Iron Deficiency Anemia

S_Yousefian.MD

Pediatrics Hematologist & Oncologist

Epidemiology

Iron deficiency is the most common nutritional deficiency and hematologic disease of infancy and childhood in worldwide in distribution.

Incidance

۱-۲Year ۹%

۵-۸Year ۵/۵%

Preadolescents ۲/۶%

Pregnant ۲۵%

Incidance

It is estimated that۴۰–۵۰% of children under ۵ years of age in developing countries are iron deficient.

ETIOLOGGY

Inadequate Intake

-Dietary Sources(little or no meat, with their nutrition derived from cultivated grasses such as rice)

-Poor Bioavailability(High gastric pH ,environmental factors by interfering with iron absorption, such as cobalt, Lead)

Inadequate Absorption

-Malabsorption (celiac disease, postgastrectomy, IBD, H.pylori infection-associated chronic gastritis)

-Antacid therapy or high gastric pH

Blood Loss

A:GI

B:Genitalia

C:Pulmonary

D:Urinary

late infancy and early childhood

Rapid growth with exhaustion of gestational iron

Low levels of dietary iron

Complicating effect of cow's milk-induced exudative enteropathy

Adolescence

Rapid growth and suboptimal iron intake

This is amplified in females due to menstrual blood loss

Infants at High Risk for IDA

Increased iron needs:

Low birth weight
Prematurity
High growth rate
Low hemoglobin level at birth

Infants at High Risk for IDA

Dietary factors:
Rate of weight gain greater than average
Low-iron formula
Breast-feeding ۶ months without iron supplements
Low socio-economic status

Infants at High Risk for IDA

Blood loss:

Perinatal bleeding(Placental ,Umbilicus)
Postnatal (Hypersensitivity to whole cow's milk)

Growth

Growth is particularly rapid during infancy and during puberty.
Each kilogram gain in weight requires an increase of۳۵–۴۵ mg body iron.

Growth

The amount of iron in the newborn is ۷۵ mg/kg. If no iron is present in the diet or blood loss occurs the iron stores present at birth will be depleted by ۶ months in a full-term infant.

Requirement

The body of a newborn infant contains about ٠٫٥ g of iron, whereas the adult content is estimated at ٥ g.

An average of ٠٫٨ mg of iron must be absorbed each day.

Requirement

To maintain positive iron balance in childhood, about ١ mg of iron must be absorbed each day because absorption of dietary iron is assumed to be about ١٠%, a diet containing ٨-١٠ mg of iron daily is necessary for optimal nutrition.

Requirement

Full-term infant :١ mg/kg start no later than four months in breastfed infants.

Infants ١٫٥–٢٫٠ kg: ٢ mg/kg/day supplemental iron.

Infants ١٫٠–١٫٥ kg: ٣ mg/kg/day supplemental iron.

Infants ١ kg: ٤ mg/kg/day supplemental iron.

Requirement

to ١٠ years old — ١٠ mg/day

years old to adult (female) — ١٥ mg/day

years old to adult (male) — ١٢ mg/day

Iron Content of Infant Foods

Food	Iron, mg	
Milk	۰/۵–۱/۵	liter
Eggs	۱/۲	each
Cereal	۳/۰–۵/۰	ounce
Vegetable(Yellow)	۰/۱–۰/۳	ounce
Vegetable(Green)	۰/۳–۰/۴	ounce
Meats(Beef, lamb)	۰/۴–۲/۰	ounce
Meats(Pork, bacon)	۶/۶	ounce
Fruits	۰/۲–۰/۴	ounce

Typical presentation of IDA

If the presentation is typical for nutritional IDA (age <٣ years, with any dietary risk factors for IDA), a CBC is sufficient

Atypical presentation for IDA

If the presentation is atypical (age ٣ to ١٢ years, or no dietary risk factors or other possible risk factors present), somewhat more extensive laboratory testing is appropriate because nutritional IDA is less common in these patients

Atypical presentation for IDA

In our program, we perform a CBC with indices, reticulocyte count, serum ferritin, and peripheral blood smear, and test stools for occult blood (three samples).
Blood lead level should be measured if there are any risk factors for lead exposure

Atypical presentation for IDA

If the results of these tests are consistent with IDA, the next step is a therapeutic trial of iron, and further evaluation is performed only if the response is inadequate.

