



Iron Deficiency Anemia

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National Anemia Action Council

www.anemia.org

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NAAC Mission



The National Anemia Action Council, Inc. (NAAC) is dedicated to raising the awareness of health care professionals and the public regarding the prevalence, symptoms, consequences, and treatment options of anemia.

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NAAC's Online Resources for Medical Professionals



- Research Reviews - Recent clinical trials reviewed
- Ask the Expert - Your anemia questions answered
- Monograph - In-office handbook on anemia
- Feature Articles - Anemia related news and research
- Anemia Alert - Free monthly e-newsletter
- Slide Sets - Educational presentations about anemia
- We have materials for your patients too!

Outline



- Definitions
- Prevalence
- Etiology & physiology of iron deficiency anemia
- Treatment for iron deficiency anemia



Iron Deficiency Anemia

Definitions

NAAC Definition Anemia



- Reduction in number of circulating red blood cells, hemoglobin (Hb) concentration, or volume of packed red cells (hematocrit [HCT])
- Women in childbearing years have lower Hb by about 1 gm/dL than men of the same age
 - Likely due to sex hormone differences

NAAC Inc. Anemia Monograph. Available at: <http://www.anemia.org/professionals/monograph/>

Laboratory Reference Ranges*



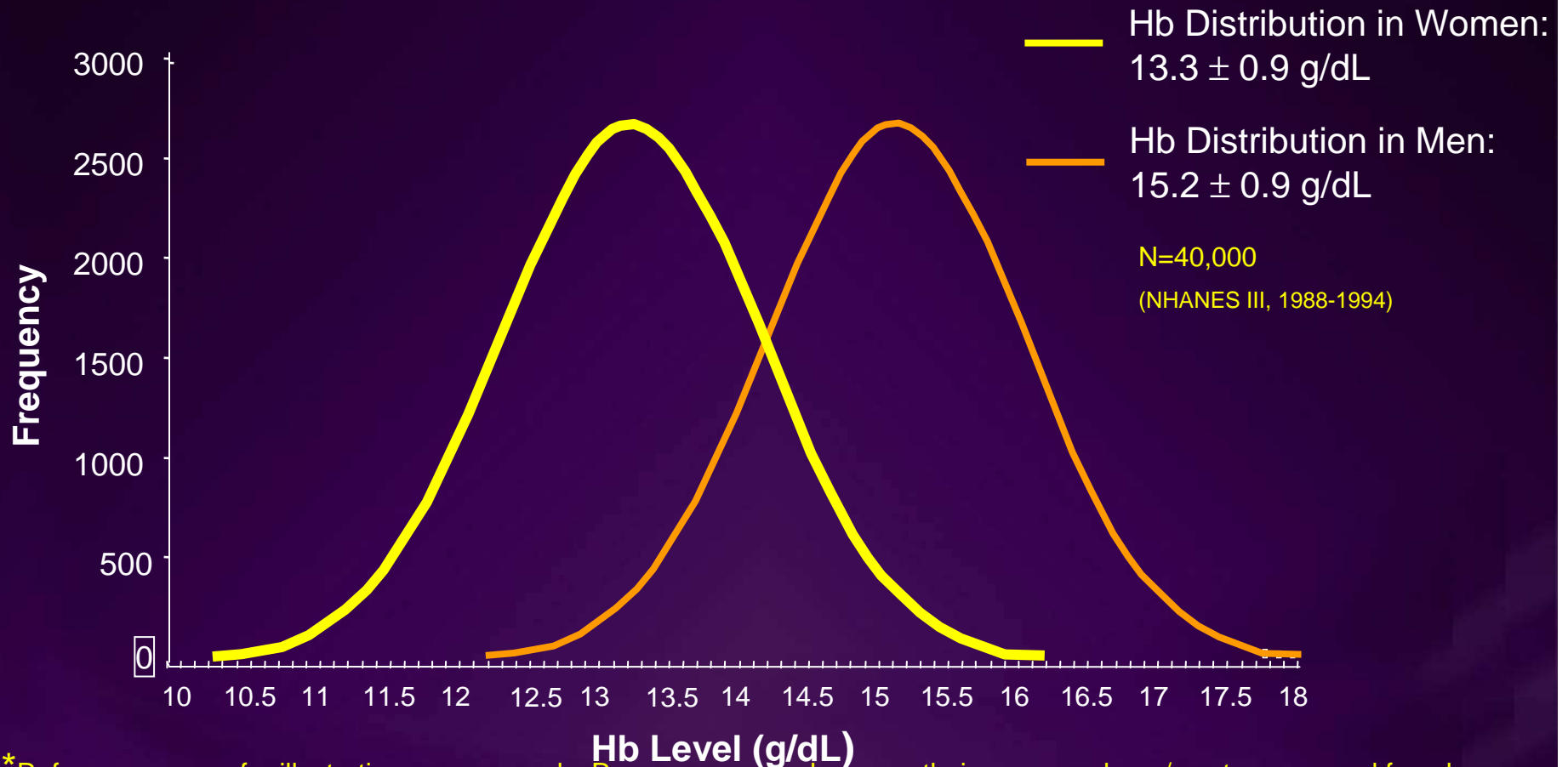
Parameter	Male	Female
Hb (g/dL)	14.0 – 17.4	12.3 – 15.3
Hct (%)	41.5 – 50.4	36.0 – 45.0
RBC count ($10^6/\mu\text{L}$)	4.5 – 5.9	4.5 – 5.1
Reticulocyte count (% of RBC count)	0.5 – 2.5	
Mean corpuscular volume (fL)	80 – 96	
Mean corpuscular Hb (MCH) (pg)	27.5 – 33.2	
MCH concentration (g/dL)	33.4 – 35.5	

