



CHAPTER

6

*Routine Iron  
Supplementation  
during  
Pregnancy*

By John W. Feightner

# Routine Iron Supplementation During Pregnancy

Adapted by John W. Feightner, MD, MSc, FCFP<sup>1</sup> from a Review prepared for the U.S. Preventive Services Task Force<sup>2</sup>

*There is currently little evidence from published clinical research to suggest that routine iron supplementation during pregnancy improves clinical outcomes for the mother, fetus or newborn. The evidence is insufficient to recommend for or against routine iron supplementation during pregnancy (C Recommendation).*

*These conclusions apply only to routine iron supplementation and do not pertain to the selection of iron containing foods as part of a healthful pregnancy diet, the use of screening tests to detect anemia during pregnancy, the proper clinical evaluation of the causes of anemia when it is discovered, or the selective use of iron supplements in pregnant women with documented iron deficiency anemia. Prevention of iron deficiency anemia in infants is addressed in Chapter 23.*

*Because relevant effectiveness data are inadequate, clinicians must use individual judgement in determining how to counsel pregnant women about dietary intake of iron containing foods and iron supplements and in deciding whether and how to screen women for anemia and iron deficiency.*

## Burden of Suffering

Both anemia and relative iron deficiency are common during pregnancy. Low hemoglobin concentrations are a normal physiologic response to the expansion in plasma volume that occurs during pregnancy. The normal pattern is for hemoglobin concentrations to fall by about 20 g/L, reaching a nadir in the second trimester, and to return to near pre-pregnancy levels by term.<sup><1></sup> Pregnant women are generally considered to be anemic when hematologic indices fall two or more standard deviations below "normal" levels, although definitions for normal vary. A recent modification of the World Health Organization definition, defines anemia in pregnancy as a hemoglobin concentration (Hgb) below 110 g/L during the first and third



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<sup>1</sup> Professor, Department of Family Medicine, McMaster University, Hamilton Ontario

<sup>2</sup> By Steven H. Woolf, MD, MPH, Assistant Clinical Professor, Department of Family Practice, Medical College of Virginia, Richmond, Virginia and Science Advisor, U.S. Preventive Services Task Force, Washington, D.C.

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trimesters and below 105 g/L during the second trimester, or an hematocrit less than 32%. In pregnancy, women require a greater amount of iron due to an expanded red blood cell volume, the needs of the fetus and placenta, and blood loss at delivery.

For years mineral and vitamin supplements have been prescribed routinely to pregnant women as a normal part of prenatal care. These supplements are often prescribed as preparations that include 25-65 mg of elemental iron, along with other minerals (e.g., calcium, zinc, magnesium, copper) and vitamins. However, few studies have examined the clinical effectiveness of prenatal vitamin preparations as a group.

## *Prevalence*

The exact prevalence of iron deficiency among pregnant women in Canada is uncertain. In the U.S., data for non-pregnant women from the National Health and Nutrition Examination Survey suggest that about 5-10% of women aged 20 to 44 years are iron deficient. The prevalence in pregnant women is thought to be higher because of the added physiologic demands of pregnancy, but exact data are lacking. Iron deficiency anemia is more common in certain high-risk groups, such as persons of low socioeconomic status or limited education; women with high parity, or those with a history of menorrhagia or multiple gestations; persons with diets that are low in both meat and ascorbic acid; persons who donate blood more than three times per year; adolescents; and persons who use aspirin regularly.

## *Effects of Anemia and Iron Deficiency on the Mother*

Among the postulated risks to the mother are increased fatigue and decreased work performance, cardiovascular stress due to inadequate hemoglobin and low blood oxygen saturation, impaired resistance to infection, and poor tolerance to heavy blood loss and surgical interventions at delivery. There is also a theoretical risk that anemic women are more likely to require blood transfusions (a risk factor for infectious diseases) and emergency caesarean section, but data to support these concerns are lacking.

