

به نام خدا

دکتر محمد جعفری

متخصص پاتولوژی

دانشیار دانشگاه علوم پزشکی همدان

**NORMAL MATURATION SERIES****Erythrocyte Series**

Figure 1A1-1

## Pronormoblast (Rubriblast)

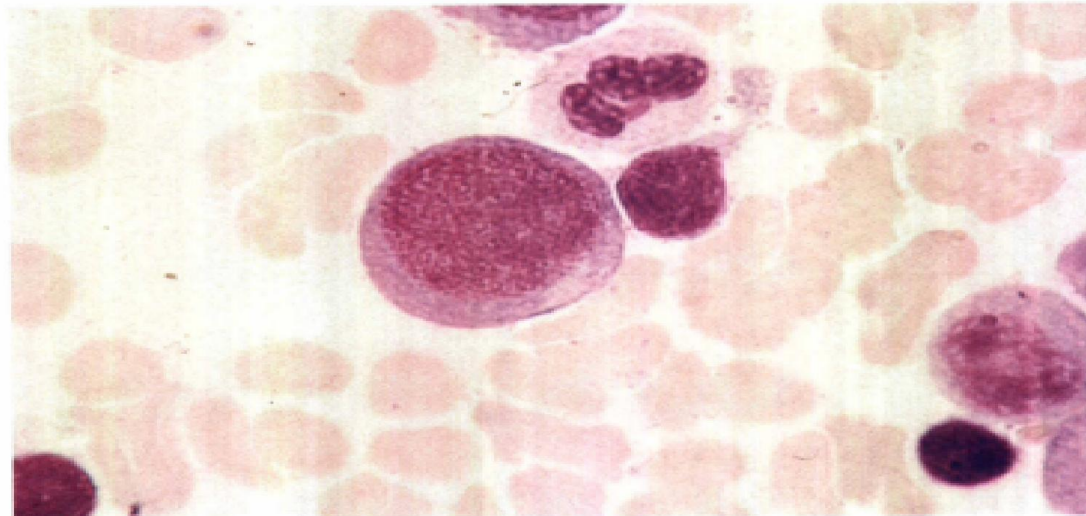


Figure IA1-2

**Size:** 14–22  $\mu$

### **Nucleus**

**Shape:** Round to slightly oval

**N/C Ratio:** 5:1–8:1

**Color:** Purple-red

**Chromatin:** Fine, but granular; parachromatin sparse

**Nucleoli:** 1–2 prominent; bluish tint

### **Cytoplasm**

**Color:** Deep blue

**Contents:** Golgi, mitochondria, which produce a lighter blue color (perinuclear halo)

### **Clinical Conditions**

- Erythroleukemia (M6a)
- Pure erythroid leukemia (M6b)
- Hemolytic disease of the newborn

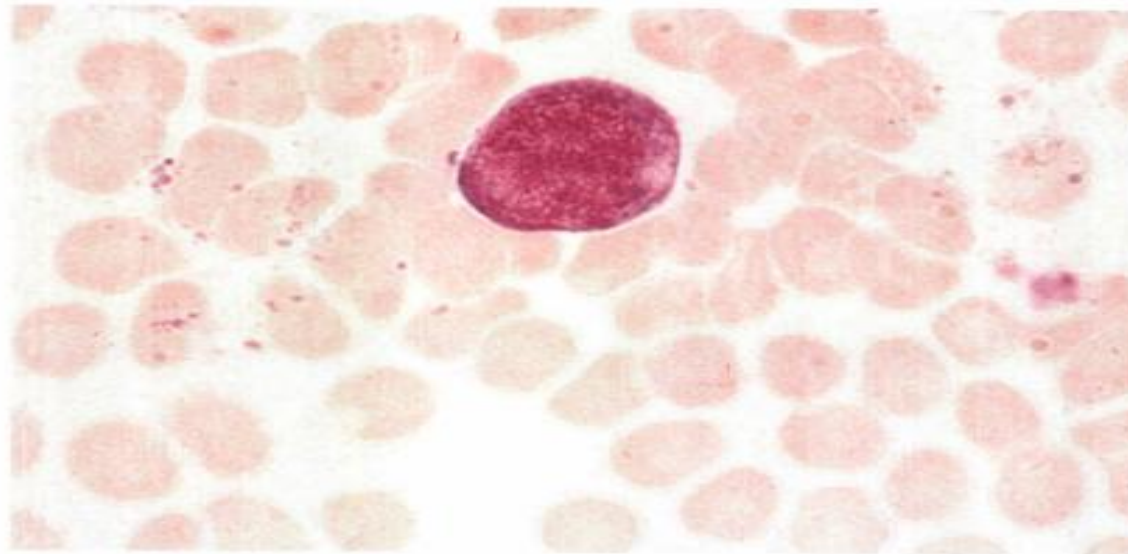
**Basophilic Normoblast (Prorubricyte)**

Figure IA1-3

**Size:** 12–17  $\mu$ **Nucleus****Shape:** Round, centered**N/C Ratio:** 4:1–6:1**Color:** Purple interspersed with light areas**Chromatin:** Coarse and somewhat condensed**Nucleoli:** Usually not visible**Cytoplasm****Color:** Deep blue**Contents:** Golgi may produce a light blue area near the nucleus, many mitochondria**Clinical Conditions**

- Erythroleukemia (M6a)
- Pure erythroid leukemia (M6b)
- Hemolytic disease of the newborn



## Polychromatophilic Normoblast (Rubricyte)

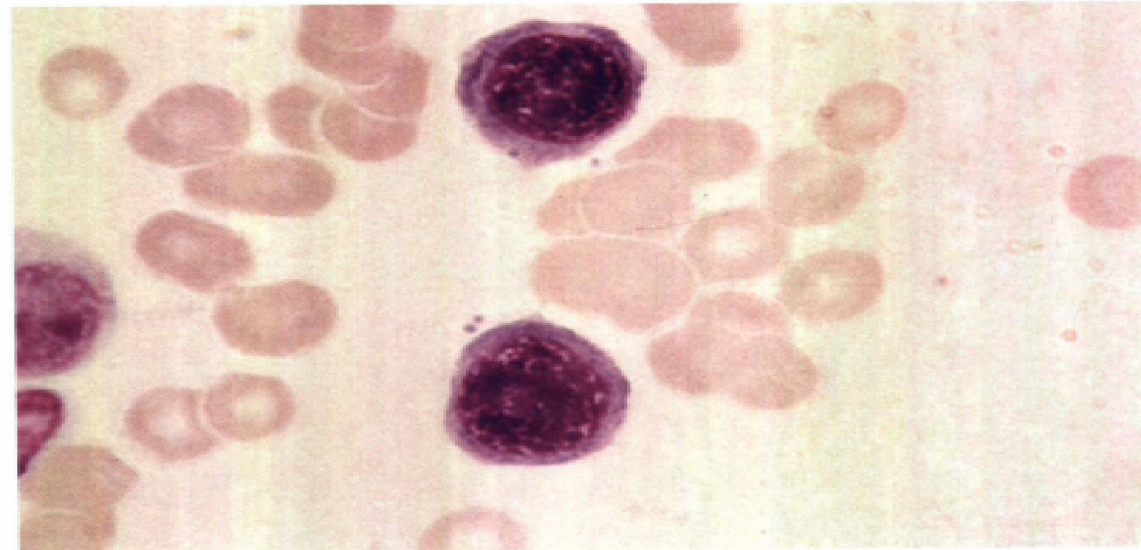


Figure IA1-4

**Size:** 11–14  $\mu$

### **Nucleus**

**Shape:** Round, centered to eccentric

**N/C Ratio:** 1:1–4:1

**Color:** Red-purple

**Chromatin:** Coarse and condensed; parachromatin distinct, producing a “checkerboard” appearance

**Nucleoli:** None

### **Cytoplasm**

**Color:** Bluish-pink to grey-blue

**Contents:** Perinuclear halo visible; increased hemoglobin, causing the pink-grey color; decreased RNA, causing the lighter blue color

### **Clinical Conditions**

- Erythroleukemia (M6a)
- Pure erythroid leukemia (M6b)
- Hemolytic disease of the newborn
- Myeloproliferative disease—chronic idiopathic myelofibrosis (CIMF), chronic myelocytic leukemia (CML)
- Hemolytic anemias
- Thalassemia major
- Sickle cell disease

## Orthochromic Normoblast (Metarubricyte)

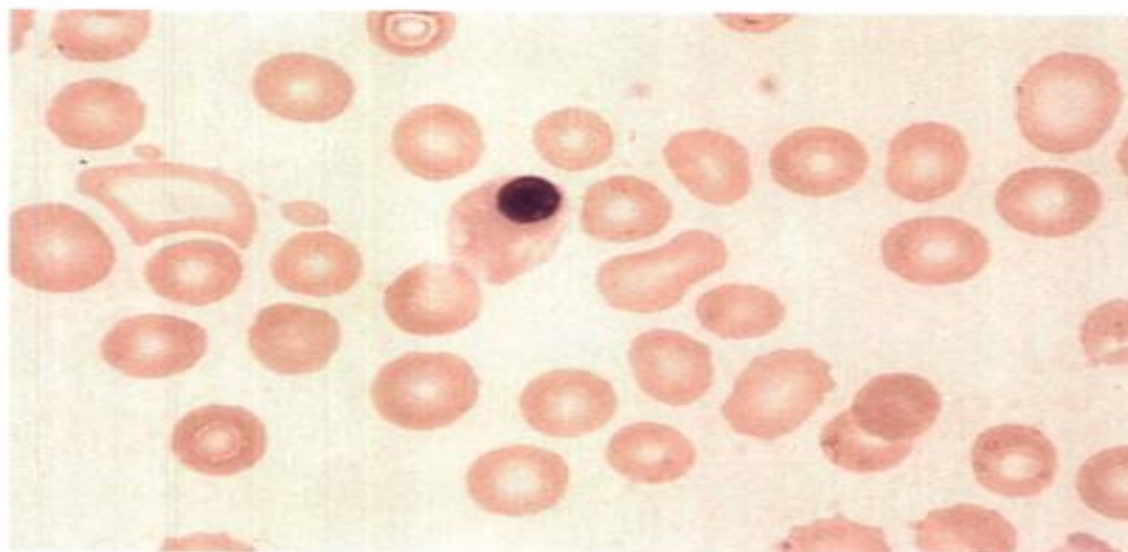


Figure IA1-5

**Size:** 8–12  $\mu$

### **Nucleus**

**Shape:** Round, centered to eccentric; may be fragmented or extruding

**N/C Ratio:** 1:4–1:2

**Color:** Blue-purple

**Chromatin:** Condensed and homogeneous (pyknotic)

**Nucleoli:** None

### **Cytoplasm**

**Color:** Pink to orange-pink, with a hint of blue

**Contents:** Hemoglobin production increased

### **Clinical Conditions**

- Erythroleukemia (M6a)
- Pure erythroid leukemia (M6b)
- Hemolytic disease of the newborn
- Myeloproliferative diseases—CIMF, CML
- Thalassemia major
- Sickle cell disease

## Polychromatophilic Erythrocyte (Reticulocyte)

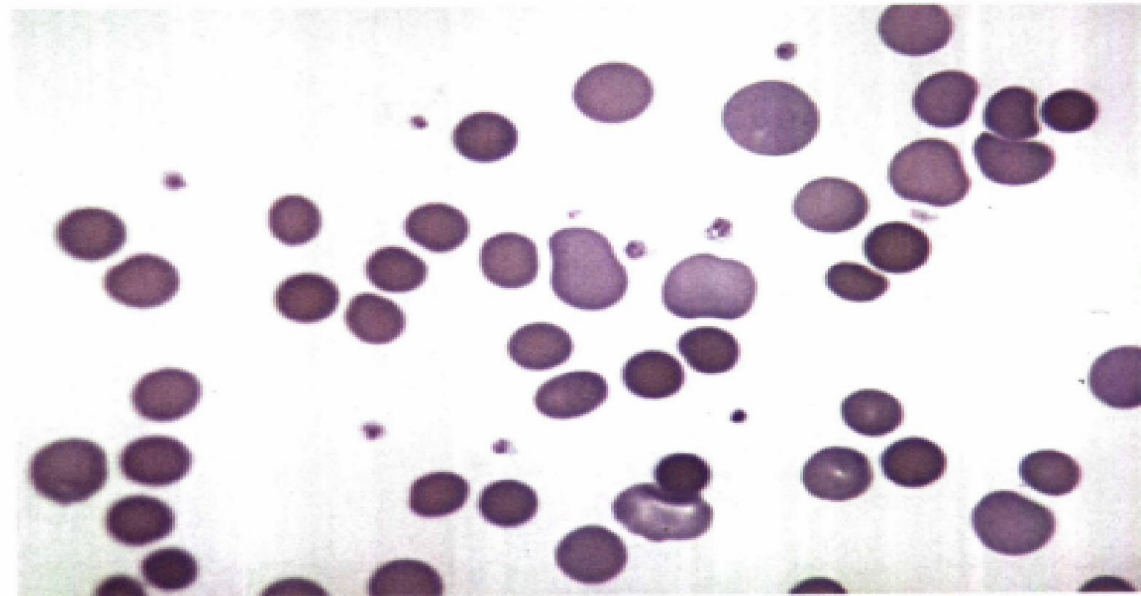


Figure IA1-6

**Size:** 8–11  $\mu$

**Nucleus**

None

**Cytoplasm**

**Color:** Pink, with a tint of blue

**Contents:** Remnants of Golgi and mitochondria, residual RNA (reticulum)

**Clinical Conditions**

- Increased erythrocyte production
- Hemolytic anemias
- Membrane disorders
- Hemolytic disease of the newborn