Hb = hemoglobin; Hct = hematocrit; RBC = red blood cell

*Reference ranges for illustrative purposes only. Ranges may vary by ethnic group or pre-and postmenopausal females

Perkins S. In: Lee G, et al, eds. *Wintrobe's Clinical Hematology (Vol. 2)*. 10th ed. Baltimore, Md: Lippincott, Williams & Wilkins; 1998:2738

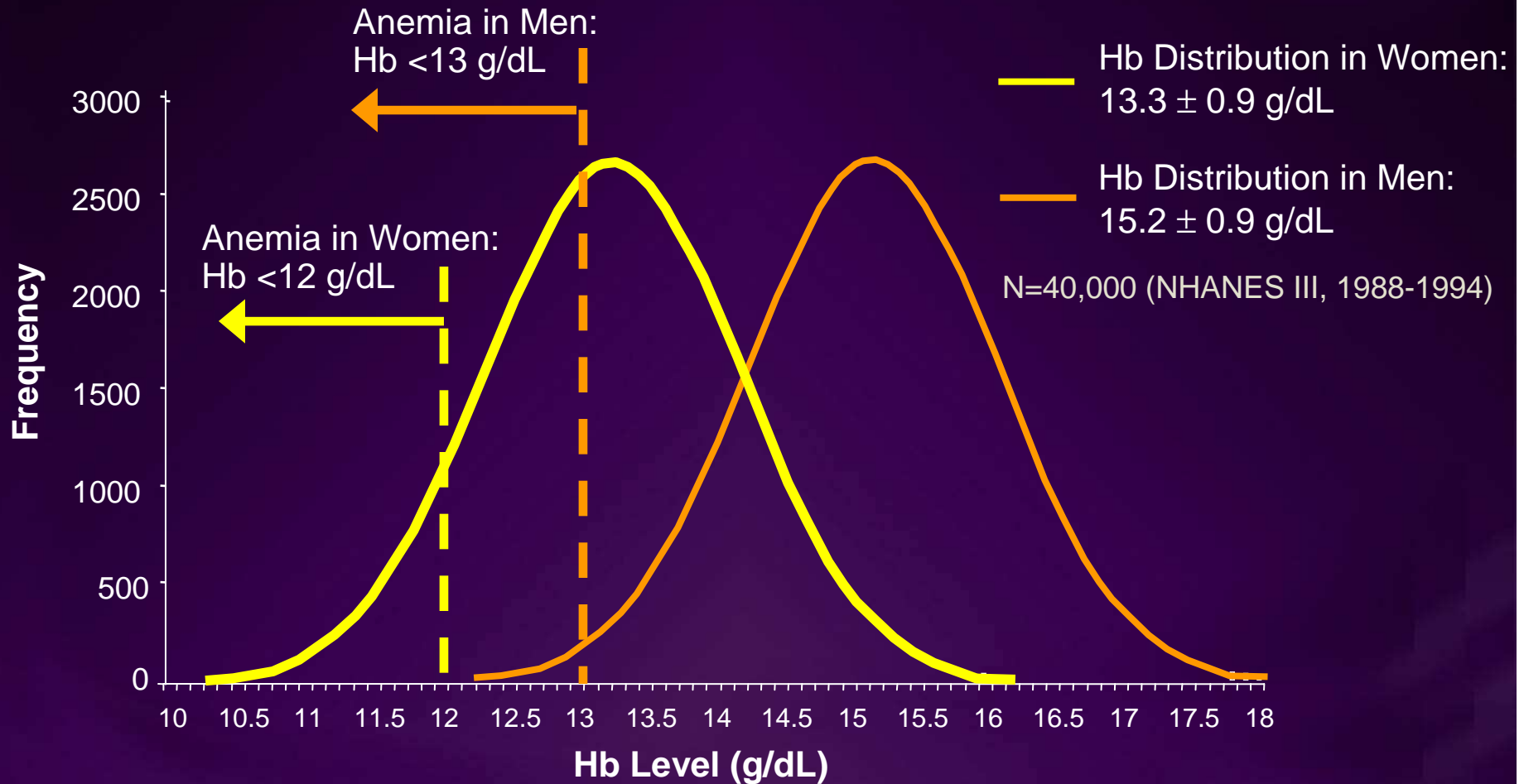
Hemoglobin Distribution in the General Population*



