
بسم الله الرحمن الرحيم

Iron Deficiency Anemia and differential diagnosis

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Normal levels of RBCs at birth range from 5.1 to 5.3 million/mm^3 for term newborns and 4.6 to 5.3 million/mm^3 for premature neonates.

Because of active in utero erythropoiesis, the reticulocyte count at birth is 3 to 7% in full-term babies and 8 to 10% in premature babies. This declines to 0 to 1% by the first week of age, reflecting diminished erythropoiesis.

The life span of adult erythrocytes is 120 days. RBCs in term neonate will survive between 60 and 90 days. Erythrocytes from premature neonates have considerably shorter life spans, ranging from 35 to 50 days

Mean Cell Volume. Early embryonic RBCs are large; diameters range from 20 to 25 μm with a mean cell volume (MCV) of 180 femtoliters (fl) or μm^3. Cell size decreases gradually during development reaching 130 fl at midgestation and 115 fl at term. MCV at 1 year of age is 82 fl.

Anaemia is defined as a low Hb concentration in blood, or less often, as a low haematocrit, the percentage of blood volume that consists of red blood cells

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The Hb and Ht range for assessing iron deficiency are:

	Hb (g/dL)	Ht (%)
Children 6 months - 5 years	11	33
Children 5 - 11 years	11,5	34
Children 12 - 13 years	12,0	36

Etiologic classification

I Impaired red cell formation

A/ Deficiency

- Decreased dietary intake
- Increased demand
- Decreased absorption
- Increased loss

B/ Bone marrow failure

- Failure of a single or all cell lines
- Infiltration

C/Dyshematopoietic anemia

II Blood loss

III Hemolytic anemia

- Corpuscular (membrane, enzymatic or hemoglobine defects)
- Extracorpuscular (immune, idiopathic)

Diagnosis of Anemia

- detailed history
- careful physical examination
- peripheral blood smear
  - red cell morphology
  - MCV
  - RDW (red cell distribution width)
  - WBC and platelet morphology
  - retic

- Additionally:

-bone marrow evaluation

-additional testing

Ferritin , Hb electrophoresis, *osmotic fragility……*

History

- Diet (iron , folate, vitB12 intake, onset of hemolysis after certain foods –e.g.,fava beans)
- family history (transfusion requirements of relatives, splenectomy, gallblader disease)
- environmental exposures (lead poissoning)
- symptoms (headache, exertion dyspnea, fatigue, dizziness, weakness, mood or sleep disturbances, tinnitis)
- melena, hematemesis, abdominal pain- chronic blood loss

Physical Examination

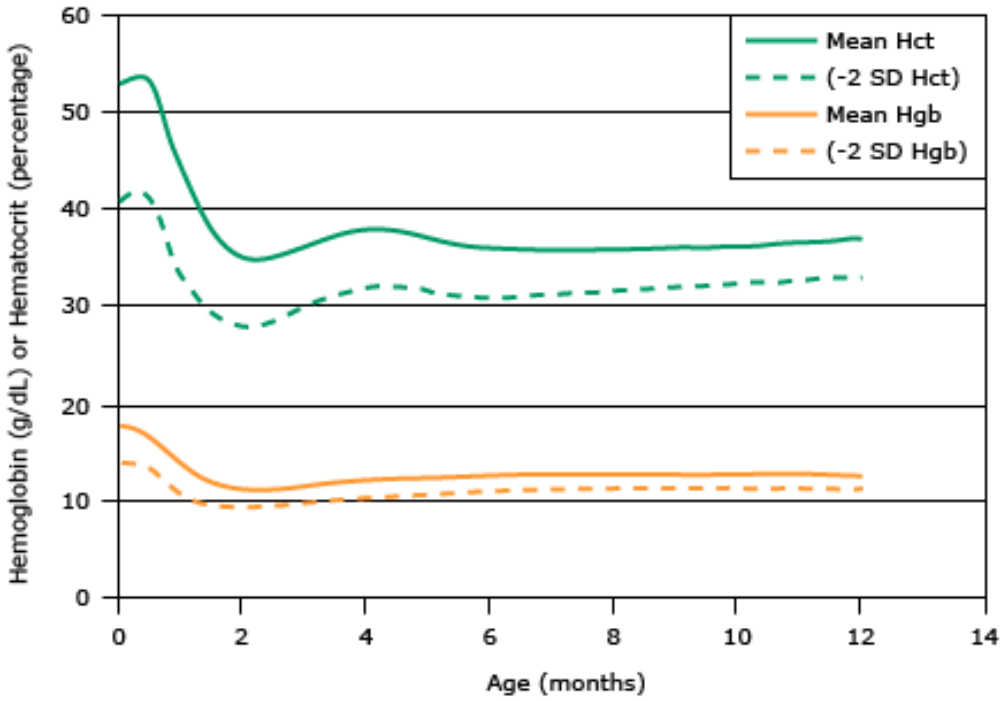
- Pallor
  (skin, oral mucosa, nail beds)
- Bone pain
- Jaundice -hemolysis
- tachycardia
- tachypnea
- orthostatic hypotension
- venous hum
- systolic ejection murmur
- peripheral edema?
- Splenomegaly?
- Hepatomegaly?
- Glossitis?
- gingival pigmentation?
- Adenopathy?
- Facial, extremity examination

