Neonatal Thrombocytopenia

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Thrombocytopenia
Definition

• Platelet count <150,000 (1-2% of healthy term infants)
  – Mild 100-150,000
  – Moderate 50-99,000
  – Severe <50,000

(Less then 5% of infants <32 weeks have platelets <104,000 and in late preterm <123,000)
Incidence

• ~18-32% of infants admitted to NICU develop thrombocytopenia during their stay.
• Increased frequency in more preterm infants.
• Increased risk for ICH, mortality, and long term neurodevelopmental disability.
Platelet production

4 steps

1. Production of Thrombopoietin (Tpo)
2. Proliferation of megakaryocytes progenitors
3. Megakaryocyte maturation

- Platelet productions starts at the end of the first trimester of pregnancy.
- There are measures of platelet production such as serum Tpo or reticulate platelet percentages (RP%) but they are not reliable in infants.
## Table 1.

**Classification of fetal and neonatal thrombocytopenias**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fetal</strong></td>
<td>Alloimmune&lt;br&gt;Congenital infection (e.g. CMV, toxoplasma, rubella, HIV)&lt;br&gt;Aneuploidy (e.g. trisomies 18, 13, 21, or triploidy)&lt;br&gt;Autoimmune (e.g. ITP, SLE)&lt;br&gt;Severe Rh haemolytic disease&lt;br&gt;Congenital/inherited (e.g. Wiskott-Aldrich syndrome)</td>
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<tr>
<td><strong>Early onset neonatal (&lt;72 hours)</strong></td>
<td>Placental insufficiency (e.g. PET, IUGR, diabetes)&lt;br&gt;Perinatal asphyxia&lt;br&gt;Perinatal infection (e.g. E coli, GBS, Haemophilus influenzae)&lt;br&gt;DIC&lt;br&gt;Alloimmune&lt;br&gt;Autoimmune (e.g. ITP, SLE)&lt;br&gt;Congenital infection (e.g. CMV, toxoplasma, rubella, HIV)&lt;br&gt;Thrombosis (e.g. aortic, renal vein)&lt;br&gt;Bone marrow replacement (e.g. congenital leukaemia)&lt;br&gt;Kasabach-Merritt syndrome&lt;br&gt;Metabolic disease (e.g. propionic and methylmalonic acidemia)&lt;br&gt;Congenital/inherited (e.g. TAR, CAMT)</td>
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<tr>
<td><strong>Late onset neonatal (&gt;72 hours)</strong></td>
<td>Late onset sepsis&lt;br&gt;NEC&lt;br&gt;Congenital infection (e.g. CMV, toxoplasma, rubella, HIV)&lt;br&gt;Autoimmune&lt;br&gt;Kasabach-Merritt syndrome&lt;br&gt;Metabolic disease (e.g. propionic and methylmalonic acidemia)&lt;br&gt;Congenital/inherited (e.g. TAR, CAMT)</td>
</tr>
</tbody>
</table>

The most common conditions are highlighted.

CMV, Cytomegalovirus; ITP, idiopathic thrombocytopenic purpura; SLE, systemic lupus erythematosus; PET, pre-eclampsia; IUGR, intrauterine growth restriction; E coli Escherichia coli; GBS, group B streptococcus; DIC, disseminated intravascular coagulation; TAR, thrombocytopenia with absent radii; CAMT, congenital amegakaryocytic thrombocytopenia; NEC, necrotising enterocolitis.

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**Neonatal thrombocytopenia: causes and management.**
Roberts I; Murray NA

Early Onset <72 hrs

• Well Appearing: Most common is autoimmune thrombocytopenia or placenta insufficiency (PIH or chronic HTN)
  – Mild to moderate thrombocytopenia
  – Nadir on postnatal day 4-5
  – Usually resolves by 7-10 days.

