No.1 Selling Book on the Subject

Fully Colored Includes Over 300 Images

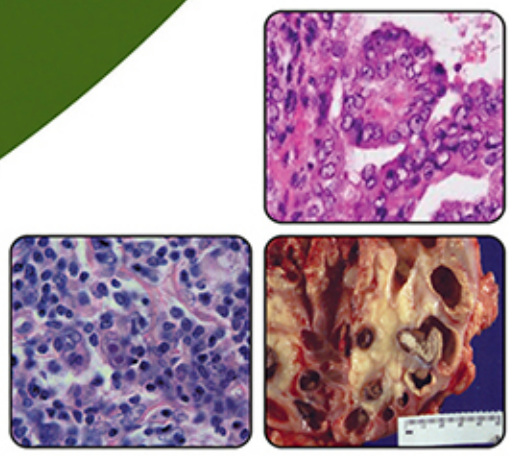
Thoroughly Revised & Updated Edition Including Latest Exam Pattern Questions

Review of PATHOLOGY AND GENETICS

A Must-buy Book for NEET-PG, INI-CET & FMG Exams

Facts and Concepts Based on Latest Editions of Robbins, Harsh Mohan, Harrison, CMDT, Wintrobe's, Williams, Ackerman's & Sternberg

Best Pathology book with Image Based Questions from Recent Exams



Gobind Rai Garg
Sparsh Gupta

14th Edition

JAYPEE

Contents

Most Recent Questions with Explanations *xxi*

Concise Summary of Chapter 1 *xxxv*

1. **Cell Injury** 1
   Most Essential Topics: Necrosis, Apoptosis, Lipofuscin and Calcification★★
   Chapter Review *1*
   Multiple Choice Questions *12*
   Explanations *18*
   Most Recent Pattern Questions with Answer *23*

2. **Inflammation** 26
   Most Essential Topic: Wound healing★★
   Chapter Review *26*
   Multiple Choice Questions *40*
   Explanations *47*
   Most Recent Pattern Questions with Answer *54*

3. **Hemodynamics**★ 57
   Chapter Review *57*
   Multiple Choice Questions *64*
   Explanations *67*
   Most Recent Pattern Questions with Answer *70*

4. **Genetics** 71
   Most Essential Topics: Pedigree Analysis (JIPMER and AIIMS) and Non-classical Inheritance★★★
   Chapter Review *71*
   Multiple Choice Questions *86*
   Explanations *93*
   Most Recent Pattern Questions with Answer *102*

5. **Neoplasia** 105
   Most Essential Topics: Genes and Diagnosis of Tumors★★★
   Chapter Review *105*
   Multiple Choice Questions *123*
   Explanations *132*
   Most Recent Pattern Questions with Answer *143*

6. **Immunity** 145
   Most Essential Topics: Amyloidosis and Autoimmune Disorders★★★
   Chapter Review *145*
   Multiple Choice Questions *164*
   Explanations *175*
   Most Recent Pattern Questions with Answer *188*

7. Anemia and Red Blood Cells **193**
Most Essential Topic: Hemolytic Anemia★★
Chapter Review *193*
Multiple Choice Questions *210*
Explanations *219*
Most Recent Pattern Questions with Answer *230*

8. White Blood Cells **233**
Most Essential Topics: Leukemia and Lymphoma★★
Chapter Review *233*
Multiple Choice Questions *250*
Explanations *258*
Most Recent Pattern Questions with Answer *270*

9. Platelets and Blood Transfusion **274**
Most Essential Topics: Bleeding Disorders★★ Blood Transfusion★★★
Chapter Review *274*
Multiple Choice Questions *283*
Explanations *288*
Most Recent Pattern Questions with Answer *295*

10. Cardiovascular System★★ **299**
Chapter Review *299*
Multiple Choice Questions *316*
Explanations *323*
Most Recent Pattern Questions with Answer *330*

11. Respiratory System★★ **333**
Chapter Review *333*
Multiple Choice Questions *347*
Explanations *353*
Most Recent Pattern Questions with Answer *361*

12. Kidney and Urinary Bladder **363**
Most Essential Topics: Kidney Theory and Biopsy Findings★★★
Chapter Review *363*
Multiple Choice Questions *381*
Explanations *391*
Most Recent Pattern Questions with Answer *403*

13. Gastrointestinal Tract★★ **405**
Chapter Review *405*
Multiple Choice Questions *419*
Explanations *426*
Most Recent Pattern Questions with Answer *433*

14. Liver★★ **437**
Chapter Review *437*
Multiple Choice Questions *447*
Explanations *453*
Most Recent Pattern Questions with Answer *462*

15. Genital System and Breast 463
Most Essential Topics: Breast (Molecular Classification and Prognostic Factors)★★★
Chapter Review *463*
Multiple Choice Questions *481*
Explanations *485*
Most Recent Pattern Questions with Answer *491*

16. Central Nervous System 493
Most Essential Topic: Tumors★★★
Chapter Review *493*
Multiple Choice Questions *502*
Explanations *506*
Most Recent Pattern Questions with Answer *512*

17. Endocrine System 513
Most Essential Topics: Thyroid and Diabetes★★
Chapter Review *513*
Multiple Choice Questions *528*
Explanations *533*
Most Recent Pattern Questions with Answer *540*

18. Musculoskeletal System 541
Most Essential Topics: Skeletal Muscle Disorders and Bone★★
Chapter Review *541*
Multiple Choice Questions *546*
Explanations *549*
Most Recent Pattern Questions with Answer *554*

19. Miscellaneous★ 555
Chapter Review *555*
Multiple Choice Questions *558*
Explanations *561*

20. Important Stains and Bodies 566

Most Important ★★★
Very Important ★★
Important ★

CHAPTER

7

ANEMIA AND RED BLOOD CELLS

Golden Points

- Erythropoiesis in organs follows the sequence of yolk sac, liver and then bone marrow.
- Ratio of fat cells to hematopoietic cells in bone marrow: 1:1.
- Myeloid to erythroid ratio in bone marrow: 3:1 or 4:1.
- Ratio of fat cells to red cells (erythroid) in bone marrow: 4:1.
- Largest number of bone marrow cells: **Metamyelocytes**.
- Best indicator of anisocytosis: red cell distribution width.
- **Hereditary spherocytosis** is the only important anemia with **increased MCHC.**
- Not a feature of hemolytic anemia Increased heptoglobin (it is decreased). However, reduced haptoglobin level in hemolysis is masked by **bile duct obstruction**.
- **Biconcave shape** of RBC is due to **Spectrin**.
- Most common defect in hereditary spherocytosis is **Ankyrin** (most common) followed by ***Band 3*** (2nd MC). Others include defective spectrin and Band 4.2 (palladin).
- Test for increased osmotic fragility in Hereditary spherocytosis: **Pink test**.
- Most common cause of spherocytes: **Immune haemolytic anemia**.
- Young female with spherocytes, investigation to be done: Coomb's test (to rule out immune hemolytic anemia).
- **Bite cells** and **Heinz body** are seen in **G-6PD deficiency.**
- Sickle cell anemia is due to a Point mutation (and not deletion).
- Sickling is affected by: Concentration of HbS (most important), deoxygenation and pH, duration of deoxygenation in microcirculation.
- Best investigation for hemoglobinopathies is HPLC.
- On Hb electrophoresis: Hb**S** moves **S**lower than HbA towards positive electrode.
- Sickle cell trait provides pretection against: Falciparum malaria.
- Gamna Gandy bodies are seen in Sickle cell anemia, chronic myeloid leukemia and cirrhosis.
- Hb**E** is common in: **E**ast India (Bengal, Assam)
- Mutation in thalassemia: Mainly point mutation (missense mutation) causing aberrant splicing.
- HbA_2 is raised (>3·5%.) in thalassemia trait whereas HbF is highly raised in thalassemia major (Cooley's anemia).
- HbH disease is due to three alpha genes deletion whereas Barts Hb is due to four gene deletions.
- Hair on end (Crew cut appearance) appearance on skull x-ray: Thalassemia, SCA, HS, G6PD deficiency.
- Paroxysmal nocturnal hemoglobinuria is due to **Acquired defect** in red cell **PIG-A gene** leading to defective Glycosylphosphatidylinositol (GPI)- linked proteins. It is best diagnosed by **FLAER flow cytometry.** *(Ref. CMDT 2018)*
- M/C collagen vascular disorder causing Coomb's positive hemolytic anemia is **SLE** whereas the leukemia causing Coomb's positive test is **CLL**.
- Donath-Landsteiner antibody is seen in: Parxysmal cold hemoglobinuria.
- Important infection causing non-immune hemolytic anemia: Malaria.
- Drugs causing warm antibody hemolytic anemia: Methyldopa, qunidine, cephalosporins, penicillin.
- Findings of microangiopathic hemolytic anemia (MAHA): Fragmented RBCs (schistocytes), Burr cells, Helmet cells, Triangle cells. Causes of microangiopathic anemia are TTP, HUS, DIC and malignant hypertension. **Macroangiopathic** anemia is seen with **cardiac prosthetic valve.**
- Important causes of microcytic hypochromic anemia: Iron deficiency, sideroblastic anemia, thalassemia, anemia of chronic disease.
- Blood index which reflects iron deficiency more accurately: MCHC.
- Mentzer index < 13: Thalassemia minor whereas Mentzer index > 13 is seen in iron deficiency anemia.
- M/C anemia in chronic renal failure is Normocytic normochromic anemia.
- Sideroblastic anemia is having production of Ringed sideroblasts and its causes include collagen vascular disorders (SLE), lead (lead poisoning leads to Inhibition of enzymes involved in heme synthesis like ferrochelatase and aminolevulinic acid dehydratase), porphyria, myelofibrosis, iron overload, alcoholism, myelodysplasia.
- Triad of megaloblastic anemia: **Oval macrocytes (earliest finding)**, hypersegmented neutrophils, Howell-Jolly bodies.

