Peripheral Blood Smear Examination: An Overview

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Abstract

A blood smear, which is also referred to as a peripheral smear for Blood cell morphology, is an important test for evaluation of blood-related problems, which are present in red blood cells, white blood cells, or platelets. The peripheral blood film (PBF) is a laboratory test that involves cytology of peripheral blood cells which is smeared on a glass slide. Very basic test but importance in investigation of various clinical diseases is invaluable. It has a wide range of uses, including distinguishing viral infections from bacterial infections, evaluating anemia, looking for causes of jaundice, and even diagnosing malaria. In addition to information about the different types of blood cells, a blood smear (especially when combined with a reticulocyte count) can often be a good measure of how well the bone marrow is functioning. This article highlights the basic technique and science behind the PBF. It expounds its laboratory applications, clinical indications and interpretations in the light of various clinical diseases. Despite advances in haematology automation, unlike other automated tests (such as a CBC), a technician or healthcare provider looks at a blood smear under the microscope in order to detect a wide range of changes that give clues to underlying diseases. For diagnosis of any pathology, there must be the triad of clinical history, physical examination and laboratory investigations. Approximately 70% of clinical diagnosis and treatment decisions are assisted by laboratory medicine.

Keywords: Blood cell morphology, Peripheral blood smear, Purpose of test, Preparation, Examination, Interpretation, Reporting.

INTRODUCTION

In patient care, for diagnosis of any pathology, there must be the triad of clinical history, physical examination and laboratory investigations. Approximately 70% of clinical diagnosis and treatment decisions are assisted by laboratory medicine.¹ Peripheral blood film (PBF) is a basic and a highly informative haematological tool at the clinician's disposal in screening, diagnosis and monitoring of disease progression and therapeutic response. An adept understanding of peripheral blood interpretation is important for a successful clinical practice.

The diagnostic importance of a peripheral blood smear (PBS) is invaluable. A simple easy to do investigation can give invaluable information's of the various diseases. The PBF exposes the morphology of peripheral blood cells, which maintains its place in the morphologic diagnosis of various blood related diseases. Its diagnostic relevance has not been lessened by advances in haematology automation and molecular techniques.

This article attempts to compile the preparation and reporting of peripheral blood film, its clinical interpretations and the common peripheral blood diagnosis. This will amplify the understanding of PBF interpretations.

PURPOSE OF TEST

Peripheral blood examination is requested by clinicians. The laboratory may initiate peripheral blood film based on abnormal findings from an automated count or patient's clinical information whose diagnosis may be supported by a peripheral blood film. A blood smear involves looking at a sample of blood under the microscope after applying special stains and looking for abnormalities or changes in red blood cells, white blood cells, and platelets. Reasons for evaluation of peripheral blood smear which include: To further evaluate abnormalities found on a complete blood count (CBC) such as a high or low red blood cell count, white blood cell count, or platelet count. To evaluate an infection (identifying the types of white blood cells present can help determine if an infection is viral, bacterial, or parasitic, as well as the severity). To look for causes of unexplained jaundice. As part of a work-up for people who have unexplained weight loss (defined as a loss of 5 percent of body weight over a 6-month period without trying). To evaluate symptoms of light-headedness and palor (paleness). To look for causes of petechiae, bruising, or excess bleeding. A low platelet count, to determine if the cause is increased degradation or decreased production (based on the size). To investigate findings suspicious for blood-related cancers. To look for malaria. To confirm sickle cell disease. To evaluate symptoms of bone pain. To look for causes of enlargement of the spleen, liver, or lymph nodes.2

A blood smear examined for the numbers and characteristics of the three types of blood cells: •Red blood cells (RBCs) are the cells that transport oxygen to the tissues •White blood cells (WBCs) are cells that fight infection among several other functions •Platelets are cell fragments that play an important role in blood clotting.

