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Review Article

Complete Blood Cell Count and Peripheral Blood Film, Its Significant in Laboratory Medicine: A Review Study

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Abstract: The aim of this review is to assist non-hematologist effective means of interpreting complete blood cell (CBC) counts results especially when encountered with abnormal result for intellectually rewarding practice and to recognize when a subspecialty consultation is reasonable and when it may be circumvented. A complete blood cell count is routine hematology tests in medicine useful for the differential diagnosis of anemia and other medical conditions. A good percentage of CBC results are reported as abnormal, therefore it is in every clinician's interest to have some understanding of the specific test basics as well as a structured action plan when confronted with abnormal results. It is a series of tests used to evaluate the composition and concentration of the cellular components of blood, which consists: red blood cell (RBC) counts, red cell indices, hematocrit, hemoglobin concentration, white blood cell (WBC) count, classification of white blood cells (WBC differential) and platelet count. CBC provides valuable information about the blood and to some extent the bone marrow, which is the blood-forming tissue. CBC can be use for the following purposes: as a preoperative test to ensure both adequate oxygen carrying capacity and hemostasis, to identify acute and chronic illness, bleeding tendencies, and white blood cell disorders such as leukemia, to monitor a medical condition and changes in the body system caused by medical treatments, to determine the effects of chemotherapy and radiation therapy on blood cell production. CBC can be performed manually using visual examination or automation by fluorescence flow cytometry and impedance. In conclusion, CBC and peripheral blood examination are one of the most commonly ordered tests that provides important information about the kinds and numbers of cells in the blood, abnormalities in any of these types of blood cells may indicate the presence of important medical disorders.

Keywords: Blood Cells, Complete Blood Cell Count, Peripheral Blood Film

1. Introduction

A complete blood count (CBC) and peripheral blood film is a blood panel hematology test requested by a physician or other medical professional which gives information about the cells in a patient's blood. The Literature reveals that as much as 70% of clinical decisions and diagnoses are supported by laboratory medicine clinical information obtained from laboratory tests, which play a key role in the diagnosis and management of patients [1]. A number of studies have shown that although physicians commonly request laboratory tests, they tend to use them for the wrong purposes, and ignore or misinterpret the results; such improper utilization and interpretation have obvious implications for the quality of patient care, and the economy as a whole [2, 3, 4]. Circulating blood cells includes red blood cells (RBCs), white blood cells (WBCs), and platelets suspended in fluid called plasma. The blood cells are produced and mature primarily in the bone marrow then released into the blood stream as needed under normal circumstances. CBC is a group of tests used to quantify the number of RBCs, WBCs, and platelets also to provide information about their size and shape of blood cells, to measure the hematocrit and RBC indices, to measure hemoglobin concentration of RBCs, to determine the percentage (relative) and absolute number of the five white blood cell types, and identify early and abnormal blood cells in the circulating system [5]. CBC count can be performed manually by visual examination or automation by fluorescence flow cytometry and impedance to determine multiple parameters of CBC. Automation provides a high

level of accuracy and precision for quantification and identification of normal white blood cells; however, this method is not sensitive at identifying abnormal or immature cells especially in WBC differential counts and is not able to accurately identifying and classifying all types of white blood cells [6, 7, 8]. To overcome this problem, most hematology automated analyzers will flag samples with possible abnormal blood cell populations, indicating the need for peripheral blood examination to identify abnormal cells by manual method. However, both automated and manual methods may not detect small numbers of abnormal cells. The false negative rate for detection of abnormal cells varies from 1-20%, depending on the instrument and the detection limit desired (1-5% abnormal cells). Disorders in CBC can be classified as quantitative or qualitative. In quantitative alterations, all cells appear normal but are present in abnormal quantities, either in excess or in defect of normal values. In qualitative defects, abnormal appearing cells or extrinsic cells are found in circulation [1, 3]. The CBC does not require fasting or any special preparation. However, patients may be asked to stop taking certain medications for several days before the sample collection. Patients on certain medicines, both prescribed and over-the-counter, supplements or vitamins, long-term use of steroids or long-term exposure to toxic chemicals (such as lye or insecticides) should be taken into consideration when interpreting their complete blood cell counts results which can cause increased or decreased in RBC, WBC, and/or platelet production or abnormal formation/morphology[3]. Apart from using blood to carryout CBC, certain body fluids can be used to perform WBC differentials, along with WBC counts. A common reason that this is done is to more directly assess one area of the body that may be infected or inflamed. For example, if meningitis is suspected, then a WBC count plus differential may be performed on a sample of cerebrospinal fluid (CSF)[6]. For clinical purposes, the parameters to focus on when examining the CBC are hemoglobin concentration and packed cell volume (as a general indicator of anemia or polycythemia), red cell indices especially MCV and RDW (is a key parameter for the classification of anemia), RBC distribution width (is relatively useful parameter in the differential diagnosis of anemia to determine the size of RBC), RBC count (an increased RBC count associated with anemia is characteristic in the thalassemia trait), platelet count (to detect either thrombocytopenia or thrombocythemia), and WBC count with differential (usually gives important clues for the diagnosis of infection, acute leukemia and chronic lymphoid or myeloid disorders as well as for the presence of leukopenia and neutropenia) [9]. Differential WBC count gives relative percentage of each type of white blood cell and also helps reveal abnormal white blood cell populations (blasts, immature granulocytes, or circulating lymphoma cells in the peripheral blood). Differential WBC count is also used along with leukocyte count (WBC) to generate an absolute value for each type of white blood cells, which usually gives more meaningful information than the percentage of each, since relative percentage can be misleading[10, 3, 11, 12]. Expressing absolute values are also useful for monitoring (monitoring neutropenia during chemotherapy or bone marrow transplantation). Using absolute values, conditions such as neutropenia, neutrophilia, lymphopenia, lymphocytosis, monocytopenia, monocytosis, eosinophilia, and basophilia can be identified, which can help differential diagnosis of patient's underlying disorders. Furthermore, patients with an abnormal WBC count, shows need to determine the type of white blood cells that is affected [10, 13]. Abnormal CBC should be interpreted within the context of an individual's baseline value because up to 5% of the general population without disease may display laboratory values outside the statistically assigned "normal" reference range. Likewise, an individual may display a substantial change from his or her baseline (personal normal) without violating the "normal" reference range. Similarly, differences in the CBC based on race and sex should be considered when interpreting results [2, 3, 8, 13]. In general, RBC-associated measurements are lower and platelet counts are higher in women compared with men, and persons of African ancestry display significantly lower hemoglobin concentration, WBC, neutrophil, and platelet counts than white persons [14]. The aim of this review is to assist non-hematologist effective means of interpreting CBC results especially when encountered with abnormal result for intellectually rewarding practice and to recognize when a subspecialty consultation is reasonable and when it may be circumvented.

2. Quantitative and Qualitative Abnormalities of Blood Cells

Blood cells disorders can be classified as quantitative or qualitative. In quantitative alterations all cells appear normal but are present in abnormal quantities, either in excess or in defect of normal values, however, in qualitative defects, abnormal appearance, abnormal function of the cells, or extrinsic cells are found in circulation.

2.1. Quantitative Abnormalities of Blood Cells

Simultaneous increase in blood cell of more than one cell line suggests overproduction of blood cells originating in an early precursor cell, this occurs in myeloproliferative neoplasm in which one cell type may predominate. However, lowering of all three types of blood cells; red blood cell, white blood cells and platelet, which may lead to low red blood cell count, low white blood cell count and low platelet count; this condition is called pancytopenia [9, 10].

Quantitative Abnormalities of Red Blood Cell

Red blood cell contains a substance called hemoglobin which transports oxygen around the body. The amount of oxygen that's delivered to body's tissues will depend on the number of red blood cells. A RBC count is usually carried out as part of a full blood cell (FBC) count. A normal red blood cell, hemoglobin and hematocrit values for male and female are 4.7 - 6.1 cells/mcL and 4.2 - 5.4 cells/mcL, 14-18 g/dL and 12-16 g/dL and 40-52% and 37-47% respectively [11, 12, 15]. RBCs have a typical lifespan of about 120 days and are

continuously renewed and replaced as they age and degrade or are lost through bleeding. A relatively stable number of RBCs is maintained in the circulation by increasing or decreasing the rate of production by the bone marrow. Some conditions affect RBC production and may cause an increase or decrease in the number of mature RBCs released into the blood circulation. Other conditions may affect the lifespan of RBCs in circulation, especially if the RBCs are deformed due to an inherited or acquired defect or abnormality [9, 6]. If RBCs are lost or destroyed faster than they can be replaced, if bone marrow production is disrupted, or if the RBCs produced do not function normally, then a person will become anemic, which affects the amount of oxygen reaching tissues. If too many RBCs are produced and released, then a person can develop polycythemia. This can cause decreased blood flow and related problems. A rise or drop in the RBC count must be interpreted in conjunction with other parameters, such as hemoglobin, hematocrit, reticulocyte count, and/or red blood cell indices [9, 16]. Blood or red cell loss that occurs suddenly or over time and diseases and conditions that decrease red blood cell production in the bone marrow will result in a low RBC count. Some causes of a low RBC count (anemia) include:

(1) Trauma
(2) Red blood cell destruction, for example hemolytic anemia caused by autoimmunity or defects in the red cell itself; the defects could be a hemoglobinopathy (sickle cell anemia), thalassemia, an abnormality in the RBC membrane (hereditary spherocytosis), or enzyme defect (G6PD deficiency)[17].
(3) Sudden (acute) or chronic bleeding from the digestive tract (ulcers, polyps, colon cancer) or other sites, such as the bladder or uterus (in women, heavy menstrual bleeding, for example)
(4) Nutritional deficiency such as iron deficiency or vitamin B12 or folate deficiency
(5) Bone marrow damage (toxin, radiation or chemotherapy, infection, drugs)
(6) Bone marrow disorders such as leukemia, multiple myeloma, myelodysplasia, or lymphoma or other cancers that spread to the marrow
(7) Chronic inflammatory disease or condition
(8) Kidney failure—severe and chronic kidney diseases lead to decreased production of erythropoietin, a hormone produced by the kidneys that stimulates RBC production by the bone marrow [9, 16, 18].

Polycythemia

Polycythemiais a condition that results in an increased level of circulating red blood cells in the bloodstream. Blood volume proportions can be measured as hematocrit, hemoglobin, or red blood cell count above the normal limits of both sex and age. Polycythemiacan be due to an increase in the number of red blood cells ("absolute polycythemia") or to a decrease in the volume of plasma ("relative polycythemia"). Polycythemia is sometimes called erythrocytosis, but the terms are not synonymous because polycythemia refers to any increase in red blood cells, whereas erythrocytosis only refers to a documented increase of red cell mass[18, 19, 20].

Absolute polycythemia

Overproduction of red blood cells may be due to a primary process in the bone marrow (myeloproliferative syndrome), or it may be a reaction to chronically low oxygen levels or, rarely, a malignancy. Alternatively, additional red blood cells may have been received through another process like over-transfusion (either accidentally or, as blood doping, deliberately) or being the recipient twin in a pregnancy, undergoing twin-to-twin transfusion syndrome. Absolute can be primary or secondary [3, 19, 21, 22].

Primary polycythemia

Primary polycythemias are due to factors intrinsic to red cell precursors. Polycythemia vera (PCV), polycythemia rubra vera (PRV), or erythremia, occurs when excess red blood cells are produced as a result of an abnormality of the bone marrow. Often, excess white blood cells and platelets are also produced. Polycythemia vera is classified as a myeloproliferative disease. Symptoms include headaches and vertigo, and signs on physical examination include an abnormallyenlarged spleen and/or liver. In some cases, affected individuals may have associated conditions including high blood pressure or formation of blood clots. A hallmark of polycythemia is an elevated hematocrit, with Hct > 55% seen in 83% of cases [19]. A somatic (non-hereditary) mutation (V617F) in the JAK2 gene is found in 95% of cases, though also present in other myeloproliferative disorders [23].

Primary familial polycythemia, also known as primary familial and congenital polycythemia (PFCP), exists as a benign hereditary condition, in contrast with the myeloproliferative changes associated with acquired polycythemia vera. In many families, PFCP is due to an autosomal dominant mutation in the EPOR erythropoietin receptor gene. PFCP can cause an increase of up to 50% in the oxygen-carrying capacity of the blood; skierEero Mäntyranta had PFCP, which is considered to have given him a large advantage in endurance events [19, 20, 21, 22, 23].

Secondary polycythemia

Secondary polycythemia is caused by either natural or artificial increases in the production of erythropoietin, hence an increased production of erythrocytes. In secondary polycythemia, there may be 6 to 8 million and occasionally 9 million erythrocytes per cubic millimeter of blood. Secondary polycythemia resolves when the underlying cause is treated.Secondary polycythemia occurs in chronic hypoxia (chronic lung disease, congenital heart disease, high-affinity hemoglobin) or aberrant erythropoietin production. Secondary polycythemia can be excluded by clinical history and examination, assessment of serum erythropoietin concentration and arterial oxygen saturation, hemoglobin electrophoresis or high performance liquid chromatography plus an oxygen dissociation curve and abnormal ultrasound examination [18].

Secondary polycythemia in which the production of erythropoietin increases appropriately is called physiologic polycythemia. Conditions which may result in a physiologically appropriate polycythemia include:

- Altitude related - This physiologic polycythemia is a normal adaptation to living at high altitudes. Many athletes train at high altitude to take advantage of this effect — a legal form of blood doping. Some individuals believe athletes with primary polycythemia may have a competitive advantage due to greater stamina. However, this has yet to be proven due to the multifaceted complications associated with this condition [22].
- Hypoxic disease-associated - as in cyanotic heart disease where blood oxygen levels are reduced significantly. It may also occur as a result of hypoxic lung disease such as COPD and as a result of chronic obstructive sleep apnea.
- Iatrogenic - Secondary polycythemia can be induced directly by phlebotomy (blood letting) to withdraw some blood, concentrate the erythrocytes, and return them to the body.
- Genetic - Heritable causes of secondary polycythemia also exist and are associated with abnormalities in hemoglobin oxygen release. This includes patients who have a special form of hemoglobin known as Hb Chesapeake, which has a greater inherent affinity for oxygen than normal adult hemoglobin. This reduces oxygen delivery to the kidneys, causing increased erythropoietin production and a resultant polycythemia. Hemoglobin Kempsey also produces a similar clinical picture. These conditions are relatively uncommon[19, 20, 21, 22, 23]

Conditions where the secondary polycythemia is not as a result of physiologic adaptation and occurs irrespective of body needs include:

- Neoplasms - Renal-cell carcinoma or liver tumors, von Hippel-Lindau disease, and endocrine abnormalities including pheochromocytoma and adrenal adenomawith Cushing's syndrome.

