GROUP A BLEEDING DISORDER IN CHILDREN
Introduction & normal physiology
Factors affect Hemostasis

- Platelets
- Coagulation factors
- Blood vessels integrity
Blood is kept in a liquid form because the endothelium produce inhibitory factors to deactivate the platelets and coagulation factors.

Healthy endothelium is crucial for hemostasis.

Injury to endothelial cells can be by: bacteria, viruses, drugs (intrinsic) OR external trauma, thermal injury (extrinsic).
Coagulation factors

- **Enzymes**, made in the liver
- some are **Vitamin K** dependent\((\text{gamma carboxylation})\)
- 10,9,7,2
- require Ionized **calcium**
- **Intrinsic pathway** \(\Rightarrow\) contact with non endothelial cell eg: Tube **activate** XII
- **Extrinsic pathway** \(\Rightarrow\) tissue lipoprotin factor, tissue thrombin ** Activate** factor VII
- **Goal:** fibrinogen \(\Rightarrow\) fibrin
Platelets

- From BM megakaryocytes
- Size 2-3 micron
- Count 150000-450000
- No nucleus
- Granules
- Receptors
- Life span 7-10 days
- Decrease number or function ➔ bleeding
Hemostasis steps

- Vasoconstriction ➔ neurogenic reflex
- endothelien ➔ by injured cells
- Von Wilibrands factors ➔ by injured cells
- Attach to platelets by Gp1b.
- platelet adhesion
- Platelet activation (TXA2) vaso.const. inc. aggregation
- Platelet aggregation
- Primary hemostatic plug AKA primary plat. Plug
- Primary hemostatic + fibrin ➔ secondary plug
<table>
<thead>
<tr>
<th>Blood vessels</th>
<th>Coagulation factors</th>
<th>Decrease platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhagic telangiectasia</td>
<td>Hemophilias (A, B, C))</td>
<td>Number</td>
</tr>
<tr>
<td>Scurvy, PEM</td>
<td>Liver diseases</td>
<td>BM depression</td>
</tr>
<tr>
<td>Henoch-Scholein purpura SLE</td>
<td>DIC</td>
<td>BM infiltration</td>
</tr>
<tr>
<td>Meningococcemia</td>
<td>Afibrinogenemia</td>
<td>Increase destruction</td>
</tr>
<tr>
<td>Infecitive endocarditis</td>
<td>Vit K deficiency</td>
<td></td>
</tr>
</tbody>
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Important Terminology

- Petichea  $<$ 3mm
- Purpura  $<$3mm$>$1cm
- Ecchymoses  $>$ 1cm
- -ve glass test
  (non blanching)
• Platelet (decrease #) or functions
• Vascular (hereditary / acquired)

• Congenital
• Acquired
Evaluation of haemostatic mechanism:

- Test for vascular and platelets disorder:
  - 1- bleeding time
  - 2- blood count
  - 3- tourniquet test
  - 4- bone marrow examination
  - 5- platelets morphology and functions.
Tests for coagulation factors:

- 1- clotting time
- 2- thrombin time N 15-20 sec
- 3- prothrombin time N 10-14 sec
- 4- partial thromboplastin time N 25-45sec
- 5- specific assessment for clotting factors
### Differences between bleeding disorders (vascular or platelets) and coagulation disorder (coagulation factors)

<table>
<thead>
<tr>
<th></th>
<th>Bleeding defects</th>
<th>Coagulation defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purpura</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>ecchymosis</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Hemarthrosis</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Precipitating factors</td>
<td>Spontaneous</td>
<td>Minor trauma</td>
</tr>
<tr>
<td>Bleeding time</td>
<td>Prolonged</td>
<td>Normal</td>
</tr>
<tr>
<td>Coagulation time</td>
<td>Normal</td>
<td>Prolonged</td>
</tr>
</tbody>
</table>
• A male child 4 years old admitted since one week, c/o fever, abdominal pain and anorexia since one week. Pallor for 3 days, red spots, bluish patches in the skin and epistaxis for one day.
Commonest platelet disorder