- MCHC is **Not increased** in megaloblastic anemia.
- False positive Schilling test: Renal insufficiency.
- Copper deficiency causes: **normocytic hypochromic** anemia
- Aplastic anemia is characterized by pancytopenia and absence of splenomegaly.
- Most common cause of Howell-Jolly bodies: Splenectomy.
- **Cabot ring** is seen in: **Megaloblastic anemia** (most common), lead poisoning (2nd MC), hemolytic anemia, thalassemia, myelodysplastic syndrome and postsplenectomy.
- Types of anemia in lead poisoning: Microcytic hypochromic (with reticulocytosis, basophilic stippling, target cells), sideroblastic anemia, hemolytic anemia.
- Blood group antigens are not found in: CSF.
- Feature of Swachman-Diamond syndrome: Pancreatic insufficiency; bone marrow dysfunc- tion; neutropenia; short stature; skeletal abnormalities.
- Best method for hemoglobin estimation: Cyanmethemoglobin method.
- Stain used for reticulocytes: Supravital stains (methylene blue and Brilliant cresyl blue).
- Conditions protecting against falciparum malaria: G-6PD deficiency, pyruvate kinase deficiency, sickle cell trait, beta thalassemia trait and HbC.

Hematology is the study of the various cells and components of the blood. Hematopoiesis is the process of production of blood cells which primarily takes place in the following organs:

Sites of Hematopoiesis

Till **3rd week** of intrauterine life: Yolk sac.
By **3rd month** of intrauterine life: **Liver** is the main site of blood formation.

At **4th month** of intrauterine life: **Bone marrow** is the main site of hematopoiesis.

Finally **by birth**, the **bone marrow** in whole of the skeleton is hematopoietically active and is the chief source of blood cells and it remains so till puberty.

After puberty, the **red marrow** is present in vertebrae, ribs, sternum, skull, pelvis and proximal epiphyseal regions of humerus and femur.

SALIENT FEATURES OF BONE MARROW

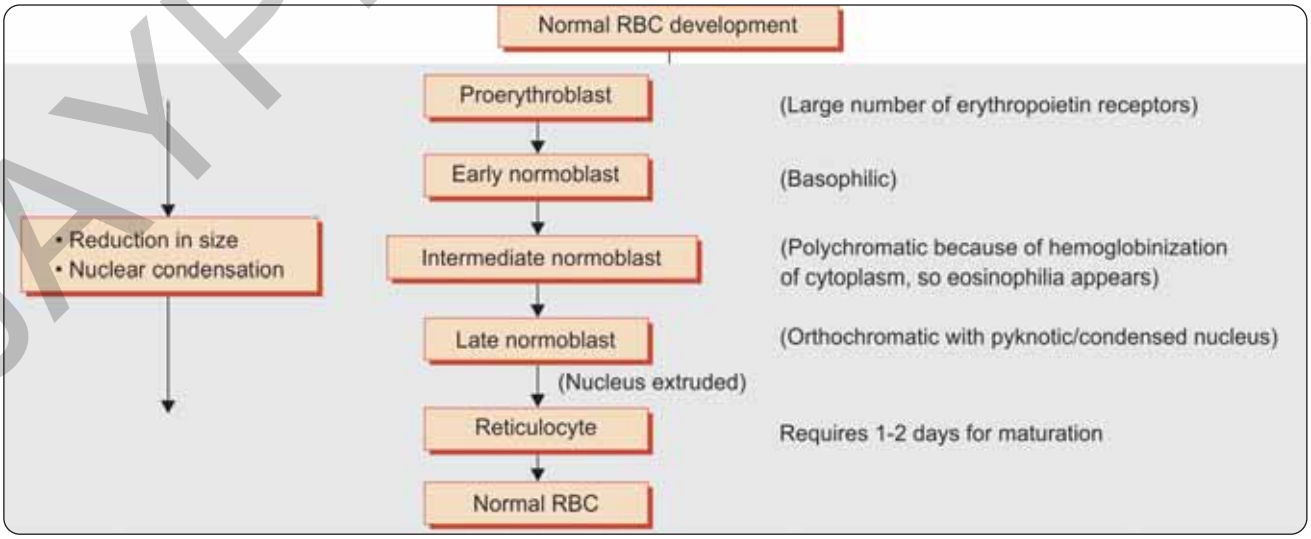
- The ratio of the fat cells and the hematopoeitic cells in an adult is 1:1. The number of the myeloid cells is more than the number of the erythroid cells (normal M:E ratio is 3 to 15:1).
- The investigations for the information about bone marrow are bone marrow aspiration and bone marrow biopsy.

Hematopoietic stem cells are pluripotent stem cells which are *CD34+ cells*. They give rise to the trilineage myeloid cells, lymphoblasts and monoblasts. The trilineage myeloid cell gives rise to the following three cells:

- Normoblast (Gives rise to RBCs)
- Myeloblast (Gives rise to neutrophils, eosinophils and basophils)
- Megakaryocyte (Gives rise to platelets).

Monoblast gives rise to monocytes whereas lymphoblast gives rise to lymphocytes.

Stages of Erythropoiesis



Recent Exam Question

First detection of hemoglobin
- By ***electron microscope***: ***Proerythroblast***
- By **giemsa** (routine) **stain**: **intermediate normoblast**

General Information About RBCs

The normal red cell is biconcave in shape and has a diameter of 7-8 mm. The cytoskeleton of the RBC is made up of proteins like spectrin, ankyrin, band 2.1, band 3, band 4.1, etc. that provide deformability to the RBCs so that they can cross through tiny blood vessels like capillaries. Importance of these proteins can be appreciated in disorders like hereditary spherocytosis. When the RBCs are of unequal size, this is referred to as *anisocytosis* and when of different shapes, it is called *poikilocytosis*.

Recent Exam Question

Spectrin is the chief protein responsible for **biconcave shape** of normal red blood cell.

- **Reticulocytes** are nonnucleated spherical cells bigger than normal RBCs and are polychromatic (having a blue color) due to the presence of free ribosomes and RNA.
- **Reticulocyte count:** Percentage of reticulocytes among the red cells present in the peripheral blood is called reticulocyte count. Normal value is around 1.5% in adults and 1.7% in the cord blood cells.

Key Point

The **reticulocyte count** is an *indicator of erythropoietic activity* of the bone marrow.

- **Absolute reticulocyte count (ARC):** Number of reticulocytes present in 1 mm^3 of blood.
  ARC = (Reticulocyte %) × Erythrocyte Count/100.
- **Reticulocyte Index (RI):** It adjusts reticulocyte count for hematocrit. It reflects bone marrow activity and is also known as *"Poor man's Bone Marrow Aspirate"*. Normal reticulocyte index is 1-3%.

RI = Reticulocyte Count × (Hb/Age and sex adjusted normal Hb level).

Table 1: Conditions affecting reticulocyte count.

Reticulocytosis (Increased RBC production)	*Reticulocytopenia (Decreased RBC production)*
Criteria Reticulocyte Index > 3% Reticulocyte Count > 1.5%	**Criteria** Reticulocyte Index < 1% Reticulocyte Count < 0.5%
Conditions • Acute blood loss or hemorrhage • Postsplenectomy • Microangiopathic Anemia • Autoimmune Hemolytic Anemia • Hemoglobinopathy (Sickle cell anemia and Thalassemia) • **Post anemia Treatment** like Folate Supplementation, Iron Supplementation and vitamin B_{12} Supplementation.	**Conditions** • Aplastic anemia • Bone marrow infiltration • Bone marrow suppression (Sepsis/Chemotherapy radiotherapy) • Blood transfusion • Liver disease • Disordered RBC maturation (Iron, B_{12}, Folate Deficiency, Hypothyroidism, Sideroblastic Anemia or Anemia of Chronic Disease)

ANEMIAS

Anemia is defined as any reduction below normal limits of the total circulating red cell mass which is characterized by the clinical features of pallor of skin and nails, dizziness, palpitations, lethargy and fatigue.