People whose testosterone levels are high because of the use of anabolic steroids, including athletes who abuse steroids, or people on testosterone replacement for hypogonadism, as well as people who take erythropoietin may develop secondary polycythemia[18].

Altered oxygen sensing

Inherited mutations in 3 genes which all result in increased stability of Hypoxia Inducible Factors (HIFs), leading to increased erythropoietin production have been shown to cause erythrocytosis:

- Chuvash polycythemia: An autosomal recessive form of erythrocytosis which is endemic in patients from Chuvashia, an autonomous republic within theRussian Federation. Chuvash polycythemia is associated with homozygosity for a C598T mutation in the von Hippel-Lindau gene (VHL), which is needed for the destruction of HIF in the presence of oxygen. Clusters of patients with Chuvash polycythemia have been found in other populations, such as on the Italian island of Ischia, located in the Bay of Naples [22]
- PHD2 erythrocytosis: Heterozygosity for loss-of-function mutations of the PHD2 gene are associated with autosomal dominant erythrocytosis and increasedHIF activity [20]
- HIF2α erythrocytosis: Gain-of-function mutations in HIF2α are associated with autosomal dominant erythrocytosis [21] and pulmonary hypertension [23]

Relative polycythemia

Relative polycythemia is an apparent rise of the erythrocyte level in the blood; however, the underlying cause is reduced blood plasma (Relative polycythemia has normal total red cell volume with reduced plasma volume). Relative polycythemia is often caused by loss of body fluids, such as through burns, dehydration and stress. A specific type of relative polycythemia is Gaisböck syndrome. In this syndrome, primarily occurring in obese men, hypertension causes a reduction in plasma volume, resulting in (amongst other changes) a relative increase in red blood cell count [18, 24].

Anemia

Anemia is the most common disorder of the blood, affecting about a quarter of the people globally [16]. Anemia is usually defined as a decrease in the amount of red blood cells (RBCs) or hemoglobin in the blood. It can also be defined as a lowered ability of the blood to carry oxygen. anemia can be diagnosis in adult men based on hemoglobin less than 130 to 140 g/L (13 to 14 g/dL), while in adult women, it must be less than 120 to 130 g/L (12 to 13 g/dL)[11, 12, 16, 25]. Further testing is then required to determine the cause. When anemia comes on slowly, the symptoms are often vague and may include: feeling tired, weakness, shortness of breath or a poor ability to exercise. Anemia that comes on quickly often has greater symptoms, which may include: confusion, feeling like one is going to pass out, loss of consciousness, or increased thirst. Anemia must be significant before a person becomes noticeably pale. Additional symptoms may occur depending on the underlying cause [16]. There are four main types of anemia: that due to blood loss, that due to decreased red blood cell production, that due to increased red blood cell breakdown and increased in body demand. Causes of blood loss include trauma and gastrointestinal bleeding, among others. Causes of decreased production include iron deficiency, a lack of vitamin B12, thalassemia, and a number of neoplasms of the bone marrow. Causes of increased breakdown include a number of genetic conditions such as sickle cell anemia, infections like malaria, and certain autoimmune diseases. Causes of increased in body demand include pregnancy especially in twins[9]. Anemia can also be classified based on the size of red blood cells and amount of hemoglobin in each cell. If the cells are small, it is microcytic anemia. If they are large, it is macrocytic anemia while if they are normal sized, it is normocytic anemia. Anemia is typically diagnosed on a complete blood count. Apart from reporting the number of red blood cells and thehemoglobin level, the automatic counters also measure the size of the red blood cells by flow cytometry, which is an important tool in distinguishing between the causes of anemia. Examination of a stained blood smear using a microscopecan also be helpful, and it is sometimes a necessity in regions of the world where automated analysis is less accessible [5, 26, 27]In modern

counters, four parameters (RBC count, hemoglobin concentration, MCV and RDW) are measured, allowing others (hematocrit, MCH and MCHC) to be calculated, and compared to values adjusted for age and sex [28]. A reticulocyte count is a quantitative measure of the bone marrow's production of new red blood cells. The reticulocyte production index is a calculation of the ratio between the level of anemia and the extent to which the reticulocyte count has risen in response. If the degree of anemia is significant, even a normal reticulocyte count actually may reflect an inadequate response. If an automated count is not available, a reticulocyte count can be done manually following special staining of the blood film. In manual examination, activity of the bone marrow can also be gauged qualitatively by subtle changes in the numbers and the morphology of young RBCs by examination under a microscope. Newly formed RBCs are usually slightly larger than older RBCs and show polychromasia [3]. Even where the source of blood loss is obvious, evaluation of erythropoiesis can help assess whether the bone marrow will be able to compensate for the loss, and at what rate. When the cause is not obvious, clinicians can use other tests, such as: ESR, ferritin, serum iron, transferrin, RBC folate level, serum vitamin B12, hemoglobin electrophoresis, renal function tests (serum creatinine) although the tests will depend on the clinical hypothesis that is being investigated. When the diagnosis remains difficult, a bone marrow examination allows direct examination of the precursors to red cells, although is rarely used as is painful, invasive and is hence reserved for cases where severe pathology needs to be determined or excluded [18, 29]

Leucocytosis

Leucocytosis can be increased in circulation by four different mechanisms: increased production, decreased egress from the circulation, demargination, and release from storage compartments. Leucocyte levels are considered elevated when they are between 15,000-20,000 per microliter. The increased number of leucocytes can occur abnormally as a result of an infection, cancer, or drug intake; however, leucocytosis can occur normally after eating a large meal or experiencing stress [3, 10, 30].

Neutrophilia: Neutrophils are commonly increased during pregnancy and acute infections, inflammation, alcohol intoxication, corticosteroid therapy and acute blood loss or red cell destruction. Combination of anemia and neutrophilia may occurs in chronic infection or inflammation and also in malignant conditions; high Hct with neutrophilia suggests polycythemia vera. Neutrophilia with an increase in platelet counts occurs in infectious or inflammatory processes or malignant conditions and during marrow recovery [13, 30]. neutroplilia with thrombocythopenia is classically seen in sepsis and occasionally in microangiopathic haemolytic anaemia.

Lymphoctosis: Lymphocytosis is a feature of certain infections, particularly infection in children. It may be especially marked in pertussis, infectious mononucleosis, cytomegalovirus infection, infectious hepatitis, tuberculosis and brucellosis. Elderly patients with lymphoproliferative disorders including chronic lymphocytic leukaemia and lymphomas often present with lymphadenopathy and a lymphocytosis [4, 13].

Monocytosis: Monocytosis, an increase in the blood absolute monocyte count to more than 800/μL (0.8 × 109/L), may occur in some patients with cancer and several unrelated conditions, such as postsplenectomy states, chronic inflammatory bowel disease, and some chronic infections (e.g., bacterial endocarditis, tuberculosis, and brucellosis), rheumatic diseases (lupus, rheumatoid arthritis), Crohn's disease and some malignant processes (Hodgkin's and non-Hodgkin's lymphoma), hematological malignancies such as chronic myeloid leukaemia and acute myeloid leukaemia [3, 30].

Eosinophilia is an abosulte increase in the number of circulating eosinophils may occur occurs in association with hypersensitivity reactions or allergic drug reactions, Extrinsic allergic alveolitisparasitic infestationsespecially those with tissue invasion, Chronic infections, Hematologic malignancies (CML, Hodgkin's disease, eosinophilic leukemia), connective tissue disorders (rheumatoid arthritis, polyarteritis nodosa), and the syndrome of pulmonary infiltrates with eosinophilia like Extrinsic asthma, Hay fever [30, 31].

Basophilia is an abosulte increase in the number of circulating basophils occurs with myeloproliferative disorders and with some allergic reactions, chronic myelogenous leukemia, Hodgkin's disease, and some chronic inflammatory and infectious disorders.

Leucopenia

Leucopenia is a decrease in the number of white blood cells circulating within blood,the immune system is severely weakened and the individual is at a greater risk of infections. Leukopenia may be caused by diseases, medications, and genetic deficiencies. Diagnosis of Leucopenia is by total WBC count with differential. It can be subdivided according to the white cell population that is affected: neutropenia, lymphopenia, eosinopenia, monocytopenia [3, 30].

Neutropenia

Normal adult peripheral blood absolute neutrophil count is $2.0 – 7.5 \times 10^9$/l, this is influenced by physical activity, age, generic factors. Neutropenia is an absolute neutropil count less than 1.5×10^9/l. Agranulocytosis implies a complete absence of neutrophil in the peripheral blood, however, in practice, the term is used to describe neutropenia that is particularly severe less than 0.3×10^9/l. A neutrophil count less than 1.5×10^9/l may be due to; decreased production or normal production but increased consumption. Severity of neutropenia can be define as Mild (1.0×10^9/l to 1.5×10^9/l), Moderate (0.5×10^9/l to 1.0×10^9/l) and Severe (less than 0.5×10^9/l). Acute neutropenia (occurring over hours to a few days) can develop from rapid neutrophil use or destruction or from impaired production. Chronic neutropenia (lasting months to years) usually arises from reduced production or excessive splenic sequestration [10, 13, 30].

Lymphocytopenia

Lymphocytopenia is a total lymphocyte count of less than

1000/μL in adults or less than 3000/μL in children less than two years. Sequelae include opportunistic infections and an increased risk of malignant and autoimmune disorders. If the CBC reveals lymphocytopenia, testing for immunodeficiency and analysis of lymphocyte subpopulations should follow. The normal lymphocyte count in adults is 1000 to 4800/μL; in children less than two years, 3000 to 9500/μL. At age six years, the lower limit of normal is 1500/μL. Both B and T cells are present in the peripheral blood; about 75% of the lymphocytes are T cells and 25% B cells. Because lymphocytes account for only 20 to 40% of the total WBC count, lymphocytopenia may go unnoticed when WBC count is checked without a differential. Almost 65% of blood T cells are CD4+ (helper) T cells [3, 30, 32]. Most patients with lymphocytopenia have a reduced absolute number of T cells, particularly in the number of CD4+ T cells. The average number of CD4+ T cells in adult blood is 1100/μL (range, 300 to 1300/μL), and the average number of cells of the other major T-cell subgroup, CD8+ (suppressor) T cells, is 600/μL (range, 100 to 900/μL).

Monocytopenia was not previously thought to be a distinct entity; however, recent evidence suggests that deficiency or absence of monocytes can occur in patients with mutations of the hematopoietic transcription factor gene, GATA2. Affected patients sometimes present with nontuberculous mycobacterial infection especially at cutaneous sites (MonoMAC syndrome) or with genital human papillomavirus infection that has a high risk of progression to genital cancer. There is risk of progression to other hematologic disorders (bone marrow failure, acute myelogenous leukemia, chronic myelomonocytic leukemia). Monocytopenia is diagnosed by CBC with differential. Treatment is experimental and may include interferon, antibodies, and allogeneic hematopoietic stem cell transplantation, depending on the severity of the condition and the development of secondary hematologic disorders [14, 30].

Eosinopenia

A low number of eosinophils in the blood (eosinopenia) can occur with Cushing syndrome, bloodstream infections (sepsis), and treatment with corticosteroids. However, a low number of eosinophils do not usually cause problems because other parts of the immune system compensate adequately. A low number of eosinophils are usually detected by chance when a complete blood count is done for other reasons. Treatment of the cause restores the normal number of eosinophils. Eosinophils play an important role in the body's response to allergic reactions, asthma, and infection with parasites. Eosinophils usually account for less than 7% of the circulating white blood cells (100 to 500 eosinophils per microliter of blood). These cells have a role in the protective immunity against certain parasites but also contribute to the inflammation that occurs in allergic disorders [27, 30]. Sometimes, eosinophils cause inflammation in certain organs and result in symptoms.

Basopenia

A decrease in the number of basophils (basopenia) can occur as a response to thyrotoxicosis, acute hypersensitivity reactions, and infections. Basophil has some role in immune surveillance (such as detecting and destroying very early cancers) and wound repair. Basophils can release histamine and other mediators and play a role in the initiation of allergic reactions [30]. Basophils account for less than 3% of the circulating white blood cells (0 to 300 basophils per microliter of blood).

Thrombocythemia and Thrombocytosis

Thrombocythemia and thrombocytosisare conditions in which blood has an abnormally high platelet count greater than 450,000/uL above normal platelets count of 150 - 450 X 10 to the 9/L. Platelets are blood cell fragments, travel through blood vessels and stick together (clot). Clotting helps stop any bleeding that may occur if a blood vessel is damaged, hence thrombocytosis can cause stroke due to platelet clot. Platelets also are called thrombocytes because a blood clot also is called a thrombus. An individual's platelet count usually remains relatively constant during life [26, 33]. The platelet count decreases normally during pregnancy (gestational thrombocytopenia). The platelet count increases to above the usual value following an acute self-limited thrombocytopenia (postsurgery thrombocytosis). The term "thrombocythemia" is preferred when the cause of a high platelet count isn't known. The condition sometimes is called primary or essential thrombocythemia.

