White Blood Cells Disorders (Part 1)

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WBCs provide the primary defense against microbial infections and are critical for mounting an immune response. Defects in WBCs can manifest as delayed healing, infection, or mucosal ulceration. To ensure the health of the patient, the dentist should be able to detect WBC abnormalities through history, clinical examination, and screening laboratory tests and should provide a prompt referral to a physician for diagnosis and treatment before invasive dental procedures are performed.

The name "white blood cell" derives from the physical appearance of a blood sample after centrifugation. The scientific term leukocyte directly reflects its description. It is derived from the Greek roots leuk- meaning "white" and cyt- meaning "cell".

WBCs make up approximately 1% of the total blood volume in a healthy adult. However, this 1% of the blood makes a large difference to health, because immunity depends on it.

White blood cells are produced from cells in the bone marrow known as **hematopoietic stem cells**. All white blood cells have nuclei, which distinguishes them from the other blood cells, the anucleated red blood cells (RBCs) and platelets. WBCs are found throughout the body, including the blood and lymphatic system.

Three groups of WBCs are found in the peripheral circulation:

1. **Granulocytes:** 90% is composed of neutrophils; the remainder consists of eosinophils and basophils.
2. **Lymphocytes:** Circulating lymphocytes are of three types:
    - T lymphocytes
    - B lymphocytes
    - Natural killer cells
3. **Monocytes**

Granulocytes are distinguished from agranulocytes by their nucleus shape (lobed versus round, that is, polymorphonuclear versus mononuclear) and by their cytoplasm granules. **Myeloid** cells (granulocytes and monocytes) are distinguished from lymphoid cells (lymphocytes) by hematopoietic lineage.

The primary function of **neutrophils** is to defend the body against certain infectious agents (primarily bacteria) through phagocytosis and enzymatic destruction. **Eosinophils** and **basophils** are involved in inflammatory allergic reactions. Eosinophils also combat infection by parasites.

T lymphocytes (T cells) are involved with the delayed, or cellular, immune reaction, whereas **B lymphocytes (B cells)** play an important role in the immediate, or humoral, immune system involving the production of plasma cells and immunoglobulins (IgA, IgD, IgE, IgG, and IgM).

Monocytes have diverse functions that include phagocytosis, intracellular killing, and mediating of the immune and inflammatory response through the production of more than 100 substances, such as cytokines and growth factors, that increase the activity of lymphocytes. Monocytes serve as antigen-presenting cells. In skin and mucosa, these antigen-presenting cells are known as **Langerhans cells**. Monocytes in tissue that phagocytose microbes are known as **macrophages**.

WBCs that circulate in the peripheral blood account for only 5% of the total WBC mass. These cells are readily available, can be called on to help fight the invading organisms. Lymphocytes localize primarily in three regions: lymph nodes, spleen, and the mucosa-associated lymphoid tissue (MALT) lining the respiratory and gastro-intestinal tracts. At these sites, microbial antigens are trapped and presented to B or T lymphocytes.

Leukocytosis and Leukopenia

The number of leukocytes in the blood is often an indicator of a disease, and thus the WBC count is an important subset of the complete blood count. The number of circulating WBCs normally ranges from 4400 to 11,000/μL in adults. The differential WBC count is an estimation of the percentage of each cell type per microliter of blood.

A normal differential count consists of:
Neutrophils, 50% to 60%;
Eosinophils, 1% to 3%;
Basophils, less than 1%;
Lymphocytes, 20% to 34%;
Monocytes, 3% to 7%.

The term **leukocytosis** is defined as an increase in the number of circulating WBCs to more than 11,000/μL, and **leukopenia** as a reduction in the number of circulating WBCs (less than 4400/μL). Many causes of leukocytosis are known. Exercise, pregnancy, and emotional stress can lead to increased numbers of WBCs in the peripheral circulation. Leukocytosis resulting from these causes is called **physiologic** leukocytosis. **Pathologic** leukocytosis can be caused by infection, neoplasia or necrosis.

Pyogenic infections increase the number of **neutrophils**. Tuberculosis, syphilis, and viral infections increase the numbers of **lymphocytes**. Protozoal infections associated with an increase in the numbers of **monocytes**. Allergies and parasitic infections increase the numbers of circulating **eosinophils**.

Leukopenia and pancytopenia (decreased WBCs and RBCs) are common complications that result from the use of chemotherapeutic drugs. Patients with leukocytosis or leukopenia may have bone marrow abnormalities that can cause thrombocytopenia. Examination of the patient's bone marrow aspirate is important for making the final diagnosis.

