CHAPTER 10

Clinical Hematology: Bleeding Disorders

PLATELETS, COAGULATION AND BLEEDING DISORDERS: LABORATORY INVESTIGATIONS

Platelet Count—Dealt in Depth Elsewhere

Capillary Fragility Test of Hess (Rumpel-Leede Sign, Tourniquet Test)

1. Inflate sphygmomanometer cuff around arm at 80 mm of Hg pressure for 5 minutes.
2. Look for petechiae in an area 5 cm in diameter just below the elbow.
3. Under normal circumstances the number of petechiae should be less than 5, more than 5 indicate a positive test.

A positive test may be found in reduced capillary resistance (or increased capillary fragility) as in non-thrombocytopenic purpura and scurvy. It may also be positive in thrombocytopenia when the platelet count is below approximately 70,000 mm^3 of blood.

Clinical Implications

1. Increased petechiae formation occurs most commonly in thrombocytopenia and less commonly in: (i) thrombasthenia, (ii) vascular purpura, (iii) senile purpura, and (iv) scurvy.
2. The number and size of petechiae are roughly proportional to the bleeding tendency and possibly to the degree of thrombocytopenia. However, the test can be positive because of capillary fragility in the presence of normal platelet count.
3. Results will be normal in coagulation disorders and vascular disorders.

Laboratory Diagnosis of Vascular Bleeding Disorders

Hess's test is positive in these

Causes and classification

1. *Hereditary*
   - Hereditary hemorrhagic telangiectasia.
2. *Acquired*
   - Simple easy bruising
   - Senile purpura
   - Purpura of infections
   - Henoch-Schonlein syndrome
   - Scurvy
   - Steroid purpura.

Interfering Factors

1. *Menstruation:* Capillary fragility is normally increased before menstruation.
2. *Infectious disease:* Capillary fragility is increased in measles and influenza.
3. *Age:* Women over 40 years with decreasing estrogen levels may have a positive test that is not indicative of a coagulation disorder.
4. *Readministration:* Repetition of test on same arm within 1 week of the first test may lead to error.
5. *Variation:* Results may vary because of differences in texture, thickness, and temperature of the skin.

LABORATORY DIAGNOSIS OF PLATELET DISORDERS

Idiopathic Thrombocytopenic Purpura (ITP)

1. Platelet count is usually 10-50 × 10^9/L.

2. The blood film shows reduced numbers of platelets, those present are often large.
3. The bone marrow usually shows increased number of megakaryocytes.
4. Sensitive tests can demonstrate antiplatelet IgG, either alone or with complement, on the platelet surface or in the serum in most patients.
5. Autologous platelet survival studies with ^{51}Cr or $DF^{32}P$-labeled platelets may be used to show reduced platelet survival. In severe cases, the mean platelet survival may be reduced to one hour.
6. Hess's test may be positive in some cases.

Drug Induced Immune Thrombocytopenia

1. Thrombocytopenia. Platelet count is often $<14 \times 10^9$/L.
2. Bone marrow may show normal or increased numbers of megakaryocytes.
3. Drug dependent antibodies against platelets may be demonstrated in sera of some patients.
   Drugs usually incriminated are:
   - Quinine
   - Quinidine
   - Sulfonamides
   - PAS
   - Rifampicin
   - Stibophen
   - Digitoxin, etc.

Disseminated Intravascular Coagulation (DIC)

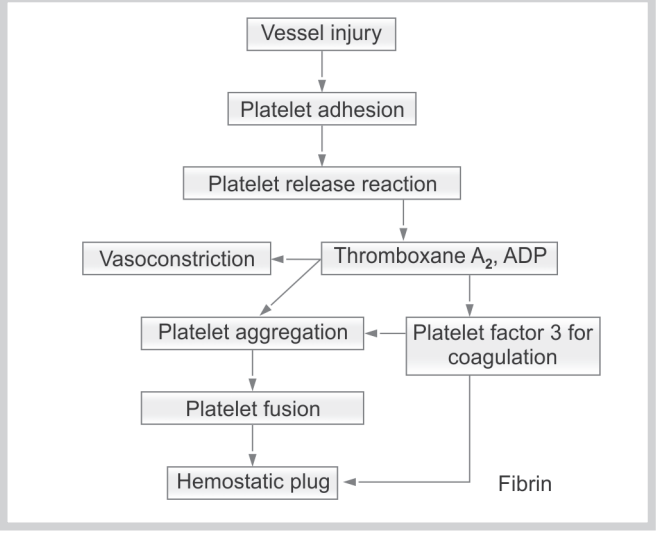
1. In acute cases blood may not clot due to gross fibrinogen deficiency.
2. Platelet count is low.
3. Fibrinogen screening tests, titers or assays indicate deficiency.
4. Thrombin time is prolonged.
5. High levels of serum fibrin/fibrinogen degradation products are found in serum and urine.
6. Prothrombin time and partial thromboplastin time are prolonged.
7. Factor V and factor VIII activity is diminished.
8. Due to microthrombi causing mechanical hemolytic anemia, RBCs may show crenation and poikilocytosis.

