Subject: Pathology 6

Topic: WBC Disorders part 1

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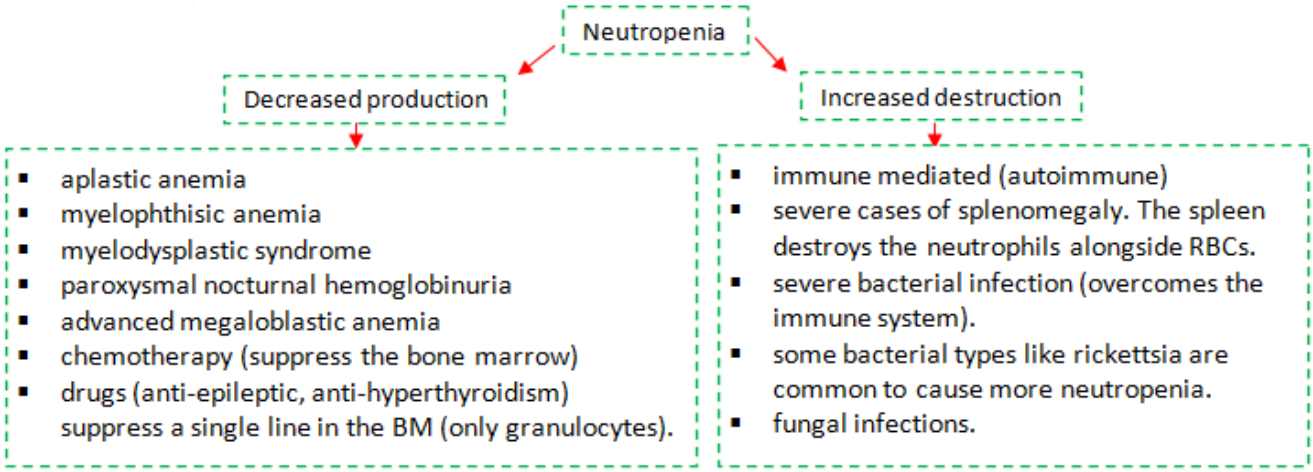
WBC Disorders

- Leukopenia
- Leukocytosis (reactive and leukemia)
- reactive lymphadenitis (acute and chronic non- specific lymphadenitis)
- Cat-Scratch Disease
- Hemophagocytic Lymphohistiocytosis / HLH (Types 1,2,3 and 4)

Basic Concepts

- Decreased WBC --> **Leukopenia**
- Increased WBC --> **Leukocytosis**
  - If benign then **reactive leukocytosis**
  - If malignant then **leukemia**
- Leukocytosis > Leukopenia
- Reactive Leukocytosis > Leukemia
- Decreased granulocytes --> **agranulocytosis**
- Decreased neutrophils --> **neutropenia**
- Absolute Neutrophil Count --> % of neutrophils multiplied by total WBC count
- if below 500, then severe neutropenia and spontaneous infection could occur.



- Reactive leukocytosis, very common, has many forms:

Neutrophilia	**Where the most predominant cell is the neutrophil,MOST COMMON,** common in **infection** (with liquefactive necrosis) and **inflammation**, like in coagulative necrosis (results from ischemia)
Lymphocytosis	Common in **viral** infections and **chronic** infections (TB, brucellosis). An exception of a bacterial strain that causes lymphocytosis is **Bordetella pertussis**.
Monocytosis	Monocytes increase in **both acute and chronic** infection but in the **chronic** infection, they become more **predominant,** inrheumatologic diseases (again chronic diseases), and in inflammatory bowel disease (chronic inflammation in the gut).
Eosinophilia	Eosinophils become predominant in asthma, **allergic diseases**(in general, either in the skin or in the systemic ones), drug hyper-sensitivity, **parasitic infections** and in some neoplasms, the most famous one is **Hodgkin Lymphoma**.
Basophilia	This is a **rare** situation, and usually **neoplastic**. It appears in myeloproliferative neoplasms.

- **Reactive Lymphadenitis** --> benign, inflammation, enlargement of LN.
- Reactive Lymphadenitis has two types:

Acute Non-specific Lymphadenitis:

- common, acute inflammation (bacteria or virus)
- swollen and painful
- red skin
- neutrophils
- liquefactive necrosis
- abscess if severe

Chronic Non-specific Lymphadenitis:

- painless
- 3 types:
  - **Follicular hyperplasia**: numerous follicles but they are benign, b cells, rheumatologic , toxoplasmosis, HIV
  - **Paracortical hyperplasia**: solid sheets, t cells, EBV, drug reactions
  - **Sinus histiocytosis**: LEAST COMMON, macrophages, with adjacent cancer.

- **Cat-Scratch Disease** --> Bartonella henselae, common in children, liquefactive necrosis and necrotizing granulomas.
- **HLH**--> rare, follows a viral infection, severe activation of macrophages.
- Symptoms : fever, splenomegaly, pancytopenia, high ferritin, high triglycerides, high IL-2, and low level of cytotoxic T cells and NKCs.

Types of HLH	
Type 1	**Type 2**
♥ **Infants** and **young** children ♥ **Homozygous defects** in gene PRF1 that encodes **perforin**. ♥ An **essential enzyme** in cytotoxic T-lymphocytes and natural killer cells	♥ **Adolescents** and **adults** ♥ **X-linked lymphoproliferative disorder (males)** ♥ Most of us have been infected with EBV but we develop immunity. ♥ Very rarely, some males, with X-linked problems in the genes, cannot fight this infection. ♥ The problem here is a **defective enzyme** called Signaling lymphocyte activation molecule **(SLAM)-associated protein** ♥ So, the Cytotoxic T Cells are inefficient in killing of EBV-infected B-lymphocyte. ♥ Infective EBV--> Proliferation of B cells--> T cells cannot counter them--> severe activation of macrophages.

Types of HLH	
Type 3	**Type 4**
♥ May be associated not with infection but with **systemic inflammatory disorders** such as rheumatologic diseases (arthritis) ♥ Patients have **heterozygous genetic defects in genes required for cytotoxic T-cells** ♥ Not a certain gene because there are many ones.	♥ **T-cell lymphomas** ♥ **Malignant** T-cells produce **abnormal cytokines** leading to dysregulation of normal cytotoxic T-cells so they cannot kill the infected cell.