• More severe NAIT

• Ill Appearing: Sepsis (Bacterial or viral), TORCH, DIC
Neonatal Autoimmune Thrombocytopenia

- Early onset, moderate-severe thrombocytopenia
- Usually a maternal history of ITP or autoimmune disease (2 in 1000 pregnancies)
- Any infant born to a mom with autoimmune disease should have a platelet count (incidence is about 10%).
- Can treat with IVIG for thrombocytopenia, may need platelet transfusion.
- Evaluate for ICH (incidence is ~1%).
- Can last from days to months.
Neonatal Alloimmune Thrombocytopenia (NAIT)

- Severe thrombocytopenia (<50,000)
- Increased risk for ICH (Incidence is 8-22%)
- May present antenatally with ICH, severe hydrocephalus, hydrops fetalis.
- Incidence 1 in 1500 pregnancies
- Due to maternal Ab to paternal Ag
- Can occur in first pregnancy
- Testing of Mother and Father for Human Platelet antigen (HPA) 1, 3, and 5. (90% of cases)
Neonatal Alloimmune Thrombocytopenia (NAIT)

- If platelets <50,000- Suggest cerebral imaging (US, CT, MRI)
- Transfuse platelets:
  - trial of random donor platelets first.
  - If ineffective: Antigen negative platelets should be used (maternal platelets or known PL A1 or PL A5 negative platelets)
- Consider IVIG 1g/kg q 24hrs x 2 doses (can be given to help patient increase own platelets or in combination with random donor transfusions.
- Consider methylprednisolone (1mg/kg q 8hrs) with IVIG.
Neonatal Alloimmune Thrombocytopenia (NAIT)

• Usually resolves with in 2 weeks
• But platelet count needs to be followed until normalized and stable.
• If persists longer may be a different diagnosis.
• Monitoring for future pregnancies and possibly treatment with maternal IVIG/steroids.
Late-Onset Thrombocytopenia

- Ill Appearing: Sepsis, NEC, IEM (Propionic Acidemia, isovaleric acidemia, methylmalonic acidemia, Gaucher Disease)
- Well Appearing: Drug induced, thrombosis, Fanconi’s Anemia
Physical Exam

• Ill or Well
• Petechia, bruising
• Fontonelle
• Liver size
• Abdominal masses (renal vein thrombosis)
• Dysmorphic features
• Forearm or thumb abnormalities (TAR syndrome or Fanconi anemia)
<table>
<thead>
<tr>
<th>Genetic Disorders Associated With Thrombocytopenia</th>
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<tbody>
<tr>
<td>Aplasia cutis, CHD, cleft lip and palate, polydactyly</td>
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<tr>
<td>IUGR, CHD, rocker-bottom feet, overlapping digits,</td>
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<tr>
<td>hypertelorism, small mouth, clinodactyly</td>
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<tr>
<td>CHD, single palmar crease, hypotonia, short neck, w/</td>
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<tr>
<td>redundant posterior folds</td>
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<tr>
<td>CHD, cubitus valgus, webbed posterior neck, broad chest,</td>
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<tr>
<td>with wide-spaced nipples, lower extremity edema</td>
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<tr>
<td>CHD, GU anomalies, facial anomalies, abnl brain imaging,</td>
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<tr>
<td>limb anomalies</td>
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<tr>
<td>Giant platelets, neutrophilic inclusions</td>
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<tr>
<td>Giant platelets, sensorineural hearing loss, cataracts,</td>
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<tr>
<td>nephritis, neutrophilic inclusions</td>
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<tr>
<td>Anemia, genitourinary abnormalities (cryptorchidism)</td>
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<tr>
<td>Abnl head size and shape, developmental delay, CHD,</td>
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<tr>
<td>cleft and high-arched palate, abnormal kidneys, optic</td>
</tr>
<tr>
<td>atrophy, valgus and varus deformities, vertebral</td>
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<tr>
<td>anomalies, coloboma, scoliosis, absent bone marrow</td>
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<tr>
<td>megakaryocytes</td>
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<tr>
<td>Immunodeficiency, small platelets, eczema</td>
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<tr>
<td>Restricted forearm pronation, proximal radioulnar</td>
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<tr>
<td>synostosis in forearm, and radioulnar synostosis</td>
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<tr>
<td>absent bone marrow megakaryocytes</td>
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<tr>
<td>Hypopigmented and hyperpigmented skin lesions, urinary</td>
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<tr>
<td>tract abnormalities, microcephaly, upper extremity</td>
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<tr>
<td>radial-side abnormalities involving the thumb, pancytopenia</td>
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<tr>
<td>(usually with onset in childhood)</td>
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<tr>
<td>Shortened/absent radii bilaterally, nml thumbs, ulnar</td>
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<tr>
<td>and hand abnormalities, abnormalities of the humerus,</td>
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<tr>
<td>CHD, eosinophilia, leukemoid reaction</td>
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<tr>
<td>Fever, HSM, hyperferritemia, hypertriglyceridemia,</td>
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<tr>
<td>hypofibrinogenemia</td>
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<tr>
<td>FTT, developmental delay, ketoacidosis,</td>
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<tr>
<td>hyperglycinemia, hyperammonemia</td>
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<tr>
<td>Odor of sweaty feet, poor feeding, hypotonia,</td>
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<tr>
<td>hyperammonemia, metabolic acidosis</td>
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<tr>
<td>Hepatosplenomegaly, Gaucher cells in bone marrow</td>
</tr>
</tbody>
</table>