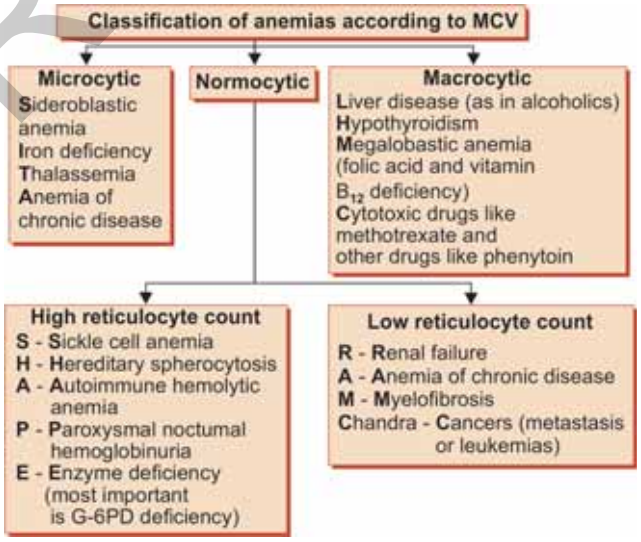
Some of the important terms used in context of anemias are as follows:

Recent Exam Question
- MCV **< 80** fl: **Microcytic** RBC.
- MCV **> *100*** fl: ***Macrocytic*** RBC.

Key Point

RDW (Red cell distribution width): is an indicator of **anisocytosis.** Its normal value is 11.5-14.5.

- **MCV (Mean cell volume):** It is the average volume (in femtolitres) of a red blood cell (normal value is 82-96 fl).
- **MCH (Mean corpuscular hemoglobin):** Average mass of hemoglobin (in picograms) per red blood cell is MCH. *Normal value is 27-33 pg.*
- **MCHC (Mean corpuscular hemoglobin concentration):** MCHC is average concentration of hemoglobin in a given volume of packed red blood cells. *Normal value is 33-37g/dL.*
- Normal RBCs have *central pallor of around a third of the diameter* (normochromic). If the color is decreased which means pallor more than one-third, the RBCs are called *hypochromic* and if color is increased (central pallor is lost), the RBCs are called *hyperchromic.*



Anemia can be caused by blood loss, reduced red cell production and excessive red cell destruction.

A. BLOOD LOSS

Blood loss causes decrease in hematocrit resulting in compensatory increased release of erythropoietin from the renal juxtaglomerular cells. Erythropoietin stimulates increased bone marrow activity. However, the *earliest change* in the peripheral blood is *leucocytosis* (caused by increased mobilization from the marginal pools) followed by reticulocytosis and thrombocytosis. Chronic blood loss is usually due to GIT lesions and gynecological disturbances.

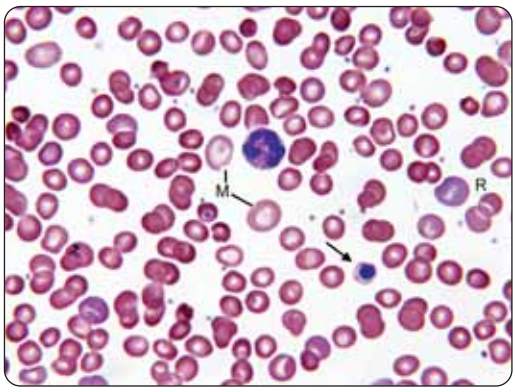
Key Point

Earliest change in the peripheral blood after acute blood loss is **leucocytosis** followed by reticulocytosis and thrombocytosis.

B. IMPAIRED RBC PRODUCTION

1. DUE TO DECREASED ERYTHROPOIESIS

This category of anemias may result from the defective DNA synthesis due to vitamin B_{12} or folic acid deficiency (called megaloblastic anemia) or impaired heme synthesis due to iron deficiency.



Megaloblastic anemia.

a. Megaloblastic Anemia

The chief feature in this anemia is impaired DNA synthesis resulting in delayed mitosis while RNA and protein synthesis is not impaired. This leads to *nuclear/cytoplasmic asynchrony* which affects all proliferating cell lines particularly cells of bone marrow and GIT cells. The chief findings are a *hypercellular bone marrow* with megaloblasts in the bone marrow along with presence of abnormal granulocytic precursors (*giant metamyelocyte and band forms*) and *large megakaryocytes* with bizarre multilobated nuclei. The presence of *ineffective erythropoiesis* can result in *pancytopenia* associated with features of hemolytic anemia including jaundice and increased levels of serum bilirubin and LDH enzyme. In the peripheral smear, there is pancytopenia with presence of macrocytes (RBCs having MCV >100 fl) lacking a central pallor. There is characteristically presence of **large and hypersegmented neutrophils** (neutrophils having **> 5 lobes**). The *earliest manifestation* of megaloblastic anemia is *presence of hypersegmented neutrophils*. **Diagnosis is made if even a single neutrophil with ≥ 6 lobes is seen or > 5% neutrophils with 5 lobes are seen.**

Concept

- **Triad** of megaloblastic anemia includes **oval macrocytes, Howell Jolly bodies and hypersegmented neutrophils**.
- MCHC is **not elevated** because hemoglobin increases proportionately to the increased volume of the RBCs.

Key Point

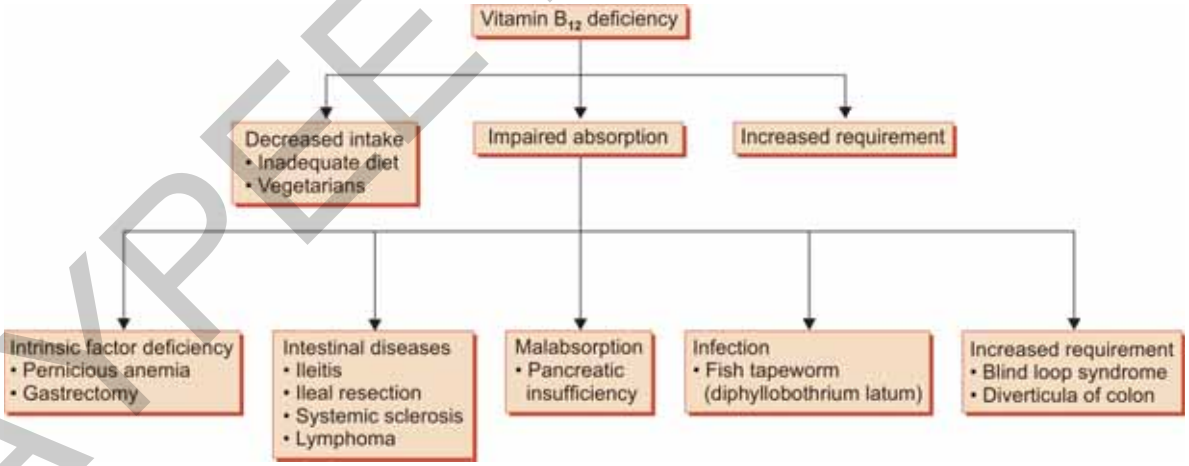
Earliest manifestation of megaloblastic anemia is presence of **macro-ovalocytosis**.

The two main causes of this anemia are vitamin B_{12} and folic acid deficiency.

(*i*) Vitamin B_{12} deficiency

Normal vitamin B_{12} metabolism

The vitamin B_{12} (or cobalamin) is present in the bound form (bound with dietary proteins) in the diet. It is freed by the action of pepsin in stomach and then binds with salivary proteins called *R-binders* (also known as cobalaphilins). In the duodenum, this cobalamin-cobalaphilin complex is broken by the action of pancreatic proteases. Free cobalamin now binds with the intrinsic factor (*Castle's factor*) secreted from the parietal cells of the stomach. Vitamin B_{12}-intrinsic factor complex is *taken by the ileal enterocytes*. Within the intestinal cells, the cobalamin gets bound with a transport protein called transcobalamin II which delivers it to the rapidly proliferating cells of the body (bone marrow and GIT cells). So, the causes of vitamin B_{12} deficiency can be:



Key Point

Vitamin B_{12}-intrinsic factor complex is taken by the **ileal enterocytes**.

Recent Exam Question

- **Diphyllobothrium latum** is associated with megaloblastic anemia[Q]
- *Ankylostoma duodenale* is associated with *iron deficiency anemia*[Q]

Pernicious anemia

It is an autoimmune disorder against parietal cells of the stomach by auto-reactive T cells resulting in chronic atrophic gastritis and parietal cells loss (responsible for decreased intrinsic factor production). The antibodies which are present in the patients are:

- Type I antibodies[Q] **(most common)**: Block binding of vitamin B_{12} to IF (in 75% patients).
- Type II antibodies: Prevent cobalamin-IF binding with ileal receptors.
- Type III antibodies: formed against the a and b subunits of gastric proton pump (seen in 90% patients but not specific as it also seen in idiopathic chronic gastritis).

It is also associated with other autoimmune disorders like autoimmune thyroiditis and adrenalitis.

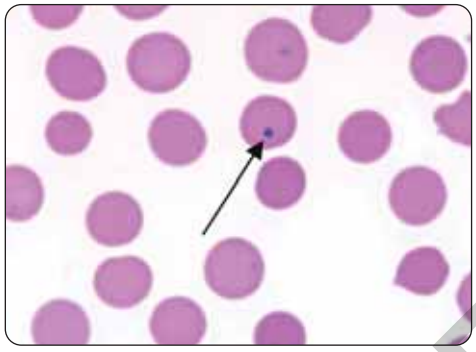
Concept

Vitamin B_{12}
- It is required for the conversion of ***homocysteine to methionine***.
- It is also involved in the conversion of **methylmalonyl CoA to succinyl CoA** which is required for the formation of normal neuronal lipids. So, any deficiency of vitamin B_{12} results in neurological features.
- **Pernicious anemia** is associated with increased risk of **gastric cancer** and increased chances of **atherosclerosis** and **thrombosis** (because of elevated homocysteine levels).