Although studies of male workers have demonstrated low productivity among iron deficient men, few studies of the health effects of iron deficiency have included women, let alone pregnant women. A Swedish survey of 1,462 women compared the complaints of 82 anemic women (Hgb <120 g/L) with those of non-anemic women and found no difference in the incidence of reported infections, fatigue, sleeping difficulties, headache, or work absenteeism.<2> Anemic women were significantly more likely to report low work productivity than non-anemic women (10% vs. 5%). Physical symptoms of anemia

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are generally unapparent unless hemoglobin values fall below 70-80 g/L.

### ***Effects of Anemia and Iron Deficiency on the Fetus and Newborn***

The postulated risks of iron deficiency on the fetus relate to the impaired delivery of hemoglobin and, thus, of oxygen to the uterus, placenta, and developing fetus.

Cross-sectional and longitudinal observational studies (grade II-2 evidence) in the U.S. and Europe have demonstrated that even mild to moderate anemia can be associated with adverse obstetrical outcomes, including preterm delivery, low birth weight and fetal death.<3,4> However, most of the studies do not control for other factors that can cause low birth weight and prematurity (e.g., poor nutrition, smoking), making it unclear whether anemia and iron deficiency are merely associated with these variables rather than having a direct influence on pregnancy outcomes.

### ***Effects of Anemia and Iron Deficiency on the Developing Child***

Another postulated risk of anemia and iron deficiency is that mothers with these conditions may give birth to infants with anemia or iron deficiency and that this may result in abnormal child development if the deficiencies are not corrected early.

However, most studies suggest that pregnant women who are iron deficient are no more likely to give birth to iron deficient newborns than women who have adequate iron stores.<5> Nor is there direct evidence that pregnant women who take iron supplements give birth to infants or children with improved mental or psychomotor performance.

### **Maneuver**

The maneuver being evaluated in this review is the routine provision of oral iron supplementation to pregnant women during the prenatal period. Doses provided in the studies reviewed were as high as 100 mg of elemental iron per day. In the clinical setting, iron is often prescribed in combination with other vitamin supplements. The effectiveness of those other supplements is not the subject of this review.



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## Effectiveness of Prevention and Treatment

The essential clinical question for routine iron supplementation is whether it can reduce the incidence of obstetrical and perinatal complications. Although evidence to date is inconclusive, a large body of data suggests that iron supplements are effective in improving the hematologic indices of the mother. Longitudinal studies in which 30-200 mg of iron were given daily have shown a statistically significant increase (10-17 g/L) in hemoglobin concentration in women taking supplements. However, maternal iron supplements do not appear to have a consistent effect on the hematologic status of the fetus or newborn.

The review by the U.S. Preventive Services Task Force of the evidence for effectiveness focused solely on the ability of iron supplements to improve clinical outcomes in either the mother or newborn (e.g. low birth weight, preterm birth). The biological effectiveness of iron supplements in changing non-clinical outcomes (e.g. hematocrit, hemoglobin, ferritin levels) was not reviewed. This chapter will focus only on studies conducted in industrialized countries.

In a prospective, controlled cohort study in Sweden, Kullander and Kallen collected data on 6,376 women in Malmö in 1963-1965.<6> They found that women who took iron and vitamin supplements were significantly less likely to give birth before 38 weeks (6-9% of births) than women who did not use such supplements (11-13% of births). The birth weight of boys (but not girls) was significantly higher in women who took iron and vitamins than in those who took no supplements. However, without proper control for confounding variables, it is difficult to know whether women who took iron supplements had other characteristics (e.g. healthier lifestyle) that reduced their risk of adverse outcomes. Conversely, a Dutch prospective study indicated no association between low maternal hemoglobin and adverse perinatal outcomes.<7>

