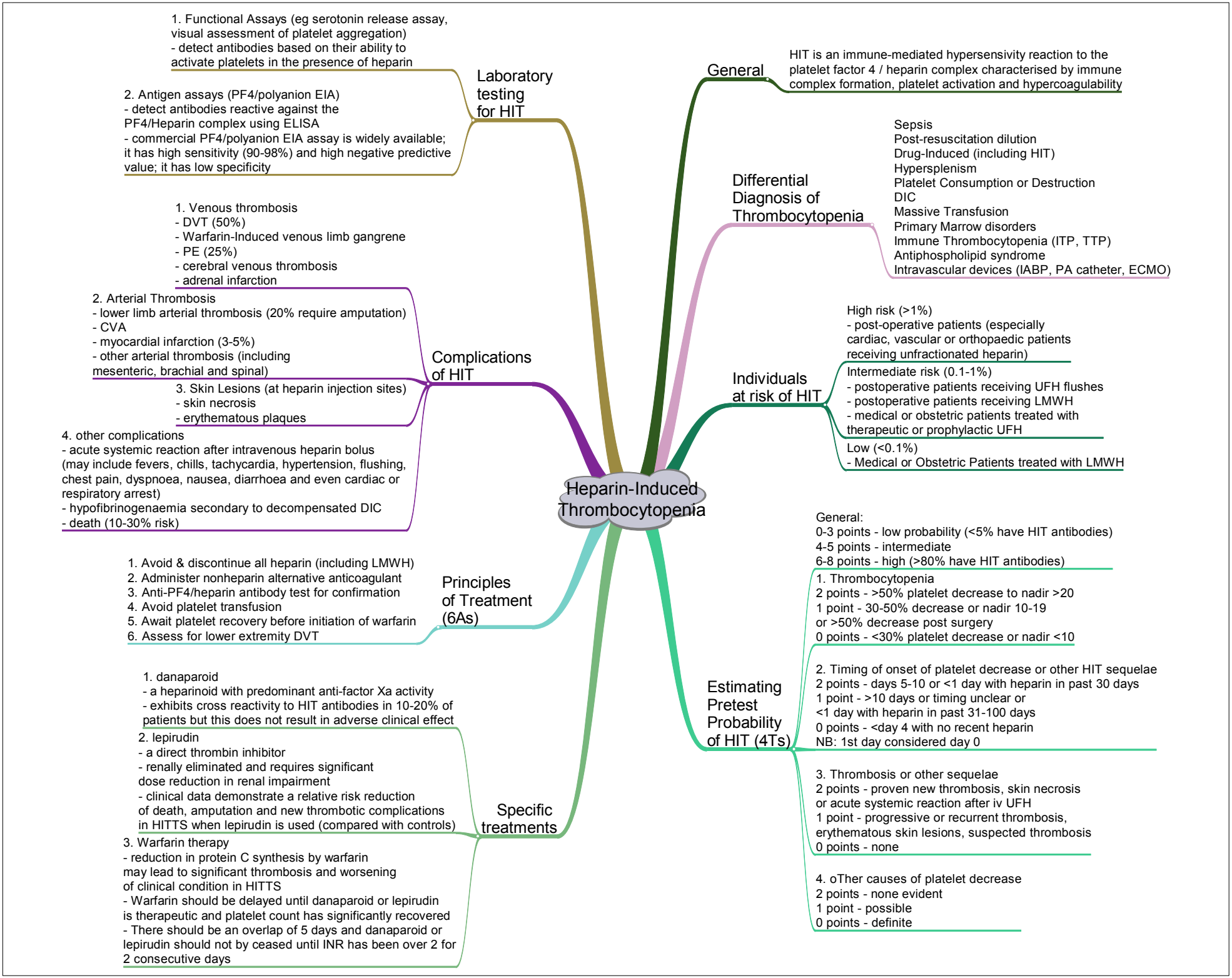
Heparin-Induced Thrombocytopenia
General
HIT is an immune-mediated hypersensivity reaction to the platelet factor 4 / heparin complex characterised by immune complex formation, platelet activation and hypercoagulability
Differential Diagnosis of Thrombocytopenia
Sepsis
Post-resuscitation dilution
Drug-Induced (including HIT)
Hypersplenism
Platelet Consumption or Destruction
DIC
Massive Transfusion
Primary Marrow disorders
Immune Thrombocytopenia (ITP, TTP)
Antiphospholipid syndrome
Intravascular devices (IABP, PA catheter, ECMO)
Individuals at risk of HIT
High risk (>1%)
- post-operative patients (especially cardiac, vascular or orthopaedic patients receiving unfractionated heparin)
Intermediate risk (0.1-1%)
- postoperative patients receiving UFH flushes
- postoperative patients receiving LMWH
- medical or obstetric patients treated with therapeutic or prophylactic UFH
Low (<0.1%)
- Medical or Obstetric Patients treated with LMWH
Estimating Pretest Probability of HIT (4Ts)
General:
0-3 points - low probability (<5% have HIT antibodies)
4-5 points - intermediate
6-8 points - high (>80% have HIT antibodies)
1. Thrombocytopenia
2 points - >50% platelet decrease to nadir >20
1 point - 30-50% decrease or nadir 10-19
or >50% decrease post surgery
0 points - <30% platelet decrease or nadir <10
2. Timing of onset of platelet decrease or other HIT sequelae
2 points - days 5-10 or <1 day with heparin in past 30 days
1 point - >10 days or timing unclear or
<1 day with heparin in past 31-100 days
0 points - <day 4 with no recent heparin
NB: 1st day considered day 0
3. Thrombosis or other sequelae
2 points - proven new thrombosis, skin necrosis
or acute systemic reaction after iv UFH
1 point - progressive or recurrent thrombosis,
erythematous skin lesions, suspected thrombosis
0 points - none
4. oTher causes of platelet decrease
2 points - none evident
1 point - possible
0 points - definite
Specific treatments
1. danaparoid
- a heparinoid with predominant anti-factor Xa activity
- exhibits cross reactivity to HIT antibodies in 10-20% of patients but this does not result in adverse clinical effect
2. lepirudin
