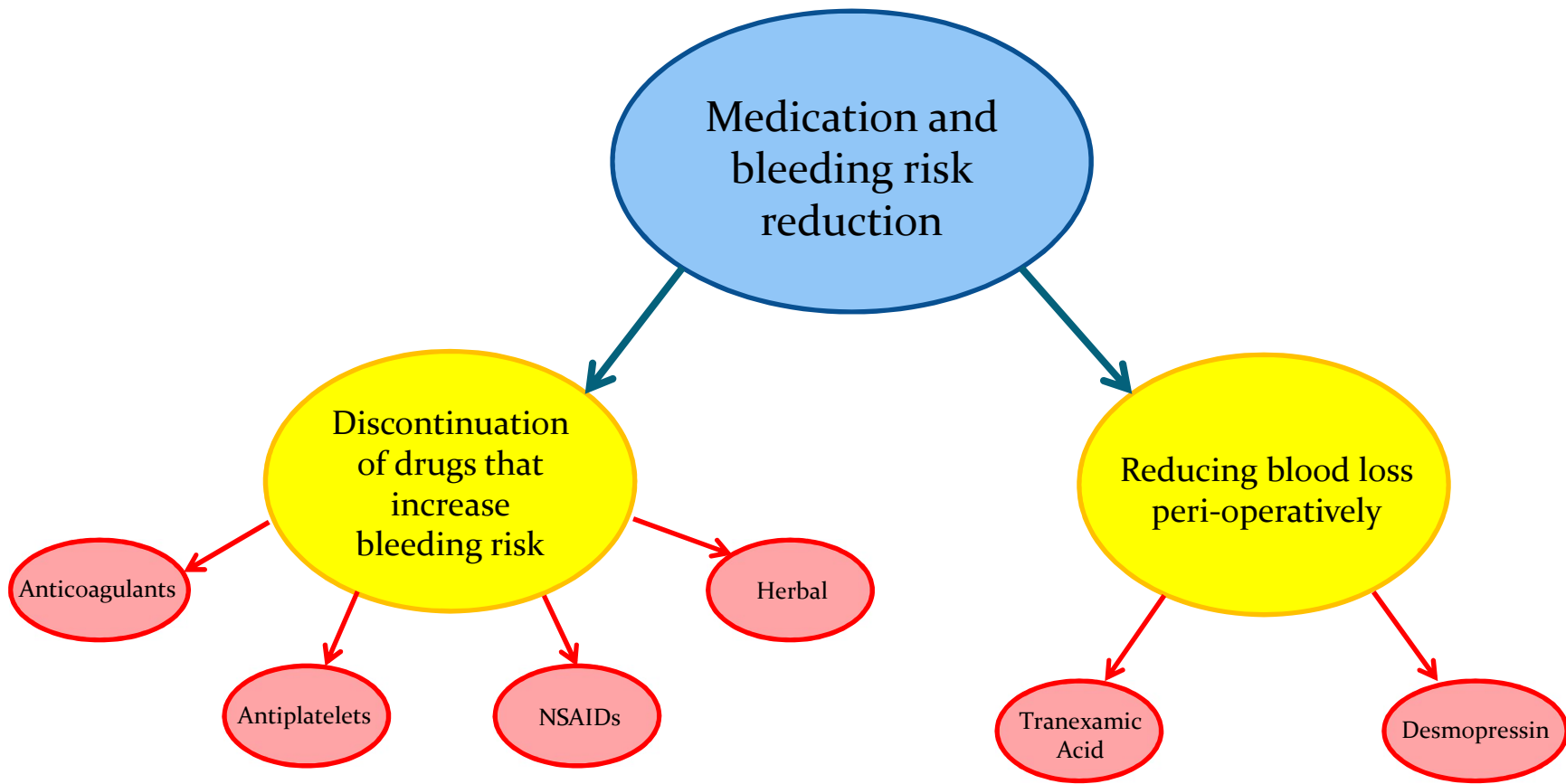


# Drugs and Blood

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# Overview



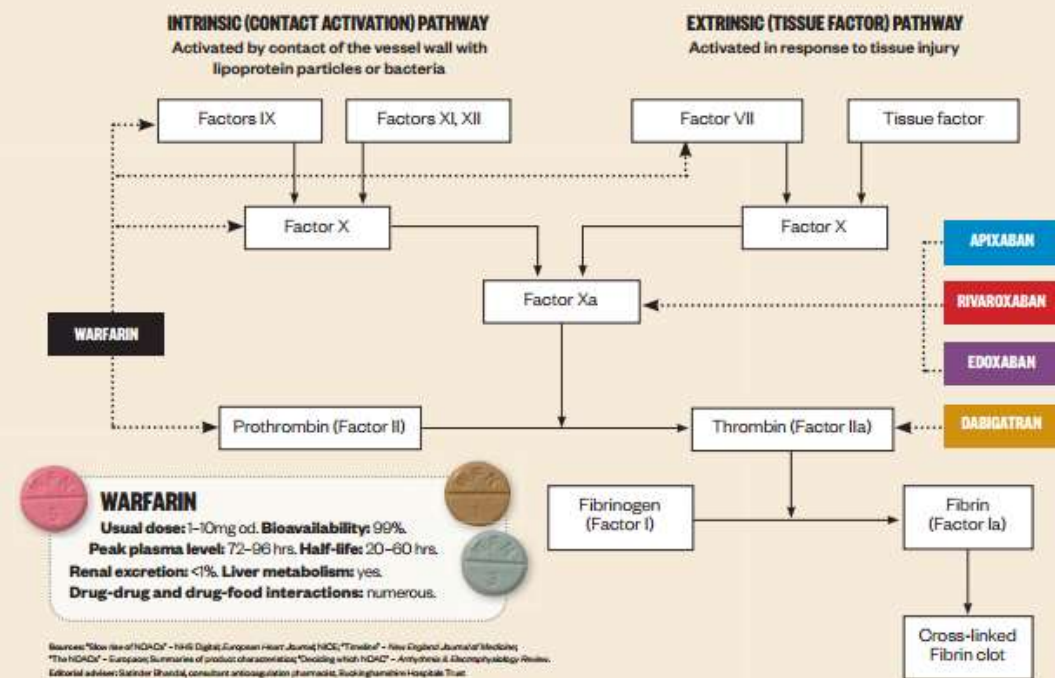
# Anticoagulants

- Anticoagulant = chemical substance that prevents or reduces coagulation of blood, prolonging the clotting time
- Indications:
  - Stroke prophylaxis in AF
  - Stroke prophylaxis in patients with mechanical heart valves
  - Treatment of DVT or PE
  - Thromboprophylaxis following hip or knee replacement surgery
- Examples:
  - Warfarin
  - NOACs
  - Low Molecular Weight Heparin

# Anticoagulants

## ANTICOAGULANT EFFECT OF NOACs

The coagulation cascade is a series of reactions involving coagulation factors that ultimately results in the formation of a blood clot. The NOACs directly inhibit one specific coagulation factor in the cascade, whereas warfarin prevents the coagulation process by suppressing the synthesis of several vitamin K-dependent coagulation factors.



# Warfarin

- Antagonises the effects of vitamin K
- Still commonly prescribed despite availability of newer agents
- Has a long half life → ~ 40 hours
- Dose prescribed is dependent on the individual patient
- Elective surgery usually requires omitting warfarin for approximately 5 days
- Can be reversed using phytomenadione (vitamin K)