Atypical presentation for IDA

Patients with nutritional IDA should have dietary counseling to address the underlying etiology .
Patients with any evidence of gastrointestinal blood loss or malabsorption should be started

Stages Of Iron Depletion

Prelatent iron deficiency

When tissue stores are depleted, without a change in hematocrit or serum iron levels.
This stage may be detected by low serum ferritin measurements.

Latent iron deficiency

The serum iron level drops and TIBC increases without a change in hematocrit.
This stage may be detected by a routine check of transferrin saturation.

The bulk of the erythrocyte population appears normal.

Frank iron deficiency anemia

Is associated with erythrocyte microcytosis and hypochromia.
It is detected when iron deficiency has persisted long enough that a large proportion of the circulating erythrocytes were produced after iron became limiting.

Laboratory tests in iron deficiency of increasing severity

	Normal	Fe deficiency without anemia	Fe deficiency with mild anemia	Severe Fe deficiency with severe anemia
Marrow reticulo-endothelial iron	**2+ to 3+**	**None**	None	None
Serum iron, µg/dL	60 to 150	60 to 150	**<60**	<40
Iron binding capacity (transferrin), µg/dL	300 to 360	300 to 390	350 to 400	**>410**
Saturation (SI/TIBC), percent	20 to 50	30	**<15**	<10
Hemoglobin, g/dL	**Normal**	**Normal**	**9 to 12**	**6 to 7**
Red cell morphology	Normal	Normal	Normal or slight hypochromia	Hypochromia and microcytosis
Plasma or serum ferritin, ng/mL	40 to 200	**<40**	<20	<10
Erythrocyte protoporphyrin, ng/mL RBC	30 to 70	30 to 70	**>100**	100 to 200
Other tissue changes	None	None	None	Nail and epithelial changes

CLINICAL MANIFESTATIONS

CLINICAL MANIFESTATIONS

The most common presentation of IDA is asymptomatic, well-nourished infant or child who has a mild to moderate microcytic, hypochromic anemia.

Infants with severe anemia, who present with lethargy, pallor, irritability, poor feeding.

Gastrointestinal tract

Anorexia-common and an early symptom

Depression of growth

Pica-pagophagia (ice) geophagia (sand)

Atrophic glossitis

Dysphagia

Esophageal webs (Kelly-Paterson syndrome)

Pica

The compulsive consumption of nonnutritive substances, is a recurrent symptom in patients with iron deficiency.

The precise pathophysiology of pica is unknown, but it is probably attributable to CNS iron deficiency.

Patients often consume laundry starch, ice,soil, or clay.

Central nervous system

Irritability

Fatigue and decreased activity

Lower mental and motor developmental test

Decreased attentiveness

Reduced cognitive performance

Breath-holding spells

Neurodevelopmental

In young children, IDA is associated with impaired neurocognitive development and have demonstrated changes on developmental assessments that persist, at least partially, even after correction of anemia with iron therapy.

Neurodevelopmental

Psycomotor development may not compeletly recover in children with moderate to severe IDA after correction of iron deficiency .

Neurocognitive Effects

The association between iron deficiency anemia and impaired neurocognitive function is well established, Iron deficiency that has not yet progressed to anemia is also associated with impaired mental and motor functioning.

Infection

Iron is an essential nutrient for bacterial proliferation.
Iron-binding proteins (transferrin and lactoferrin) have bacteriostatic effects and when the iron-binding proteins are saturated with iron, the bacteriostatic effect may be lost, with an increased risk for progression of infection.

Infection

Patients with IDA and protein malnutrition, aggressive treatment with iron resulted in rapid saturation of iron-binding proteins and reactivation or progression of dormant infections, such as malaria or tuberculosis.