The strongest evidence on which to evaluate the effectiveness of routine iron supplementation comes from randomized controlled trials. Most clinical trials of iron supplementation have not demonstrated significant improvements in maternal or neonatal outcomes. Sample sizes in these trials are small, and thus statistical power is generally inadequate to prove that iron supplementation is ineffective. A quasi-experimental study in India reported improved birth weights with supplementation but that may have been confounded by improper randomization.<8> A Scottish randomized controlled trial of 3,600 patients found no difference in the incidence of a wide range of adverse obstetrical outcomes between those receiving iron and those receiving placebo.<9> In a randomized controlled trial with 3,000 women, Hemminki and Rimpela compared routine versus selective iron supplementation.<10> The "routine"



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group was advised to take 100 mg of elemental iron daily beginning by the 17th week of gestation, while the “selective” group was advised to take iron only if certain hematologic parameters were present. Women in the “selective” group were more likely to report poor overall health, to require transfusion and operative delivery, and to have newborns with reduced gestational age at birth. The difference in gestational age was not clinically significant, however, and the authors conjectured that lack of blinding may have contributed to the higher complication rate in the selective group.

### **Adverse Effects**

Iron supplements can cause unpleasant gastrointestinal symptoms (e.g., nausea, constipation), but these usually occur at higher doses than are recommended for routine supplementation. Iron supplements may complicate preexisting gastrointestinal disorders such as ulcerative colitis. Complications of excessive iron storage, including hemochromatosis and hemosiderosis, are possible but very uncommon in women who take only oral (and not parenteral) iron supplements. Finally, a potential hazard of iron supplements is unintentional overdosage by children in the home.

### **Recommendations of Others**

The recommendations of the U.S. Preventive Services Task Force are those outlined in this chapter and, hence, the same as those of the Canadian Task Force.<11>

In 1988, the *U.S. Surgeon General's Report on Nutrition and Health* concluded that iron supplementation is a “reasonable approach” to the prevention of iron deficiency and included pregnant women among the groups that “may need iron supplements.” The report also recommended that pregnant women receive laboratory evaluation for anemia and nutritional advice on methods to ensure adequate iron intake and to enhance iron bioavailability from the diet.

In 1989, the U.S. Public Health Service Expert Panel on the Content of Prenatal Care recommended that health promotion activities during routine preconception and prenatal visits should include counselling on vitamin and iron supplementation “on indication”, for women at risk. The evidence on which this recommendation was based was classified as “fair.” The panel also recommended routine hemoglobin and hematocrit measurements.

In a major report in 1990 on nutrition during pregnancy, the Food and Nutrition Board of the Institute of Medicine recommended routine use of daily iron supplements (30 mg/day) after about the twelfth week of gestation, in conjunction with a well-balanced diet that contains enhancers of iron absorption (ascorbic acid, meat). It also

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recommended that either hemoglobin or hematocrit should routinely be determined at the first prenatal visit. The report recommended that anemia accompanied by a low serum ferritin concentration should be treated with 60-120 mg of ferrous iron daily until a normal hemoglobin concentration is reached, after which the dose should be lowered to 30 mg daily.

## Conclusion and Recommendations

There is currently little evidence from published clinical research to suggest that routine iron supplementation during pregnancy is beneficial in improving clinical outcomes for the mother, fetus or newborn. The evidence is insufficient to recommend for or against routine iron supplementation during pregnancy (C Recommendation).

Although observational data (grade II-2 evidence) suggest that pregnant women with anemia (hemoglobin less than 100 g/L) are at increased risk of preterm birth, low birth weight, or other adverse outcomes, it is unclear from such evidence whether anemia is responsible for these outcomes and whether they can be prevented through iron supplementation. Similarly, it is unclear whether iron supplementation during pregnancy can reduce the incidence of iron deficiency in infants, a condition that has been associated with delayed psychomotor development. Although iron supplementation can improve maternal hematologic indices, controlled clinical trials (grade I and II-1 evidence) have failed to demonstrate that iron supplementation or changes in hematologic indices actually improve clinical outcomes for the mother or newborn.

