Review Article

Risk of suboptimal iron and zinc nutriture among adolescent girls in Australia and New Zealand: causes, consequences, and solutions

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Surveys in Australia, New Zealand and other industrialised countries report that many adolescent girls have dietary intakes of iron and zinc that fail to meet their high physiological requirements for growing body tissues, expanding red cell mass, and onset of menarche. Such dietary inadequacies can be attributed to poor food selection patterns, and low energy intakes. Additional exacerbating non-dietary factors may include high menstrual losses, strenuous exercise, pregnancy, low socioeconomic status and ethnicity. These findings are cause for concern because iron and zinc play essential roles in numerous metabolic functions and are required for optimal growth, immune and cognitive function, work capacity, sexual maturation, and bone mineralization. Moreover, if adolescents enter pregnancy with a compromised iron and zinc status, and continue to receive intakes of iron and zinc that do not meet their increased needs, their poor iron and zinc status could adversely affect the pregnancy outcome. Clearly, intervention strategies may be needed to improve the iron and zinc status of high risk adolescent subgroups in Australia and New Zealand. The recommended treatment for iron deficiency anaemia and moderate zinc deficiency is supplementation. Although dietary intervention is often recommended for treating non-anaemic iron deficiency and mild zinc deficiency, it is probably more effective and appropriate for prevention than for the treatment of suboptimal iron and zinc status. Many of the strategies for enhancing the content and bioavailability of dietary iron are also appropriate for zinc.

Key words: adolescent, anaemia, Australia, bioavailability, diet, girls, iron, New Zealand, zinc.

Introduction

Adolescence is defined by the World Health Organization as the period between childhood and adulthood, spanning from 10 to 19 years of age. During adolescence, physiological requirements for iron and zinc peak at the time of the pubertal growth spurt, which in girls generally occurs between 10 and 15 years. Several other physiological processes that accompany puberty in females have a major impact on their requirements for iron and zinc, including sexual maturation, onset of menarche, and increased erythropoiesis.[1,2] Even when the growth spurt has ceased, adolescents may require additional iron and zinc to replete body iron stores and depleted tissue zinc pools as a result of these increased demands.[3,4]

Unfortunately, many adolescents fail to meet these high physiological requirements for iron and zinc during puberty. The quality of their diets is often poor. This has been attributed to poor food selection patterns, and low energy intakes arising from concerns about body weight, and possibly from a sedentary lifestyle.[5] Furthermore, among this age group, the interest in vegetarian dietary patterns has increased, often resulting in a reduced consumption of red meat and high intakes of plant-based foods. Flesh foods are readily available sources of iron and zinc, whereas many plant-based foods are high in dietary fibre, phytates, and polyphenols. These food components are known to interfere with iron and zinc absorption. As a result, intakes of available iron and zinc are often low for adolescent girls.[5]

Several non-dietary factors, such as, high menstrual losses, frequent blood donations, other sources of blood loss (e.g. nose bleeds), and intense physical exercise, may further exacerbate suboptimal iron and zinc nutriture.[6,7] Hence, it is not surprising that suboptimal iron status has been reported among adolescents in Australia, New Zealand (NZ),[8–12] and elsewhere.[5,13–16] Biochemical data on the zinc status of adolescents, however, are more limited. Nevertheless, the prevalence of suboptimal zinc status is likely to be comparable to that of iron deficiency, because the factors associated with the aetiology of iron deficiency also induce zinc deficiency. Indeed, low serum zinc concentrations have been reported in young women with low serum ferritin values from NZ and Canada as well as the USA.[16–18]

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This paper discusses the risk of suboptimal iron and zinc nutriture among adolescents in Australia and NZ, the potential aetiological factors and adverse health consequences associated with deficiencies of these two trace elements, and strategies for their treatment and prevention.

Prevalence of suboptimal iron and zinc status among adolescents in Australia and New Zealand

The prevalence of iron deficiency (ID) and iron deficiency anaemia (IDA) among adolescent girls in Australia, NZ, and elsewhere is compared in Table 1. Note that of the available estimates based on nationally representative samples, USA adolescents aged 16–19 years have the highest prevalence of iron deficiency,[15] whereas NZ adolescents have the highest prevalence of IDA.[11] Available national estimates for ID among school children in Australia correspond more closely to those reported in the USA NHANES (National Health and Nutrition Evaluation Survey) III survey.[8,15] For certain high-risk subgroups, such as, vegetarians, athletes, Pacific people, NZ Maori, and pregnant women, the prevalence of ID and IDA during adolescence is often much higher (M Skeaff, unpubl. data, 1994).[5,11,12,14,19] Caution must be used when comparing these prevalence estimates because the criteria and cut-offs used to define ID and IDA vary widely among studies.