Essential or primary thrombocythemia is a myeloproliferative disorder involving overproduction of platelets because of a clonal abnormality of a hematopoietic stem cell. A markedly elevated platelet count with impaired platelet functionis typically associated. Essential thrombocythemia has highest platelet count which may exceed 1 million. When another disease or condition causes a high platelet count, the term "thrombocytosis" is preferred. This condition often is called secondary or reactive thrombocytosis. Secondary thrombocytosis is more common than primary thrombocythemia [1].

Reactive thrombocytosis or secondary thrombocythemia is an overproduction of platelet in response to another disorder, increased platelet levels may last for days to weeks, although platelet function is normal. There are many causes, including acute and chronic blood loss acute infection, chronic inflammatory disorders (inflammatory bowel disease, tuberculosis, sarcoidosis rheumatoid arthritis) splenectomy, iron deficiency, rebound thrombocytosis in recovering alcoholics or patients on chemotherapy and certain cancers. Reactive thrombocytosis is not typically associated with an increased risk of thrombosis [33]

Thrombocytopenia

This is an abnormally low platelet count of less than 50,000/uL, is the most common cause of abnormal bleeding. The various explanations for thrombocytopenia differ depending on the clinical setting. For patients who present to the emergency room with acute, severe thrombocytopenia, certain life-threatening disorders must be considered, such as thrombotic thrombocytopenia purpura (TTP), drug-induced immune thrombocytopenic purpura (D-ITP), and acute leukemia. In postoperative patients, the timing of onset of thrombocytopenia is important since early thrombocytopenia is usually due to postoperative hemodilution, whereas

later-onset thrombocytopenia suggests heparin-induced thrombocytopenia, septicemia, or other postoperative complications [2]. Thrombocytopenia in the intensive care unit is often due to poorly defined platelet consumption complicating multiorgan system dysfunction. However, causes of thrombocytopenia can be classified by mechanism and include decreased platelet production, increased splenic sequestration of platelets with normal platelet survival, increased platelet destruction or consumption (both immunologic and nonimmunologic causes), dilution of platelets, and a combination of these mechanisms. Increased splenic sequestration is suggested by splenomegaly [6]. A large number of drugs may cause thrombocytopenia, typically by triggering immunologic destruction. Overall, the most common specific causes of thrombocytopenia include: Gestational thrombocytopenia, Drug-induced thrombocytopenia due to immune-mediated platelet destruction (commonly, heparin, trimethoprim/sulfamethoxazole), Drug-induced thrombocytopenia due to dose-dependent bone marrow suppression (chemotherapeutic agents), Thrombocytopenia accompanying systemic infection, Immune thrombocytopenia (ITP, formerly called immune thrombocytopenic purpura)

Platelet dysfunction

In this condition, platelet count may be normal but malfunction. Platelet dysfunction may stem from an intrinsic platelet defect or from an extrinsic factor that alters the function of normal platelets. Dysfunction may be hereditary or acquired. Hereditary disorders of platelet function consist of von Willebrand disease, the most common hereditary hemorrhagic disease, and hereditary intrinsic platelet disorders, which are much less common. Acquired disorders of platelet function are commonly due to diseases (renal failure) as well as to aspirin and other drugs [33].

2.2. Qualitative Abnormalities of Blood Cells

Qualitative abnormalities may involve all the blood cells; red cell morphology evaluation include examination for deviations in size, shape, distribution, concentration of hemoglobin, color and appearance of inclusions. White cell morphology evaluation consists of differentiation white blood cells and their overall appearance which includes nuclear abnormalities, cytoplasmic abnormalities and the presence of abnormal inclusions that denote a disease process. Platelet count should be verified and in addition the smear should be reviewed for platelet shape and size abnormalities and for clumping

Morphology of Red Blood Cells, Interpretations and Clinical Significant

Red blood cells are the major cellular component of blood. Mature red blood cells are biconcave discs that lack nucleus and most cell organelles such as lysomes, endoplasmic reticulum and mitochondria [13]. However, variable abnormal erythrocyte morphology is found in various pathological conditions:

(1) Anisocytosis: Variation in size
(2) Variation in color
(3) Poikilocytosis: Variation in shape
(4) Presence of inclusion bodies

(1) Anisocytosis is the Variation in size of RBC. The normal size of RBC is 7.5+/-0.2 micrometer in diameter. Nucleus of small lymphocyte is useful guide to the size of RBC. When the appearance of RBCs (RBC morphology) is normal, it is often reported as normochromic and normocytic. Anisocytosis is divided into Macrocytosis and Microcytosis. Variation in erythrocyte size is now measured by the red cell distribution width (RDW). Always take the RDW into account when interpreting the mean corpuscular volume (MCV) as shown in figure A5 of the appendix.

- Microcytosis: RBCs smaller than the normal size are considered as microcytes. Microcytosis is seen in: Iron deficiency anemia, thalassemia, lead poisoning, sideroblastic anemia and anemia of chronic disorders as shown in figure A6 of the appendix.
- Macrocytosis: RBCs larger than the normal size are considered as macrocytes. Macrocytosis is seen in: Liver diseases, hypothyroidism, megaloblastic anemia, chemotherapy, post splenectomy and some other causes of elevated erythropoiesis as shown in figure A7 of the appendix [2, 6, 13].

(2) Variation in color: RBCs that appear disc shaped (biconcave) and having an area of central pallor that occupies approximately one-third of the cell's diameter (containing normal amount of hemoglobin) are considered as normochromic RBCs due to the hemoglobin inside the RBCs, they appear pink or red in color with a pale center after staining the blood smear with Rowmanosky dye because the hemoglobin content of the red cell picks up eosin, the acidophilic components of the dye. The color of the red cells is reflected by its haemoglobin content. Increased haemoglobinization is termed hyperchromia. Decreased haemoglobination is hypochromia [6, 9].

- Hypochromic: RBCs that have an area of pallor that is larger than the normal are called hypochromic. This variation is seen in: Iron deficiency anemia, anemia of chronic diseases, thalassemia, some hemoglobinopathies, sideroblastic anemia and any of the conditions leading to microcytosis as shown in figure A2 and A3 of the appendix.
- Polychromasia: It lack central pallor, red cells stain shades of blue-gray as a consequence of uptake of both eosin (by haemoglobin) and basic dyes (by residual ribosomal RNA). Often slightly larger than normal red cells and round in shape - round macrocytosis. This variation is seen in:Any situation with reticulocytosis - for example bleeding, haemolysis or response to haematinic factor replacement. also, it can occur in small cells such as microspherocytes (densely haemoglobinized) during immune haemolytic anaemia (splenic macrophages bite off portions of the membrane

with the bound antibody and the cell reseals with a smaller volume) or an abnormally shaped cell like irreversible sickled red cells, spherocytes and irregularly contracted cells (ICC) or pyknocytes. ICC lacks central pallor with irregularly (non- uniform) margins and is seen in haemoglobin SC, CC disease, oxidant injury and unstable haemoglobinopathy, in burns and less frequently micro angiopathy [6, 9] as shown in figure A24 of the appendix.

- Dimorphic Blood Picture is the two distinct populations of red cells. The populations may differ in size, shape or haemoglobin content. Found in: Anaemic patient after transfusion, Iron deficiency patient's taking supplements, Combined B12 / folate and iron deficiency, Sideroblastic anaemia [1, 13] as shown in figure A4 of the appendix.

(3) Poikilocytosis is the Variation in the shape of RBC is called poikilocytosis. RBCs exist as biconcave discs in large blood vessels but their shape changes to parachute like confirmation in capillaries. Following are some abnormal RBC shapes as shown in figure A11 of the appendix:

- Spherocytes: RBCs lacks the biconcave shape and becomes more spherical, no central pallor is present with increased hemoglobin content. Spherocytes are found in : hereditary spherocytosis, immune hemolytic anemia, Zieve's syndrome,
  Microangiopathic haemolytic anaemia and post transfusion reaction [17] as shown in figure A23 of the appendix.
- Ovalocytes: Oval shaped RBCs. Ovalocytes are found in: Thalassemia major, hereditary ovalocytosis, sickle cell anemia as shown in figure A13 of the appendix.
- Elliptocytes: The RBCs are ovaal or elliptical in shape, long axis is twice the short axis. Elliptocytes are found in: hereditary elliptocytosis, megaloblastic anemia, IDA, thalassemia, myelofibrosis as shown in figure A13 of the appendix.
- Target cells: Red cells have an area of increased staining which appears in the area of central pallor. Target cells are found in: obstructive liver disease, severe IDA, thalassemia, Hemoglobinopathies (S and C), post splenectomy as shown in figure A11, A15 and A18 of the appendix.
- Teardrop cells: RBCs having the shape like teardrop or pear. These are usually microcytic and often hypochromic. Teardrop cells are found in : myelofibrosis, megaloblastic anemia, IDA, thalassemia as shown in figure A11 and A28 of the appendix [2].
- Schistocytes: These are helmet or triangular shaped, fragmented or greatly distorted RBCs smaller than normal size. Schistocytes are seen in: Thalassemia, microangiopathic hemolytic anemia, mechanical hemolytic anemia, uremia, artificial heart valves, DIC as shown in figure A21 of the appendix.
- Acanthocytes: RBCs with irregularly spaced projections. Projections vary in width but usually contain a rounded end. Spherical cells with 2 - 20 spicules of unequal length and distributed unevenly over the red cell surface. Acanthocytes are found in: liver diseses, post splenectomy, anorexia nervosa and starvation, alcoholism, vitamin C deficiency, they are also present in an inherited disorder called a beta lipoproteineimia [34] as shown in figure A14 of the appendix.
- Stomatocytes: Red cells with a central linear slit or stoma. Seen as mouth shaped form in peripheral smear. Stomatocytes are found in: excess alcoholism, alcoholic liver disease, hereditary stomatocytosis, Hereditary spherocytosis as shown in figure A20 of the appendix.
- Keratocytes: These are half-moon shaped cells with two or more spicules. Keratocytosis is seen in G6PD deficiency, pulmonary embolism, disseminated intravascular coagulation.
- Burr cells: Red cells with uniformly spaced pointed projections on their surface. Burr cells are found in hemolytic anemia, uremia, megaloblastic anemia as shown in figure A15 of the appendix.
- Sickle cells: These are sickle-shaped Red Blood Cells. Sickle cells are seen in Hb-S disease/ sickle cell anemia[6] as shown in figure A19 of the appendix.
- Cigar Cells: Red cells shaped like a cigar or pencil. Found in: Iron deficiency as shown in figure A8 of the appendix
- Echinocytes: Red cells are covered with 10 - 30 short spicules of regular form. Found in: Uraemia, Severe burns, EDTA artifact, Liver disease as shown in figure A22 of the appendix
- Red cell agglutinate: These are irregular clumps of RBCs. These are found in cold agglutinations, warm autoimmune hemolysis as shown in figure A10 of the appendix.
- Rouleaux Formation: Stacks of RBCs resembling a stack of coins. These are found in hyperglobulinemia, hyperfibrinogenaemia [1, 13] as shown in figure A9 of the appendix.

(4) Presence of inclusion bodies: Red blood cells have different morphological variations depending upon following type of inclusion bodies:

- Howell-Jolly bodies: Small round cytoplasmic red cell inclusion with same staining characteristics as nuclei. These are fragments of DNA. Usually seen in post splenectomy, MBA, hemolytic anemia as shown in figure A27 of the appendix.
- Heinz bodies: These represent denatured hemoglobin (methemoglobin) within a cell. With a supravital stain like crystal violet, Heinz bodies appear as round blue precipitates. Seen in G6PD Deficiency, splenectomy [6].
- Haemoglobin H inclusions are seen in alpha-thalassemias giving rise to the characteristic ‘golf ball’ appearance of the erythrocytes. Red cells with bluish reticular fragments (ribosomal proteins and RNA) on supravital staining are reticulocytes.
- Reticulocytes appear as polychromatic cells on Rowmanosky stained slides. They are immature red cells newly released from the marrow sinusoids and takes

about a day or two to mature in the peripheral circulation in those with intact spleen [35] as shown in figure A29 of the appendix.

- Nucleated red cells are not normally seen in the periphery except in neonates. Their presence on blood film suggests a severe stress on the marrow forcing their premature release. Circulating nucleated red cells (erythroblasts) may be associated with increased circulating neutrophil precursors; in which case the term 'leucoerythroblastic' is used. Leucoerythroblastosis occurs in the setting of marrow fibrosis, marrow stressors as seen in hypoxia, severe anaemia (haemolytic or haemorrhagic) and severe sepsis, marrow infiltrations (due to leukaemia, lymphoma, myeloma or secondary metastasis), marrow challenge with growth factors such as G-CSF and extramedullary haemopoiesis. The circulating erythroblasts may be normoblasts (normal maturation) or megaloblasts (megaloblastic changes). [35, 36]
- Pappenheimer bodies or Siderotic granules or pappenheimer bodies appear purple on Rowmanosky stain, blue on Perl's stain and are seen in disorders of iron utilization like sideroblastic anaemias: These represent iron deposits which as dense blue, irregular granules in wright stain. Pappenheimer bodies are found in RBCs with hemolytic anemia, splenectomy, sideroblastic anemia, thalassemia [2].
- Basophilic stippling: These are considerable amount of small basophilic inclusions in red cells which represent precipitated RNA. Seen in: haemoglobinopathies thalassemia, sideroblastic anaemia, megaloblastic anaemia and a rare inherited condition, pyrimidine 5' nucleotidase deficiency, severe infections, hemolytic anemia, liver damage, heavy metal (lead or arsenic) poisoning [37] as shown in figure A25 of the appendix.
- Cabbot's ring: Reddish, purple, thread-like rings in RBCs of severe anemias. These are the remnants of nuclear membrane.
- Parasites of red cells: Protozoan parasites, delicate rings with 1 or 2 chromatin dots. Often more than one ring in a red cell like one of the four species of the malaria parasite may be seen in case of malarial infection [1, 4, 8, 13] as shown in figure A30 of the appendix.

