Ring in Red Blood Cells

Ring or twisted strands of basophilic material appear in the periphery of the RBCs. This is also called the Goblet ring. This appears in the RBCs in certain types of anaemia.

Howell-Jolly Bodies

In certain types of anaemia, some nuclear fragments are present in the ectoplasm of the RBCs. These nuclear fragments are called Howell-Jolly bodies (Figs 2.5 and 2.6).

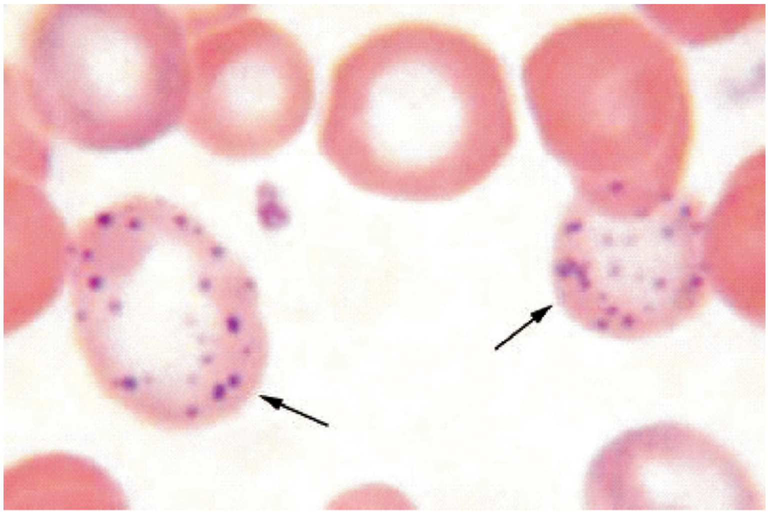

Fig. 2.4: Punctuate basophilia

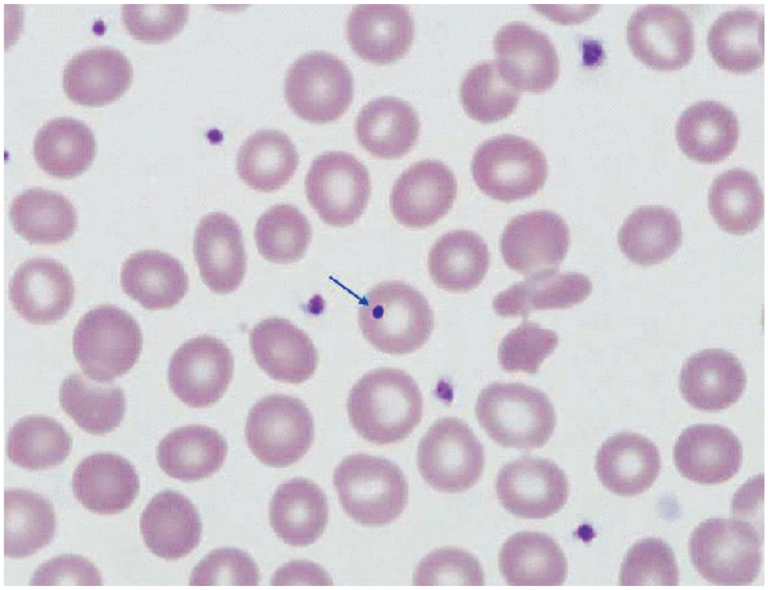

Fig. 2.5: Howell-Jolly bodies

ii. Thyroxine

Being a general metabolic hormone, thyroxine accelerates the process of erythropoiesis at many levels. So, hyperthyroidism and polycythemia are common.

iii. Haemopoietic Growth Factors

Haemopoietic growth factors or growth inducers are the interleukins and stem cell factor (steel factor). Generally these factors induce the proliferation of PHSCs. Interleukins (IL) are glycoproteins, which belong to the cytokines family. Interleukins involved in erythropoiesis:

a. Interleukin-3 (IL-3) secreted by T-cells.
b. Interleukin-6 (IL-6) secreted by T-cells, endothelial cells and macrophages.
c. Interleukin-11 (IL-11) secreted by osteoblast.

iv. Vitamins

Some vitamins are also necessary for the process of erythropoiesis. Deficiency of these vitamins cause anaemia associated with other disorders.

Vitamins necessary for erythropoiesis

a. Vitamin B: Its deficiency causes anaemia and pellagra (disease characterised by skin lesions, diarrhoea, weakness, nervousness and dementia).
b. Vitamin C: Its deficiency causes anaemia and scurvy (ancient disease characterised by impaired collagen synthesis resulting in rough skin, bleeding gum, loosening of teeth, poor wound healing, bone pain, lethargy and emotional changes).
c. Vitamin D: Its deficiency causes anaemia and rickets.
d. Vitamin E: Its deficiency leads to anaemia and malnutrition.

MATURATION FACTORS

Vitamin B_{12}, intrinsic factor and folic acid are necessary for the maturation of RBCs.

1. Vitamin B_{12} (Cyanocobalamin)

Vitamin B_{12} is the maturation factor necessary for erythropoiesis.