Infection

There is no conclusive evidence that iron supplementation of ١ to ٢mg/kg had no apparent harmful effect on the incidence of infectious in theimmunocompetent host, even in the face of active infection.

Diagnosis

Diagnosis

Hb,Platelet count ,PBS
MCV,MCH,MCHC,RDW
Reticulocyte count
Ferritin
Serum Iron ,Iron Saturation Percentage
Therapeutic Trial

Hemoglobin

The minimum laboratory screen for IDA is measurement of hemoglobin.
Common definitions of low hemoglobin is <١١ in children ٠/٥ to <٥ years of age, and <١١/٥ in children ٥ to <١٢ years.

Hemoglobin

Use of hemoglobin to screen children because only the later stages of iron deficiency result in anemia, relying on hemoglobin to screen for iron deficiency misses many children who are iron deficient and in whom adverse consequences, such as potentially irreversible nurocognitive impairment.

Peripheral Blood Smear

Hypochromic microcytic red cells, confirmed by RBC indices:

(١) MCV less than acceptable normal for age

(٢) MCH less than ٢٧/٠ pg

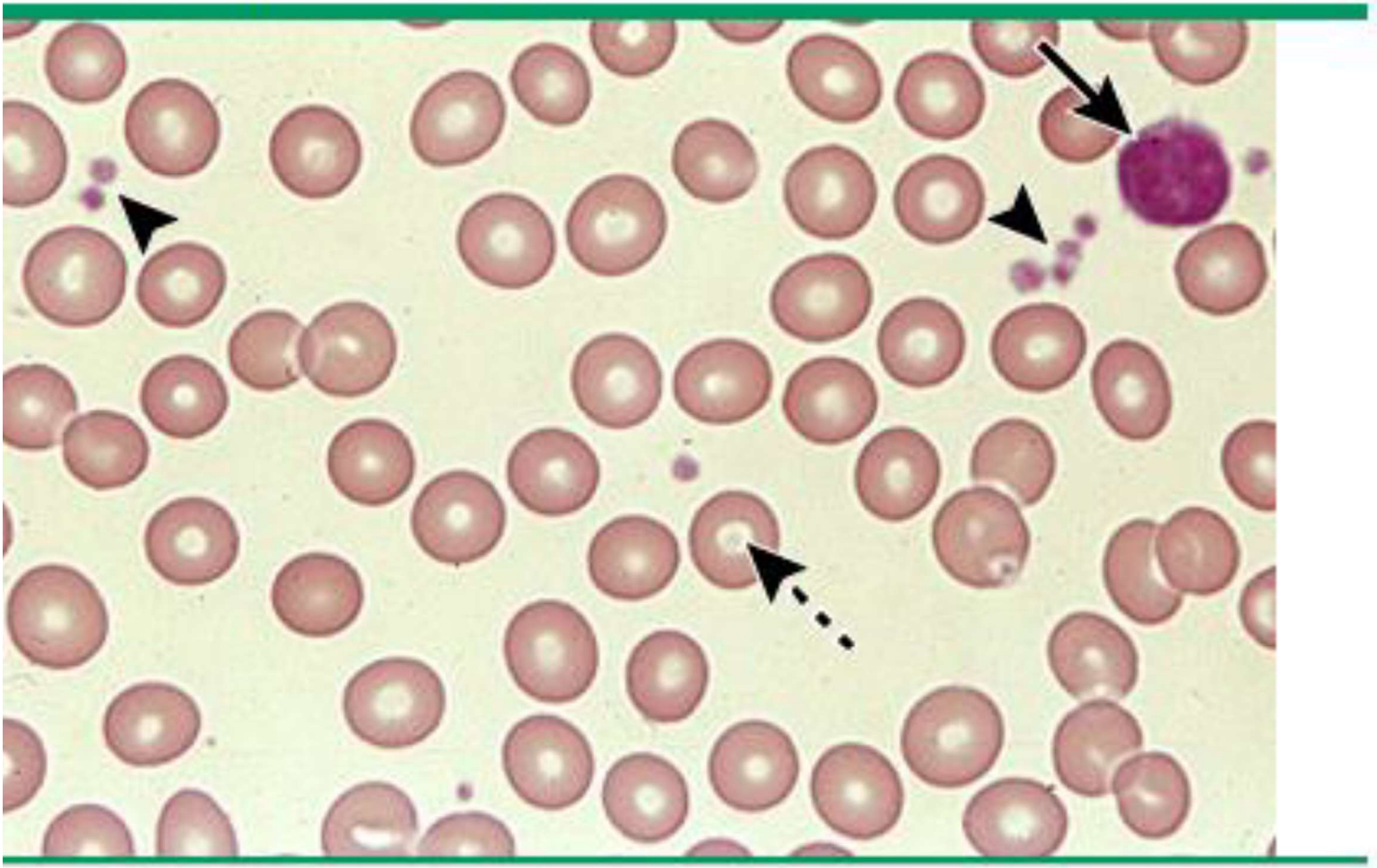
(٣) MCHC less than ٣٠%

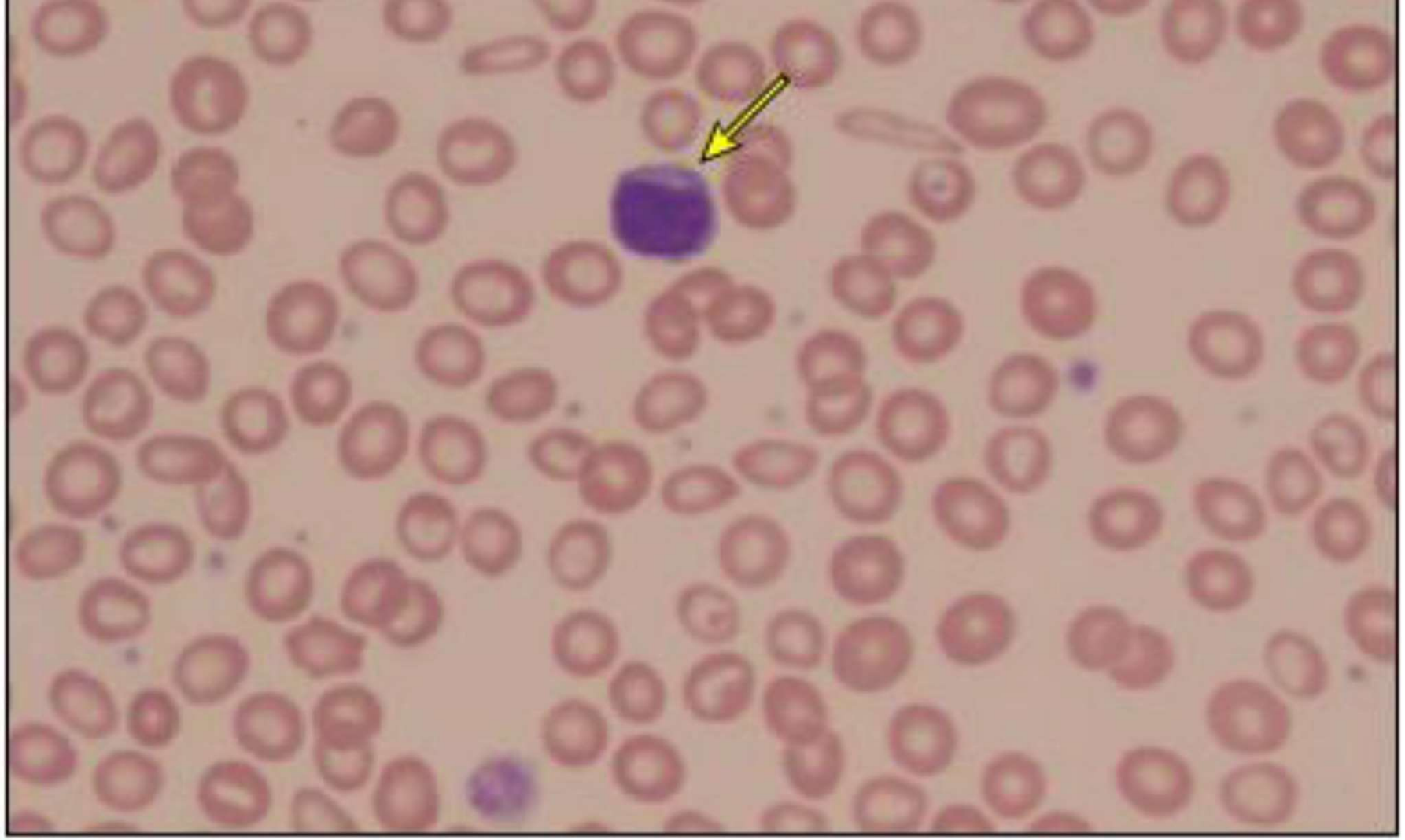
(٤)Wide red cell distribution width (RDW) greater than ١٤/٥%

