



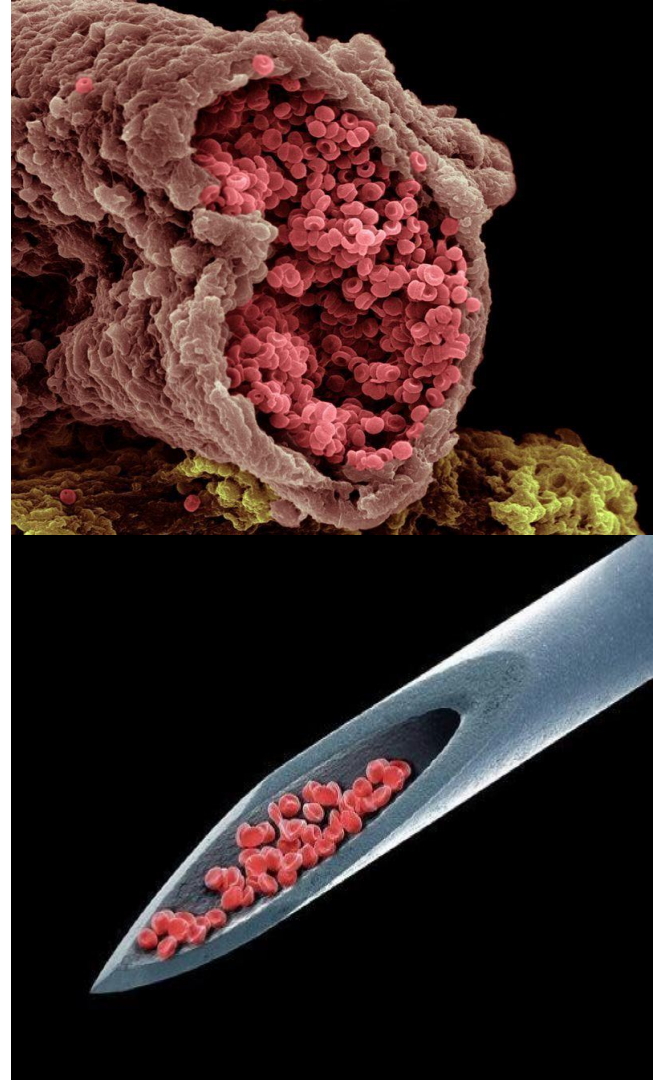
Lecture 6

Normal and Abnormal Red Blood Cells Morphology



Outlines

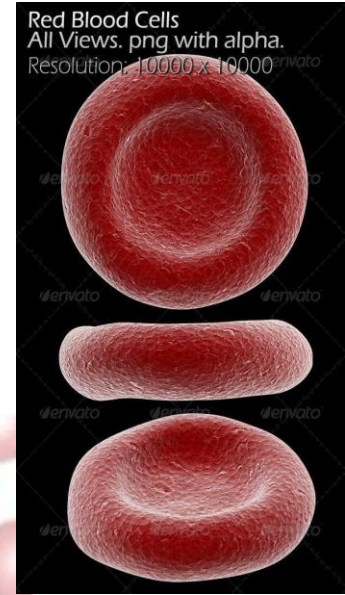
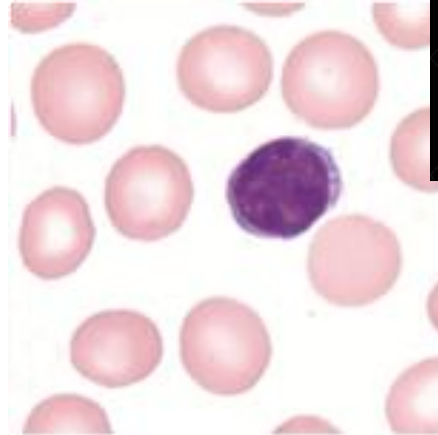
- I. Normal Red Blood Cell Morphology
- II. The Different Types of Variations of Red Blood Cells Abnormalities.



I. Normal Red Blood Cell Morphology

Red blood cell morphology

- Normal RBCs are **biconcave** in shape with a central pale area that accounts for 1/3 of the diameter of the cell.
- RBCs with normal color are described as **normochromic**.
- The average size of RBCs is about 7-8 μm in diameter (Normocytic).



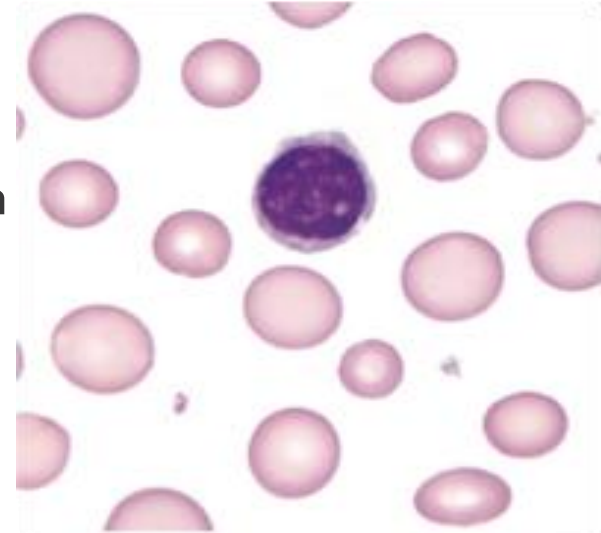
II. Variations of Red Blood Cells Abnormalities

Red Cell Abnormalities

- Causes of the presence of abnormal RBC:
 - 1) Abnormal erythropoiesis (production of RBC only).
 - 2) Decreased Hb formation.
 - 3) RBC damage after production.
 - 4) Changes due to an increase in Erythropoiesis.
- These causes result in the following variation:
 1. Anisocytosis → variation in size (Microcytic or Macrocytic).
 2. Poikilocytosis → variation in shape.
 3. Variation in color → (Hypochromic or hyperchromic).
 4. Variation in content → The presence of inclusions in erythrocytes.

1. Anisocytosis

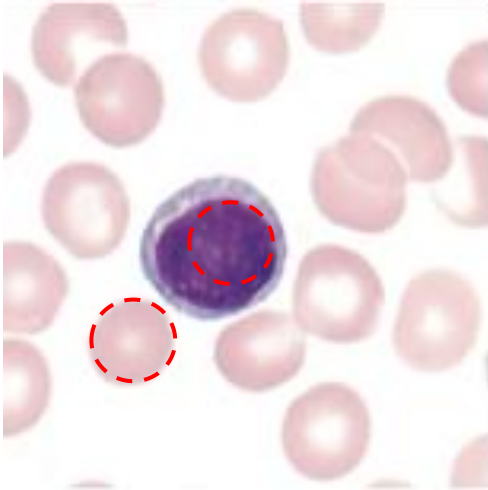
- **Anisocytosis** (aniso-unequal) is the variation in red blood cell diameter (or volume) on a blood film.
- This variation correlates with the **red blood cell distribution width (RDW)**.
 - **Macrocytic:** associated with Megaloblastic anemias and alcohol intake.
 - **Microcytic:** Microcytosis is characteristic of iron deficiency and thalassemia.



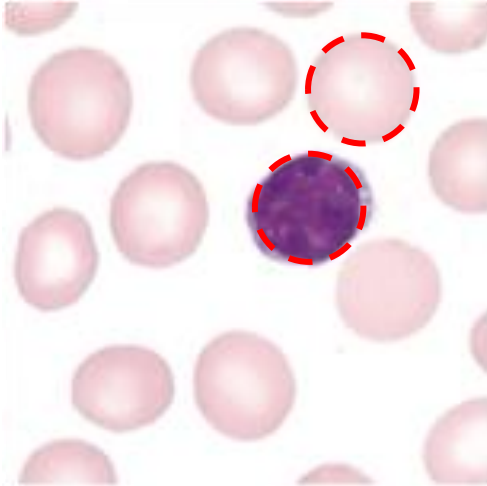
A *heterogeneous* population of erythrocytes, indicating *anisocytosis (RDW > 14.5%)*.

1. Anisocytosis

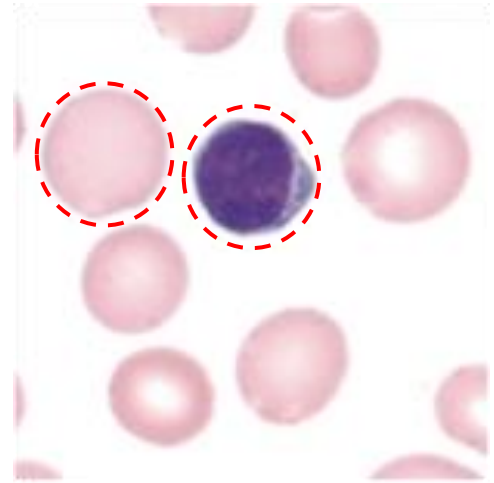
* Remember, comparison of the **RBC** with **normal small mature lymphocytes** is helpful in classifying them as normocytic, microcytic, or macrocytic.



Microcytes (MCV < 80 fL.).



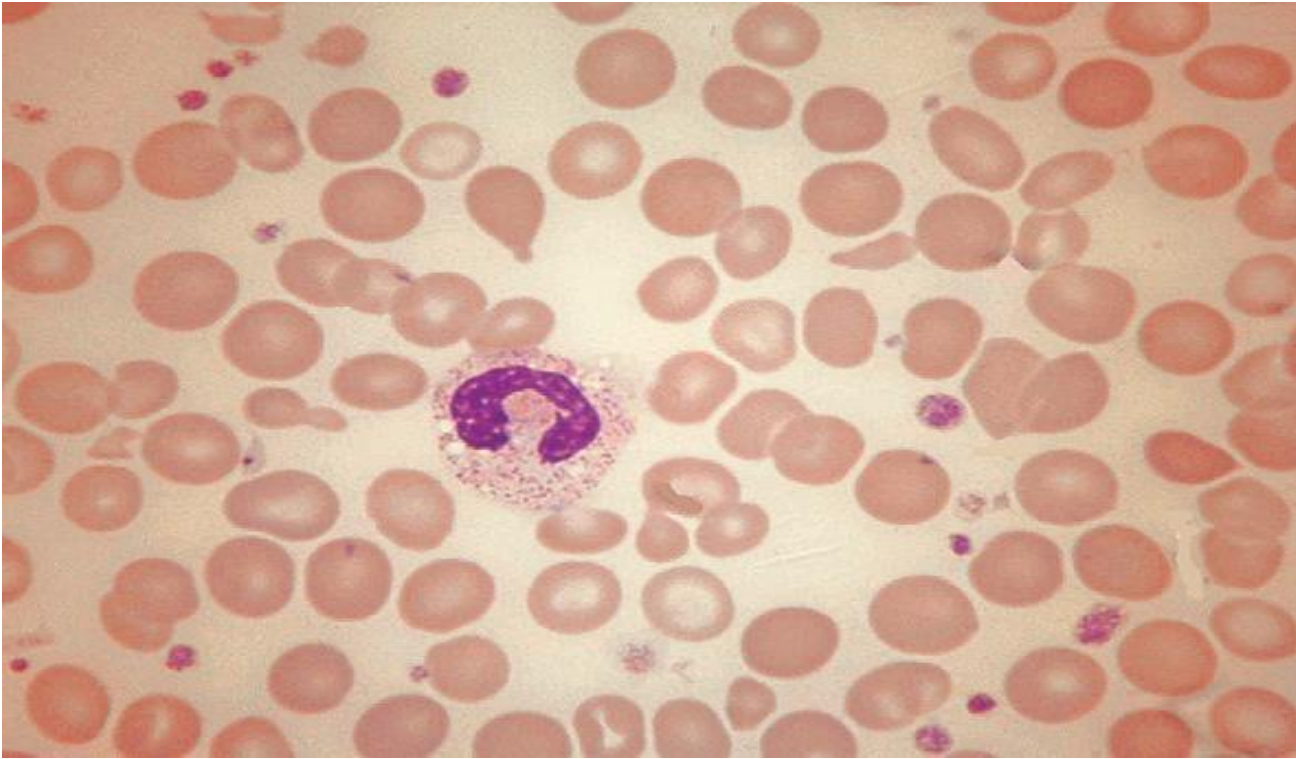
Normocytes (MCV 80-100 fL.).



