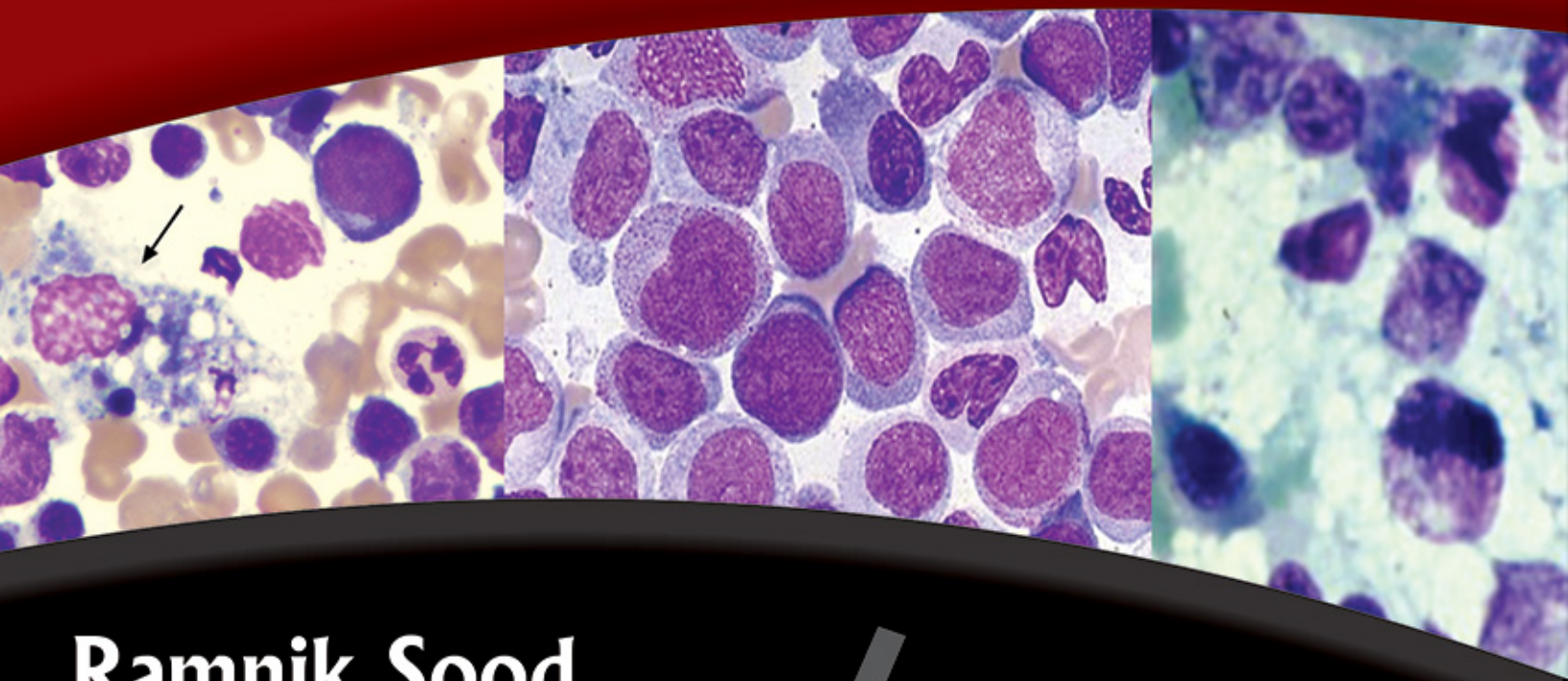
HEMATOLOGY

for Students and Practitioners



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Sixth Edition

JAYPEE

Contents

4 Basic Principles in Diagnosing and Treating Anemias

INVESTIGATIONS

Before proceeding further one should assess whether or not the patient is anemic. If anemia is confirmed one would like to know the type of anemia that the patient is suffering from and lastly to be able to treat one must clearly understand the cause of anemia.

IS THE PATIENT ANEMIC?

a. Proper history and a thorough examination of the patient are must.

History

History to be sought from every suspected case of anemia.