However, morphology of Red blood cell can be used to classify anaemia based on the size of red blood cells. The size is reflected in the mean corpuscular volume (MCV), If the cells are smaller than normal (under 80 fl), the anemia is said to be microcytic; if they are normal size (80–100 fl), normocytic; and if they are larger than normal (over 100 fl), the anemia is classified as macrocytic. This scheme quickly exposes some of the most common causes of anemia; microcytic anemia is often the result of iron deficiency. In clinical workup, the MCV will be one of the first pieces of information available, so even among clinicians who consider the "kinetic" approach more useful philosophically, morphology will remain an important element of classification and diagnosis. Limitations of MCV include cases where the underlying cause is due to a combination of factors - such as iron deficiency (a cause of microcytosis) and vitamin B12 deficiency (a cause of macrocytosis) where the net result can be normocytic cells [9, 38, 39]

Morphology of White Blood Cells, Interpretations and Clinical Significant

As part of a blood smear evaluation, a manual WBC differential is performed. Typically, at least 100 WBCs are found, counted, and categorized according to type. The percentage of each type is calculated. Normally, about 2 to 5 leukocytes per high power field (HPF) can be seen. As a rule, a leucocyte/hpf approximates about 200 and 2000 cells in peripheral blood at x10 objective and x100 objective respectively. The field factor is calculated by dividing total leucocyte counts by the average number of leucocytes seen on ten fields [1]. Leucocytosis is suspected when WBC greater than 5 leucocytes/hpf and leucopenia less than 2 cells/hpf. The more the number of cells counted, the better the accuracy of the cell count estimates. In addition, the appearance (morphology) and stage of development of the WBCs are noted. White blood cells have a nucleus surrounded by cytoplasm. All WBCs are derived from bone marrow stem cells. In the bone marrow, they differentiate into two groups: granulocytic and lymphoid cells [10].

Neutrophils: Neutrophils has (10-18 μm) with normal range of (40–75%). They are cells that have cytoplasm with pink or purple granules. The half-life of mature neutrophils in circulation is about 7 hours. They irreversibly traverse the vascular endothelium into the tissues, where they die after 1 or 2 days. They compose the majority of WBCs in a healthy adult. They are involved in the defense against infections [2, 27].

- Drumstick: Drumstick shaped nuclear appendage. ± 1,5 μm in diameter and attached to the nucleus by a filament. Inactive X chromosome of the female. Found in: Neutrophils of females Males with Klinefelter syndrome as shown in figure A41 of the appendix
- Sessile Nodule: Inactive X chromosome found as nodule on neutrophils of females. Found in: Neutrophils of females as shown in figure A42 of the appendix
- Hypersegmentation or right shift of neutrophil nuclei: Average lobe count increased or increased % of neutrophils with 5 - 6 lobes or greater than 3% neutrophils with 5 lobes or more. Found in: Megaloblastic anaemia, Iron deficiency, Chronic infection, renal failure,Liver disease, Uraemia, Hereditary as shown in figure A31of the appendix
- Ring shaped nuclei: Nucleus ring or doughnut shaped Found in:Acute myeloid leukemia, Chronic granulocytic leukaemia, Megaloblastic anaemia, MDS as shown in figure A44 of the appendix
- Detached nuclear fragments: Detached nuclear material in cytoplasm. Found in: Dysgranulopoiesis,Patients on anti cancer chemotherapy, HIV as shown in figure A43 of the appendix
- MPO deficiency: Neutrophils appear normal on Romanowsky stain but are not counted as neutrophils by the cell counters employing a myeloperoxidase stain.

Found in: Inherited, Refractory anaemia, Blast crisis of CML as shown in figure A70 of the appendix

- Toxic Granulation: Increased granulation. Granulation more basophilic and larger than normal. Found in: Severe bacterial infection, Non specific finding - seen in tissue damage of various types, Normal pregnancy, herapy with cytokines. Toxic granulations are seen in the neutrophils cytoplasm due to compensatory increase in microbicidal granules [10] as shown in figure A33 of the appendix
- Hypogranulation: Reduced granulation in neutrophil cytoplasm. Found in: Myelodysplastic syndromes as shown in figure A35 and figure A37 of the appendix
- Vacuoles: Vacuoles in the cytoplasm of granulocytes Found in: Infection, Toxic effect of ethanol, Jordan's anomalyas shown in figure A40 and figure A71 of the appendix
- Döhle Bodies: Small pale blue cytoplasmic inclusions, often in the periphery of the cell. Found in: Infective and inflammatory states, Severe burns, Tuberculosis, Post chemotherapy, Pregnancy as shown in figure A38 of the appendix
- Phagocytosed Parasites: Malaria - Plasmodium falciparum Found in: Severe malaria infection as shown in figure A45 of the appendix
- Phagocytosed Organisms: DF2 organism. Rod shaped organism in vacuoles in cytoplasm of neutrophils Found in: Dog bite as shown in figure A73 of the appendix
- Phagocytosed Platelet: Platelet in vacuole in neutrophil cytoplasm Found in Infection as shown in figure A46 of the appendix
- Phagocytosed Red blood cell: Red cell in vacuole in cytoplasm of neutrophil Found in:Infection, Auto immune haemolytic anaemia, Incompatible blood transfusionas shown in figure A47 of the appendix
- Auer Rods: Small azurophil rods in the cytoplasm of myeloblasts and promyelocytes. Sometimes found in mature neutrophils Found in: Acute myeloblastic leukemia, Myelodysplastic syndromes as shown in figure A48 of the appendix
- Macro Neutrophils: Twice the size of a normal neutrophil with tetraploid DNA content. Found in:Occasionally in the blood of healthy subjects, Inherited, Administration of G-CSF, Megaloblastic anaemia,Chronic infection as shown in figure A49 of the appendix
- Necrobiotic / Apoptotic neutrophil: Dense homogenous nuclei (pyknotic) Found in: Occasionally in healthy subjects, In vitro artifact, AML as shown in figure A51 of the appendix
- Shift to the Left: Presence of precursor of granulocytes in the peripheral blood Found in: Normal in pregnancy or neonate, Infections, Bone marrow fibrosis, Bone marrow infiltration by malignancies. Severe neutrophilia with left shift is termed leukaemoid reaction [4, 14, 32] as shown in figure A32 of the appendix
- Pseudo Pelger Hüet Anomaly: Bilobed neutrophils with more condensed chromatin. Found in:Inherited Myelodysplastic syndromes, Idiopathic myelofibrosis, Chronic granulocytic leakaemia, Therapy with colchicine, ibuprofen Infectious mononucleosis, malaria, myxoedema, CLL as shown in figure A72 of the appendix
- Neutrophil aggregation: Small clumps of neutrophils. Happens in vitro if EDTA anticoagulated blood is allowed to stand. May lead to incorrect WBC Found in: In vitro finding, Infectious mononucleosis, Bacterial infections, Auto immune disease [1, 2, 4, 8, 10, 13] as shown in figure A39 of the appendix.

Eosinophils: (10-15 μm) are easily recognized in stained smears with their large, red-orange granules. It has life time of 8–12 days (circulate for 4–5 hours). Generally low in number $0.02–0.5\times10^9$/l (1–6%), they most often increase in number in individuals with allergies and parasitic infections [30]

- Eosinophilia: Increase in number of eosinophils in peripheral blood Found in: Parasitic infections, Allergic reactions, Drug hypersensitivity, Hodgkin's disease. However, marked eosinophilia (>1500/ml) suggest hypereosinophilic syndrome (especially with associated tissue damage) or a neoplastic entity especially when there is an associated cellular dysplasia as in chronic eosinophilic leukaemia as shown in figure A52 of the appendix
- Left shift Eosinophil: Eosinophil metamyelocyte in peripheral blood Found in: Reactive eosinophila, Myeloproliferative disorders, AML [2, 10] as shown in figure A53 of the appendix

Basophils: Basophils (12-15 μm) have large, black granules and are the least often seen type of WBC (1%). It has life time of a few hours to a few days. Basophils constitute about $0.02–0.1\times10^9$/l (< 1–2%) of circulating leukocytes [30]

- Basophilia: Increase in the number of basophils in the peripheral blood. Found in: Myeloproliferative disorders, Myxoedema, Ulcerative colitis, Hyperlipidaemia, hypersensitivity states and malignant conditions like lymphomas and chronic myeloid leukaemia [2, 30]as shown in figure A54 of the appendix

Lymphocytes: Small lymphocytes 7–8 μm and large lymphocytes 12–15 μm diameters. Lymphocyte has $1.0–3.0\times10^9$/l (20–40%) circulating leukocytes It has a small amount of cytoplasm and often a smooth, round nucleus. In the peripheral blood, approximately 15 to 25% of lymphocytes are B cells and 40 to 75% are T cells. It has life time of Years for memory cells, weeks for all else [30, 31].

- Atypical Lymphocytes: Pleomorphic. Large with diameter of 15 - 30 μm. Abundant, strongly basophilic cytoplasm. Basophilia may be confined to the cytoplasmic margins. Found in: Viral infections - EBV, CMV, Hep A, Measles , Bacterial infections - brucella, tuberculosis, Protozoa – malaria, Immunization, SLE as shown in figure A55 of the appendix
- Plasmacytoid Lymphocyte: Lymphocyte with basophilic cytoplasm and eccentric nucleus. Found in: Reactive phenomenon as shown in figure A57 of the appendix

- Mott cell: Plasmacytoid lymphocyte with globular inclusions composed of immunoglobulin. Found in: Reactive changes in peripheral blood as shown in figure A58 of the appendix
- Large Granular Lymphocyte: Small eosinophilic granules in the cytoplasm of large lymphocytes Found in: Natural killer cells, Lymphokine activated T cells [2, 10, 30] as shown in figure A59 of the appendix.

Monocytes: Monocytes are usually the largest of the WBCs (12-20 μm) and are often referred to as scavenger cells (phagocytes). It has life time of hours to days. They can ingest particles such as cellular debris, bacteria, or other insoluble particles.

- Monocyte Vacuolization: Vacuoles in the cytoplasm of monocytes Found in: Infections[10, 30] as shown in figure A60 of the appendix

Morphology of Platelets, Interpretations and Clinical Significant

It is expected that we see approximately 7– 15 platelets on x100 objective with 2-4 by 0.5 microns in dimension (which is about a third of a normal sized red cell) having coarse cytoplasmic granules. A platelet/hpf is equivalent to approximately 15,000- 20,000 platelets in circulation. Platelets circulate for 7 to 10 days; about one third are always transiently sequestered in the spleen. The platelet count is normally 140,000 to 440,000/μL [1]. However, the count can vary slightly according to menstrual cycle phase, decrease during near-term pregnancy (gestational thrombocytopenia), and increase in response to inflammatory cytokines (secondary, or reactive, thrombocytosis). Platelets are eventually destroyed by apoptosis, a process independent of the spleen [2] as shown in figure A 61 of the appendix.

- Platelet Satellitism: Platelets clumped around neutrophils. Found in: EDTA in vitro induced change of no clinical significance except false low platelet count (in vitro) as shown in figure A63 of the appendix.
- Giant Platelets: Platelet larger than a normal red cell. Found in: Increased platelet turnover, Myeloproliferative disorders, Myelodysplastic disorders as shown in figure A64 of the appendix
- Large Platelets: Large platelets - larger than one third but less than the size of a red cell. Found in: Increased turnover of platelets, Myeloproliferative disorders, Myelodysplastic disorders, May Hegglin anomaly, Grey platelet syndrome, Bernard Soulier as shown in figure A65 of the appendix
- Micro Clots: Fibrin strands, platelets and white cells (in this case - neutrophils) clumped together. Found in: In vitro artefact caused by poor venesection technique, Leads to false low counts - can influence white cell, red cell and platelet counts [6, 33] as shown in figure A66 of the appendix
- Platelet Clumping: Small clumps of platelets. Found in: In vitro artefact caused by EDTA or cold and leads to false low platelet count, difficult venesection as shown in figure A67 of the appendix
- Wiskott Aldrich Syndrome: Small platelets. Found in: Wiskott Aldrich syndrome as shown in figure A68 of the appendix
- Grey Platelet Syndrome: Platelets appear degranulated. Found in: Grey platelet syndrome, Discharge of platelet granules in vivo (cardiopulmonary bypass, hairy cell leukemia), Discharge of platelet granules in vitro (poor venesection technique), [8, 13, 14, 32] as shown in figure A69 of the appendix.

3. Laboratory Techniques for Complete Blood Cell and Differential White Cell Count Test

Leukocytes can be evaluated through several techniques both manually and automation of varying complexity and sophistication. Both quantitative and qualitative properties can be assessed in the laboratory.

A manual review of automated counts with peripheral blood film (PBF) should be performed when flagging occurs due to excess counts. Falsely elevated leucocyte count may be generated by the automated or manual counts due to circulating nucleated red cells. A PBF examination can be used to correct the error in white blood cell counts [37]. The correcting formula is given thus.

Corrected WBC=[estimated WBC/(100+Number of nucleated RBC among 100 WBC)] x 100%.

Peripheral blood film is often used as a follow-up test to abnormal results on a complete blood count (CBC) to evaluate the different types of blood cells [1]. It may be used to help diagnose and/or monitor numerous conditions that affect blood cell populations. Presence of abnormal white blood cells (WBCs), red blood cells (RBCs), and/or platelets can be identifying with peripheral blood film. Peripheral blood film is used to categorize and/or identify conditions that affect one or more type of blood cells and to monitor individuals undergoing treatment for these conditions [7, 11, 12]. Usually, only normal, mature or nearly mature cells are released into the bloodstream, but certain circumstances can induce the bone marrow to release immature and/or abnormal cells into the circulation. When a significant number or type of abnormal cells are present in the circulation, it can suggest a disease or condition and prompt a health practitioner to do further testing. The results of a blood smear typically include a description of the appearance of the red blood cells, white blood cells, and platelets as well as any abnormalities that may be seen on the slide [4, 39].