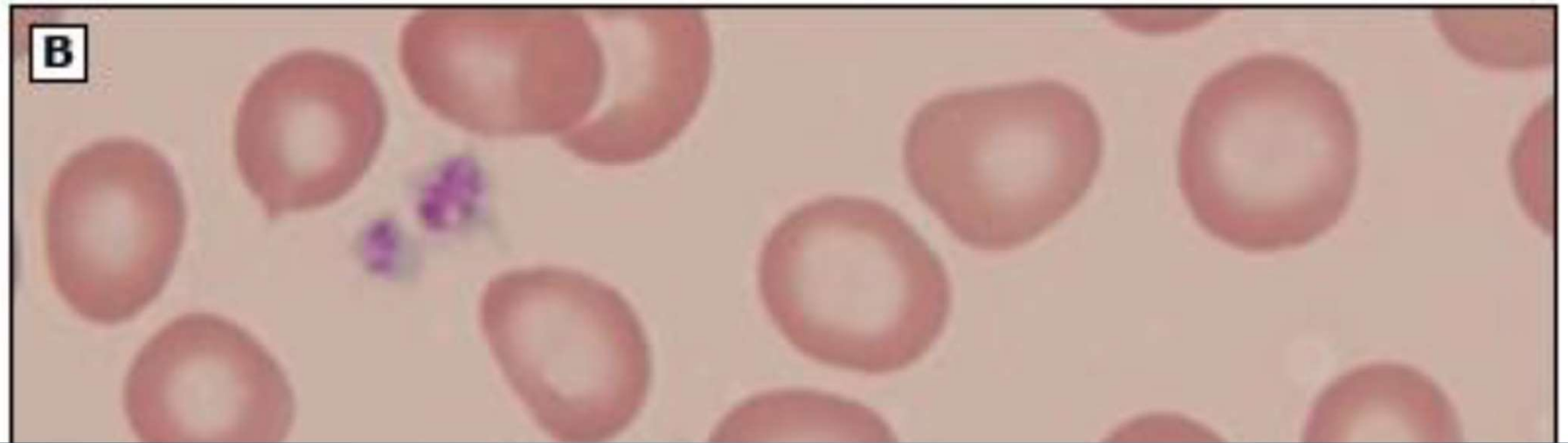
(RDW, MCV)

Widened red cell distribution width (RDW) in association with a low MCV is one of the best screening tests for iron deficiency.

The RDW is high (١٤٫٥%) in iron deficiency and normal in thalassemia (١٣%).



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Platelet count

The platelet count varies from thrombocytopenia to thrombocytosis.

Thrombocytopenia is more common in severe iron-deficiency anemia.

Thrombocytosisis present when there is associated bleeding from the gut.

Reticulocyte count

Reticulocyte count is usually normal but, in severe iron-deficiency anemia associated with bleeding, a reticulocyte count of ۳–۴% may occur.

Serum iron

Serum iron estimation as a measure of iron deficiency has serious limitations.