## Mature Red Blood Cell (Mature Erythrocyte)

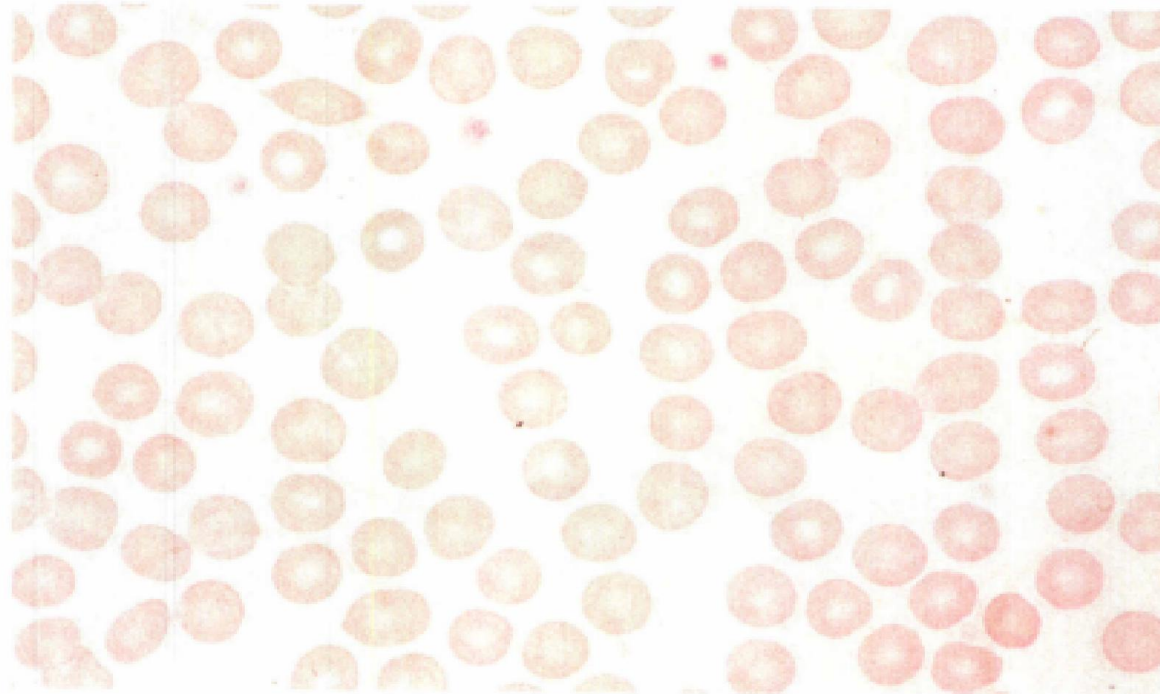


Figure IA1-7

**Size:** 7–7.5  $\mu$

**Nucleus**

None

**Cytoplasm**

**Color:** Pink, central pallor about 1/3 of the cell

**Contents:** No mitochondria

**MEGALOBlastic MATURATION SERIES****Megaloblastic Series**

Figure IA1-8



## Promegaloblast (Megaloblastic Rubriblast)

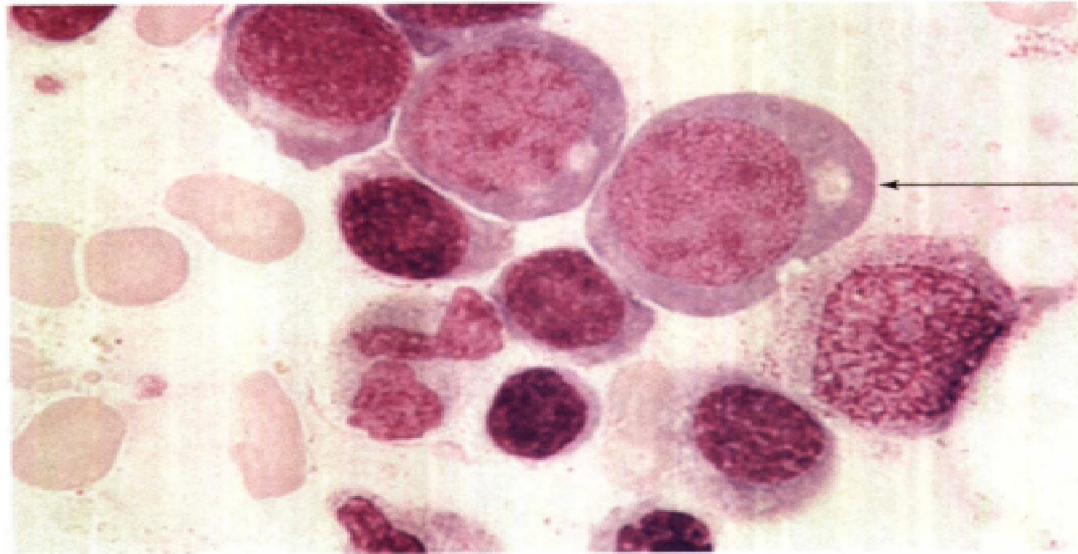


Figure IA1-9

**Size:** 19–27  $\mu$

### **Nucleus**

**Shape:** Round or irregular

**N/C Ratio:** 5:1

**Color:** Purple

**Chromatin:** Fine and closely meshed

**Nucleoli:** Multiple

### **Cytoplasm**

**Color:** Deep blue

**Contents:** Nongranular with perinuclear halo

### **Clinical Conditions**

- Vitamin B<sub>12</sub> deficiency
- Folic acid deficiency
- Congenital dyserythropoietic anemia

### Basophilic Megaloblast (Megaloblastic Prorubricyte)

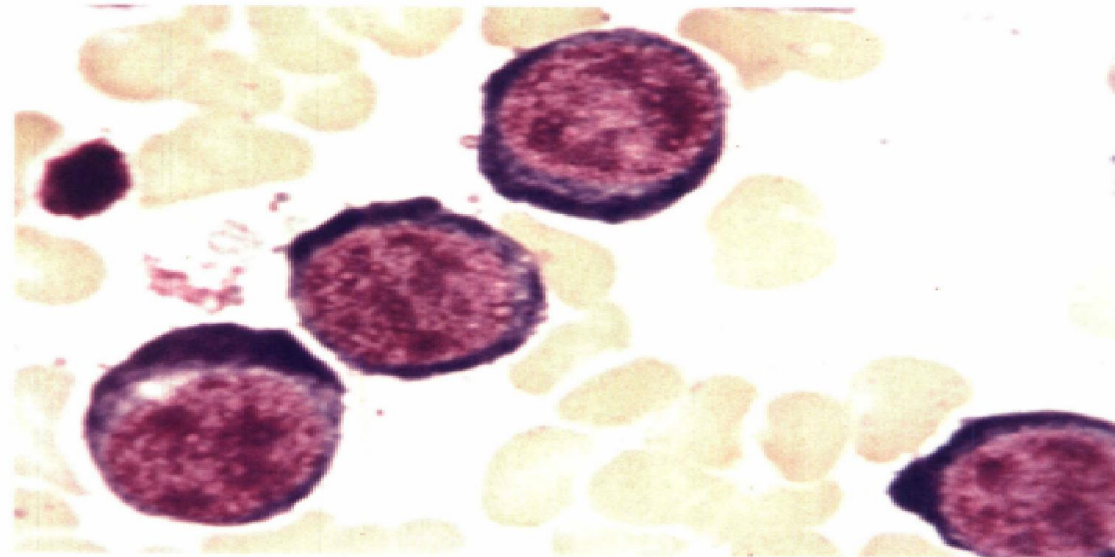


Figure IA1-10

**Size:** 17–24  $\mu$

#### **Nucleus**

Shape: Round

N/C Ratio: 4:1

Color: Purple

Chromatin: Coarser than previous cell but still fine and open

Nucleoli: Not visible

#### **Cytoplasm**

Color: Deep blue

Contents: Faint perinuclear halo

#### **Clinical Conditions**

- Vitamin B<sub>12</sub> deficiency
- Folic acid deficiency
- Congenital dyserythropoietic anemia

### Polychromatophilic Megaloblast (Megaloblastic Rubricyte)

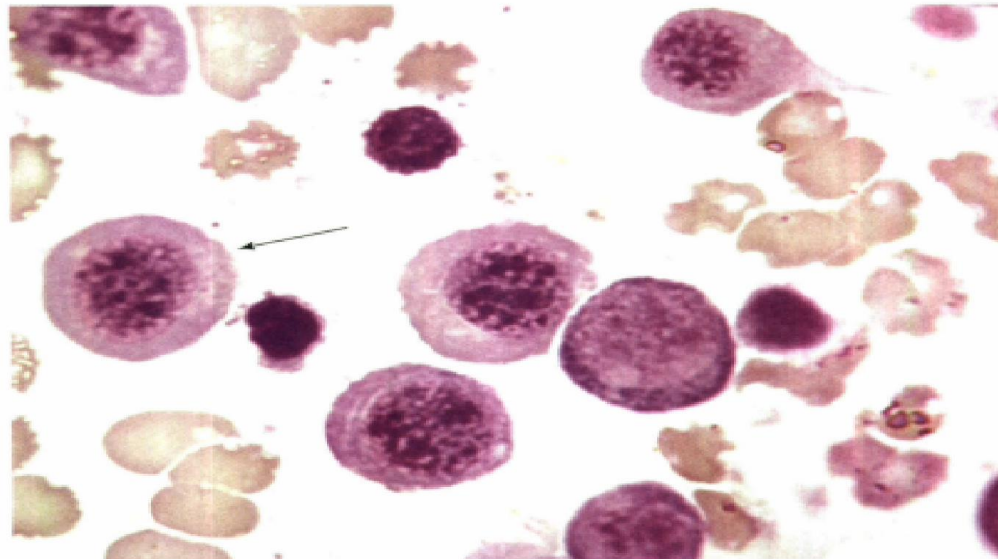


Figure IA1-11

**Size:** 15–20  $\mu$

#### **Nucleus**

**Shape:** Round and central

**N/C Ratio:** 2:1

**Color:** Purple

**Chromatin:** Minimal clumping, loosely defined

**Nucleoli:** Not visible

#### **Cytoplasm**

**Color:** Blue-grey to pink-grey

**Contents:** More cytoplasm than in normoblastic cell

#### **Clinical Conditions**

- Vitamin B<sub>12</sub> deficiency
- Folic acid deficiency
- Congenital dyserythropoietic anemia



### Orthochromic Megaloblast (Megaloblastic Metarubricyte)

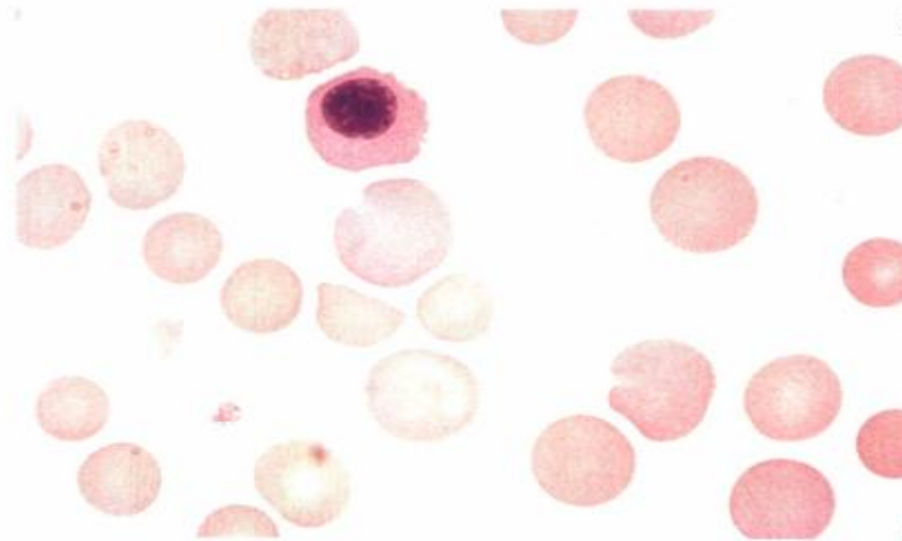


Figure IA1-12

**Size:** 10–15  $\mu$

#### **Nucleus**

**Shape:** Round to slightly irregular, central or slightly eccentric

**N/C Ratio:** 1:1

**Color:** Deep purple but still some chromatin structure

**Chromatin:** Clumped, but less than in normoblastic cell

**Nucleoli:** Not visible

#### **Cytoplasm**

**Color:** Pink, with a hint of blue

**Contents:** More cytoplasm than in normoblastic cell

#### **Clinical Conditions**

- Vitamin B<sub>12</sub> deficiency
- Folic acid deficiency
- Congenital dyserythropoietic anemia

## Polychromatophilic Megalocyte (Megaloblastic Reticulocyte)

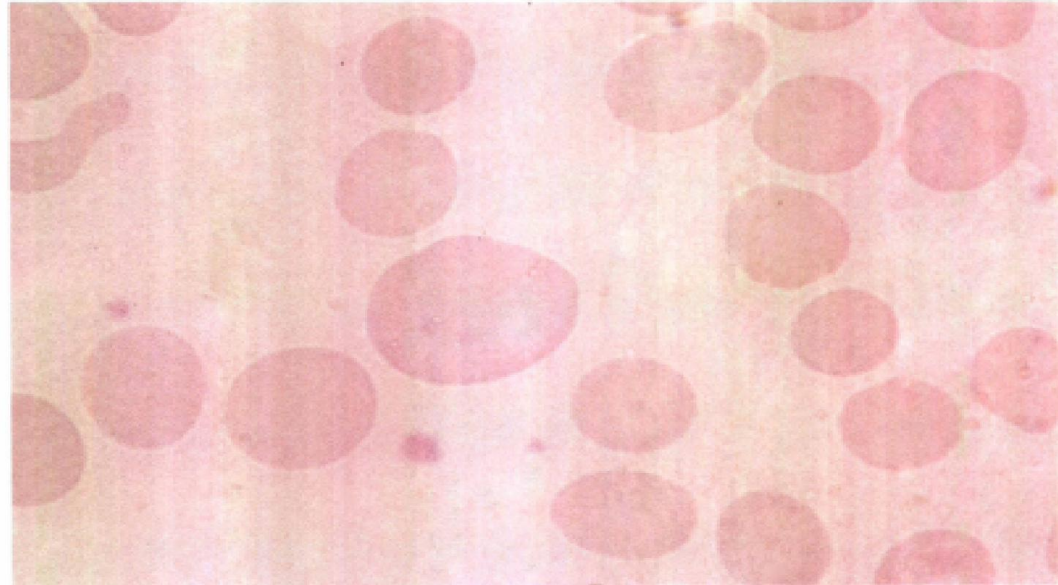


Figure IA1-13

**Size:** 9–15  $\mu$

**Nucleus**

None

**Cytoplasm**

**Color:** Pink, with a hint of blue

**Clinical Conditions**

- Vitamin B<sub>12</sub> deficiency
- Folic acid deficiency
- Congenital dyserythropoietic anemia