Peripheral Blood Components

important! Different values dependent on age!

- RBC
- Hgb
- HCT
- MCV – 80 – 100 fl/L (a calculated value)
- MCH
- RDW
- Reticulocyte Count

Normal values for hematocrit and hemoglobin during the first year of life in healthy term infants



Data from:
1. Jopling J, Henry E, Wiedmeier SE, et al. Reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period: data from a multihospital health care system. Pediatrics 2009; 123:e333.
2. Oski FA, Naiman JL. Hematologic problems in the newborn, 2nd ed, WB Saunders, Philadelphia 1972; p.13.
3. Saarinen UM, Siimes MA. Developmental changes in red blood cell counts and indices of infants after exclusion of iron deficiency by laboratory criteria and continuous iron supplementation. J Pediatr 1978; 92:412.

Normal values for hemoglobin, hematocrit, and mean corpuscular volume in children

Age			Hemoglobin (g/dL)		Hematocrit (%)		MCV (fL)		
			50th percentile	Lower limit*	50th percentile	Lower limit*	50th percentile	Lower limit*	Upper limit*
1 year¶	Caucasian		12.5	11	37	32	80	71	89
	African American		12	11	36	31	77	63	88
2 to 3 years	Caucasian		12.6	11	37	33	82	74	89
	African American		12	11	36	32	80	64	89
4 to 6 years	Caucasian		12.9	11.7	38	34	84	77	91
	African American		12.5	11	37	33	83	67	91
7 to 10 years	Caucasian		13.5	12	40	35	85	78	91
	African American		12.7	11.2	38	34	84	72	92
11 to 14 years	Caucasian	Female	13.7	12.3	40	36	87	80	94
		Male	14.3	12.6	42	36	87	80	94
	African American	Female	12.9	10.6	38	33	86	71	95
		Male	13.6	11.8	40	35	86	73	95
15 to 18 years	Caucasian	Female	13.7	11.5	40	34	89	81	96
		Male	15.4	13.7	46	40	89	81	96
	African American	Female	12.8	10.7	38	32	87	71	96
		Male	14.9	12.9	44	38	87	75	96

Hypochrom Microcytic Anemia

Iron deficiency anemia

Thalassemia

Hb E

Lead poisoning

Sideroblastic anemia

Pyropoikilocytosis

Chronic disorders

Developmental Stages of Iron Deficiency Anemia (WHO)

- Pre-latent –
  - reduction in iron stores without reduced serum iron levels
  - Hb, MCV, Transferrin saturation- Normal, Iron absorption - increase, Serum ferritin and marrow iron reduced
  - no clinical manifestation
- Latent-
  - iron stores are exhausted, but the blood hemoglobin level remains normal
  - index of the blood within the standard
  - clinical picture is caused by the sideropenic syndrome
- Iron Deficiency Anemia
  - blood hemoglobin concentration falls below the lower limit of normal
  - the clinical manifestations in the form of sideropenic syndrome and general anemic symptoms

Differential Diagnosis of Microcytic, Hypochromic Anemias

	RDW	Serum Iron	TIBC	Serum Ferritin	FEP
Iron Deficiency	Inc	Dec	Inc	Dec	Inc
Alpha Thal	Norm	Norm	Norm	Norm	Norm
Beta Thal	Norm	Norm	Norm	Norm	Norm
Hgb E Disease	Norm	Norm	Norm	Norm	Norm
Anemia of Chronic Disease	Norm	Dec	Dec	Inc	Inc
Sideroblastic Anemia	Inc	Inc	Norm	Inc	Dec
Lead Poisoning	Norm	Norm	Norm	Norm	Inc

Iron treatment restores HbA_2 levels in patients with IDA; also reveals BTT in the BTT-IDA patient

Table 2

Table 2. Comparison of basic hematological parameters, Hb-A_2 and serum ferritin levels before and after treatment in patients with IDA and patients with co-pathological condition (IDA+BTT).