Findings that are noted are as •the number of the type of blood cells. •With white blood cells, the number and proportion of the different subtypes of white blood cells, including lymphocytes, neutrophils, basophils, eosinophil's, and monocytes. •The relative size of the cells, as well as a variation in size. •The shape of the blood cells. •Other characteristics such as

inclusions in the blood cells, clumping of cells, or cell fragments other than platelets. •Other findings in the blood such as the presence of malaria parasites

PREPARATION OF A PERIPHERAL BLOOD FILM SLIDE

For accurate and reliable results, pre-analytical variables are important because they can affect the quality of film. Which include patient preparation and consent, blood sampling technique, transport to the laboratory and sample preservation. Commonly, blood is obtained from peripheral veins and stored in anticoagulant bottle. Blood to anticoagulant ratio should be in the right proportion. Rarely, capillary blood may be obtained by finger-prick. Care should be taken to ensure minimal tissue damage because excess tissue fluid affects the distribution of the cellular components of blood. Ethylene diamine tetra-acetic Acid (EDTA) is the anticoagulant of choice for peripheral blood film preparation. Samples should be sent to the laboratory as soon as possible. Samples are best analysed within 2 hours of blood collection. Delay in preparation of blood smear may allow for the degeneration of the cellular elements of blood and may result in a pseudo-thrombocytopenia (falsely reduced platelet count) due to formation of platelet aggregates.³ Slide preparation is done by trained personnel preferably a medical laboratory technologist, who can ensure quality slides for microscopy. Laboratory assistants can also be trained in the art of slide preparation.

One require slides, pipette/capillary tube and blood spreader to make PBF smear. The 'push' (wedge) or cover-slip method is used.4, 5 The former is more commonly used. In the wedge method, a drop of well mixed blood (minimum of 10 gentle inversions) is placed on the base of a slide close to one end (about 1 cm from the edge) with a pipette/capillary tube. A spreader slide with chipped edges is placed on the base slide in front of the blood and moved backwards to touch the drop of blood which makes the blood spread along the base slide-width. The spreader slide should have a smooth end to prevent the tail end of the smear from being irregular. Then, a smear is made with the spreader inclined at an angle of about 30 to 45 degrees to the blood.₆ Care should be taken not to apply excessive pressure on the spreader slide when smearing. This can lead to slide breaks and laboratory accidents. Smear artifacts may be caused by dirty slides, fat droplets or poor quality slides. Laboratory safety precautions should be observed when working on any clinical specimen. Every blood specimen should be treated as potentially high risk. Though stains commonly used are intercalating agents that destroy microbes, they do not offer protection against HIV and HBV. The smear should cover twothirds of the base slide length and should have an oval feathered end. As a rule, the faster and steeper the smear, the thicker it is.7 For instance, steeper and faster smear may be adapted for anaemic samples. The smear is properly air dried. Avoid high humidity (causes inadequate drying) when making a smear as it commonly accounts for the artefactual sharp refractile border demarcating the area of central pallor, thus making hypochromia difficult to assess. Then proceed to label the slide with pencil or crayon on the frosted end of the slide or the head end. The dried smear is fixed with absolute methanol or ethyl alcohol and stained with a Rowmanosky stain. A properly air dried smear should be fixed within 4 hours of preparation but preferably within one hour. Good fixation requires about 10 to 20 minutes. Improper fixation causes artefactual burr cells (crenated red cells with refractile borders).

Romanosky stains are mixtures of acidic dye and basic dyes that give a differential staining of the different cellular components.⁸ Commonly used stain in our environment is Leishman stain which is composed of polychrome methylene blue (basic component) and eosin (acidic component). May-Grunwald Giemsa or Wright-Giemsa stain can also be used.⁸ The intensity of the staining varies with the duration of stain contact time and concentration of the stain. It is important to determine the adequate contact time with each new batch of stain made or procured.

The smear is floored with stain for about 5-10 minutes, then double diluted with buffered water and allowed for another 5–10 minutes for the cells to pick the stain. After this, the slide is properly rinsed under running water. Attempts should be made to wipe the underside of the slide with cotton wool to remove excess stain. Finally, the slide is placed on a rack with the feathered end sloping upwards to dry. Stain artifact such as debris and precipitates may be caused by over-staining (excess stain contact time) and inadequate washing under running water. Occasionally, large cells such as monocytes may be pushed to the periphery and feathery end of the film and this should be noted when interpreting the film. Infrequently, smears are made from buffy layer (white area between the plasma and red cell layer, rich in white cells and platelets) after heavy spin centrifugation especially in neutropenic specimens.