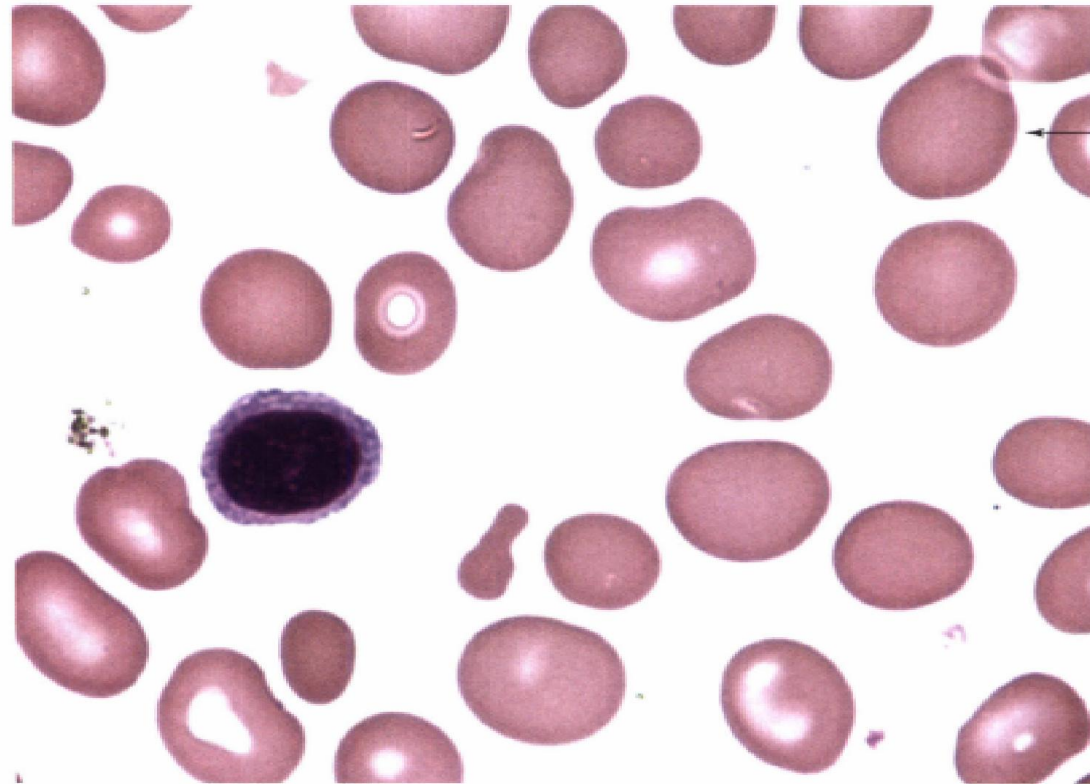
**Megalocyte (Oral Macrocyte)**

Figure IA1-14

**Size:** 9–12  $\mu$ **Nucleus**

None

**Cytoplasm****Color:** Pink, central pallor less distinct**Contents:** Increased hemoglobin content**Clinical Conditions**

- Vitamin B<sub>12</sub> deficiency
- Folic acid deficiency
- Congenital dyserythropoietic anemia
- Myelodysplastic syndromes
- Newborn