Idiopathic thrombocytopenia purpura
Platelets

Count: 150,000-400,000/mm^3

Life span: 8 to 9 days

Normally account for 1 out of 10,000
Idiopathic Thrombocytopenic Purpura

- Thrombocytopenia less than 100,000/mm$^3$
- Presence of antiplatelet in plasma
- Short life span
- Normal / increased # of megakaryocyte
- No primary disease
• Megakaryocytes hematopoietic stem cells in BM

- Its lobulated nucleus responsible for the production of blood thrombocytes (platelets), which are necessary for normal blood clotting.
Definition :-

- Autoimmune thrombocytopenic purpura is a common disorder that usually precedes by a viral infection, usually late winter and spring.
- Usually EBV, RUBELLA
- 1-4 wks after exposure.
- Commonly affect children between 1-4 years.
- 1/20,000 children.
Pathogenesis
Pathogenesis:

- Platelets destruction
- Antiplatelets antibodies IgG, IgM
- FC receptor recognition
- Splenic macrophage
- IgG against Megakaryocyte
1. common 1-4 years old

2. sudden onset of Generalized Petechiae and Purpura

3. bleeding from the gums and mucous membrane
   Platelets <10,000

4. History of a preceding viral infection 1 to 4 wks before onset of the thrombocytopenia.
CLASSIFICATION :-

Use to *assess severity of bleeding* basis of symptoms and signs, but *not platelet count*:

- **NO SYMPTOMS**
- **MILD SYMPTOMS**
- **MODERATE**
- **SEVER**
Class 1

- NO SYMPTOMS

Class 2

- Mild Symptoms
  - Bruises and petechiae,
  - Minor epistaxis
  - Interference with daily life.
Class 3

- Moderate
- More severe skin and mucosal lesions
- More severe epistaxis

Class 4

- Severe
- Bleeding episodes
- Epistaxis
- Melena
- Requiring transfusion or hospitalization
- Symptoms more interfering with the quality of life
INVESTIGATIONS :-

History and examination

• A- Laboratory investigation:

  1- CBC

  - In acute cases usually (HB, WBC, and differential count are normal).

  - Severe thrombocytopenia (platelet count <20 × 10⁹/L)

  - Platelet size is normal or increased
• **2- bone marrow**
  - Normal or increased numbers of megakaryocytes
Indications for bone marrow aspiration or biopsy

- Abnormal WBC count or differential
- Unexplained anemia
- Signs suggestive bone marrow disease on history and physical examination.
• In case of adolescents with new-onset ITP, ANA test should **evaluate** for SLE.
• **A coombs** should be done in unexplained anemia to rule out **EVAN SYNDROME** (autoimmune hemolytic anemia & thrombocytopenia)
Treatment :-

• 1- In case of minimal, mild, and moderate no treatment is required → Counselling and educations of the family.

• 2- For sever and moderate thrombocytopenia (Platelets count <10,000/mm^3) therefore Intravenous immunoglobulin (IVIG) 0.8–1.0 g/kg/day for 1–2 days lead to rapid rise in platelet within 48h.
• 3- Intravenous anti-D therapy:
  - For Rh positive patients
  - IV anti-D at a dose of 50–75μg/kg causes a rise in platelet count to >20× 10⁹/L in 80–90% of patients within 48–72h
• 4- Prednisone:
• Corticosteroid therapy 1–4 mg/kg/24 h.
• Continued for 2-3 wks or until rise in platelets count $>20 \times 10^9$/L than rapid taper.
5- Splenectomy reserved for 1 of 2 circumstances:
1- >4 years child with severe ITP lasting >1y.
2- Symptoms not controlled by medical therapy.
3- Platelets count cannot be corrected rapidly by (BT, IVIG, & Corticosteroid)
Differential Diagnosis

- 1- Leukaemia
- 2- Aplastic anemia
- 3- allergic purpura <henoch –shonlein
- 4- collagen vascular disease < SLE
Collagen vascular disease
SLE
In a class of diseases known as **autoimmune disorders**, the body’s immune system attacks its own tissues. Some of these diseases are similar to each other such as arthritis and inflammation of arteries in the tissues. People who developed these disorders were previously said to have "connective tissue" or "collagen vascular" disease. We now have names for many of many specific conditions such as:

- Ankylosing spondylitis
- Dermatomyositis
- Polyarteritis nodosa
- Psoriatic arthritis
- Rheumatoid arthritis
- Scleroderma
- Systemic lupus erythematosus

