Contents

Practical Anaesthesia

Decreasing VTE Risk PeriOp

Preoperative

1. Preop Assessment & use of bridging LMWH where required depending on pt VTE risk (AF, mechanical heart valve, pre VTE event, carotid stenosis)
2. Hydration – minimising starvation time, supplemental IVF once starved
3. Prophylactic LWMH prior to surgery (20-40mg SC clexane, >12 hours so option of a neuraxial block can be performed if required) – most effective strategy in the low to moderate risk patient
4. Education regarding importance of mobilising and bed exercises post-operatively
5. TED stocking
6. Weight loss
7. Stopping smoking

Intraoperative

1. Hydration – IV fluid
2. Intermittent pneumatic calve compressors & graduated compression stockings (ie not TEDS) – shown to be effective in combination with low dose heparin in major surgery. Needs to be instituted pre, intra and post op, expensive.
3. Regional anaesthesia –
    - ↓shown to decrease DVT risk in peripheral vascular surgery, theoretical reduction in hypercoagulable state and improved blood flow,
    - But may worsen immobility post op (use low dose LA + opioid epidural infusion)
4. Minimal intraoperative duration and high quality surgery (minimal trauma)
5. Graduated compression stockings
6. Optimal cardiac output

Postoperative

1. Adequate analgesia to increase chance of early mobilisation
2. Early mobilisation
3. Post-operative pharmacological options: LMWH 20-40mg SC OD, aspirin 100-300mg/day, heparin 5000IU SC , IV heparin -> titrated to an APTT of 60-40 seconds
4. TED stocking
5. Adequate hydration
6. Bed lower limb exercises, physio and mobilise
7. Early discharge from hospital

Anticoagulated Patient

Overview

- assessment based on balance of 3 factors:
  - patient thrombosis risk
  - patient risk of bleeding
  - surgical risk of bleeding

Patient Thrombosis Risk

ATRIAL FIBRILLATION

- base line risk peri-operative risk of arterial thromboembolism in AF with no anticoag (& no valve dysfunction) = ~1%
- CHADS2 to calculate annual stroke risk:
  - heart failure = 1
  - HTN = 1
  - Age
    - 65-74 = 1
    - >75 = 2
  - DM
  - prior TIA/stoke = 2 points
  - female = 1
  - Vasc = any of: periph arterial disease, prev MI, aortic plaque = 1

- scores:
  - 0 = low risk ⟹ no anti-coat consider aspirin
  - 1 = mod risk ⟹ aspirin/warf
  - ≥2 = mod/high risk ⟹ warfarin or NOAC

- yearly incidence of stoke based on score:
  - 0 = 2%; 1 = 3%, 2 = 4%, 3 = 6%, 4 = 8.5%,, 5 = 12.5%, 6 = 18%

- other factors (not in CHADS) which can make you high risk:
  - thromboembolism within 30 days,
  - AF with mitral valve disease

MECHANICAL HEART VALVES

- base line annual risk = 17% or ~0.4% for 8d period
- with thromboprophylaxis = 2%
- high risk: mural thrombus, recent valve replacement, multiple prosthetic valves, cage-ball valve, mitral position, AF, poor LV function
- intermediate risk: bi-leaflet or tilting-disk prosthesis, >90 days since replacement, previous thromboembolism
- low risk: nil! (all mechanical valves are high risk)

CAROTID STENOSIS

- high risk: asymptomatic stenosis, bruit or previous TIA, recent symptoms
- aim = continuation of aspirin perioperatively

VTE

- high risk: recent VTE (<30 days), major surgery, pregnancy
- intermediate risk: VTE in last 3 months, obesity, malignancy, familial prothrombotic state, preoperative immobility
- low risk: thrombotic event >3 months

Patient Risk of Bleeding

- Anaemia = indeed RF of mortality & need for transfusion

- HAS-BLED score = 1 point for each:
    - H ypertension
    - A bnormal liver or renal function
    - S troke
    - B leeding history
    - L abile INR
    - E lderly >65yrs
    - Drugs ie aspirin, NSAIDs, alcohol
- score
    - 0 = low risk
    - 1-2 = standard
    - ≥3 = high risk

Surgical Risk Bleeding

HIGH RISK

- major procedures involving airway, joints, head and neck and body cavities
- neurosurgery, orthopaedic, plastic and opthalmological procedures

- must stop warf 5d prior to surgery
- dont re-start LMWH or warf until 48hrs post procedure if high risk of bleeding

LOW RISK

- =
    - minor dental procedure
    - superficial, skin and subcutaneous surgery
- can proceed with no change to oral anticoagulants

Guidelines for Perioperative Management

- need good, robust pre-admission set up with involvement of GP and district nurses.
- needs good monitoring of INR preoperatively
- can reverse INR with vitamin K, FFP and prothrombinex
- can perform neuroaxial technique if INR < 1.3 and no contraindications
- if INR 1.3-1.5 you need to take into account other anti-platelet agents
- no neuroaxial block within 12hrs of prophylactic LMWH
- no neuroaxial block within 24 hrs of therapeutic LMWH
- remember other methods: intermittent calve compressors, TEDS, good hydration and analgesia.

Anticoagulation Plan

- Treat based on 3 factors;
- if need to stop warf must do 5 days prior to surgery
- RF stratification:
    - All low risk = low risk
    - All high risk = high as below
    - Anything intermediate = complicated in middle

LOW RISK

- low risk of surgical bleeding -> keep oral anti-coagulation going or
- cease warfarin 5 days preoperative
    - no bridging
    - (or ultra low dose 20mg LMWH SC OD)
    - time OT at least 12 hours after last dose

INTERMEDIATE

- cease warfarin 5 days (D1) pre-OT (aim = INR <1.5)

- commence thromboprophylaxis (D3) 3 days prior to surgery
- 40mg LMWH SC OD
- time OT 12 hours after last dose

HIGH
- ideally delay surgery
- stop warfarin 5 day preoperatively
- 1.5mg/kg LMWH SC OD (some give 80% of that) 3 days prior to surgery
- time OT 12-24 hours after last dose

VERY HIGH RISK
- ideally delay surgery
- stop warfarin 5 day preoperatively
- admit 4 days prior to surgery -> IV heparin infusion 1000unit/hr and adjusted to APTT
- stop heparin infusion 6hr prior to surgery

During Surgery
- Use SCDs routinely
- no benefit of using compression stockings & SCDs at same time
- TEDS likely not of benefit unless full leg & fitted accurately

Management of Bleeding
- decide if surgical or coagulopathy;
  - coag: if bleeding from multiple sites or slow
- surgical control of bleeding a priority
- use coagulation testing:
  - coag screen
  - TEG - see cardiac SSU notes
- products:
  - prc's:
    - lack factor V, VIII, XI especially
  - platelets - 1 bag
  - FFP
    - replace natural coag factors incl antithrombin III & protein C
    - does contain fibrinogen (but not a lot)
    - 15ml/kg or 4 units in average adult
  - cryo $\Rightarrow$
    - 2 pools or 10U to keep fibrinogen >1
  - TXA 15-30mg/kg
  - VIIa - consider