**IRON-DEFICIENT MATURATION SERIES****Iron-Deficient Series**

Figure IA1-15

### Iron-Deficient Pronormoblast (Iron-Deficient Rubriblast)

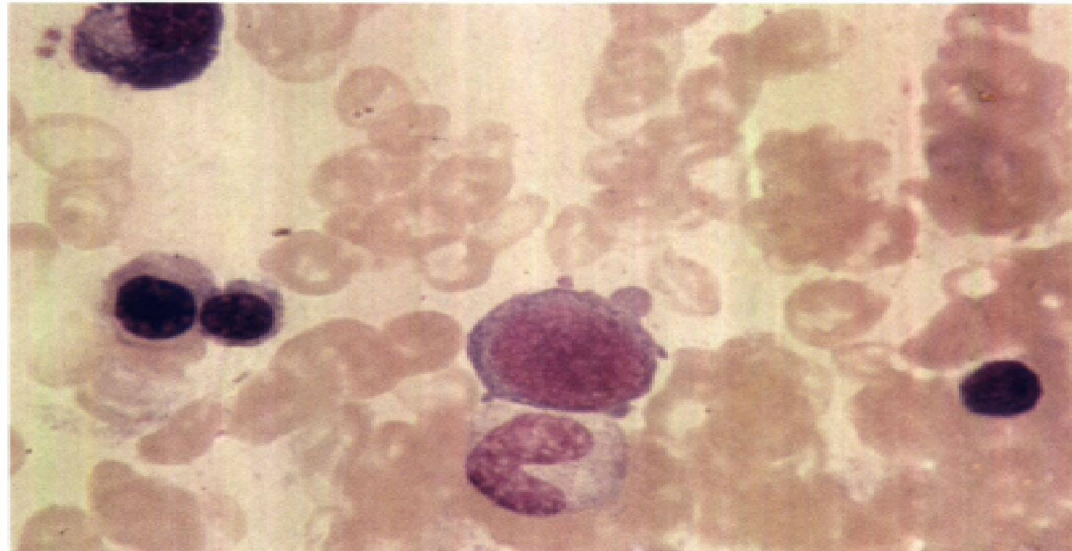


Figure IA1-16

**Size:** 14–20  $\mu$

#### **Nucleus**

**Shape:** Irregularly round to slightly oval

**N/C Ratio:** 5:1

**Color:** Purple-red

**Chromatin:** Fine, but granular

**Nucleoli:** Present, but not distinct

#### **Cytoplasm**

**Shape:** Irregular

**Color:** Deep blue

**Contents:** Golgi; mitochondria, which produce a lighter blue perinuclear halo

#### **Clinical Conditions**

- Iron deficiency
- Anemia of chronic disease



### Iron-Deficient Basophilic Normoblast (Iron-Deficient Prorubricyte)

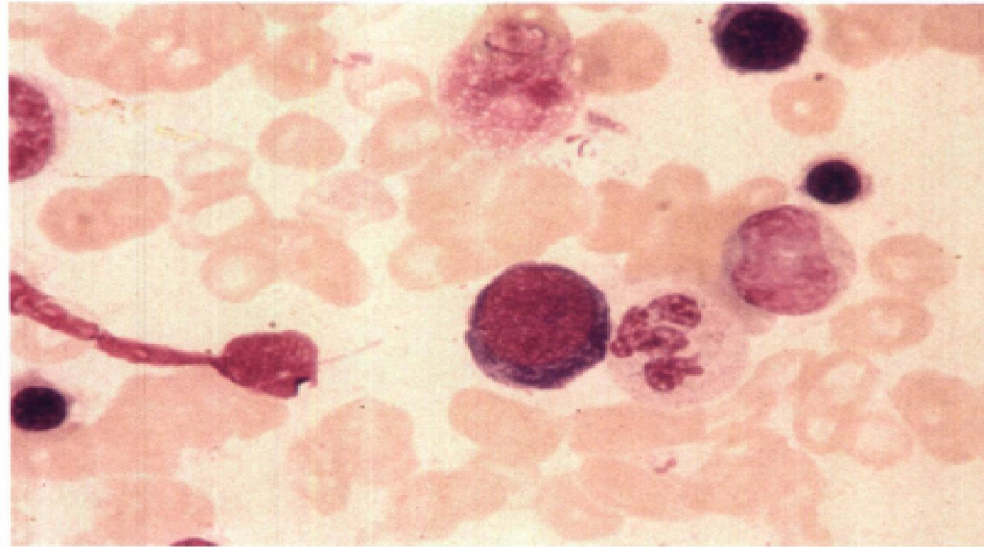


Figure IA1-17

**Size:** 10–15  $\mu$

#### **Nucleus**

**Shape:** Round, centered

**N/C Ratio:** 5:1

**Color:** Purple, interspersed with light areas

**Chromatin:** Granular to slightly lumpy

**Nucleoli:** Usually not visible

#### **Cytoplasm**

**Shape:** Irregular

**Color:** Deep blue

**Contents:** Golgi may produce a light blue area near the nucleus; many mitochondria

#### **Clinical Conditions**

- Iron deficiency
- Anemia of chronic disease

### **Iron-Deficient Polychromatophilic Normoblast (Iron-Deficient Rubricyte)**

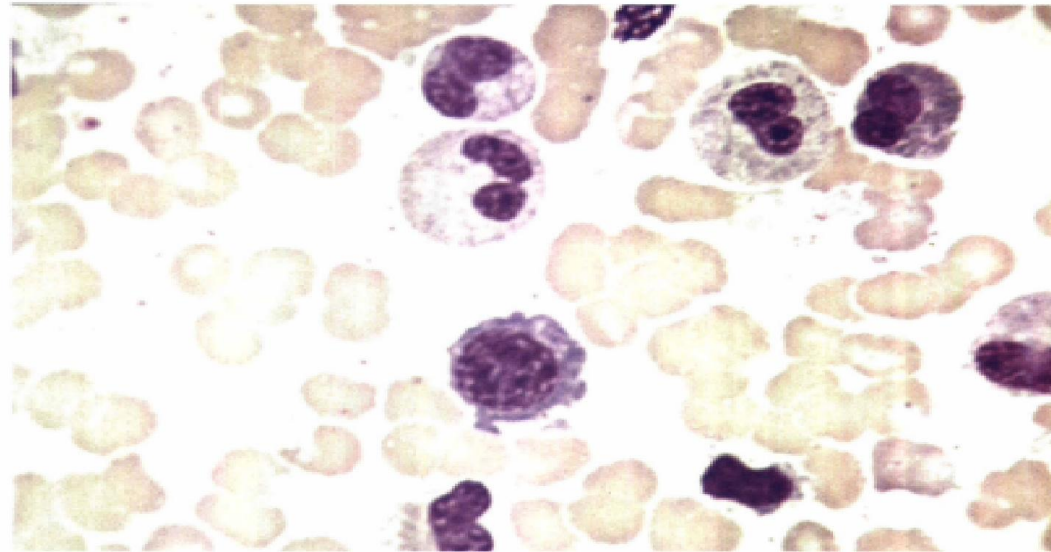


Figure **IA1-18**

**Size:** 9–12  $\mu$

#### **Nucleus**

**Shape:** Round

**N/C Ratio:** 2:1

**Color:** Purple-red

**Chromatin:** Lumpy, with lighter parachromatin

**Nucleoli:** None

#### **Cytoplasm**

**Color:** Bluer than in normoblastic maturation

**Contents:** Lesser amount with shaggy blunt extensions

#### **Clinical Conditions**

- Iron deficiency
- Anemia of chronic disease

### Iron-Deficient Orthochromic Normoblast (Iron-Deficient Metarubricyte)

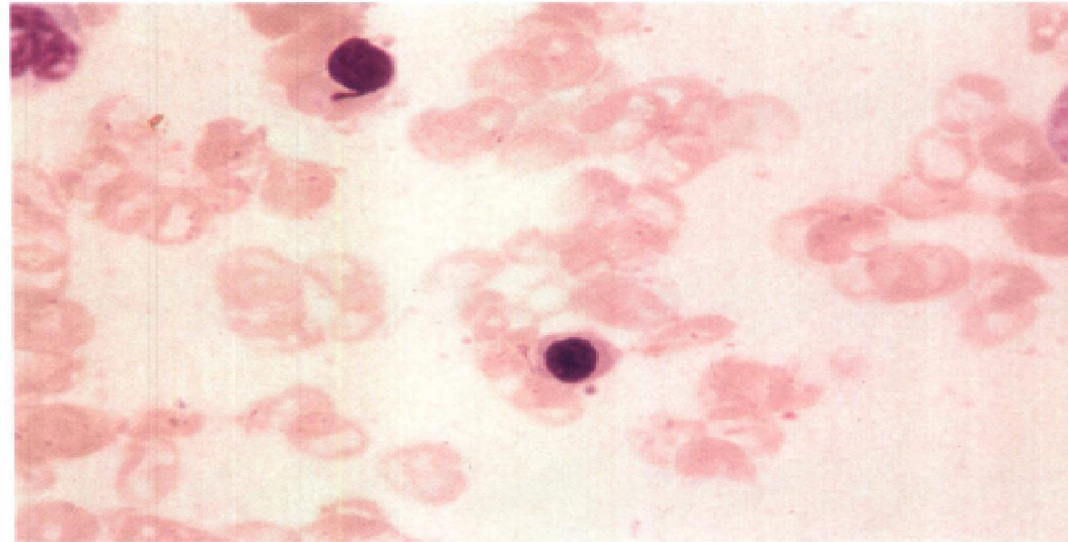


Figure IA1-19

**Size:** 7–11  $\mu$

#### **Nucleus**

**Shape:** Round

**N/C Ratio:** 1:2

**Color:** Blue-purple

**Chromatin:** Condensed and homogeneous

**Nucleoli:** None

#### **Cytoplasm**

**Shape:** Irregular

**Color:** Pink, with residual blueness of RNA

#### **Clinical Conditions**

- Iron deficiency
- Anemia of chronic diseases



## Iron-Deficient Polychromatophilic Erythrocyte

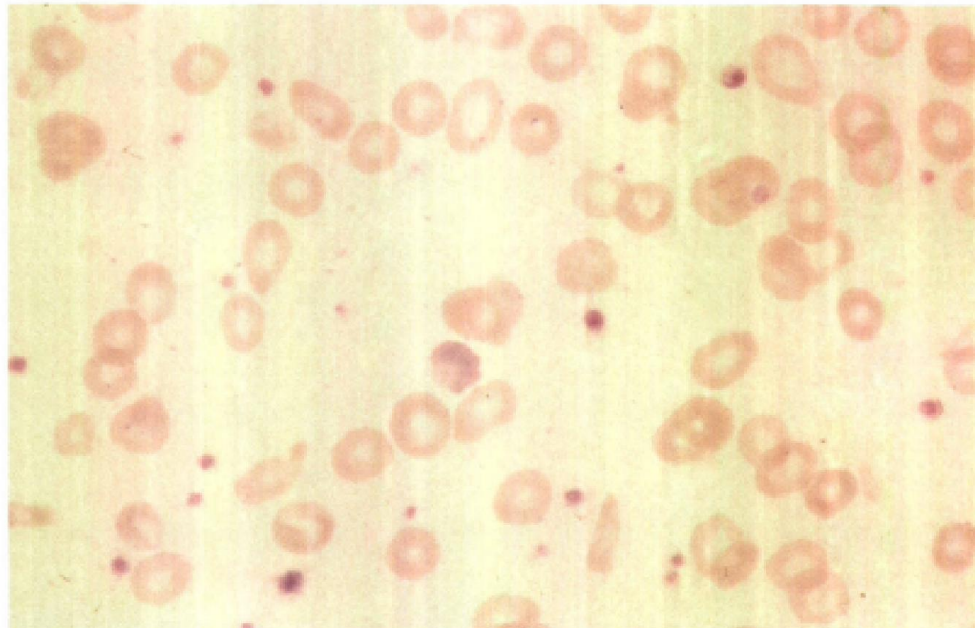


Figure IA1-20

**Size:**  $<6.5\text{--}10\ \mu$

**Nucleus**

None

**Cytoplasm**

Color: Pink, with a hint of blue

**Clinical Conditions**

- Iron deficiency
- Anemia of chronic diseases

### Iron-Deficient Erythrocyte (Hypochromic/Microcytic)

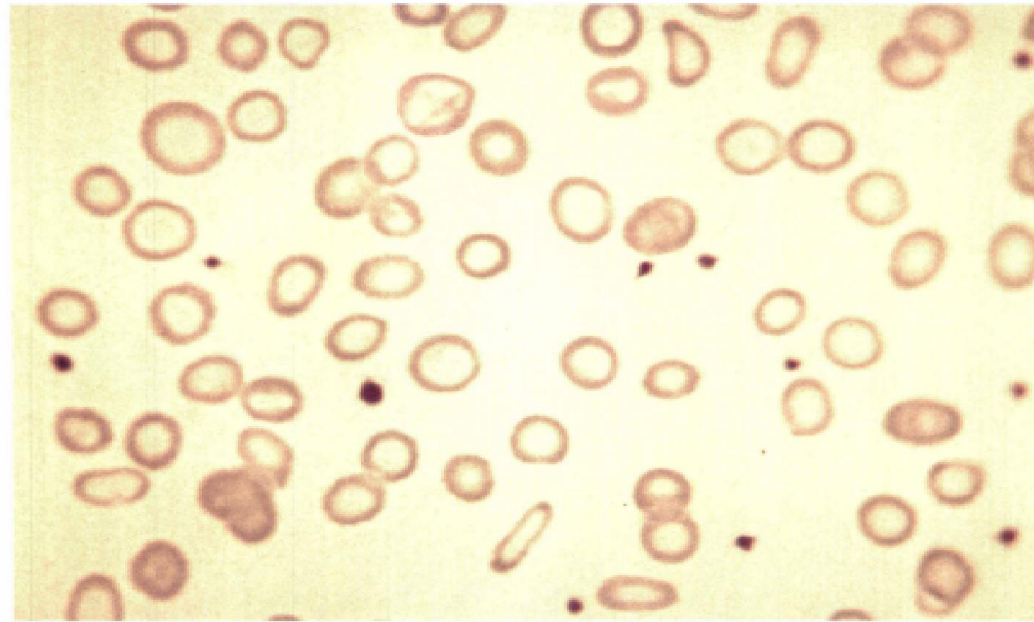


Figure IA1-21

**Size:**  $< 6.5 \mu$

**Nucleus**

None

**Cytoplasm**

**Color:** Pink, central pallor greater than one-third of cell

**Contents:** Hemoglobin decreased

**Clinical Conditions**

- Iron deficiency
- Anemia of chronic disease

## DISTRIBUTION

## Agglutination

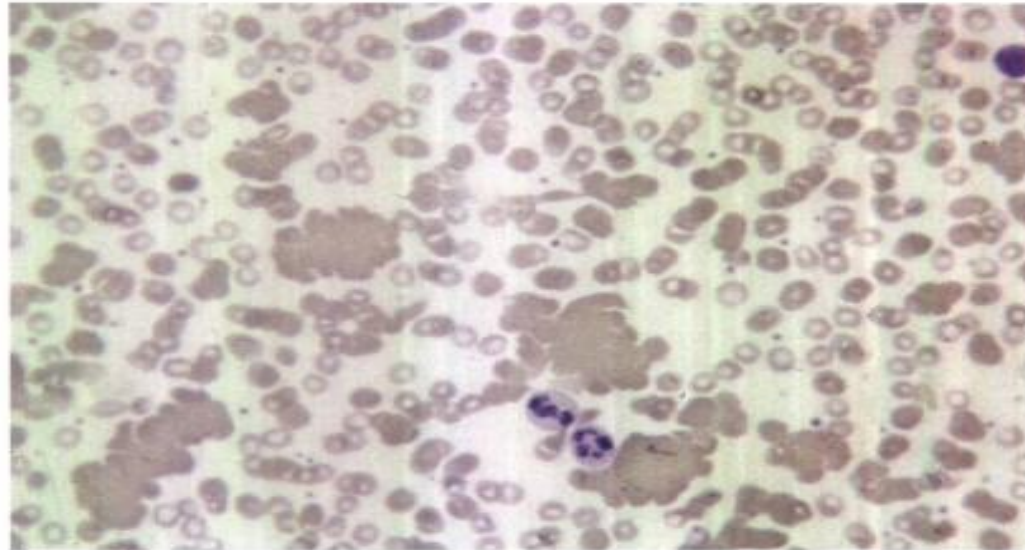


Figure IA1-22

### **Cell Type**

Mature red blood cells

### **Description**

Random masses or clusters of cells

### **Clinical Conditions**

- Exposure to a variety of antibodies
- Hemolytic anemia (autoimmune)
- Atypical pneumonia
- Staphylococcal infections
- Trypanosomiasis
- Cold agglutinin disease

## Rouleaux

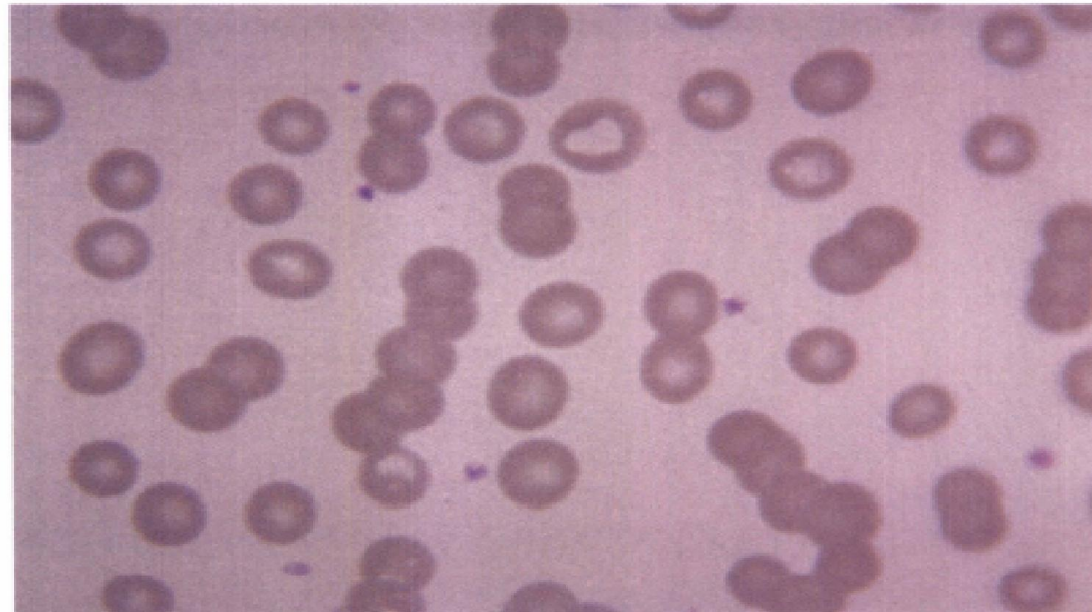


Figure IA1-23

### **Cell Type**

Mature red blood cell

### **Description**

Short or long stacks of cells (three or four or more) resembling coins; often a blue-staining background is also present

### **Clinical Conditions**

- Hyperproteinemia
- Multiple myeloma
- Macroglobulinemia
- Increased fibrinogen (infection, pregnancy)



## SHAPES

### Acanthocyte

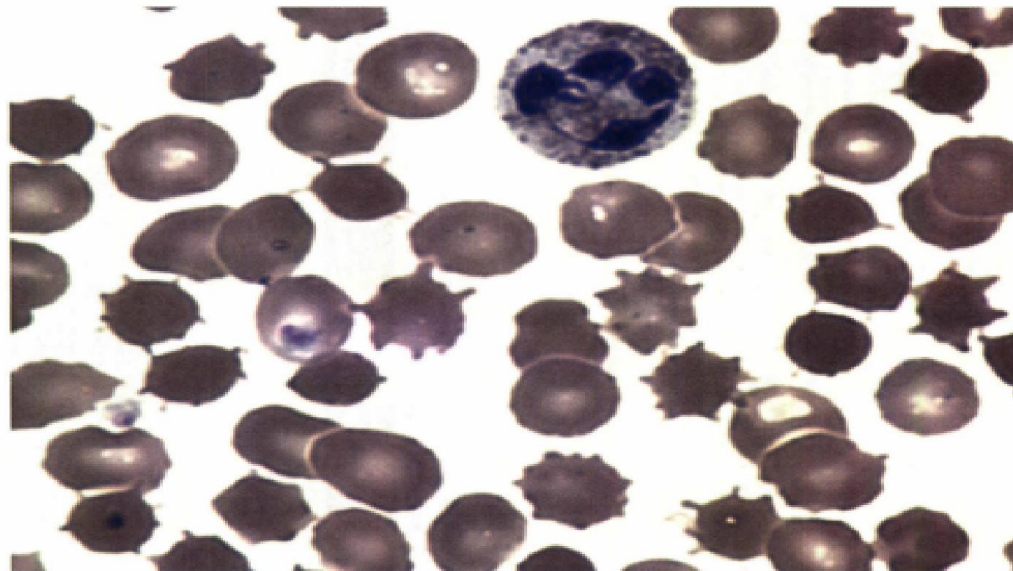


Figure IA1-24

#### **Cell Type**

Mature red blood cell

#### **Description**

Spherical and densely stained cell with 3–12 spicules of uneven length and width around the surface

#### **Clinical Conditions**

- Inherited lipid disorder (abetalipoproteinemia)
- Alcoholic cirrhosis
- Malabsorption states
- Neonatal hepatitis
- Pyruvate kinase deficiency

## Codocyte (Target Cell)

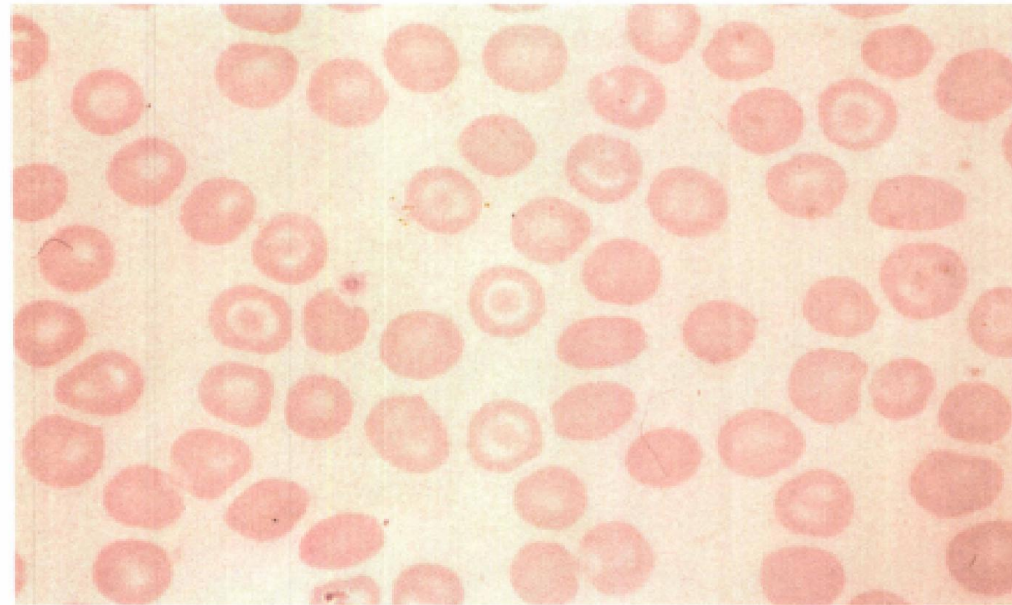


Figure IA1-25

### **Cell Type**

Mature red blood cell

### **Description**

Bell shaped, with a thin wall having a greater-than-normal surface membrane:volume ratio; central area of hemoglobin, a clear ring, and a peripheral ring of hemoglobin, giving an appearance of a bull's eye

### **Clinical Conditions**

- Hemoglobinopathies
- Thalassemia
- Obstructive liver disease
- Iron deficiency anemia

## Dacryocyte (Teardrop Cell)

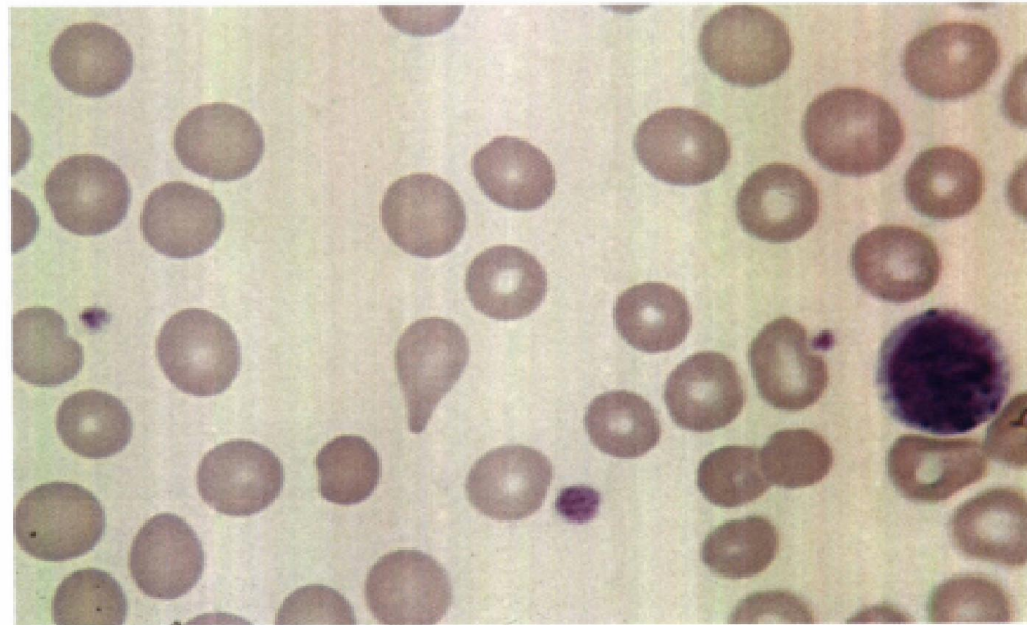


Figure IA1-26

### **Cell Type**

Mature red blood cell

### **Description**

Pear-shaped cell with a blunt pointed projection

### **Clinical Conditions**

- Extramedullary hematopoiesis (myelofibrosis, myelophthisic anemia)
- Megaloblastic anemia
- Thalassemia
- Hypersplenism
- Renal disease