Macrocytes (MCV > 100 fL.).

Normal erythrocytes are approximately the same size as the nucleus of a small lymphocyte.

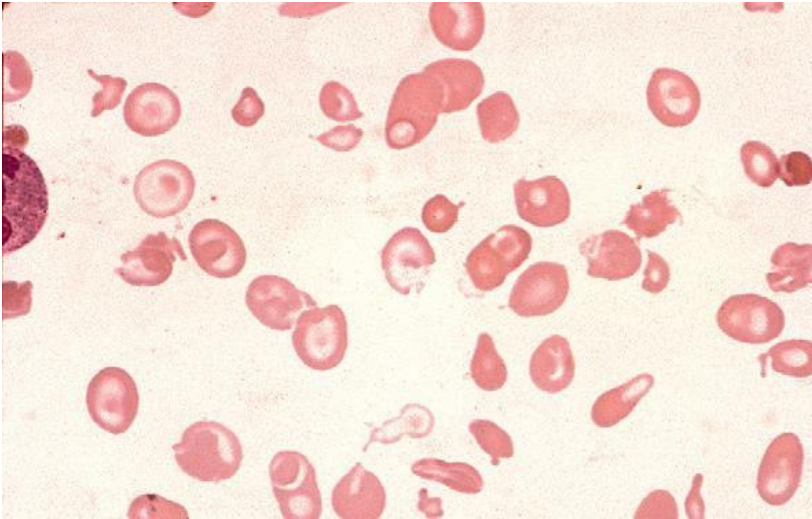
1. Anisocytosis



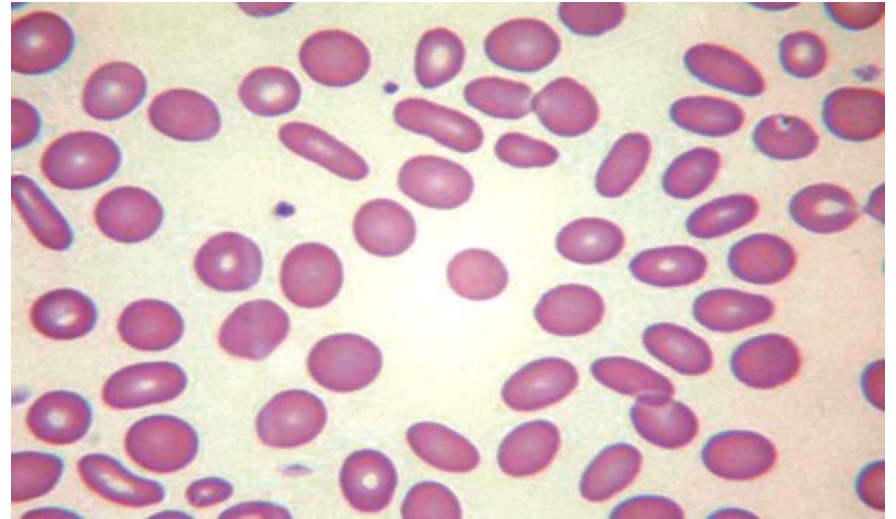
Shows moderate anisocytosis and poikilocytosis.

2. Poikilocytosis

- **Poikilocytosis** (poikilo- varied): variation in shape.
- Poikilocytosis is a general term for the presence of abnormally shaped red blood cells.



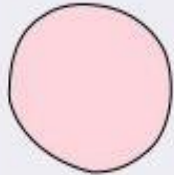







Shows marked anisocytosis and poikilocytosis.



Shows many erythrocytes in elliptical or oval shape.

2. Poikilocytosis

	Red cell abnormality	Causes		Red cell abnormality	Causes
	Normal			Microspherocyte	Hereditary spherocytosis, autoimmune haemolytic anaemia, septicaemia
	Macrocyte	Liver disease, alcoholism. Oval in megaloblastic anaemia		Fragments	DIC, microangiopathy, HUS, TTP, burns, cardiac valves
	Target cell	Iron deficiency, liver disease, haemoglobinopathies, post-splenectomy		Elliptocyte	Hereditary elliptocytosis
	Stomatocyte	Liver disease, alcoholism		Tear drop poikilocyte	Myelofibrosis, extramedullary haemopoiesis

2. Poikilocytosis

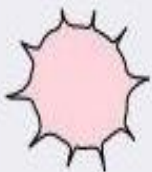
Red cell abnormality

Causes



Pencil cell

Iron deficiency



Echinocyte

Liver disease,
post-splenectomy,
storage artefact



Acanthocyte

Liver disease, abetalipo-
proteinaemia, renal failure

Red cell abnormality

Causes



Basket cell

Oxidant damage—
e.g. G6PD deficiency,
unstable haemoglobin



Sickle cell

Sickle cell anaemia



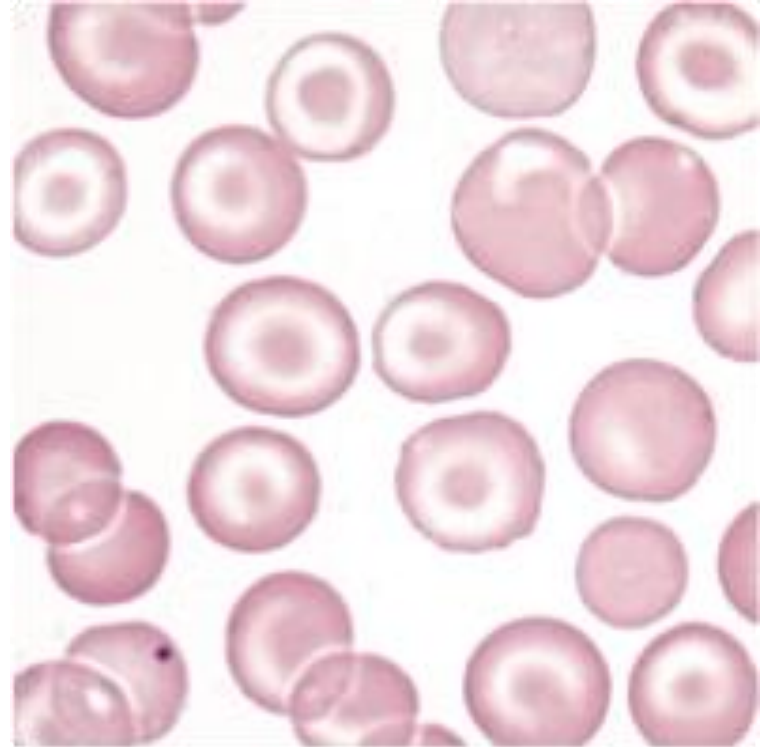
Microcyte

Iron deficiency,
haemoglobinopathy

2. Poikilocytosis

Target cells

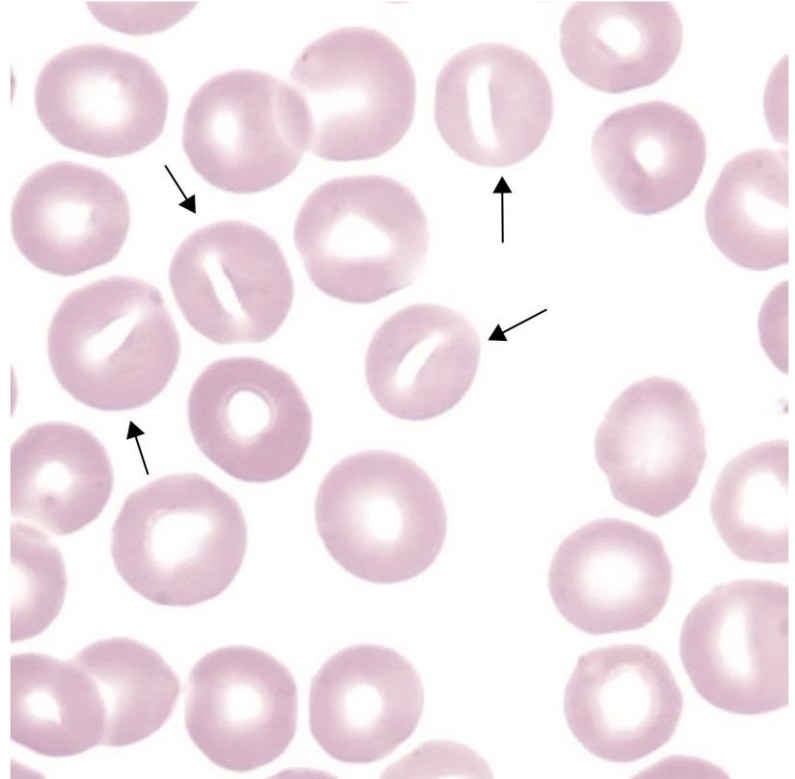
- **Shape:** Bull's eye; central concentration of hemoglobin surrounded by a colorless area with a peripheral ring of hemoglobin resembling bull's eye.
- **Associated with:** Hemoglobinopathies, thalassemia, iron deficiency anemia, splenectomy, obstructive liver disease



2. Poikilocytosis

Stomatocytes

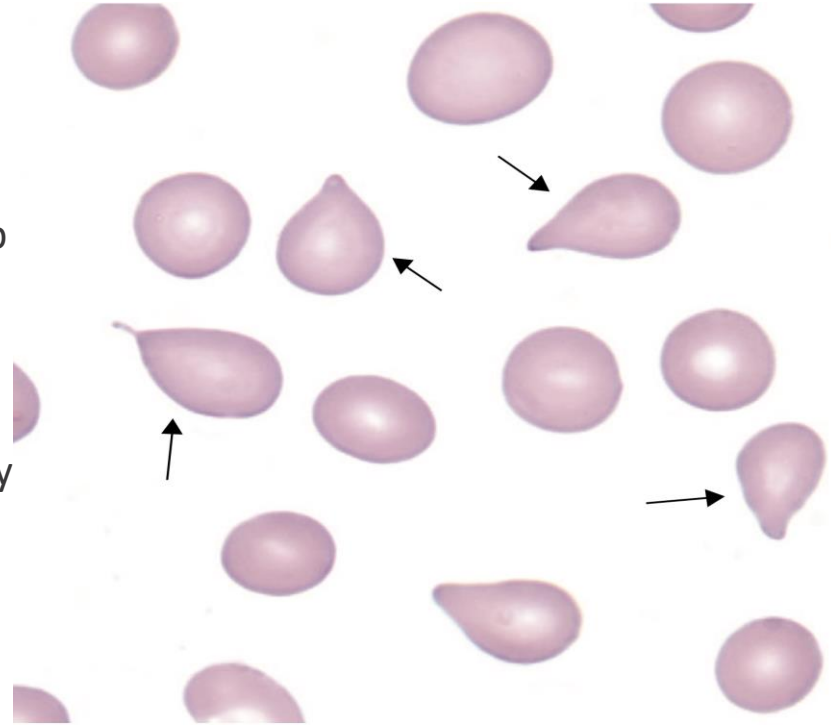
- **Description:** Erythrocyte with a slitlike area of central pallor (similar to a mouth or stoma).
- **Associated with:** Hereditary stomatocytosis, alcoholism, liver disease.