Leukemia and Lymphoma

Patients with leukemia or lymphoma are gravely ill if they are not properly identified and do not receive appropriate medical care. Patients are usually immunosuppressed because of the disease or treatment. Hence, they are prone to develop a serious infection and often bleed easily because of thrombocytopenia.

Leukemia

Leukemia (cancer of the WBCs) is characterized by a great increase in the numbers of circulating immature leukocytes. Leukemia affects the bone marrow and circulating blood. It involves exponential proliferation of a clonal myeloid or lymphoid cell and occurs in both acute and chronic forms. Acute leukemia is a rapidly progressive disease that results from accumulation of immature, **functionless** WBCs in the marrow and blood. Chronic leukemia has a slower onset, which allows the production of larger numbers of more mature, **functional** cells.

There are four common types of leukemia:

(1) Acute lymphoblastic leukemia (ALL)
(2) Acute myeloid leukemia (AML)
(3) Chronic lymphoblastic leukemia (CLL)
(4) Chronic myeloid leukemia (CML)

Myeloproliferative disorders

- Acute myeloid leukemia: immature neoplastic malignancy of myeloid cells
- Chronic myeloid leukemia: mature neoplastic malignancy of myeloid cells

Lymphoproliferative disorders

- Acute lymphoblastic leukemia: immature neoplastic malignancy of lymphoid cells
- Chronic lymphocytic leukemia: mature neoplastic malignancy of lymphoid cells

Leukemia occurs in all races, at any age, more common in **men**. Leukemia is much more common in **adults** than in children, with more than half of all cases occurring **after age 65 years**. The most common types of leukemia in adults are **acute myeloid leukemia**. The most common form of leukemia among people younger than 19 years of age is **acute lymphoblastic leukemia**.

The cause of leukemia remains unknown. Increased risk is associated with large doses of ionizing radiation or infection with specific viruses (e.g., Epstein-Barr virus). Cigarette smoking and exposure to electromagnetic fields also have been proposed to be causative.

Lymphomas

Lymphoma is a cancer of the lymphoid organs and tissues. Lymphomas are classified by **Cell type** (B cell, T cell, MALT, plasma cell), **Appearance** (small or large cell) and **Clinical behavior** (low, intermediate, and high grade). These diseases are of importance in dental management because initial signs often occur in the mouth and in the head and neck region, and precautions must be taken before any dental treatment is provided.

Intraoral lymphoma most commonly involves Waldeyer's ring (soft palate and oropharynx); less often, the salivary glands and mandible are affected. Intraoral lymphomas appear as rapidly expanding (or chronic), unexplained swellings of the head and neck lymph nodes, palate, gingiva, buccal sulcus, or floor of the mouth. The presence of these orofacial abnormalities requires prompt evaluation by biopsy using a needle, incisional, or excisional techniques.

Most Common Types of Lymphomas

- **Hodgkin lymphoma:** is a malignant neoplasm of B-lymphocytes, primarily in lymph nodes. This neoplasm contains a characteristic tumor cell called the **Reed-Sternberg cell**. Symptoms may include fever, night sweats, and weight loss. Often there will be non-painful enlarged lymph nodes in the neck.

- **Non-Hodgkin lymphoma:** includes all types of lymphoma except Hodgkin's lymphomas. B or T cell malignant neoplasms, many types and locations; most are of B cell lineage.
- **Burkitt lymphoma:** aggressive non-Hodgkin B cell lymphoma involving bone and lymph nodes.
- **Multiple myeloma:** overproduction of malignant plasma cells that results in multiple tumorous masses scattered throughout the skeletal system.

Dental care considerations:

1. Risks of infection and excessive bleeding in patients receiving chemotherapy.
2. Risk of osteonecrosis, mucositis and xerostomia in patients treated by radiation to the head and neck region.
3. Petechiae or ecchymoses if thrombocytopenia presents because of tumor invasion of bone marrow.
4. Cervical lymphadenopathy.
5. The dentist can biopsy extranodal or osseous lesions to establish a diagnosis; patients with lesions involving the lymph nodes should be referred for excisional biopsy.
6. Before invasive procedures, a complete blood count should be obtained to determine risks for bleeding and infection.
7. Consider prophylactic antibiotics if the WBC count is less than 2000/µL.

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- ***Denis Parsons Burkitt*** (1911–1993), an Irish surgeon who first described the disease (Burkitt lymphoma) in 1958 while working in equatorial Africa.
- Hodgkin's lymphoma was first described in an 1832 report by ***Thomas Hodgkin*** (1798–1866); a British physician and one of the most prominent pathologists.