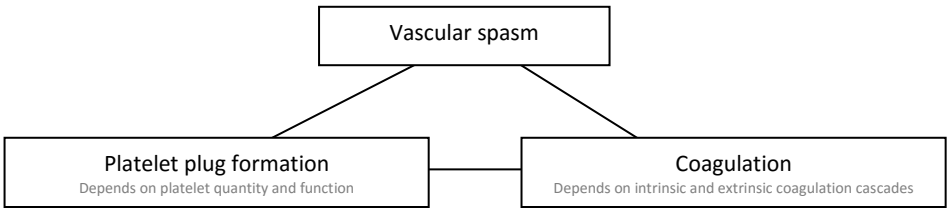
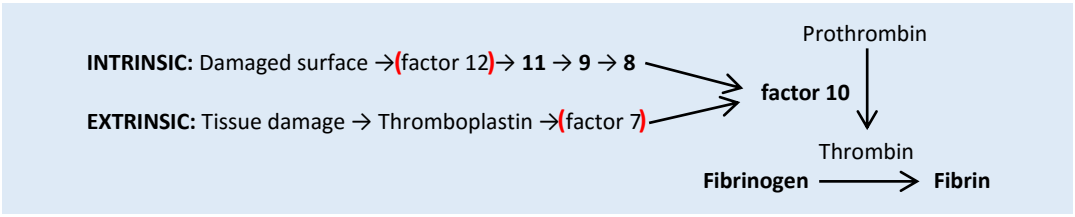
Interpretation of Coagulation Screen

Background knowledge

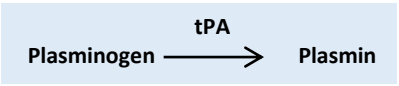
- Haemostasis process:



- Coagulation cascade:



- Clot dissolution:



- Natural anticoagulants: protein C&S, heparin, antithrombin
- Vitamin K dependant clotting factors: 2, 7, 9, 10 (+ protein C&S)
- Most coagulation factors are synthesised by the liver

Tests

Basic

- **PT and INR = EXTRINSIC**
  - Thromboplastin is added to blood to activate the extrinsic pathway. Clotting time is measured in seconds (PT). This is compared to the normal value (12-13s) to get the INR for ease of comparison (normal 0.8-1.2).
  - *Aid to memoire:* ***WEPT*** ***W****arfarin* ***E****xtrinsic* ***P****rothrombin* ***T****ime*
  - Prior to the common pathway, only factor 7 is involved (of which isolated deficiencies are rare) so PT/INR is *only really affected by global reduced clotting factor synthesis or increased consumption:*
    - *Warfarin/vitamin K deficiency*
    - *Liver disease*
    - *DIC*
- **APTT = INTRINSIC**
  - Phospholipid, a contact activator and calcium are added to blood to activate the intrinsic pathway. Clotting time is measured in seconds (normal = 30-50s)
  - Involves similar clotting factors to the extrinsic pathway PLUS some others (8, 9, 11) so *affected by:*
    - *Warfarin/vitamin K deficiency*
    - *Liver disease*
    - *DIC*

    ] Like the extrinsic path
    - *PLUS anything which affects factors 8 (haemophilia A/Von Willebrands), factor 9 (haemophilia B), factor 11 (haemophilia C)*

    Note: factor 12 is also involved in the intrinsic pathway but deficiencies are rare
    Note: anti-phospholipid syndrome (explained below) is a common cause of a misleadingly prolonged APTT, due to antibody-mediated inactivation of the phospholipid added to activate the intrinsic pathway in the laboratory
- **Bleeding time = PLATELET FUNCTION**
  - Involves making a patient bleed and timing how long it takes to stop
  - Measures platelet plug formation so *only affected by conditions involving platelet quantity/function*
- **Thrombin time = FIBRINOGEN TEST**
  - Thrombin is added to blood to test the conversion of fibrinogen to fibrin to form a clot
  - This tests the level and function of fibrinogen

Other relevant tests

- **Full blood count** – to check platelet count and other haematological abnormalities
- **Liver function tests** – to exclude liver function abnormalities as a cause for clotting problems
- **Albumin** – gives an indication of nutrition e.g. a high INR (with no clear cause) and low albumin suggests vitamin K deficiency

- **D-dimer/fibrin degradation products** – tests the level of fibrin degradation products predicting recent clot formation (e.g. DVT, PE, DIC etc)

Advanced tests

- **Anti-phospholipid antibodies** (e.g. anti-cardiolipin, lupus anticoagulant) – to look for anti-phospholipid syndrome
- **Factor assays ± factor inhibitor antibodies** (e.g. factor 8, 9, 11) – the level of individual clotting factors may be tested to look for common deficiencies (e.g. haemophilia A, B, C respectively)

