IS DIAGNOSIS FROM BLOOD SMEAR STILL ON ACTUALITY?

GABRIELA ARIADNA GAVRILĂ[1], LIVIA DRĂGHILĂ[2]

[1,2]*Emergency County Clinical Hospital Sibiu*

Keywords: *peripheral blood smear, importance*

Abstract: *Peripheral blood smear is one of the most frequent analyzes in hematology laboratory. This procedure is a time-consuming one and it demands a well trained laboratory specialist doctor. There are two circumstances which require the blood smear: physician's request or laboratory hematologist request. Each laboratory has its own policy on the criteria for the examination of a laboratory-initiated blood smear. Sometimes, blood smear offers sufficient information for a definitive diagnosis (leukemia), otherwise, it opens the way for upcoming investigations. Blood film has an important role in the differential diagnosis of anemia and thrombocytopenia. To eliminate diagnostic errors of the haematological disorders, the peripheral smear is a pivot between the clinical context of the patient and the other modern investigations.*

On the era of over-performing hematology analyzers, flow cytometry and advanced molecular biology techniques, the question remains: is there any place for peripheral blood smear in the rapid changes of the hematology laboratory?

"Reading" of peripheral blood smear is often done by physicians in USA, while in Europa only a well-trained laboratory specialist are allowed to perform it. In our country, the rules of the National Health Insurance House require that the blood smear has to be executed and interpreted by a laboratory specialist doctor. If the automated blood count is a rapid procedure, reading of a blood smear is a time consuming, labour-intensive and a relatively expensive technique, so we have to use it judiciously. However, peripheral smear remains one of the most frequent analyzes in hematology laboratory.

There are two circumstances who require the blood smear: on the one hand is the physician's request on the basis of clinical patient data or an anterior abnormality in total blood count data or to evaluate the effectiveness of treatment, but on the other hand the laboratory hematologist is the one who request, response on automatic blood cell counting flags or other abnormality.

Table no. 1. Clinical Criteria for Blood Smear Examination (1,2)

Unexplained anaemia, leucopenia or thrombocytopenia;
Unexplained leukocytosis, lymphocytosis or monocytosis;
Unexplained jaundice/ haemolysis;
Skin rushes, abnormal bruising/ petechiae;
Splenomegaly, bone pains;
Sudden weight loss (suspected chronic or acute myeloproliferative disease, chronic lymphoproliferative diseases);
Suspected organ failure such as renal or liver failure;
Hyperviscosity syndrome (leukaemic hyperleucocytosis, paraproteinaemias, polycythaemia);
Severe infection (bacterial sepsis or parasitic infections);
Malignancies with possible bone marrow involvement;
Monitoring of therapeutic response in haematological diseases or side-effects of chemotherapy.

Each laboratory has its own policy on the criteria for the examination of a laboratory-initiated blood smear according to International Society for Laboratory Hematology recommendations.

Table no. 2. Criteria for the examination of a laboratory-initiated blood smear (3)

	Adults
1. Automated cells count	
WBC ($x10^9$ / L)	> 20
Hb (g/dL)	< 7
PLT ($x10^9$ / L)	< 100 or > 1000
2. Automated Diff count	
Neutrophils ($x10^9$ / L)	< 1
Lymphocytes ($x10^9$ / L)	> 5
Eosinophils ($x10^9$ / L)	> 1,5
Basophils ($x10^9$ / L)	> 0.3
Monocytes ($x10^9$ / L)	> 1,5
3. Not realized automated Diff count	
4. Qualitative Flags	Immature granulocytes, Left shift, Atypical lymphocytes, Blasts, NRBC (erythroblasts), Schistocytes, Platelet aggregates; Abnormal histogram: WBC abnormal histogram, double red blood cell population.

WBC = white blood cells; Hb = hemoglobin; PLT = platelet

Blood smear typically provided information of the red blood cells, white blood cells and platelets morphology or other abnormalities (presence of abnormal peripheral cells like plasma cells, metastatic cells, parasites and other bacteria). Morphological abnormalities includes detail in the appearance, shape, size, inclusions, distribution of blood cells. So, the blood film is an important tool in the differential diagnosis (of anemia and thrombocytopenia) or in the identification and characterization of lymphoma and leukemia. Sometimes, blood smear offer sufficient information for a definitive diagnosis, otherwise opens the way for upcoming investigation. We will further describe significant changes in erythrocyte, leukocyte and platelet morphology and we will exemplify with imagery from our own collection of smears.

