

Iron deficiency (ID) is the most common micronutrient deficiency worldwide. In Canada, ID is recognized as a “*Public Health Problem*” in infants and young children. Preterm infants are at high risk of developing ID due to lower iron stores at birth, rapid post-natal growth, frequent blood sampling and inadequate iron intake. Iron deficiency in infancy may lead to permanent neurodevelopmental impairment.

### Why is prevention of iron deficiency important?

Iron is an essential nutrient required for the growth and development of the central nervous system. Both ID and ID anemia are detrimental to brain development. ID alone (even without onset of anemia) during infancy affects motor development, socio-emotional behavior and leads to impaired learning, memory and poorer auditory recognition. Prevention of ID is extremely important since the negative effects of ID can’t be reversed by later diagnosis and iron supplementation.

### What are the recommendations for prophylactic iron supplementation in preterm infants?

Human milk contains very little iron, it is incredibly important for breast-fed preterm infants (receiving human milk for half or more of their feeds) to receive prophylactic iron supplements. Infant formulas usually contain higher iron levels than human milk however, iron fortified formula alone may not provide adequate iron for all preterm infants.

**Table 1:** For infants born less than 37 weeks gestation, the IWK recommendations for prophylactic iron supplementation and treatment for iron deficiency anemia are below:

Birth Weight (kg) and fed with human milk	Elemental Iron (mg/kg/day)
Less than or equal to 1 kg	3-4 mg/kg/day
1.01 to 1.5 kg	2-3 mg/kg/day
>1.5 kg	2 mg/kg/day
Birth Weight (kg) and fed with standard iron-rich formula	Elemental Iron (mg/kg/day)
Less than or equal to 1 kg	2 mg/kg/day
1.01 to 1.5 kg	1 mg/kg/day
>1.5 kg	No additional iron supplementation necessary
Iron Deficiency Anemia	4-6 mg/kg/day of elemental iron divided once or twice daily

**Note:** Infants receiving 150 mL/kg/day of standard iron-rich formula receive approximately 2 mg/kg/day of elemental iron. This intake may be low in infants receiving low-iron formulas or for infants who are partially formula feeding.

### **How iron should be adjusted after hospital discharge in preterm infants?**

Iron supplementation should be adjusted as the infant grows or as the diet changes post discharge (switch from formula to breast milk). It is important to adjust the iron dose post-hospital discharge to ensure the infant continues to receive the minimum recommended intake (see Table 1).

Some infants may also be discharged on a treatment dose of iron which could be higher than above recommendations (refer to the NICU discharge summary for guidance). It is important these infants continue to receive at least recommended minimum intake. Health care practitioners may consider doing a CBC, reticulocyte hemoglobin and ferritin at 3-4 months corrected age to guide iron dosage.

### **How long should the iron supplements be continued in preterm infants?**

Supplemental iron should be continued until at least 12 months corrected age. Iron supplements may be discontinued after 12 months corrected age if the infant is eating a wide variety of iron rich foods at least 2-3 times per day. Health care providers may consider re-checking iron stores (CBC, reticulocyte hemoglobin and ferritin) at 12-15 months corrected age before discontinuing supplemental iron.

### **What should I do if the baby is not tolerating their iron supplements or is experiencing constipation?**

Side effects related to oral iron therapy may include abdominal pain, constipation, diarrhea, and darker than normal stools. Given the importance of iron supplementation in the preterm population, it is recommended treating the constipation rather than discontinuing iron supplementation.

Abdominal massage and bicycling exercises of the legs may be helpful in relieving constipation. Other treatment measures for constipation may include, extra water (ideally for use with older infants and should not be added to formula or replace regular feedings), diluted prune juice (for infants 4 months and older and should not replace regular feedings), a stool softener (e.g. Restoralax). Changing the formula may be helpful. Reassurance can be provided about darker stools.

### **When should solids be introduced?**

Iron rich complementary foods are recommended once the infant is at least 6 months corrected age and developmentally ready to start solids. These first foods would include iron fortified infant cereal, pureed meat, or meat alternative iron rich food sources such as tofu, legumes, nuts, seeds, spinach etc. For formula-fed infants, cow's milk should not become the main source of milk until 12 months corrected age to ensure they continue to receive iron from the formula.

## What is the practice about iron supplementation at the IWK NICU and Perinatal Follow-Up Program of Nova Scotia?

At the IWK Health NICU, all preterm infants (<37 weeks) are supplemented with prophylactic iron starting at 2-3 weeks of chronological age. The iron stores are routinely monitored during the NICU stay. For the preterm infants born less than 31 weeks gestation or weighing less than or equal to 1500 grams and followed by the Perinatal Follow-Up Program of Nova Scotia, routine blood testing for CBC, ferritin and reticulocyte hemoglobin is again performed at 3-4 months corrected age to check their iron stores and guide iron supplementation. Note: This testing is not performed for infants seen through travel clinics.

