MANAGEMENT OF THROMBOCYTOPENIA AND THROMBOCYTOSIS

Background

- Commonest cause of bleeding problems in the neonate
- Defined as a platelet count < 150 x 10^9/L (same as adults) and classified as early (within 3 days of birth) or late onset (after 3 days)
- Further defined as mild (100 - 149 x 10^9/L), moderate (50 - 99 x10^9/L) or severe (< 50 x 10^9/L).
- Risk increases with decreasing gestational age and with multiple risk factors.

General Causes

• **Onset**	• **Most common aetiology**	• **Less common aetiology**
• Foetal	• Placental insufficiency (IUGR, diabetes, PET) • Chorioamnionitis • Congenital Infection (Viral [rubella, CMV, HSV, HIV] or bacterial [toxoplasmosis) • Aneuploidy (trisomies/triploidy) • Alloimmune- Neonatal alloimmune thrombocytopenia (NAIT) • Autoimmune (ITP/SLE)	• Severe rhesus disease • Congenital/inherited (Fanconi's anaemia, Thrombocytopenia absent radii TAR)
• Early Onset (<72hr) • Often preterm deliveries complicated by placental insufficiency / foetal hypoxia	• Placental insufficiency (IUGR, diabetes, PET) • Perinatal asphyxia • Chorioamnionitis • Hypoxia/sepsis/shock • Consumption by haemorrhage (IVH, pulmonary haemorrhage) • DIC • NAIT/Autoimmune (ITP/SLE) • Thrombotic events	• Congenital infection • Bone marrow disorders (congenital leukaemia, neonatal neuroblastoma) • Metabolic disease • Congenital heart disease • Giant Haemangiomata • Post exchange transfusion
• Late Onset (>72hr)	• Late onset sepsis • NEC • Thrombotic events	• Congenital Infection • NAIT/autoimmune • Kasabach-Merritt • Metabolic disease • Congenital heart disease

General Diagnosis and Investigations

- Thorough examination considering differential diagnoses a listed above
- Blood tests: FBC and film (confirm count), group & save, clotting screen, blood gas, cultures, CRP, liver function tests, consider: maternal platelet count, viral TORCH screen, , NAIT bloods (see below), genetic tests
- Specialist advice if required

General Management

- Symptomatic treatment: platelet transfusion of ideally ABO compatible/CMV negative platelets in **10 – 20 ml/kg** increments (in haemorrhagic emergency transfuse O negative emergency platelets)
- See flowchart for suggested transfusion thresholds.
- In strongly suspected or confirmed NAIT use HPA-1A negative platelets whenever possible, always transfuse under 50 x 10^9/L, transfuse under 100 x 10^9/L if significant bleeding
- Causative treatment depending on the diagnosis
- PlaNeT-2/Matisse trial: higher mortality and major bleeding in babies in higher transfusion threshold group (< 50 x 10^9/L) than in lower transfusion threshold group (< 25 x 10^9/L). BPD rates higher in higher transfusion threshold group. Also evidence to suggest an increase in IVH in babies with higher transfusion threshold (< 100 x 10^9/L)
- Always consider risk of transfusion related adverse effects such as related acute lung injury (TRALI) and transfusion associated circulatory overload (TACO)
- Highest bleeding risk include < 28 weeks gestation, early onset severe thrombocytopenia and NEC

Neonatal alloimmune thrombocytopenia (NAIT)

- Incidence potentially as high as 1 in 1000
- Mother's platelet count usually normal
- Commonest platelet antigen HPA-1A. Mother HPA-1A negative → destruction of infant platelets by anti HPA-1A antibodies

Clinical presentation

- Most neonates mild-moderately affected with resolution within first week of life, 20% severely affected
- Greatest risk IVH (up to 80% in utero), excessive bruising and oozing may occur

Diagnosis

- Often diagnosed as previous baby had low platelet count often with complications
- Detection of specific antibodies in maternal serum and on infant's platelets
- NAIT investigation request form:
  Hospitals & Science website https://hospital.blood.co.uk/ → Diagnostic Services → Histocompatibility and Immunogenetics → H&I test request forms → Platelet immunology
  - Maternal sample: 6 ml clotted blood + 6 ml EDTA blood
  - Paternal sample: 6 ml EDTA blood
  - Baby sample: 1 ml EDTA blood

Management

- Not all infants require treatment but should be observed
- Avoid random platelet transfusions (less effective), if possible use HPA-1A negative or specific HPA compatible platelets
- Seek specialist haematological advice, refer to local haematology team for outpatient monitoring

Maternal idiopathic thrombocytopenia (and SLE)

- Mother's platelet count usually reduced (unless splenectomised)
- May result in thrombocytopenia if maternal antiplatelet IgG cross placenta
- No correlation between maternal platelet count and the impact on foetus
- Severity variable: may be confined to bruising with jaundice and secondary anaemia or may be as severe as intracranial haemorrhage
- Process self-limiting, platelet count should rise by 3rd week and normalise by 2-3 months

- In severe cases seek specialist haematological advice and refer to local haematology team for outpatient monitoring

Management:

- Infants with a platelet count < 30 x 10^9/L consider 1 g/kg/ of IVIG as a single dose, can be repeated if < 30 x 10^9 by day 5.
- No routine use of platelets recommended unless clinically indicated.

Thrombocytosis

- Defined as platelet count > 450 x 10^9/L
- Often unspecific finding
- Often thought to be due to higher levels of and increased sensitivity to thrombopoietin
- Other causes include infectious and inflammatory causes
- No specific treatment available or required

Platelet transfusion thresholds (not NAIT)