When a specific disease cannot be diagnosed, more general terms may be used. These include as undifferentiated systemic rheumatic (connective tissue) diseases or overlap syndromes.
Systemic lupus erythematosus (SLE) is an autoimmune disease. In this disease, the body’s immune system mistakenly attacks healthy tissue. It can affect the skin, joints, kidneys, brain, and other organs.
Signs and symptoms

• Joint manifestations
• Skin and mucous membrane manifestations
• Cardiopulmonary manifestations
• Lymphoid tissue
• Neurologic manifestations
• Renal manifestations
• Obstetric manifestations
• Hematologic manifestations
• GI manifestations
Causes:

• The cause of autoimmune diseases is not fully known.
• SLE is more common in women than men. It may occur at any age
• most often in people between the ages of 15 and 44. The disease affects African Americans and Asians more often than people from other races.
• Certain drugs may also cause SLE.
• The most common medicines known to cause drug-induced lupus erythematosus are:
  • Isoniazid
  • Hydralazine
  • Procainamide
Diagnosis

• Clinical criteria
• Cytopenias
• Autoantibodies

Laboratory testing differentiates SLE from other connective tissue disorders. Routine testing should include the following:

• Antinuclear antibodies (ANA) and anti–double-stranded (ds) DNA
• CBC
• Urinalysis
• Chemistry profile including renal and liver enzymes
• Fluorescent ANA
• Screening for renal involvement
Treatment

- NSAIDs and often antimalarials for mild disease
- Corticosteroids and often immunosuppressants for severe disease

- Mild or remittent disease
- Severe disease
Increased Platelet Destruction

• The hallmark of increased platelet destruction is increased marrow megakaryocytes or, when available, high reticulated platelet count. Platelet destruction results from various immune conditions, including the following:
  • Immune thrombocytopenic purpura (ITP)
  • Thrombotic microangiopathies
  • Post-transfusion purpura (PTP)
  • Heparin-induced thrombocytopenia (HIT)
  • Disseminated intravascular coagulation (DIC)

**Disorders of Platelet Function**
• Types of platelet function disorders:-
  • 1-hereditary
  • 2-acquired
Disorders of platelet adhesion
bernard-soulier syndrome
• Hereditary disorders:-
• 1-disorder of platelet adhesion(bernard-soilier syndrome)
• 2-disorders of platelet aggregation(glanzmann thrombasthenia)
• 3-disorder of platelet secretion
• 4-disorders of platelet procoagulant activity
• is a rare autosomal recessive coagulopathy (bleeding disorder) that causes a deficiency of glycoprotein Ib (GpIb), the receptor for von Willebrand factor
disorders of platelet aggregation (Glanzmann thrombasthenia)

• is an abnormality of the platelets. It is an extremely rare coagulopathy (bleeding disorder due to a blood abnormality), in which the platelets contain defective or low levels of glycoprotein IIb/IIIa (GpIIb/IIIa), which is a receptor for fibrinogen. As a result, no fibrinogen bridging of platelets to other platelets can occur, and the bleeding time is significantly prolonged.
Disorders of platelet adhesion
bernard-soulier syndrome
Acquired Abnormalities of Platelet Function

- MYELOPROLIFERATIVE DISEASE
- DYSPROTEINEMIA
- CARDIOPULMONARY BYPASS
- UREMIA
- LIVER DISEASE
- DRUG INHIBITION
- Infections
MYELOPROLIFERATIVE DISEASE

- Patients with myeloproliferative disorders (ie, polycythemia vera, myeloid metaplasia, idiopathic myelofibrosis, essential thrombocythemia, and chronic myelogenous leukemia) frequently exhibit abnormal platelet function.

- Some of these patients have very high platelet counts and demonstrate either abnormal bleeding, or a tendency for arterial or venous thrombosis, or even both. Although the height of the platelet count alone does not correlate with the bleeding or thrombotic tendency, thrombocytosis in excess of 1 million/µL is considered to be a risk factor.
Signs and symptoms

- Perioperative (and postoperative bleeding)
- Bleeding gums
- Bruising Epistaxis (nosebleeds)
- Abnormal bleeding (from small injuries)
- Unusual menstrual periods
CLINICAL FEATURES

Bleeding gums

Easy Bruising
There are no specific symptoms or signs that indicate a platelet functional defect.