Parameters	Patients with IDA			Patients with co-pathological condition (IDA + BTT)		
	Before Tx	After Tx	*P*	Before Tx	After Tx	*P*
Hb (g/dL)	9.4±0.4	12.7±0.8	0.001	8.9±0.2	11.5±0.5	0.002
RBC ($\times 10^6/\mu L$)	3.4±0.3	4.3±0.4	0.02	3.2±0.2	5.1±0.1	<0.001
MCV (fL)	64.8±3.1	77.4±2.4	0.001	64.0±2.9	67.0±2.6	0.005
MCH (pg)	22.6±1.6	28.1±1.1	0.001	22.1±1.4	25.1±1.7	0.050
MCHC (g %)	25.4±2.7	29.8±1.0	0.003	24.4±1.7	28.8±0.8	0.043
Hb-A_2 (%)	1.7±0.1	2.9±0.3	0.001	2.6±0.6	5.2±0.3	<0.001
Serum ferritin (ng/mL)	2.91±1.2	29.8±7.1	<0.001	5.1±1.5	33.8±6.8	<0.001

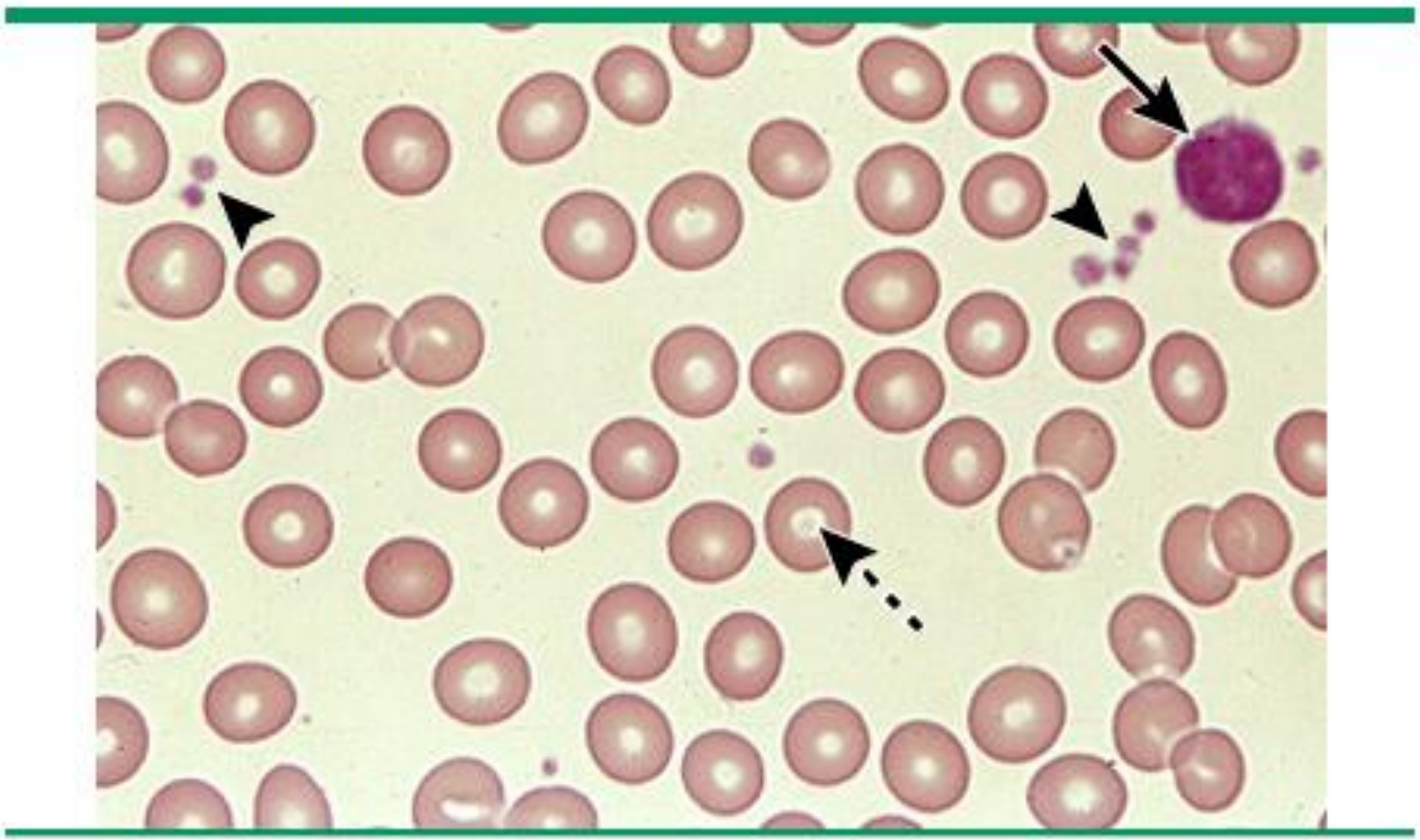
Abbreviations: IDA, iron deficiency anemia; BTT, beta thalassemia trait; Tx, treatment.