Drugs

Warfarin

- = oral anticoag which prevents liver synthesising functional vit K dependant factors: 2,7,9,10, protein C &S
- prolongs PT
- INR targets:
  - 2-2.5 for DVT prophylaxis
  - 2.5 for treatment of DVT/PE, prophylaxis in AF, cardioversion
  - 3.5 recurrent DVT/PE or mechanical heart valves

Reversal

No Bleeding

- INR < 4.5 - reduce or omit dose
- INR 4.5-10 - cease dose + Vit K 2mg po or 1mg IV
- INR >10 -
  - cease dose +
  - Vit K 5mg po or 1mg IV,
  - consider Prothrombin VF 15-50 IU\kg
  - measure INR in 12-24hr

Bleeding

- INR >1.5 and life threatening bleed:
  - vit K 10m IV
  - prothrombinex VF 50units/kg
    - ↳ if unavailable give FFP 15ml/kg
  - FFP 150-300ml (ie 1 bag)
- INR >2 and critically significant bleeding (but not life threatening):
  - vit K 10mg IV
  - prothrombinex VF 35-50unit/kg
    - ↳ if unavailable give FFP 15ml/kg
- Minor bleeding with INR >4.5 or bleeding risk high:
  - vit K 2mg orally or 1mg IV
- any other INR with minor bleeding:
  - omit and adjust dose

Prothrombinex

- human plasma derivative
- note comes in different forms:
  - HT/VF version = 3 factor ie 2, 9, 10
  - only one prep is 4 factor ie added factor 7
- complete reversal of INR within 15mins
- but factors half lifes similar to endogenous ones ∴ must give vit K at same time

Adv over FFP

- rapid reconstitution
- small volume of infusion over 20mins
- fast onset action
- no requirement to check pts blood gp
- minimal infection risk
- ↓transfusion reactions

Contraindications

- thrombosis

- DIC
- contains small amount heparin - caution in HITT

Adverse effects

- allergy
- PE
- phlebitis
- DVT
- anaphylaxis
- vomiting
- fever
- rash
- urticaria
- SOB
- pain
- thrombocytopenia

Dose

-> 15-50 IU\kg
(1 IU\kg of Factor IX raises the Factor IX by 1%)

Other Important Notes

Monitor INR >6 carefully
Vit K works within 6-12 hours

Dabigitran

Pharmacology

- direct thrombin inhibitor
- 85% renally excreted
- half life 12-24hrs **but** longer in renal dysfunction
- peak plasma conc 2 hours post dose

Monitoring

- no regular monitoring required
- Ax renal function prior to starting
- monitor renal function during acute illness

Converting

- to Dabigitran :stop warfarin & start dabigitran when INR <2
- to warfarin:
    - norm renal function: start warf 3 days before stopping dabigitran
    - impaired renal function: start warf 1-2 days before stopping dabigitran

Dosing

- AF: 150mg bd (>80yrs 110mg bd)
- DVT/PE Rx:
    - 150mg bd after at least 5 days of other anticoags
    - Rx for 6months
- DVT/PE prophylaxis:
    - as Rx
- Ortho surgery prophylaxis:
    - 1-4hrs post surgery = 110mg (delay if hamestasis not secure)
    - then 220mg once daily for
        - TKR 10days
        - THJ 28-35days

- renal function dosing based on Creat clearance
    - <30ml/min = do not use
    - >30ml/min = normal dosing

Neuraxial
- time after Drug Before Block:
  - CrCl >80 = 2days
  - CrCl 50-80 = 3days
  - Cr Cl <50 = 4days
- time after block/catheter out before next drug dose:
  - 6hrs

Interactions
- avoid concurrent other anticoagulants
- use with caution with aspirin/clopidogrel
- NSAIDs fine
- interaction ↑ing dabigitran conc with P-glycoprotein inhibitors:
  - amiodarone
  - verapamil
  - clartihromycin

Reversal
- limited but:
  - time
  - haemodialysis
  - FEIBA (activated prothrombin complex concentrate)

Rivaroxaban

Pharmacology
- Factor Xa inhibitor
- highly protein bound
- 33% renal excreted unchanged
- half life 5-9hrs (up to 13hrs in elderly)
- no age dose adjustment
- peak plasma conc 2-4hrs post dose

Contraindications
- hypersenitivity
- bleeding
- liver disease & coagulopathy
- cautin in impaired renal function
- pregnancy/breast feeding
- mechanical heart valves

Dosing
- standard
  - = 20mg/d
  - CrCl 30-50 = 15mg/d
  - CrCl <15 dont use
- VTE Rx:
  - 15mg bd for 3 weeks then 20mg daily
  - CrCl 15-50 then maintenance dose = 15mg
- ACS Rx:
  - 2.5mg bd to standard antiplatelt therapy for 12months 24hrs post event
- Ortho prophylaxis:
  - 10mg od 10hrs post surgery once haemostasis secure
    - 14days TKJR
    - 35days THJR

Neuraxial
- time after Drug Before Block:
  - CrCl >50 = 18hrs
  - CrCl 30-50 = 24hrs
  - CrCl <30 = 48hrs

- time after block/catheter out before next drug dose:
    - 6hrs

Reversal

- limited but:
    - time
    - prothrombinex

Perioperative Dabigitran/Rivaroxaban

Elective Surgery on Dabigitran/Rivaroxaban

- no LMWH bridging needed
- timed cessation of drug based on CrCl & bleeding risk of surgery

(timings below essentially 1 day less conservative than regional guidelines)

Table 6 Preoperative interruption of new oral anticoagulants: a suggested management approach[21–24]

Drug (doses)†	Renal function	Low bleeding risk surgery‡ (2 or 3 drug half-lives between last dose and surgery)	High bleeding risk surgery§ (4 or 5 drug half-lives between last dose and surgery)
Dabigatran (150 mg twice daily)			
Half-life, 12–17 h	Normal or mild impairment (CrCl ≥ 50 mL/min)	Last dose: 24 h before surgery	Last dose: 48–72 h before surgery
Half-life, 13–23 h	Moderate impairment (CrCl 30–49 mL/min)	Last dose: 48–72 h before surgery	Last dose: 96 h before surgery
Rivaroxaban (20 mg once daily)			
Half-life, 5–9 h (healthy)	Normal or mild impairment (CrCl ≥ 50 mL/min)	Last dose: 24 h before surgery	Last dose: 48–72 h before surgery
Half-life, 9–13 h	moderate impairment (CrCl 30–49 mL/min)	Last dose: 48 h before surgery	Last dose: 72 h before surgery