Inherited defects are rare and are generally characterized by a relatively mild bleeding tendency. von Willebrand disease (vWD) is an exception to this rule, since certain vWD subtypes are associated with severe and even fatal bleeding.

Patients with platelet functional defects generally present with:
- Easy bruisability
- Mucocutaneous bleeding of a purpuric nature
- Bleeding from the gastrointestinal and genitourinary tracts (often with severe menorrhagia) rather than the petechial bleeding that characterizes thrombocytopenia.

It is not unusual for the bleeding tendency to escape detection until aggravated by another abnormality. For example, the defect may first be suspected because of excessive bleeding following minor surgery or a dental extraction or unusual mucocutaneous bleeding following the administration of anticoagulants or a platelet inhibitor such as aspirin. Therefore, a history of unusual bleeding, a family history suggestive of a congenital abnormality, and the clinical picture can provide important clues.
1. BLEEDING TIME AND TESTS FOR FACTOR DEFICIENCIES

• The bleeding time (BT) has traditionally been used as a screening test for the presence of a platelet functional defect. If performed carefully in a well-standardized manner, the BT correlates with both platelet number and function.

• With platelet counts greater than 100,000/µL, the BT should be less than 8 minutes. As the count falls below this level, the BT lengthens, reaching times of 20 to 25 minutes when the count falls to 10,000/µL.

• Patients with functional defects, such as severe vWD, can show BTs in excess of 20 minutes with a normal platelet count. Patients with an acquired functional defect secondary to aspirin therapy or uremia show more modest prolongations of the BT (8 – 20 minutes).
2. COMPLETE BLOOD COUNT AND BLOOD FILM

- A complete blood count (CBC) with examination of the blood film can also be helpful.

- The CBC can provide evidence of hematopoietic disease, especially a myeloproliferative disorder where high numbers of circulating platelets are associated with abnormal function.

- Platelet morphology can help in diagnosing disorders such as Bernard-Soulier syndrome and Î±-granule deficiency (gray platelet syndrome).
3. MEASUREMENTS OF PLATELET ACTIVATION/AGGREGATION

- Direct measurements of platelet activation/aggregation are possible using an aggregometer or flow cytometer.

- The aggregometer provides a graphic display of the wave of platelet aggregation seen in response to agonists such as ADP, epinephrine, or collagen, and the agglutination response to ristocetin. Specific functional defects respond differently to these agonists.

- For example, patients with vWD specifically show decreased or absent agglutination with ristocetin [ristocetin-induced platelet agglutination assay (RIPA)], whereas other disorders such as storage pool disease demonstrate poor responses to ADP, epinephrine, and collagen.
ASSAYS FOR VON WILLEBRAND FACTOR

• Full evaluation of the patient with vWD requires an array of tests, including assays for factor VIII activity, vWF antigen, vWF activity, and vWF multimer pattern by agarose gel electrophoresis.

• Together with the patient's bleeding history, family history, and BT, these assays will diagnose and classify vWD into one of several clinically important subtypes.
• How can bleeding difficulties in patients with platelet function disorders be treated?
TREATMENT for abnormalities of platelet function

• Abnormalities in platelet function are often first appreciated as a complication of an acute illness or surgery and multiple aggravating factors may play a role in determining the severity of the bleeding tendency.

• An accurate diagnosis is not usually easily made

• Hence, treatment should address as many potential contributing factors as possible.

• This list includes discontinuing drugs that inhibit platelet function, empirically replacing vWF or treating with DDAVP (Desmopressin) and, according to the severity of the patient's bleeding, transfusing normal platelets.

• Although this approach lacks precision, it is effective. Both acquired and congenital disorders of platelet function can be acutely reversed in order to control severe clinical bleeding.
Treatment cont’d

• Long-term management of a platelet functional defect should be based on an accurate diagnosis. Patients with congenital defects should be counseled to avoid drugs that can aggravate the functional abnormality and cause bleeding.

• Obviously, aspirin and nonsteroidal analgesics are prime offenders. vWD and thrombasthenia patients demonstrate significant prolongations of the bleeding time with aspirin ingestion and are at greater risk for clinical bleeding.