Hemoglobin E

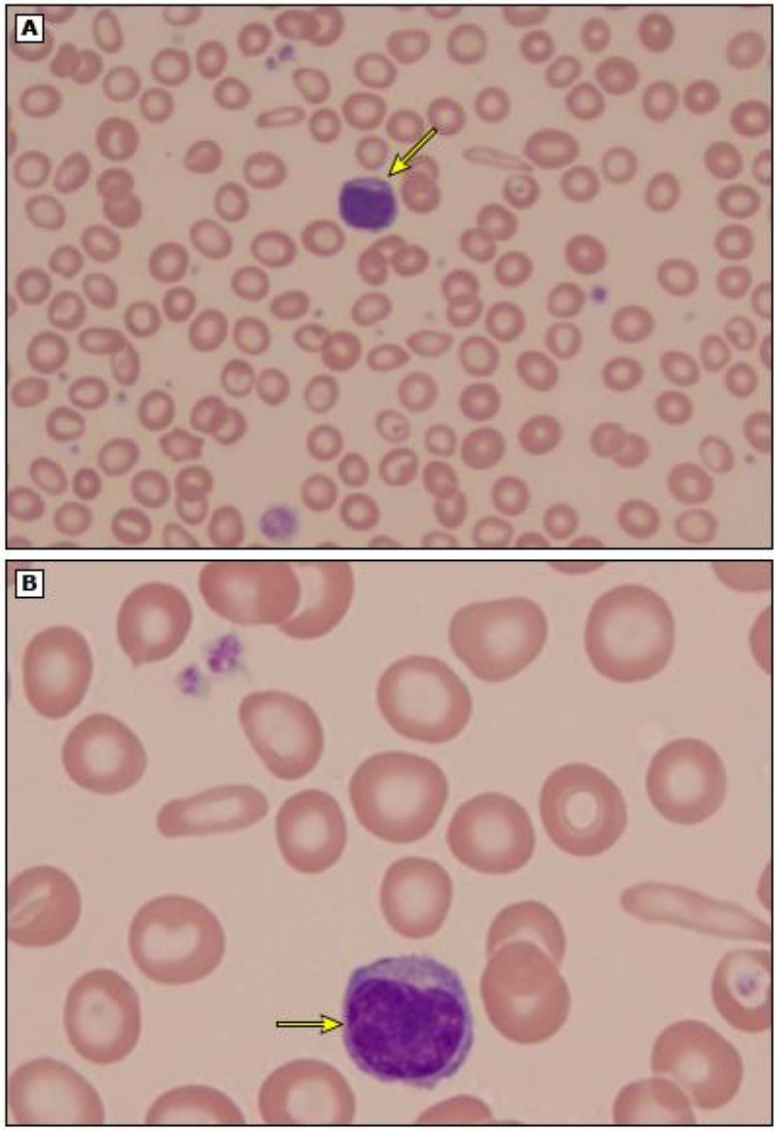
Hb E Disorders

Condition	*Genotype*	*Clinical*
Hb E Trait	A/E	30% Hb E ±| MCV
Hb E Disease	E/E	90% Hb E,| MCV
Hb E-β-thal	E/beta$^{0,+}$	Hb E 40-85%, Hb F 10-60%, ⍰ MCV, Hb
Hb SE disease	S/E	resembles Hb S-β^{+} thal