Important conditions

- Factor synthesis problems
    - **Vitamin K deficiency**: vitamin K is a fat-soluble vitamin so may be deficient in fat malabsorption (e.g. in biliary obstruction – check LFTs) or a simple dietary deficiency. Deficiency reduces the vitamin K dependant clotting factors (2, 7, 9, 10) and, hence, affects both the intrinsic and extrinsic clotting pathways. If due to dietary deficiency, treat with 5-10mg oral vitamin K (phytomenadione) OD for 3 days; if due to fat malabsorption, IV vitamin K or menadiol (a water-soluble vitamin K derivative) can be used.
    - **Liver failure**: the liver synthesises most clotting factors so liver failure can result in a global decline in clotting factors which affects both the intrinsic and extrinsic clotting pathways. Platelets may also be reduced due to hypersplenism. Liver-relate coagulopathy is difficult to manage and is mainly supportive (FFP, cryoprecipitatie, platelet transfusions etc as required). Vitamin K may be given if a deficiency is suspected.
- Consumption
    - **DIC**: in a severe systemic illness dying cells release procoagulant agents that activate coagulation, resulting in fibrin generation that occludes small vessels. Platelets and clotting factors are used up and result in bleeding elsewhere. Blood tests reveal thrombocytopenia, increased PT/INT and APTT, and raised D-dimer and fibrin degradation products. Treat by removing cause and supportive therapies (blood, platelets, FFP, cryoprecipitate).
- Drugs
    - **Warfarin (vitamin K antagonist)**: reduces vitamin K dependant clotting factors (2, 7, 9, 10) and, hence, affects both the intrinsic and extrinsic clotting pathways. See below for more information.
    - **Heparin**: heparin is a natural anticoagulant that potentiates antithrombin (which inactivates factors 2, 9, 10, 11, 12) and inactivates thrombin. Types of heparin that are commonly used include:
        - Subcutaneous LMWH (e.g. enoxiparin) – most commonly used for prophylactic and therapeutic anticoagulation. Consists of only short chain heparins and, therefore, only binds to a specific part of antithrombin, which results in inhibition of factor 10A only. This means the effects are more predictable than standard (unfractionated) heparin. Monitoring is not required but effect can be measured by anti-factor 10A.
        - IV or subcutaneous unfractionated (standard) heparin – consists of heparin chains with a variety of molecular lengths and, therefore, has more and less predictable effects. Subcutaneous therapy may be used for prophylactic anticoagulation in patients with reduced renal function (unfractionated heparin is partially cleared by the liver, whereas LMWH is not). IV therapy may be used for therapeutic anticoagulation pre-op or if there is significant risk of bleeding, due to its short half-life (effect stops within 4 hours of infusion stopping). It must be monitored regularly using APTT and dose adjusted (as per hospital guidelines).

    Heparin can be reversed with protamine sulphate if required.
- Deficiencies
    - **Haemophilia** A (factor 8 deficiency), B (factor 9 deficiency), C (factor 11 deficiency): clinical features depend on level of affected factor but characteristically include haemarthroses and muscle haematomas
    - **Von Willebrands disease**: deficiency of von Willebrand factor which is involved in platelet aggregation and adhesion, and binds factor 8 preventing it from destruction. Hence von Willebrands disease produced a platelet disorder picture of bleeding (petichiae, menorrhagia, contact bleeding e.g. gums)
- Autoimmune
    - **Anti-phospholipid syndrome:** anti-phospholipid antibodies (anti-cardiolipin, lupus anticoagulant) react against proteins that bind to plasma membrane phospholipids, which results in arterial and venous thrombosis. Anti-phospholipid syndrome misleadingly causes a prolonged APTT because the antibodies inactivate the phospholipid added to activate the intrinsic clotting cascade during the laboratory measurement of APTT.

	Haemophilia A	Von Willebrands disease	Vitamin K deficiency
Bleeding time	N Because platelets not affected	↑ Because vWF is mainly involved in platelet adhesion	N Because platelets not affected
PT/INR	N Because factor 8 not involved in extrinsic pathway	N Because vWF is mainly involved in platelet adhesion	↑ Because vitamin K dependant clotting factors are used in extrinsic pathway
APTT	↑ Because factor 8 is involved in intrinsic pathway	↑± Because vWF binds factor 8	↑ Because vitamin K dependant clotting factors are used in intrinsic pathway
vIIIic	↓↓ Because factor 8 is deficient	↓ Because vWF binds factor 8	N Because factor 8 is not vitamin K dependant
vWF	N Because vWF not affected	↓ Because vWF is deficiency	N Because vWF not affected

Warfarin

Therapeutic test (INR)

- Warfarin therapy is monitored using the INR
- Aims:
    - INR 2-3: DVT/PE, hypercoagulable states, AF
    - INR 2.5-3.5: aortic metallic heart valves (higher pressure blood flow reduced embolic risk)
    - INR 3-4: mitral metallic heart valves

Reversal

- Major bleeding → stop warfarin, prothrombin complex concentrate, 5-10mg IV vitamin K
- Non-major bleeding
    - INR >8 → stop warfarin, PLUS 0.5-2.5mg PO vitamin K if other risk factors for bleeding
    - INR 6-8 → stop warfarin
    - INR 3-6 → reduce/stop warfarin

Stop warfarin for 2-4 days to see effect
Oral vitamin K takes 24-48 hours, IV vitamin K takes 6 hours, prothrombin complex concentrate takes 15 minutes
FFP may be used instead of prothrombin complex concentrate if this is unavaliable
For pre-op warfarin reversal, see pre-op assessment notes