PostOp Resumption

Table 8 Postoperative resumption of new oral anticoagulants: a suggested management approach

Drug	Low bleeding risk surgery	High bleeding risk surgery
Dabigatran	Resume 24 h after surgery, 150 mg twice daily	Resume 48–72 h after surgery, 150 mg twice daily†
Rivaroxaban	Resume 24 h after surgery, 20 mg once daily	Resume 48–72 h after surgery, 20 mg once daily‡

Emergency Surgery

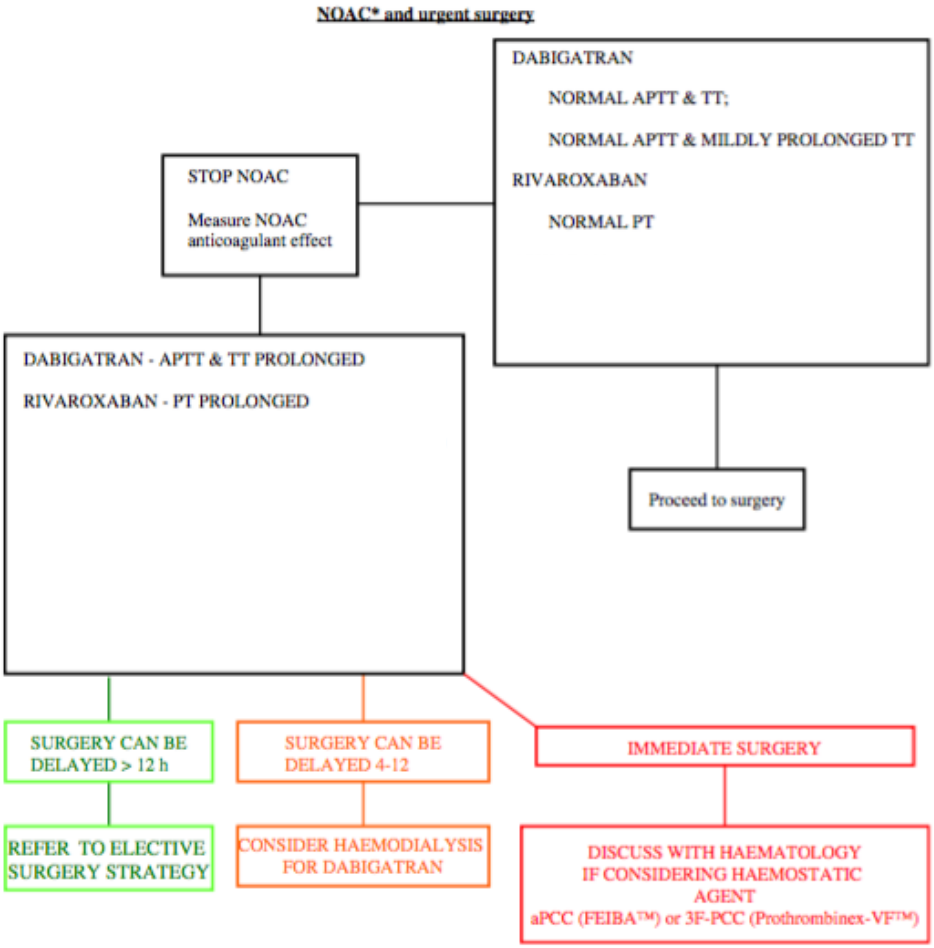

Figure 2 Suggested management of patients receiving NOAC requiring urgent surgery.
*Routine coagulation tests are insensitive to apixaban. Anti-Xa testing for apixaban is not currently available. Refer to Laboratory testing and NOAC section. aPCC, activated prothrombin complex concentrate; 3F-PCC, 3-factor prothrombin complex concentrate. APTT, activated partial thromboplastin time; PT, prothrombin time; TT, thrombin time.

- dabigitran & other agents:
  - no haemostatic agent shown in vivo to reverse anticoagulant effectively
  - evidence in vitro/animal to use:
    - dabigitran = FEIBA (an activated prothrombin complex concentrate)
    - rivaroxaban = prothrombinex