2. Poikilocytosis

Tear drop cells

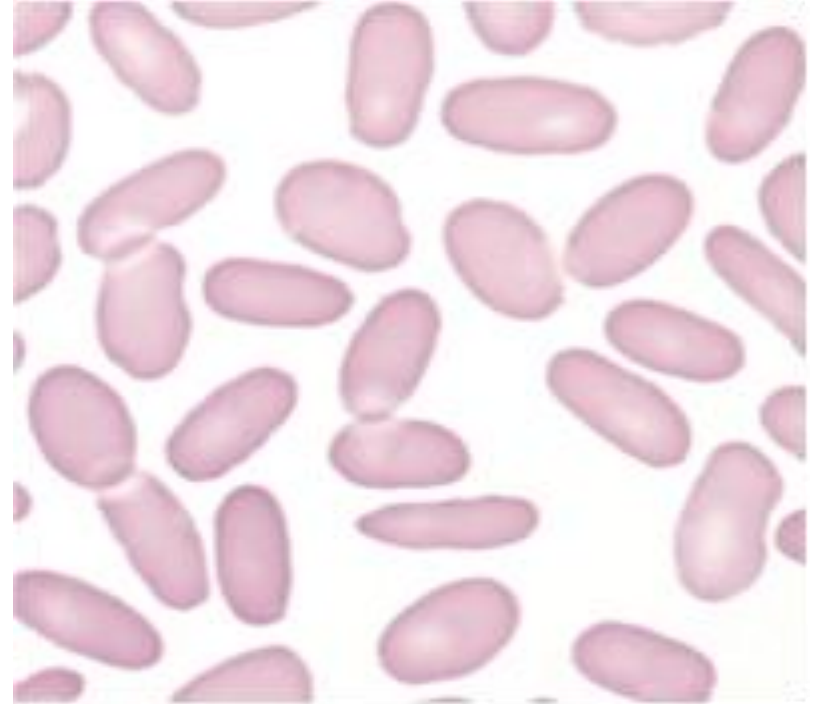
- **Description:** Erythrocyte shaped like a tear drop or pear; may have one blunt projection.
- **Associated with:** Primary myelofibrosis, thalassemia, and other causes of extramedullary hematopoiesis.



2. Poikilocytosis

Elliptocytes

- **Description:** Elliptocyte—cigar-shaped erythrocyte.
- **Associated with:** Hereditary elliptocytosis.



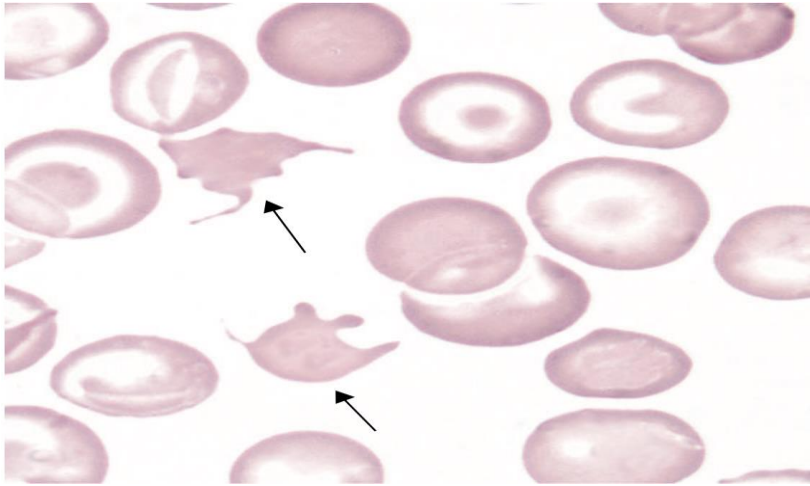
2. Poikilocytosis

Sickle cells

- **Shape:** Elongated cell with a point on each end; may be curved or S-shaped
- **Composition:** Hemoglobin S
- **Associated with:** Sickle Cell Anemia (Homozygous hemoglobin S patient).



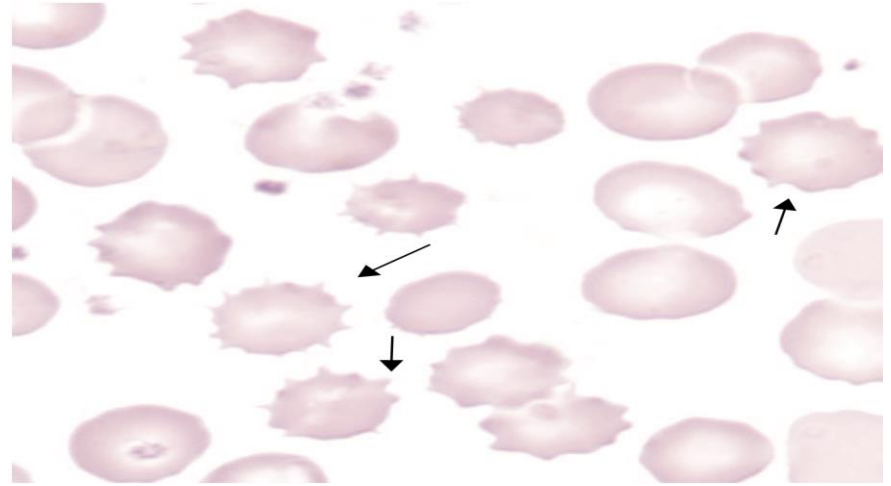
2. Poikilocytosis



Acanthocytes

Description: Erythrocytes with irregularly spaced projections that vary in width, length, and number; usually dense, lacking central pallor.

Associated with: Severe liver disease, splenectomy.



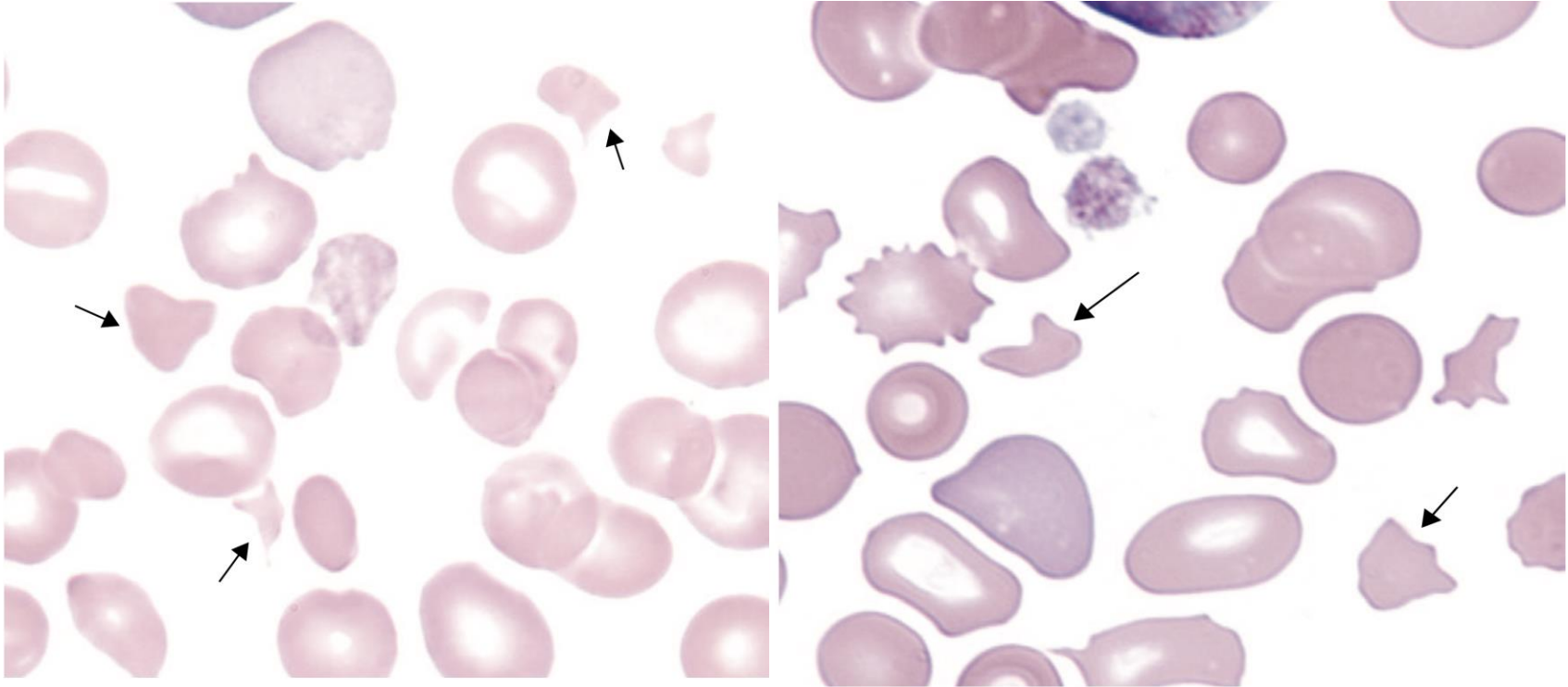
Echinocytes/burr cells

Description: Erythrocyte with short, evenly spaced projections, usually with central pallor.

Associated with: Uremia, pyruvate kinase deficiency, microangiopathic hemolytic anemia, neonates (especially premature), storage artifacts.