Slide preparation can be quite laborious especially if large numbers of specimens are to be handled. However, automated slide stainers such as a dipping- style slide stainer are available.8 Two or more slides should be made per specimen and the quality of the slide should be assessed immediately. Poor quality slides should be discarded and new ones produced. It is safer to produce a new slide than to interpret a poor quality slide. Quality of the film produced depends on a proper smearing technique and quality of the staining process.9 For a quality differential staining to be achieved, the stain requires an adequate contact time to avoid over or under staining. For quality control, the stain quality should be compared with a well-made, normal, cover-slipped slide on day to day basis to detect deterioration in stain quality which is virtually inevitable over time with use and storage.

INTERPRETING A PERIPHERAL BLOOD FILM

The interpretation may be done by haemato-morphologist who is trained laboratory technologist but preferably a pathologist. The slide is viewed at the body of the smear, usually beginning about one millimetre away from the tail (the monolayer part). The head of the smear should be avoided as the cell density or overcrowding and overlapping of cells is twice in comparison to the tail. The head portion of the blood film might be of interest when investigating for presence of malaria parasites or microfilaria. The feathered end may be examined for platelet clumps and large cells like monocytes and blasts._{10,11}

Microscopy requires a skilled systematic approach. A quick assessment of a smear can be made within 3 minutes but an abnormal film would require longer time for wider view and differential cell counts. Peripheral blood smear can be used for estimation of manual blood counts. With the advent of automated cell counters which are more reliable and accurate, manual differential counts of white blood cells using PBF is gradually fading in routine haematology laboratory practice. However, in resource deprived/ poor regions where http://www.webology.org

automated counters are not readily available, assessing differential cell counts from PBF is a good option.

Morphology of the blood cells on a PBF smear is best discussed in line with each haemopoietic cell lineage. The distribution, size, shape, colour, cellular inclusions of the red blood cell (RBC) and morphology of the other major cell lines should be carefully assessed. However, there are some abnormalities like broken cells (or smudge cells) may be interfere and should be taken into consideration when reporting.

RED CELL MORPHOLOGY

The normal red cell is biconcave disc-shaped, measures about $7-8 \,\mu\text{m}$ in diameter, has central pallor (approximately a one third of the red cell diameter) and lacks intra-cytoplasmic inclusions. Red cells are pink in colour when stained with Rowmanosky stains because the haemoglobin content of the red cell picks up eosin, the acidophilic components of the dye. Abnormal variations in cell size, shape, colour, presence of intracellular inclusions and pathologic arrangement of the cells suggests a host of abnormalities. On microscopy, a normal sized red cell is comparable to the size of the nucleus of a small lymphocyte. Normally, red cells exhibit narrow variations in size as reflected by normal red cell distribution width (RDW) of 11-15%. A wide variation in cell size is described as anisocytosis. Abnormalities of cell size can be microcyte (smaller) or macrocyte (larger RBC). Anisocytosis correlates with mean cell volume (MCV) except in combined deficiency states. The normal MCV range is 76-96 femtoliters. MCV <76fl suggests microcytosis while MCV >96fl suggests macrocytosis. 14 Macrocytes may be oval (ovoid) or round in shape and this has diagnostic implications. Oval macrocytosis is associated with Megaloblastic anaemias (folate or cobalamin deficiency), myelodysplasia and use of drugs like hydroxycarba-mide. Round macrocytes are seen in liver disease and alcoholism.

Red cell inclusions often result from defective maturation of the erythrocytes, oxidant injury to the cells or infections. Howell jolly bodies are DNA remnants seen in post-splenectomy patients and in anatomical or functional asplenia due to loss of pitting action of the spleen. Basophilic stipplings or punctuate basophilia are denatured RNA fragments dispersed within the cytoplasm and are associated with haemoglobinopathies (thalassemias), lead or arsenic poisoning, unstable haemoglobins, severe infections, sideroblastic anaemia, megaloblastic anaemia and a rare inherited condition, pyrimidine 5' nucleotidase deficiency. 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. Intracellular parasites such as plasmodium or babesia may also be seen. Some other red cell inclusions can only be appreciated with supravital staining (reticulocyte preparations). Heinz bodies are denatured haemoglobin (seen in oxidant injury, G6PD deficiency). 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.

