Problem 4 – Unit 6 – Immunology: mechanism of ITP



- <u>ITP</u>: platelets will be cleared (high turnover) in an abnormal pattern because of the presence of antibodies (IgG) on the surface of platelets. These antibodies will be directed against GPIIb/IIIa & GPIb receptors. Platelets coated with antibodies will be destructed by macrophages present in the spleen (RE system).
- Primary ITP: is always autoimmune (also known as idiopathic).
- ITP can be secondary to SLE, HIV, Lymphomas or chronic lymphocytic leukemia.
- <u>In Acute ITP</u>, the patient has a history of infections such as chickenpox, upper respiratory tract infections or measles.

- Sequence of events (Figure 1):

- Antibodies (IgG) will coat the platelets.
- Platelets will be taken by macrophages in the RE system (especially the spleen).
- These macrophages will act as antigen presenting cells (APC).
- They will present the antigens to Tlymphocytes which in turn will activate Blymphocytes and lead to the production of specified antibodies directed against the platelets.
- They cycle will continue again and there will be increased clearance of platelets by spleen and other fixed phagocytes.

- ELISA (Figure 2):

- In ITP autoantibodies are attached to the surface of platelets (to GPIIb/IIIa & GPIb).
- Platelets are solubilized.
- Monoclonal antibodies are added against GPIIb/IIIa
- Anti-human immunoglobulin (which is enzyme linked) is added and binds to the autoantibodies.

How to rise platelet count in ITP:

- Steroids: and this will lead to the blockage of Fc receptors on macrophages so they will be unable to destroy the platelets coated with the antibodies and this will increase their survival.
- High-dose IV immunoglobulins: blockage of Fc receptors on macrophages or modification of autoantibody production.
- Immunosuppressive drugs (azathioprine).
- Monoclonal antibodies (rituximab).
- Thrombopoietin receptor agonists are given to those patients who are contraindicated for steroids.
- Splenectomy.
- Platelets transfusions: their benefit will only last a few hours (for emergency).
- SCT: for very severe cases.



