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## Iron supplementation: is less better?

Iron deficiency affects more than a quarter of the world's population.[1] The optimum long-term intervention strategy is iron fortification of food, but in developing countries where iron deficiency is most prevalent it is often difficult to identify a foodstuff that is centrally processed and widely consumed. Consequently, distribution of iron tablets is the mainstay of efforts to alleviate iron deficiency despite its dismal record of success. Among several reasons why iron supplementation programmes are ineffective,[2] poor compliance is generally believed to be the most important.

A proposed innovation in iron supplementation programmes is a reduction in frequency of administration to less than once daily. The efficacy of intermittent supplementation was evaulated recently by Schultink and colleagues[3] who compared daily with twice weekly iron administration in a randomised double-masked field trial in 2–5-year-old preschoolchildren in eastern Jakarta, Indonesia. 87 children with a baseline haemoglobin concentration of less than 112 g/L were given anthelminthic treatment and then randomly assigned to receive 30 mg iron as liquid ferrous sulphate either daily or twice weekly for 2 months. Correction of iron deficiency as measured by an increase in haemoglobin or decrease in erythrocyte protoporphyrin concentration was two-fold greater in 32 children given iron daily than in 33 children given iron twice daily. However, after statistical adjustment for the lower initial haemoglobin concentration in children given iron daily, the difference was not statistically significant. The researchers concluded that the effectiveness of daily and intermittent administration schedules was equivalent. Their findings would have been strengthened if a control group had been included to assess the haematological effects of deworming and the magnitude of regression to the mean of laboratory measurements. Because iron administration was supervised by health workers in the home, compliance was not evaluated in this study. However, the fact that a quarter of the children in both groups refused to continue in the trial suggests that there was a high frequency of gastrointestinal side-effects from iron doses as high as 4 mg/kg body weight. A more important question is whether a busy mother will be more consistent with intermittent than with daily iron administration; compliance has been a major limitation with weekly antimalarial prophylaxis as a public health measure.[4]

An argument in support of intermittent supplementation is derived from rat studies showing that iron absorption is inhibited when preceded by massive doses of oral iron that would be highly toxic in human beings if given on a body weight basis.[5,6] This mucosal block to iron absorption is assumed to occur with daily dosage. Theoretically, less frequent adminstration of iron should enhance absorption sufficiently to offset the reduction in weekly dose of iron. However, in a recent radioisotopic study, there was no significant difference in absorption of 50 mg of iron as ferrous sulphate when subjects were given oral iron for the preceeding six days.[7] Whilst any increase in iron intake is likely to be of some benefit, a central question with intermittent supple-mentation is whether a 3–7-fold reduction in the weekly dose of iron will have an impact on the prevalence of iron deficiency anaemia. Estimations from isotopic measurements show that 50 mg of iron given twice weekly with food provides less than 10% of the iron requirements during the third trimester of pregnancy.[7] More effective approaches to circumventing the gastrointestinal side-effects of iron would be to use formulations that delay iron release in the stomach[8,9] or perhaps to reduce the daily dose of iron.[10] More than twenty studies have been planned or are in progress in developing countries to assess the efficacy of intermittent iron supplementation schedules.[11] This heavy investment in a theoretical concept may not represent the best use of limited resources.

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## Male fertility in cystic fibrosis

Infertility in males, which is generally accepted as an almost inevitable component of cystic fibrosis (CF), results from congenital bilateral absence or atrophy of the vas deferens (CBAVD).[1] The body of the epididymis is also affected but the testicular efferent ducts tend to be spared and some may be dilated.[2] These features are usually established by the time of birth, although there is evidence of postnatal progression in some individuals. Semen analysis reveals azoospermia in almost all adult males with CF.[3]

CBAVD may also occur as an isolated abnormality.[4,5] In a study of 102 patients without any other clinical manifestations of CF who were investigated for abnormalities in the CFTR gene, 19 had mutations in