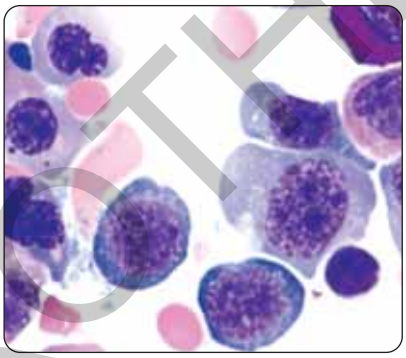
Morphology

The principal organs affected are the bone marrow, GIT and CNS which show the following features:

Bone marrow
Megaloblasts, hypersegmented neutrophils and precursors of granulocytes along with megakaryocytes are seen. Megaloblasts with sieve like chromatin are seen due to nuclear cytoplasmic asynchrony.
GIT
There is presence of shiny and ***"beefy" tongue*** due to atrophic glossitis, almost complete loss of parietal cells and replacement of gastric mucosa by mucus secreting goblet cells ***(intestinalization)***.
CNS
The combined involvement of the axons in the ascending tracts of posterior column and the ***descending pyramidal tract*** is a characteristic feature of vitamin B12 deficiency giving the term as **subacute combined degeneration of the spinal cord**.



Howell Jolly body representing **basophilic nuclear remnants (clusters of DNA)** in circulating erythrocytes.



Megaloblasts with **sieve-like chromatin** due to nuclear cytoplasmic asynchrony.

Clinical Features

They are as follows:
- Megaloblastic anemia
- Pancytopenia (Leucopenia with hypersegmented neutrophils, thrombocytopenia)
- Jaundice due to ineffective hematopoiesis and peripheral hemolysis
- Neurological features due to posterolateral spinal tract involvement.

Key Point

Schilling test: It is performed to distinguish between different causes of vitamin B_{12} deficiency. It is **not used** for the diagnosis of vitamin B_{12} deficiency.

Laboratory Tests

- Serum antibodies against intrinsic factor are present.
- *Achlorhydria even after histamine stimulation*.
- Increased serum levels of methylmalonic acid and homocysteine.
- **Schilling test:** It is performed to distinguish between different causes of vitamin B_{12} deficiency.

Recent Exam Question

- Gene for **reduced folate transporter** is present on **chromosome 21q**.
- Megaloblastic anemia caused due to folic acid deficiency is **NOT** associated with neuro-logical abnormalities.

(*ii*) *Folic acid deficiency*

Megaloblastic anemia caused due to folic acid deficiency is clinically indistinguishable from vitamin B_{12} deficiency anemia. However, folic acid deficiency is **NOT** associated with neurological abnormalities.

b. Due to defective hemoglobin synthesis

(*i*) ***Iron deficiency***

It is the *commonest cause of anemia worldwide.*

Normal iron metabolism

The metabolism of iron can be divided in the following headings:

Absorption

Iron is present in two forms in the food: heme and nonheme iron. The iron is absorbed more completely from the heme form (present in the nonvegetarian food) as compared to nonheme form. The factors affecting absorption of iron include:

Factors increasing absorption	Factors decreasing absorption
• Ferrous form (Fe^{2+}) • Acid (HCl) in the stomach • Ascorbic acid • Amino acid and sugars in the food • Iron deficiency • Physiological conditions (pregnancy and hypoxia)	• Ferric form (Fe^{3+}) • Achlorhydria (absence of HCl secretion) • Alkaline food (pancreatic secretions) • Phytates, tannates and phosphates in diet • Iron overload • Tetracyclines and EDTA • Inflammatory disorders

Iron is *absorbed primarily from the duodenum* in the ferrous form. It is transported inside the enterocytes by an apical transporter called DMT1 (Divalent Metal Transporter 1) and from here, it enters the plasma by two basal membrane transporters **(ferroportin and hephaestin)**. A fraction of ferrous iron gets converted into ferric state by intracellular oxidation. Most of the iron absorbed from the gut is lost because of mucosal lining shedding whereas in increased requirements it is absorbed in a greater percentage.

Concept

A regulatory protein called **hepcidin** regulates the absorption of iron from the gut. In case of iron depletion the level of this negative regulatory protein is decreased thereby increasing the absorption of iron and vice versa. **Mutation** of the gene coding for hepcidin is implicated in the causation of **hemochromatosis.**

Recent Exam Question

- ***Hepcidin*** is the **master regulator** of ***human iron metabolism.***
- **Iron** is absorbed primarily from the **duodenum** in the **ferrous** form.

Transport and storage of iron

From the enterocytes, the absorbed iron is transferred to a plasma protein called **transferrin** that delivers it to different cells of the body expressing high levels of transferrin receptors on their surface. These cells include *hepatocytes and the developing erythroblasts* in the bone marrow. The serum transferrin saturation is an indicator of serum iron concentration. Normally, transferrin is 33% saturated (one-third saturation) with iron. Since, the serum transferrin concentration is nearly 300-350 µg/dL (also called as total iron binding capacity or TIBC), the normal serum iron levels are in the range of 100-120 µg/dL. The iron which is not immediately required by the cells is stored in the form of **ferritin** which is a protein iron complex present in all the tissues especially liver, spleen and bone marrow. It is the *ferric form of iron which is present in ferritin*. A small amount of ferritin is also present in the plasma which is derived from the storage pools of the body iron; so, **serum ferritin is an indicator of body iron stores**. Intracellular iron is converted into hemosiderin which stains positively with potassium ferrocyanide giving a positive Prussian blue stain.

Key Point

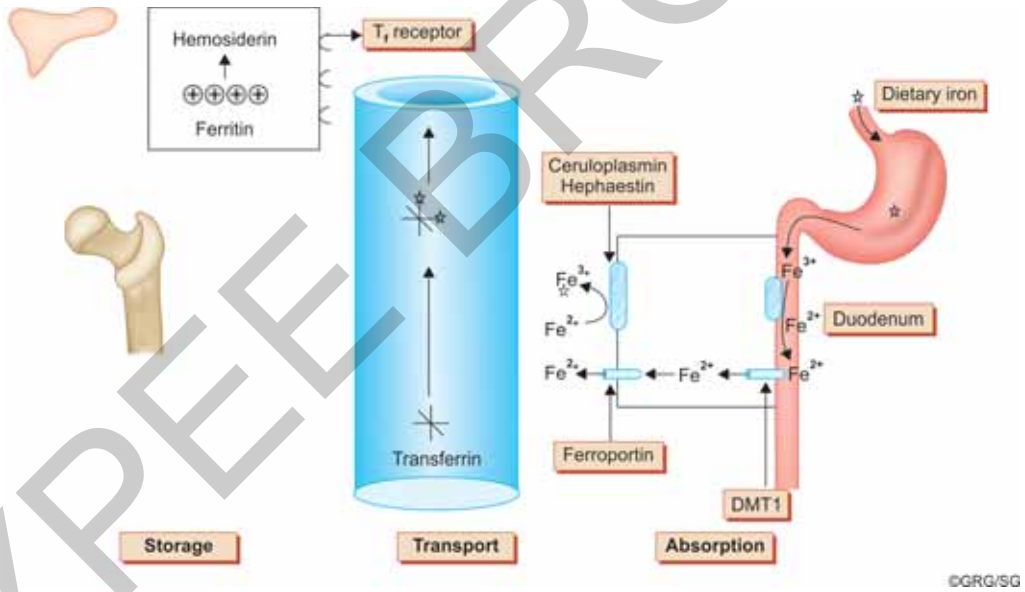
Absorbed iron is transferred to a plasma protein called transferrin.

Recent Exam Question

Each molecule of **transferrin** can transport **two** molecules of iron to the desired areas.

The normal requirement of iron in the diet is nearly 1 mg/dL. The causes of iron deficiency anemia include the following:

Dietary lack	Impaired absorption	Increased requirement	Chronic blood loss
• Infants • Children • Low socio-economic status • Elderly	• Steatorrhea • Sprue • Chronic diarrhea • Gastrectomy	• Growing infants and children • Pregnant females • Premenopausal women	• GIT (peptic ulcer, gastric cancer, hemorrhoids, hookworm disease) • Urinary tract (renal, pelvic or bladder cancers) • Genital tract (uterine cancer, menorrhagia)



Normal iron metabolism.

FEATURES OF IRON DEFICIENCY ANEMIA

It is characterized by the following stages:

Stage I or stage of negative iron balance

This is a stage characterized by decreased amount of storage iron manifesting as decreased serum ferritin concentration and reduced amount of bone marrow iron staining with Prussian blue stain. *The serum iron and red cell protoporphyrin levels are absolutely normal*. Though TIBC is marginally increased, the *red cell indices and morphology are normal*.

Stage II or stage of iron deficient erythropoiesis

This is a stage of reduced circulating iron in addition to decrease storage form of iron. So, this stage is characterized by deficient iron stores, *reduced serum ferritin, decreased % saturation of serum transferrin and increased TIBC*. The *red cell morphology is normal*.

Stage III or stage of iron deficiency anemia

It is characterized by all features of stage II and in addition *abnormal morphology of the red cells*, i.e. the presence of microcytic and hypochromic cells.

Recent Exam Question

Most of the body's iron is contained in **hemoglobin** and *not ferritin*.