2. Poikilocytosis

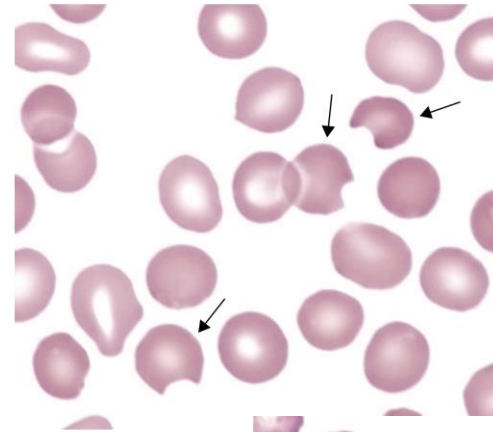
Schistocytes are fragmented parts of a red blood cell.



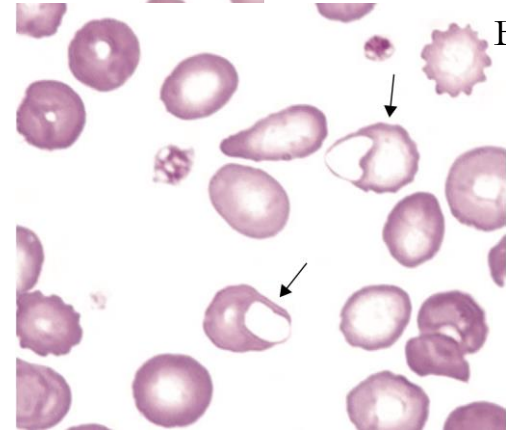
2. Poikilocytosis

Bite and blister cells

- Associated with: G6PD deficiency.
- Bite and blister cells are the **results of splenic pitting of Heinz bodies**.



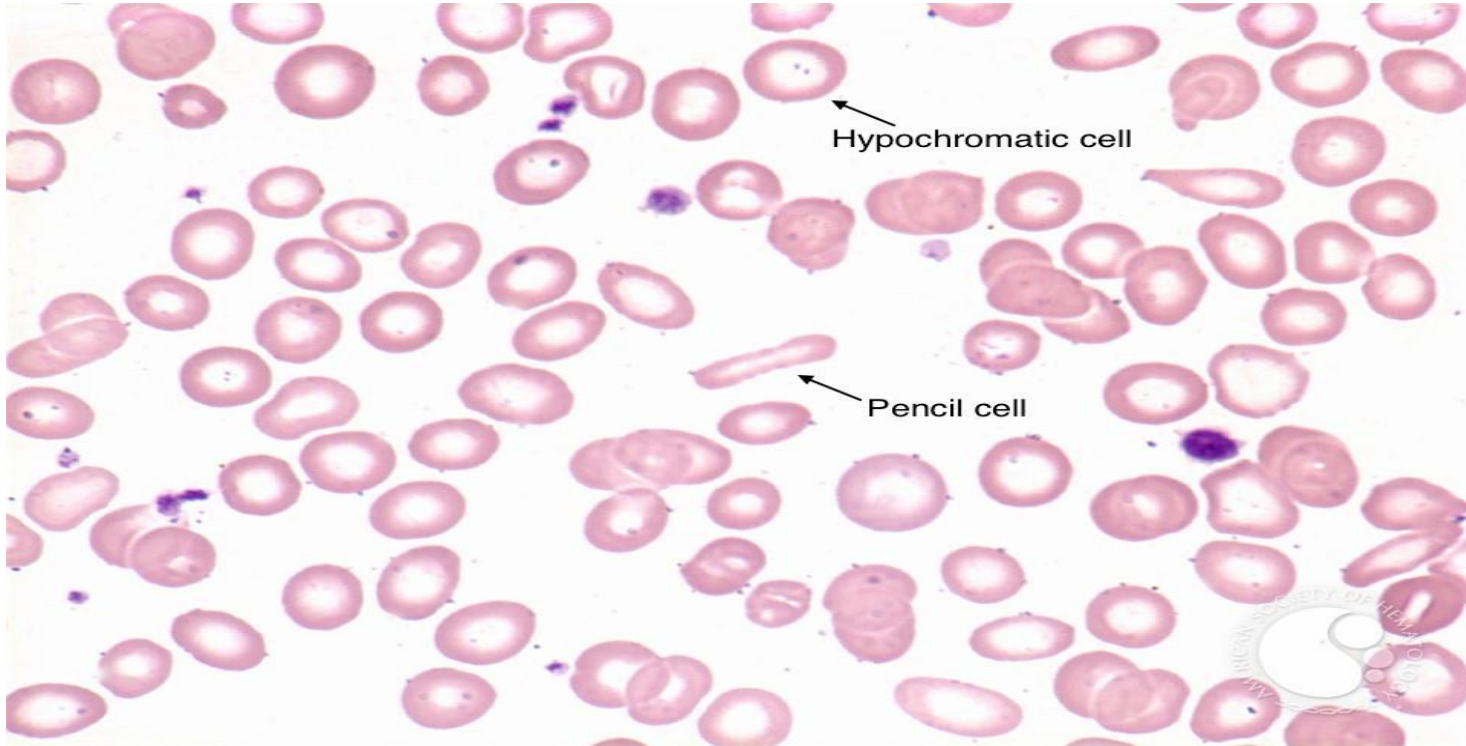
Bite cells.



Blister cells.

2. Poikilocytosis

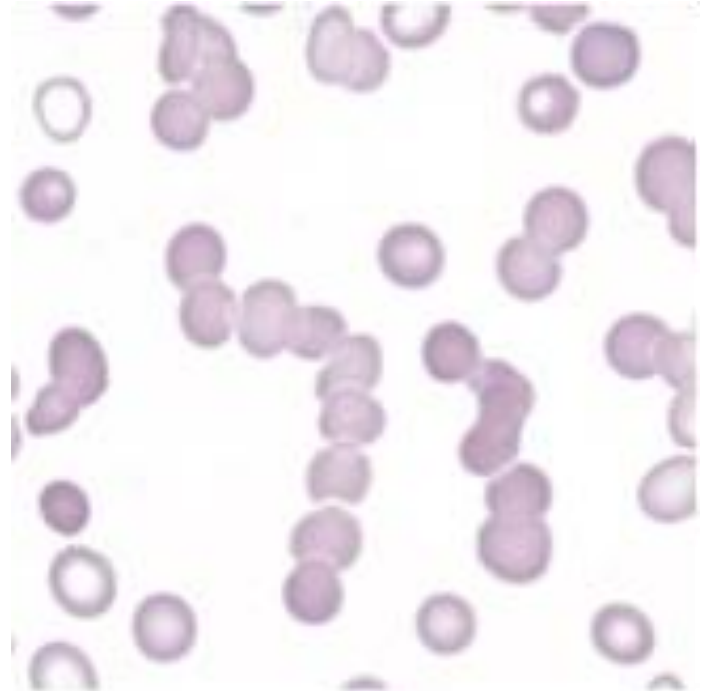
Pencil cell Associated with iron deficiency anemia (IDA).



2. Poikilocytosis

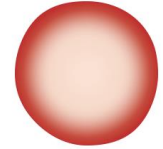
ROULEAUX

- **Description:** Erythrocytes are arranged in rows like stacks of coins.
- **Associated with:** Acute and chronic inflammatory disorders, plasma cell myeloma(increased production of Antibody).

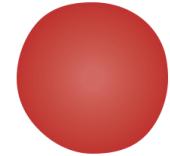


3. Variation in color of Erythrocytes

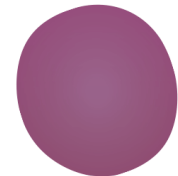
- **Hypochromia** (hypo-under): pale red cell.
 - **Associated with:** Iron deficiency anemia (commonly), thalassemia.
- **Hyperchromasia** (hyper-over): deep staining of the red cells with a lack of central pallor.
- **Polychromesia** (Poly-many and chromesia - color) is present due to immature red blood cells which uptake Eosin Y –Red (Hb) and Azure B –Blue (RNA). They have a grayish-blue color.
 - **Associated with:** Acute and chronic hemorrhage, hemolysis, effective treatment for anemia, neonates.