## Degmacyte (Bite Cell)

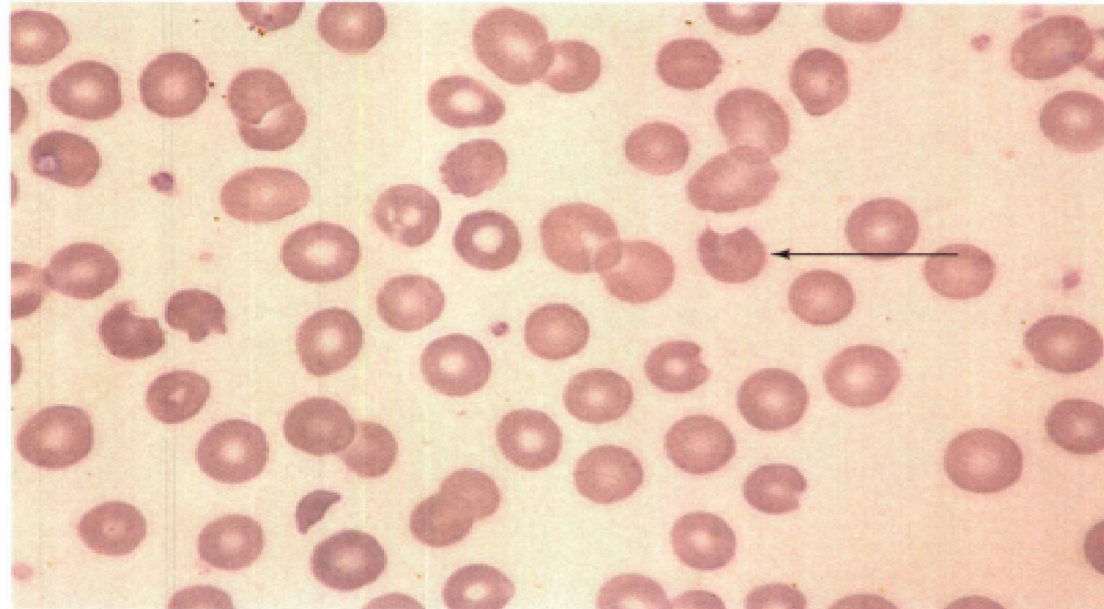


Figure IA1-27

### **Cell Type**

Mature red blood cell

### **Description**

Semicircular area (denatured and precipitated masses of hemoglobin) of cell removed by spleen; these cells may show multiple peripheral defects

### **Clinical Conditions**

- Drug-induced anemias
- Glucose-6-phosphate dehydrogenase deficiency
- Thalassemia
- Unstable hemoglobinopathies



## Drepanocyte (Sickle Cell)



Figure IA1-28

### **Cell Type**

Mature red blood cell

### **Description**

Elongated cell due to polymers of abnormal hemoglobin; terminal projections, causing the cell to take on an irregular shape; usually lacks a central pallor

### **Clinical Conditions**

■ Hemoglobinopathies (SS, SC, SD, S- $\beta$  thalassemia)

## Echinocyte (Burr Cell)

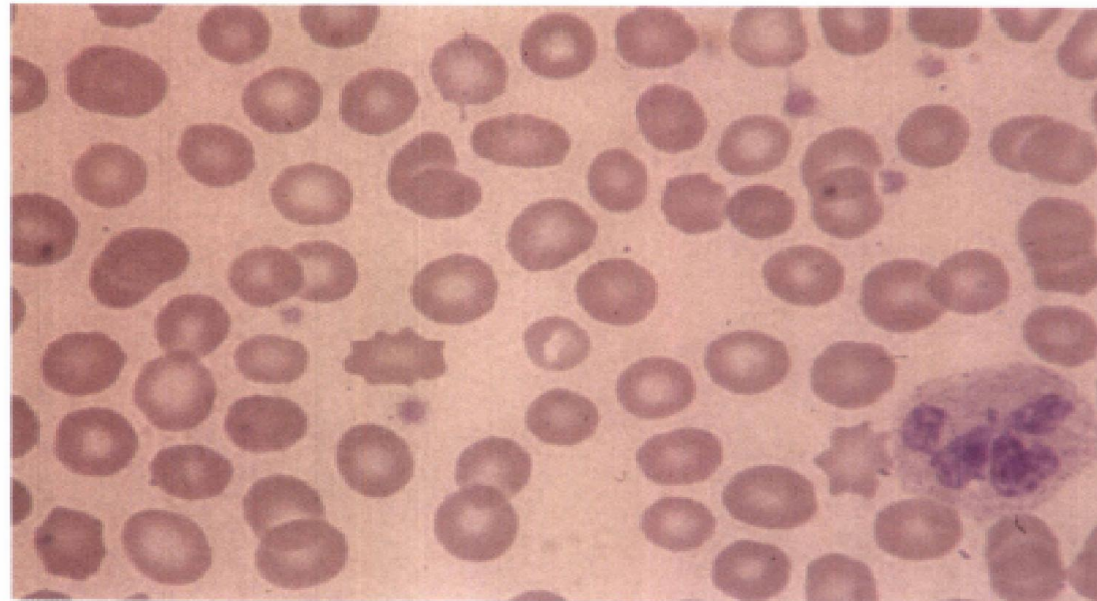


Figure IA1-29

### **Cell Type**

Mature red blood cell

### **Description**

Cell with evenly distributed, short spicules; the spicules have a blunt end; retains central pallor

### **Clinical Conditions**

- Slow drying in high humidity
- Renal insufficiency
- Pyruvate kinase deficiency
- Stored blood
- Severe dehydration
- Burns

## Keratocyte (Horn Cell)

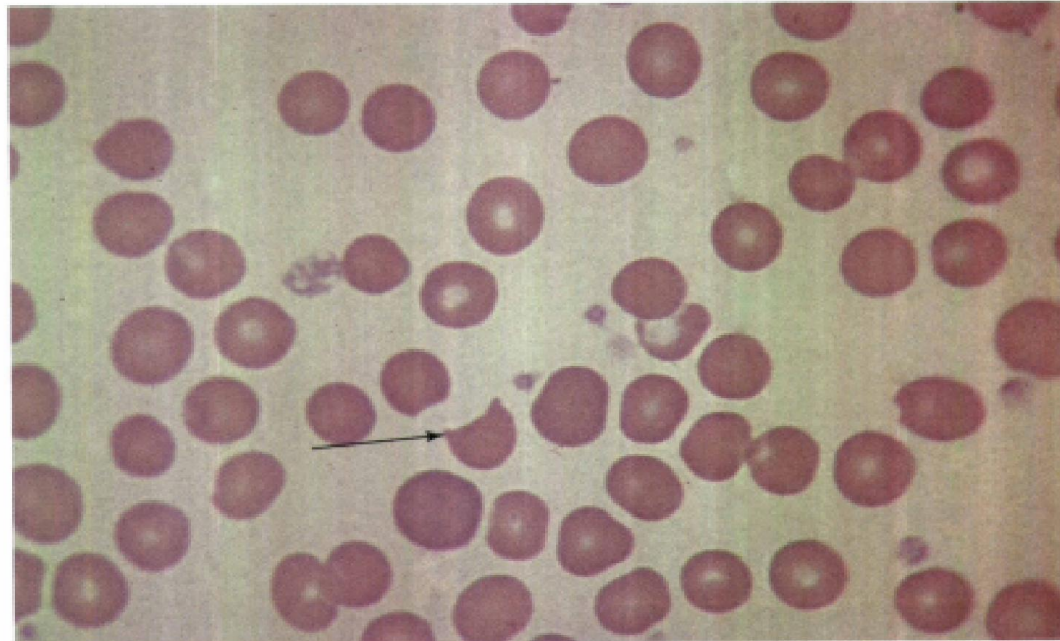


Figure IA1-30

### **Cell Type**

Mature red blood cell

### **Description**

Cell with projections (usually two) that resemble horns

### **Clinical Conditions**

- Microangiopathic hemolytic anemia
- Glomerulonephritis
- Waring Blender syndrome
- Pyruvate kinase deficiency

## Knizocyte (Pinch Cell)

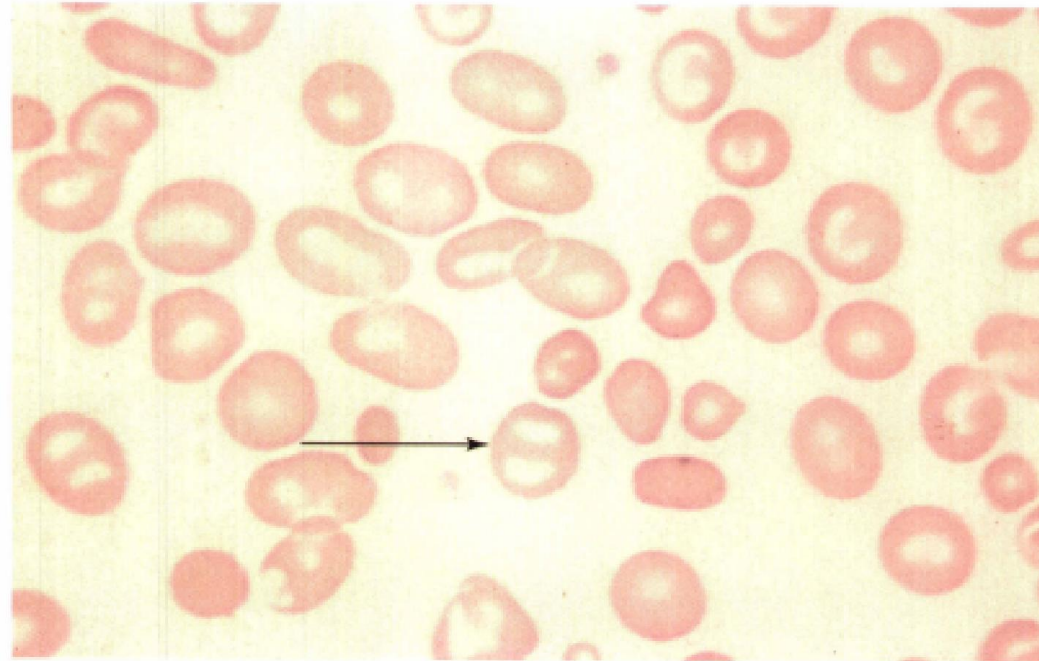


Figure IA1-31

### **Cell Type**

Mature red blood cell

### **Description**

Cell with triconcave shape having two central pallors

### **Clinical Conditions**

- Hemolytic anemia
- Hemoglobinopathies
- Pancreatitis



## Ovalocyte (Elliptocyte)

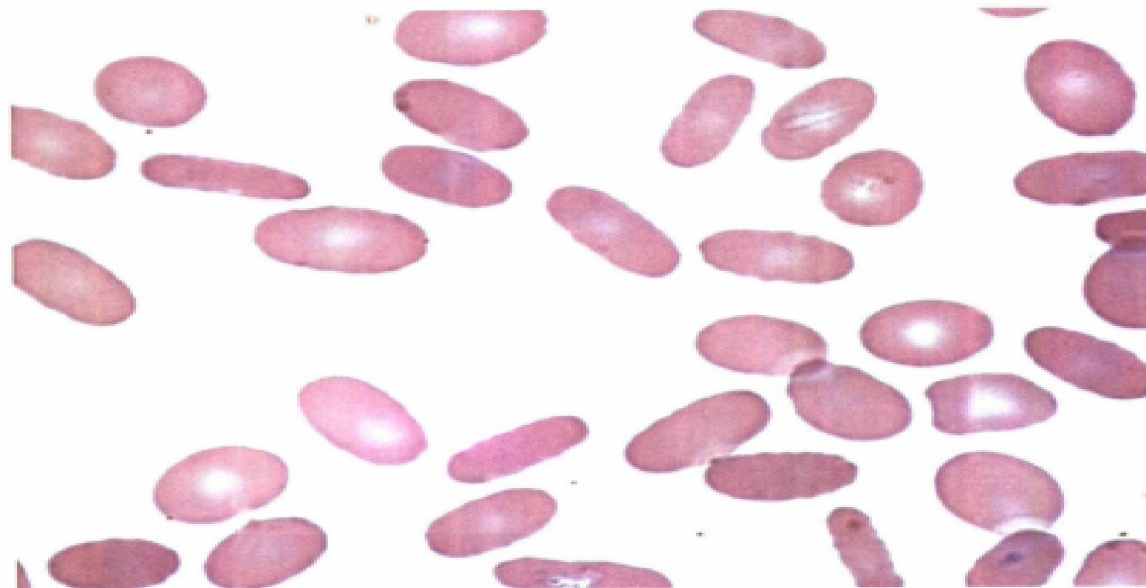


Figure IA1-32

### **Cell Type**

Mature red blood cell

### **Description**

Oval-shaped cell (may be slightly egg, rod, or pencil shaped); hemoglobin is concentrated at two ends; normal central pallor

### **Clinical Conditions**

- Hereditary elliptocytosis
- Iron deficiency anemia
- Myelophthisic anemia
- Megaloblastic anemia
- Thalassemia
- Sideroblastic anemia
- Congenital dyserythropoietic anemia