Source vitamin B_{12} is called extrinsic factor since it is obtained mostly from diet. Its absorption from intestine requires the presence of intrinsic factor of Castle. Vitamin B_{12} is stored mostly in liver and in small quantity in muscle. When necessary, it is transported to the bone marrow to promote maturation of RBCs. It is also produced in the large intestine by the intestinal flora.

Action

Vitamin B_{12} is essential for synthesis of DNA in RBCs. Its deficiency leads to failure in maturation of the cell and reduction in the cell division. Also, the cells are larger with fragile and weak cell membrane resulting in macrocytic anaemia. Deficiency of vitamin B_{12} causes pernicious anaemia. So, vitamin B_{12} is called antipernicious factor.

Intrinsic Factor of Castle

Intrinsic factor of castle is produced in gastric mucosa by the parietal cells of the gastric glands. It is essential for the absorption of vitamin B_{12} from intestine. In the absence of

2. Exposure to industrial chemicals such as

i. Aromatic amines.
ii. Fluorides.
iii. Irritant gases like nitrous oxide and nitrobenzene.
iv. Propylene glycol dinitrate.

3. Drugs

i. Antibacterial drugs like sulfonamides.
ii. Antimalarial drugs like chloroquine.
iii. Antiseptics.
iv. Inhalant in cyanide antidote kit.
v. Local anaesthetics like benzocaine.

4. Hereditary trait

Due to deficiency of NADH-dependant reductase or presence of abnormal haemoglobin M. Haemoglobin M is common in babies affected by blue baby syndrome (a pathological condition in infants, characterised by bluish skin discolouration (cyanosis), caused by congenital heart defect).

3. Sulfhaemoglobin

Sulfhaemoglobin is the abnormal haemoglobin derivative, formed by the combination of haemoglobin with hydrogen sulphide. It is caused by drugs such as phenacetin or sulfonamides. Normal sulfhaemoglobin level is less than 1% of total haemoglobin. Sulfhaemoglobin cannot be converted back into haemoglobin. Only way to get rid of this from the body is to wait until the affected RBCs with sulfhaemoglobin are destroyed after their lifespan.

Blood Level of Sulfhaemoglobin

Normally, very negligible amount of sulfhaemoglobin is present in blood which is nondetectable. But when its level rises above 10 gm/dL, cyanosis occur. Usually, serious toxic effects are not noticed.

Synthesis of Haemoglobin

Synthesis of haemoglobin actually starts in proerythroblastic stage. However, haemoglobin appears in the intermediate normoblastic stage only. Production of haemoglobin is continued until the stage of reticulocyte. Haeme portion of haemoglobin is synthesised in mitochondria. And the protein part, globin is synthesised in ribosomes.

Synthesis of Haeme

Haeme is synthesised from succinylCoA and the glycine. The sequence of events in synthesis of haemoglobin (Fig. 4.3):

1. First step in haeme synthesis takes place in the mitochondrion. Two molecules of succinylCoA combine with two molecules of glycine and condense to form-aminolevulinic acid (ALA) by ALA synthase.
2. ALA is transported to the cytoplasm. Two molecules of ALA combine to form porphobilinogen in the presence of ALA dehydratase.

acid, vitamin B_{12} [cyanocobalamin], vitamin C, pyridoxine; and riboflavin), and hormones (androgens and thyroxine).

In addition to the common deficiencies of iron and folate, there is a growing body of evidence to implicate vitamin A (important for cell growth and differentiation maintenance of epithelial integrity and normal immune function) and Zn (important in protein synthesis and nucleic acid metabolism) in nutritional anaemias.

In anaemia there is low circulating haemoglobin (Hb) in which concentration has fallen below a threshold lying at two standard deviations below the median of a healthy population of the same age, sex and stage of pregnancy. The WHO definition for diagnosis of anaemia in pregnancy is a Hb concentration of less than 11 gm/dL (7.45 mmol/L) and a haematocrit of less than 33%.

TYPES OF ANAEMIA

Physiological Anaemia

In pregnancy there is a disproportionate increase in plasma volume, RBC volume and haemoglobin mass. The plasma volume increase more than the RBC mass haemodilution occurs and is called physiological anaemia of pregnancy.

Criteria are

a. RBC 3.2 million/cmm.
b. Haemoglobin 10 gm%.
c. RBC morphology on peripheral smear is normal, i.e. normocytic, normochromic.
d. PCV 30%.

Pathological Anaemia

WHO definition of Anaemia in Pregnancy

- Haemoglobin less than 11 gm/dL is considered as anaemia.
- In India, FOGSI recommends haemoglobin less than 10 gm/dL during pregnancy is considered as anaemia.

Table 6.1: Classification of anaemia

	ICMR	*WHO*
Mild	10–11 gm/dL	9–11 gm/dL
Moderate	7–10 gm/dL	7–9 gm/dL
Severe	4–7 gm/dL	<7 gm/dL
Very severe	<4 gm/dL	

CDC definition of Anaemia in Pregnancy

Hb <11 gm/dL uring first and third trimester and <10.5 gm/dL in the second trimester (to allow for the physiological fall due to haemodilution in second trimester).