Hypochromic RBC

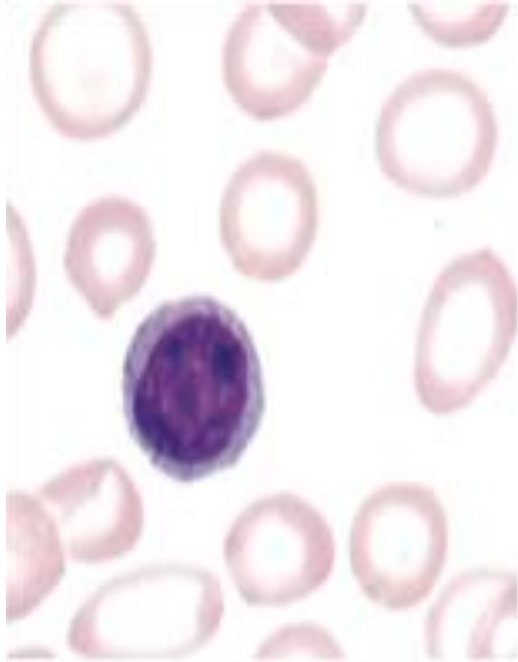


Hyperchromic RBC

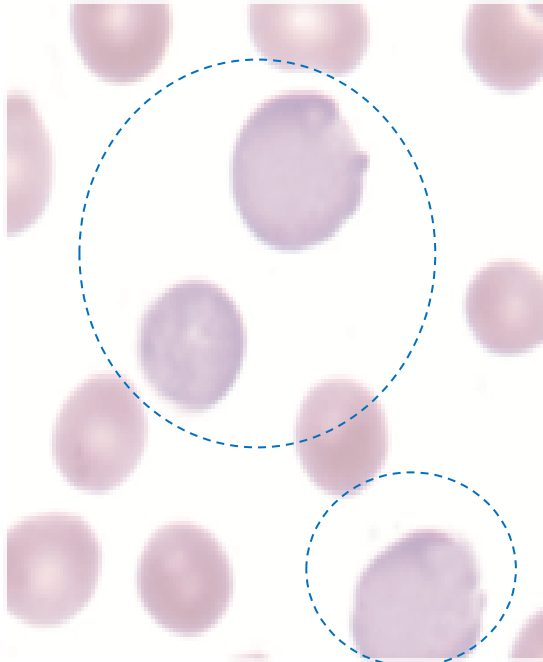


Polychromic RBC

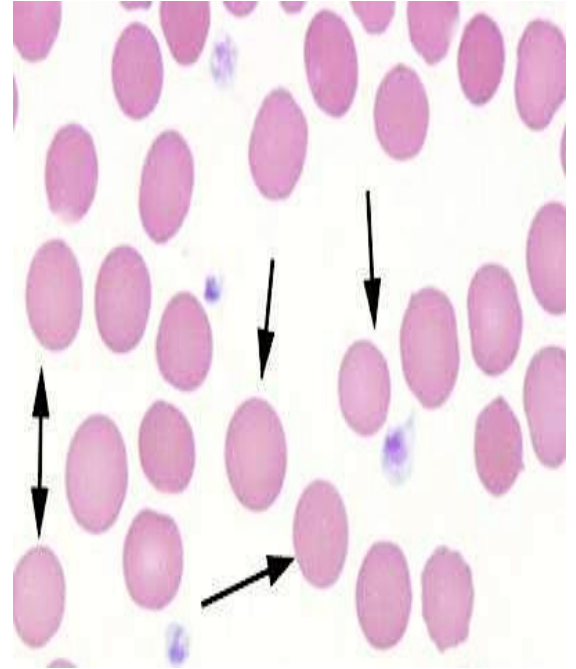
3. Variation in color of Erythrocytes



Hypochromic erythrocytes

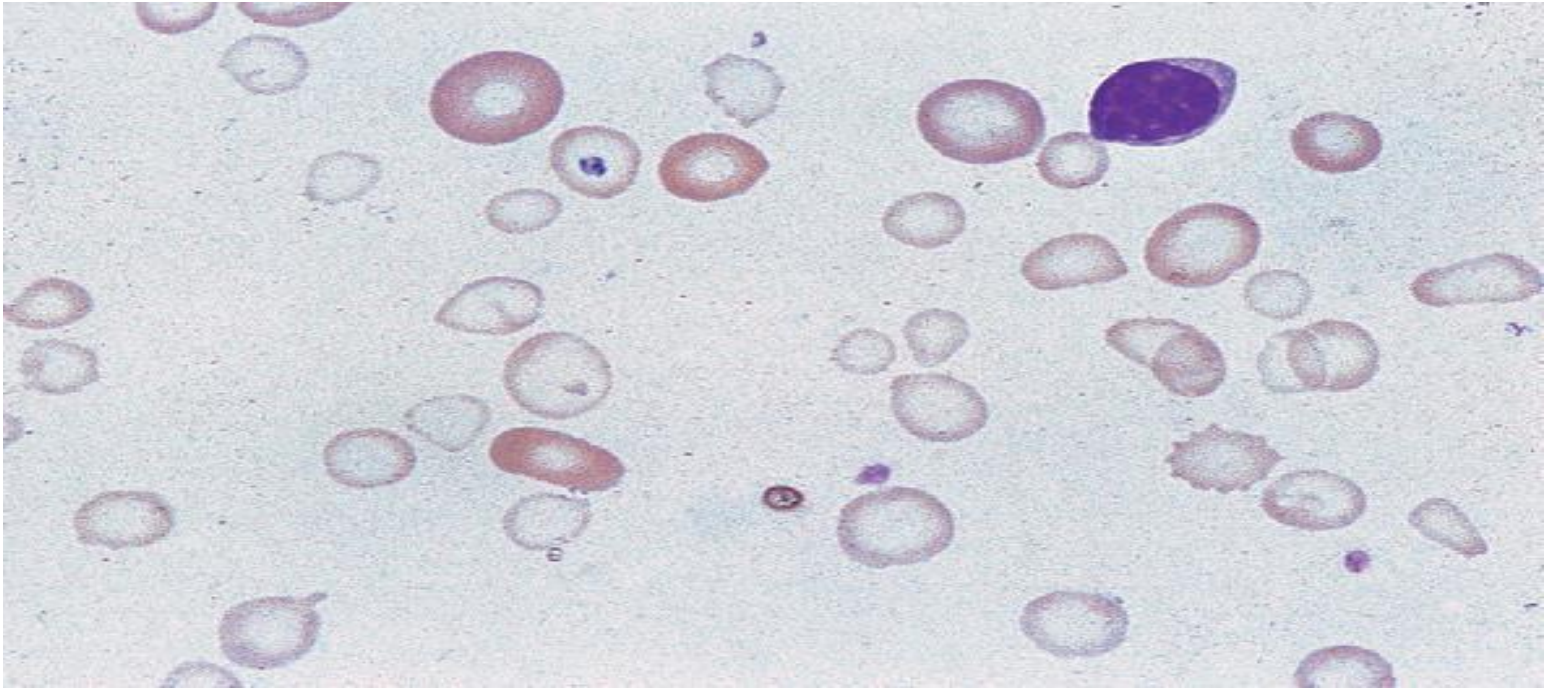


Polychromatic RBCs containing RNA residues








Hyperchromic erythrocytes

3. Variation in color of Erythrocytes



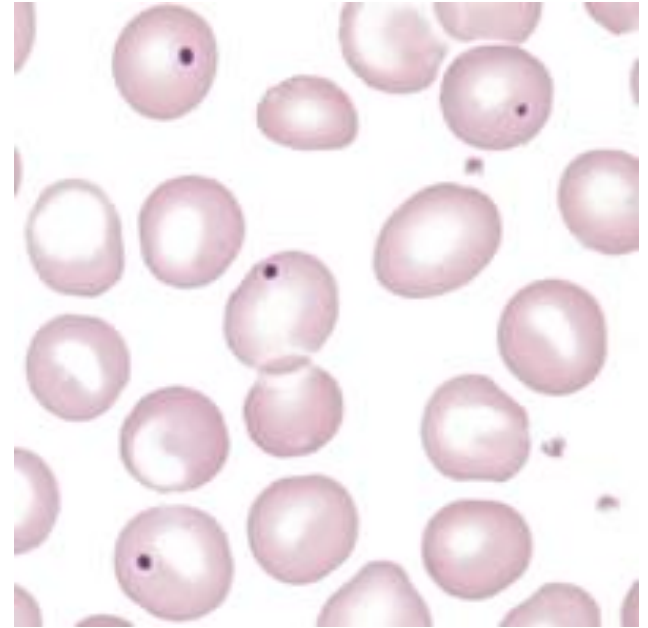
Shows a marked degree of microcytosis, marked anisocytosis, and mild poikilocytosis;

4. Variation in the content

Common RBC Inclusions	Cartoon Image	Inclusion	May be associated with
Howell Jolly Bodies		DNA	Hyposplenism Asplenism Severe hemolytic anemia
Heinz Bodies	 <i>Supravital stain</i>	Hemoglobin	G6PD deficiency Oxidant drugs Unstable hemoglobin
Pappenheimer Bodies		Iron deposits	Thalassemia Sideroblastic anemia Hemolytic anemia Post-splenectomy
Hemoglobin H Inclusion	 <i>Supravital stain</i>	Hemoglobin	Hemoglobin H disease
Basophilic Stippling		Ribosomes	Lead poisoning Thalassemia Sickle cell anemia MDS

4.1 Howell-Jolly bodies

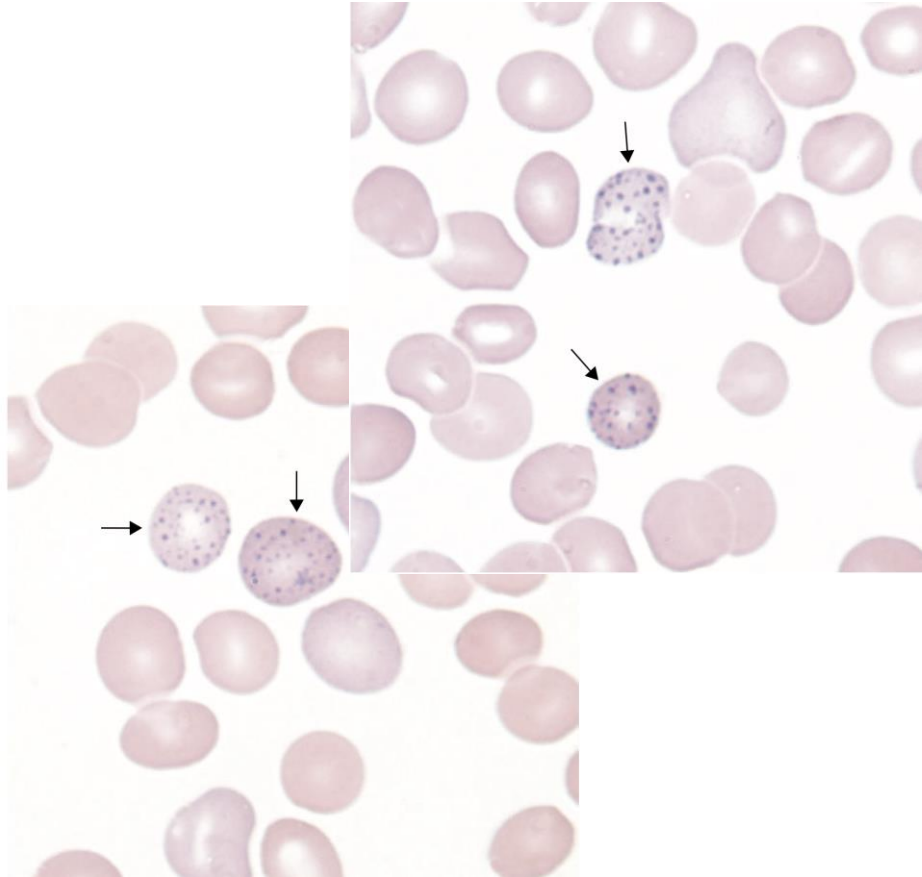
- **Shape:** Round to oval
- **Number Per Cell:** Usually 1.
- **Composition:** DNA
- **Associated with:** Splenectomy, hyposplenism, megaloblastic anemia, hemolytic anemia



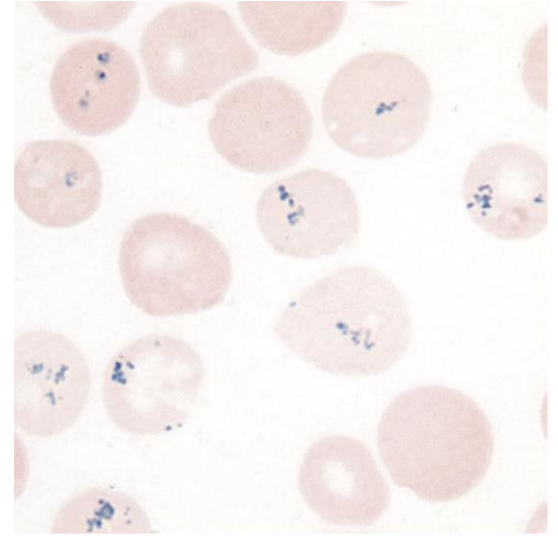
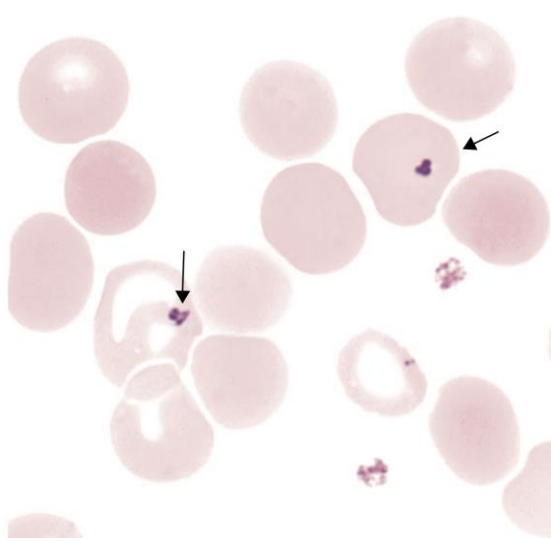
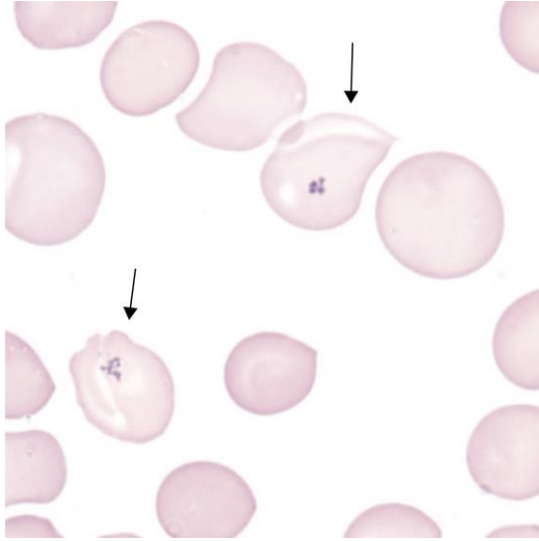
Howell-Jolly bodies.