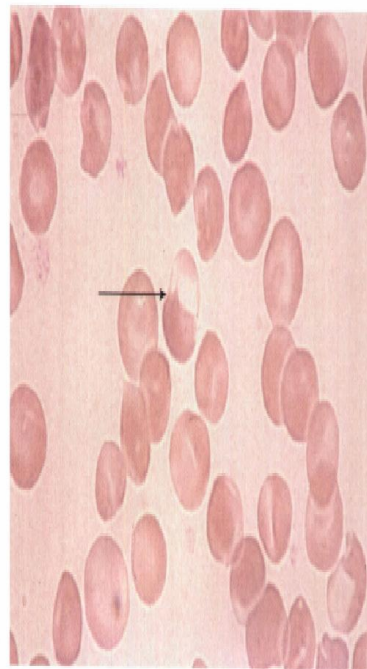
**Pyknocyte (Blister Cell)**

Figure 1A1-33

**Cell Type**

Mature red blood cell

**Description**

Cell with a clearing on one side and a concentrated area of hemoglobin on the other side

**Clinical Conditions**

- Infantile pyknocytosis
- Infantile viremia

## Schistocyte (Schizocyte)

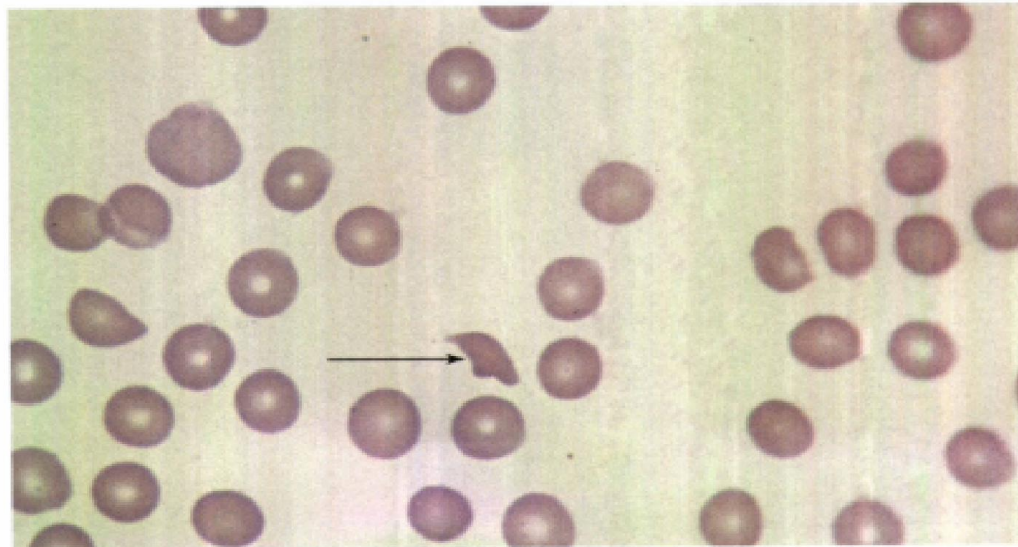


Figure IA1-34

### **Cell Type**

Mature red blood cell

### **Description**

Irregular shape or fragment of cell; results from damaged membrane

### **Clinical Conditions**

- Microangiopathic hemolytic anemias
- Traumatic hemolytic anemias
- Waring Blender syndrome

## Spherocyte

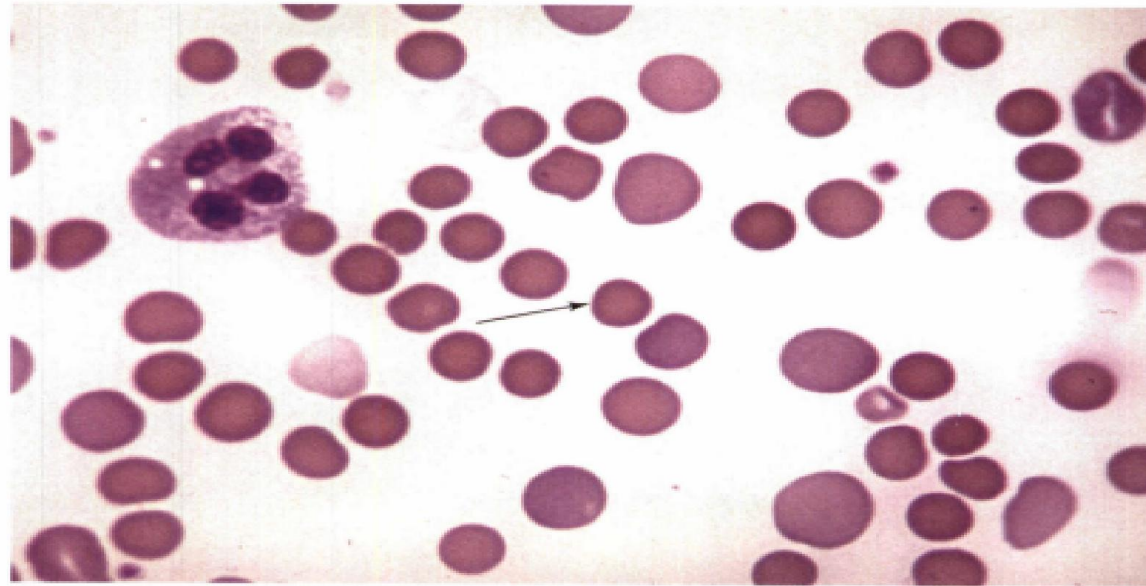


Figure IA1-35

### **Cell Type**

Mature red blood cell

**Size:** 6.1–7.0  $\mu$

### **Description**

Round cells; increased staining intensity with no central pallor; smaller volume than a normal cell (decreased surface:volume ratio)

### **Clinical Conditions**

- Hereditary spherocytosis
- Immuno-hemolytic anemias
- Heinz body hemolytic anemia
- Severe burns (microspherocytes seen); microspherocytes are  $<4.0 \mu$
- Hypersplenism



## Stomatocyte

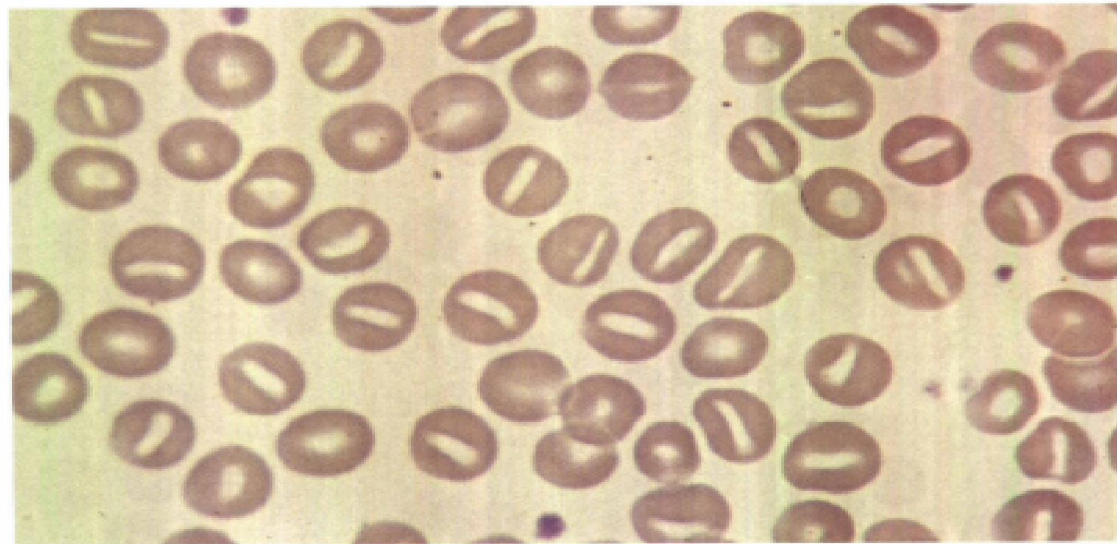


Figure IA1-36

### **Cell Type**

Mature red blood cell

### **Description**

Cell having a slitlike area of central pallor

### **Clinical Conditions**

- Hereditary stomatocytosis
- Alcoholism
- Obstructive liver disease
- Cirrhosis
- Rh-null disease

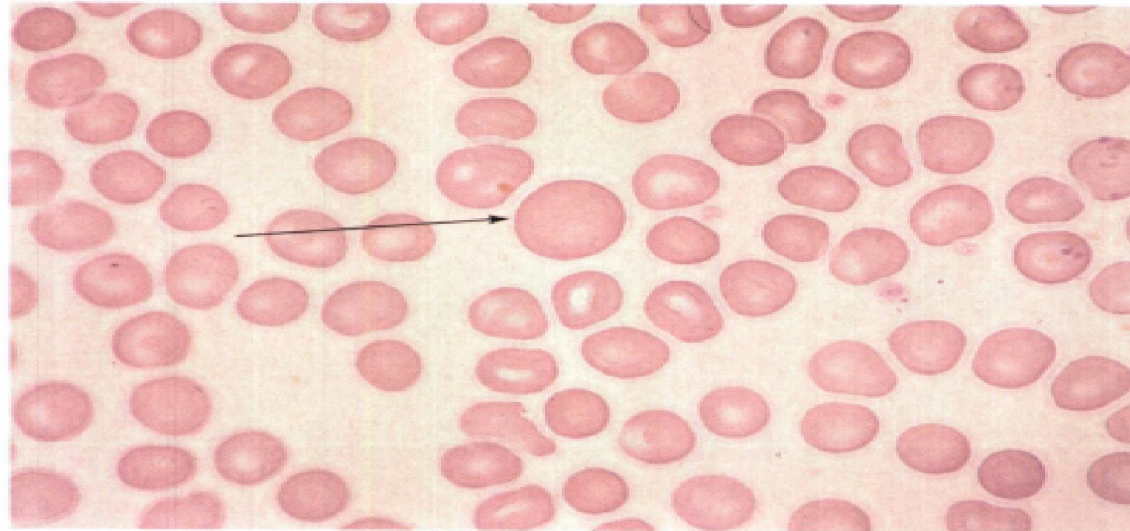
**SIZE****Macrocyte**

Figure IA1-37

**Size:**  $> 7.8 \mu$ **Cell Type**

Mature red blood cell

**Description**

Large cell, mean corpuscular volume usually  $> 100$  fL; usually normochromic; may be round or oval; cytoplasm is pink-red

**Clinical Conditions**

- Liver disease (round macrocytes seen)
- Megaloblastic anemias (oval macrocytes seen)
- Myelodysplastic syndrome
- Acute blood loss
- Chemotherapy

## Microcyte

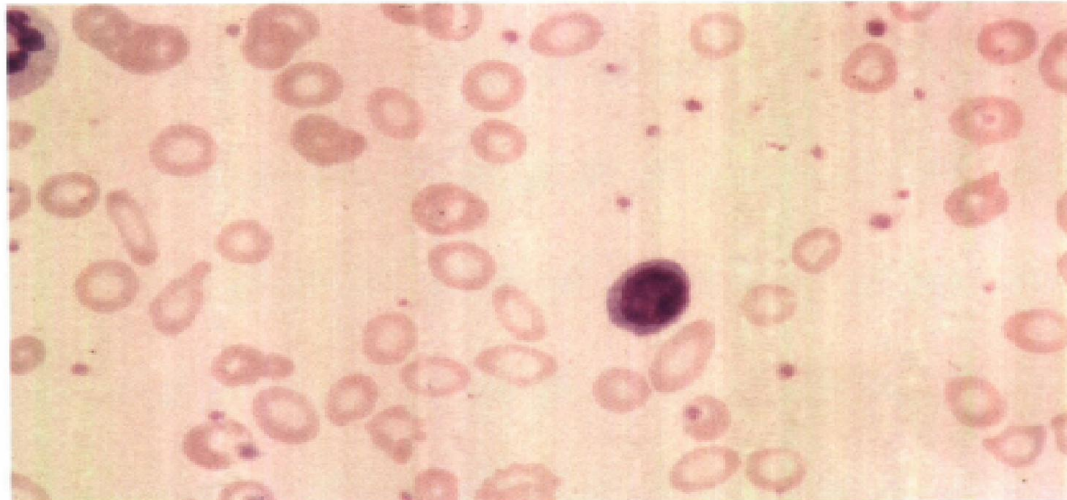


Figure IA1-38

**Size:**  $< 6.5 \mu$

**Cell Type**

Mature red blood cell

**Description**

Smaller than a normal cell; mean corpuscular volume usually  $< 80$  fL; has a central pallor; normochromic or hypochromic

**Clinical Conditions**

- Iron deficiency anemia
- Thalassemias
- Lead poisoning
- Anemia of chronic disease
- Sideroblastic anemia

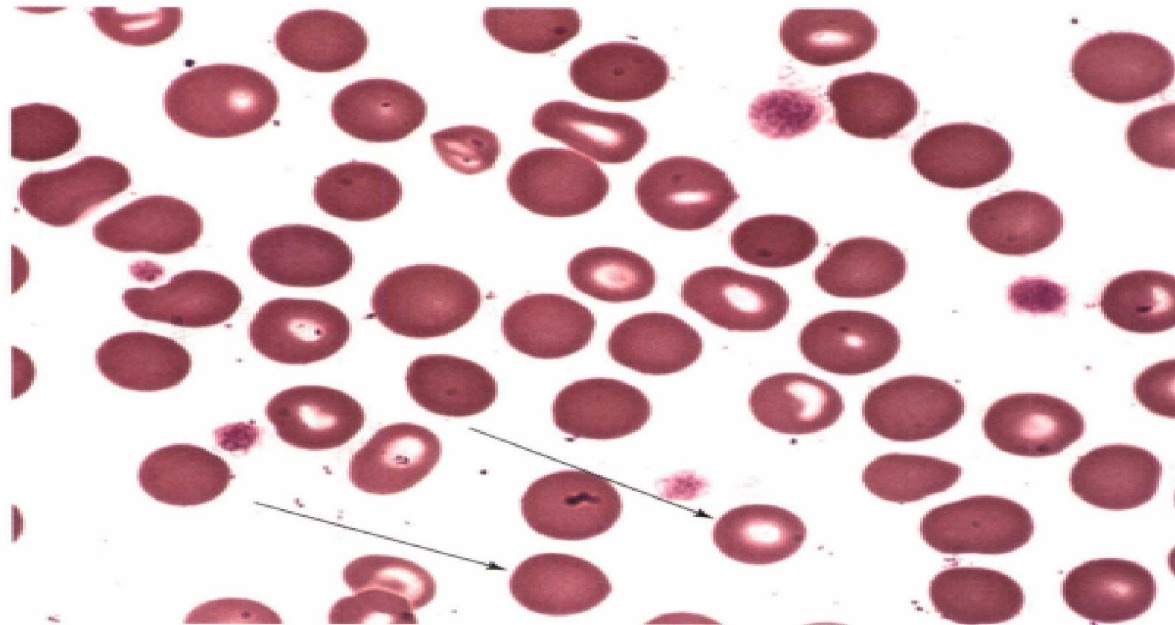
**COLORING****Dimorphic**

Figure IA1-39

**Cell Type**

Mature erythrocytes

**Size:** 6–11  $\mu$

**Description**

Dual population of cells, normocytic and microcytic; normocytic and macrocytic; may also exhibit normochromia and hypochromia

