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Iron-deficiency and health consequences in Children

Introduction

What is iron, and why is it important?

Iron, a trace metal found in the earth's crust, is a constituent of many enzymes in the human body and is especially important to ensure oxygen carrying capacity of hemoglobin. Clinical consequences of iron-deficiency include anemia, impaired psychomotor and neurocognitive development and impaired immune function.

How common is iron deficiency?

Iron deficiency is the most common single nutrient deficiency worldwide. 20-40% of infants are iron deficient by 1 to 2 years of age, of which 4-12% are anemic (Sandoval et al., 2005). Iron deficiency in Canada has declined over the last few decades, but is still prevalent. In BC, about 7% of otherwise healthy infants are iron deficient, with increased incidence in First Nations and Indo-Canadians secondary to diet (Guidelines and protocols advisory committee in BC, 2004).

How is iron regulated in the body?

Iron is absorbed in the duodenum and upper jejunum and is transported in the blood by transferrin. Iron is found primarily in hemoglobin (biologically active), but is also stored as ferritin in reticuloendothelial cells (spleen, liver, bone marrow). The iron concentration in the body is regulated by absorption – the human body has no mechanism of excreting excess.

Risk factors

Table1: Risk factors for Iron deficiency

↓intake/low stores	↑loss	Increased demand
'Milk babies'	Menorrhagia	Prematurity
Poor dietary habits	GI Bleed	Infancy
Strict vegatarian	Meckel's diverticulum	Adolescence
	Esophagitis	
	Peptic ulcer	
	IBD	
	Parasitic infection	

*adapted from Sandoval et al. (2004).

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Which groups are most vulnerable in pediatrics?

There are 3 groups that are most vulnerable to iron deficiency in the pediatric population. Each group is at elevated risk for different reasons:

1) Infants

Infants, during their first year, need to absorb about 1.2mg of elemental iron daily to meet demands of normal hemoglobin synthesis. Full-term infants have adequate iron stores to meet demands for the first 4 months of life. After 6 months of age, full term infants may develop iron-deficiency if not given foods rich in iron.

a. 0-6mnths: Premature and low birth weight neonates have fewer iron stores, and therefore become iron-deficient more quickly than full-term infants.

b. 6-12mnths: The introduction of cow's milk before 1 year can lead to iron deficiency due to excess milk intake. Milk is low in iron and replaces foods rich in iron. Also, dairy products interferes with the absorption of iron. This is an especially vulnerable stage of rapid psychomotor development.

2) Toddlers up to pre-school

Toddlers, as the previous group discussed, are at risk if they have excessive milk intake. They are by nature "picky eaters" putting them at risk. After the age of 1 year, a child should consume no more than two 8oz bottles of milk per day.

3) Adolescents

Iron deficiency in this population can be due to low intake from poor dietary habits, increased demand from growth spurts, and increased blood loss from menstruation. Females and vegetarians are identified as high risk. Also, IBD, malabsorption and blood loss (which may be occult) should be considered.

General Presentation

What does iron-deficiency 'look' like?

In the early stages, iron deficiency is occult and is generally only discovered when anemia has developed. The complications of iron deficiency can be divided into hematologic and non-hematologic:

Table 2: Consequences of Iron-deficiency and clinical presentation

Hematologic	Non-hematologic
Anemia – pallor, tachycardia, flow murmur, irritability	Epithelial – angular stomatitis, glossitis, koilonychias, alopecia Behavioural – pica (eating dirt and ice) Neurocognitive – delayed development

Iron-deficiency anemia is a microcytic hypochromic anemia. Clinical findings due to the anemia include fatigue, pallor, tachycardia, flow murmur (if severe) and irritability.

Pica is a behavioural manifestation of iron deficiency and presents with geophagia (eating dirt) and pagophagia (eating ice). Pica generally resolves with the correction of the iron deficiency. Pica places the child at risk for lead poisoning, which may compound the diagnosis of microcytic anemia.