These conclusions apply only to routine iron supplementation and do not pertain to the selection of iron containing foods as part of a healthful pregnancy diet, the use of screening tests to detect anemia during pregnancy, the proper clinical evaluation of the causes of anemia when it is discovered, or the selective use of iron supplements in pregnant women with documented iron deficiency anemia.

Because relevant effectiveness data are inadequate, clinicians must use individual judgement in determining how to counsel pregnant women about dietary intake of iron-containing foods and iron supplements and in deciding whether and how to screen women for anemia and iron deficiency.

## Unanswered Questions

Further research, including randomized controlled trials with adequate sample size and statistical power or carefully performed meta-analyses of existing studies, is needed before definitive conclusions can be reached about the effectiveness or ineffectiveness of routine iron supplementation. Future studies need to address clinical outcomes that are relevant to the health of the mother, fetus,

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and newborn. Data examining the effects of iron supplementation during pregnancy on long-term pediatric outcomes (e.g., growth, cognitive development, school performance) are currently unavailable and should be a focus of future research. Moreover, there are inadequate data to determine whether giving iron supplements only to pregnant women with documented iron deficiency is less or more cost effective than routine supplementation.

## Evidence

The review sought all observational studies and clinical trials published between 1966 and 1991 in the English language literature. Studies were excluded if they did not measure clinical outcomes in either the mother or the newborn. The review was initiated by the Canadian Task Force in April 1993 and the recommendations were finalized in January 1994.

## Selected References

1. Institute of Medicine: *Nutrition During Pregnancy Part II: Nutrient Supplements*. Washington, D.C.: National Academy Press, 1990: 272-298
2. Lennartsson J, Bengtsson C, Hallberg L, *et al*: Characteristics of anemic women: the population study of women in Göteborg 1968-1969. *Scand J Haematol* 1979; 22: 17-24
3. Scholl TP, Hediger ML, Fischer RL, *et al*: Anemia vs. iron deficiency: increased risk of preterm delivery in a prospective study. *Am J Clin Nutr* 1992; 55: 985-988
4. Murphy JF, O'Riordan J, Newcombe RG, *et al*: Relation of hemoglobin levels in first and second trimesters to outcome of pregnancy. *Lancet* 1986; 1: 992-994
5. Lao TT, Loong EP, Chin RK, *et al*: Relationship between newborn and maternal iron status and hematological indices. *Biol Neonate* 1991; 60: 303-307
6. Kullander S, Kallen B: A prospective study of drugs and pregnancy. *Acta Obstet Gynecol Scand* 1976; 55: 287-295
7. Knottnerus JA, Delgado LR, Knipschild PG, *et al*: Hematologic parameters and pregnancy outcome: a prospective cohort study in the third trimester. *J Clin Epidemiol* 1990; 43: 461-466
8. Agarwal KN, Agarwal DK, Mishra KP: Impact of anemia prophylaxis in pregnancy on maternal hemoglobin, serum ferritin, and birth weight. *Indian J Med Res* 1991; 95: 277-280
9. Willoughby MLN: An investigation of folic acid requirements in pregnancy. II. *Br J Haematol* 1967; 13: 503-509

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10. Hemminki E, Rimpela U: A randomized comparison of routine versus selective iron supplementation during pregnancy. *J Am Coll Nutr* 1991; 10: 3-10
  11. U.S. Preventive Services Task Force: Routine iron supplementation during pregnancy: policy statement. *JAMA* 1993; 270: 2846-2848



## Routine Iron Supplementation During Pregnancy

MANEUVER	EFFECTIVENESS	LEVEL OF EVIDENCE <REF>	RECOMMENDATION
Routine oral iron supplementation in pregnant women	Mixed results have been reported in terms of pre-term birth and birth weight.  Trials have not demonstrated clinically significant benefit but have suffered from methodologic limitations or small sample size.	Cohort and case-control studies<6,7> (II-2)  Randomized controlled trials and quasi-randomized controlled trials<8-10> (I;II-1)	There is insufficient evidence to recommend for or against the routine use of oral iron supplements in pregnant women (C)