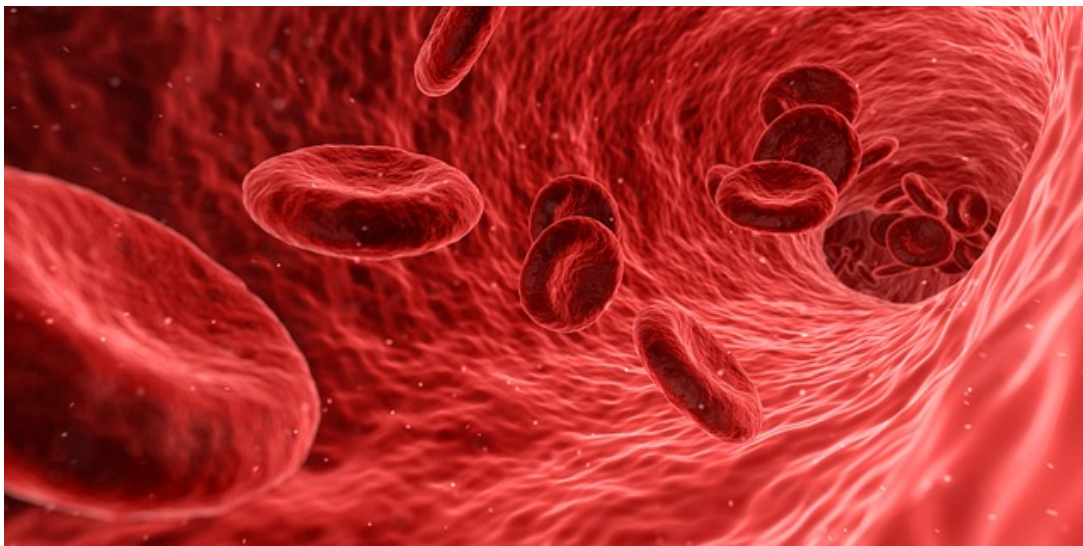


Investigation and Diagnosis of Blood Disorders: Approach to a Patient, Investigation of the Blood System & Additional Investigations

[See online here](#)

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:

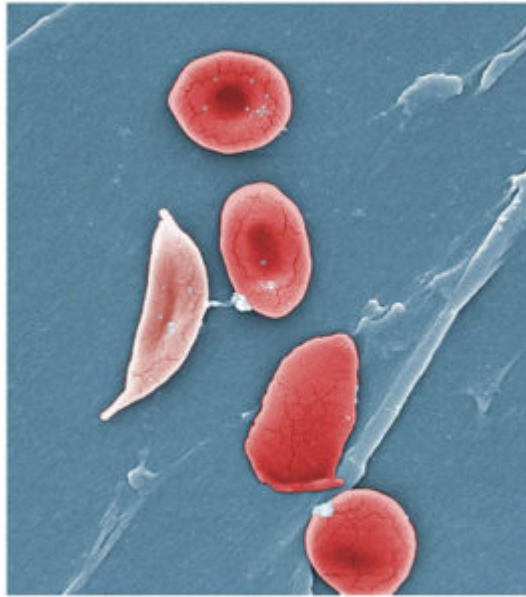


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Red cell disorders: Iron deficiency anemia, anemia of chronic disease, pernicious anemia, thalassemia, sickle cell anemia, spherocytosis, polycythemia vera, and erythrocytosis

White cell disorders: Leukopenia, leukocytosis, leukemia, lymphoma, multiple myeloma, and myelodysplastic syndrome

Platelet disorders: Idiopathic thrombocytopenia, thrombotic thrombocytopenia, and essential thrombocytosis

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

Approach to the Patient

Patients with blood disorders can present with features suggesting disease etiology:

- Anemia will present with features of inadequate tissue oxygenation, such as hypoxia, syncope attacks, and palpitations.
- Leukopenia will present with recurrent infections.
- Increased cellularity disorders will present with leukocytosis within the blood vessel and ischemia of distant organs.
- Plasma/coagulation factor deficiency disorders will present with minor bleeding, easy bruising, a 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 infections
- Excess white cells in malignant disease can cause lumps and swelling
- Platelet disorders 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, e.g. trauma, dental extraction, etc., should be determined.

The nature of bleeding should also be established because the mucosal and cutaneous bleeding point to vascular or platelet deficiency problems. Bleeding into deep tissues and joints indicate clotting factor deficiency.

It is also important to obtain a history of the patient's medications, such as chloramphenicol (aplastic anemia), and anti-fibrinolytic or anti-platelet drugs. A history of previous blood transfusion is important since it indicates underlying chronic disease.

A history of recurrent infections could indicate leukopenia or other bone marrow abnormalities.

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

Patients over 40 years with persistent, unexplained bone pain, especially nocturnal, should be evaluated for 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, koilonychia, tachycardia, and 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, which is deep soft tissue or muscle bleeding, may be noticed in coagulation factor defects. **Hepatomegaly is a finding in liver failure cases**, while splenomegaly indicates excessive red cell lysis, such as in hereditary spherocytosis, 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 for signs suggesting leukemia or lymphoma
- Excessive bruising is seen in platelet disorders

Laboratory tests for 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

A normal red cell count is around $4-6 \times 10^{12}/l$. The normal hemoglobin concentration 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 lymphoma.

Prothrombin time (PT): Might be elevated in patients with liver disorders or liver failure

Partial thromboplastin time (PTT): May indicate a bleeding disorder, such as hemophilia, autoimmune disorders affecting coagulation, or Vitamin K deficiency.

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 indicate multiple myeloma.

Bone marrow examination is indicated in patients being screened for 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 in patients with multiple myeloma and Waldenström's macroglobulinemia.

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.



Image: "PET CT scan" by Jacopo Werther. License: [CC BY-SA 2.0](https://creativecommons.org/licenses/by-sa/2.0/)

PET CT scan is indicated in multiple myeloma to differentiate between solitary

plasmacytoma versus multiple myeloma.

Cytogenetic studies are required when the patient is being screened for 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](#) via aafp.org

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

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

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