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Table

Red cell shape abnormalities and their differentials

Red Cell Shapes	Differential Diagnosis
Irreversibly sickled red cells (drepanocytes)	Sickle cell syndromes (SS, SC, Sβthalassemia)
Target cells (codocytes, mexican hat cells)	Sickle cell disease, haemoglobin C trait, haemoglobin CC disease, thalassemias, iron deficiency, Liver disease (cholestasis), asplenia,
-	Thrombotic micro-angiopathic haemolytic anaemias such as Disseminated intravascular coagulopathy (DIC), thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome.
Burr cells (echinocytes, crenated red cells)	In-vitro artifact following prolonged storage or slow drying of the smear due to high humidity, uraemia, Malnutrition
Spur cells (acanthocytes)	Liver disease, Renal failure, Abetalipoproteinaemia, Spur cell anaemia, pyruvate kinase deficiency
Tear drop cells (dacrocytes)	Myelofibrosis, Myelophthisia (marrow infiltrations), Extramedullary haemopoiesis, Hereditary elliptocytosis, Hereditary pyropoikilocytosis, Severe iron deficiency, Megaloblastic anaemia, Thalassemias, Myelodysplastic syndrome
Bite cells (degmacytes)	G6PD deficiency, Oxidative stress, unstable haemoglobins, congenital heinz body anaemia
Pencil cells	Iron deficiency
Stomatocytes	Artifact(due to slow drying in humid environment), Liver disease, alcoholism, Rh-null disease, Obstructive lung disease
Elliptocytes	Hereditary Elliptocytosis (>25%)
Basket cells (half ghost cells/Blister cells) Spherocytes	Oxidant damage, G6PD deficiency, Unstable haemoglobins Hereditary spherocytosis, ABO incompatibility, Autoimmune hemolytic anemia (warm antibody type), Severe burns

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. 12.13 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 extra medullary Hemopoiesis. The circulating erythroblasts may be normoblasts (normal maturation) or megaloblasts (megaloblastic changes). The colour of the red cells is reflected by its haemoglobin content. Increased haemoglobinization is termed hyperchromia. Decreased haemoglobination is hypochromia. Hyperchromic cells lack central pallor and can occur in the setting of large cell such as polychromatic cells, small cells such as microspherocytes or an abnormally shaped cell. Shape abnormalities associated with hyperchromia include irreversible sickled red cells, spherocytes and irregularly contracted cells (ICC or pyknocytes). Spherocytes are seen in hereditary spherocytosis. Small cells termed microspherocytes (densely haemoglobinized) occur in immune haemolytic anaemia (splenic macrophages bite off portions of the membrane with the bound antibody and the cell reseals with a smaller volume); burns and less frequently micro angiopathy. Hypochromia reflects low haemoglobin content in the red cell and commonly results from iron deficiency.

WHITE CELL MORPHOLOGY

Aberrations in leukocyte morphology are consistent with a number of pathologies. A quick assessment of cell counts can be made. Normally, you see about 2 to 5 leukocytes per high power field (HPF). 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. Leucocytosis is suspected when WBC >5 leucocytes/hpf and leucopenia <2 cells/hpf. The more the number of cells counted, the better the accuracy of the cell count estimates. Therefore, cell count estimation of leucocytes will give a better representation at low power especially in leucopenic specimens.

In the peripheral blood, the proportion of polymorphonuclear (PMN) cells to mononuclear cells varies with age but in adults' neutrophils is the most abundant. They constitute about 40 to 75% of entire leucocytes, lymphocytes about 20-45%, eosinophils 1 to 6%, monocytes 2- 10% and basophils <1%. Reductions or increase in any of the white cell series may be absolute or relative. For example, relative lymphocytosis means total white cell count is adequate but the lymphocytes predominate. Mature neutrophils have segmented nucleus with 2 to 5 lobes joined by a thin filament. Less mature forms include bands (stab, juvenile) forms, metamyelocyte, myelocyte, promyelocyte and myeloblast in that order. The cytoplasm of a mature neutrophil is pink or nearly colorless and possesses moderate azurophilic and specific granules. The bands have unsegmented nuclear morphology. Myeloblasts are the earliest recognizable granulocyte precursors and may spill over into the periphery in situations that cause marked left shift.₁₄ Myeloblasts are large with round to oval nucleus, basophilic cytoplasm, 2 to 5 nucleoli and fine reticular chromatin pattern. Promyelocytes are slightly larger with primary granules, http://www.webology.org

nucleoli and the chromatin pattern is slightly more condensed. Myelocytes are smaller with oval or round nucleus, no nucleoli, condensed chromatin and more cytoplasm. Metamyelocytes are similar to myelocytes but have indented nucleus.