Clinical features include fatigue, impaired growth and development, pica (eating noedible substances like mud, etc. in children), koilonychia (angular or spoon shaped nails), angular stomatitis (ulceration at the angle of mouth), dysphagia (as in Plummer Vinson syndrome) and palpitations (because of hyperdynamic circulation which can even precipitate congestive heart failure).

Peripheral blood

Microcytic and hypochromic red cells with slight reticulocytosis whereas TLC is normal. Usually, microcytosis is seen before appearance of hypochromia. Poikilocytosis is seen in form of small and elongated red cells called *pencil cells.* It is also characteristic feature of this disease. There is increased red cell distribution width also.

Bone marrow

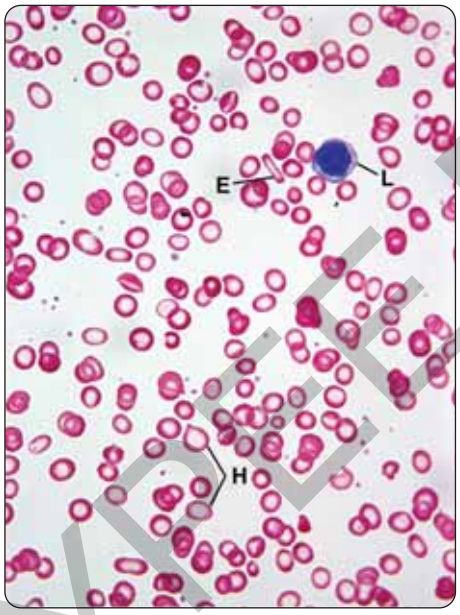
Hypercellular bone marrow (having increased erythroid progenitors) with depleted bone marrow iron stores. There is presence of ***micro-normoblasts***.

Additional findings

- **Serum** *ferritin and serum iron are decreased whereas serum transferrin and TIBC are increased*.
- **Red cell protoporphyrin levels** *are increased* because there is decrease in the availability of heme (due to reduced iron availability) resulting in elevated free erythrocytic protoporphyrin levels. RBC free protoporphyrin is normally 30-50 µg/dL whereas its value reaches > 200 µg/dL in iron deficiency anemia.

Key Point

Serum ferritin is an *indicator* of body **iron stores**.



Iron deficiency anemia.
(H: Hypochromic cell; E: Elliptocyte)

Key Point

The normal requirement of iron in the diet is nearly **1 mg/d**.

The treatment of anemia is with the help of either oral or parenteral iron therapy the response of which is clinically assessed with improvement in symptoms and increase in the reticulocyte count on **about** 8th–9th **day**.

Recent Exam Question

In the bone marrow, **Micronormoblasts** are present with persistent basophilia.

Differential diagnosis of microcytic hypochromic anemia

Tests	Iron deficiency	Inflammation	Thalassemia	Sideroblastic anemia
Peripheral smear	Micro/hypo	Normal micro/hypo	Micro/hypo with targeting	Variable
SI	< 30	< 50	Normal to high	Normal to high
TIBC	> 360	< 300	Normal	Normal
Percent TS	< 10	10-20	30-80	30-80
Ferritin (mcg/L)	< 15	30-200	50-300	50-300
Hemoglobin pattern	Normal	Normal	Abnormal	Normal

SI, serum iron; TIBC, total iron-binding capacity; TS, transferrin saturation.

(*ii*) **Thalassemia**

It is discussed in detail with other hemolytic diseases.

There are many indices to differentiate between iron deficiency anemia (IDA) and beta-thalassemia (BT): Two examples include:

Mnemonic

TIBC levels at
Top = **I**ron deficiency (In iron deficiency anemia, TIBC is raised)
Bottom = **C**hronic disease (In Anemia of Chronic Disease, TIBC is low).

Index	Formula	Value for Iron deficiency anemia	Value for beta-thalassemia
Mentzer index	MCV/RBC count	> 13	< 13
Srivastava index	MCH/RBC	> 3.8	< 3.8

a. **Miscellaneous**

(i) **Anemia of Chronic Disease (AOCD)**

It is characterized by the *decreased utilization of iron* from the storage from of iron, i.e. ferritin. In chronic inflammatory conditions, there is increased secretion of cytokines like IL-1, TNF, IFN-γ, etc. that cause release of the ***protein hepcidin***[Q] because of which release of iron from the storage pool is inhibited. This result in the high serum ferritin levels, reduced TIBC, reduced % transferrin saturation and decreased serum iron levels.

Recent Exam Question

AOCD causes **normocytic normochromic** anemia **more commonly** but may also lead to microcytic hypochromic anemia (less commonly).

Recent Exam Question

- Anemia of chronic disease is caused by **hepcidin.**
- **Hepcidin inhibits ferroportin** to reduce the utilization of iron.

- In the **peripheral blood smear** there is presence of microcytic and hypochromic red cells.
- In the **bone marrow** there is absence of hypercellularity because of inhibition of erythropoetin secretion by renal cells due to the action of cytokines like IL-1, etc.
- Common clinical conditions having AOCD include diseases like rheumatoid arthritis, regional enteritis, osteomyelitis, lung abscess and cancers like Hodgkin's lymphoma, carcinomas of breast and lung.

Concept

Anemia of chronic disease is differentiated from iron deficiency anemia morphologically by the fact that **microcytosis follows hypochromia** *(microcytosis precedes hypochromia in IDA)*.

Mnemonic

During a chronic inflammation (microbial or RA)… the microbes want iron, so our body reacts by locking all of its iron within the macrophages and loosing the key.
The good news is that the microbe does not get any iron… However, the bad news is that our body doesn't get iron either, which reduces the amount of heme (no iron, no heme), which reduces the amount of hemoglobin. hence, microcytic anemia.

(*ii*) **Anemia due to marrow infiltration**

This type of anemia is caused due to *infiltration of the bone marrow* resulting in *myelophthisic anemia.* It is characterized by presence of immature erythroid and myeloid precursors in the blood (this is called as leukoerythroblastosis). Metastasis from cancers like breast, lung and prostate are the most common cause of marrow infiltration.

Recent Exam Question

Leukoerythroblastosis and **tear drop RBCs** are seen with **bone marrow infiltration** which is most commonly caused by **metastasis.**

(*iii*) **Sideroblastic anemia**

Sideroblastic anemia is characterized by the *presence of ringed sideroblasts.* These are normoblasts having pin point iron granules (easily demonstrable with the help of Prussian blue dye) in the cytoplasm or perinuclear region. Sideroblastic anemia can be *hereditary* (due to decreased ALA synthase activity) *or acquired* (secondary to leukemias, myelodysplastic syndrome, alcoholism, copper deficiency, pyridoxine deficiency or lead poisoning). The pathogenesis of the diseases involves defective heme synthesis resulting in ineffective erythropoiesis which thereby contributes to iron overload.

Key Point

- **Sideroblastic anemia** is characterized by the presence of **ringed sideroblasts**.
- There is **increase** in serum **iron**, serum **ferritin**, % **transferrin saturation** and free erythrocyte porphyrin whereas ***TIBC is decreased***.

  – Peripheral smear is characterized by presence of *microcytic hypochromic cells* which also demonstrate the presence of anisopoikilocytosis. There is *increase in serum iron, serum ferritin, % transferrin saturation and free erythrocyte porphyrin whereas TIBC is decreased.*

NOTE

Abnormal sideroblasts are also seen in *thalassemia, megaloblastic anemia and hemolytic anemias.*

2. DUE TO DECREASED STEM CELLS PROLIFERATION

a. **Aplastic anemia**

This is a disorder characterized by marrow failure associated with pancytopenia (anemia, thrombocytopenia and leukopenia). The causes are:

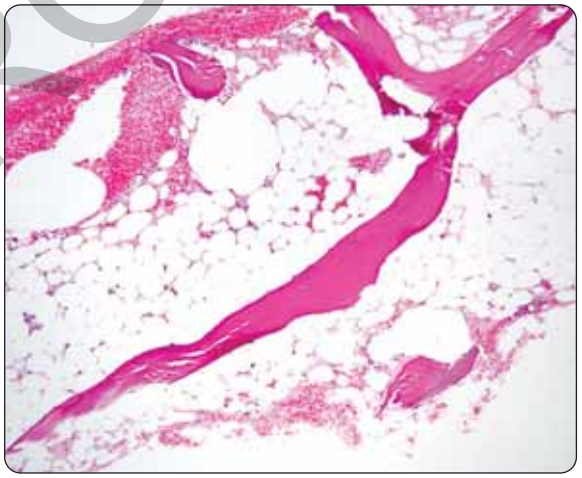
Acquired	Inherited
• Primary stem cell defect • Irradiation • Viral infections [hepatitis (non A, non B , non C, non G), CMV, EBV, varicella zoster virus] • Chemical agents (alkylating agents, antimetabolites, benzene, chloramphenicol, phenylbutazone, arsenicals, insecticides like DDT, parathion)	Fanconi anemia

Recent Exam Question

- **Fanconi anemia** is the most important **inherited** cause of **aplastic anemia**.
- **Bone marrow aspiration** in aplastic anemia reveals **"dry tap"**.

It has been postulated that the etiological agents cause alteration in the stem cells thereby activating the T cells of the body against them resulting in destruction of the stem cells contributing to the pancytopenia.

