeding-purpura, bruising
- bleeding from the gums
- blood in the urine
- bloody or dark tarry stool
- a nosebleed
- vomiting blood.
- An unusual headache or a headache that is more severe than usual may signal intracerebral bleeding.

**☐ Seek treatment immediately if you experience the following signs**

- Skin-brusing, purpura
- Coughing up large amounts of bright red blood
- Vomiting blood
- Bleeding that will not stop
- Dark red or dark brown urine
- Bright red blood in stool/Dark tarry stools
- Fall or injury to the head
- Headache that is severe or unusual
- Severe headache, confusion, weakness or numbness

**❑ Some simple changes to decrease the risk of bleeding while taking warfarin include the following:**

- Use a soft-bristle toothbrush
- Shave with an electric razor rather than a blade
- Take care when using sharp objects, such as knives and scissors
- Avoid activities that have a risk of falling or injury (e.g., contact sports)

## ☐ **Pregnancy**

- Not recommended during pregnancy
- If you become pregnant while on warfarin inform doctors immediately.
- Need to change the drug due to risk of teratogenicity in T1 & risk of fetal haemorrhage later
- Contraception-



## ☐ **Breast feeding-Safe**

## ☐ **Renal & liver failure** -Avoid if severe

## ☐ **Travel**

Check with your healthcare provider if you expect to travel. While traveling, carry your medication with you at all times.

## ☐ **Surgery/Dental and Other Medical Procedures**

Inform healthcare providers that you are taking warfarin. You may need to stop taking warfarin.

## ❑ Warfarin Interacts With Other Medications

### Read

#### ❑ Alcohol -

- Alcohol intake can affect how the body metabolizes warfarin.
- Increase risk of GIT bleeding
- Should avoid drinking alcohol on a daily basis.
- Alcohol should be limited to no more than 1 to 2 servings of alcohol occasionally.
- This means an average of one to two drinks per day for men and one drink per day for women.

## ❑ **Food -**

- Some food can interfere with the effectiveness of warfarin.
- Eat what you normally eat and not to make any major changes in your diet without contacting your healthcare provider.

## ❑ **Vitamin K**

- Eating an increased amount of food rich in vitamin K can lower the PT and INR, making warfarin less effective
- Should aim to eat a relatively similar amount of vitamin K each week.

# Common Do's and Don'ts

What to Do	What Not to Do
Do watch for signs and symptoms of bleeding.	Never double a dose because you missed a dose.
Do tell your healthcare provider when you get sick or hurt.	Don't start new medications, herbals, or supplements without talking to your healthcare provider.
Do take warfarin exactly as prescribed.	Don't make changes to your warfarin dose without talking to your healthcare provider.
Do tell anyone giving you medical or dental care that you are taking warfarin.	
Do keep appointments for blood tests.	



**Thank you**