Causes of DIC

1. DIC may be caused by entry of procoagulant material into circulation, for example,
   - Amniotic fluid embolism
   - Premature placental separation
   - Widespread mucin secreting adenocarcinoma
   - Severe falciparum malaria
   - Hemolytic transfusion reaction
   - Promyelocytic leukemia
   - Some snake bites.
2. DIC may also be initiated by extensive endothelial damage and collagen exposure, for example
   - Endotoxemia
   - Gram-negative and meningococcal septicemia
   - Septic abortion
   - Certain viral infections (purpura fulminans)
   - Severe burns
   - Hypothermia.
3. Massive intravascular platelet aggregation can also precipitate DIC as occurs in some:
   - Bacterial and viral infections
   - Immune complexes may have a direct effect on platelets.

Functional Platelet Disorders

Platelet reactions in the hemostatic process.



Laboratory Diagnosis

1. Platelet count normal.
2. Prolonged bleeding time.
3. Abnormal platelet aggregation studies with ADP, adrenaline, collagen and ristocetin.
4. Abnormal adhesion studies and nucleotide pool measurement.
5. Factor VIII clotting assay (for von-Willebrand's disease).

Abnormal platelet function should be suspected in cases where bleeding is prolonged despite a normal platelet count. Various causes included in this are as follows:

Hereditary Disorders

1. *Platelet storage pool disease:* There is defective release

of ADP and 5HT due to an intrinsic deficiency in the number of dense granules.
2. *Thrombasthenia (Glanzmann's disease):* There is failure of primary platelet aggregation.
3. *Bernard-Soulier syndrome:* Platelets are larger than normal, lack surface glycoprotein and fail to make phospholipid available or to adhere to vessel walls.
4. von Willebrand's disease: There is defective platelet adhesion as well as coagulation factor VIII deficiency.

Acquired Disorders

1. *Aspirin therapy:* It may lead to abnormal bleeding time although purpura is rare. Aspirin leads to impaired thromboxane-A_2 synthesis. So, there is failure of the release action aggregation with ADP and adrenaline.
2. *Hyperglobulinemia:* Interferes with platelet adherence, release and aggregation.
3. *Myeloproliferative disorders:* Intrinsic abnormalities of platelet function may occur in patients with essential thrombocythemia and other myeloproliferative disorders.

Bleeding Time

The duration of bleeding from a standard puncture wound of the skin is a measure of the function of platelets as well as the integrity of the vessel wall.

Duke's Method

Requirements

- Stop watch
- Lancet
- Filter paper
- Glass slide
- Alcohol sponges.

Method

1. Clean the lobe of the ear or tip of a finger with alcohol and let dry.
2. For ear—glass slide is placed behind the ear lobe and held firmly in place. This provides a firm site for incision.
3. Pierce the lobe of the ear by a firm stroke against the glass slide (or pierce the finger-tip). Discard the glass slide if ear lobe has been incised. Start the stop watch when the stab was made.
4. Bleeding of the wound should be allowed to proceed without pressure and the blood is allowed to drop on the filter paper. The paper should be moved so that each drop will fall on a fresh area. When bleeding slows, the wound is touched gently with a fresh area of the filter paper at 30 second intervals. When blood no longer stains the filter paper, the watch is stopped and the time recorded.

Normal Values

The normal range is up to 6 minutes. Between 6 and 10 minutes, the results are borderline. Over 10 minutes is definitely abnormal.

Precautions

1. In children, heel should be used.
2. In suspected cases of a bleeding disorder, the bleeding may not be controlled easily from the ear lobe hence, fingertip puncture wounds are better.
3. The area to be punctured should not be congested.
4. The size and depth of the wound may vary if one does not have a standardized technique.
5. If bleeding persists for more than 15 minutes it should be stopped by placing a dry gauge sponges over the site and applying finger pressure (the filter paper used to collect the drops of blood can be dried and saved as a record of the procedure).

Ivys's Method

(Preferred because of greater ease of standardization).

Method

1. Cleanse the inner aspect of the forearm with spirit and let dry.
2. Place a blood pressure cuff on the upper arm, inflate at 40 mm Hg, and maintain the same throughout the test.
3. Select an area on the forearm—Volar aspect which is devoid of superficial veins. Stretch the skin laterally between the thumb and forefinger and hold in a taut position.
4. Take a cork, through which a no. 11 surgical blade has been inserted with the tip extending 3 mm beyond the cork surface (both cork and blade should have been sterilized before), the blade should be withdrawn from the cork and autoclaved before being used again.
5. Hold the cork with the thumb and forefinger of the free hand, and with the heel of the hand resting on the patient's arm, quickly make two skin punctures (actually they are small incisions) in the selected area. It is important that the surface of the cork meet the skin to ensure a 3 mm deep incision. Holding the skin taut prevents the test area from being depressed when the blade enters the skin.
6. Timing is begun as soon as the incisions are made and bleeding starts.
7. Using the edge of a piece of a filter paper to collect the blood, gently touch paper to the drop of blood, which