3.1. Manual Techniques

Manual technique uses specially designed chambers (Neubauer) to count white blood cells, however to determine the white blood cells differential, a drop of blood is thinly spread over a glass slide, air dried, and stained with a Romanosky stain, most commonly the Leishman, Wright or May-Grunewald-Giemsa technique. One hundred cells are then counted and classified in percentage. [11, 12]. Manual technique has ability and reliability to discover morphologic abnormalities. Manual technique can be used to look for

quantitative abnormalities in morphologically normal WBC population such as in the diagnosis of infectious or allergic diseases and for therapeutic monitoring of cytotoxic or myelotoxic drugs by calculating relative WBC from absolute WBC (This requires a high level of precision and accuracy). It can also used to look for morphologic abnormalities of white blood cells (when circulating abnormal white blood cell population such as immature or atypical cells is suspected for diagnostic or monitoring reasons; this requires a high level of clinical sensitivity) [39].

3.2. Principleand Procedure for Staining Thin Blood Film

Staining usually take place at a neutral pH. pH of blood is 7.4, when buffered at pH 6.8, it brings the pH to neutral pH i.e. pH 7.0. Unlike charges of stain and blood will attract, the basic part of stain methylene blue stained the acidic part of the cell i.e. the nucleus while the acidic part of stain eosin stained the basic part of the stain i.e. cytoplasm. Thin blood film was made on clean grease free glass slide and stained using Leishman staining technique; the procedure was described by Monica Cheesbrough, 2005. Thin blood film was made from well mixed EDTA anticoagulated blood; the film was allowed to air dry and flooded with Leishman stain for 3minutes. The slide was diluted with buffered distilled water and allowed to stain for 10minutes. Slide was rinsed with water; back of the slide was cleaned with damped cotton wool in methylated spirit. The slide was allowed to air dry and examined under microscope using X100 objective lens [40, 41, 42].

3.3. Automation Techniques (Electronic Blood Cell Counting) Its Principle and Procedure

Electronic blood cell counting is based upon the principle of impedance (resistance to current flow). Some hematology analyzers combine both impedance counting with light scattering to measure platelets. A small sample of well mixed EDTA blood is aspirated into a chamber (the WBC counting bath) and diluted with a balanced isotonic saline solution that is free of particles. The diluted blood sample is split into two parts, one for counting RBCs and platelets and the other for counting WBCs. The RBC portion is transferred to the RBC/platelet counting bath where it is diluted further. The other portion remains in the WBC bath and a detergent (lysing agent) is added to destroy (hemolyze) the red blood cells. A small portion of the diluted fluid in each bath is allowed to flow past a small aperture. An electrical current is produced in each aperture by two electrodes, one on the inside and the other on the outside of the aperture. The saline solution is responsible for conducting current between the electrodes [7, 43]. The cells move through the aperture one at a time, when a cell enters the aperture, it displaces a volume of electrolyte equal to its size. The cell acts as an electrical resistor, and impedes the flow of current. This produces a voltage pulse, the magnitude of which is proportional to the size of the cell. Instrument electronics are adjusted to discriminate voltage pulses produced by different cells, these adjustments are called thresholds. For example, the threshold for counting a RBC is equivalent to a cell volume of 36 femtoliters or higher. Voltage pulses that are equivalent to volumes of 2–20 femtoliters are counted as platelets. This process is repeated two more times so that the RBC, WBC, and platelet counts are performed in triplicate. Each time frame for counting is several seconds and many thousands of cells are counted. The computer processes the counting data first by determining the agreement between the three counts. If acceptable criteria are met, the counts are accepted and used to calculate the result. The hemoglobin concentration is measured optically using the solution in the WBC bath. The lysing agent contains potassium cyanide that reacts with the hemoglobin to form cyanmethemoglobin. The optical density of the cyanmethemoglobin is proportional to hemoglobin concentration. The voltage pulses produced by the white blood cells depend upon the size of the cell and its nuclear density. Therefore, the pulses may be analyzed to differentiate between the types of WBCs found. For example, lymphocytes are the smallest WBCs and comprise the lower end of the size scale [15, 44]. Monocytes, prolymphocytes, and immature granulocytes comprise the central area of the WBC histogram, and mature granulocytes comprise the upper end. In addition to cell sizing, automated instruments may use any of three other methods to distinguish between subpopulations. These are radio frequency conductance, forward and angular light scattering, and fluorescent staining [11, 12]. The automated differential blood count provides a high level of accuracy and precision (correct and consistent results) for quantification and identification of normal white blood cells; however, this method is not sensitive at identifying abnormal or immature cells and is not able to accurately identifying and classifying all types of white blood cells. To overcome this problem, most automated analyzers will flag samples with possible abnormal white blood cell populations, indicating the need for peripheral smear examination to be examined by trained personnel to identify abnormal cells [1, 38]

4. Conclusion

Complete blood cell count and peripheral blood film can be truly diagnostic for a disease condition; examination of blood smear morphology remains an indispensable tool to the hematology practice. It remains a frontline diagnostic in unraveling mysteries behind cryptic symptoms and signs in primary and secondary haemopathies. However, further laboratory test or more advanced investigations may be required to confirm the diagnosis.

Recommendation

Baseline parameters of complete blood cell count and peripheral blood film is necessary especially for patients to be placed on medication or chemotherapy, this will help in monitor their response to treatment.

Appendix

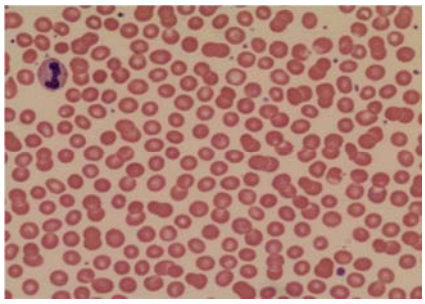

Figure A1. *NORMOCYTES.*

Comment: The picture shows normal erythrocytes seen at the correct part of the slide. Only a few erythrocytes overlap, but in all other cells there are distinct central halos

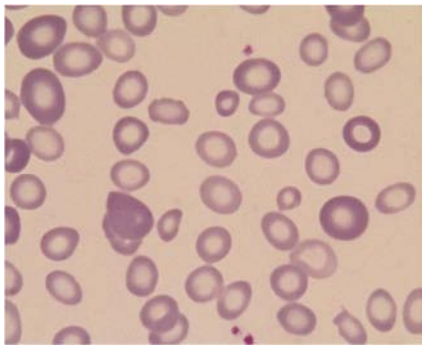

Figure A2. *HYPOCHROMIA.*

Definition: Excessive central pallor in the erythrocyte, exceeding one third of its diameter. It is due to insufficient hemoglobinization

Comment: Considerable hypochromia, only three cells are normocytes; moreover microcytosis and numerous ovalocytes are present. Found in: Iron deficiency, Thalassaemia and any of the conditions leading to microcytosis

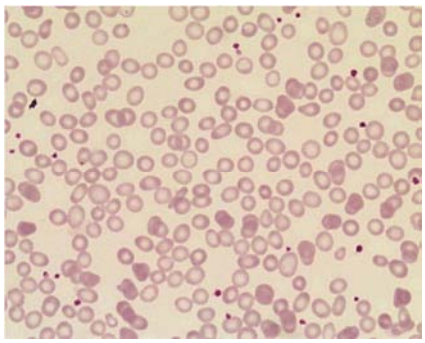

Figure A3. *HYPOCHROMIA.*

Definition: Excessive central pallor in the erythrocyte, exceeding one third of its diameter. It is due to insufficient hemoglobinization

Comment: Most cells show extremely large perinuclear halo (hypochromic cells), which account for more than one third of the cell diameter. Only a few cells are normocytes.

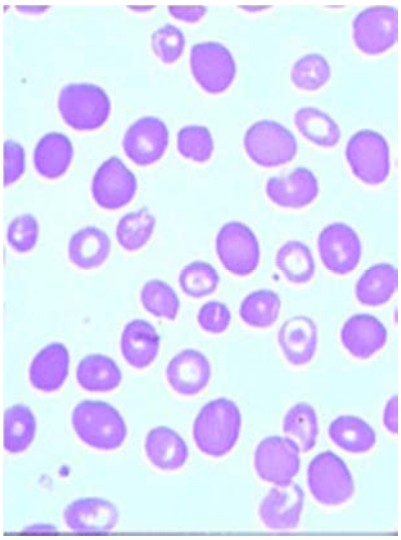

Figure A4. *MORPHIC BLOOD PICTURE.*

Morphology: Two distinct populations of red cells. The populations may differ in size, shape or haemoglobin content. Found in: Anaemic patient after transfusion Iron deficiency patient during therapy Combined B_{12} / folate and iron deficiency, Sideroblastic anaemia

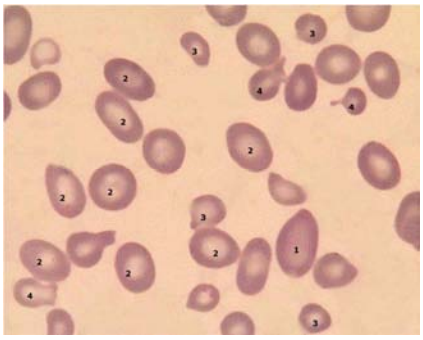

Figure A5. *ANISOCYTOSIS.*

Morphology: An increase in the variability of red cell size. Variation in erythrocyte size is now measured by the red cell distribution width (RDW). Alway take the RDW into acount when interpreting the mean corpuscular volume (MCV).

Comment: Distinct anisopoikilocytosis. One megalocyte and numerous macro- and microcytes are present. Most cells are ovalocytes, also schistocytes are visible.1. megalocyte, 2. macrocyte, 3. microcyte, 4. schistocyte

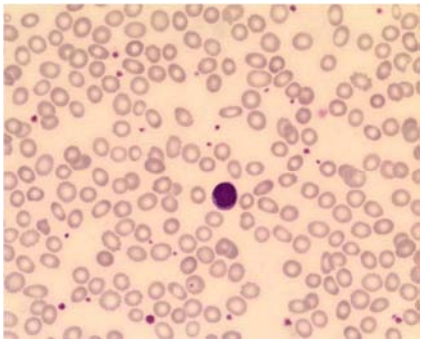

Figure A6. *MICROCYTES.*

Morphology: Decrease in the red cell size. Red cells are smaller than ± 7µm in diameter. The nucleus of a small lymphocyte (± 8,µm) is a useful guide to the size of a red cell. Found in:Iron deficiency anaemia Thalassaemia Sideroblastic anaemia Lead poisoning Anaemia of chronic disease.

Comment: In the picture the visible erythrocytes are microcytes and their diameters are much smaller than the diameters of the small lymphocyte (its diameter is 10-12 µm). The erythrocytes are hypochromic. Besides, normal platelets are present.

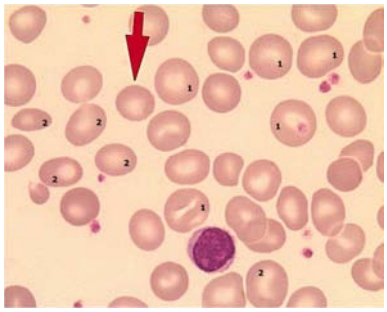

Figure A7. *MACROCYTES.*

Morphology: Increase in the size of a red cell. Red cells are larger than 9µm in diameter. May be round or oval in shape, the diagnostic significance being different. Found in: Folate and B12 deficiencies (oval), Ethanol (round), Liver disease (round), Reticulocytosis (round).

Comment: The arrow indicates normocyte. Most erythrocytes are macrocytes (compare with the lymphocyte). Five ovalocytes are seen 1. macrocyte, 2. Elliptocyte

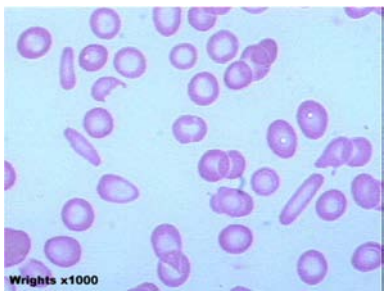

Figure A8. *CIGAR CELLS.*

Morphology: Red cells shaped like a cigar or pencil Found in: Iron deficiency

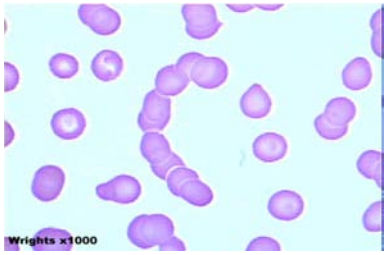

Figure A9. *ROULEAUX FORMATION.*

Morphology: Stacks of RBC's resemblinga stack of coins. Found in: Hyperfibrinogenaemia, Hyperglobulinaemia

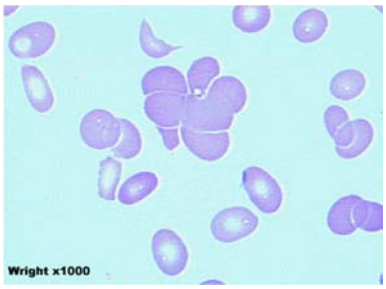

Figure A10. *RED CELL-AGGLUTINATION.*

Morphology: Irregular clumps of red cells Found in:Cold agglutinins Warm auto immune haemolysis.

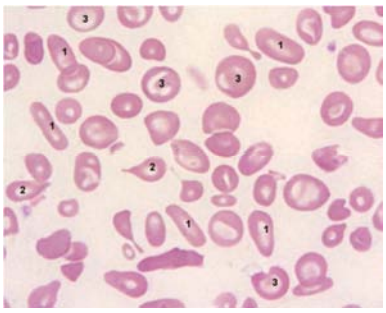

Figure A11. *POIKILOCYTES.*

Definition: Simultaneous occurrence of differently shaped of erythrocytes in blood.