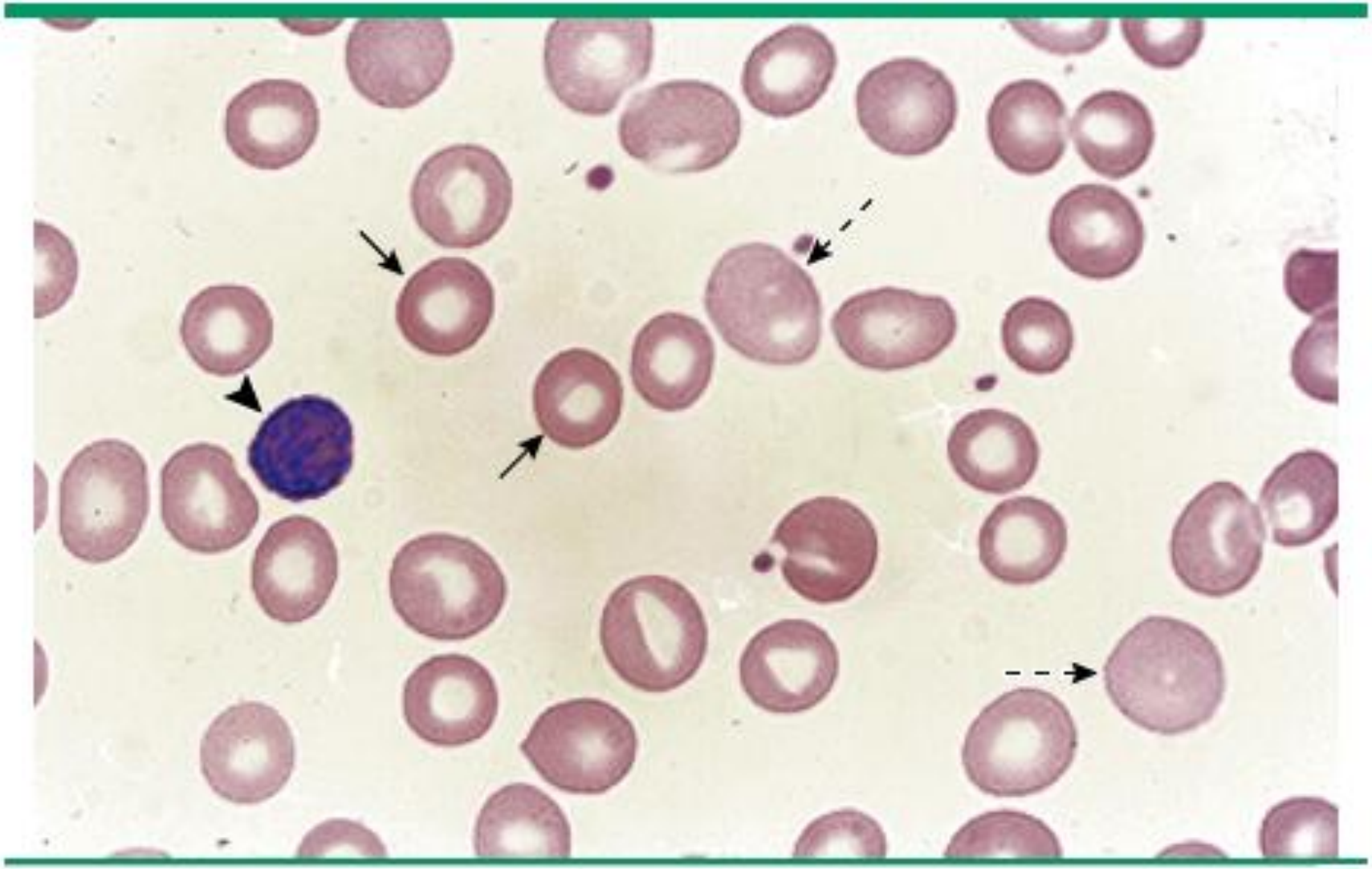
Normal peripheral blood smear



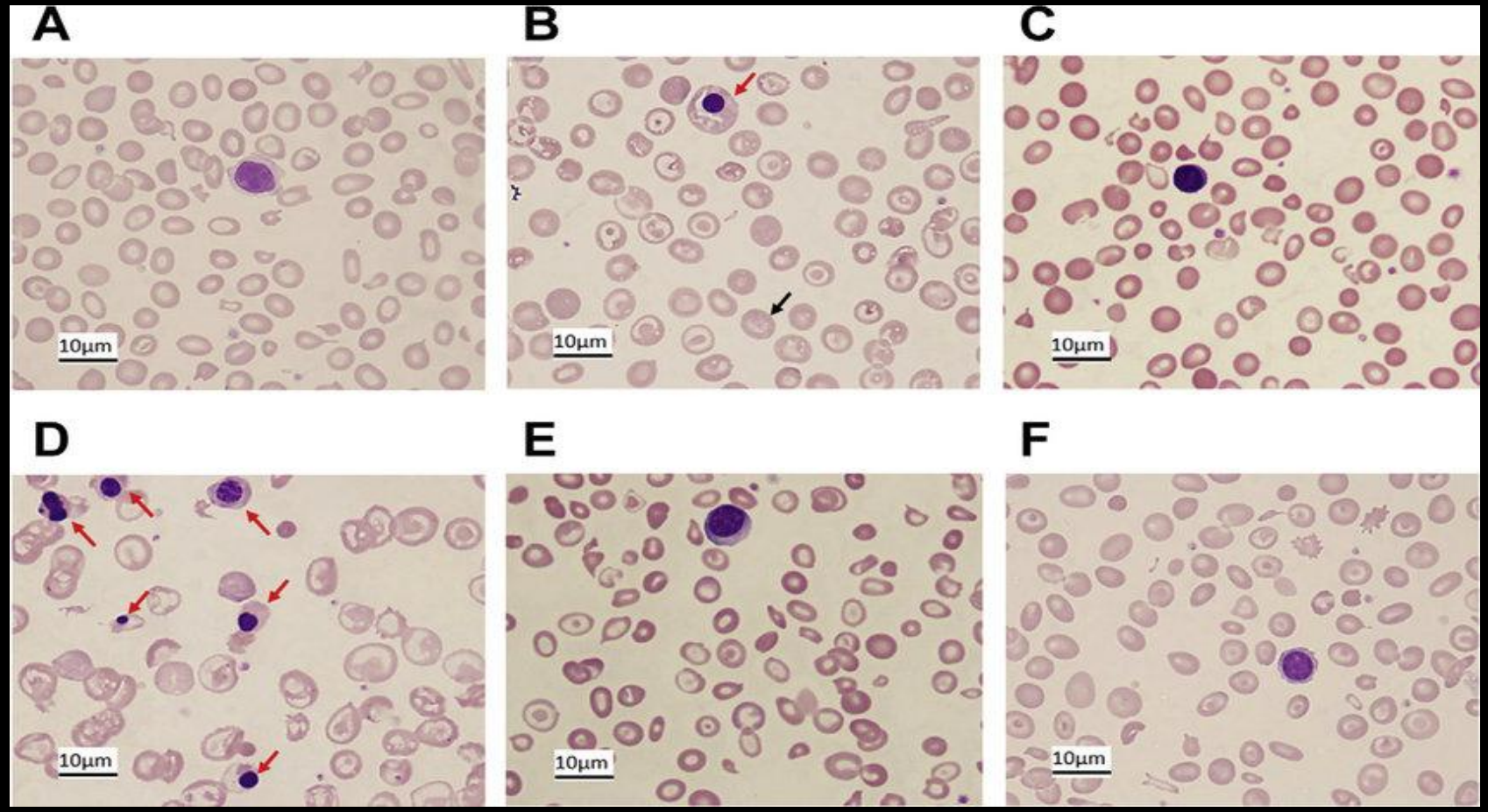
Peripheral blood smear in iron deficiency