A complete clinical history should be taken with special reference to the following points:

Age, Sex

Onset
- Rapid or gradual

Blood loss
- Hematemesis
- Malena
- Bleeding hemorrhoids
- Menorrhagia
- Metrorrhagia
- Epistaxis
- Hematuria
- Hemoptysis

Alimentary System

- Appetite
- Weight loss
- Dysphagia
- Abdominal pain
- Diarrhea
- Constipation
- Jaundice
- Soreness of tongue
- History of abdominal operations
- Passage of worms

Reproductive System

- Detailed menstrual history
- Number and interval of pregnancies
- Abortions

Urinary System

- Nocturia

Central Nervous System

- Paraesthesia, difficulty in walking

Bleeding Tendencies

- Easy bruising
- Prolonged bleeding after minor cuts
- Bleeding from many sites

Skeletal System

- Bone pain
- Arthralgia
- Arthritis

Drug Ingestion

Occupational History

Dietary History

Social History

- Alcoholism

Past History

- Previous anemia: Diagnosis, treatment and response to it.

Family History

- Anemia
- Recurrent jaundice

Temperature

- Fever
- Night sweats

a. Estimate hemoglobin—preferably by the cyanmet-hemoglobin method or by the oxyhemoglobin method: Sahli's acid hematin method is obsolete and not a very reliable exercise.

b. Anemia is said to be mild if the Hb is more than 9 gm percent. Anemia is labelled as moderate if Hb is between 6-9 gm percent. Any anemia where the Hb is less than 6 gm percent is severe anemia.

WHAT IS THE TYPE OF ANEMIA?

Careful examination of a well made and stained peripheral blood smear is the single most important test to diagnose the type of anemia. The cell size, shape and degree of hypochromia should be noted. Other features are also good indicators.

CAUSE OF ANEMIA

The cause can be ascertained by correlating the clinical presentation of the patient coupled with results of relevant investigations done in a particular case.

The Table 4.1 provides relationship between various clinical pictures with the type/cause of anemia associated with each one of them.

Other Investigations which should be done routinely **(Besides Hb and peripheral smear examination)**

a. *Preferably about 2-3 ml venous blood should be withdrawn and added to the right anti-coagulant.*

b. *Do a total and differential while cell count.*

c. *Perform PCV estimation*
- Enables calculation of MCHC
- Plasma color gives useful clues as to the etiology of anemia.

d. *Reticulocyte count*

Before and after institution of therapy. A rise in reticulocyte count indicates that a correct diagnosis was made and that the patient is responding well.

Raised reticulocyte count occurs

With erythroid hyperplasia in the bone marrow: which may occur naturally as in severe hemolytic anemia or may be a response to therapy given.
- It may also be increased in disorders causing marrow infiltration.

e. *Erythrocyte Sedimentation Rate*

Reflects mainly changes in plasma protein pattern. ESR gives a lead regarding an underlying organic cause and is a good prognostic tool.

EXAMINATION OF BLOOD FILM

Method

1. *Mount* Cover the slide using a neutral mounting medium.
2. *Low power field examination* look for–
   - Quality of film
   - Number, distribution and staining of WBCs.
   - For RBCs examination, select an area where they just touch each other without overlapping, i.e. between tail and body of the film.
3. *High power field examination*
   - Assess RBC
     - Size
     - Shape
     - Hemoglobin concentration

Table 4.1: System manifestation

		Common to all anemias	*Suggests specific disorders*	*Remarks*
1.	Skin and mucous membranes	Pallor		Inconstant- m. membranes more reliable.
		Bruising	Bruising	May be seen in any severe anemia. Suggests associated thrombocytopenia. When ecchymoses are extensive, they may be cause of anemia (blood loss).
			Lemon yellow color	Megaloblastic anemia
			Follicular petechiae	Scurvy
			Leg ulcers	Sickle cell disease, chronic hemolytic anemia
			Fissures of lips	Iron deficiency
			Brittle nails, spooning	Iron deficiency
			Atrophy of papillae	Vitamin B_{12}, folic acid or iron deficiency. of tongue, glossitis
			Dermatitis	Nutritional deficiency
2.	Cardiovascular	Dyspnea, tachypnea,	Thrombotic events tachycardia, palpitations, angina, heart failure, claudication	Sickling disorders, paroxysmal nocturnal hemoglobinuria
3.	Nervous system and eye	Irritability, dizziness, fatigue, headache, tinnitus	Delirium	Vitamin B_{12} deficiency, Thrombotic thrombocytopenic purpura
			Convulsions	Sickling, lead poisoning
			Subacute combined	Vitamin B_{12} deficiency degeneration of cord
			Peripheral neuritis	Vitamin B_{12} deficiency, nutritional deficiency, neoplasia
			Retinal vein tortuosity	Sickle cell disease
			Retinal hemorrhage	Vitamin B_{12} or folic acid deficiency, leukemia, may be in any severe anemia or with associated bleeding disorder
			Intraocular hemorrhage, retinal vessel arborisation	Sickle cell C disease
4.	Gastrointestinal		Anorexia; nausea, flatulence, diarrhea, constipation, jaundice	Vitamin B_{12} or folic acid deficiency, may accompany other anemias
			dysphagia	Hemolytic anemia
			splenomegaly	Iron deficiency anemia
				Hemolytic anemias, pernicious anemia, iron deficiency, congestive splenogemagly, neoplasia
			Abdominal pain	Sickling disorders, spherocytosis
5.	Others		Bone tenderness	Myeloid metaplasia, leukemia, myeloma
			Arthritis	Leukemia, collagen vascular disease
			Gout	Myeloproliferative disorders
			Limb pain	Sickling disorders
			Hypermetabolism	Leukemia
		Fever		Infection (but may be seen in acute hemolytic anemia, acute leukemia, sickle crisis, pernicious anemia and others).