The **bone marrow** biopsy shows it is characteristically hypocellular being replaced by fat cells (in contrast to aleukemic leukemia and myelodysplastic syndrome in which we have pancytopenia associated with hypercellular marrow) whereas *bone marrow aspiration reveals "dry tap".*



Aplastic anemia.
(Fat cells replace hematopoietic cells in bone marrow)

Clinical features are caused because of anemia (pallor, weakness and dyspnea), thrombocytopenia (petechiae) and neutropenia (recurrent infections). *Red cells are normocytic and normochromic.*

Concept

Characteristically, ***splenomegaly is absent and reticulocytopenia is the rule*** in aplastic anemia.

It is treated with either bone marrow transplantation (in young patients) or antithymocyte globulin (in old patients).

b. **Anemia of chronic disease (**has been discussed above)

c. **Anemia of renal failure**

It is characterized by inadequate release of erythropoetin resulting in development of anemia. The other contributory factors are:

– Iron deficiency secondary to increased bleeding tendency (seen in uremia)
– Extracorpuscular defect induced hemolysis

MULTIPLE CHOICE QUESTIONS

RBC: GENERAL ASPECTS

1. Which of the following is associated with an intrinsic defect in the RBC membrane? *(AIIMS May 2012)*
(a) Autoimmune hemolytic anemia
(b) Hereditary spherocytosis
(c) Microangiopathic haemolytic anemia
(d) Thermal injury causing anemia

2. Which of the following is not a stem cell of the bone marrow? *(AI 2012)*
(a) Lymphoblast (b) Myeloblast
(c) Myoblast (d) Normoblast

3. Which of the following surface glycoproteins is most often expressed in human hematopoietic stem cell? *(AIIMS May 2008)*
(a) CD 22 (b) CD 40
(c) CD 15 (d) CD 34

4. Reticulocytosis is seen in all *except*: *(AIIMS May 2007)*
(a) P.N.H.
(b) Hemolysis
(c) Nutritional anemia
(d) Dyserythropoietic syndrome

5. Which of these are seen on Romanowsky stain? *(PGI Dec 2004)*
(a) Reticulocytes
(b) Basophilic stippling
(c) Heinz bodies
(d) Howell-Jolly bodies
(e) Cabot ring

6. Which of the following surface glycoproteins is most often expressed in human hematopoietic stem cell? *(Delhi PG 2010)*
(a) CD22 (b) CD40
(c) CD15 (d) CD34

7. Inappropriate erythropoietin level is found in all *except*: *(UP 2001)*
(a) Renal cell carcinoma
(b) Lung disease
(c) High altitude
(d) Benign liver tumor

8. The size of the red blood cells is measured by: *(UP 2007)*
(a) MCV (b) MCHC
(c) ESR (d) MCH

Most Recent Questions

9. Anemia which is associated with pancytopenia is:
(a) Hemolytic (c) Megaloblastic
(b) Iron deficiency (d) All

10. Hematuria with dysmorphic RBCs are seen in:
(a) Acute glomerulonephritis
(b) Renal TB
(c) Renal calculi
(d) Chronic renal failure

11. MCHC is increased in:
(a) Iron deficiency anemia
(b) Spherocytosis
(c) Thalassemia
(d) All

12. In polycythemia vera, all are raised *except*:
(a) Hematocrit
(b) Platelet count
(c) RBCs
(d) Erythropoietin

13. The type of anemia seen in chronic renal failure is:
(a) Microcytic
(b) Normocytic
(c) Macrocytic
(d) All of the above

14. Burr cell is seen in:
(a) Uremia
(b) Hepatocellular carcinoma
(c) Gastric carcinoma
(d) Ovarian carcinoma

15. Acanthocytes are seen in:
(a) Abetalipoproteinemia
(b) Hartnup disease
(c) Whipple disease
(d) None

16. Reticulocytes are stained with:
(a) Methyl violet
(b) Brilliant Cresyl blue
(c) Sudan black
(d) Indigo carmine

17. Storage form of iron:
(a) Ferritin
(b) Transferrin
(c) Hepcidin
(d) Ferroportin

18. Hb is a good buffer because of:
(a) Histidine residues
(b) Protein nature
(c) Acidic nature
(d) Iron molecule

19. Normal platelet count is found in:
(a) Wiskott Aldrich syndrome
(b) Henoch Schonlein purpura
(c) Immune thrombocytopenia
(d) Dengue fever

20. In an adult man, there is about how much grams of hemoglobin in the circulating blood?
(a) 350 (b) 500
(c) 900 (d) 1000

21. The longest living WBC is which one of the following?
(a) Lymphocyte (b) Eosinophil
(c) Neutrophil (d) Monocyte

22. Freezing point of normal human plasma is:
(a) 4°C (b) 0°C
(c) –0.54°C (d) –1.54°C

23. The normal albumin: globulin (A/G) ratio blood is:
(a) 5:1 (b) 2:1
(c) 1:2 (d) 1:1

24. Thrombosthenin is:
(a) Coagulation protein
(b) Contractile protein
(c) Thrombus inhibiting protein
(d) Protein for platelet production

25. The best method for estimation of hemoglobin concentration in blood is:
(a) Acid hematin method
(b) Alkali hematin method
(c) Cyanmethemoglobin method
(d) Any of the above

26. The number of Fe^{2+} atoms in one Hb molecule:
(a) 1 (b) 2
(c) 4 (d) 8

27. Linzenmeyer is used to measure:
(a) Bleeding time
(b) Clotting time
(c) Prothrombin time
(d) ESR

28. Serum contains all the clotting factors *except*:
(a) Plasma thromboplastin
(b) Labile factor
(c) Hageman factor
(d) Christmas factor

29. Progenitor hematopoetic stem cells originate in which of the following?
(a) Bone marrow
(b) Thymus
(c) Lymph node
(d) Spleen

30. Haematocrit is the ratio of:
(a) WBC to whole blood
(b) Platelets to whole blood
(c) RBCs to whole blood
(d) Total blood cells to plasma

31 The anaemia associated with leukaemia is:
(a) Iron deficiency
(b) Megaloblastic type
(c) Myelophthisic type
(d) None of the above

32. Which of the following is a distinguishing feature of reticulocyte?
(a) Constitute 10% of the red cells
(b) No nucleus
(c) Smaller in the size than RBCs
(d) Mature in lymph nodes

33. Life span of RBCs in infant is:
(a) 100–120 days
(b) 60–80 days
(c) 80–100 days
(d) 40–60 days

34. Increase in MCHC is associated with:
(a) Iron deficiency anemia
(b) Megaloblastic anemia
(c) Anemia of chronic disease
(d) Hereditary spherocytosis

35. MCHC criteria to diagnose iron deficiency anemia:
(a) <32 (b) <34
(c) <28 (d) <30

MEGALOBLASTIC ANEMIA, APLASTIC ANEMIA

36. Which of these does not indicate megaloblastic anemia? *(AIIMS Nov 2012)*
(a) Increased reticulocyte count
(b) Raised Bilirubin
(c) Mild splenomegaly
(d) Nucleated RBC

37. A patient with Hb-6 gm%, TLC 1200, platelet-60,000, MCV 12 fl, what is the diagnosis? *(AIIMS May 2008)*
(a) Aplastic anemia
(b) Megaloblastic anemia
(c) PNH
(d) Myelofibrosis

38. Macrocytosis in complete blood count can be diagnosed by: *(PGI Dec 2006)*
(a) ↑ MCV
(b) ↑ MCHC
(c) ↑ Hematocrit
(d) ↑ Red cell distribution width

39. Which is the true statement regarding megaloblastic anemia? *(PGI Dec 01)*
(a) Megaloblastic precursors are present in bone marrow
(b) Mean corpuscular volume is increased
(c) Serum LDH is increased
(d) Thrombocytosis occurs
(e) Target cells are found

40. Macrocytic anemia may be seen in all of these *except*: *(PGI June 2002)*
(a) Liver disease
(b) Copper deficiency
(c) Thiamine deficiency
(d) Vitamin B_{12} deficiency
(e) Orotic aciduria

41. Causes of vitamin B_{12} deficiency megaloblastic anemia are: *(PGI June 2005)*
(a) Fish tap worm infestation
(b) Dilantin therapy
(c) Gastrectomy
(d) Ileal resection
(e) Methotrexate

42. Aplastic anemia can progress to all *except*: *(Delhi PG 2010)*
(a) AML
(b) Myelodysplastic anemia
(c) Pure red cell aplasia
(d) Paroxysmal nocturnal hemoglobinuria

43. Serum vitamin B_{12} level is increased in all *except*: *(UP 2000)*
(a) Hepatitis
(b) Cirrhosis of liver
(c) Hepatocellular carcinoma
(d) Cholestatic jaundice

EXPLANATIONS

1. **Ans. (b) Hereditary spherocytosis** *(Ref: Robbins 10/e p632)*
Regarding Hereditary spherocytosis;
Direct quote from Robbins....'*this inherited disorder is caused by* intrinsic defects in the red cell membrane *that render red cells spheroid, less deformable, and vulnerab le to splenic sequestration and destruction*'
Other disorders with intrinsic defect in red cell membrane are hereditary elliptocytosis and abetalipoproteinemia.