١-Wide normal variations (age, sex, laboratory methodology)

٢-Subject to error from iron ingestion

٣-Diurnal variation circadian changes (as much as ١٠٠ µg/dl during the day)

٤-Falls in mild or transient infection

Ferritin

The level of serum ferritin reflects the level of body iron stores.
Ferritin is quantitative, reproducible, specific and sensitive and requires only a small blood sample.

Ferritin

A low serum ferritin is always consistent with iron deficiency, but normal or elevated ferritin does not exclude iron deficiency

Measure of inflammation index, such as C-reactive protein (CRP), may be assessed to validate the results of serum ferritin.

Ferritin

Concentration of less than ١٢ ng/ml for children <٥ years, and <١٥ ng/ml for children ٥ to <١٢ years is considered diagnostic of iron.
In the setting of inflammation, ferritin, a positive acute phase reactant,may overestimate iron stores.

Ferritin

Normal ferritin levels, however, can exist in iron deficiency when bacterial or parasitic infection, malignancy or chronic inflammatory conditions co-exist because ferritin is an acute-phase reactant and its synthesis increases in acute or chronic infection or inflammation.

Serum transferrin receptor (STfR)

The STfR is increased in instances of hyperplasia of erythroid precursors such as iron-deficiency anemia and thalassemia.

It is unaffected by infection and inflammation.

Serum transferrin receptor (STfR)

Great value in distinguishing iron deficiency from the anemia of chronic disease and in identifying iron deficiency in the presence of chronic inflammation or infection.

Therapeutic trial

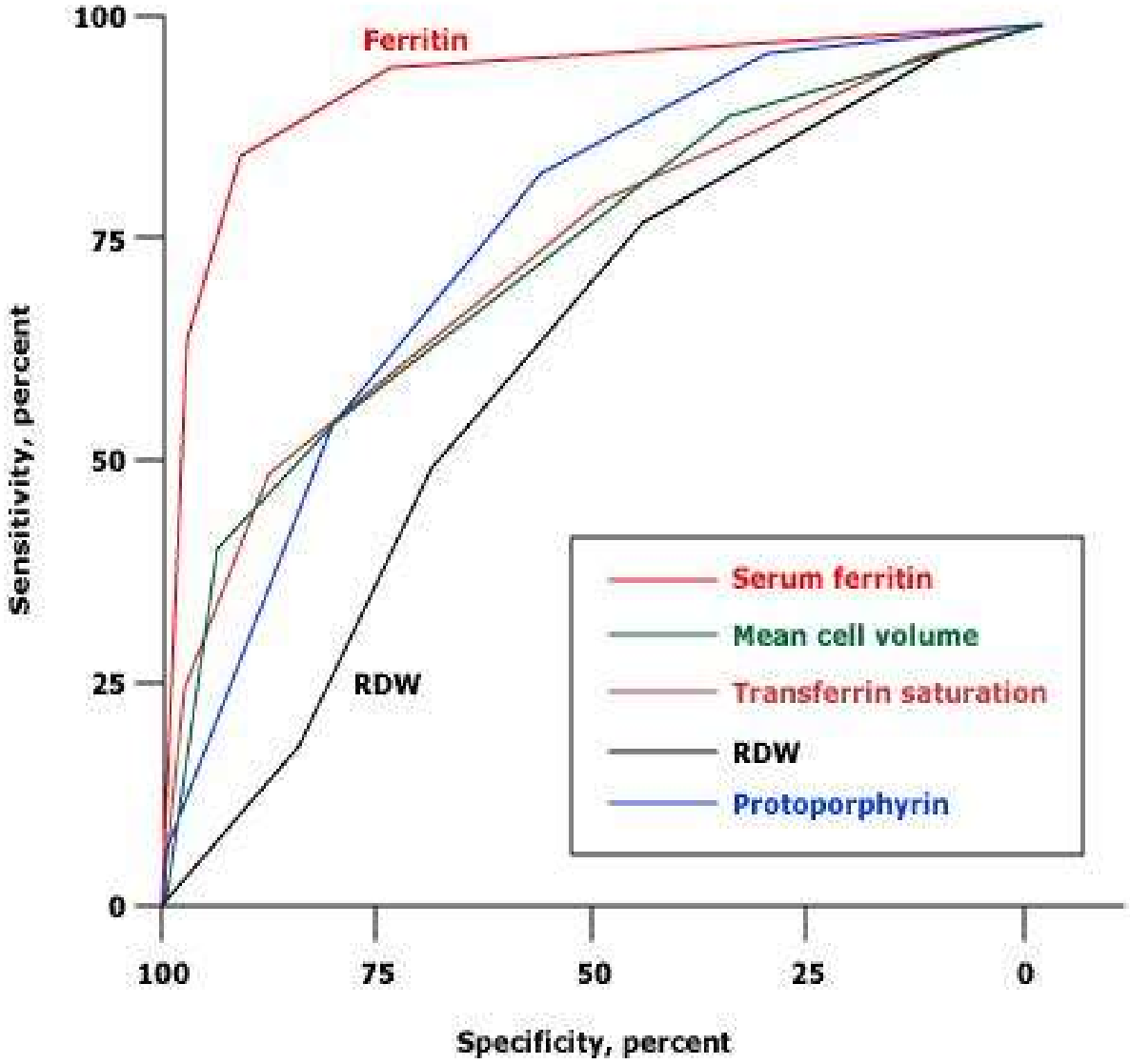
The most reliable criterion of iron-deficiency anemia is the hemoglobin response to an adequate therapeutic trial of oral iron.