• These patients should also be educated regarding the nature of their abnormality and should carry identification or wear a medical alert bracelet. This information can be invaluable as a guide to appropriate transfusion therapy in an emergency situation.
Treatment Cont’d

• As a general principle, the nature of the functional abnormality will guide the choice of therapy.

• For example, the vWD patient who lacks normal amounts of vWF will respond to agents that increase plasma vWF levels. In this situation, the platelets will function normally once the vWF abnormality is corrected. In contrast, patients with congenital defects of platelet receptor expression, granule content, or platelet metabolism will require platelet transfusion.

• As for the acquired abnormalities of platelet function, the best approach to therapy lies somewhere in between. There is clinical evidence that patients with acquired defects secondary to drug ingestion, uremia, and liver disease will respond to DDAVP, vWF replacement, or both. These data suggest that an increase in plasma vWF levels may partially compensate for a platelet-based defect.
infections

- May be bacterial characterized by bloody and puruloid mucus stool, and is often accompanied by fever, tenesmus, and severe abdominal pain. Pathogenic bacteria causing the inflammatory diarrhea syndrome include Salmonella, Vibrio, Shigella, enteroinvasive and enterohemorrhagic Escherichia coli, Campylobacter, Yersinia, Chlamydia, and Clostridium difficile
• May be Hemorrhagic fevers which can be caused by many different types of virus.
• The viruses most often associated with hemorrhagic fever are Filoviruses, such as Ebola and Marburg viruses (Ebola Virus and Marburg Virus Infections), which occur mainly in parts of Central Africa Arenaviruses, such as Lassa fever virus in West Africa and Junin virus in South America (Lassa Fever and South American Hemorrhagic
• Fevers) Bleeding occurs because the viruses make the blood vessels leak. These infections are often fatal. Many other viruses, including the dengue virus (Dengue), hantavirus (Hantavirus Infection), and yellow fever virus (Yellow Fever), can cause hemorrhagic symptoms. Some of these viruses naturally reside in animals. Some are spread by the bite of a tick or mosquito.
• Henoch-shoulei purpura:

characterized by sudden development of purpura rash arthritis, abdominal pain, renal involvement.

The rash:
- Consist of petechiae and often palpable purpura
- Involve lower extremities and buttocks
- In kidney causes focal glomerulonephritis.
• **Ethiler- Danlos syndrome:**
  - Disorder of collagen structure that causes easy bruising and poor wound healing.
  - Skin is hyperelastic: joint lax
  - The most serious form have been associated with sudden rupture of visceral organ.
• **Acquired disorder:**
  - Survey, chronic corticosteroids therapy, and severe malnutrition associated with weakening of collagen matrix that support blood vessels.
Coagulation disorders

CONGENITAL & ACQUIRED
Von-Willebrand Disease
• VWD is a congenital bleeding disorder characterized by a lifelong tendency toward easy bruises, frequent epistaxis and menorrhagia.

• It’s a family of bleeding disorders caused by an abnormality of VWF.

• VWD is the most common hereditary bleeding disorder.
• VWF is a large glycoprotein required for normal platelet adhesion and also functions as the carrier protein for factor VIII.

• As such VWF functions in both primary and secondary homeostasis.

• VWD is due to abnormality either qualitative or quantitative of the VWF.
**Types**

- **TYPE (1) VWD:**
  - Account for 70-80% of cases
  - Characterized by partial quantitative decrease in VWF and FVIII
  - Pt generally has mild symptoms
  - Inherited as autosomal dominant
• **Type (2) VWD:**
  - Accounts for 15-20% of cases
  - Qualitative defect of VWF
  - Can be either autosomal dominant or recessive

• **Type (3) VWD:**
  - Is the rarest and most severe form
  - Inherited as autosomal recessive trait
  - Characterized by marked deficiencies of both VWF and FVIII
**presentation**

- May be asymptomatic
- Easy bruising
- Recurrent epistaxis
- Menorrhagia
- Post-operative bleeding
D/Dx:

• Hemophilia A,B or C
• Platelet disorders
Laboratory studies:

- CBC
- BT, PT, aPTT
- VWF levels
- FVIII activity
- VWF antigen
- Gene studies
Treatment:

- Vasopressin analogues (desmopressin)
- Plasma products
- Aminocarporic acid (Amicar)
- Pt-Education
Haemophilia
Definition:

- It is most common and serious congenital coagulation factor deficiencies.
- It is an inherited bleeding disorder, it is sex linked recessive.
- Females are carriers.
- Occurs in males.
- **Types:**
  - Hemophilia A (classic type), (factor 8 deficiency):
  - Occurs in 1 in 5000 males and represents 85% of all hemophilia.