*Reference ranges for illustrative purposes only. Ranges may vary by age, ethnic group and pre / postmenopausal females

Dallman PR, et al. In: *Iron Nutrition in Health and Disease*. London, UK: John Libbey & Co; 1996:65-74

WHO Definition of Anemia v. Hb Distribution General Population



1. World Health Organization. Geneva, Switzerland; 2001

2. Dallman PR, et al. In: *Iron Nutrition in Health and Disease*. London, UK: John Libbey & Co; 1996:65-74

Definition: Iron Deficiency Anemia (IDA)



- Iron deficiency anemia is the condition in which there is anemia due to lack of iron
- Iron deficiency anemia develops when available iron is insufficient to support normal red cell production

Adamson J. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, Isselbacher KJ, eds. *Harrison's Online. Harrison's Principles of Internal Medicine*, 16th Ed. McGraw-Hill Companies, Inc. 2005: Chap 90. Part 5, Section 2.



Iron Deficiency Anemia

Prevalence

Iron Deficiency Anemia Prevalence

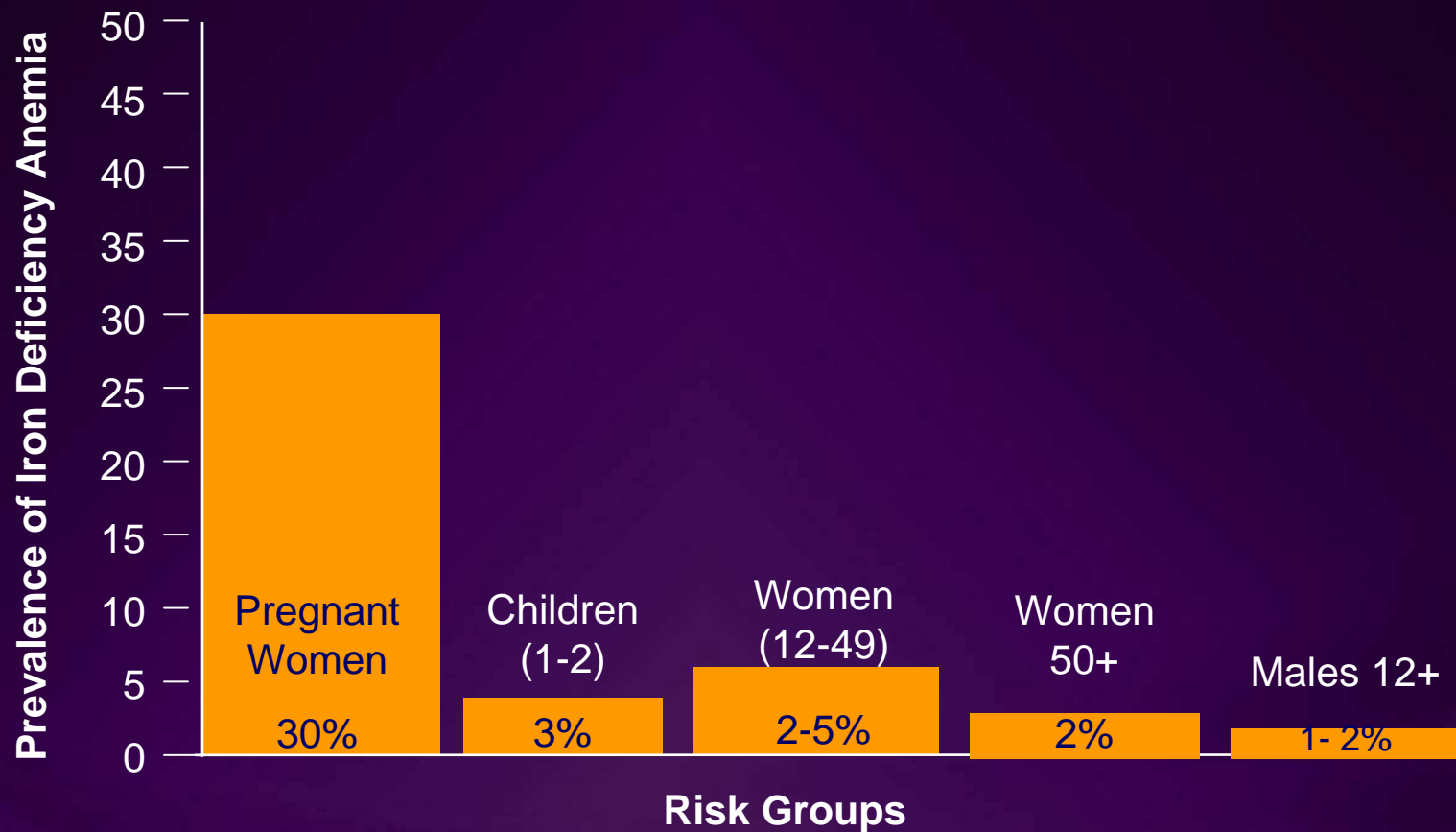


- 3.4 million people in the U.S. are living with anemia
- 2 billion people worldwide are anemic (30% of world's population)
- Many of these anemias are due to iron deficiency

Medical Professional: Anemia Monograph. *National Center for Health Statistics, 1996.* 2006 NAAC <http://anemia.org>