## How common is iron deficiency in preterm infants in Nova Scotia?

A recent retrospective cohort study done on preterm infants born in Nova Scotia found that 1/3 of infants born less than 31 weeks gestational age are iron deficient at 4-6 months corrected age. Many of these preterm infants have their iron discontinued by this age or receiving an unadjusted dose of iron resulting in lower iron stores. The most common reasons why the iron supplement tends to be discontinued are either these infants are formula feeding, there are issues with constipation or solids have been introduced.

Health care providers should strive to eliminate ID by meeting iron supplementation recommendations and adjusting iron doses as infants grow during the first year of life. Parents should be encouraged to re-start iron supplementation if it has been stopped prior to 12 months corrected age.

## What are the recommended cut-offs for ID and ID anemia during infancy?

**Table 2**

Indication	Biomarker	Newborn	2 months	4 months	6-24 months
<b>ID</b>	Serum ferritin (µg/l)	<35	<40	<20	<10-12
<b>ID anemia</b>	Hemoglobin (g/l)	<135	<90	<105	<105
<b>Iron overload (very rare)</b>	Serum ferritin (µg/l)	>300	>300	>250	>200

Adapted from *Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines*, by from Koletzko et al., 2014, p. 122. Copyright 2014 by S. Karger.

### **Key Recommendations:**

1. Prevention of ID is important in preterm infants to avoid negative neurodevelopmental consequences.
2. Follow IWK recommendations for prophylactic iron supplementation in preterm infants <37 weeks of gestation (See Table 1)
3. Preterm infants should be continued on iron supplements for the first year of life.
4. Iron dose should be adjusted as the infant gains weight.

**Contributing Authors:** Satvinder Ghotra, Lisa Morrison, Michelle Higgins, Joyce Ledwidge

### **Here is a list of IWK handouts that could be shared with families:**

Iron for your Health

<https://www.iwk.nshealth.ca/clinical-nutrition/resources#/content/iron-your-diet-pl-0374>

Constipation in Infants

<https://www.iwk.nshealth.ca/clinical-nutrition/resources#/content/constipation-babies-pl-0582>

Guidelines for Feeding Your Baby 6-12 months of age

<https://www.iwk.nshealth.ca/clinical-nutrition/resources#/content/guidelines-feeding-your-baby-6-12-months-age-pl-0369>

Ferrous Sulfate/Iron

[PL-1206-Final-FerrousSulfate-Nov21-2019.pdf \(nshealth.ca\)](#)

## References

- Hartfield D. Iron deficiency is a public health problem in Canadian infants and children. *Paediatrics & child health*. 2010;15(6):347-350.
- Zlotkin SH, Ste-Marie M, Kopelman H, Jones A, Adam J. The prevalence of iron depletion and iron-deficiency anaemia in a randomly selected group of infants from four Canadian cities. *Nutr Res*. 1996(5):729-733.
- Lozoff B. Iron deficiency and child development. *Food and Nutrition Bulletin*. 2007;28(4):S571.
- Georgieff MK. Long-term brain and behavioral consequences of early iron deficiency. *Nutr Rev*. 2011;69(SUPPL. 1):43-48.
- Domellöf M, Braegger C, Campoy C, et al. Iron requirements of infants and toddlers. *J Pediatr Gastroenterol Nutr*. 2014;58(1):119-129.
- Baker, R.D. & Greer, F.R. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). *Pediatrics*. 2010;126(5):1040-1050.
- Greer, F.R. & Kleinman, R.E. *Pediatric Nutrition 8<sup>th</sup> edition* American Academy of Pediatrics. 2020. Chapter 19. Iron
- Parkin, PC, Borkhoff, CM. Practical tips for paediatricians: Assessment and management of young children with iron deficiency. *Paediatrics & Child Health*. 2018;433-434.
- Unger, S. et al. Iron requirements in the first 2 years of life. *Pediatr Child Health*. 2019;24(8):555
- Tudehope, D. et al. Nutritional Needs of the Micropreterm Infant. *J Pediatr*. 2013; 162:S72-80.
- Agostoni C, Buonocore G, Carnielli VP, et al. Enteral nutrient supply for preterm infants: Commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. *J Pediatr Gastroenterol Nutr*. 2010;50(1):85-91.
- Koletzko B et al. Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines. *World Rev Nutr Diet*. 2014(110):121-139
- Powers, J. & Mahoney, D. 2020. Iron deficiency in children < 12 years: Screening, prevention, clinical manifestations and diagnosis. In K.Motil (Ed.) *UptoDate*. Retrieved Nov 20, 2021. From <https://www.uptodate.com/contents/iron-deficiency-in-infants-and-children-less-than12-years-screening-prevention-clinical-manifestations-and-diagnosis>
- Landry et al. Post discharge iron status in very preterm infants receiving prophylactic iron supplementation after birth. *J Pediatr*. 2022 May 14;S0022-3476(22)00424-3.
- IWK Pediatric Neonatal Drug Dose Guidelines [iron \(oral\) – Neonatal Drug Dosing Guidelines – IWK Drug Information Resource \(nshealth.ca\)](#)