2. **Ans. (c) Myoblast** *(Ref: Robbins 10th/e p580)*
Bone marrow cells include

- **Hematopoietic stem cells** include **lymphoblast, myeloblast** and **normoblast**.
- **Marrow stromal cell**/multipotent stem cells (MSC) including **myoblast, osteoblasts, chondrocytes, adipocytes** and **endothelial cell precursors**. Myoblast is an example of MSC giving rise to muscle cells or myocytes.

3. **Ans. (d) CD 34** *(Ref: Robbins 10th/e p590)*

CD34 is expressed on pluripotent hematopoietic stem cells and progenitor cells of many lineages

4. **Ans. (c) Nutritional anemia**
(Ref: Harrison 18th/454, 17th/359-361 and Ghai 6th/306) ...see Table 7.1

Reticulocytes are nonnucleated spherical cells bigger than normal RBCs and are polychromatic (having a blue color) due to the presence of free ribosomes and RNA.

5. **Ans. (b) Basophilic stippling; (d) Howell-Jolly bodies; (e) Cabot ring** *(Ref: PJ Mehta 16th/372, T. Singh 1st/34)*
- **Romanowsky dyes** are used for staining blood films. They are made up of combination of acid and basic dyes. The nucleus and neutrophilic granules are basophilic and stains blue. Hemoglobin is acidophilic and stains red.
- Various modifications available are **Leishman's stain, Wright's stain, Giemsa and Jenner's stain.**
- Basophilic stippling, Howell-Jolly body and Cabot rings are seen by Romanowsky stain.

- **Basophilic stippling:** These are small blue or black granules in red cells seen in megaloblastic anemia, heavy metal poisonings, etc.
- **Howell-Jolly Body:** These are remnants of the nucleus seen as small, round dark blue particles near the periphery of the cells; found in postsplenectomy, asplenia and severe hemolytic anemia.
- **Cabot ring:** These are pale staining nuclear remnants in the form of rings or figure of eight seen in hemolytic anemia, megaloblastic anemia, leukemia and after splenectomy. These are arginine rich and acidophilic.
- Heinz bodies are denatured hemoglobin which does not stained with Romanowsky stain. It is demonstrated by supravital stains such as crystal violets. Reticulocytes also require Supravital staining.

6. **Ans. (d) CD 34** *(Ref: Robbins 10/e p590)*

7. **Ans. (d) Benign liver tumor** *(Ref: Robbins 10/e p331)*

8. **Ans. (a) MCV** *(Ref: Robbins 10/e p630)*

9. **Ans. (c) Megaloblastic** *(Ref: Robbins 10/e p645)*

10. **Ans. (a) Acute glomerulonephritis** *(Ref: Robbins 10/e p898)*

11. **Ans. (b) Spherocytosis** *(Ref: Robbins 10/e p633)*

12. **Ans. (d) Erythropoietin** *(Ref: Robbins 10/e p656)*

13. **Ans. (d) All of the above** *(Ref: Harrison 18 Table 280 (5))*

14. **Ans. (a) Uremia** *(Ref: Tejinder Singh 1st/38)*

15. **Ans. (a) Abetalipoproteinemia** *(Ref: Tejinder Singh 1st/38)*

16. **Ans. (b) Brilliant Cresyl blue** *(Ref: Robbins, 10/e p635)*
- **Reticulocytes** are stained in **living state** *in vitro* so staining with dyes like brilliant cresyl blue and **new methylene blue (Best stain)** is referred to as ***supravital staining***.

17. **Ans. (a) Ferritin** *(Ref: Robbins 10/e p650)*

18. **Ans. (a) Histidine residues**
Harper mentions …'Hemoglobin also functions in CO_2 and proton transport from tissues to lungs. Release of O_2 from oxy Hb at the tissues is accompanied by uptake of protons due to lowering of the p*Ka* of ***histidine residues***.'

19. **Ans. (b) Henoch Schonlein purpura**
(Ref: Robbins 10/e p526-527)
All other options have decreased platelet count except Henoch Schonlein purpura. Though it has the name purpura, but the ***platelet count in this condition is normal***. The skin manifestations in HSP are due to **small vessel vasculitis**.

20. **Ans. (c) 900... About 900 g[Q] of hemoglobin is present in the circulating blood of an adult man.**

21. **Ans. (a) Lymphocyte**

- **Lymphocyte** is the **longest living**[Q] white blood cell.
- **Neutrophil** is the most **numerous**[Q] white blood cell.

22. **Ans. (c) –0.54° C**

- The **freezing point** of normal **human plasma** averages **-0.54 °C**[Q], which corresponds to an osmolal concentration in plasma of **290 mOsm/L**[Q].
- The term **tonicity** is used to describe the osmolality of a solution relative to plasma
- A **0.9% saline solution** and **5% glucose solution is isotonic** when initially infused intravenously.

Also know how to calculate osmolality: medicine link!

Osmolality (mOsm/L) = 2[Na+] (mEq/L) + 0.055 [Glucose] (mg/dL) + 0.36[BUN] (mg/dL)

23. **Ans. (b) 2:1**
- Normal **albumin-globulin ratio** is **1.8 : 1 to 2 : 1**[Q].
- Synthesis of **albumin exclusively occurs in liver** but many ***globulins (immunoglobulins) are synthesized by B-lymphocyte.***

Conditions with altered albumin globulin ratio

High Albumin Globulin Ratio	Low Albumin Globulin Ratio
• Hypothyroidism • Hypogammaglobulinemia • Leukemia • Glucocorticoid excess	• Overproduction of globulins in conditions like **multiple myeloma, chronic infections** and in some autoimmune diseases. • Under production of albumin in conditions like **liver cirrhosis, malnutrition and nephrotic syndrome**.

24. Ans. (b) Contractile protein

(Ref: Harsh Mohan 5th/ 177, The Circulating Platelet/ 215-8)

- Thrombosthenin is a contractile protein in platelets that is active in the formation of blood clots.

25. Ans. (c) Cyanmethemoglobin method

Hemoglobin estimation		
Visual Colorimetric method	Sahli's (acid hematin method) Alkali hematin method	Most popular method
Photocolorimetric method	Cyanmethemoglobin method	**Most accurate** and currently used

26. Ans. (c) 4

Hemoglobin is a globular molecule made up of four subunits. Each subunit contains a **heme** moiety conjugated to a polypeptide. Heme is an iron-containing porphyrin derivative. So, **hemoglobin = 4 globins + 4 heme groups**

Since each heme molecule contains an iron, so total iron atoms present in hemoglobin are 4 in number.

- **70%** of the iron in the body is in **hemoglobin**, 3% in myoglobin, and the rest in ferritin, which is present not only in enterocytes, but also in many other cells.

27. Ans. (d) ESR *(Ref: A Textbook of Hematology p133)*

28. Ans. (b) Labile factor

If whole blood is allowed to clot and the clot is removed, the remaining fluid is called **serum.** Serum has essentially the same composition as plasma, except that:

- **Fibrinogen (factor I)** and clotting factors **II**, **V**, and **VIII** have been **removed** and.
- Has **higher serotonin content** because of the breakdown of platelets during clotting.

Also know that **factor 5** is called as **labile factor**[Q].

29. Ans. (a) Bone marrow *(Ref: Robbins 10/e p580)*

By birth, marrow throughout the skeleton is hematopoietically active and hepatic hematopoiesis dwindles to a trickle, persisting only in widely scattered foci that become inactive soon after birth.

30. Ans. (c) RBCs to whole blood *(Ref: Robbins 10/e p631)*

Haematocrit (also known as packed cell volume) is the volume percentage (%) of red blood cells in blood.

31. Ans. (c) Myelophthisic type *(Ref: Robbins 10/e p655)*

- *Myelophthisic anemia* describes a form of marrow failure in which space-occupying lesions replace normal marrow elements. **The commonest cause is metastatic cancer**, most often carcinomas arising in the breast, lung, and prostate.

32. Ans. (b) No nucleus *(Ref: Wintrobe 11th/200)*

33. Ans. (b) 60-80 days *(Ref: Oski's Hematology /28)*

- Premature infant: 35-50 days
- Term infant: 60-70 days
- Adult: 100-120 days

34. Ans. (d) Hereditary spherocytosis *(Ref: Robbins 10th/e p633)*

35. Ans. (b) <34 *(Ref: Park's PSM textbook/Nutrition and health)*

At all ages **the normal MCHC should be 34**; values below that indicate that red cells are hypochromic, which occurs in iron deficiency anaemia.

36. Ans. (a) Increased reticulocyte count

(Ref: Robbins 10/e p645; Wintrobe's 12th/1151-3)

Direct quote from Robbins … *'The reticulocyte count is low'*. Please be clear of the concept friends that the ***reticulocyte count is increased*** when the megaloblastic anemia is being treated with ***vitamin B_{12} and folate supplementation*** i.e. after the initiation of the treatment in these patients.

- Nucleated red cell progenitors occasionally appear in the circulating blood when anemia is severe.
- The derangement in DNA synthesis causes most precursors to undergo apoptosis in the marrow (ineffective hematopoiesis) and leads to pancytopenia. The anemia is further exacerbated by a mild degree of red cell hemolysis. This leads to raised bilirubin.
- Wintrobe mentions … 'Mild reversible splenomegaly is present in megaloblastic anemia'.