# Factor Xa Inhibitors

- Rivaroxaban, apixaban and edoxaban
- Prevents thrombin formation and development through inhibiting factor Xa
- More stable pharmacokinetics than warfarin
- For surgery:
  - Rivaroxaban & apixaban = 48 hours prior to procedure
  - Edoxaban = 24 hours prior to procedure
- Restart 24-48 hours post-op
- There is currently no antidote for factor Xa inhibitors
- Andexanet – approved by FDA, no license in Europe

# Dabigatran

- Reversible direct thrombin inhibitor
- For surgery:

Renal Function (eGFR in ml/min)	Timing of last dose
>80	2 days
>50 to ≤80	3 days
>30 to ≤50	4 days
<30	>5 days

- Assays do exist for the emergency situation
- Restart 24-48 hours post-op
- Can be reversed using Praxbind<sup>®</sup> (idarucizumab)
  - Dose = 5g
  - Cost = £1700

# Low Molecular Weight Heparin

- Dalteparin, enoxaparin, tinzaparin
- Indications:
  - Thromboprophylaxis
  - Bridging therapy
- Risk of heparin induced thrombocytopaenia (HIT)
- Stop 12-24 hours prior to surgery, epidural or spinal anaesthesia



# “to bridge or not to bridge”

- Type of anticoagulant
- Consequence of withholding anticoagulant
  - Indication
  - Patient risk factors
- Bleeding risk associated with individual, surgery or procedure
- Alternative anticoagulation available for patient