**Clinical Conditions**

- Sideroblastic anemia
- Myelodysplastic syndromes



## Hypochromic

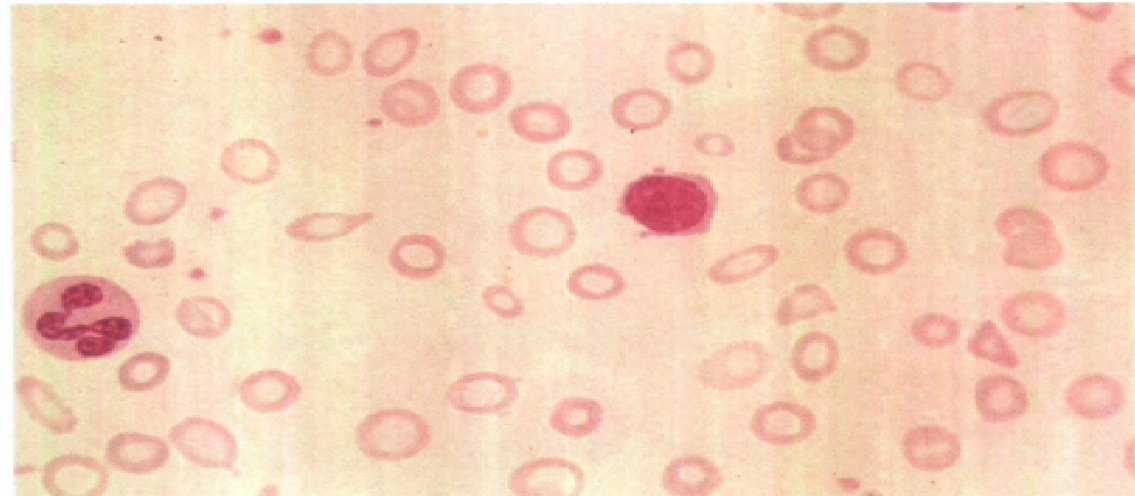


Figure IA1-40

### **Cell Type**

Mature red blood cell

### **Description**

Cells possess a greater central pallor than normal (greater than one-third); may lack hemoglobin and have a decreased mean corpuscular hemoglobin concentration or may be abnormally thin

### **Clinical Conditions**

- Iron deficiency anemia
- Thalassemia
- Anemia of chronic disease
- Sideroblastic anemia
- Myelodysplastic syndromes



## Polychromatophilic

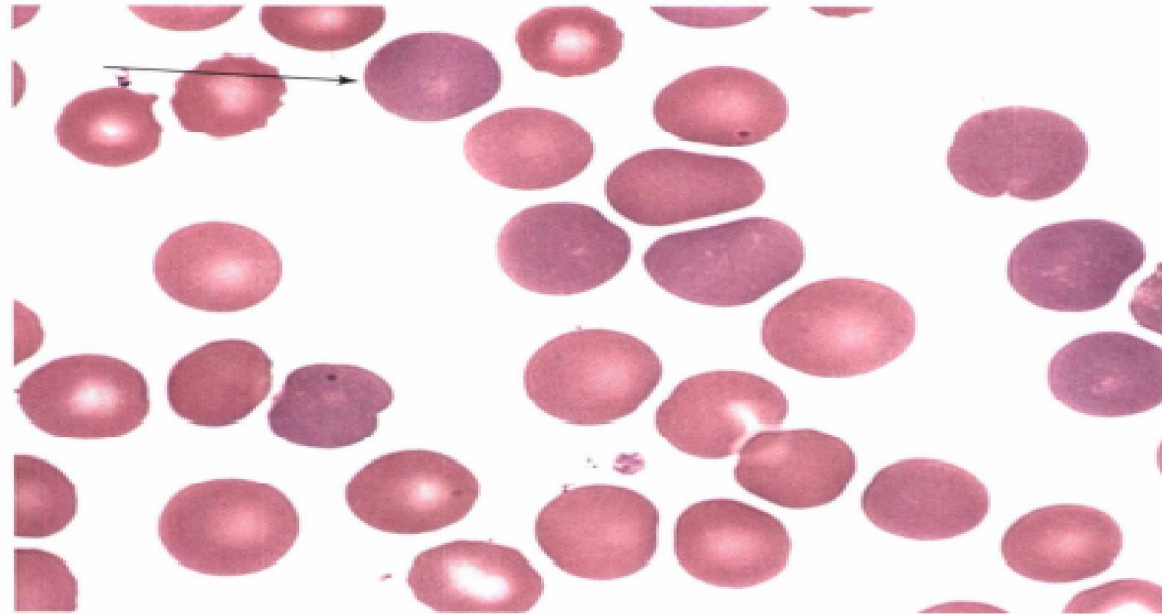


Figure IA1-41

### **Cell Type**

Young red blood cell with no nucleus

**Size:** 8–11  $\mu$

### **Description**

Contains residual RNA, which stains diffusely blue; identified as reticulocyte when stained with a supravital dye

### **Clinical Conditions**

- Increased erythrocyte production
- Hemolytic anemias
- Membrane disorders
- Hemolytic disease of the newborn

## INCLUSIONS

### Basophilic Stippling (Punctuate Basophilia)

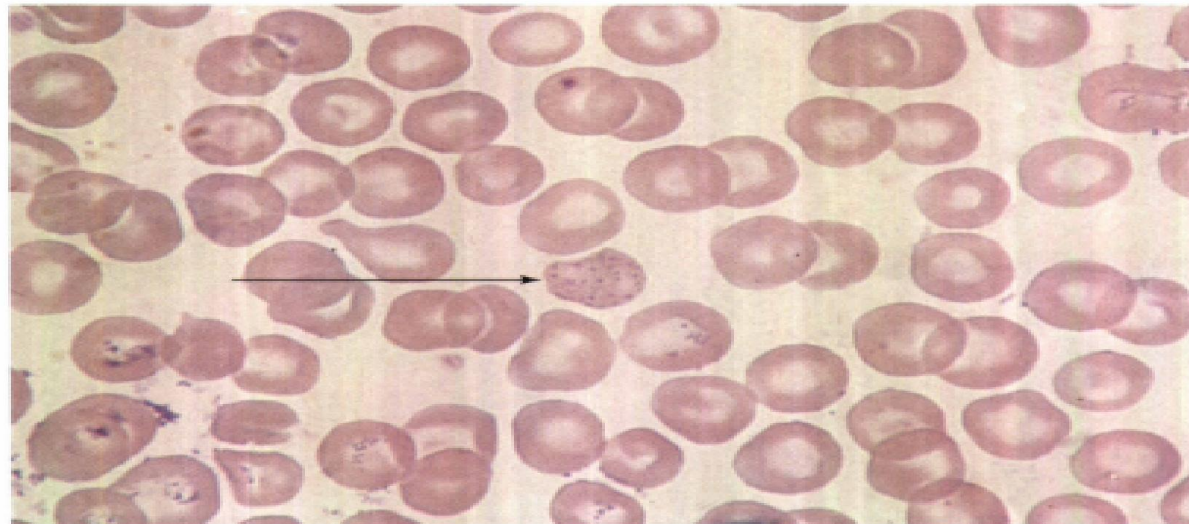


Figure IA1-42

#### **Cell Type**

Mature red blood cell

#### **Description**

Coarse, deep blue inclusions; irregularly aggregated or clumped ribosomes throughout the cell; mitochondria and siderosomes may also aggregate

#### **Clinical Conditions**

- Altered hemoglobin biosynthesis
- Lead intoxication
- Thalassemia
- Megaloblastic anemia
- Alcoholism
- Sideroblastic anemia
- Pyrimidine-5'-nucleotidase deficiency

## Cabot Ring

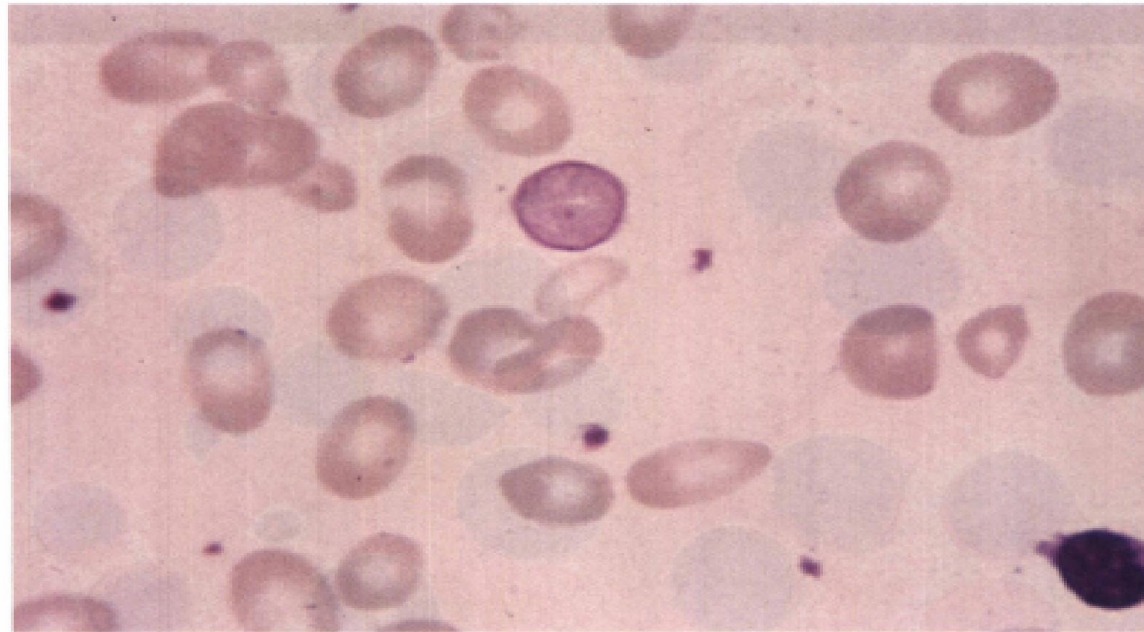


Figure IA1-43

### **Cell Type**

Mature red blood cell

### **Description**

Oval or figure eight–shaped inclusion; red-violet; usually one per cell; consists of nuclear remnants or part of the mitotic spindle

### **Clinical Conditions**

- Severe anemias
- Dyserythropoiesis

## Heinz Bodies

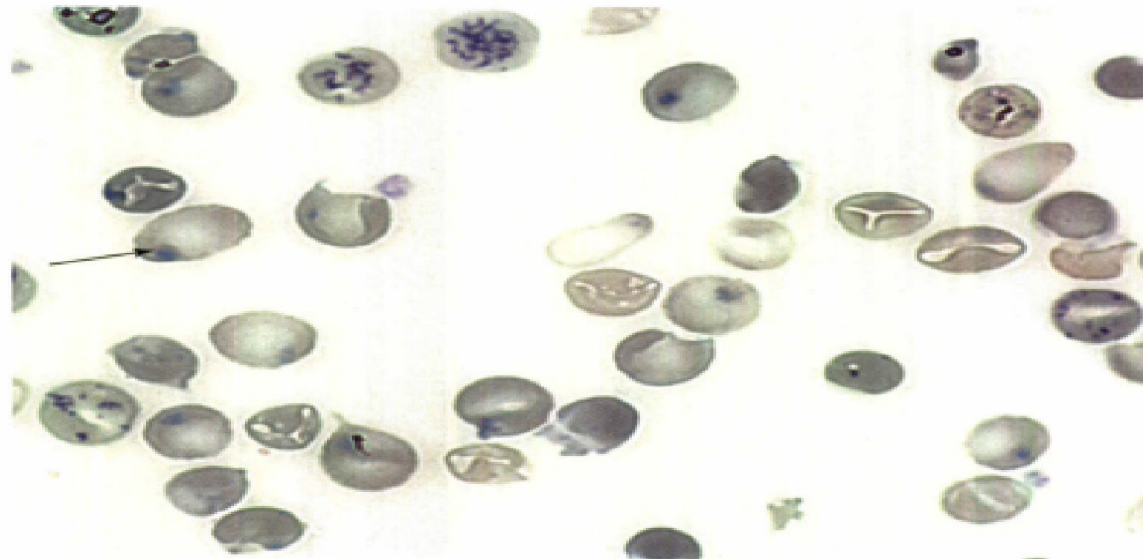


Figure IA1-44

### Cell Type

Young and mature red blood cells

**Size:** 1–2  $\mu$

### Description

Round, refractile inclusions found on the periphery of the cell when stained with a supravital dye; consists of denatured globin produced by the destruction of hemoglobin; they may occur in multiple numbers

### Clinical Conditions

- Drug-induced anemias
- Thalassemia
- Glucose-6-phosphate dehydrogenase deficiency and other red blood cell enzymopathies
- Unstable hemoglobinopathies



