PYRUVATE KINASE DEFICIENCY

- **Background**
  - Active enzyme in Embden-Meyerhof pathway
  - Deficiency leads to defective red cell glycolysis and decrease ATP production
  - Red cells are rigid and deformed, metabolically and physically vulnerable with decreased red cell survival
GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

Oxidative radicles
H₂O₂

₂H₂O + O₂

GSH
(Reduced Glutathione)

GSSG
(Oxidized Glutathione)

G6PD
NADP

NADPH
GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

• Pathophysiology
  - Reduced half-life of G6PD in red blood cells.
    • Mildly reduced → may not have hemolysis
    • Markedly reduced → chronic hemolysis

• Genetics
  - X-linked recessive
  - More common in African American and Mediterranean ancestry
GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

• Episodes of hemolysis produced by:
  – Drugs
    • Antioxidant drugs include:
      – Aspirin
      – Sulfonamides
      – Antimalarials
      – Usually 24-48 hours after exposure
  – Fava beans
  – Infections
  – Neonatal jaundice
GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

- Normocytic anemia
- Heinz bodies seen in unstained red blood cells due to hemoglobin precipitation
- Bite cells
- Diagnosis demonstrated by reduced G6PD activity in RBCs should be few weeks after the hemolytic episode
GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

- Treatment
  - Avoidance of agents
  - Transfusion as needed
  - Folic acid supplementation
  - Splenectomy
    - Severe chronic anemia
    - Hypersplenism
    - Splenomegaly
Female G6PD

- G6PD deficiency is X-linked and therefore predominantly affects males.
- **Females** who are heterozygotes are usually clinically normal as they have about half the normal G6PD activity.
- Females may be affected either if they are *homozygous* or, more commonly, when by chance more of the normal than the abnormal X chromosomes have been inactivated (extreme Lyonisation – the Lyon hypothesis is that, in every XX cell, one of the X chromosomes is inactivated and that this is random).
- 45xo
AUTOIMMUNE HEMOLYTIC ANEMIA

- Etiology
  - Antibodies against antigens on RBCs surface
  - IgG against Rh complex is the most common in children
  - IgM cold antibodies usually associated with infections e.g. *Mycoplasma*, and *EBV*

- Clinical presentation
  - Pallor
  - Jaundice
  - Pyrexia
  - Hemoglobinuria
  - Splenomegaly
Direct Antibody Test or Coombs test

Looking for antibodies attached to red cell surface
Indirect Antibody Testing

Recipient’s antibodies from serum and donor’s blood sample: cross match and antibody screen
AUTOIMMUNE HEMOLYTIC ANEMIA

- Profound anemia
- Reticulocytosis
- Jaundice (unconjugated)
- Positive Direct antiglobulin (Coombs) test
- High MCHC, and spherocytosis
- High cold agglutinin (IgM) titer (in cases of mycoplasma or EBV)
AUTOIMMUNE HEMOLYTIC ANEMIA

• Treatment
  – Supportive treatment for mild cases
  – Corticosteroids for IgG mediated disease
  – Blood transfusion (blood unit with the least reaction by Coomb’s technique)
  – IVIg
  – Splenectomy in persistent cases
FANCONI ANEMIA

• Genetics
  – Autosomal Recessive, mutation in FANCA and FANCC genes

• Clinical Presentation
  – Skin abnormalities in 65% of cases
    • Hyperpigmentation of the trunk and intertriginous areas, café-au-lait spots, vitilgo
  – Short stature - 60%
  – Upper limb anomalies – 50%
    • Absent thumb
    • Triphalangeal thumb
    • Congenital hip dysplasia
  – Anemia (macrocytic)
  – café-au-lait spots
  – Short stature
  – Triphalangeal thumbs or absent thumb
  – Intellectual disability
FANCONI ANEMIA

• Clinical Presentation
  
  – Genital anomalies
  – Facial anomalies
    • Microcephaly, small eyes, epicanthal folds, abnormal shape ears, or absent ears
  – Intellectual disability—10%
  – Kidney abnormalities
    • Horseshoe kidney, absent or duplicate kidney
FANCONI ANEMIA

- **Laboratory**
  - Macrocytic anemia
  - Variable progression to full blown pancytopenia due to aplasia
  - Diepoxybutane (DEB) DNA analysis

- **Complications**
  - Acute leukemia
  - Carcinoma of head and neck, and upper esophagus
<table>
<thead>
<tr>
<th>Shape</th>
<th>Causes</th>
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<tbody>
<tr>
<td>Hypersegmented PMNs (6 or more lobes)</td>
<td>Megaloblastic anemia</td>
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<tr>
<td>Howell-Jolly bodies “Residual nuclear remnants”</td>
<td>Functional asplenia</td>
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<tr>
<td>Heinz bodies</td>
<td>G6PD</td>
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<tr>
<td>Schistocytes Shearing of the cell</td>
<td>Micronangiopathy, DIC, TTP, HUS</td>
</tr>
<tr>
<td>Spherocytes “Loss of membrane”</td>
<td>Spherocytosis, AIHA, enzymopathy, and hemoglobinopathy</td>
</tr>
<tr>
<td>Target cells “Excess membrane”</td>
<td>Thalassemia, liver disease</td>
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