anemia showing microcytic, hypochromic red blood cells



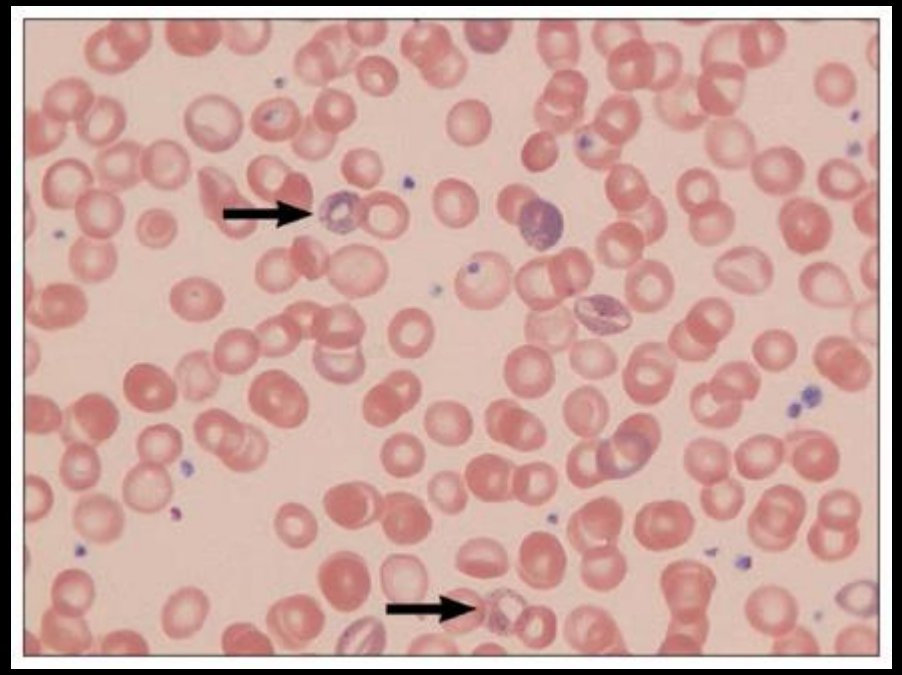
Polychromatophilia due to increased reticulocytes