## Hemoglobin C Crystals

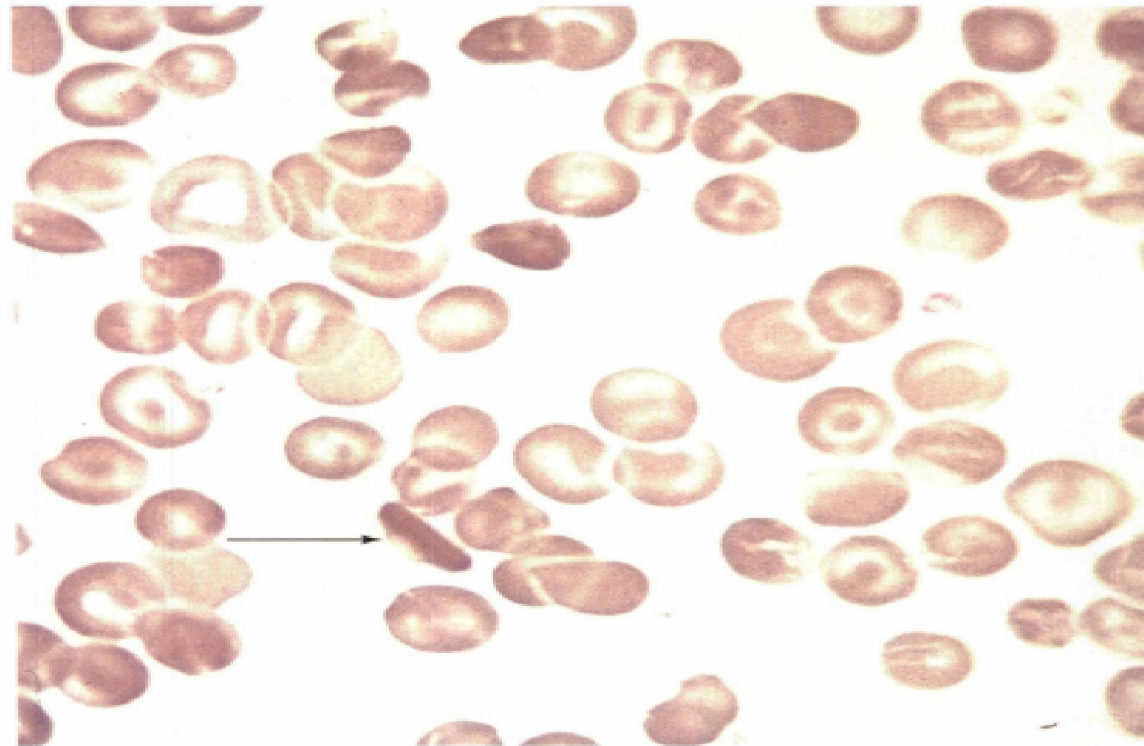


Figure IA1-45

### **Cell Type**

Mature red blood cells

### **Description**

Hexagonal, rod-shaped inclusions with blunt ends that stain very dark; formed within the cell membrane; remainder of cell has a clear area

### **Clinical Condition**

■ Hemoglobin CC disease



## Hemoglobin H Inclusions

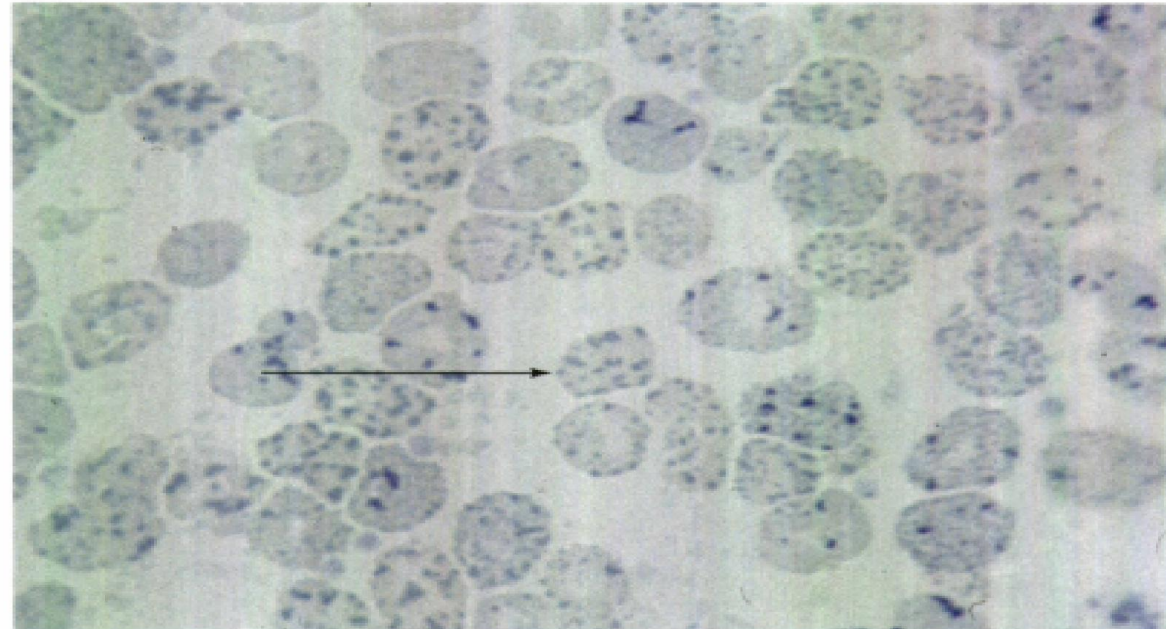


Figure IA1-46

### **Cell Type**

Nucleated and nonnucleated red blood cells

### **Description**

Unpaired beta-chains form small, greenish-blue inclusions when stained with brilliant cresyl blue; uniformly dispersed throughout the cell; when present in multiple numbers, they give the cell a “golf ball” appearance

### **Clinical Condition**

■ Hemoglobin H disease

## Hemoglobin SC Crystals



Figure IA1-47

### **Cell Type**

Mature red blood cell

### **Description**

Darkly stained condensed hemoglobin; crystals may be straight with parallel sides and a blunt protruding end or have several fingerlike projections from the center; crystals may protrude from the cell membrane; remainder of cell has pallor or distorted membrane

### **Clinical Condition**

■ Hemoglobin SC disease

## Howell-Jolly Body

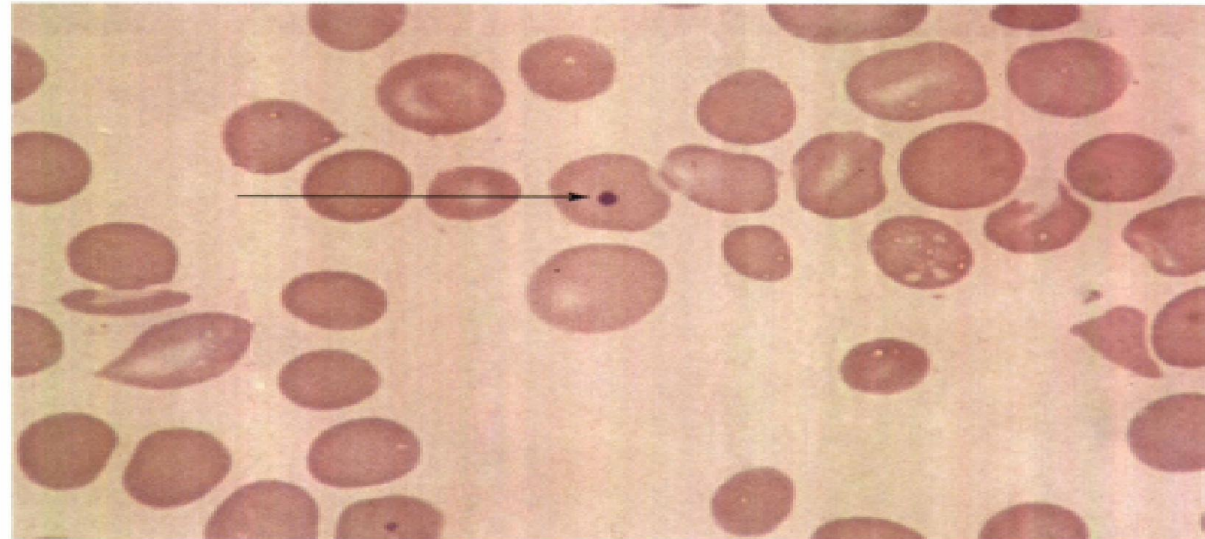


Figure IA1-48

**Size:** 0.5–1.0  $\mu$

### **Cell Type**

Nucleated and nonnucleated red blood cells

### **Description**

Round fragments of nucleus (DNA); reddish-blue to deep purple; usually one per cell but occasionally may be two or more; represents chromosomes that have been separated from the mitotic spindle during abnormal mitosis; may also appear to arise from nuclear fragmentation or abnormal expulsion of the nucleus

### **Clinical Conditions**

- Megaloblastic anemia
- Hemolytic anemias
- Hyposplenism
- Splenectomized persons
- Alcoholism
- Sickle cell anemia



## Malaria

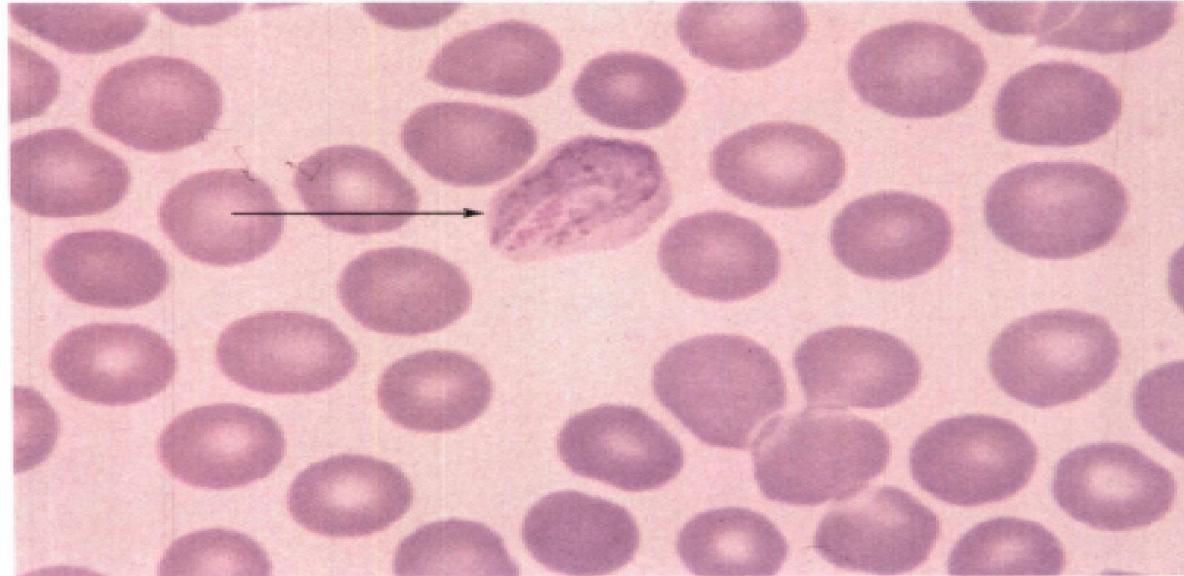


Figure IA1-49

### Cell Type

Red blood cell

### Description

Depends on the species of *Plasmodium* that infects the cells:

*Plasmodium vivax* infection enlarges the cell; Schüffner's granules may be present

*Plasmodium malariae* infection does not enlarge the cell

*Plasmodium falciparum* infection produces delicate ring forms; cells are not enlarged; Schüffner's granules are not present

*Plasmodium ovale* infection produces large, oval cells; Schüffner's granules are present

### Clinical Conditions

■ *Plasmodium* infections

## Pappenheimer Body

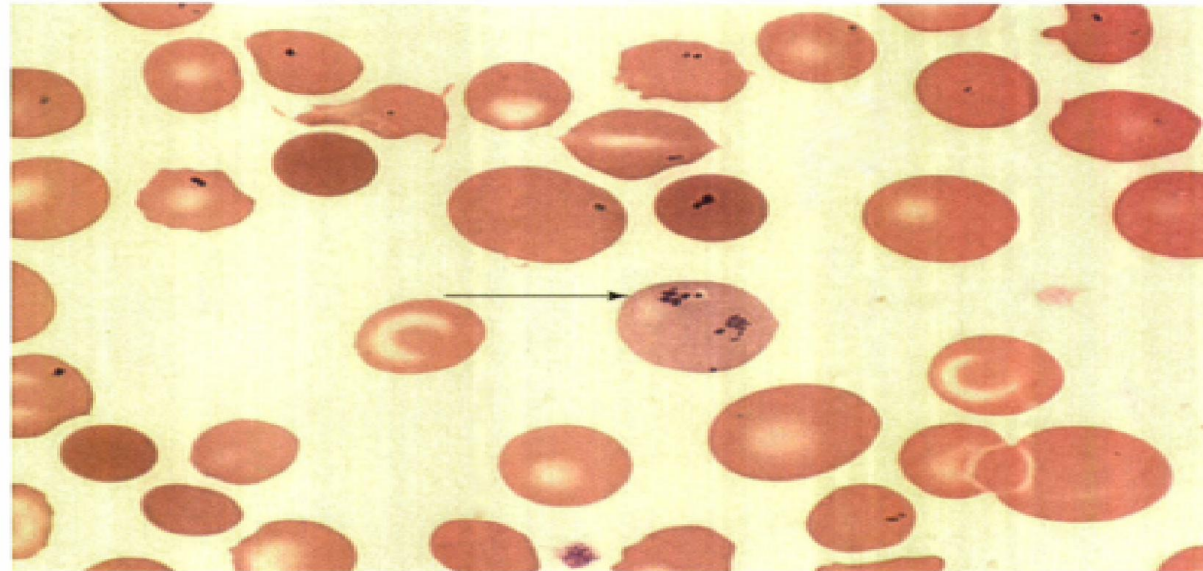


Figure IA1-50

### **Cell Type**

Mature red blood cells, reticulocytes, metarubricytes

### **Description**

Small, irregular, pale blue- to dark-staining granules; usually found on the periphery of the cell and in groups; smaller than Howell-Jolly bodies; represent siderosomes, which stain positive with Perls' Prussian blue stain and indicate iron content

### **Clinical Conditions**

- Disturbed hemoglobin synthesis
- Sideroblastic anemia
- Dyserthropoietic anemias
- Thalassemia
- Myelodysplastic syndromes



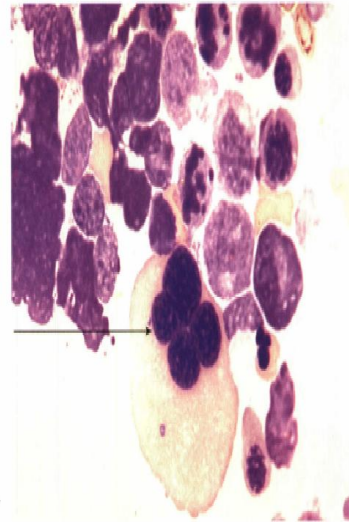
**ABNORMAL MATURATION****Dyserythropoiesis**

Figure IA1-51

**Cell Type**

Red blood cell precursors

**Description**

Abnormal findings in red blood cell precursors, including abnormal nuclear shapes, more than one nucleus, nuclear fragments, megaloblastoid and/or megaloblastic maturation, and vacuolated cytoplasm

**Clinical Conditions**

- Myelodysplastic syndromes
- Megaloblastic anemias
- Erythroleukemia (M6a)
- Pure erythroid leukemia (M6b)
- Arsenic poisoning