Therapeutic trial

Ferrous sulfate,in a dose of ٣ mg/kg per day is given for one month. (a hemoglobin rise of more than ١ g/dl in one month).

Absence of these changes implies that iron deficiency is not the cause of the anemia.

Testing for iron deficiency



Receiver operating characteristic (ROC) curves showing the sensitivity and specificity of various tests for the diagnosis of iron deficiency [ferritin, red cell protoporphyrin, transferrin saturation, mean red cell volume (MCV), and red cell volume distribution width (RDW)]. Note that, at any given level of sensitivity or specificity, serum ferritin outperforms all the other tests shown.

Differential Diagnosis

Hemoglobinopathies(Thalassemia,hemoglobinCC; EE; koln;Lepor)

Sidroblastic Anemia

Cooper Deficiency

Lead Intoxication

Chronic Infections

	Thalassemia Trait	Iron Deficiency
MCV/RBC	<١٣	>١٣
٢(MCV) x MCH	<١٥٣٠	>١٥٣٠
MCV - RBC -(٥ x Hb) - ٨/٤	Negative values	Positive values

TREATMENT

TREATMENT

IDA should be treated with oral iron therapy, and the underlying etiology should be corrected so the deficiency does not recur.

Oral Iron Medication

١- Product: Ferrous iron (e.g., ferrous sulfate, ferrous gluconate, ferrous ascorbate, ferrous lactate, ferrous succinate, ferrous fumarate).

٢- Dose:. ١–٢ mg/kg & ٤-٦ mg/kg elemental iron three times daily.

٣- Duration: ٦–٨ weeks after hemoglobin level and the red cell indices return to normal.

Absorbtion

Iron is not absorbed in the stomach and is absorbed best from the duodenum and proximal jejunum.

Therefore, enteric coated or sustained release capsules, which release iron further down in the intestinal tract, are less efficient sources of iron.

Absorbtion

Enhancers of iron absorption:
heme iron (meat, poultry, and fish) & vitaminC.

Inhibitors of iron absorption:

polyphenols (in certain vegetables), tannins (in tea), phytates
(in bran), and calcium (in dairy products).
Vegetarian diets :low in heme iron.
iron bioavailability in a vegeterian diet can be increased by careful planning of meals to include other sources of iron and enhancers of iron absorption

Absorbtion

Iron should be given two hours before, or four hours after, ingestion of antacids.