- while hemophilia B (factor 9 deficiency) occurs in approximately 1 in 25000.

- The lack of factor 8 or 9 delays the generation of thrombin, which is important for forming a normal functional fibrin clot and solidifying the platelet plug that has formed in areas of vascular injury.
• Factors 8 and 9 cross placenta, so the presentation starting early (neonatal bleeding).
• Patients with less than 1% (severe hemophalia) Factor 8 or 9 may have spontaneous bleeding into muscle, GIT, joint and soft tissues OR bleeding with minor trauma.
• Patients with (1-5%) (moderate hemophalia) Factor 8 or 9 usually require moderate trauma to induce bleeding episodes.
• In mild hemophalia (less than 5% factor 8 or 9) Significant trauma is necessary to induce bleeding.
Clinical picture:

- **At birth**: unusual bleeding from umbilicus OR circumcision site.

- **Later**:
  - 1/ external bleeding: epistaxis, dental bleeding, hematuria and gastrointestinal.
  - 2/ internal bleeding: intracranial hemorrhage, muscles hematoma.
  - 3/ skin: echymosis and hematoma.
  - 4/ hemarthrosis: mainly in big joints of lower limb: Joint become swollen, red, hot, tender with limited mobility, later on: fibrosis and ankylosis.
Diagnosis:

1/ diagnostic:

Diagnosis is based on activated partial thromboplastin time (PTT).

When an abnormal PTT is obtained, specific factor assay (factor 8 and 9 level) are needed to make a precise diagnosis to determine the appropriate factor replacement therapy.

Early appropriate replacement therapy is the hallmark of excellent hemophilia care.
Cont..

2/ carrier detection:
- *direct gene mutation analysis
- *F VIII/ Vwf ratio (less than 1%)

3/ prenatal diagnosis:
- *DNA analysis
- *fatal blood sample at (18-20) weeks.
**Treatment**

- **.1/ prophylactic treatment:**

- Early institution of factor replacement and continuous prophylaxis starting in early childhood should prevent the chronic joint disease associated with hemophilia.

- Regular F VIII replacement (20 unite/kg three times a week.)

- Hepatitis B vaccine.

- Avoid trauma, IM injection and aspirin.
• 2/ during bleeding attacks:
• A- factor VIII replacement:
  • 1/ recombinant factor VIII dose (25-50 unite/kg) according to severity.
• 2/ others:
  • *fresh frozen plasma
  • * factor VIII concentrate.
• **B- adjuvant drugs:**

• **1/ desmopressin** (DDAVP): increase plasma F VIII by 4 folds.

• **2/ antifibrinolytics**: inhibit fibrinolysis, so stabilize the clot (e.g: Tranexamic acid)

• Indication: mucosal bleeding, menorrhagia.

• **3/ prednisone**: (short coarse) in hemarthrosis and hematuria.
Cont...

- **C/ special cases:**
  - **1/ intracranial hemorrhage:** high dose of F VIII
    - (50-75 unite/Kg) for 2 weeks.
  - **2/ hemarthrosis:**
    - Local: cold compresses.
    - F VIII replacement + prednisone (short coarse).
    - Rest for 48 hr then physiotherapy to avoid ankylosis.
complication

• Of bleeding:
  • 1/ severe blood loss: hypovolemic shock.
  • 2/ severe intracranial hemorrhage.
  • 3/ hemophilic arthropathy: joint stiffness.
  • 4/ muscle atrophy.
Of treatment:

Treatment may be complicated with:

1/ F8 antibodies development, which is treated using high levels of the factor VIII (100-200 unite/kg) or using procine F8.

2/ allergic reaction.

3/ risk of acquiring blood-borne disease especially hepatitis C.