4.2 Basophilic stippling

- **Shape:** Fine or coarse punctate granules.
- **Number Per Cell:** Numerous with fairly even distribution.
- **Composition:** RNA.
- **Associated with:** Lead intoxication, thalassemia, abnormal heme synthesis.



4.3 Pappenheimer bodies



Pappenheimer bodies (Wright stain). Pappenheimer bodies (Wright stain).

Siderotic granules (iron stain).

Shape: Fine irregular granules in clusters

Number Per Cell: Usually one cluster; may be multiples; often at the periphery of the cell.

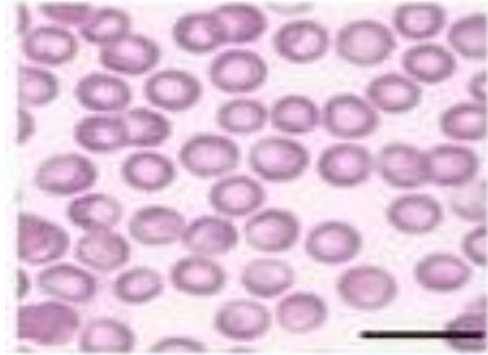
Composition: Iron

Associated with: Splenectomy, hemolytic anemia, sideroblastic anemia, megaloblastic anemia, hemoglobinopathies

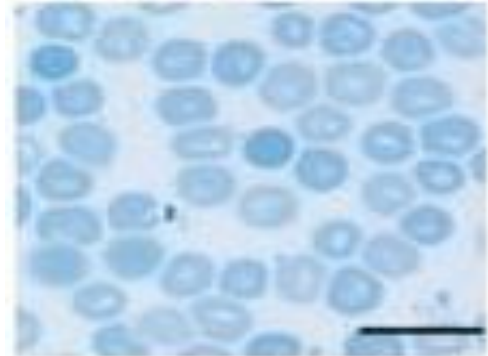
4. Inclusions With Supravital Stain

Inclusions Observed With Supravital Stains are:

1. Heinz bodies.
 2. Hemoglobin H.
 3. Reticulocytes.
- The most commonly used supravital stains in hematology are new methylene blue and brilliant cresyl blue.



Wright-Giemsa



Brilliant
cresyl blue

4.4 Heinz bodies

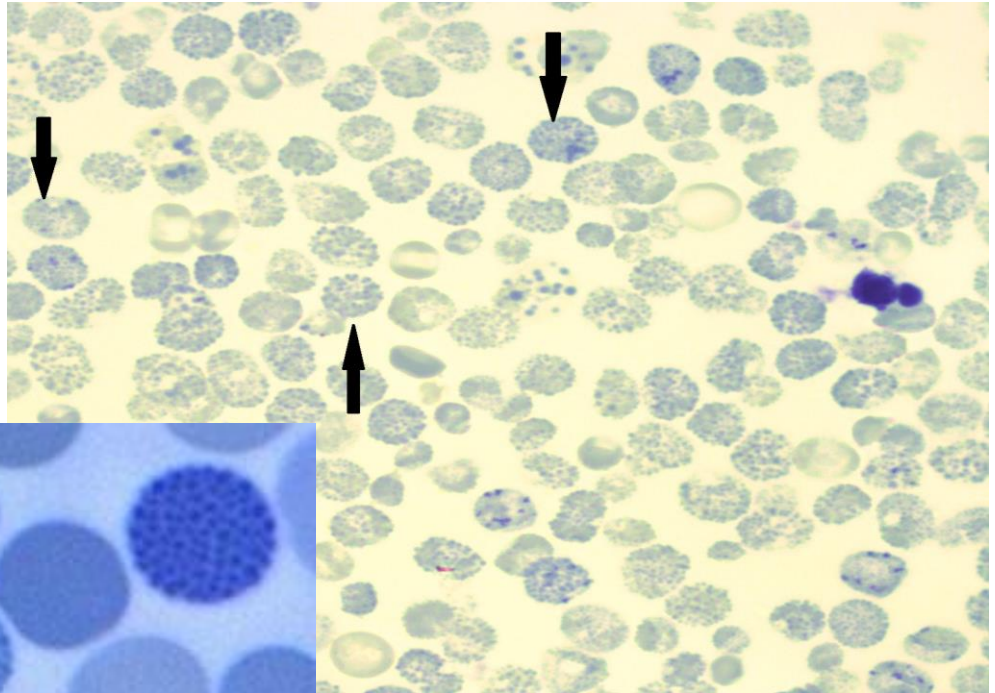
- **Cell:** Mature erythrocyte
- **Composition:** Precipitated oxidized hemoglobin.
- **Number:** Single or multiple, generally membrane- Bound
- **Associated with:** Unstable hemoglobin, some hemoglobinopathies, some erythrocyte enzyme deficiencies (e.g., glucose-6-phosphate dehydrogenase(**G6PD**)).



Stained with New Methylene Blue

4.5 Hemoglobin H

- **Cell:** Mature erythrocyte.
- **Composition:** Hemoglobin beta chains.
- **Number:** Multiple evenly dispersed granules described as “golf balls” or “raspberries”
- **Color:** Dark blue

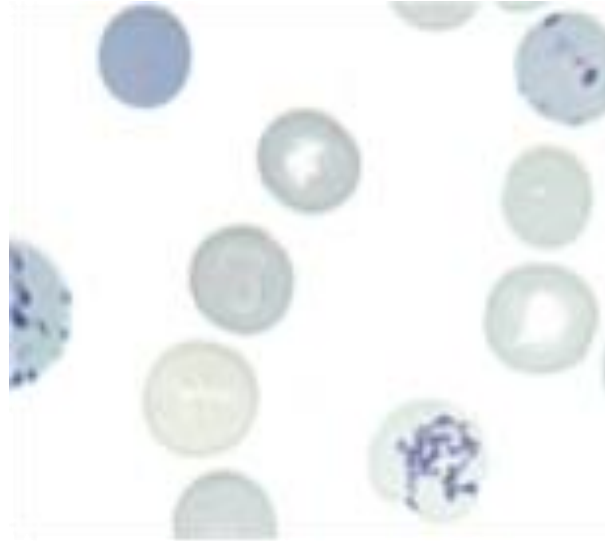


4.6 Reticulocytes

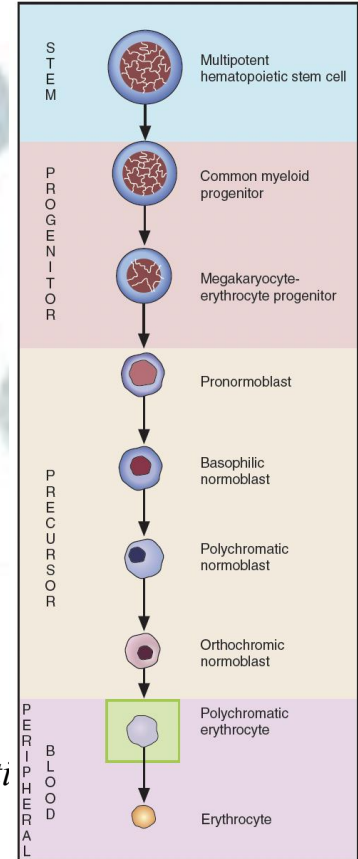
- **Cell:** Anuclear immature erythrocyte.
- **Composition:** Precipitated RNA
- **Number:** >2 per cell
- **Color:** Dark blue

Reference Interval:

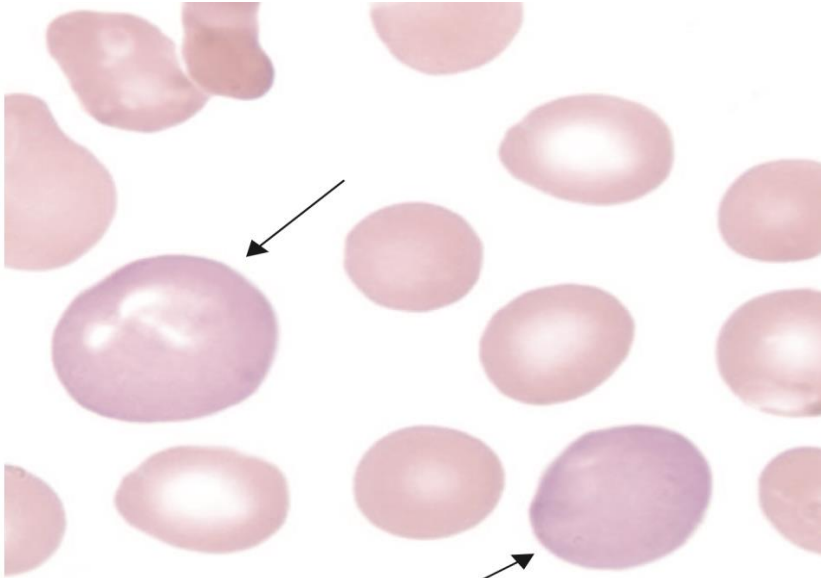
- Bone Marrow: 1%
- Peripheral Blood: 0.5% to 2.0%
- If present in peripheral blood, more than 2% is associated with Hemolytic anemias and Blood loss.



Erythrocyte sequence—polychromati erythrocyte (reticulocyte).



4.6 Reticulocytes

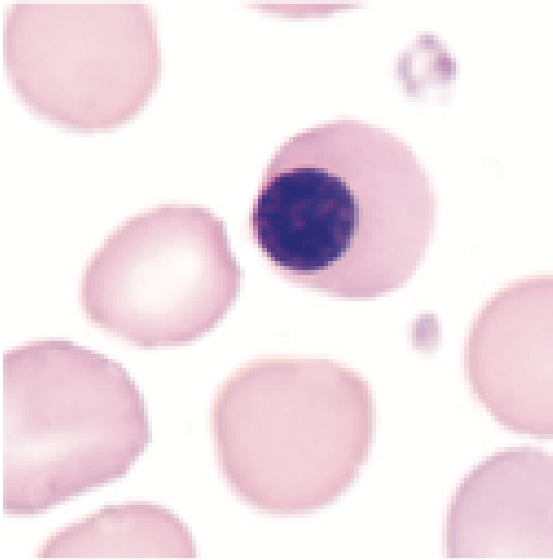


Polychromatic erythrocyte stained with Wright stains appears Slight gray-blue color.