Comment: Marked anisopoikilocytosis including ovalocytes, target cells and lacrymocytes. 1. ovalocyte, 2. lacrymocyte, 3. target cell

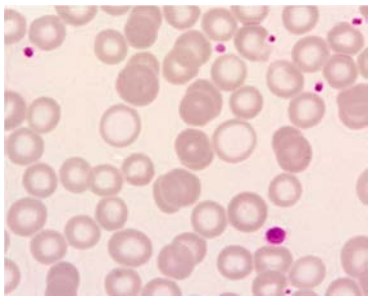

Figure A12. *LEPTOCYTES.*

Definition: Erythrocyte with excessive central pallor and very thin area of stained cytoplasm. The diameter of this cell is larger than the diameter of normocyte, but the volume is the same. **Comment:** Two leptocytes are visible in the field

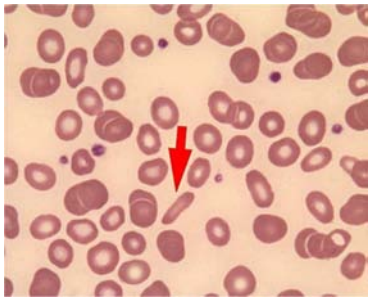

Figure A13. *ELLIPTOCYTES (OVALOCYTES).*

Definition: Oval or elliptical erythrocytes

Morphology: The red cells are oval or elliptical in shape. Long axis is twice the short axis. Found in: Hereditary elliptocytosis, Megaloblastic anaemia, Iron deficiency, Thalassaemia, Myelofibrosis

Comment: Indicated by the arrow extremely elongated ovalocyte is sometimes called pencil-like cell. Besides it other six ovalocytes less elongated are seen. Also distinct anisocytosis is present. Normal platelets are present.

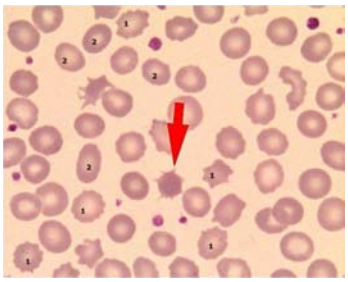

Figure A14. *ACANTHOCYTE.*

Definition: Erythrocytes with irregular, long, sharply pointed and bent spicules of cytoplasm. Presence of spicules of cytoplasm results in an absence of central pallor.

Morphology: Spherical cells with 2 - 20 spicules of unequal length and distributed unevenly over the red cell surface. Found in: Liver disease, Post splenectomy, Anorexia nervosa and starvation.

Comment: In the picture a single acanthocyte is seen. Besides it, separatedovalocytes and echinocytes. 1. burr-cell 2. Elliptocyte

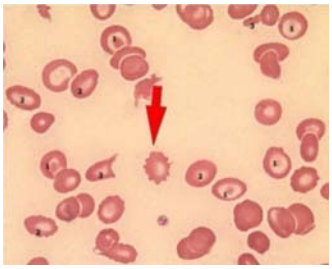

Figure A15. *BURR-CELLS(ECHINOCYTES).*

Definition: Erythrocytes with regular, short spicules of cytoplasm. The cells are usually biconcaved

Comment: The arrow indicates an echinocyte. Besides it, there are ovalocytes, target cells and schistocytes. Also slight anisocytosis. 1. target-cell, 2. elliptocyte, 3. schistocyte

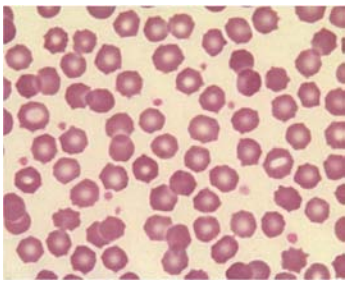

Figure A16. *CRENATED RED BLOOD CELLS.*

Definition: Erythrocytes with crimpsy cytoplasm. This is a typical artefact. They appear in vitro while making a blood film. Comment: All erythrocytes, that are shown in the picture, are crenated red blood cells with shrinked cell membrane.

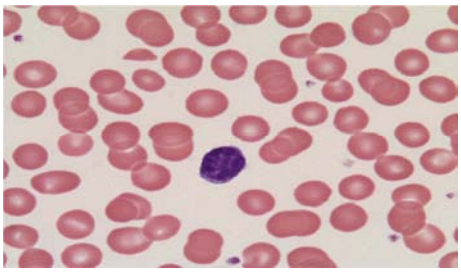

Figure A17. *LYMPHOCYTES.*

Comment: Typical small lymphocyte in blood. Also a single schistocyte

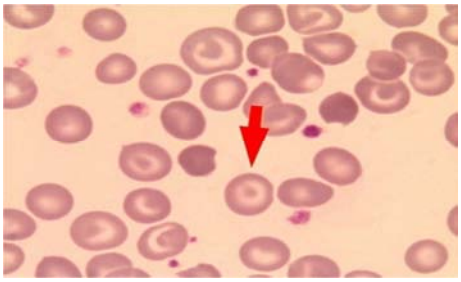

Figure A18. *TARGET CELLS.*

Definition: Erythrocyte containing dark stained central area **Morphology:** Red cells have an area of increased staining which appears in the area of central pallor. Found in: Obstructive liver disease, Severe iron deficiency, Thalassaemia, Haemoglobinopathies (S and C), Post splenectomy

Comment: In the picture seven target cells are present. Also slight anisocytosis of the erythrocytes and platelets. surrounded by lightly stained ring of cytoplasm without hemoglobin.

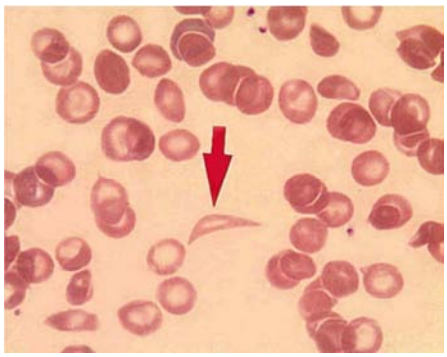

Figure A19. *SICKLE CELLS.*

Definition: Elongated erythrocytes, usually curved with sharply pointed one or two poles.

Morphology: Sickle shaped red cells. Found in: Hb-S diseaseComment: Single sickle cell. Also distinct anisopoikilocytosis and staining disturbance of erythrocytes.

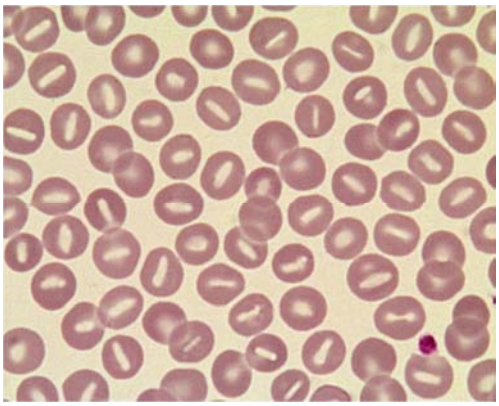

Figure A20. *STOMATOCYTES.*

Morphology: Red cells with a central linear slit or stoma. Seen as mouth-shaped form in peripheral smear. Found in: Alcohol excess, Alcoholic liver disease, Hereditary stomatocytosis, Hereditary spherocytosis

Definition: The erythrocyte with elongated central palor.

Comment: Very numerous stomatocytes in the course of inherited stomatocytosis

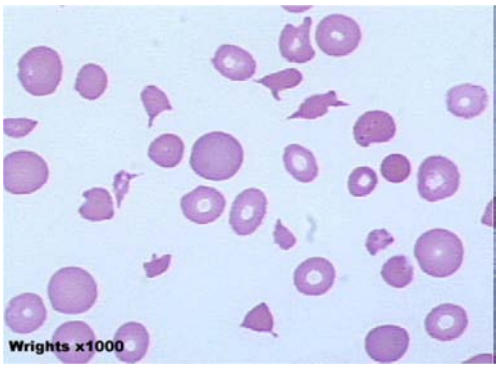

Figure A21. *SCHISTOCYTOSIS.*

Morphology: Fragmentation of the red cells. Found in: DIC, Micro angiopathic haemolytic anaemia, Mechanical haemolytic anaemaia

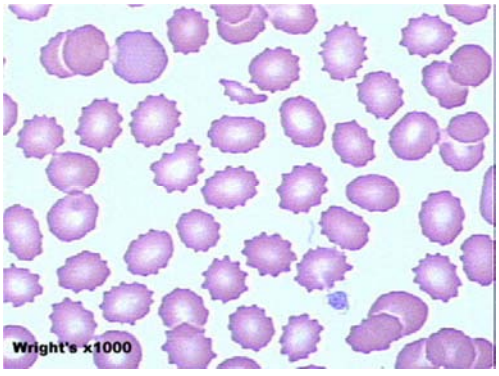

Figure A22. *ECHINOCYTES.*

Morphology: Red cells are covered with 10 - 30 short spicules of regular form. Found in: Uraemia, Severe burns, EDTA artifact, Liver disease

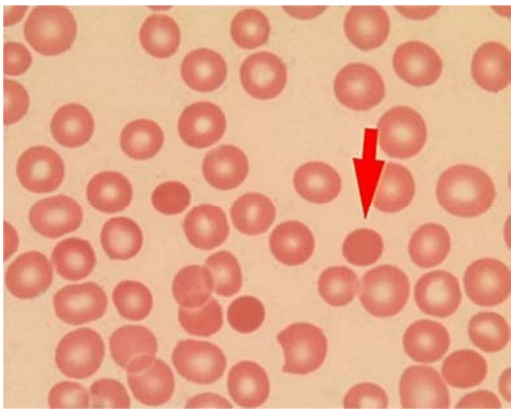

Figure A23. *SPHEROCYTES.*

Morphology: Red cells are more spherical. Lack the central area of pallor on a stained blood film. Found in: Hereditary spherocytosis Immune haemolytic anaemia Zieve's syndrome Microangiopathic haemolytic anaemia.

Definition: Spheroidal erythrocyte of lower diameter in comparison with normal red cell; without central pallor and more dark than normocyte.

Comment: Three spherocytes, one of them is indicated by the arrow. Also not much expressed anicytosis of the erythrocytes are shown

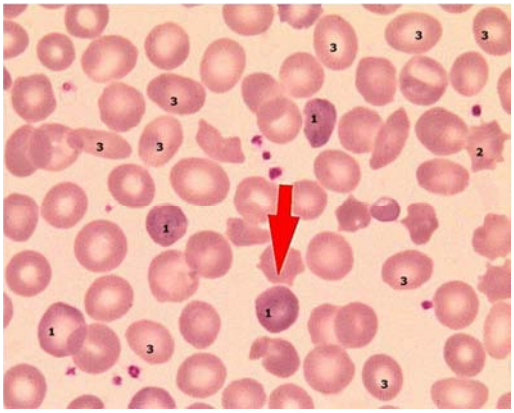

Figure A24. *POLYCHROMASIA.*

Definition: The red cell takes the basic and the acid dyes and exhibits violet tint, which results from the presence of ribonucleic acid in the cell. These cells are reticulocytes.

Morphology: Red cells stain shades of blue-gray as a consequence of uptake of both eosin (by haemoglobin) and basic dyes (by residual ribosomal RNA). Often slightly larger than normal red cells and round in shape - round macrocytosis. Found in: Any situation with reticulocytosis - for example bleeding, haemolysis or response to haematinic factor replacement

Comment: In the picture four cells are polychrpmatophilic cells (one is indicated by the arrow). Also a few ovalocytes, acanthocyte, and normal platelets are seen. 1. polychromatic erythrocyte 2. acanthocyte 3. elliptocyte

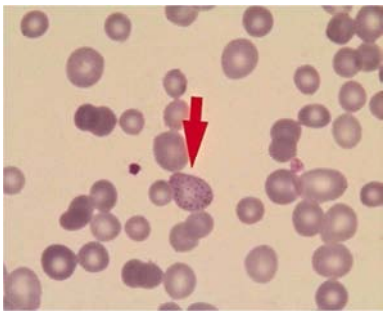

Figure A25. *BASOPHILIC STIPPLING.*

Definition: Very fine, pinpoint cytoplasmic granules distributed evenly in the cytoplasm.

Comment: The cell with basophilic stippling. Also erythrocytes anisocytosis

Morphology: Considerable numbers of small basophilic inclusions in red cells. Found in: Thalassaemia Megaloblastic anaemia Haemolytic anaemia Liver disease Heavy metal poisoning.

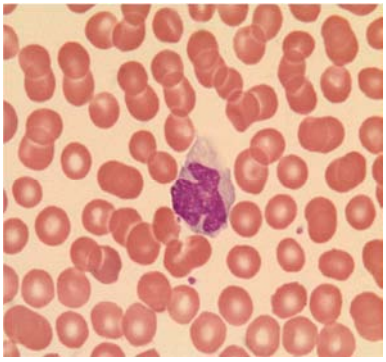

Figure A26. *MONOCYTES.*

Comment: Typical monocyte with abundant purple-blue cytoplasm containing small vacuoles.

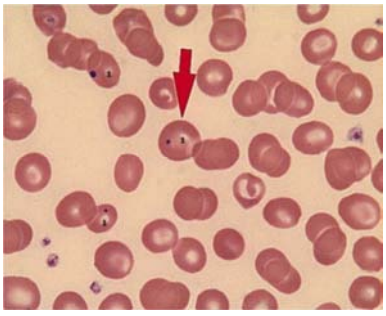

Figure A27. *HOWELL-JOLLYBODIES.*

Definition: Round chromatin fragments remaining in the cytoplasm of mature erythrocyte, resulting from abnormal division of erythroblast.

Morphology: Small round cytoplasmic red cell inclusion with same staining characteristics as nucleus. Found in:Haemolytic anaemias, Post splenectomy, Megaloblastic anaemia

Comment: In the picture three cells with Howell-Jolly bodies are shown. One of them is indicated by the arrow. 1. Howell-Jolly body

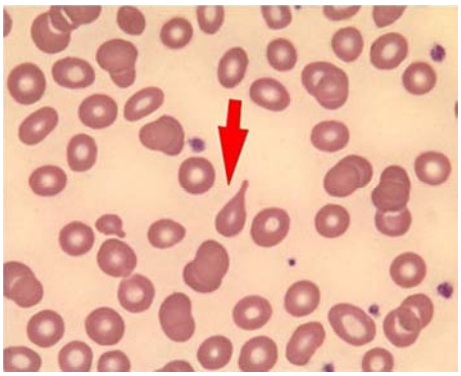

Figure A28. *LACRYMOCYTES.*

Definition: Erythrocyte with a tear-drop shape. The central pallor shall be seen (the cells are different from pseudolacrymocytes, which have pinched cytoplasm on one of the poles. These cells are observed excessively at the thin parts of the blood film).