Neurocognitive deficits are the most devastating. Iron is critical in oligodendrocyte and dopaminergic metabolism. Iron deficiency can lead to hypomyelination and may be the basis for the neurocognitive deficits. It is still unclear whether correcting iron-deficiency will reverse the impacts on psychomotor development.

Questions to ask

- Prenatal history (infants)
  - Premature? Low birth weight? Congenital conditions?
- Diet history
  - Infant: Breastfeeding? If over 6mnths, iron fortified cereal? Cow's milk?
  - Toddler: Milkaholic? Malabsorption?
  - Adolescent: Vegetarian? Poor eating habits?

- Developmental assessment
  - Any concerns of delay, possibly attributable to iron deficiency
- Other
  - Growth spurts, menstruating/menorrhagia, blood loss, malabsorption?
- Symptoms
  - Fatigue? Irritable? Pallor? Disturbed sleep? Edema or swelling? Skin changes? Pica? Hematochezia? Loose/pale stools? Hematemesis?
- Differential
  - Thalassemia – family history
  - Anemia of chronic disease – general review of systems
  - Lead exposure (for more info http://www.cmaj.ca/cgi/content/full/166/10/1287 see Box 1)

Physical Examination

What pertinent physical findings are there for iron deficiency?

General - irritability, pallor, tachycardia, growth parameters
Specific findings - increased HR, pallor, blue sclera, angular stomatitis, spoon nails, flow murmur, headache
Neurological examination – appropriate development for developmental age?

Laboratory Investigations

The gold standard test for iron deficiency is a bone marrow aspirate to test for iron stores, however this is an invasive test, and generally hematology is used, including looking at a peripheral blood smear and interpreting measured parameters. The peripheral blood smear shows microcytic, hypochromic RBC with anisocytosis and poikilocytosis. Measured parameters are summarised in the table below:

Table 3: Hematologic Profile of Iron deficiency

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Test	Finding
Ferritin[1]	↓
CBC	**↓Hemoglobin** **↓MCV**
RDW	↑
Peripheral Smear	**Hypochromic microcytosis**
Fe[2]	↓
TIBC[3]	↑
Transferrin Saturation (serum Fe/TIBC)	↓

[1]Falsely elevated in inflammatory and liver disease, neoplasm, hyperthyroidism
[2]varies daily
[3]Total Iron binding capacity – measure of total transferrin in blood, high specificity for decreased iron, low sensitivity

Treatment

How do you treat iron-deficiency?
Iron supplements come as ferrous sulphate, ferrous gluconate, or ferrous fumarate. Ferrous sulphate is preferred as it is the least expensive, however may have more side effects (constipation). Dosages dependent on age of child, but generally 3-6mg/kg/day of elemental iron divided in 2 to 3 doses is a therapeutic dose. Supplements should be taken with vitamin C to enhance absorption. It should be given in between meals and not with milk.

How do you follow up on treatment?
After initiating iron therapy, reticulocytes will increase after one week. Hemoglobin will normalize by about 10g/L per week. Follow-up after therapy (repeat blood work) should be done about 4 weeks after initiating iron supplementation.

References

1. Guidelines and Protocols Advisory Committee in BC. (2004) Investigation and Management of Iron Deficiency, BC Health Services.
2. http://www.hlth.gov.bc.ca/msp/protoguides/gps/irondef.pdf

3. Sandoval, C, et al. (2004). Trends in diagnosis and management of iron deficiency during infancy and early childhood. *Hematol Oncol Clin N Am*. 18:1423-1438.

Website links

1. Iron needs of babies and children (for parents): http://www.caringforkids.cps.ca/babies/IronReq.htm

2. Australian Iron Status advisory panel: http://www.ironpanel.org.au/AIS/AISdocs/index.html

3. Disordered Iron Metabolism (for more in depth information on the physiology of Iron metabolism, and info on iron deficiency) (Bridges, K) http://sickle.bwh.harvard.edu/menu_iron.html

4. Sanborn, MD et al. (2002) Identifying and Managing adverse environmental health effects. 3. Lead exposure. http://www.cmaj.ca/cgi/content/full/166/10/1287 (reviews questions to ask when assessing for lead exposure)