Neutrophilia is commonly a response to bacterial infections especially pyogenic infections. Other associations of neutrophilia include any form of acute inflammation (such as myocardial infarction), burns, corticosteroid use (inhibits neutrophil margination), malignancy, chronic myelogenous leukaemia. Left shift is a term used to describe an abnormal rise in the proportion of circulating neutrophil precursors. Normally, mature segmented neutrophils are seen with band neutrophil population less than 8% and metamyelocytes less than 0.5%. 9 However, an increase in the proportion of myeloid precursors is termed left shift. Severe neutrophilia with left shift is termed leukaemoid reaction. In severe infections, toxic granulations are seen in the neutrophils cytoplasm due to compensatory increase in microbicidal granules. Right shift or neutrophil hypersegmentation is a diagnostic feature of megaloblastic anaemia. It is defined by the presence of at least one neutrophil with 6 or more nuclear segments or at least 5% of circulating neutrophils with 5 nuclear segments. Neutrophil hypersegmentation may be familial, associated with iron deficiency anaemia or renal failure.₁₅

Lymphoid cells in the periphery exhibit differing morphologies. Commonly seen is the small lymphocyte population. Small lymphocytes are round with high nuclear cytoplasmic ratio (N: C ratio) and scanty paledark blue cytoplasm. In the large lymphocytes, the N: C ratio is lower and the nucleus may be round oval or indented with less condensed chromatin. When large lymphocytes have cytoplasmic granules, there are termed large granular lymphocytes and they represent cytotoxic T lymphocytes or NK cells. On the other hand, reactive (activated) lymphocytes are large with indented or irregular nucleus, abundant cytoplasm (which tends to flow around surrounding red cells) and may possess nucleoli. Neoplastic lymphoid blasts when seen on blood film are also large with a size comparable to activated lymphocytes but have a high N: C ratio. Lymphoma cells are seen in leukaemic phase of Non-Hodgkins lymphomas and usually show varying sizes and various nuclear morphologies. Some have single deep nuclear cleavage (follicular cells), some have multiple indentations and clefts (mantle cells). Lymphoplasmacytoid, lymphocytes have eccentric nucleus, blue cytoplasm and some perinuclear halo. Villous lymphocytes seen in splenic marginal zone lymphoma have a bipolar cytoplasmic projection while hairy cells seen in hairy cell leukemia have feathery cytoplasmic projections distributed round the cytoplasm. Relative lymphocytosis is normally seen in children age less than 5 years.₁₆ Other causes of relative lymphocytosis include acute viral infections, connective tissue diseases, thyrotoxicosis and adrenocortical insufficiency. Causes of absolute lymphocytosis include reactive conditions like infectious mononucleosis, hepatitis, Cytomegalovirus infections, pertussis, chronic intracellular bacterial infections (such as Tuberculosis or brucellosis), chronic lymphocytic leukaemia, acute lymphoblastic leukaemia and leukaemic spills of lymphomas.

Eosinophils are slightly larger than polymorphs and the nucleus is usually bilobed. Their defining characteristic is the presence of orange-red granules in the cytoplasm. Significant eosinophilia may be seen in allergies and parasites infections. However, marked eosinophilia (>1500/ml) suggest hypereosinophilic syndrome (especially with associated tissue damage) or 3177 http://www.webology.org

a neoplastic entity especially when there is an associated cellular dysplasia as in chronic eosinophilic leukaemia. Basophils are slightly smaller than polymorphs and have large deeply basophilic (bluish) granules that may even totally obscure the nucleus. Basophilia is seen in hypersensitivity states and malignant conditions like lymphomas and chronic myeloid leukaemia. Monocytes are the largest cells in the periphery with blue-grey ground glass cytoplasm. Its nucleus is large and assumes various shapes but often horse shoe shaped. Monocytosis is seen in chronic bacterial infections such as tuberculosis, inflammatory conditions like Crohn's disease, haematological malignancies such as chronic myeloid leukaemia and acute myeloid leukaemia.₁₇