Morphology: Red cells shaped like a tear drop or pear Found in:Bone marrow fibrosis, Megaloblastic anaemia, Iron deficiency, Thalassaemia

Comment: The arrow points a single lacrymocyte. Also numerous ovalocytes and normal plateles are present**.**

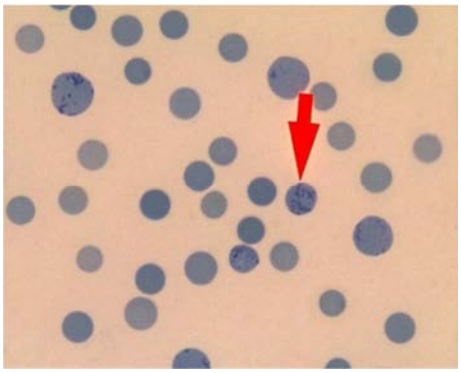

Figure A29. *RETICULOCYTES.*

Comment: The indicated reticulocyte contains fine granules (remnants of the rybonucleic, substances). In the picture six reticulocytes are present**.**

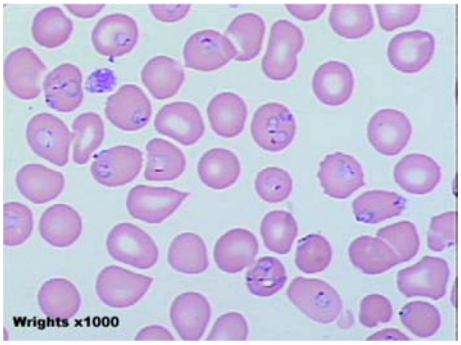

Figure A30. *MALARIA PARASITIES PLASMODIUM FALCIPARUM.*

Morphology: Ring form of Pl falciparum in red cells. Delicate rings with 1 or 2 chromatin dots. Often more than one ring in a red cell. Accolé forms are found. Found in: Malaria

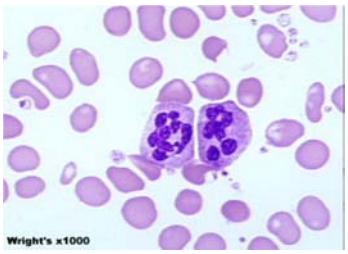

Figure A31. *HYPERSEGMENTATION OR RIGHT SHIFT OF NEUTROPHIL NUCLEI.*

Morphology: Average lobe count increased OR increased % of neutrophils with 5 - 6 lobes OR > 3% neutrophils with 5 lobes or more. Found in: Megaloblastic anaemia Iron deficiency Chronic infection Liver disease Uraemia Hereditary

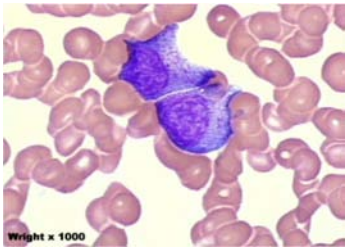

Figure A32. *NEUTROPHIL WITH SHIFT TO THE LEFT.*

Morphology: Presence of precursor of granulocytes in the peripheral blood Found in: Normal in pregnancy or neonate Infections Bone marrow fibrosis Bone marrow infiltration by malignancies

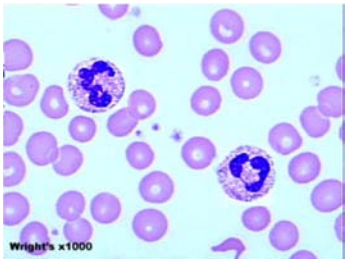

Figure A33. *NEUTROPHIL WITH TOXIC GRANULATION.*

Morphology: Increased granulation. Granulation more basophilic and larger than normal. Found in: Severe bacterial infection Non specific finding - seen in tissue damage of various types. Normal pregnancy Therapy with cytokines

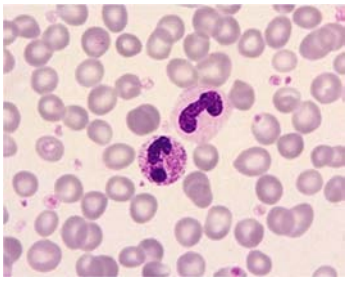

Figure A34. *GRANULATION HETEROGENEITY.*

Comment: The heterogeneity of granulation in two neutrophils. One (on the left side) shows toxic granulation. The other is nearly agranular. There are slight disturbances in platelets' granulation.

Occurrence in blood: normally not present

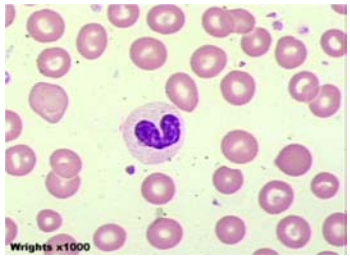

Figure A35. *NEUTROPHIL WITH HYPOGRANULATION.*

Morphology: Reduced granulation in neutrophil cytoplasm. Found in: Myelodysplastic syndromes

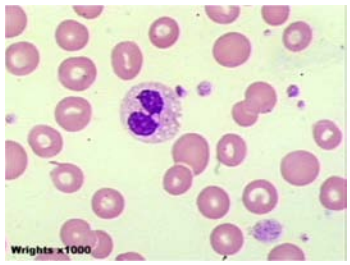

Figure A36. *PSEUDO PELGER HÜET ANOMALY.*

Morphology: Bilobed neutrophils with more condensed chromatin. Found in: Inherited Myelodysplastic syndromes Idiopathic myelofibrosis Chronic granulocytic leakaemia Therapy with colchicine, ibuprofen Infectious mononucleosis, malaria, myxoedema CLL

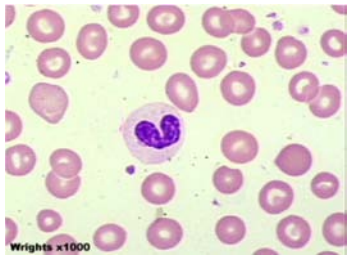

Figure A37. *NEUTROPHIL WITH HYPOGRANULATION.*

Morphology: Reduced granulation in neutrophil cytoplasm. Found in: Myelodysplastic syndromes

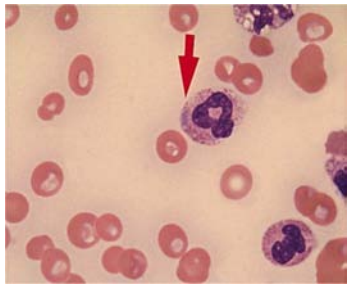

Figure A38. *NEUTROPHIL WITH DÖHLE BODIES.*

Morphology: Small pale blue cytoplasmic inclusions,

often in the periphery of the cell. Found in: Infective and inflammatory states Severe burns Tuberculosis Post chemotherapy Pregnancy

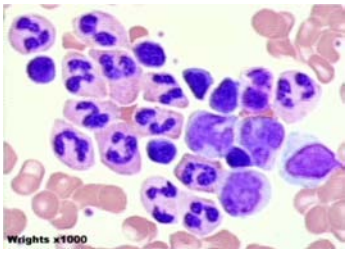

Figure A39. *NEUTROPHIL AGGREGATION.*

Morphology: Small clumps of neutrophils. Happens in vitro if EDTA anticoagulated blood is allowed to stand. May lead to incorrect WBC Found in: In vitro finding Infectious mononucleosis Bacterial infections Auto immune disease

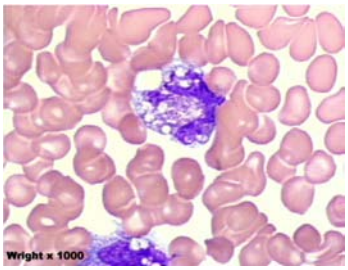

Figure A40. *NEUTROPHIL WITH VACUOLATION.*

Morphology: Vacuoles in the cytoplasm of granulocytes Found in: Infection Toxic effect of ethanol Jordan's anomaly

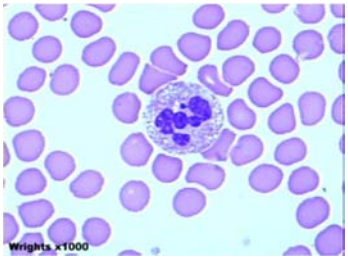

Figure A41. *DRUMSTICK.*

Morphology: Drumstick shaped nuclear appendage. ± 1,5 µm in diameter and attached to the nucleus by a filament. Inactive X chromosome of the female. Found in: Neutrophils of females Males with Klinefelter syndrome

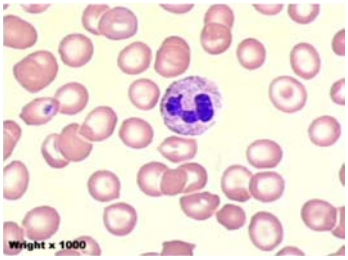

Figure A42. *SESSILE NODULE.*

Morphology: Inactive X chromosome found as nodule on neutrophils of females. Found in: Neutrophils of females

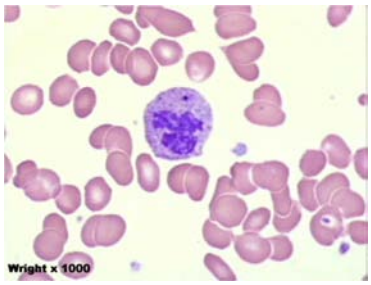

Figure A43. *NEUTROPHIL WITH DETACHED NUCLEAR FRAGMENTS.*

Morphology: Detached nuclear material in cytoplasm. Found in: Dysgranulopoiesis Patients on anti cancer chemotherapy HIV

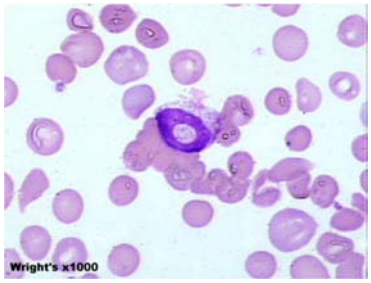

Figure A44. *NEUTROPHIL WITH RING SHAPED NUCLEI.*

Morphology: Nucleus ring or doughnut shaped Found in: Acute myeloid leukemia Chronic granulocyticleukaemia Megaloblastic anaemia MDS

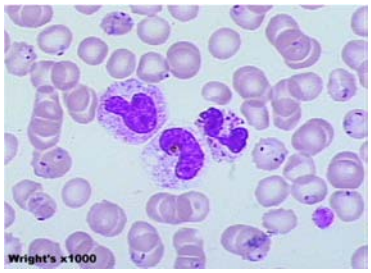

Figure A45. *NEUTROPHIL WITH PHAGOCYTOSED PARASITES.*

Morphology: Malaria - Plasmodium falciparum Found in: Severe malaria infection

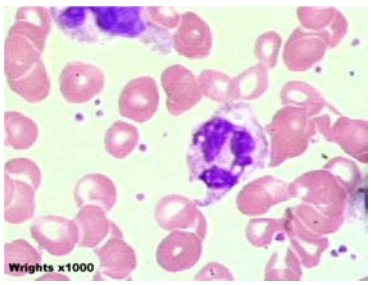

Figure A46. *NEUTROPHIL WITH PHAGOCYTOSED PLATELET.*

Morphology: Platelet in vacuole in neutrophil cytoplasm Found in Infection

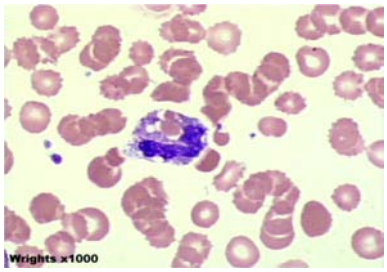

Figure A47. *PHAGOCYTOSED RED BLOOD CELL.*

Morphology: Red cell in vacuole in cytoplasm of neutrophil Found in: Infection Auto immune haemolytic anaemia Incompatible blood transfusion

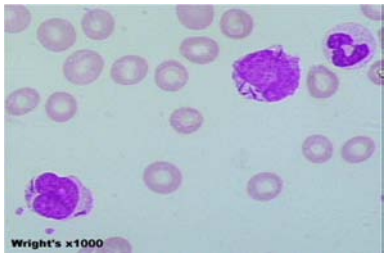

Figure A48. *NEUTROPHIL WITH AUER RODS.*

Morphology: Small azurophil rods in the cytoplasm of myeloblasts and promyelocytes. Sometimes found in mature neutrophils Found in: Acute myeloblastic leukemia Myelodysplastic syndromes

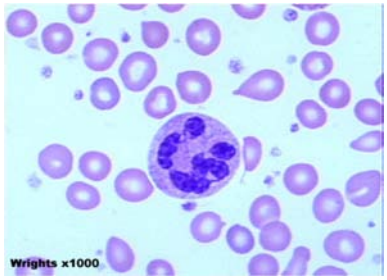

Figure A49. *MACRO NEUTROPHILS.*

Morphology: Twice the size of a normal neutrophil with tetraploid DNA content. Found in: Occasionally in the blood of healthy subjects Inherited Administration of G-CSF Megaloblastic anaemia Chronic infection

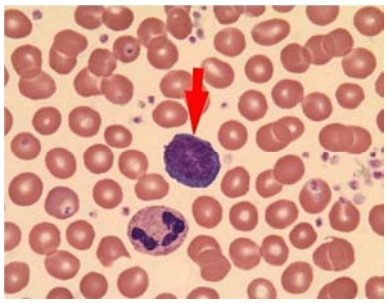

Figure A50. *LYMPHOPLASMOCYTES OR REACTIVE LYMPHOCYTE.*

Comment: Lymphoplasmocyte often has irregular shape of the nucleus, dark marbled chromatin and very strong basophilic staining of the cytoplasm. Platelets are normal.