37. Ans. (d) Myelofibrosis *(Ref: Harrison 17th/661, 674, 646)*

The findings in the given question are:
Anemia (Hb = 6 g)
Reduced leukocyte count (TLC= 1200)
Reduced platelet count (60000)
Reduced MCV (12 fL)

- Normal value of MCV is 80-100 fL. It is the measure of size of RBC. Reduced MCV means microcytic and increased MCV means macrocytic RBCs. Normal TLC is 4000-11000, normal platelet count is 1,50,000 to 4,50,000 and normal Hb is above 12 g/dL.
- Now, considering the options one by one:

- **Aplastic anemia** has reduced RBC, WBC as well as platelet counts. Anemia is normocytic normochromic, thus it can be easily ruled out.
- **Paroxysomal nocturnal hemoglobinuria (PNH)** typically presents with anemia which is usually normomacrocytic. If MCV is high, it is due to reticulocytosis. Neutropenia and thrombocytopenia may or may not be present. Therefore, this option also cannot be the answer.
- **Megaloblastic anemia** presents with raised MCV. There may be leukopenia as well as thrombocytopenia. Severity of these changes parallels the degree of anemia.
- **Myelofibrosis** usually presents with anemia, leukopenia and thrombocytopenia. Mostly anemia is normocytic but in 30% cases microcytic anemia can be present.

Based on the above discussion, the most probable answer is 'Myelofibrosis'.

However, the value of MCV given is 12 fL which is practically not possible. Normal value of MCV is 80-100 fL. MCV < 50 fL is considered to be extremely low. Therefore, one

MOST RECENT PATTERN QUESTIONS WITH ANSWER

1. A boy after playing football complaining fatigue and abdominal pain. He also had a history of hand swelling in past. On ultrasonography, he has shrunken spleen. What is the likely diagnosis of this patient? *(NEET 2020 like pattern)*

(a) Sickle cell anemia
(b) Iron deficincy anemia
(c) Acute pancreatitis
(d) Intermittent porphyria

Ans. (a) Sickle cell anemia *(Ref: Robbins 10th/e p636-7)*

Presence of fatigue is likely to be due to anemia. Shrunken spleen is likely to be due to autosplenectomy and swelling of the hand can be attributed to dactylitis or 'hand foot syndrome'. So, the clinical picture given in the stem of the question is likely to be associated with sickle cell anemia.

Shrunken spleen and hand swelling is not seen in other options like iron deficiency anemia, pancreatitis and intermittent porphyria.

2. A young male presented with history of fatigue and tiredness. On investigating, he had a hemoglobin of 8 g/dL, MCV of 101 fL, hematocrit of 33% with the peripheral smear showing macrocytes and hypersegmented neutrophils. Which of the following is the most likely cause of the findings in this patient? *(NEET 2020 like pattern)*

(a) Lead poisoning
(b) Chronic alcohol
(c) Chronic renal failure
(d) Hemolytic anemia

Ans. (b) Chronic alcohol > (c) Chronic renal failure *(Ref: Robbins 10th/e p649)*

The clinical picture given in the question is suggestive of anemia with high MCV and hypersegmented neutrophils which means megaloblastic anemia. Out of the given options in the questions, alcohol is a commoner cause of folate deficiency. So, it can be associated with development of megaloblastic anemia.

3. A 30-year-old women came with complaints of easy fatigability, exertional dyspnea and weight loss. She also has a complaint of frequent fall. Physical examination revealed there was bilateral decrease in vibration sense. Her hemoglobin levels were 8.2 g%. She was treated with folate. Her anemia improved but neurological symptoms worsened. Which of the following is the most probable reason for her condition? *(NEET 2020 like pattern)*

(a) Folate not absorbed
(b) Folic acid deficiency unmasked pyridoxine deficiency
(c) Deficiency of folate reductase in CNS
(d) Folate therapy caused rapid use of B12 stores aggravating symptoms

Ans. (d) Folate therapy caused rapid use of B12 stores aggravating symptoms *(Ref: Robbins 10th/e p649)*

The clinical is suggestive of anemia (features of fatigability and exertional dyspnea with low hemoglobin). However, it is important to know that megaloblastic anemia with neurological symptoms respond to vitamin B12 administration. If by mistake, the patient is administered folate first, the neurological complications are likely to worsen as had happened in this case.

4. Hepcidin inhibits which of the following? *(AIIMS Nov 2019 like pattern)*

(a) Hephaestin (b) DMT-1
(c) Ceruloplasmin (d) Ferroportin

Ans. (d) Ferroportin *(Ref: Robbins 10th/e p650)*

- Iron absorption is regulated by *hepcidin*, a peptide that is synthesized and released from the liver in response to increases in intrahepatic iron levels.
- *Hepcidin inhibits iron transfer from the enterocyte to plasma by binding to ferroportin* and causing it to be endocytosed and degraded.
- When the body is replete with iron, high hepcidin levels inhibit its absorption into the blood.

5. Iron entry into enterocytes is done by which of the following? *(AIIMS Nov 2019 like pattern)*

(a) DMT-1 (b) Ferroportin
(c) Transferrin (d) Hepcidin

Ans. (a) DMT-1 *(Ref: Robbins 10th/e p650)*

- Fe^{2+} iron is then transported across the apical membrane of the enterocytes in the duodenum by divalent metal transporter 1 (DMT 1).
- Iron that enters the duodenal cells and is destined for the circulation is transported from the cytoplasm across the basolateral enterocyte membrane by ferroportin.
- Transferrin is involved in the transport of iron in the blood.

6. Which of the following findings are there in iron deficiency anemia? *(AIIMS Nov 2019 like pattern)*

(a) ↑ TIBC, ↑ Ferritin, ↓ Transferrin saturation
(b) ↑ TIBC, ↓ Ferritin, ↓ Transferrin saturation
(c) ↓ TIBC, ↓ Ferritin, ↓ Transferrin saturation
(d) ↓ TIBC, ↓ Ferritin, ↑ Transferrin saturation

Ans. (b) ↑ TIBC, ↓ Ferritin, ↓ Transferrin saturation *(Ref: Robbins 10th/e p652)*

As discussed in the text in detail, the patients with iron deficiency anemia have the following changes:

- Serum iron: reduced
- Serum ferritin: reduced
- Transferrin saturation: reduced
- Total iron binding capacity: increased

7. Which of the following is downregulated by hepcidin? *(AIIMS May 2019 like pattern)*

(a) Ferroportin
(b) Transferrin
(c) DMT 1
(d) Hephaestin

Ans. (a) Ferroportin *(Ref: Robbins 10th/e p650)*

Review of PATHOLOGY AND GENETICS

Salient Features

* Thoroughly revised and updated by a professional board of editors
* New NBE-based pattern (wider coverage, concept development, one-liner approach)
* Special points like 'NEET busters' have been added to facilitate last minute revision
* Picture MCQs with Answers (According to Recent Examinations)
* Golden points at the beginning of each chapter
* Most authenticated question bank
* Solved MCQs (PGMEEs 2022–1985) including All Recent Questions of 2022
* Chapterwise concise complete text in a new layout for enabling the students to study antegrade
* New conceptual and clinically relevant information has been highlighted in the text
* Provides the advantage of both antegrade as well as retrograde study
* Large number of diagrams and flow charts to quickly revise the topics
* References from 10th edition of Robbins and Cotran Pathologic Basis of Disease
* Golden points and additional information from 10th edition of Robbins have been given separately
* Previous years' MCQs and other potential questions highlighted in the text
* Large number of easy-to-grasp Mnemonics
* Chapter on important stains and bodies included
* Includes new topics being asked recently in the examinations
* Authentic and complete Question Banks of various years with latest references and correct answers of the following States' examinations have been added:

Rajasthan PGMEE, UP PGMEE, AP PGMEE, Tamil Nadu PGMEE, Kolkata PGMEE, Bihar and Jharkhand PGMEE, Kerala PGMEE, MP PGMEE, DNB, Odisha PGMEE, Delhi PGMEE and Maharashtra PGMEE.

Gobind Rai Garg completed his MBBS and MD (Pharmacology) from University College of Medical Sciences, New Delhi, India. He has been among the toppers and got a Gold Medal in Community Medicine. He has written many books and papers. He is currently the Director of Ayush Institute of Medical Sciences and is involved in teaching pharmacology to the undergraduate and postgraduate students. Recently, he has launched his mobile application 'Pharmacology by Dr Gobind Rai Garg' containing video lectures of entire Pharmacology. It is available to download at both Play store and Apple store.

Sparsh Gupta completed his MBBS and MD (Pharmacology) from University College of Medical Sciences, New Delhi, India. He was a brilliant student in MBBS and MD, and got a Gold Medal in Forensic Medicine. He is a topper of UPSC (teaching specialist, Pharmacology), and is presently involved in teaching the undergraduate and postgraduate students.

Printed in India

Available at all medical bookstores or buy online at www.ejaypee.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
EMCA House, 23/23-B, Ansari Road,
Daryaganj, New Delhi - 110 002, INDIA
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers
Follow us on instagram.com/JaypeeMedicalPublishers

Shelving Recommendation
PATHOLOGY

ISBN 978-93-5465-876-1
9 789354 658761