PLATELET MORPHOLOGY

Platelets (thrombocytes) are approximately 2-4 by 0.5 microns in dimension (which is about a third of a normal sized red cell) with coarse cytoplasmic granules. They are formed from budding off of the cytoplasm of megakaryocytes in the marrow. It is expected that we see approximately 7–15 platelets on x100 objective. A platelet/hpf is equivalent to approximately 15,000-20,000 platelets in circulation. An increase in platelet count is termed thrombocytosis while a decrease is termed thrombocytopenia. Qualitative abnormalities of platelets are termed thrombosthenia and require platelet functional studies to identify them.₁₈

Thrombocytopenia can result from reduced production as in bone marrow failure syndromes, increase peripheral destruction (as in disseminated intravascular coagulopathies and other thrombotic microangiopathies) or increased splenic sequestration (as in hypersplenism). Thrombocytopenia may be spurios (pseudo-thrombocytopenia) in EDTA-induced platelet aggregation or presence of clots in the blood specimen. Causes of thrombocytosis include major surgeries, post splenectomy, preterm infants, haemorrhage, acute haemolysis, iron deficiency, infections, connective tissue diseases (e.g. systemic lupus erythematosus, rheumatoid arthritis), use of cytokines (thromomimetics), and certain drugs. Thrombocytosis can be associated with malignant conditions especially myeloproliferative neoplasms (Polycythaemia Vera, myelofibrosis, essential thrombocythaemia). Large platelet forms may also be seen. Usually, large platelets are caused by hyperactivity of megakaryocytes due to increased demand. Reticulated platelets (younger larger forms) are released faster. Falsely elevated automated platelet counts may be due to red cell fragments in microangiopathic haemolytic anaemias, fragments of leukaemic cells or even fungi. Giant platelet (about the size of a normal red cell or more) is seen in inherited conditions like Bernard Soulier syndrome, May-Haggelin anomaly or Wiskott Aldrich syndrome and acquired states like megaloblastic anaemia and myeloproliferative disorders.₁₉.

REPORTING A PERIPHERAL BLOOD FILM

When laboratory results are generated, they must be transcribed into reports and signed by the haematologist especially when there is a significant PBF abnormality. The typical reporting format begins with the patient's bio-data, hospital number, requesting physician, date of request, date of report and clinical summary/details of the patient. The body of the report includes detailed characterization of each of the major haemopoietic cell lines: erythrocytes, leucocytes and the platelets. This is followed by a summary of the significant findings, likely http://www.webology.org

diagnosis with differentials, other recommended laboratory evaluations and authorizing signature of the laboratory physician with date.

Reports are generated in duplicates and stored in a retrieval system (electronic or manual or both). Films/ slides should also be stored and preserved for a minimum length of time (as stipulated by local guidelines) for possible retrieval or review. Slides are stored in shelves away from light exposure. Use of coverslip also helps prolong shelf life.

CONCLUSION

The list of the various abnormalities in each cell line discussed above is by no means exhaustive. You may need to refer to standard textbooks for more details. Making diagnosis from a PBF requires a sound clinical database of the various possible cytological abnormalities, their aetiologies and a wealth of laboratory experience. Conclusions from a PBF can be truly diagnostic for a disease condition such as a blood film diagnosis of sickle cell disease or chronic myeloid leukaemia. In other cases, it is at best suggestive and requires further laboratory work-ups or more advanced investigations such as cytochemistry, flow cytometry, cytogenetics or molecular techniques especially when dealing with malignancies.

Despite the major advances in genetic and molecular techniques in diagnosis of various diseases the examination of blood smear morphology remains an indispensable tool to the haematology practice. It remains a frontline diagnostic jigsaw in unraveling mysteries behind cryptic symptoms and signs in primary and secondary haemopathies.

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