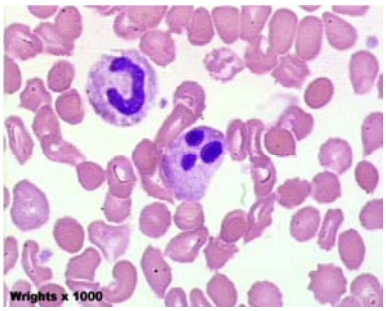

Figure A51. *NECROBIOTIC / APOPTOTIC NEUTROPHIL.*

Morphology: Dense homogenous nuclei (pyknotic) Found in: Occasionally in healthy subjects In vitro artifact AML

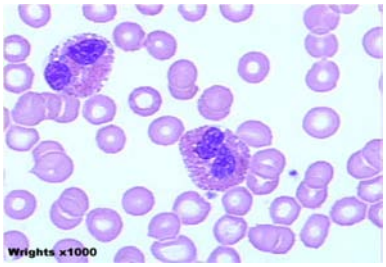

Figure A52. *EOSINOPHILIA.*

Morphology: Increase in number of eosinophils in peripheral blood Found in: Parasitic infections Allergic reactions Drug hypersensitivity Hodgkin's disease

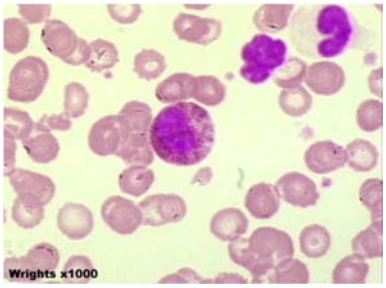

Figure A53. *LEFT SHIFT: EOSINOPHIL.*

Morphology: Eosinophil metamyelocyte in peripheral blood Found in: Reactive eosinophila Myeloproliferative disorders AM L

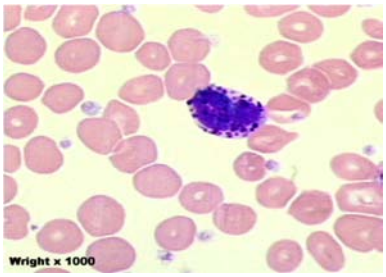

Figure A54. *BASOPHILIA.*

Morphology Increase in the neumber of basophils in the peripheral blood. Found in: Myeloproliferative disorders

Myxoedema Ulcerative colitis Hyperlipidaemia

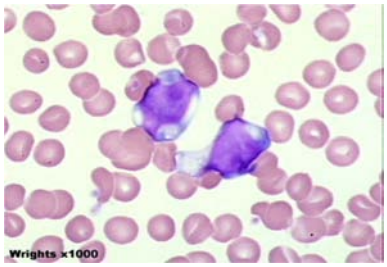

Figure A55. *ATYPICAL LYMPHOCYTES.*

Morphology: Pleomorphic. Large with diameter of 15 - 30 µm. Abundant, strongly basophilic cytoplasm. Basophilia may be confined to the cytoplasmic margins. Found in: Viral infections - EBV, CMV, Hep A, Measles Bacterial infections - brucella, tuberculosis Protozoa – malaria Immunization SLE

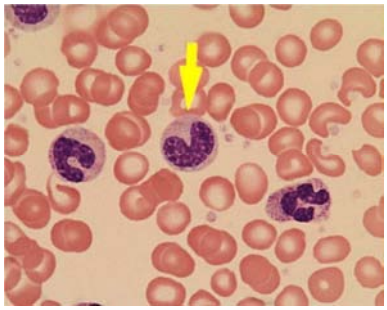

Figure A56. *NEUTROPHIL METAMYELOCYTES.*

Comment: Neutrophil metamyelocyte indicated by the arrow is present in blood. Besides, neutrophil segmented and band-forms leucocytes are seen. Platelets not rich in granules.

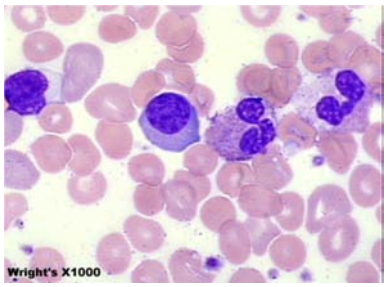

Figure A57. *PLASMACYTOID LYMPHOCYTE.*

Morphology: Lymphocyte with basophilic cytoplasm and eccentric nucleus. Found in: Reactive phenomenon

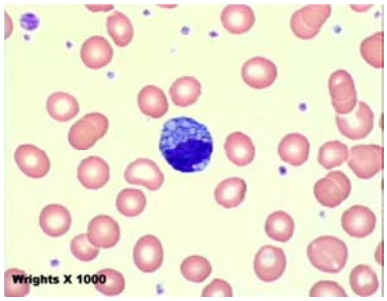

Figure A58. *MOTT CELL.*

Morphology: Plasmacytoid lymphocyte with globular inclusions composed of immunoglobulin. Found in: Reactive changes in peripheral blood

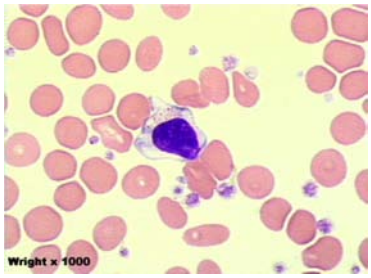

Figure A59. *LARGE GRANULAR LYMPHOCYTE.*

Morphology: Small eosinophilic granules in the cytoplasm of large lymphocytes Found in: Natural killer cells Lymphokine activated T cells

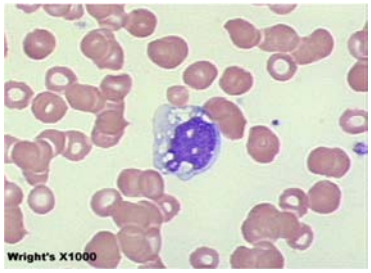

Figure A60. *MONOCYTE VACUOLIZATION.*

Morphology: Vacuoles in the cytoplasm of monocytes Found in: Infections

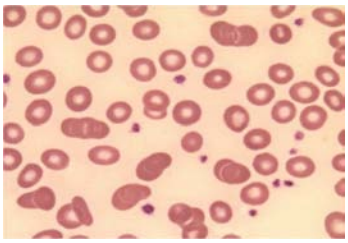

Figure A61. *PLATELETS.*

Comment: Normal platelets with correct level of granulation. Size of the cell: 1 - 4 mm Shape of the cell: round or oval, with irregularly jagged marginColour of cytoplasm: blue Granularity: fine, violet granules filling central area of platelet. Thin margin without granules on the periphery of the cell. Decrease or disappearance of granules in platelets is a morphological anomalyNucleus: not present

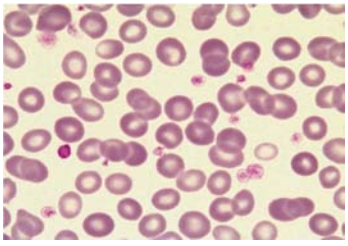

Figure A62. *PLATELETS ANISOCYTOSIS.*

Definition: simultaneously occurrence of platelets of different size, including giant forms in blood

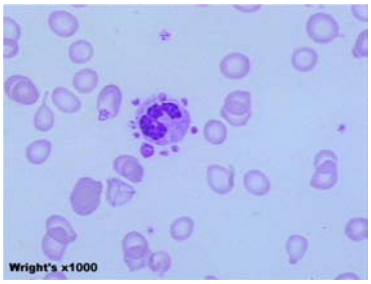

Figure A63. *PLATELET SATELLITISM.*

Morphology: Platelets clumped around neutrophils. Found in: EDTA in vitro induced change of no clinical significance except false low platelet count (in vitro).

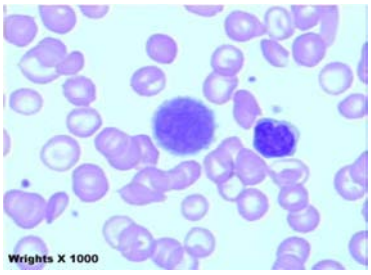

Figure A64. *GIANT PLATELETS.*

Morphology: Platelet larger than a normal red cell. Found in: Increased platelet turnover Myeloproliferative disorders Myelodysplastic disorders

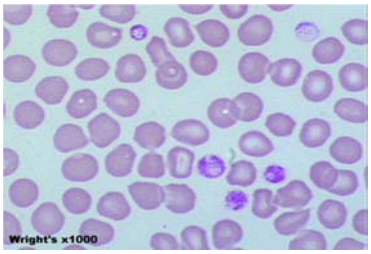

Figure A65. *LARGE PLATELETS.*

Morphology: Large platelets - larger than one third but less than the size of a red cell. Found in: Increased turnover of platelets Myeloproliferative disorders Myelodysplastic disorders May Hegglin anomaly Grey platelet syndrome Bernard Soulier

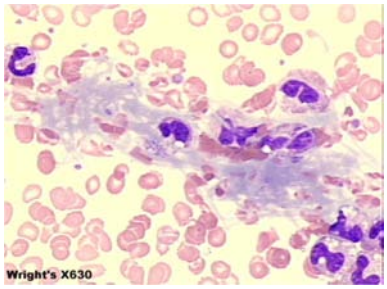

Figure A66. *MICRO CLOTS.*

Morphology: Fibrin strands, platelets and white cells (in this case - neutrophils) clumped together. Found in: In vitro artefact caused by poor venesection technique Leads to false low counts - can influence white cell, red cell and platelet counts

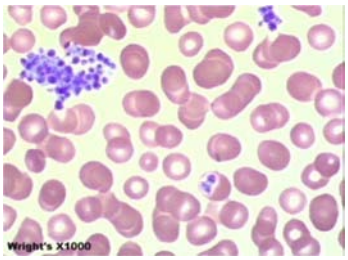

Figure A67. *PLATELET CLUMPING.*

Morphology: Small clumps of platelets. Found in: In vitro artefact caused by EDTA or cold and leads to false low platelet count Difficult venesection

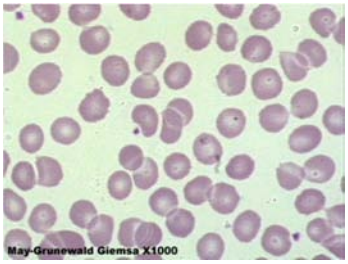

Figure A68. *WISKOTT ALDRICH SYNDROME.*

Morphology: Small platelets. Found in:Wiskott Aldrich syndrome

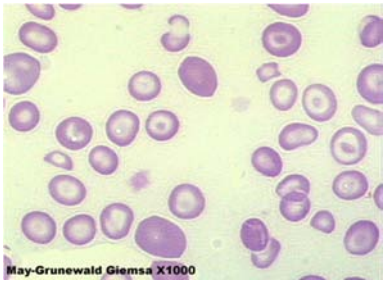

Figure A69. *GREY PLATELET SYNDROME.*

Morphology: Platelets appear degranulated. Found in: Grey platelet syndrome Discharge of platelet granules in vivo (cardiopulmonary bypass, hairy cell leukemia) Discharge of platelet granules in vitro (poor venesection technique)

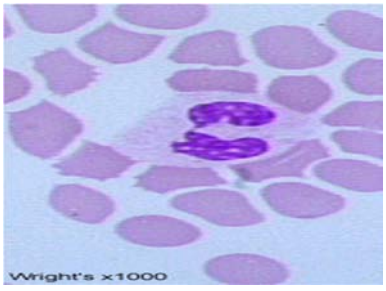

Figure A70. *MPO DEFICIENCY.*

Morphology: Neutrophils appear normal on Romanowsky stain but are not counted as neutrophils by the cell counters employing a myeloperoxidase stain. Found in: Inherited Refractory anaemia Blast crisis of CML

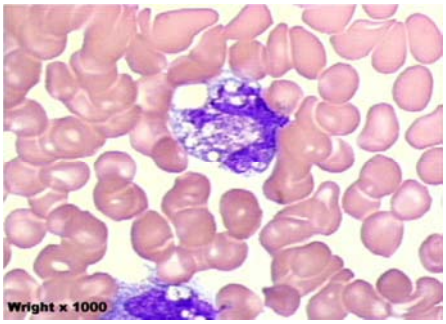

Figure A71. *VACUOLES.*

Morphology: Vacuoles in the cytoplasm of granulocytes. Found in: Infection Toxic effect of ethanol Jordan's anomaly.

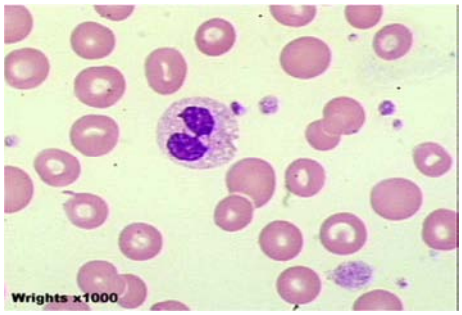

Figure A72. *PSEUDO PELGER HÜET ANOMALY.*

Morphology: Bilobed neutrophils with more condensed chromatin. Found in: Inherited Myelodysplastic syndromesIdiopathic myelofibrosis Chronic granulocytic leakaemiaTherapy with colchicine, ibuprofen Infectious mononucleosis, malaria, myxoedema CLL

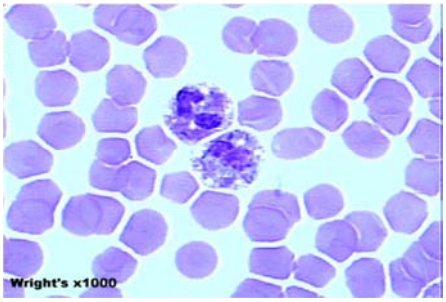

Figure A73. *PHAGOCYTOSED ORGANISMS.*

Morphology: DF2 organism. Rod shaped organism in vacuoles in cytoplasm of neutrophils Found in: Dog bite

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