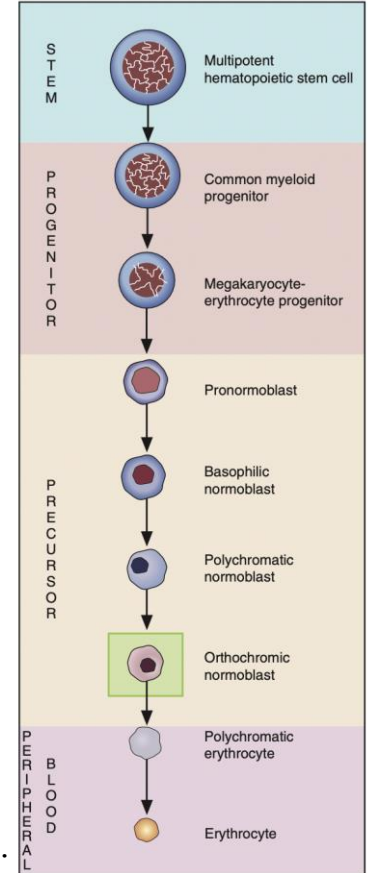
Reticulocytes Stained with supravital stain (new methylene blue) shows precipitated ribosomal material.

4.7 Nucleated RBCs



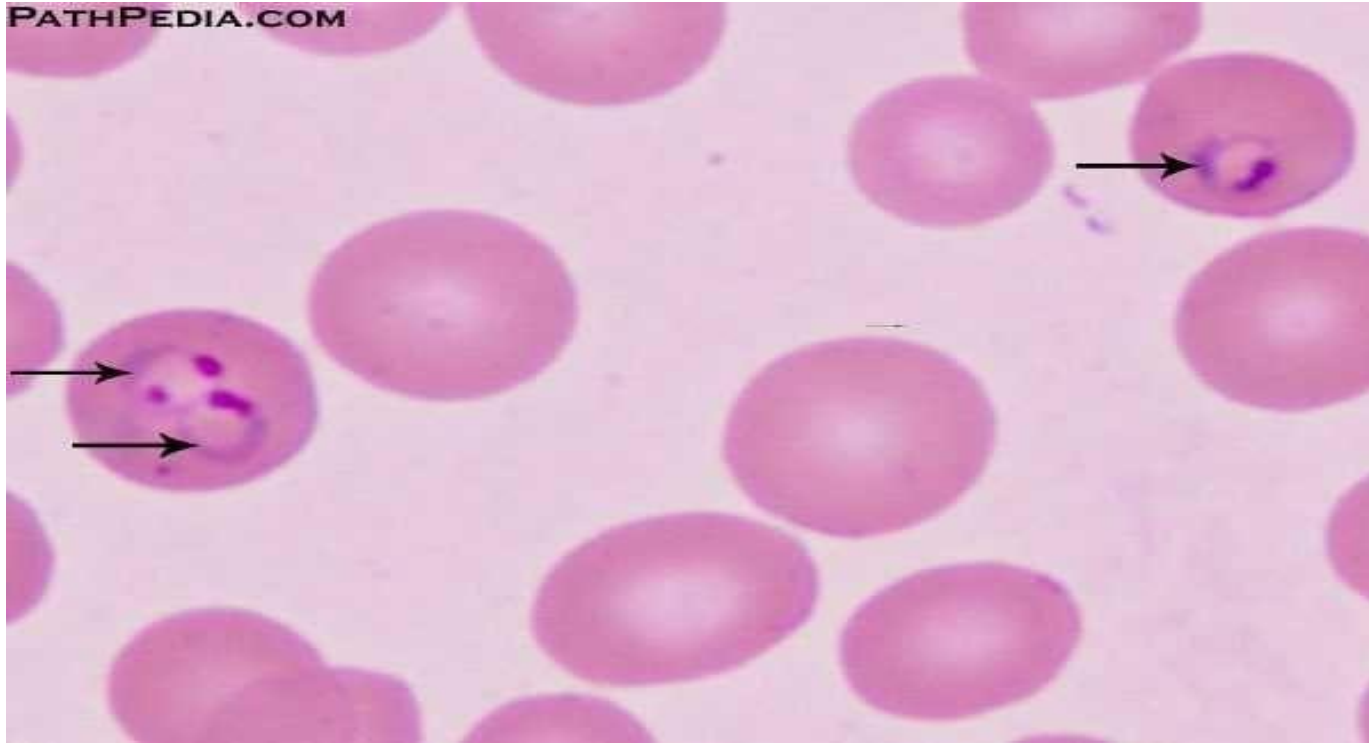
Reference Interval:

- Bone Marrow: 5% to 10%
- Peripheral Blood: 0%
- If present in peripheral blood is associated with ineffective erythropoiesis.

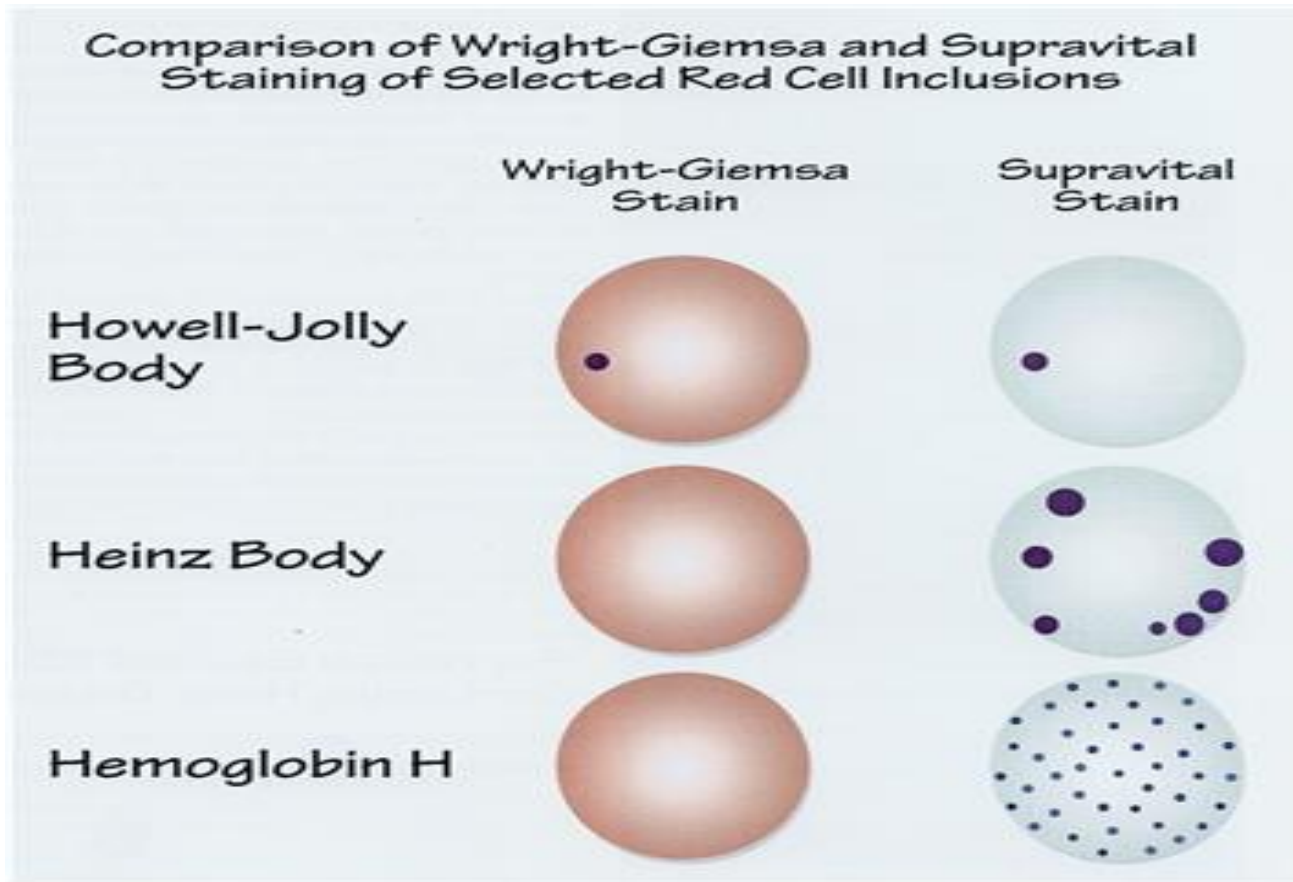


Erythrocyte sequence—orthochromatic normoblast (nucleated RBCs).

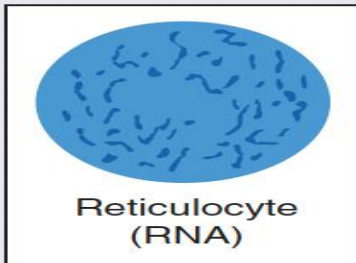
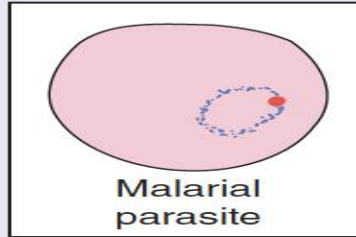
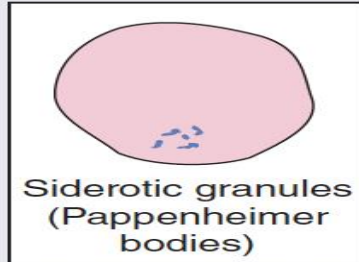
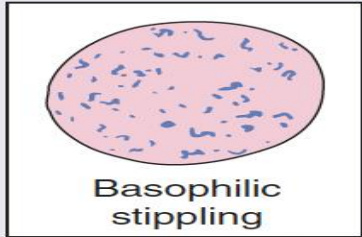
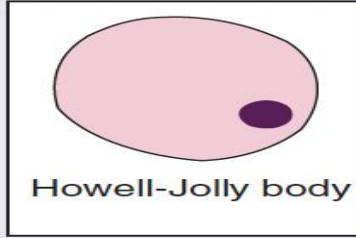
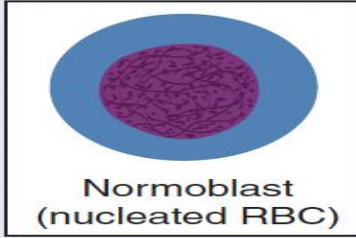
4.8 *Plasmodium* spp. (malaria)



4. Variation in the content



4. Variation in the content



Red blood cell (RBC) inclusions which may be seen in the peripheral blood film in various conditions.

