Hemorrhagic disease of the newborn

- A moderate decrease in factors II, VII, IX, X normally occurs in all newborn infants by 48-72 hours after birth, this is probably due to lack of free Vit K from the mother and absence of bacterial intestinal flora normally responsible for Vit K synthesis.

- Rarely in term and more frequently in preterm accentuation and prolongation of this deficiency between the 2nd and the 7th days of life result in spontaneous and prolonged bleeding.

- Breast milk is a poor source of Vit K and hemorrhagic complications are more frequent in breast fed than artificially fed infants.
• The most common sites of hemorrhage or bleeding are: gastrointestinal, nasal, subgaleal, intracranial, or postcircumcision

• **Types:**
  1. classic
  2. early onset: very rare, 0-24 hr, maternal drugs: phenobarbital, phenytoin, warfarin, rifampin, INH; they interfere with Vit K
  3. late-onset vitamin K deficiency (1-6 mo) bleeding include:
     • Malabsorption
     • Hepatitis, biliary atresia
     • Cystic fibrosis
     • Alpha1-antitrypin deficiency
     • Short bowel syndrome
     • Intestinal bacterial overgrowth
     • Chronic exposure to broad spectrum antimicrobials
• DDX:
  1. DIC   2. Inherited coagulopathy

Investigations:
PT, PTT are prolonged
blood coagulation time is prolonged
The levels of factors II, VII, XI, X are low

Prevention of vitamin K deficiency bleeding with intramuscular vitamin K is of primary importance in the medical care of neonates. A single dose of intramuscular vitamin K after birth effectively prevents classic vitamin K deficiency bleeding particularly in term infants.
• Vitamin K is the mainstay for prevention of and treatment of vitamin K deficiency bleeding (VKDB). Other coagulation factors are rarely needed. Severe bleeding may warrant the use of fresh frozen plasma.
Genetic Disorders of Metabolism

inborn errors of metabolism or inherited metabolic disorders: hereditary biochemical disorders caused by single gene mutations that encode specific proteins.

These mutations can result in the alteration of primary protein structure or the amount of protein synthesized. The function of a protein, whether it is an enzyme, receptor, transport vehicle, membrane, or structural element, may be relatively or seriously compromised.
Common Characteristics of Genetic Disorders of Metabolism

1. The affected infant is normal at birth and becomes symptomatic later on in life.

2. Variation in severity of the phenotype in different families.

3. The earlier the appearance of clinical symptoms the more severe is the disease.

3. The majority of conditions are inherited as autosomal recessive traits.

4. Most of the genetic metabolic conditions can be controlled successfully by some form of therapy, and a few can be potentially cured by the use of bone marrow or liver transplants if diagnosed and treated early, before irreversible damage to organs, especially to the brain, occurs.
1. Defects in metabolism of aminoacids:
   a. phenylalanine: phenylketonuria
   b. Tyrosine: tyrosinemia, Albinism
   c. Methionine: homocystinuria
   d. Valine, Leucine, Isoleucine: Maple Syrup Urine Disease
   e. Ammonia: urea cycle and Hyperammonemia

2. Defects in metabolism of carbohydrate:
   a. Glycogen storage diseases
   b. Galactoseemia: Milk and dairy products contain lactose, the major dietary source of galactose. The metabolism of galactose produces fuel for cellular metabolism through its conversion to glucose-1-phosphate
Galactosemia denotes the elevated level of galactose in the blood resulting from complete or partial deficiency of galactose-1-phosphate uridyl transferase (galactokinase, and uridine diphosphate galactose-4-epimerase to less extent) Without the transferase enzyme, the infant is unable to metabolize galactose-1-phosphate, the accumulation of which results in injury to kidney, liver, and brain.
The diagnosis of uridyl transferase deficiency should be considered in newborn or young infants with any of the following features: jaundice, hepatomegaly, vomiting, hypoglycemia, seizures, lethargy, irritability, feeding difficulties, poor weight gain or failure to regain birth weight, aminoaciduria, nuclear cataracts, vitreous hemorrhage, hepatic failure, liver cirrhosis, ascites, splenomegaly, or mental retardation.

The preliminary diagnosis of galactosemia is made by demonstrating a reducing substance in several urine specimens.
Direct enzyme assay using erythrocytes establishes the diagnosis.

Various non–lactose containing milk substitutes are available (casein hydrolysates, soybean-based formula). Elimination of galactose from the diet reverses growth failure and renal and hepatic dysfunction. Cataracts regress, and most patients have no impairment of vision. Early diagnosis and treatment have improved the prognosis of galactosemia
3. Defects in metabolism of lipids

4. Mucopolysaccharidoses: hereditary, progressive diseases caused by mutations of genes coding for lysosomal enzymes needed to degrade glycosaminoglycans (acid mucopolysaccharides)
# Recognition Pattern of Mucopolysaccharidoses

<table>
<thead>
<tr>
<th>Manifestations</th>
<th>Type I-H</th>
<th>Type I-S</th>
<th>Type II</th>
<th>Type III</th>
<th>Type IV</th>
<th>Type VI</th>
<th>Type VII</th>
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<tbody>
<tr>
<td>Mental deficiency</td>
<td>+</td>
<td>–</td>
<td>?</td>
<td>+</td>
<td>–</td>
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<td>?</td>
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<tr>
<td>Coarse facial features</td>
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<td>+</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>?</td>
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<tr>
<td>Corneal clouding</td>
<td>+</td>
<td>+</td>
<td>–</td>
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<td>(+)</td>
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<td>Visceromegaly</td>
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<td>+</td>
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<tr>
<td>Short stature</td>
<td>+</td>
<td>(+)</td>
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<td>–</td>
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<tr>
<td>Joint contractures</td>
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</tr>
</tbody>
</table>
5. Disorders of Purine and Pyrimidine Metabolism

5. Progeria

6. The Porphyrias