4. *Oil immersion examination*
   - Assess atypical cells or note fine details, e.g. inclusion bodies.

Always Note

RBCs (Table 4.2)

Size

- Macrocytes, microcytes, normocytes
- Anisocytosis (Variation in size)

Shape

- Abnormal shape: oval, pencil, tear, pear, oat and sickle-shaped cells; fragmented cells, target cells, spherocytes, crenated cells, burr cells, acanthocytes, stomatocytes (poikilocytosis).

Hemoglobin

Normochromic, hypochromic.

Table 4.2: Description and significance of various forms of red blood corpuscles

Type of cell	*Description*	*Physiologic significance*	*Clinical disorders*
Macrocyte	Larger than normal (>7.7 µm in diameter). Well filled with hemoglobin	1. Young RBC (?Skipped generation; early loss of nucleus) 2. DNA Synthesis-impaired, megaloblastic maturation	1. Accelerated erythropoiesis. 2. B_{12} or folate deficiency
Thin macrocyte	Diameter increased but MCV normal; often hypochromic (see target cells)	Membrane cholesterol and lecithin increased	Liver disease, postsplenectomy
Microcyte	Smaller than normal (<6.7µm)	Differs according to whether or not a. Well filled with hemoglobin b. Normal in shape	See below
Hypochromic cell	Exaggeration of central pallor (>central 1/3rd); usually also microcytic	Failure of hemoglobin due to i. Lack of iron ii. Defective globin synthesis iii. Defective porphyrin synthesis	Iron deficiency anemia, anemia of chronic disease (?) Thalassemia, some hemoglobinopathies (C,E) Sideroblastic anemias.
Target cell	Hypochromic, with central pigment; thin cell; surface/volume ratio increased	1. Splenectomy decreases rate and extent of loss of lipids from reticulocytes. 2. Accumulation of both cholesterol and phospholipid on RBC. 3. Congenital	As for hypochromic cells. Also 1. Postsplenectomy 2. In liver disease, especially obstructive jaundice 3. LCAT deficiency
Leptocyte	Thin, hypochromic cell, diameter normal, MCV decreased		Thalassemia
Spherocyte	Spherical, not hypochromic; usually also microcytic; surface/volume ratio decreased, no central pallor	1. RBC membrane abnormality 2. RBCs lose fragment after impact with fibrin strands, walls of diseased vessels and artificial surfaces in circulation	1. Hereditary spherocytosis 2. Acquired immunohaemolytic anemia.
Elliptocyte	Elliptical in shape not hypochromic	1. Herediatry abnormality 2. Acquired alteration	1. Herediatry elliptocytosis 2. In various anemias especially megaloblastic.
Sickle cell	Sickle-shaped, form assumed under hypoxia (deprivation of oxygen)	Molecular aggregation of HbS	HbS trait or disease also seen in some other hemoglobinopathies HbC Harlm, Hb Capetown, etc.

Contd...

Table 4.2 contd...

