Severe iron-deficiency anemia in infants and young children

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Background
There is good evidence of major adverse health impacts associated with both severe and moderate iron-deficiency anemia (IDA) in otherwise healthy infants and young children. The most likely cause of IDA is excessive consumption of cow’s milk in the context of a rapidly growing child with a rapidly increasing red blood cell mass. Cow’s milk is deficient in absorbable iron and additionally may cause enteric blood loss. The cause of the enteric blood loss is not clearly understood but is likely an allergic type reaction between a milk protein and enterocytes lining the gastrointestinal tract.

Severe anemia is associated with decreased oxygen-carrying capacity of red blood cells. If acute or prolonged, this condition can lead to congestive heart failure and ultimately death. There is also good evidence that moderate anemia is associated with changes in motor and cognitive development in young children. Similar evidence is not available for severe anemia and developmental outcomes, but one may logically assume that, if development is impacted by moderate anemia, it would be similarly impacted by a more severe form. There is agreement that both moderate and severe anemia should be prevented if possible and treated if present.

In Canada, there is extremely limited data on the prevalence of moderate or severe IDA in infants and children in otherwise good health. Moderate and severe anemia is, however,
well described in association with various pathological conditions, such as malabsorption syndromes, allergic colitis, clotting disorders, haemolytic conditions, chronic infections or inflammatory conditions and others. Mild anemia is often seen with acute non-severe infections, such as upper respiratory tract infections or otitis media. Mild anemia is defined as a hemoglobin value of more than 100 g/L, but less than 110 g/L, or 120 g/L depending on the age of the infant or child.

The Canadian Paediatric Society (CPS) recommends exclusive breastfeeding for six months, followed by the introduction of iron-containing complementary foods. These two recommendations should prevent anemia from developing in most full-term infants. Although cow’s milk is an important food for the growing child, the CPS recommends restricting its introduction until after nine months of age, while the AAP recommends restricting its introduction until after 12 months of age. These recommendations were based on the observed association between enteric loss of blood and resulting IDA, specifically in infants who received cow’s milk at an age earlier than is recommended.

Although the CPS recommendation to restrict the introduction of cow’s milk has been in place for many years, there is no published data on adherence to this recommendation or to the impact of failing to adhere to it. Since IDA is the only major outcome associated with the early introduction of cow’s milk, a study of this condition in infants and young children 6 to 36 months of age will provide indirect evidence of the success of this recommendation.

**Methods**

New cases of severe IDA will be identified through the CPSP. Participants who identify cases through the monthly reporting form will be asked to complete a detailed questionnaire to ensure the case definition is met.

**Objectives**

- Ascertain the incidence of severe IDA among otherwise healthy Canadian infants and young children by identifying all newly diagnosed cases over a two-year period.
- Determine the significant health complications of severe IDA, such as urgent paediatric consultation, emergency department care or hospitalization, need for blood transfusion or the development of congestive heart failure.
- Determine the ethnicity of infants and young children presenting with severe IDA.
- Obtain demographic and medical information which will assist in:
  - the identification of risk factors for development of severe IDA in Canada;
  - the evaluation of current preventive strategies.
- Supply data that will help develop novel public health policies to prevent severe IDA among children living in Canada.
- Determine adherence to the CPS recommendation on exclusive breastfeeding for six months and restriction of cow’s milk until after nine months of age in children with severe IDA in Canada.
**Severe iron-deficiency anemia in infants and young children (continued)**

**Case definition**
Report all otherwise healthy infants and young children from six months to 36 months of age with severe iron-deficiency anemia defined as:

Hemoglobin <80 g/L and low mean corpuscular volume (MCV; below normal for age) plus one or more of the following:

- low ferritin
- low iron
- high transferrin receptor
- high free-erythrocyte protoporphyrin
- correction of anemia with iron therapy

**Exclusion criteria**

- Chronic disease known to be associated with anemia
- Diseases associated with malabsorption
- Conditions associated with blood loss, such as trauma, surgery, and frequent bloodletting
- Known congenital hemoglobinopathy
- Known disorders of clotting
- Blood loss due to acute or chronic disease causing gastrointestinal bleeding

**Duration**
October 2009 to September 2011

**Expected number of cases**
Based on a cross-sectional study and an emergency departmental study done at a paediatric tertiary care hospital, the expected number of new cases is 600 per year.

**Ethical approval**
Research Ethics Board, The Hospital for Sick Children, Toronto

**Analysis and publication**
An annual interim analysis of the collected data will be done. Dissemination of completed study results will be submitted for publication to appropriate peer-reviewed journals and presented at national and international meetings.

**Bibliography**