- The reticulocyte RNA and Heinz bodies are only demonstrated by supravital staining (e.g. with new methylene blue).
- Heinz bodies are oxidized denatured haemoglobin.
- Siderotic granules (Pappenheimer bodies) contain iron. They are purple on conventional staining but blue with Perls' stain.
- The Howell-Jolly body is a DNA remnant. Basophilic stippling is denatured RNA.



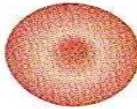

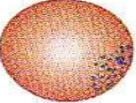
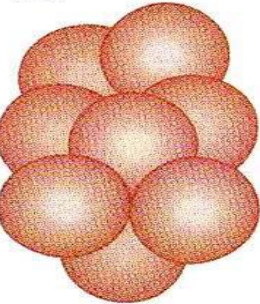




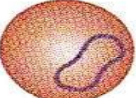
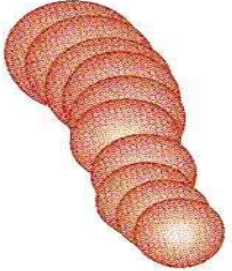


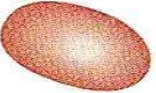


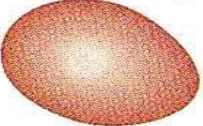


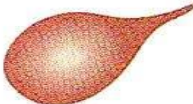

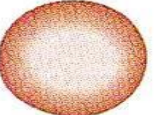





4. Variation in the content

TABLE 12-1 Staining Qualities of Erythrocyte Inclusion Bodies

Inclusion	Composition	Wright- Giemsa Stain	New Methylene Blue (or Other Supravital Stain)	Prussian Blue (Iron)
Howell-Jolly body	DNA	+	+	0
Basophilic stippling	RNA	+	+	0
Pappenheimer body	Iron	+	+	+
Cabot ring	Remnant of mitotic spindle	+	+	0
Heinz body	Unstable hemoglobin	0	+	0
Hemoglobin H	β chains	0	+	0

+, Positive; 0, negative.

RED BLOOD CELL MORPHOLOGY

Size variation	Hemoglobin distribution	Shape variation		Inclusions	Red cell distribution
Normal 	Hypochromia 1+ 	Target cell 	Acanthocyte 	Pappenheimer bodies (siderotic granules) 	Agglutination 
Microcyte 	2+ 	Spherocyte 	Helmet cell (fragmented cell) 	Cabot's ring 	
Macrocyte 	3+ 	Ovalocyte 	Schistocyte (fragmented cell) 	Basophilic stippling (coarse) 	
Oval macrocyte 	4+ 	Stomatocyte 	Tear drop 	Howell-Jolly 	
Hypochromic macrocyte 	Polychromasia (Reticulocyte) 	Sickle cell 	Burr cell 	Crystal formation HbSC  HbC 	



Normal Erythrocyte



Sickle Cell



Dacrocyte



Keratocyte



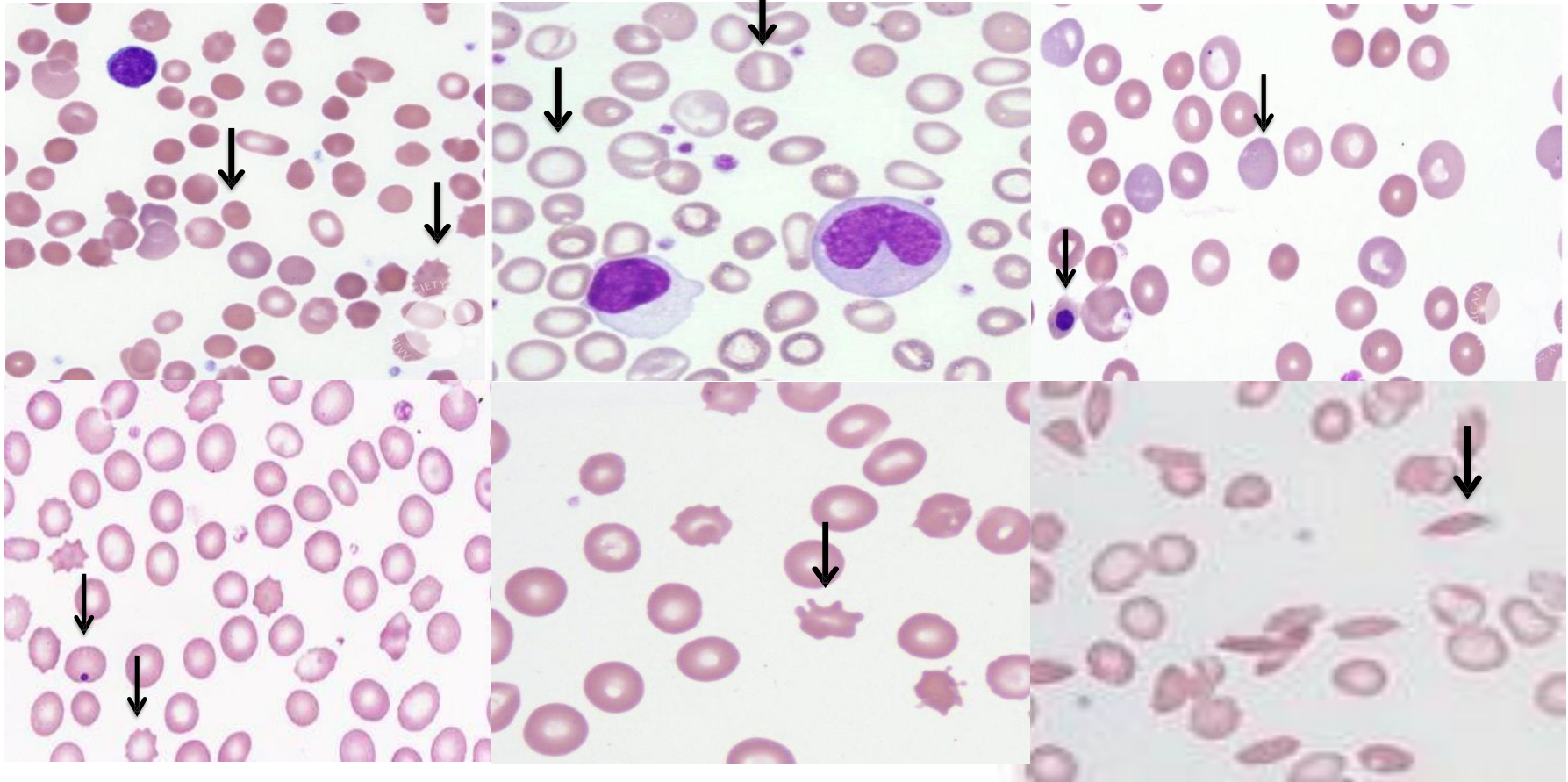
Knizocyte



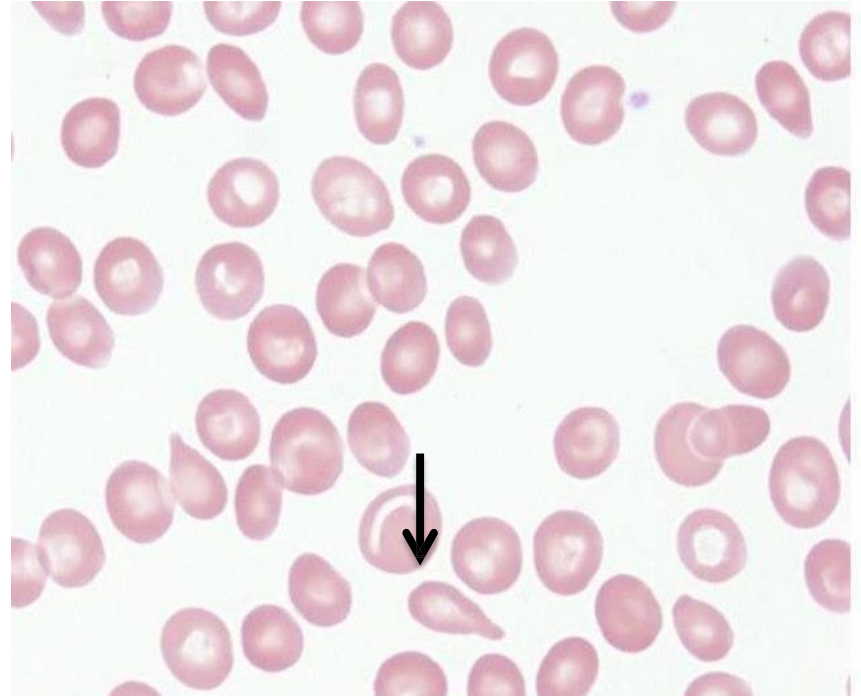
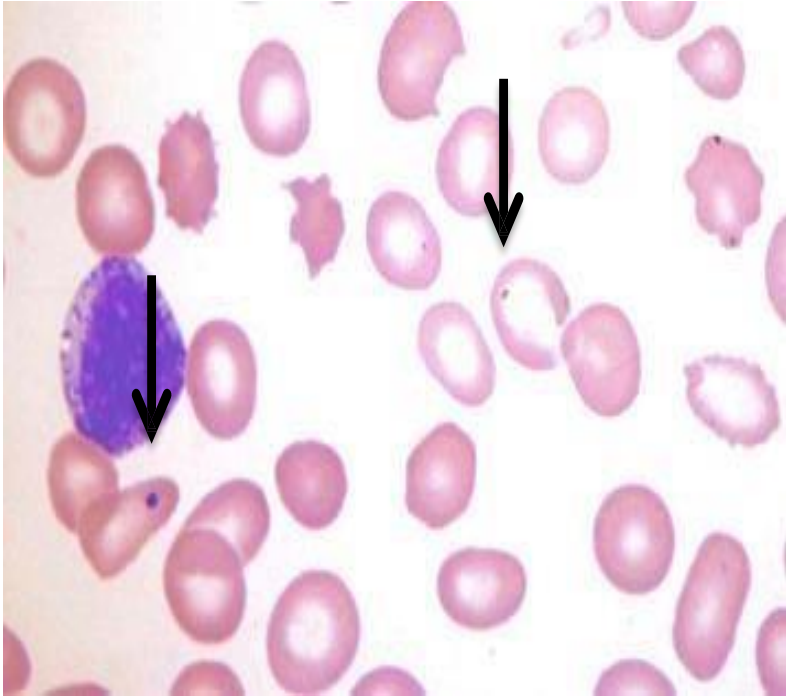
Stomatocyte

FOTORESEARCH

Review



Review



Microscopy check list

Practice finding all of the following cells:

1. Normal red cell
2. Elleptocyte
3. Schistocyte
4. Microcytic hypochromic cell
5. Macrocytic cell
6. Sickle cell
7. Target cell
8. Normocytic hypochromic cell
9. Tear drop cell
10. Howel jolly bodies
11. Bite cell
12. Polychromisia
13. Nucleated RBC
15. Spherocyte (hyperchromic microcytic)
16. Malaria