World Health Organization. Micronutrient deficiencies: Iron deficiency anemia <http://www.who.int/nutrition/topics/ida/en.html>

Iron Deficiency: The Most Common Cause for Anemia



Looker AC et al. JAMA. 1997;277:973



Iron Deficiency Anemia(IDA)

Etiology and Pathophysiology

Etiology of Iron Deficiency Anemia



Iron-deficiency anemia can arise from blood loss, inadequate iron absorption, or loss of iron in the urine due to excessive blood destruction

Causes of Iron Deficiency



- Too little iron in diet - Especially children with dietary iron deficiency or a low caloric diet
- Poor iron absorption - Patients with conditions influencing gastric acidity or small bowel absorption
- Chronic blood loss – GI, menstruation, intravascular red cell destruction with iron loss in the urine
- Increased iron demand – Pregnancy and breast feeding, rapid growth in adolescence

(90% of IDA is linked to menstrual blood loss, gastrointestinal blood loss, or pregnancy)

Medline Plus at: <http://www.nlm.nih.gov/medlineplus/ency/article/000584.htm>

Iron Absorption



- Iron balance is achieved primarily by regulation of iron absorption in the duodenum
- Insufficient dietary iron intake is uncommon in adults
- Malabsorption can occur due to atrophic gastritis, GI surgery and from gastric or small bowel disease
 - *Helicobacter pylori*, celiac disease