  ↳ but clearly no standard of care in place

Reversal if Bleeding

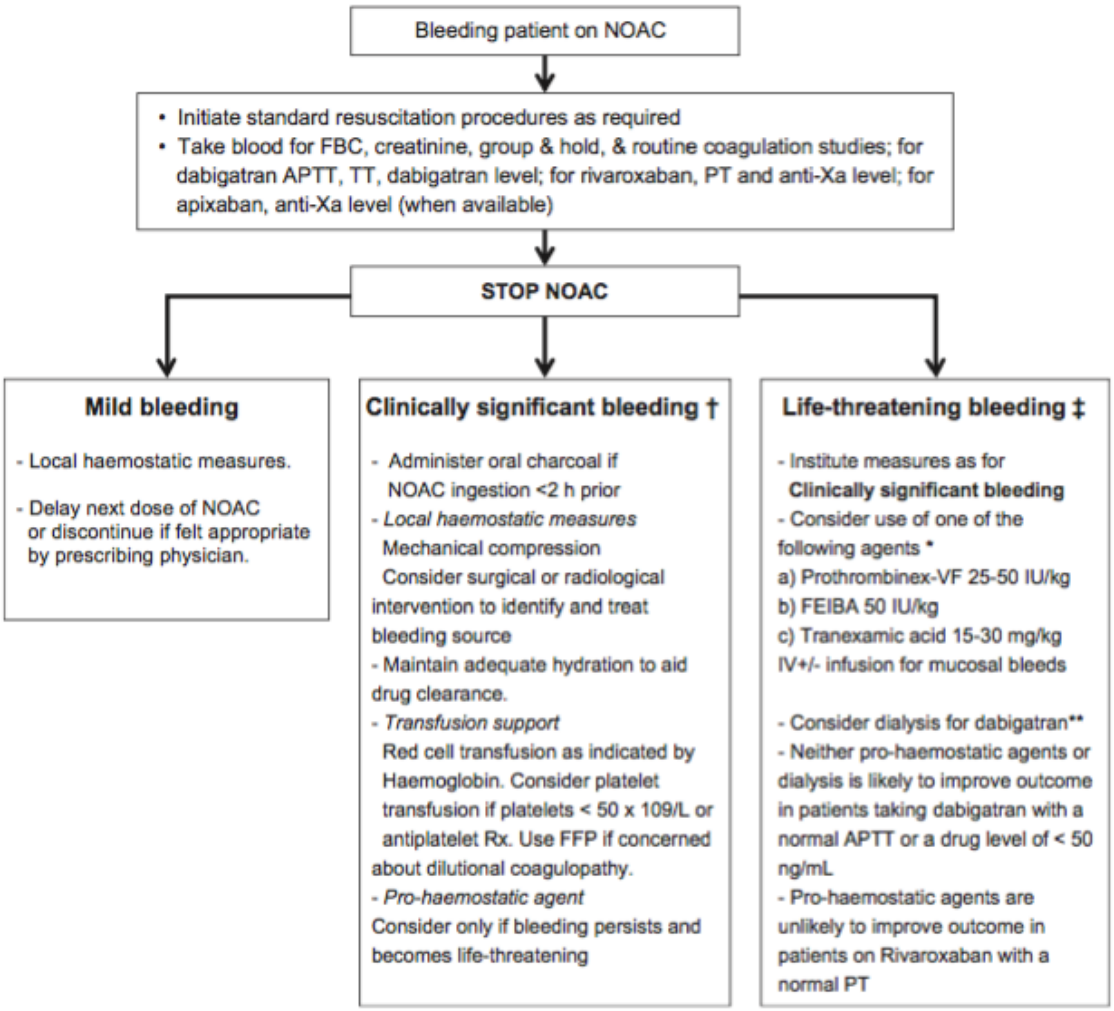

Figure 3 Management of new oral anticoagulants (NOAC)-associated bleeding.[26–33,33,34] †Clinically significant bleeding – reduction in Hb ≥ 20g/L, transfusion of ≥2 units of red cells. ‡Life-threatening bleeding – bleeding in critical area or organ (intraocular, intracranial, intraspinal, compartment syndrome, retroperitoneal or pericardial), hypotension not responding to resuscitation. *This is an off license use of FEIBA and Prothrombinex-VF and the risk of thrombotic complications with these agents when used for this indication is unclear. Their use is supported by laboratory data but clinical evidence supporting an improvement in clinical outcomes is lacking. **Dialysis is indicated if dabigatran level is high as indicated by excessively prolonged activated partial thromboplastin time (APTT) > 80 s or dabigatran level > 500 ng/mL and/or impaired renal function. Four hours of haemodialysis will reduce drug level by ~60%.[26] FBC, full blood count; FFP, fresh frozen plasma.

key points:

- tests:
  - standard: FBC, creatinine, G&H, coag screen
  - dabigitran tests: TT, dabigitran level
  - rivaroxaban: anti Xa level
- clinically sig bleeding:
  - charcoal <2hrs prior ingestion
  - standard product support eg transfusion of prc's & platelets if indicated
  - prohaemostatic agent only if specifically indicated
- life threatening bleed:
  - For all: TXA 15-30mg/kg
  - Dabigitran:
    - if normal APTT or drug level <50ng/ml then nothing will help
    - otherwise: FEIBA 50u/kg
  - Rivaroxaban:
    - if normal PT then nothing will help
    - otherwise: prothrombinex 25-50u/kg

Heparin

- acts by potentiating antithrombin III ⟹
  - ↑inactivation of thrombin & F10
    - UFH 10a:2a = 1:1
    - LMWH 10a:2a = 4:1
  - high doses via AT3 ⟹ inactivates 9,11,12 & ↓platelet aggregation

UFH

- IV bolus: 1000 units or 80u/kg
- infusion 18U/kg/hr
- check APTT at 6hrs: target is APTT 1.5-2.5x normal lab value
- follow local policy
- half life 1-2hr

LMWH

- mostly replaced UFH due to ease of dosing & monitoring
- ↑ed antiXa activity compared to UFH
- anti Xa levels can be monitored in renal failure
- ↓dose in renal failure

Heparin Induced Thrombocytopaenia & Thrombosis Syndrome

- HIT = heparin induced thrombocytopaenia
- if concurrent thrombosis = HITTS:
  - Platelet Factor -4 + heparin + IgG complex on platelet surface ⟹ inappropriate activation of platelets ⟹ hypercoag state ⟹ thrombosis
- 1-6% incidence (much less with LMWH)
- diagnoses 4 Ts:
  - **T** hrombocytopaenia = >50% fall
  - **T** iming - within 5-10 days starting heparin
  - **T** hrombosis - venous or arterial
  - no o **T** her explanation
- Tests:
  - antibody test - best
  - platelet activation assay
  - clinical scoring systems available to quantify risk
- more frequent with bovine lung heparin
- 2 types:
  - type 1:
    - day 1-4
    - transient/self limiting ↓platelets to ~50
    - = direct heparin induced plt agglutination ie non immune mechanism
  - type 2:
    - Day 4-14 days after 2nd exposure to heparin
    - platelet ↓ to ~10 & assoc with thromboembolic phenomena
    - immune mediated plt aggregation by IgG & IgM antibodies
    - development of antibodies to platelets following 1st heparin exposure. ie occurs on next exposure
    - = type II hypersensitivity reaction
    - usually resolves rapidly on stopping heparin (can last for 2/12)
    - must avoid UFH forever, but can use LMWH (with caution)
- Rx:
  - stop heparin immediately
  - use altervative
  - postpone warf until platelets >150 (initiate without loading dose)
  - monitor for thrombosis
  - avoid platelet transfusions

Protamine

- made from fish
- allergy & hypotension on administration
- UFH:
  - 95% neutralising activity on Xa inhibition
  - given within 15mins: 1mg protamine reverses 100unit heparin
- LMWH:
  - 55% neutralising activity on Xa inhibiton
  - <8hrs since admin: 1mg protamine reverses 1mg enoxaparin (=100units UFH)
  - >8hrs since admin: 50% dose ie 0.5mg protamine for every 1mg enoxaparin

Aspirin

- = a non specific COX inhibitor ⇒ ↓peripheral production of prostaglandins & thromboxane
- CVS specifically:
  - platelet actions:
    - irreversible inhibition of platelet COX by irreversible acetylation of the active site of the enzyme
    - ↓thromboxane A_2 in platelets:
      - TXA_2 causes ↑ADP release ⇒ VasoC & ↑platelet aggregation
      - aspirin ⇒ vasoD & ↓platelet aggregation
    - effect lasts for life of platelet (approx 3-5/7)
    - occurs at very low doses of aspirin
  - endothelial action:
    - ↓endothelial PGI2 (prostacycline) production:
    - PGI2 role (opposite to TXA2) ie vasoD & ↓platelet aggregation
    - ∴ ↓PGI2 ⇒ vasoC & ↑platelet aggregation
      - but NET effect is of TXA2 inhibition (vasoD & ↓aggregation) because of:
        - endothelium able to remanufacture more PGI2 (platelet not)
          - because endothelium has a nucleus & able to remanufacture COX
        - aspirin (especially at low dose) more selective for TXA2 inhibition
    - proposed that diseased patients have a dysfunctional endothelium ∴ baseline low PGI2 production ∴ use of aspirin helps to restore correct equilibrium

PeriOp

- should stop 7-9days prior to have no residual effect
- few trials looking at periop bleeding & aspirin
- use around surgery depends on balance of bleeding risk of surgery & thrombosis risk of patient:
  - CABG & aspirin = ↑risk of bleeding but ↑graft patency
  - TURP & aspirin = considerable ↑periop bleeding
  - minor skin surgery = continue aspirin
  - retinal/intracranial surgery = stop asirin