Note; hemophilia occurs in female with turner`s syndrome.
Hemophilia B: (Christmas disease)

- Factor IX deficiency.
- Sex linked recessive disorder.
- As hemophilia A but milder.
- Treated by recombinant F IX OR F IX concentrate given / 24 hr.
Hemophilia C:

Factor XI deficiency.

Autosomal recessive disorder, so can affect both sexes.

Very mild disease.

Treated by fresh frozen plasma given / 48 hr.
DIC is a condition that results from widespread activation of coagulation in the circulation.

- This result in:
  - Consumption of some coagulation factors and platelets
  - Fibrin deposition and secondary fibrinolysis.
• Etiology:
  • Severe infection such as septicemia.
  • Extensive tissue damage in burn and major surgery.
  • Shock
  • Heat stroke
  • Acute liver failure
  • Neoplastic disorders as promyelocytic leukemia, adenocarcinoma.
CLINICAL FEATURES

1. Acute hemorrhagic manifestation:
   • Hematemesis
   • Bleeding from injection site
   • Intracranial hemorrhage
   • Melena

Ischemia and necrosis:
   • Skin gangrene
   • Kidneys acute cortical necrosis leading to renal failure.
   • Hemolytic anemia due to destruction of RBCs lead to pallor and red urine.
Laboratory finding

- Thrombocytopenia
- Prolonged prothrombin time
- Deficiency of factors I, II, V, VIII
- Increased concentration of fibrin degradation products specially D dimers

**TREATMENT**

- Correction of the cause [shock, infection, hypoxia]
- Infusion of fresh frozen plasma
- Heprin small dose 100 units/6 hours
- In newborn exchange transfusion with fresh blood.
Vitamin K deficiency
• Is now the preferred term for haemorrhagic disease of the newborn (HDN).
• Vitamin K is required for the production of clotting factors II, VII, IX, X.
• Is present in some plant and it's also synthesised by some E. Coli in the gut.
• All newborn infants have low level of vitamin K are at risk of developing VKDB.
Classification

• 1) early VKDB: present within 24 hrs of birth.
• 2) classic VKDB: present between day 1 and day 7 of life.
• 3) late VKDB: present between week 2 and week 12 of life.
Risk factors

• 1) children who are entirely breast-fed have a 20 times greater risk of developing VKDB than those who receive formula milk.
• 2) several drugs such as isoniazid, rifampicin, anticonvulsion and anticoagulant agent which have taken by the mother.
• 3) warm environmental temperature.
• 4) unsuspected liver disease especially alpha-1 antitrypsin deficiency.
• 5) malabsorption of fat soluble vitamin due to diarrhoea, coeliac disease or cystic fibrosis.
Presentation

• *Early :
  • Present with bleeding at sites related to trauma of birth
  • 1_bleeding from scalp monitor site.
  • 2_cephalhaematomas especially after ventous delivery.
  • 3_intracranial bleeding after traumatic delivery.
  • 4_intrathoracic bleeding
  • 5_intraabdominal bleeding.
• *classic:
• Bleeding most often affect non vital organs
  1_gastrointestinal bleeding.
  2_bleeding from skin and mucous membrane.
  3_prolong bleeding following circumcision.
•  4_bleeding from umbilical stump.
• *late :
• It typically present with intracranial haemorrhage and is often caused by undiagnosed cholestasis with resultant malabsorption of vitamin K.
• Produce the greatest morbidity and mortality amongst the infant due to sudden bleeding into CNS.
If VKDB is suspected it is important to go over certain aspect at history:

- 1. drugs taken in pregnancy
- 2. gestation at delivery.
- 3. type and length of delivery.
- 4. feeding history.
Investigation

• 1_FBC.
• 2_clotting screen.
• 3_CXR or ultrasound scan
• 4_MRI or CT.
Management

• When VKDB is suspected vitamin K should be given as soon as possible.
• This will result in reduction in bleeding time within a few hrs.
• The injection should be subcutaneous.
• Infant of mother taking drugs that inhibit vitamin K are at risk of early VKDB should receive 1mg IM as soon as possible after delivery.
• Babies with severe bleeding or intracranial haemorrhage may require fresh frozen plasma to be given in addition to vitamin K.
Thank you