Dohil R, et al. *J Pediatr*. 1998;132:155-159

Gasché C, et al. *Am J Gastroenterol*. 2001;96:2382-2387

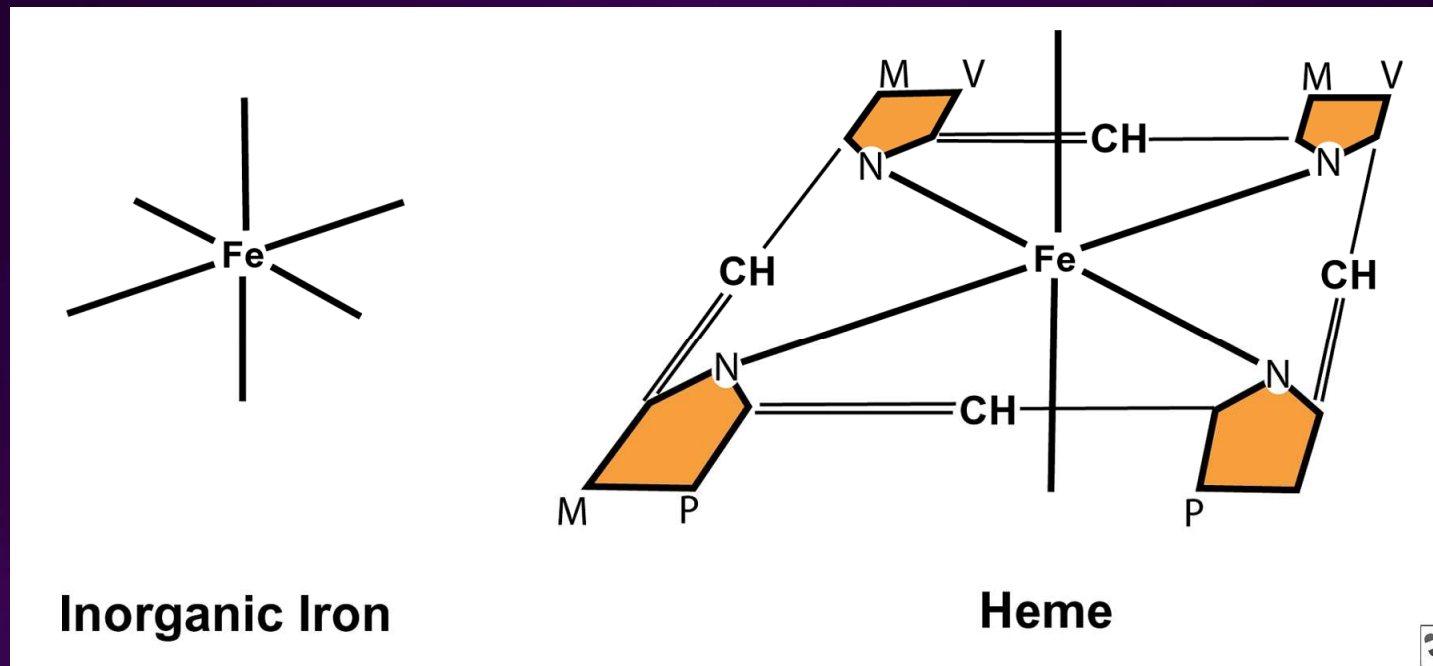
Gasché C, et al. *Digestion*. 1999;60:262-267

Driscoll RH, et al. *Med Clin North Am*. 1978;62:185-201

Iron Uptake



- Two separate pathways for proximal small bowel iron uptake
 - Heme iron pathway
 - Inorganic iron pathway



Physiology of Iron Absorption



- Heme/non-heme iron absorbed into enterocyte non-competitively
- Heme enters cell as intact metalloporphyrin
 - Degraded within enterocyte by heme oxygenase with release of iron
 - Traverses basolateral cell membrane in competition with non-heme iron to bind transferrin in plasma

Physiology of Inorganic Iron Absorption



- Dietary inorganic iron is absorbed mainly from duodenal enterocyte
 - Dietary iron (ferric 3+) in the acid environment of the stomach is chelated by ascorbic acid, sugars and amino acids
 - The chelated iron is reduced to the ferrous (2+) state by ferric reductase in the alkaline environment of the duodenum
 - The ferrous iron is transported across enterocyte cell membrane by the divalent metal transporter 1 (DMT1)
 - The ferrous iron is stored as intracellular ferritin or transported to plasma
 - Transfer to plasma transferrin is facilitated by ferroportin and oxidation by ceruloplasmin

Fleming RE, Bacon BR. *Orchestration of Iron Homeostasis*. N Engl J Med, 28Apr2005;352(17):1741-4