1. Red blood cells

a. anisocytosis:

- microcytes (iron deficiency anemia, thalassemia, anemia of chronic disease, lead poisoning, sideroblastic anemias);
- macrocytes (folate or vitamin B12 deficiency, obstructive jaundice, alcoholism, impaired DNA synthesis from chemotherapy or inherited diseases, myeloproliferative disorders, myelodysplastic syndromes, splenectomy).(4)

[1]Corresponding author: Gabriela Ariadna Gavrila, B-dul. Coposu, Nr. 2-4, Sibiu, România, E-mail: gcocisiuu@yahoo.com, Phone: +40766 449285
Article received on 17.10.2017 and accepted for publication on 29.11.2017
ACTA MEDICA TRANSILVANICA December 2017;22(4):72-74

- erythrocytic dimorphism with both macrocytes and microcytes, (red blood cell transfusions, myelodysplasia, erythropoietin therapy, hemolytic anemia with a reticulocyte response).

b. poikilocytosis:

- ovalocytes (hereditary ovalocytosis, megaloblastic anemias -macro-ovalocytes);
- echinocytes (artifact, uraemia, malnutrition);
- elliptocytes (iron deficiency, hereditary elliptocytosis, primary myelofibrosis);(5)
- acanthocytes (pyruvate kinase deficiency, liver disease, renal disease, abetalipoproteinaemia),
- keratocytes, sickle cells (sickle cell anemia, hemoglobin disease);
- teardrop cells (myelofibrosis with myeloid metaplasia and other infiltrative disorders of the bone marrow – leukemia, metastatic carcinoma);
- target cells or codocytes (thalassemias, iron deficiency, chronic liver disease, asplenia);
- bite cells (glucose-6-phosphate dehydrogenase deficiency);
- spherocytes (hereditary spherocytosis, hemolytic transfusion reactions, hemolytic anemia, severe burns, bacterial toxins from Clostridium perfringens);(5)
- schistocytes (disseminated intravascular coagulopathy, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura).(6)

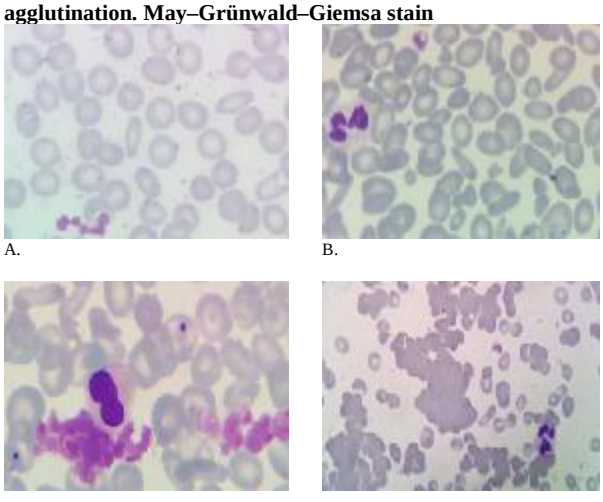
c. intra-cytoplasmic inclusions:

- basophilic stippling (lead poisoning, sideroblastic anemia, thalassemia, megaloblastic anemias);
- Howell Jolly bodies (splenectomies or hyposplenism, hemolytic anemia, pernicious anaemia, and sometimes in celiac disease);
- Heinz bodies (unstable hemoglobin).(6,7)

d. abnormal distribution:

- rouleaux (very high serum protein concentrations due to multiple myeloma or to macroglobulinemia);
- agglutination (cold agglutinins).(6)

Figure no. 1. Red bood cell changes. A. Iron deficiency anemia with microcytes, elliptocytes and hypochromia. B. Pyropoikilocytosis with elliptocytosis, microcytes, polychromasia, bizarrely shaped cells, fragmentation and microspherocytes. C. Splenectomies with Howell Jolly bodies and codocytes. D. Cold agglutinin disease with eritocytes agglutination. May–Grünwald–Giemsa stain



A. B. C. D.

2. White blood cells

a.hyper granulation (inflammatory states, bacterial infection, burns, trauma, exposure to hematopoietic growth factors);

- hipo granulation (myelodysplastic syndromes, some of myeloid leukemia);(4)

b. Dohle bodies (infections, burns, pregnancy, after cytotoxic chemotherapy, tissue damage, G-CSF administration), Auer rodes (acute myeloid leukemia, myelodysplastic syndromes;(8)

c. neutrophilic hypersegmentation (vitamin B_{12} or folic acid deficiency, myelodysplasia or myeloproliferative disorders, uremia, cytotoxic treatment with methotrexate);