Dipydridamole

- used with low dose aspirin post CABG, valve replacement or stroke/TIA
- MOA by:
  - ↓adenosine uptake by rbcs ⇒ ↑serum adenosine ⇒ inhibit ADp induced platelet aggregation
  - reversible inhibition of platelet phosphodiesterase 5 ⇒ ↓TXA creation
- half life ~10hrs and is reversible effect
- controversy on when to stop:
  - stop 24hrs - 7 days prior to surgery
  - (no need to stop when placing neuraxial)

Clopidogrel

- = prodrug which blocks ADP receptors on platelet membranes irreversibly
- needs to be stopped 7days pre-op
- If rapid reversal required:
  - platelet transfusion can be useful

- as is a prodrug ideally need to wait >24hrs after last clopidogrel dose prior to platelet dosing

Ticagrelor

- ADP receptor reversible antagonist ie similar to clopidogrel
- = pro drug
- 9hr ½ life
- Stop 5 days prior to surgery

Glycoprotein IIb/IIIa Inhibitors

- block binding of fibrinogen to IIb/IIIa receptor
- commonly used in ACS
- eg
  - tirofibran -
    - reversible antagonist
    - if norm renal function ⟹ full reversal in 4-8hrs
    - rapid reversal:
      - platelet transfusions - but if free drug circulating may be of limited use
      - FFP may be beneficial
  - abciximab -
    - monoclonal antibody
      - stop 7d prior to surgery

Fibrinolytics

- act as thrombolytics by activating plasminogen ⟹ plasmin ⟹ degradation of fibrin ⟹ dissolution of thrombus
- used in ACS & stroke
- alteplase by infusion, reteplase/tenecteplase (bolus dose)
- need to be given within 12 hours of symptom onset - ideally 1hr
- used in combo with LMWH & aspirin
- severe bleeding is indication for cessation of therapy & +/- reversal:
  - crypoprecipitate - high level VIII & fibrinogen
  - FFP - factor V ^ VIII
  - platelets
  - anti-fibrinolytics - TXA
- bleeding times ↑ed for 24hrs post drug admin
- urokinase also used to unblock catheters:
  - 5000 to 25000 units plus saline into line to fill lumen
  - leave for 20-60 min then aspirate out

Anti-fibrinolytics

Tranexamic Acid

- = synthetic derivatives of lysine (amino acid)
- MOA: reversible binding to plasminogen ∴ blocking its binding to fibrin
- TXA x10 more potent than aminocaproic acid
- excreted 95% renally unchanged (half life 2-11hr)
- can ↓seizure threshold
- not been shown to ↑risk of VTE
- Used to ↓bleeding:
  - trauma
  - intraop - cardiac surgery, ortho, obstetrics, prostatectomy, dental extractions
  - hemophiliacs
- contraindicated in DIC & ureteric bleeding (clot retention)
- IV dose = 15-30mg/kg
- PO dose 1g tds

Desmopressin

- analogue of arginine vasopressin
- induces release of vWF from vasc endothelium ⟹ ↑vWF & factor VIII
- 0.3mcg/kg in 50ml saline over 30min
- indications:
  - haemophilia A
  - vWD (except 2b)
  - ↓platelet function in renal failure & aspirin

Factor VIIa

- recombinant factor acts at tissue factor:VIIa complex on damaged endothelium
- ∴ effect localised to site of vessel damage rather than body wide
- side effects of ↑thrombogenic risk
- licensed indications:
  - haemophilia
  - prophylaxis in pts with congenital VII deficiency
- is used in major bleeding protocols but off license:
  - should weigh benefits & risk
  - pre conditions:
    - pH >7.2, temp >35, significant other product used
    - 90mcg/kg in discuss with haematologist

By Disease

Anaemia

Preoperative

- = male <130
- = female <120
- = pregnancy <110

Cause Classification

1. **Decreased production** – renal failure, folate/B12 deficiency, marrow infiltration or suppression, anaemia of chronic disease, hypothyroidism
2. **Bleeding** – acute or chronic
3. **Increased consumption** – haemolysis ->
    - inherited (thalasaemias, sickle cell, spherocyctosis)
    - acquired (autoimmune, drugs, infections, mechanical valves, DIC)

or by size of rbc:

Microcytic	Normocytic	Macrocytic	
		Megaloblastic	Normoblastic
Iron Deficiency	Acute blood loss	B12 def	Alcohol
Thalassaemia	Renal	folate def	Liver
Sideroblastic disease	Marrow failure		Reticulocytosis
Chronic disease	Haemolytic		
	Endocrine		

HISTORY

- fatigue
- SOB
- palpitations
- headaches
- angina

- FHx
- medications: NSAIDS, aspirin, ET-OH

- exercise capacity

EXAMINATION

- pallor
- P and BP
- general examination looking for causes

INVESTIGATIONS

- Hb - should be measured for all major surgery & anyone with sig PMH esp CVS/Resp disease
- Other testes
    - Fe studies
    - B12/folate
    - reticulocyte count
    - direct Coombs test – antibodies attached to RBC's causing their destruction

- liver and hepatic function
- bone marrow

MANAGEMENT

- treat cause
- delay surgery where possible
- Fe supplementation:
    - oral - notoriously poorly compliant
    - IV Fe+ -
        - modern preps = low risk, iron replete within 20mins. 10 day for max response
- B12 injections
- transfusion if indicated (more conservative approach now c/o morbidity associated with transfusions and understanding that we can tolerate much lower Hb than first thought)

Intraoperative & Postoperative

- Number of studies :
    - ↑mortality with ↑blood transfusion
    - limited evidence for diff in mortality via restrictive vs liberal regime BUT is ↑morbidity:
        - infection
        - CVS events
- Transfusion Triggers:
    - fit and healthy – Hb 70
    - if renal failure, neuro disease, IHD then trigger is unclear ⟹ suggest 80 & reAx

Porphyria

Preoperative

= group of disorders where patients have a inability to synthesis Hb resulting in an accumulation of precursors oxidised to porphyrins
- hepatic and erythropoietic varieties

- only the 3 hepatic forms effect anaesthesia practise (autosomal dominant - but with variable expression)

(1) AIP - acute intermittent porphyria (sweden)
(2) VP - variegated porphyria (afrikaners). Dermal photosensitivity
(3) HCP - hereditary coporporphyria (rare - dermal hypersensitivity)

HISTORY

Female
30-40 yrs
FHx
May never have had symptoms ∴ **FH impt (do not ignore & must be Rx'ed as has disease)**

