WHY IS IT IMPORTANT?

Iron deficiency (ID) peaks in prevalence in early childhood, 1 to 3 years of age. Studies in Canadian children suggest a prevalence of 12% or higher for nonanemic ID, and a prevalence of 1.5% or higher for ID anemia (1). ID is considered ‘an inadequately addressed and significant public health problem among Canadian infants and children’ (1). ID in infancy is associated with neuro-cognitive impairments. Long-term follow-up of children with ID in infancy to 25 years of age shows that these deficits persist, and include cognitive impairments and functional impairments such as noncompletion of secondary school and poor emotional health (2). Animal studies confirm impairments in memory and cognition.

PRACTICAL TIP #1: CLINICAL ASSESSMENT

Several studies have identified key risk factors for ID in young children aged 1 to 3 years. Practitioners can identify these by history and physical examination. These
include: prematurity or low birth weight, weaning to noniron fortified foods, introduction of cow’s milk before 9 to 12 months, bottle use beyond 12 months of age, cow’s milk consumption more than 500 mL per day, breastfeeding beyond 12 to 15 months without iron supplementation, meat and meat alternative consumption less than twice per day, overweight or obese (3).

**PRACTICAL TIP #2: LABORATORY ASSESSMENT**

There are many laboratory indices of iron status, and practitioners may find it challenging to select the most informative laboratory test. A systematic review of studies in adults, comparing several laboratory tests to bone marrow aspirate (gold standard) concluded that serum ferritin has the highest diagnostic accuracy and should therefore be the ‘only blood test ordered’ (4). Mean corpuscular volume, which is routinely available with the complete blood count, was also found to be a useful test when less than 70 fl, but not as accurate as serum ferritin (4). For children, there are little data to establish a link between the serum ferritin cut-off value and a gold standard (such as bone marrow aspirate) or optimal health outcomes. Future studies should examine the relationship between serum ferritin and developmental outcomes. Furthermore, laboratory reference intervals for serum ferritin are very wide and may not be informative for determining whether or not a young child has ID. A recent study in Canadian children aged 1 to 3 years examined the relationship between hemoglobin and serum ferritin; this analysis suggests that for this age group the optimal hemoglobin is more than 120 g/L (based on the fact that hemoglobin peaks at that level) which is usually associated with a serum ferritin >18 μg/L (5). As serum ferritin is an acute phase reactant, practitioners should concurrently measure C-reactive protein. If the C-reactive protein is elevated, the serum ferritin level may be falsely elevated and should be interpreted with caution.

**PRACTICAL TIP #3: MANAGEMENT**

There are many oral iron preparations and brand names, from which practitioners must select the most effective with the least adverse effects. Many oral iron supplements are over-the-counter natural health products which have a separate regulatory system from prescription drugs. The recommended dose is 2 to 6 mg/kg/day
of elemental iron, which may be given once daily, or divided into two or three daily doses, for a duration of 3 to 6 months (6).

Common forms of iron include ferrous and ferric iron salts. Ferrous iron salts are the most commonly used iron preparations (6). Ferrous sulfate and ferrous fumarate are available in liquid forms, with brand names including Fer-In-Sol® (ferrous sulfate) and Palafer® (ferrous fumarate). More recently, ferric iron salts mixed with a saccharide and water has led to the production of polysaccharide iron complex. Brand names include NovaFerrum® (a liquid) and FeraMAX® (a powder).

A 2017 publication reported on a trial that randomized young children aged 9 to 48 months with nutritional ID anemia to a 12-week course of ferrous sulfate or polysaccharide iron complex (6). While children in both groups demonstrated improved hemoglobin and serum ferritin, children receiving ferrous sulfate had significantly greater improvements, and a larger proportion with complete resolution of ID anemia (29% versus 6%) (6). A significant proportion of children in both groups had persistent ID at 12 weeks (6). There were more reports of diarrhea in the polysaccharide iron complex group than in the ferrous sulfate group (6).

**SUMMARY OF PRACTICAL TIPS**

In young children 1 to 3 years of age, practitioners should:

- Assess clinical risk factors for ID
- In children at risk, measure hemoglobin, mean corpuscular volume, serum ferritin and C-reactive protein
- If ID, select an iron product that is the most effective with the least adverse effects (typically a ferrous salt)
- Treat ID for at least 12 weeks followed by repeat laboratory assessment to determine if treatment needs to continue, aiming for a hemoglobin >120 g/L and serum ferritin >18 µg/L

Conflicts Of Interest
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References

   Google Scholar  CrossRef  PubMed

   Google Scholar  CrossRef  PubMed

   Google Scholar  CrossRef  PubMed

4. Guyatt GH, Oxman AD, Ali M, Willan A, McIlroy W, Patterson C. Laboratory diagnosis of iron-

Google Scholar  CrossRef  PubMed


Google Scholar  CrossRef  PubMed


Google Scholar  CrossRef  PubMed

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