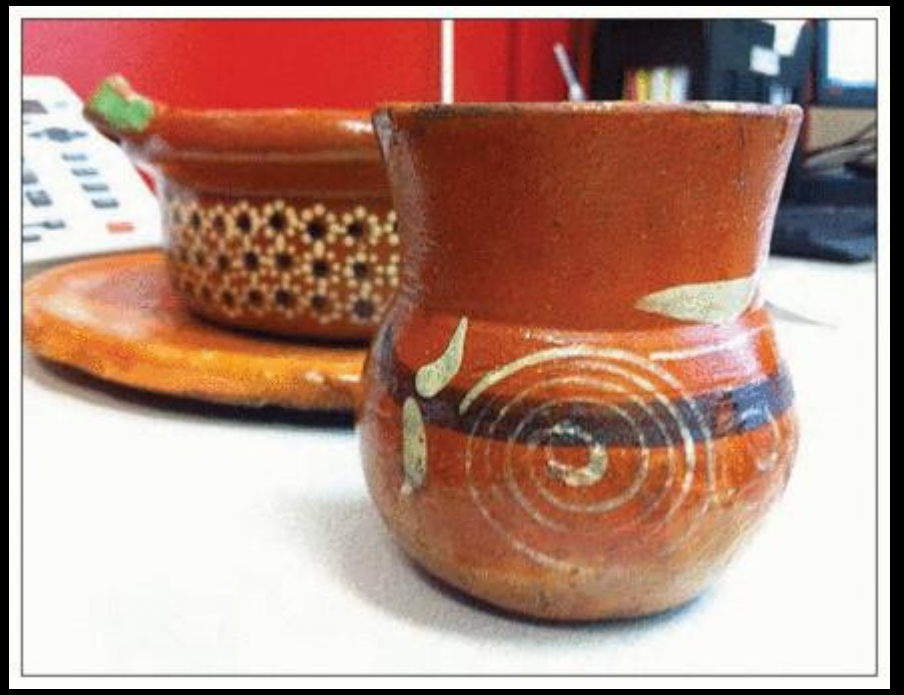


(A) Hb H disease. (B) Hb H/Hb CS disease. (C) b-Thalassemia intermedia. (D) Homozygous b-thalassemia (after splenectomy). (E) Hb E/b 0-thalassemia. (F) AE Bart's disease (Hb H disease with Hb E trait)