Porphyric Crises

- Many precipitants - drugs, stress, infection, alcohol, menstruation, pregnancy, starvation, dehydration
- Symptoms incl:
  - Abdo pain
  - Vomiting
  - Motor and sensory neuropathy
  - Autonomic dysfunction
  - Cranial nerve palsies
  - Confusion
  - Coma
  - Seizures
  - Fever
- symptoms may mimic surgical pathology

EXAMINATION

- as directed by history

INVESTIGATIONS

(may be normal between attacks)
- urinary porphyrins & porphyrin precusors (ALA and PBG)
- serum porphyrins
- faecal porphyrins
- erythrocyte porphyrins
- DNA testing

MANAGEMENT

- avoidance of precipitants
- premedication to decrease stress
- minimise preoperative fasting (IVF)

Intraoperative

- invasive monitoring during crisis (autonomic instability)
- RA:
  - bupiv safe
  - should avoid if concurrent crises as neuropathy may be rapidly progressing
- GA - TIVA with fentanyl & sux or vec

- intra-op problems:
  - hypertension and tachycardia -> beta blockers
  - convulsions -> midazolam, propofol, MgSO4

Anaesthetic Drugs & Safety

	Def Unsafe	Maybe	Probably Safe
Induction	thio etomidate	ketamine	Propofol
Volatiles	Enflurane	iso sevo	Nitrous
NMBs		panc atrac roc	Sux vecuronium
Reversal			Atropine Glyco Neo
Analgesia		dicofenac	aspirin & paracetamol alfent, fent, morphine naloxone
LAs	Ropiv	Lignocaine	Bupiv Prilocaine
Sedatives	nitrazepam	Diazepam	Midazolam Chloral hydrate
Antiemetics	metoclopramide	ondansetron Ranitidine	Droperidol
CVS Drugs	Hydralazine Nifedpine Phenoxybenzamine	Diltiazem verapamil SNP	Adrenaline α & ß agonists Mg ß blockers phentolamine
Others	OCP phenytoin sulfonamides aminophylline	Steroids	

Postoperative

- crisis may be delayed for up to 5d

Management of Prophyric Crisis

Goals
(1) stop precipitating agent
(2) reverse factors that increase haem production (ALA synthase activity)

- Call for help
- Stop administering precipitent
- Haem arginate 3mg/kg IV OD for 4/7 (inhibits ALA synthase activity)
- Analgesia – opioids (avoid RA)
- Supportive care: infection, dehydration, electrolyte imbalance

- Give glucose (20g/hr)
- Beta-blockers (manage haemodynamics + decreases activity of ALA)
- Plasmapheresis
- Monitor closely (HDU/ICU)

Hereditary Spherocytosis

Preoperative

- autosomal dominant condition
- RBC's have a smaller surface to volume ratio + abnormally permeable to Na+
- spherocytes -> phagocytosed in spleen

HISTORY

- anaemia symptoms
- asymptomatic

EXAMINATION

- splenomegally

INVESTIGATIONS

- microspherocytic anaemia
- reticulocytosis
- RBC increased osmotic fragility

MANAGEMENT

- splenectomy ->
  - ↑50% survival of rbc
  - ideal <6yrs old
  - need vaccinations prior: pneumococcal, meningococcal and HIB
  - lifelong penicillin

Anaesthesia

- nil specific issues

Glucose 6 Phosphate Dehydrogenase Deficiency

(G6PD Deficiency)

Preoperative

- this enzyme responsible for production of NADPH -> involved in cells defence against
  - **oxidative stresses** (ie. infections)
  - **oxidation of drugs** (aspirin, quinolones, chloramphenicol, isoniazid, quinine, sulphonamides, vitamin K)
- also required for reduction of methaemoglobinaemia (thus SNP and prilocaine contraindicated)
- x-linked
- haemolysis of rbcs occurs 2-5d after exposure to precipitant

HISTORY

- Black American or Mediterranean
- ingestion of broad beans (fava) -> haemolysis
- 2/7 later: abdominal pain

EXAMINATION

- anaemia

- jaundice

INVESTIGATIONS
- haemoglobinaemia
- haemoglobinuria
- high bilirubin (unconjugated)
- Heinz bodies
- RBC G6PD assay (may be false high in acute crisis)

MANAGEMENT
- discontinuation of offending agent
- transfusion

Anaesthesia
- avoid precipitants - NSAIDs

Thalassaemias

Preoperative
- absent or deficient synthesis of alpha or beta globin chains of Hb
- severity related to degree of impaired globin synthesis
- regardless of cause classifed as:
  - major - transfusion dependant. Sig issues with Fe overload
  - intermediate
  - minor

HISTORY
- anaemia symptoms
- Mediterranean, African and Asian
- degree of organ involvement from iron overload
- high output cardiac failure

EXAMINATION
- heart failure signs
- hyperplastic marrow -> overgrowth of bone and facial bone deformity $\Longrightarrow$ diff airway

INVESTIGATIONS
- mild -> severe anaemia
- Hb electrophoresis +/- globin chain analysis

MANAGEMENT
- severe forms = transfusion dependent
- cross match to identify any antibodies that may exist
- thorough airway assessment

Anaesthesia
- as guided by above

Sickle Cell Anaemia
- inherited sickling haemoglobinopathy
- different states:
  - homozygous state (HbSS) - true sickle cell anaemia
  - heterzygous (HbSA) = trait

    - combo with another Hb ß chain abnormality (HbSC, HbSD, ß thalassaemia)
- Sickling process proportional to concentration of HbS:
    - trait = unusual as HbS <50%
    - HbF inhibits sickling process
- endemic in parts of Africa, Med, Middle East, India
- pathology is from vaso-occlusion by sickled rbcs ⟹ haemolysis & infarction
- precipitants:
    - hypoxia
    - hypothermia/fever
    - acidosis
    - hypovolaemia
    - infection

Features

- great variability
- diff types of crises:
    - vaso-occlusive (commonest):
        - presentations:
            - acute abdo
            - acute chest syndrome- pneumonia like
            - stroke
            - priapism
            - proliferative retinopathy
        - most functionally asplenic by teens ∴ ↑risk of sepsis
    - aplastic crisis:
        - =temp shutdown of marrow
        - ↓↓Hb with no reticulocytes
        - precipitants = parvovirus with B12 or folate deficiency
    - sequestration crises:
        - mainly in paeds
        - sudden pooling of rbcs in spleen ⟹
            - hypotension
            - ↓↓↓Hb
        - death unless transfusion
    - haemolytic:
        - ↓Hb with ↑reticulocytes & ↑bili
        - usually accompany veno-occlusive crises
        - chronic haemolysis ⟹ gallstones

Investigations

- Screening test: deoxygenates HbS ⟹ positive for HbSS & HBSA
- Hb electrophoresis distinguishes specific types

- Hb 60-90
- ↑retics
- film -
    - sickled cells & target cells
    - Howell-Jolly bodies (if spleen atrophic)