- a direct thrombin inhibitor
- renally eliminated and requires significant dose reduction in renal impairment
- clinical data demonstrate a relative risk reduction of death, amputation and new thrombotic complications in HITTS when lepirudin is used (compared with controls)
3. Warfarin therapy
- reduction in protein C synthesis by warfarin may lead to significant thrombosis and worsening of clinical condition in HITTS
- Warfarin should be delayed until danaparoid or lepirudin is therapeutic and platelet count has significantly recovered
- There should be an overlap of 5 days and danaparoid or lepirudin should not by ceased until INR has been over 2 for 2 consecutive days
Principles of Treatment (6As)
1. Avoid & discontinue all heparin (including LMWH)
2. Administer nonheparin alternative anticoagulant
3. Anti-PF4/heparin antibody test for confirmation
4. Avoid platelet transfusion
5. Await platelet recovery before initiation of warfarin
6. Assess for lower extremity DVT
Complications of HIT
1. Venous thrombosis
- DVT (50%)
- Warfarin-Induced venous limb gangrene
- PE (25%)
- cerebral venous thrombosis
- adrenal infarction
2. Arterial Thrombosis
- lower limb arterial thrombosis (20% require amputation)
- CVA
- myocardial infarction (3-5%)
- other arterial thrombosis (including mesenteric, brachial and spinal)
3. Skin Lesions (at heparin injection sites)
- skin necrosis
- erythematous plaques
4. other complications
- acute systemic reaction after intravenous heparin bolus (may include fevers, chills, tachycardia, hypertension, flushing, chest pain, dyspnoea, nausea, diarrhoea and even cardiac or respiratory arrest)
- hypofibrinogenaemia secondary to decompensated DIC
- death (10-30% risk)
Laboratory testing for HIT
1. Functional Assays (eg serotonin release assay, visual assessment of platelet aggregation)
- detect antibodies based on their ability to activate platelets in the presence of heparin
2. Antigen assays (PF4/polyanion EIA)
- detect antibodies reactive against the PF4/Heparin complex using ELISA
- commercial PF4/polyanion EIA assay is widely available; it has high sensitivity (90-98%) and high negative predictive value; it has low specificity