Iron is best absorbed as the ferrous (Fe^{2+}) salt in a mildly acidic medium. As a result, we usually add a ٢٥٠ mg ascorbic acid tablet at the time of iron administration to enhance the degree of iron absorption.

Iron bioavailability

Iron bioavailability depends on dietary composition.

Heme iron: meat, poultry, and fish.

Non-heme iron: plantbased foods and iron-fortified foods .

The bioavailability of non-heme iron is strongly affected by the kind of other foods ingested at the same meal.

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Response

a. Peak reticulocyte count on days ٥–١٠ following initiation of iron therapy.

b. Following peak reticulocyte, hemoglobin rises on average by ٠/٢٥–٠/٤ g/dl/ day or hematocrit rises ١%/day during first ٧–١٠ days.

c. Thereafter, hemoglobin rises slower: ٠/١–٠/١٥ g/dl/day.

Response

٤-٣٠ days Increase in hemoglobin level.

Iron medication should be continued for ٨ wk after blood values are normal.

Because ١-٣ mo repletion of stores.

Oral Supplementation

Administration of iron on an empty stomach at night will lessen the gastrointestinal difficulties.

The decreased gastrointestinal motility of sleep will also enhance absorption.

Failure to respond to oral iron

-Poor compliance
-Inadequate iron dose ,Ineffective iron preparation, Insufficient duration
-Persistent or unrecognized blood loss
-Incorrect diagnosis (thalassemia, sideroblastic anemia)

Failure to respond to oral iron

-Coexistent disease that interferes with absorption or utilization of iron (e.g., chronic inflammation, IBD)

-Impaired GI absorption due to high gastric pH (e.g., antacids,histamine-٢ blockers, gastric acid pump inhibitors)

Gastrointestinal blood loss

Negative guaiac tests for occult bleeding may occur if bleeding is intermittent; for this reason, occult bleeding should be tested for on at least five occasions when gastrointestinal bleeding is suspected.

The guaiac test is only sensitive enough to pick up more than ۵ ml occult blood.

Parenteral Iron Replacement

-Oral iron is poorly tolerated or noncompliance
-Rapid replacement of iron stores is needed
-GI Iron absorption is compromised
-Erythropoietin therapy is necessary(dialysis)

Iron sucrose (Venofer)

The most common form of IV iron utilized in children.

Rates of adverse events including anaphylaxis are very low.

No test dose or routine premedications are indicated.

Blood Transfusion

-Severe anemia requiring correction more rapidly than is possible with oral iron or parenteral iron.

-IDA with infection,especially when signs of cardiac dysfunction are present .

- Hemoglobin level is ٤ g/dl or less.

Iron Replacement In Infants

Iron Replacement In Infants

Because the fetus accumulates iron at the mother's expense in the third trimester of pregnancy, full-term infants are born with adequate iron stores to last approximately ٦ months.

Preterm infants are at greater risk for iron deficiency, with their stores depleted by ٣ to ٤ months of age.

Effects Of Maternal Iron Stores

When the mother is iron deficient, the placenta is concerned only with the welfare of the fetus and will continue to remove iron from the mother to support fetal development, even at the cost of negative maternal iron balance.

AAP Recommendetion

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-Breast milk should be provided for at least ٥ to ٦ months .

Iron supplementation of ١-٢ mg/kg/day should be provided to infants who are exclusively fed breast milk beyond ٦ months of age.

AAP Recommendetion

-Infants who are not breast-fed should be nourished with an iron supplemented formula (at least ١٢ mg/L)until the end of the first year of life.

AAP Recommendetion

-Iron enriched cereals should be among the first food introduced with a solid diet.

-- Cow's milk should be avoided during the first year because it contains substances that chelate iron and it sometimes induces occult gastrointestinal hemorrhage.

AAP Recommendetion

-Exclude cow's milk from the infant's diet in the first year of life,limit subsequent consumption of cow's milk to ٢٤ ounces per day.

-Evaporated milk or soy-based formula should be used when iron-deficiency is due to hypersensitivity to cow’s milk.

Thanks For Attention