Complete Blood Counts with Differential Results: a Guide for Clinicians

Key highlights

- Most hematologic abnormalities are not specific but instead due to an increase or decrease in hematologic parameters
- Abnormalities that are significant, such as acute leukemias, chronic myeloproliferative disorders, hemolytic anemia and many lymphomas, can be detected by the laboratory
- Contact Labcorp discipline directors with any questions regarding nonspecific abnormalities

Introduction

Most hematologic abnormalities are nonspecific and due to an increase or decrease in one or more hematologic parameters. Significant hematologic abnormalities, such as acute leukemias, chronic myeloproliferative disorders, hemolytic anemia and many lymphomas, can be detected routinely by the laboratory. This guide is intended to inform clinicians on the interpretation of nonspecific abnormalities.

Anemias

To ascertain the cause of the anemia, examination of the MCV (mean corpuscular volume) and MCH (mean hemoglobin concentration) is essential.

- **Microcytic hypochromic anemia (low MCV and MCH):** The differential diagnosis includes iron deficiency anemia, anemia of chronic disease and thalassemia minor. The latter condition is usually marked by high RBC count and low MCV with a normal hemoglobin. Thalassemia minor should be differentiated from polycythemia vera as both conditions could present with similar indices. Iron studies are recommended for further differentiation of iron deficiency anemia from anemia of chronic disease. Other rare causes of microcytic anemia include lead poisoning (clinical correlation is important) and certain hemoglobinopathies (Hemoglobin C disease and trait and hemoglobin E) If a hemoglobinopathy is suspected, order a hemoglobin electrophoresis.[1]
- **Normochromic Normocytic anemia (normal MCV and MCH):** Normocytic anemias are due to diverse causes including iron deficiency, chronic disease, renal insufficiency, blood loss and hemolysis. Based upon the clinical picture, additional testing including iron studies, reticulocyte count and renal function tests, may be ordered.[2] Microangiopathic hemolytic anemia and spherocytic hemolysis are routinely identified by the laboratory.
- **Macrocytosis/macrocytic anemia (high MCV):** B12 deficiency is the most common cause of macrocytic anemia. Other causes of macrocytic anemia include drug effect, folate deficiency (uncommon in the United States), hypothyroidism and excessive alcohol consumption. Rare causes of macrocytic anemia include congenital disorders and myelodysplastic syndrome.[3]

Erythrocytosis

Common causes of erythrocytosis include chronic hypoxia (COPD, tobacco exposure, dehydration) or as a reaction to certain drugs (i.e., testosterone therapy). Persistent erythrocytosis without cause raises the possibility of polycythemia vera. Determination of serum erythropoietin level and *JAK2* testing may be indicated.[4]

Neutrophilia

Reactive neutrophilia occurs most commonly in acute and chronic infections and inflammatory states. Rare causes include heat stress, metabolic and endocrine disorders, tissue hypoxia and damage, and occult malignancy.[5]

Neutropenia

Common causes of neutropenia include viral infections (influenza, infectious hepatitis, infectious mononucleosis, etc.) and certain bacterial infections (i.e., typhoid fever). A variety of drugs can cause neutropenia either as a dose-dependent or idiosyncratic reaction. Other less common causes of neutropenia include immune neutropenia, endocrine disorders and alcoholism.[6]

Monocytosis

Reactive causes of monocytosis are relatively common and occur in chronic infections, autoimmune conditions and with certain medications. Transient monocytosis can also be seen after splenectomy and with acute infections.[7]

Persistent monocytosis (>1000 X 106/µL) cause may be indicative of a chronic myeloproliferative disorder/chronic myelomonocytic leukemia, especially in an older patient.[8]

Eosinophilia

Eosinophilia can be characterized as mild (500-1500 x 106/L), moderate (> 1500 x 106/L) and severe (>5000 x 109/L). Reactive causes of eosinophilia are relatively common and may be due to parasitic infection, allergies, autoimmune diseases and drug effect.[9] If the eosinophil count is moderately or severely elevated without cause, a chronic myeloproliferative disorder or clonal eosinophilic disorder should be considered.[10]

Lymphocytosis

Common causes of lymphocytosis include viral infections (EBV, rubella, influenza, etc.) and certain bacterial infections (*Bordetella pertussis*). Cigarette smoking, splenectomy and Addison's disease can also cause a benign lymphocytosis.[11-12]

If the absolute lymphocytosis is persistently above 5,000/µL and without cause, recommend flow cytometric analysis to exclude a chronic lymphoproliferative disorder.[13] This threshold may be lower in patients above age 65.[14]

Lymphocytopenia

Lymphocytopenia can be due to a variety of causes including viral infection, autoimmune diseases, immunodeficiencies, splenomegaly and corticosteroids.[15]

Thrombocytosis

The most common causes of thrombocytosis are reactive and related to infection or inflammatory state. Post surgical states, post splenectomy and iron deficiency anemia can also cause a reactive thrombocytosis.[1]

If the platelet count >450 x 109/L persistently without reactive causes, the differential diagnosis includes a chronic myeloproliferative disorder.[16]

Thrombocytopenia

Thrombocytopenia can occur due to several mechanisms including decreased production and increased destruction/consumption of platelets. Blood loss can also cause thrombocytopenia.

Decreased platelet productions can occur in a variety of settings. Congenital thrombocytopenia is rare but may be associated with May-Hegglin anomaly, Bernard-Soulier syndrome and other abnormalities. Contact Labcorp's discipline directors if there is concern for congenital abnormalities. Acquired causes are most commonly secondary to drug effect.

Increased platelet destruction/consumption is relatively common and is mostly an acquired condition. Auto-immune disorders and drug-induced immune thrombocytopenia are common causes. Thrombocytopenia can rarely occur after certain viral infections such as infectious mononucleosis.[1]

Platelet aggregates

Platelet aggregates are occasionally observed on complete blood counts (CBCs). When a patient has platelet aggregates for the first time, the cause is most likely preanalytical. Repeat the platelet count and ensure that the redrawn specimen is collected without significant trauma and the tube is mixed adequately and immediately after collection.

If a patient repeatedly demonstrates platelet aggregation, please arrange to have the sample collected and immediately run in your local laboratory. Keeping the sample close to 37°C and immediately running the sample on the instrument may minimize platelet aggregation.

Concern for blood parasites

If there is concern for blood parasites (i.e., Plasmodium, Babesia, microfilaria, Ehrlichia, etc.) order **Parasite Examination, Whole Blood [008185]**. A routine CBC will not effectively detect blood parasites.

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