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How much iron does a healthy pregnant woman require?

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Dietary reference values for iron in pregnancy vary widely. For example, the US Estimated Average Requirement (EAR) for pregnant women (aged 18 years and above) is 22 mg/d, based on factorial modeling with the assumption that 18% of dietary iron is absorbed during the first trimester and 25% in the second and third trimesters (1). This compares with an EAR in nonpregnant women of 8.1 mg/day. In contrast, the UK Department of Health (2, 3) and the European Food Safety Authority (EFSA) (4) both concluded that there is no need for additional dietary iron during pregnancy, provided there are adequate iron stores at conception. According to the UK Dietary Reference Values (DRVs), the EAR for pregnant women is 11.4 mg/d, whereas EFSA gives an EAR for pregnant women of 7 mg/day (4). The EFSA used factorial modeling to calculate the quantity of absorbed iron required to meet maternal and fetal needs and reached broadly similar values to the Institute of Medicine, but they used different values for iron absorption; heme iron absorption was assumed to be 25% and values for nonheme iron absorption were assumed to be 7.2% in the first trimester, 36.3% in the second trimester, and 66.1% in the third trimester, as reported by Barrett et al. (5). These values were selected on the basis that the test meals administered by Barrett et al. (5) were more reflective of dietary iron intakes than those in some of the other studies, in which higher levels of iron were given as iron salts. The limited data for dietary iron absorption during pregnancy is the main reason for the substantial difference in reference values between these 2 authorities, but there are many other unanswered questions relating to iron metabolism in pregnancy.

Two articles are published in this edition of the *American Journal of Clinical Nutrition* that provide data on iron absorption during pregnancy using stable isotope techniques. Stoffel et al. (6) measured fractional iron absorption (FIA) in normal weight and overweight pregnant women during the second and third trimesters. Women were given a bread roll test meal, labeled with 12 mg of stable isotopically enriched iron, and absorption was calculated from RBC isotope enrichment 14 days after ingestion. In normal weight women, the median FIA values were 13.6% and 23.9% in the second and third trimesters, respectively. The FIA in overweight pregnant women was 13.5% in the third trimester, significantly lower than that in normal weight women. The authors concluded that impaired upregulation of iron absorption in overweight women during the third trimester is associated with inflammation, but is independent of serum hepcidin. This is an important finding, as it concurs with data from animal models demonstrating that fetal signals drive maternal iron absorption (7). The study by Delaney et al. (8) gave 20 mg of iron as ferrous sulphate and reported 9% and 20% iron absorption in the second and third trimesters, respectively, which are similar 2-fold increases to the findings of Stoffel et al. (6) for normal weight women. They found that total body iron, calculated from serum ferritin and a soluble transferrin receptor, explained well over half the variance in iron absorption but, again, there was no association with the hepcidin concentration.

Iron absorption data from these 2 studies will be a useful addition to the literature, the results of which are summarized in Delaney et al. (8) and can be used for future updates of dietary reference values for iron. However, a seemingly intractable question remains unresolved: namely, how much additional iron is required to support a pregnancy? Pregnancy is a normal physiological state, and the high prevalence of iron deficiency in pregnant women and the widespread need for iron supplements is puzzling. The most likely explanation is an inadequate dietary supply of iron in women of child-bearing age that results in low body iron stores, combined with insufficient absorbable dietary iron during pregnancy. Over the course of evolution, physiological adaptations that favored a positive outcome for pregnancy were conserved, but diets were very different at that time, and iron absorption from preagricultural diets has been estimated to be much higher than that from present-day diets (9). In comparison, it could be argued that depletion or even exhaustion of maternal iron stores during pregnancy is a normal physiological mechanism and that repletion should take place in the months and years after delivery: for example, facilitated by the amenorrhea of lactation.

The study by Delaney et al. (8) sheds light on how iron is delivered to the fetus and the importance of red blood cells, particularly in women with low iron stores. The study by Stoffel et al. (6) shows the inability of overweight pregnant women to upregulate iron absorption and transfer sufficient iron to the fetus. Thus, in addition to modern diets containing iron of low bioavailability, inflammation induced by overweight is another phenomenon that may have an adverse impact on the iron statuses of both mothers and infants. The fetus is able

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to accumulate iron normally in the presence of maternal iron deficiency, most likely through compensatory upregulation of placental iron transport, but with severe anemia the fetal iron status becomes compromised, with undesirable consequences (7). It is widely accepted that the fetus acts as a parasite on the mother, but we still do not know whether maternal iron depletion during pregnancy represents a normal physiological state and to what extent efforts should be made to prevent it. The study by Delaney et al. (8) demonstrates that red blood cell iron turnover is faster in women with diminished iron stores and that red blood cell iron is a significant source for fetal iron. This pool of iron will be smaller with anemia, illustrating how important it is to avoid anemia in pregnancy, and also to enter pregnancy with sizeable body iron stores. However, we still do not know whether depletion of iron stores has any adverse effects on the mother or fetus and whether preventative actions are desirable, such as taking iron supplements. Further to the Cochrane review on iron supplementation in pregnancy (10), in which intermittent regimens and daily supplementation produced similar maternal and infant outcomes, an analysis of the risks and benefits of iron supplements in pregnancy is needed. Consensus on iron requirements in pregnancy is urgently required. The 2 papers published in this volume of the *American Journal of Clinical Nutrition* contain data that will help to update dietary reference values for iron, which will in turn inform future public health policies and worldwide strategies focused on the important goal of reducing iron deficiency in women and infants.

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