↳ may all be norm in trait

MANAGEMENT

- supportive care:
    - folic acid supplements
    - vaccinations
    - penicillin prophylaxis
- crises care:
    - rest
    - IVF
    - antibiotics
    - O2
    - warming cares

    - good analgesia
- blood transfusion (discuss with haematologist first!):
    - some vaso-occlusive crises
    - transfuse to target of HbS <30%

Anaesthesia

- discuss pt with haematologist prior to all operations
- attention to hypoxia, dehydration, infection, acidosis, hypothermia, pain
- Regionals - not contraindicated
- Tourniquet: can be used if limbs are meticulously exsanguinated prior to inflation

Coagulation Disorders

- extrinsic & intrinsic pathways now thought in vitro only
- common pathway:

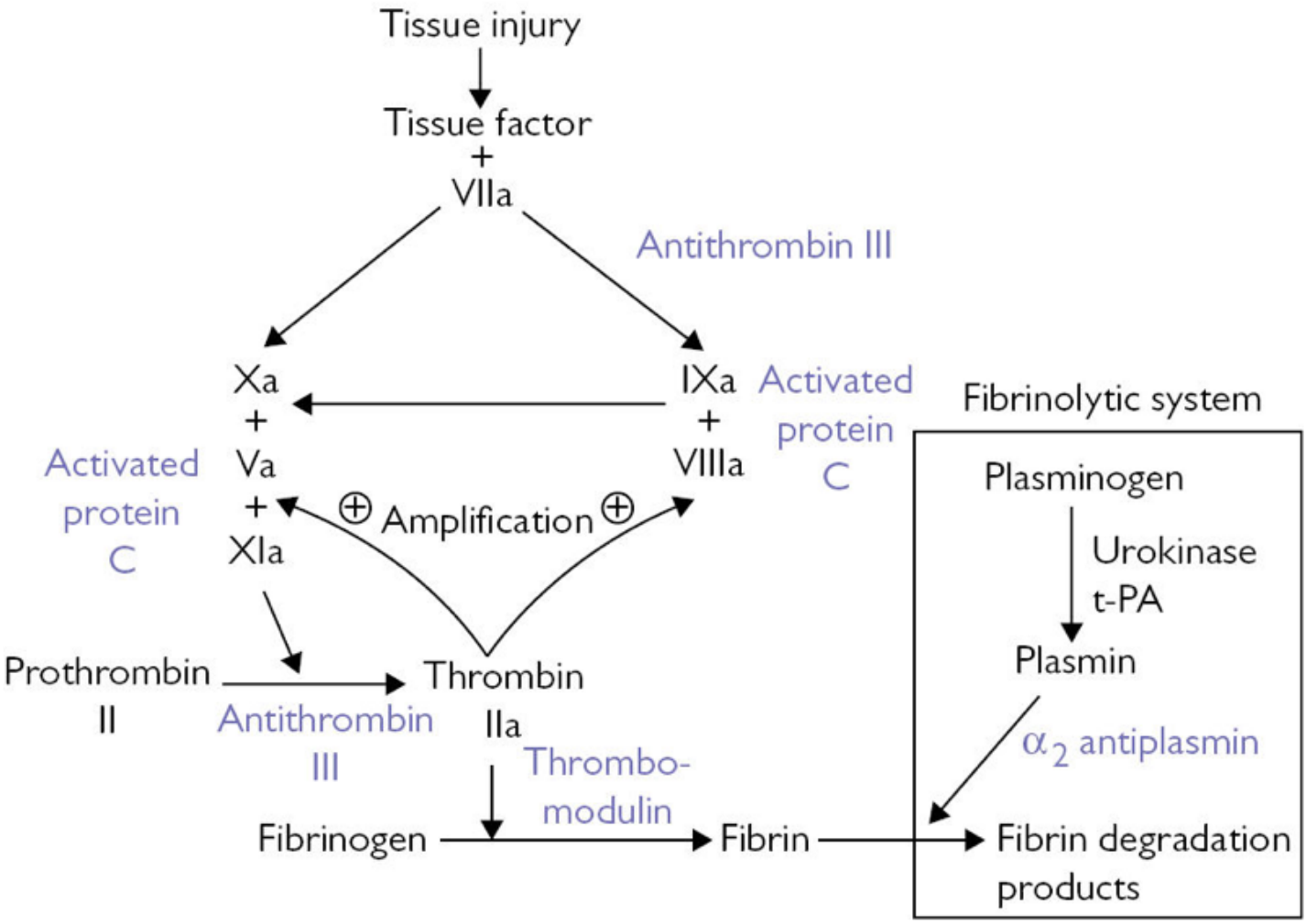

Fig. 10.1 Coagulation cascade (colour indicates inhibitor).
t-PA, tissue plasminogen activator.

- ie……damage to vascular bed ⟹ tissue factor & VIIa ⟹ activate IX & X ⟹ generate small amount of thrombin
- Amplification of thrombin ⟹ activate V & VIII ⟹ massive thrombin ⟹ fibrin

- sources of disease:
  - congenital - present in adulthood with precipitant
  - acquired:
    - lack of synthesis of factor
    - ↑consumption
    - production of substances interfering with factor function
- PMH relevant:
  - liver disease:
    - coag screen misleading. TEG better
    - give vit K 10mg daily +/- FFP 15ml/kg
  - malabsorption - vit K deficiency
  - infection
  - malignancy (DIC)
  - autoimmune (SLE, RA)

- meds eg anticoags, aspirin, NSAIDs

Haemophilia

Preoperative

- types:

1. haemophillia A (X-linked recessive defect in factor VIII activity):
   - severe (spont bleeding) = factor VIII <2%
   - mod = 2-5%
   - mild (bleeding only after trauma)= 5-30%
2. haemophilia B (X-linked recessive defect in factor IX activity -> Christmas disease)

- affects males (females are carriers but can have mild disease)
- female homozygotes die in utero

HISTORY

- bleeding into muscles, joints and internal organs

EXAMINATION

- evidence of bleeding/bruising

INVESTIGATIONS

- bleeding time normal
- APTT prolonged
- INR normal
- fibrinogen normal
- reduced specific factors levels
- von Willibrands factor levels normal

MANAGEMENT

- discuss with haematologist
- treated as required with recombinant factor:
  - aim for factors level 50-100% pre op
  - maintain levels for 2-7d post procedure

Intraoperative

- minimise blood loss and transfusion of products
- avoid anti-platelets and anti-coagulants
- avoid IM injections

MILD BLEEDING RISK

- DDAVP 0.3mcg/kg over 30min
- transexamic acid infusion 20mg/kg IV over 5 min TDS

MODERATE TO SEVERE BLEEDING RISK

- replace with recombinant factors and maintain over 2-7 days post-operatively
- cryoprecipitate (factor VIII) and FFP (factor XI) should only be used in emergencies