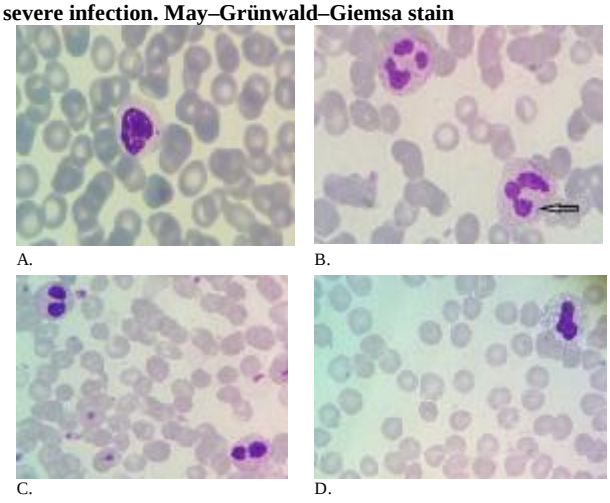
- neutrophilic hyposegmentation or Pelger-Hüet cells (myelodysplastic and myeloproliferative disorders, rarely in accelerated phase chronic myelogenous leukaemia);(6)

d. cytoplasmic vacuolation and toxic granulations (severe infection, toxic states, poisoning, burns, chemotherapy).(7)

e. bacteria in the cytoplasm of neutrophils or within vacuoles (meningococcal and pneumococcal septicaemia). (5)

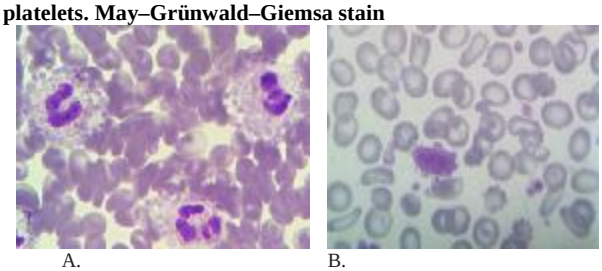
f. pyknotic or apoptotic neutrophils (infection).

Figure no. 2. White blood cell changes. A. Hipogranular and dysplastic granulocyte in myelodysplastic syndromes. B. Toxic granulation and Döhle bodies in severe infectious processes. C. Pelger- Hüet neutrophils in a Pelger- Hüet anomaly case. D. neutrophilic cytoplasmic vacuolation in severe infection. May–Grünwald–Giemsa stain



A. B. C. D.

Figure no. 3. Platelets changes. A. Trombocytopenia due to platelets satelitism. B.Myelodysplastic syndrome with giant platelets. May–Grünwald–Giemsa stain



A. B.

3. Platelets cells abnormalities

a. confirm trombocytopenia and looking for the causes: platlet clumping (EDTA anticoagulant causes), platelet satellitism (antiplatelet autoantibodies causes or healthy individuals), small clots;

b. large and giant platelets (increased platelet production during bleeding or stress, hyposplnism, Bernard Soulier syndrome, May-Haggelin anomaly, Wiskott Aldrich syndrome,

megaloblastic anaemia or myeloproliferative disorders), bizarre platelets (myelodysplastic syndromes);
c.platelet hypogranularity (myeloproliferative disorders, myelodysplastic syndromes, grey platelet syndrome).(4)

In conclusion, to eliminate diagnostic errors of the haematological disorders, the peripheral smear is at the cross-over between clinical context of the patient and the other modern investigations.

REFERENCES

1. Bain BJ. Diagnosis from the Blood Smear. N Engl J Med. 2005;353:498-507.
2. Adewoyin AS, Nwogoh B. Peripheral blood film - A review. Ann Ibd Pg Med. 2014;12(2):71-79.
3. Suggested Criteria for Action Following Automated CBC and WBC Differential Analysis, The International Consensus Group for Hematology Review. 2015 [cited 9 September 2017]. Available from: http://www.islh.org/web/consensus_rules.php
4. Shagana JA. Diagnostic Cells in the Peripheral Blood Smear. J Pharm Sci & Res. 2014;6(4):213-216.
5. Bain BJ, Bates I, Laffan MA, Lewis M. Dacie and Lewis Practical Haematology. 11th ed. Livingstone: Elsevier Churchill; 2011. p. 71-99.
6. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition.1990. [cited 9 September 2017]. Available from: https://www.ncbi.nlm.nih.gov/ books/NBK263/.
7. Carr JH, Rodak BF. Clinical Hematology Atlas. 4th ed. St. Louis, Missouri: Elsevier Inc.; 2013. p. 93-117.
8. Bain BJ. Auer rods or McCrae rods? Am J Hematol. 2011;86:689.