Blood disorders include abnormalities of the red cells, white cells, platelets, their precursors in the bone marrow and clotting factor deficiencies. Several blood disorders are asymptomatic and difficult to diagnose. A detailed history and physical examination, followed by hematological laboratory tests, are essential to identify the specific disorder which can range from leukemia to aplastic anemia to clotting factor deficiencies.

Types of Blood Disorders

Depending on the cell affected, the disorders can be grouped as:
Red cell disorders: Iron deficiency anemia, Anemia of chronic disease, Pernicious anemia, thalassemia, sickle cell anemia, spherocytosis, Polycythemia vera, Erythrocytosis

White cell disorders: Leukopenia, leukocytosis, leukemia, Lymphoma, Multiple myelomas, myelodysplastic syndrome

Platelet disorders: Idiopathic thrombocytopenia, Thrombotic thrombocytopenia, Essential Thrombocytosis

Plasma/Coagulation disorders: coagulation factor deficiencies, disseminated intravascular coagulation, deep vein thrombosis and hypercoagulable states

Approach to a Patient

Patients with blood disorders can present with features suggesting the etiology of the disease i.e.

Disorders due to deficiency of a certain lineage of cells present with features indicating the deficiency of that function:

- Anemia will present with features of inadequate tissue oxygenation, such as hypoxia, syncope attacks and palpitations as red blood cells contain hemoglobin which is responsible for carrying oxygen to various parts of the body,
- Leukopenia will present with recurrent infections.

Disorders of increased cellularity will present with leukocytosis within the blood vessel and ischemia of distant organs.

Disorders of deficiency in coagulation factors will present with minor bleeding, easy bruisability, and fever of unknown origin or abnormal laboratory test results which are often noticed incidentally.

A thorough history and detailed examination are essential to reach a diagnosis.
History of Blood Disorders

Taking a history in a patient with a blood disorder depends on the type of clinical problem:

- Red cell problems usually present with anemia (fatigue, shortness of breath)
- White cell deficiency leads to unusual or prolonged infection
- Excess white cells in malignant disease can cause lumps and swelling
- Disorders of platelets lead to bruising and bleeding

The age and sex of the patient at presentation often provide a clue to the diagnosis; for example, coagulation disorders present in infancy and childhood. Hemophilia is more common in males, while women presenting with menorrhagia or excessive bleeding during childbirth should be evaluated for a coagulation factor deficiency or hypercoagulable state. Triggers for bleeding should be inquired e.g. trauma, dental extraction etc.

The nature of bleeding should also be established as mucosal and cutaneous bleeding points towards vascular or platelet deficiency problems while bleeding into deep tissues and joints indicate clotting factor deficiency.

It is also important to obtain history about medications taken by the patient, such as chloramphenicol (aplastic anemia), herbal medications like XXX and anti-fibrinolytic or anti-platelet drugs. History of any previous blood transfusion is important as it indicates underlying chronic disease. A history of recurrent infections could indicate leukopenia or other bone marrow abnormalities.

Other information like a positive family history (for thalassemia/sickle cell anemia/hemophilia); nutritional deficiencies (iron deficiency anemia), alcohol use (megaloblastic anemia, clotting factor deficiency); hepatic or renal disease (anemia of chronic disease) should also be obtained.

Persistent unexplained bone pain, especially nocturnal, in patients over the age of 40 years should raise suspicion of multiple myeloma.

Examination of Blood Disorders

A physical examination should include an assessment of the skin and mucous membrane inspection for pallor, bruising and petechiae. In severe anemia, conjunctival pallor, koilonychias, tachycardia, and the cardiac murmur may be present. Platelet disorders should be suspected if excessive bruising, bleeding after minor dental procedures or epistaxis and menorrhagia are noted.

Hemarthrosis, deep soft tissue or muscle bleeding may be noticed in coagulation factor defects. Hepatomegaly is a finding in cases of liver failure, while splenomegaly is an indication of excessive red cell lysis such as in hereditary spherocytosis or malignancies or idiopathic thrombocytopenic purpura.

The broad general examination requires:

- Examination of the nails, skin and mucous membranes may suggest anemia
- Examination of the lymph nodes may suggest leukemia or lymphoma
- Excessive bruising is seen in platelet disorders
Laboratory tests of Blood Disorders

A hematologic workup is required to detect a bleeding disorder. These usually include:

**Complete blood count**

This is usually the first investigation that is done. **There are three main components:**

- Red cell count and hemoglobin
- Total and individual white cell counts
- Platelet count

In the red cell count and hemoglobin, the normal red cell count is around $4-6 \times 10^{12}/l$. The hemoglobin concentration is expressed in grams per decilitre. The normal range in men is 13.5-17.5 g/dl. The normal range in women is 11.5-15.5 g/dl.

A peripheral blood smear is used to detect the morphology of red cells and platelets and to confirm the presence of thrombocytopenia. Normocytic normochromic anemia with rouleaux formation occurs in multiple myeloma.

**Erythrocyte sedimentation rate (ESR):** May be elevated in patients with multiple myeloma, leukemia, and lymphomas.

**Prothrombin time (PT):** Values may be elevated in liver disorders or liver failure

Partial thromboplastin time (PTT).

**Coagulation factor studies:** If coagulation factor deficiencies are suspected, then von Willebrand factor antigen, ristocetin cofactor activity, and Factor VIII levels have to be evaluated.

**Liver function tests:** Abnormal values or elevated liver enzyme levels may be detected in liver failure or hepatic disorders.

**Renal function tests:** Elevated blood urea nitrogen and serum creatinine with renal insufficiency may be a finding in cases of multiple myeloma.

**Bone marrow examination** is indicated in patients suspected with leukemia, lymphoma or multiple myeloma. While sheets and clusters of plasma cells are seen in multiple myeloma; a complete absence of cells with fat infiltration may be seen in aplastic anemia.

**Chromosomal studies** may reveal plasma cell karyotype abnormalities.

**Serum and urine protein electrophoresis** with immunofixation will reveal Bence Jones proteins in urine and elevated free light chain immunoglobins in serum.

**Serum calcium:** Hypercalcemia is a typical finding in multiple myeloma. A skeletal survey which includes plain X-rays of the long bones, skull, pelvis, spine, and ribs may show punched out osteolytic lesions in multiple myeloma.
**PET CT scan** is indicated in multiple myeloma to differentiate between solitary plasmacytoma versus multiple myeloma.

**Cytogenetic studies** are required in suspected cases of leukemia.

**Diagnosis of aplastic anemia**

- Absolute neutrophil count < 500 /microlit.
- Absolute reticulocyte count < 60,000 /microlit.
- Platelet count < 20,000 /microlit.
- Bone marrow cellularity <30%.

**References**

[Clinical Evaluation of Bleeding and Bruising in Primary Care](https://aafp.org) via aafp.org

[Identification and Basic Management of Bleeding Disorders in Adults](https://jabfm.org) via jabfm.org

[Diagnosis and Management of Bleeding Disorder in a Child](https://journals.sagepub.com) via journals.sagepub.com

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