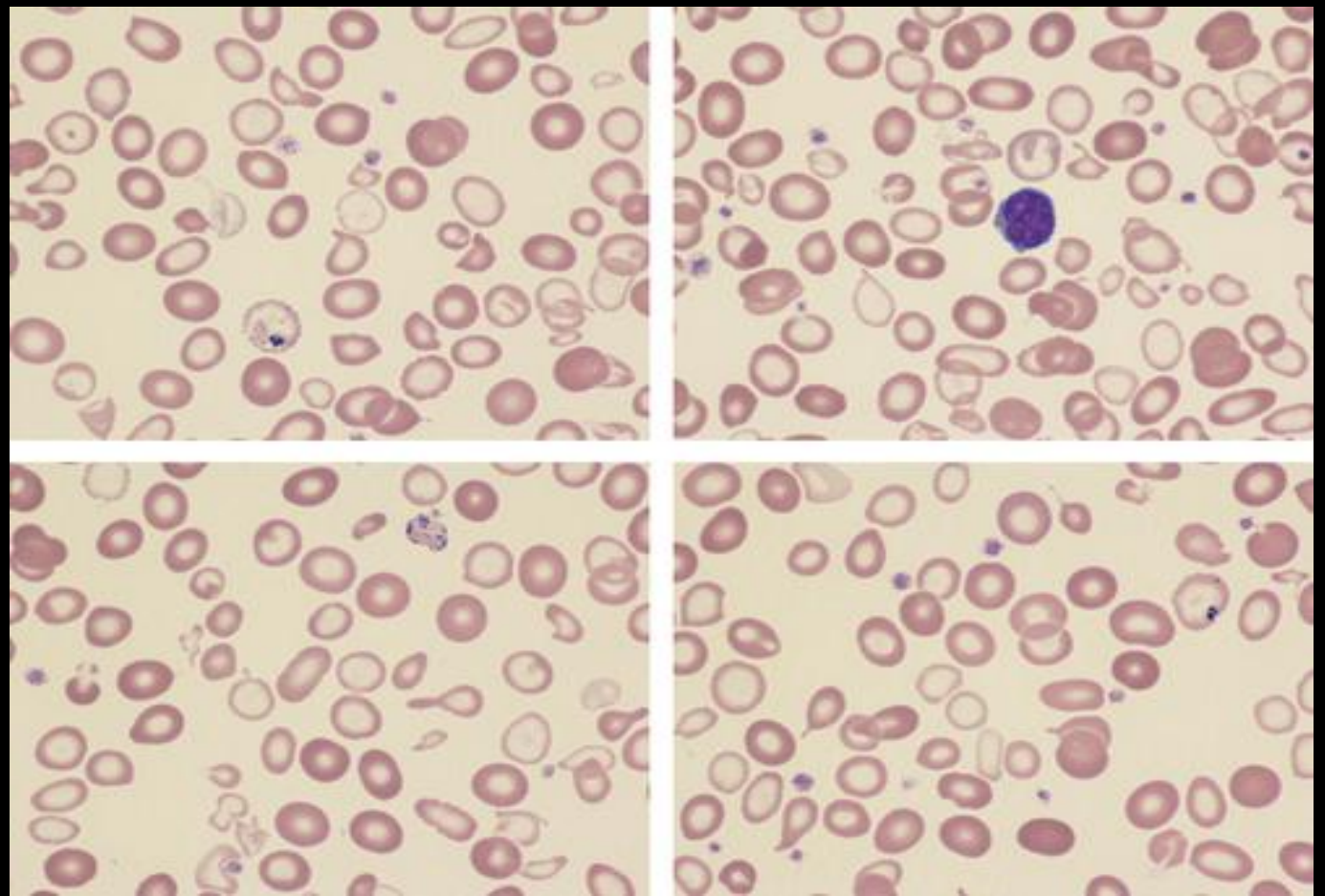


Lead Poisoning





Sideroblastic Anemia



Case 1

A15 *month old boy comes the Dr.'s office for evaluation of a cold. Further hx reveals introduction of whole cow's milk at* 5 months with copious quantities and no well baby visits.

He appears quite pale and has the following findings:

Hgb 5.3, RBC 2400000 MCV 48, plts 780, WBC 12.5 and retic 1.7%

What does he have?

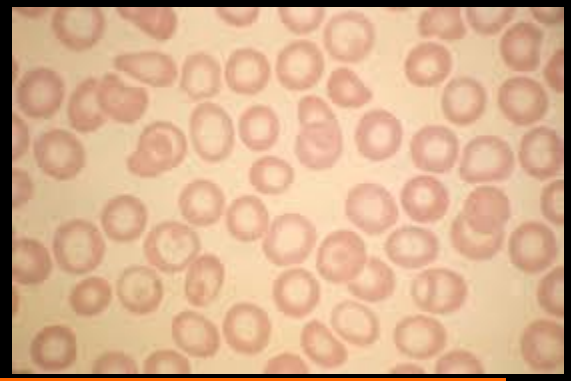
Case #1 Questions

- What lab tests are abnormal?
- How much milk should a 24 month old be allowed?
- Is it surprising the child was asymptomatic?
- Why is iron important?

Case 1

- Iron deficiency anemia

Case #2



- 24 month old boy is being seen for a follow-up for his anemia. He was prescribed iron 5 months ago .
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- Repeat CBC shows Hgb 10.0, RBC 5500000, and MCV 60. Smear shows hypochromic, microcytic red cells.
- Physical Exam is unremarkable.

Thalassemia Trait

1. Is there anything else you want to know in the history?
2. Is there any other laboratory testing that you would like done?
3. What is the diagnosis?

Case 3

- A one years old girl comes for routine check .
- PE: mild pallor
- Hb 11.3
- WBC 7600 poly 47% lymph 45%
- RBC 4500000
- Plt 250000
- MCV 67
- MCH 23
- RDW 14
- What are the differential diagnosis?

Case 3

- Ferritin 32
- Hb A 97%
- Hb A2 2%
- HB F 1%
- What do you do for confirmation of diagnosis?

Alfa thalassemia minor

An 18 month old girl was in good health until she developed a cold 10 days ago.

Now she is pale but without visible jaundice.

The CBC shows a Hgb of 6.8, MCV of 78 and retic of 0.1%,

WBC 7800 poly 35% lymph57%

Plt 340000 are normal as is the peripheral blood smear.

What does she have?

Transient erythroblastopenia of childhood