Physiology of Inorganic Iron Absorption



- Liver-derived hepcidin controls how much iron is absorbed from gut or released from storage sites
 - Feedback between iron needs and absorption:
 - Increased absorption
 - Increased bone marrow activity
 - Decreased hemoglobin concentration
 - Decreased blood oxygen concentration
 - Decreased absorption
 - Anemia of Inflammation (anemia of chronic disease)

Fleming RE, Bacon BR. *Orchestration of Iron Homeostasis*. N Engl J Med, 28Apr2005;352(17):1741-4

Physiology of Inorganic Iron Absorption



- Iron released into circulation binds to transferrin
 - For transport to sites of cell usage and storage
- The hepcidin-ferroportin mediated release of iron from enterocytes, macrophages, and hepatocytes is the critical determinant of iron homeostasis

Fleming RE, Bacon BR. *Orchestration of Iron Homeostasis*. N Engl J Med, 28Apr2005;352(17):1741-4

Physiology of Inorganic Iron Absorption



- Hepcidin is now considered the principle hormone involved in iron regulation
 - It senses body iron status
 - It modulates the ferroportin-mediated cell iron release system
- Factors regulating intestinal iron absorption also regulate expression of hepcidin by the liver
 - In particular, anemia or erythropoietin down regulate hepcidin expression
 - Treatment of hepcidin-related illnesses such as anemia of inflammation may now be possible

Fleming RE, Bacon BR. *Orchestration of Iron Homeostasis*. N Engl J Med, 28Apr2005;352(17):1741-4

Dietary Factors Affecting Iron Absorption



- The body absorbs iron best from ingestion of meat (heme-iron pathway)
- Absorption of iron can be increased by adjunct ingestion of the following:
 - Absorption of iron can be enhanced by foods high in vitamin C
- Iron absorption can be blocked by coffee, tea, egg yolk, milk, fiber and spinach

Factors Affecting Iron Absorption



- Quantity in diet
 - 7 mg per 1000 calories
 - Chemical form; heme iron versus inorganic iron
- pH (antacids, H2 blockers)
- Gastrointestinal motility
- Chelation due to antacids, phylates, tannins
- *Helicobacter pylori*
- Gastrointestinal disorders (gastrectomy, Celiac disease, hemochromatosis)
- Chronic anemia (hepcidin deficit)
- Inflammatory disorders (hepcidin excess)

Mucosal Factors Affecting Iron Absorption



- Anatomic factors
 - Decreased absorptive surface
 - Gastric surgery
- Mucosal cell defects
 - Gastric atrophy
 - Celiac disease
 - Inflammation

Host Factors Affecting Iron Absorption



- Body iron stores
- Iron needs
 - Rate of erythropoiesis
 - Tissue hypoxia
- Dietary history

IDA Laboratory Workup



- CBC
 - Chronic IDA red cell indices show microcytosis and hypochromia (MCV and MCHC below normal range)
 - Reference range values: MCV 83-97 fl; MCHC 32-36 g/dL
 - Platelet count may be elevated prior to iron therapy (>450,000/mm³)
- Serum Ferritin <14 ng/ml
- Total Iron Binding Capacity >400 mcg/ml
- Transferrin Saturation <20%
- Serum Iron <30 mcg/ml



Treating Iron Deficiency Anemia



Iron Supplementation

- Start with oral supplementation
 - Avoid taking iron with antacids or antibiotics
- Improvement should be seen within a month

Types of Iron Supplementation



Supplement	Route Administered
Ferrous fumarate	Oral
Ferrous gluconate	“
Ferrous sulfate	“
Iron polysaccharide	“
Iron dextran*	Parenteral
Iron sorbital	“
Iron sucrose	“
SFGC **	“

*Test dose should be administered and anaphylaxis kit available

**SFGC: sodium ferric gluconate complex

Optimal Therapeutic Regimen



- The Centers for Disease Control (CDC) recommends three months of iron supplementation for adults with iron deficiency anemia
- Oral iron supplementation may result in normal hemoglobin levels after a few weeks. To replenish iron stores requires an extended course of iron supplementation, usually 3 months

Summary



- Iron deficiency and iron deficiency anemia are prevalent and associated with adverse outcomes
- Iron deficiency may signal an underlying serious medical condition
- Appropriate identification and treatment of iron deficiency are imperative
- Correction of anemia improves quality of life

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