Type of cell	Description	Physiologic significance	Clinical disorders
Schistocyte	Helmet or triangular-shaped, fragmented or greatly distorted RBC; smaller than normal	RBC's lose fragments after impact with fibrin strands, walls of diseased vessels and artificial surfaces in circulation.	1. Microanglopathic hemolytic anemia 2. Hemolytic anemia due to physical agents 3. Also in uremia, malignant hypertension
"Teardrop" RBC	Shape of drop; usually microcytic, often also hypochromic	Distorted or fragmented RBC	1. Especially in myelosclerosis 2. Less frequently in other forms of anemia, e.g. thalassemia
Spicule Cell may be; a. Acanthocyte ('Spur Cell')	RBC with tiny projection on surface. Has 5-10 spicules of various lengths irregular in spacing and thickness	Differs according to type: a. Ratio of cholesterol/lecithin of RBC membrane increased when associated with liver disease. Can be converted to normal shape by non-ionic detergents	1. In abetalipoproteinemia 2. Liver disease with hemolytic anemia 3. Postsplenectomy (few) 4. Pyruvate kinase deficiency
b. Echinocyte (Sea-urchin cell, crenated cell, burr cell)	Has 10-30 spicules, evently distributed over surface of the RBC	b. Result of alteration of intra and extra-cellular environment. Can be brought about by accumulation of fatty acid or lysolecithin on RBC surface, or both, as result of changes in plasma or in RBC metabolism	1. Uremia 2. Neonates 3. Pyruvate kinase deficiency 4. Phosphoglycerate kinase deficiency
Pyknocyte	Distorted and contracted RBC, similar to echinocyte		Infantile Pyknocytosis
Stomatocyte	Uniconcave, as contrasted with normal biconcave RBC; slit-like instead of circular area of central pallor in RBC	1. Hereditary. Primary defects in membrane structure of function resulting in abnormalities of cation permeability, content and flux	1. Hereditary stomatocytosis Several forms
		2. Acquired alteration in cation content and flux	2. Smaller number seen in alcoholic cirrhosis, acute alcoholism, obstructive liver disease, malignancies, etc. and perhaps artifacts.

Immature Forms

Polychromatic, stippled or nucleated red cells.

Inclusion Bodies

Howell Jolly bodies, Cabot rings, Pappenheimer bodies, malarial parasites.

Arrangement

Auto-agglutination, excess rouleaux formation.

WBCs

Number

Normal, increased, decreased.

Abnormal or Immature Forms

Immature forms, hypersegmented macropolycytes, abnormal forms.

Platelets

Number

Normal, increased, decreased.

Form

Abnormalities of size and shape.

TREATMENT

Before embarking on treatment have the accurate diagnosis of the cause of anemia.

Treatment Includes

- Rectification of the disorder causing anemia.
- Administration of specific hematinics.
- Relief from symptoms.

Treatment of Disorder Causing Anemia

1. Arrest of bleeding acute or chronic.
2. Supplement the deficiencies.
3. Relieve the causative systemic disorder. Take care of infection, renal failure, malignancies: hematological or otherwise, liver disease, autoimmune disorder or endocrine deficiency.
4. Remove the toxic chemical agent or drug.
5. Correct any anatomical gastrointestinal abnormality if present.

Administration of Hematinics

Folic acid, Vitamin B_{12} and iron when given therapeutically are called hematinics. The logic behind giving their extracts is that they contain the important hemopoietic vitamins.

The most common anemia seen in practice is that caused by iron deficiency; iron, therefore, is most commonly needed. Vitamin B_{12} and folic acid deficiencies are on the increase and the anemia caused thereby needs specific vitamins for rectification. In certain disorders non-specific marrow stimulation may be needed and for this testosterone is employed. Erythropoietin (EPO) is now being used to stimulate bone marrow in many situations.

General Considerations

1. Always establish the kind of anemia and its cause before embarking on treatment regimens.
2. Give supplementation of only the specific deficient substance.
3. Give adequate doses of an effective preparation for a sufficient length of time.
4. Do not give shotgun preparations containing iron, vitamin B_{12} and folic acid, etc. For instance, if the patient does improve on shotgun preparations one would not know about the actual substance to which the patient has responded. In the case of Vitamin B_{12} and intrinsic factor deficiency, if folic acid is given alone, sub-acute combined degeneration of the cord may be precipitated.

Hematology *for* Students and Practitioners

The most up-to-date concise yet exhaustive and adequately complete book of hematology for medical students and practitioners—All in color, as one sees everything through the lenses of the microscope. True-to-life picture quality enhances easy understanding and permanent retention of the knowledge accrued and gained.

The charts, tables, flow diagrams, algorithms, figures (all in color) and recapitulation sections (at the end of each chapter) provide for easily assimilable understanding of hematology. Should one desire details also; well, within the covers of this book you will find them all! All answers to what, how, why, when and where—as related to hematology are presented in this book in an easily digestible format. Students and practitioners would find it extremely helpful in acquiring knowledge of theory as well as practice of hematology.

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