Postoperative

- monitoring for bleeding
- close management with haematologist

Von Willebrands Disease

Preoperative

- von Willibrands factor = protein involved in platelet adhesion and carriage of factor VIII
- deficiency produces
  - factor VIII deficiency
  - abnormal platelet adhesiveness
  - abnormal vascular endothelium

- autosomal dominant inheritance

- types:
  - 1 = (90% of cases)
    - quantitative reduction in vWB factor
    - mild/asymptomatic
    - heterzygous
  - 2 = (9%)
    - qualitative abnormality in vWB factor
    - 4 subtypes A, B, N, M
    - DDAVP contraindicated in 2B (risk of ↓platelets & ↑thrombosis)
      ↳ 2B = gain of function defect ie ↑risk of clotting
  - 3 = (1%)
    - similar to type 1.
    - but severe symptoms
    - homozygous
    - autosomal recessive inheritance

HISTORY

- epistaxis
- bruising
- haemarthosis
- haematoma
- mennorrhagia

EXAMINATION

- as per history

INVESTIGATIONS

- platelets count normal
- INR normal
- APTT increased
- fibrinogen normal
- factor VIII level decreased
- vWB factor level decreased
- increased bleeding time
- increased platelet functional assay time

MANAGEMENT

- define responders and non-responders to DDAVP (0.3mcg/kg over 30min IV) -> measurement of vWB factor level pre and post.

Intraoperative

- responders should have DDAVP for prophylaxis and bleeding
- non-responders should have factor VIII concentrates or cryoprecipitate
- can also use tranexamic acid 20mg/kg IV TDS

Postoperative
- monitor for bleeding
- consult haematologist

Thrombocytopaenia

Preoperative
= <150 x 10^9/L
- causes:
1. decreased production (hereditary, drugs, ET-OH, viral infection, marrow failure)
2. dilution (massive transfusion)
3. increased consumption (ITP, drugs, viral infection, SLE, lymphoproliferative disorders, DIC, bypass, TTP, hypersplenism)

- spont bleeding v uncommon until <10-20

HISTORY
- bleeding
- bruising

EXAMINATION
- large spleen

INVESTIGATIONS
- FBC + repeat sample
- film
- bone marrow

MANAGEMENT
- as per cause
- ITP:
    - transfusion of platelet reserved for major haemorrhage as platelets die quickly
    - better to prep for surgery: steroids or high dose Ig
- platelet targets:
    - >50 to insert invasive lines, transbronchial biopsy, liver biopsy or laparotomy
    - >80 for LP, epidural,
    - >100 critical surgery ie neurosurgery or eye surgery

Intraoperative
- manage bleeding
- if ongoing bleeding despite platelets >50 ⟹ DIC -> FFP and cryo
- renal failure, haemophilia and vWB disease: DDAVP 0.3mg/kg IV over 30min

Postoperative
- standard

Disseminated Intravascular Coagulation

Acute DIC
- acute DIC = most common cause of coag abnormality in surgical setting
- causes:
    - infection - esp gram -ve
    - placental abruption
    - amniotic fluid emobolism

    - major trauma
    - burns
    - hypoxia/hypovolaemia
    - severe liver disease
- leads to varied clinical presentation:
    - haemorrhage ⟹ predominates
    - thrombosis ⟹ multi organ dysfiunction 2nd to microthrombosis
    - both

Chronic DIC

- causes:
    - aneurysms
    - hemangiomas
    - carcinomatosis
- may have limited clinical effect

Diagnosis

- variable depending on severity of DIC:
    - ↓Hb
    - prolonged APTT, INR
    - ↓ing or low platelets
    - low fibrinogen
    - high D dimer
- DIC score:
    - simple scoring system based on platelet count, PT, D dimer & fibrinogen levels
    - sensitivity 93% & specificity 98%

Differential

- primary fibrinolysis
- dilutional coagulopathy from masseive transfusion
- trauma induced coagulopathy
- post thromboylsis
- venom induce consumptive coagulopathy ⟹ snake bite

Treatment

- treat cause
    - FFP ⟹ INR >1.5
    - cryo ⟹ fib <1
    - platelets ⟹ platelets <50
    - consider VIIa
    - consider heparin - if not bleeding ie chronic DIC

Hypercoagulability Syndromes

Polycythaemia

- polycythaemia = Hb >175 in males and >155 in females (+ increased RCC and haematocrit)

Causes

- **primary** = polycythaemia vera (PCV)
- **secondary** =
  - compensatory ↑ EPO:
    - altitude
    - Cardioresp disease eg cyanotic, OSA, metHb, heavy smoking
  - inappropriate ↑EPO:
    - renal disease - hydronephrosis, cycts, carcinmoa
    - massive uterine fibromyomata
    - hepatocellular Ca
    - cerebellar haemangioblastoma
- **relative**:
  - stress
  - dehydration/hypovolaemia
  - burns
  - enteropathy

Polycythaemia Vera

PreOperative

HISTORY

- headaches
- SOB
- chest pain
- vertigo
- pruritis
- epigastric pain
- HT
- gout
- thrombotic episodes (retinal)

EXAMINATION

- splenomegaly

INVESTIGATONS

- thrombocythaemia (↑platelets)
- FBC - as above
- AG
- bone marrow aspiration
- EPO levels
- genetic testing - JAK2 mutation in 90-95% of PV patients

MANAGEMENT

- venesection - aim normal Hb prior to surgery
- myelosuppresive drugs - 10% of patients ⟹ develop myelofibrosis & rarely acute leukaemia
- monitoring for transformation -> myelofibrosis and leukaemia

Intraoperative

- DVT prophylaxis: SCDs & LMWH

Postoperative
- DVT cares: SCDs & LMWH

Essential Thrombocythaemia
- megakaryocyte proliferation ⟹ ↑platelets >450
- closely related to PV
- clinical features = recurrent haemorrhage & thrombosis

Investigations
- blood film show
    - abnormal large platelets
    - megakaryocyte fragments
- platelet function tests abnormal

Differential
- haemorrhage
- chronic infections
- malignancy
- PV
- myelosclerosis
- chronic granulocytic leukaemia

Treatment
- hydroxycarbamide

Antiphospholipid Syndrome
- rare but ↑ing diagnoses
- clinical result is:
    - arterial or venous thrombosis
    - recurrent miscarriage

Associations
- autoimmune diseases eg SLE

Clinical Features
- thrombosis ⟹ subacute migraine to heart failure or stroke
- arterial thrombosis should make you think of antiphospholipid syndrome

Investigations
- +ve antiphospholipid antibody
- +/- lupus anticoagulant:
    - actually causes prolongation of coag screen eg APTT
- need careful & thorough investigation

Treatment
- aspirin
- if confirmed thrombotic event ⟹ lifelong warfarin

Peri-Op Management
- very high risk of thrombosis:
    - should use IV heparin pre-&post op