Decision to stop treatment is always a balance  
between risk and benefit

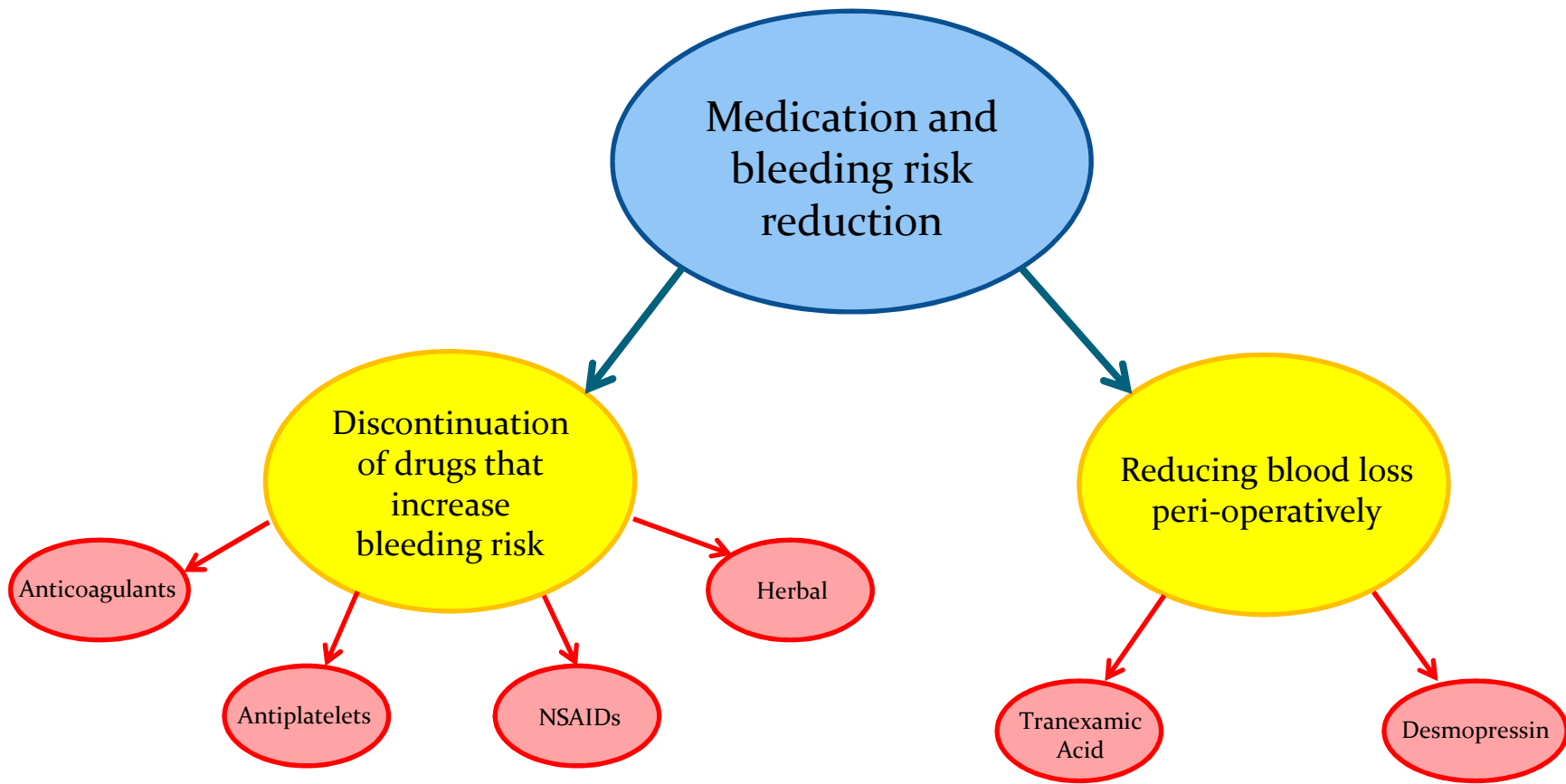
# Antiplatelets

- Decrease platelet aggregation and inhibit thrombus formation
- Usual Indications
  - Prevention of atherothrombotic events in patients with a history of ischaemic disease or in Acute Coronary Syndrome
  - Prevention of atherothrombotic or thromboembolic events in AF (if warfarin is unsuitable)
  - Treatment of TIA or acute stroke
- Examples:
  - ADP receptor antagonists – clopidogrel, prasugrel & ticagrelor
  - COX inhibitors – aspirin
  - PDE inhibitors – dipyridamole
  - GP IIb/IIIa inhibitors – tirofiban, abciximab
- ? when / if to stop

# Others

- NSAIDs
  - Associated with an increased risk of bleeding due to antiplatelet effect
  - COX2 specific inhibitors (celecoxib, meloxicam, etodolac) are not associated with an increased bleeding risk
  - Benefit vs. risk
- Herbal medicines
  - Often not disclosed by patients
  - Always remember to ask about herbal meds

# Overview



# Tranexamic Acid

- Indication:
  - Prevention and treatment of haemorrhage due to local or general fibrinolysis
- Inhibits fibrinolysis and reduces clot breakdown
- Inhibits plasminogen activation and therefore prevents conversion to plasmin
- Renal impairment:
  - Severe – contraindicated (risk of accumulation)
  - Mild to moderate – dose reduction (based on serum creatinine)
- Reduces the probability of receiving a blood transfusion by over 30% (depending on the type of surgery)
- Risk of thromboembolic events occurring
- ADRs
  - Convulsions, hypersensitivity reactions, visual disturbances, nausea and diarrhoea

# Desmopressin

- Synthetic analogue of vasopressin
- Increases the plasma levels of factor VIII and vWF
- Enhances platelet adhesion to the wall
- Used for mild to moderate haemophilia or von Willebrands disease patients undergoing surgery or following trauma
- Lack of clinical evidence to support use in patients who do not have congenital bleeding disorders
- Dose can be repeated at 12 hourly intervals
  - Response can diminish after successive doses
- Caution to prevent fluid overload in patients
- Vasodilation may occur resulting in tachycardia, hypotension and facial flushing