Q1. What are the two major classification of platelet disorders?
- a. Quantitative Disorder
- b. Qualitative Disorder

Q2. What are the two major quantitative platelet disorders? What are their distinguishing characteristics?
- a. Thrombocytosis: >450,000/ uL or $450x10^9$/L
- b. Thrombocytopenia: <100,000/uL or $100x10^9$/L

Q3. What could be the possible risk if a patient has a platelet count of <50,000/uL?
- a. INCREASED PROGRESSIVE RISK for bleeding

Q3. What could be the possible risk if a patient has a platelet count of less than <10,000/uL?
- a. HIGH RISK for severe spontaneous bleeding

Q4. What can you say about the relationship between the platelet concentration and risk for the severity of bleeding?
- a. INVERSELY PROPORTIONAL:
  - INCREASED/HIGH platelet concentration = DECREASED/LOW risk of severe bleeding
  - DECREASED/LOW platelet concentration = INCREASED/HIGH risk of severe bleeding

Q5. What are the conditions related to thrombocytosis?
- a. MPNS
- b. Relative/Secondary Hemostasis

Q6. What are the conditions related to thrombocytopenia?
- a. IMPAIRED/DECREASED platelet production
- b. INCREASED platelet destruction
- c. INCREASED sequestration
- d. ABNORMALITIES of distribution or dilution
- e. INCREASED consumption

Q7. What happens when there is an increased sequestration?
- a. Increased sequestration is usually associated with "big spleen" syndromes or splenomegaly, where normally produced platelets are sequestered in spleen. So, because there is an increased sequestration, platelets stay on the spleen and are not released in circulation. As a result, if we would test or measure the platelet count, platelet level is very low (thrombocytopenia).

Q8. What happens where are abnormalities in the distribution or dilution?
- a. Thrombocytopenia: same as with the sequestration but this time, it is caused by dilution. Remember that hemodilution can cause a false decrease in the number of not only platelets but the over all blood elements (such as RBCs and WBCs.

Q9. What will happened if there is an increased consumption of platelet?
- a. Thrombocytopenia: Since platelets are used/consumed during clot formation, especially in secondary hemostasis, if the bone marrow cannot keep up with the production of platelets. So, here, there is an increased consumption rather than production of platelets.

Q10. What does reactive thrombocytosis mean? When do they usually occur?
- a. Reactive Thrombocytosis: is the sudden rise in platelet count for a limited period of time but it does not exceed 800,000/uL, usually around 450,000-800,000/uL. Platelet counts that reaches 1-2 million/uL is rarely seen. Reactive thrombocytosis usually happens due to some underlying conditions like acute blood loss, splenectomy, childbirth, tissue necrosis following after surgery, chronic inflammatory diseases, infection, exercise, iron, deficiency anemia, hemolytic anemia, renal disorders, and various malignancies. During reactive thrombocytosis, platelet function, megakaryocyte, and morphology are normal. So, that means that RT is not caused by the platelets itself rather it is caused by the underlying and unrelated conditions.
- b. Sidenotes: In this condition, platelet production remains responsive to TPO [the normal regulatory stimuli, hormone that is produced chiefly in the liver parenchyma and secondarily in kidney] and morphologically normal platelets are produced at a moderately increased rate.
- c. If bone marrow examination is done in patients with reactive thrombocytopenia:
  Results: Normal to increased number of megakaryocytes that are morphologically normal
- d. Platelet aggregation test in RT patients: Normal platelet function

What is the effect of normal marrow replacement to the platelet concentration?

- If one's normal marrow is replaced with malignant cells like in the case of Myelophthisic anemia, then there would be no space for the Megakaryocytes, therefore, there would also be no production of platelets. So platelet concentration decreases.

What is the effect of megaloblastic anemia to the platelet concentration?

- For this case, there is a decreased B12 and folic acid, in which, both are needed for DNA synthesis. Knowing this, we could also say that not only RBCs and WBCs are affected but so are the platelets.

Explain TAR syndrome.

- TAR syndrome: Thrombocytopenia with Absent Radius. A rare autosomal recessive disorder characterized by severe neonatal thrombocytopenia and congenital absence or extreme hypoplasia of the radial bones of the forearms with absent, short, or malformed ulnae and orthopedic abnormalities.
- Associated with a mutation in the RBM8A gene located in the long arm of chromosome 1.
- Platelet count is decreased (>10,000/uL to 30,000/uL) during the first 2 years of infancy.
- Platelet count usually increase over time, with normal levels usually achieved by the time these children reach school age.
- TAG LINES: GENE MUTATION = DEFECTIVE TPO = EXTREME HYPOPLASIA OF MEG. = DECREASED PLATELET PRODUCTION = DECREASED PLATELET COUNT

Explain May-Hegglin Anomaly.

- MHA: A rare autosomal dominant disorder whose exact frequency is unknown.
- Large platelets are present in peripheral blood films
- Dohle bodies are present in neutrophils and occasionally in monocytes.
- Characterized by abnormally enlarged or misshapen platelets.
- Platelet function in response to platelet-activating agents is usually normal.
- In some patients, megakaryocytes is increased and their ultrastructure is abnormal.
- Mutation in the MYH9 gene that encodes for non-muscle myosin heavy chain have been reported and is believed to be responsible for the abnormal size of platelets in this disorder.

What are the other three disorders that also have mutation in MYH9 gene?

- Sebastian syndrome:
  - Inherited as autosomal dominant disorder
  - Abnormalities: Large platelets, thrombocytopenia, granulocytic inclusions
- Fechtner syndrome
  - Abnormalities: the same with SS accompanied by deafness, cataracts and nephritis
- Epstein syndrome
  - Abnormalities: large platelets associated with deafness, ocular problems, glomerular nephritis

What is Congenital Amegakaryocytic Thrombocytopenia?

- An autosomal recessive disorder reflecting bone marrow failure.
- Caused by mutations in MPL gene on chromosome 1 (1p34.1), resulting in the complete loss of thrombopoietin receptor function resulting in reduced megakaryocyte progenitors and high thrombopoietin level because even there is high amount of TPO but there is no megakaryocyte receptor, megakaryocytes cannot produce platelets.
- Affected infants: platelet count is less than or equal to 20,000/uL at birth, petechiae and evidence of bleeding at or shortly after birth.

What is Autosomal Dominant Thrombocytopenia?

- Caused by mutations in ANKRD26 gene on the short arm of chromosome 10 (10p12.1)
- Mutation in ANKRD26 gene lead to incomplete megakaryocyte differentiation and resultant thrombocytopenia.
- Although, platelet morphology and size are still normal.
- Bleeding is absent or mild, because platelet function is still normal.

What is X-linked Thrombocytopenia?

- Caused by the mutation in WAS (Wiskott-Aldrich Syndrome) gene on the X chromosome (Xp11.23) or mutations in GATA1 gene also on the X chromosome at Xp11.
- Mild thrombocytopenia with small platelets
- Absent or mild bleeding to large platelets with severe bleeding