**Chromosomal:**
- Trisomy 13: Aplasia cutis, CHD, cleft lip and palate, polydactyly
- Trisomy 18: IUGR, CHD, rocker-bottom feet, overlapping digits, hypertelorism, small mouth, clinodactyly
- Trisomy 21: CHD, single palmar crease, hypotonia, short neck, w/ redundant posterior folds
- Turner syndrome: CHD, cubitus valgus, webbed posterior neck, broad chest, with wide-spaced nipples, lower extremity edema

**Familial:**
- May-Hegglin anomaly: Giant platelets, neutrophilic inclusions
- Sebastian syndrome: Giant platelets, sensorineural hearing loss, cataracts, nephritis, neutrophilic inclusions
- Fechtner syndrome: Anemia, genitourinary abnormalities (cryptorchidism)
- Bernard-Soulier syndrome: Abnl head size and shape, developmental delay, CHD, cleft and high-arched palate, abnormal kidneys, optic atrophy, valgus and varus deformities, vertebral anomalies, coloboma, scoliosis, absent bone marrow megakaryocytes

**Metabolic:**
- Propionic acidemia, methylmalonic acidemia: FTT, developmental delay, ketoacidosis, hyperglycinemia, hyperammonemia
- Isovaleric acidemia: Odor of sweaty feet, poor feeding, hypotonia, hyperammonemia, metabolic acidosis
- Gaucher disease: Hepatosplenomegaly, Gaucher cells in bone marrow
Management

• Any doubt repeat sample
  – Errors from improper collection or unrecognized platelet clumping

• Blood culture +/- antibiotics depending on history, clinical picture and severity.

• Review peripheral smear and MPV (Jacobsen and Fechtner syndromes present with large platelets and Wiskott-Aldrich syndrome and X-linked thrombocytopenia present with small platelets)
Management

• Transfuse platelets: (volume reduction not necessary)
  – <30,000- if clinically stable term or preterm > 1 week of age and no ICH
  – <50,000 for ill term infants or preterm infants (<33 weeks) in the first week of age.
  – <100,000 if ICH or signs of active bleeding.

• Andrew et al 1993 showed preterm infants tx at < 150000 vs <50,000 no differences in freq or severity of ICH

• Murray et al 2002 retrospective review no major hemorrhage in infants if platelets >30,000.
Management

• 10-15ml/kg random-donor platelets
  – Either CMV neg or leukoreduced
  – Irradiation to reduce GVHD

• Platelet transfusions associated with TALI and increased mortality

• If neonate responds to transfusion:
  – But needs transfusions on a weekly basis more likely due to decreased platelet production (congenital amegakaryocytic thrombocytopenia)
  – If needed every 1-2 days more likely increased platelet consumption.
References

• Saxonhouse et al. Thrombocytopenia in the neonatal intensive care unit. Neoreviews 2009;10;e435-445
• Sola, M. Evaluation and treatment of severe and prolonged thrombocytopenia in neonates. Clinics in Perinatology 2004; 31; 1-14