To date, the true prevalence of zinc deficiency among adolescents in Australia and NZ is unknown because no national surveys have included biochemical assessment of zinc status. Indeed, to our knowledge, the USA NHANES II 1976–1980 survey and the UK National Diet Survey for adolescents are the only national surveys that have included serum or plasma zinc assessments on adolescents.[20,21] Serum zinc concentrations, although of limited use at the individual level, are a useful indicator of zinc deficiency for population subgroups. They are sensitive to changes in diet[17,22–24] and functional outcomes (e.g. linear growth velocity) after zinc supplementation.[25] Table 2 summarises the available data on average serum zinc concentrations and the prevalence of low levels in adolescent females from studies in NZ and elsewhere.[26–29] Note that the prevalence of low serum zinc values varies markedly. In general, prevalence estimates based on convenience samples tend to be higher than in the USA NHANES II and UK nationally representative samples,[20,21] with the exception of a Finnish study.

Aetiological factors associated with iron and zinc deficiency among adolescents

Homeostatic regulation of iron and zinc metabolism is achieved by regulating absorption from the diet, and for zinc, by regulation of daily basal losses and secretion of endogenous reserves.[1,30] Suboptimal iron and zinc nutriture develops when homeostasis is disturbed because of increased physiological requirements and/or excessive losses, and inadequate dietary supply.

High physiological requirements

The estimated average requirements (EAR) for iron and zinc during adolescence have recently been recalculated by the US Institute of Medicine and are shown in Table 3.[2] They are based on the factorial approach; with menstrual iron losses calculated as 0.5 mg/day on average. Because physiological requirements for absorbed iron and zinc peak at the time of the pubertal growth spurt, dietary requirement estimates for iron and zinc at this time are more than double those for toddlers.[2,4,31] Indeed, in NZ Maori adolescents, their higher prevalence of depleted iron stores (21% cf. 6%; serum ferritin < 12 μg/L) and low serum zinc (14% cf. 4%; serum zinc < 10.7 μmol/L) concentrations compared to non-Maori adolescents has been attributed to their earlier peak

Table 1. Median serum ferritin, and prevalence of depleted iron stores, iron deficiency, and iron deficiency anaemia among adolescent girls

Country (year)	*n*	Age (years)	Serum ferritin (μg/L)	Depleted iron stores* (%)	Iron deficiency† (%) deficiency anaemia‡ (%)	Iron
Australia NDS[8] (1985)	195	12	33	11§	2	?
Australia NDS[8] (1985)	143	15	27	28	9	?
Australia[10] (1995)	264	15–30	29	12	7	4
New Zealand** (1993)	357	13–15	32	10	?	< 3
New Zealand NNS[11] (1997)	89	15–19	29	7	0	5
UK NDS[21] (2000)	128	11–14	28	14¶	?	?
UK NDS[21] (2000)	136	15–18	23	27¶	?	?
Canada[17] (1995)	72	14–19	18	25	?	?
US NHANES III[15] (1997)	516	12–15	?	?	9	2
US NHANES III[15] (1997)	405	16–19	?	?	11	3

*Serum ferritin < 12 μg/L.

†Multiple criteria.

‡Multiple criteria including low haemoglobin.

§Serum ferritin < 10 μg/L.

¶Serum ferritin < 15 μg/L.

**M Skeaff, unpubl. data, 1994.

NDS, National Diet Survey; NHANES, National Health and Nutrition Examination Survey; NNS, National Nutrition Survey.

Table 2. Median serum zinc and prevalence of low serum zinc values among adolescent girls

Country (year)	*n*	Age (years)	Serum zinc (μmol/L)	Serum zinc < 10.71 μmol/L (%)
NZ, Dunedin[27] (1983)	207	11	13.9	11
NZ Dunedin & Gisborne‡ (1993)	309	13–15	12.6	4
US NHANES II[20] (1984)	1342	9–19	12.9	1.3
USA[28] (1989)	92	14–19	12.9	10
Canada[38] (1995)	72	14–19	11.3	26
Canada Health Survey[29] (1981)	1146	15–19	13.0	8
Finland[26] (1988)	296	15	14.2	1
UK NDS[21] (2000)	139	11–14	14.5*	1†
UK NDS[21] (2000)	147	15–18	13.6*	1†

*Plasma zinc.

†Plasma zinc < 10 μmol/L.

‡M Skeaff, unpubl. data, 1994.

NDS, National Diet Survey; NHANES, National Health and Nutrition Examination Survey.

Table 3. USA estimated average dietary requirements (EAR) for iron and zinc (mg/d) in children, adolescent and adult females*

Age (years)	Iron	Zinc
1–3	3.0	2.2
4–8	4.1	4.0
9–13	5.7	7.0
14–18	7.9	7.5
19–30	8.1	6.8

*Data from the US Institute of Medicine.[2]

Table 4. Blood loss characteristics of New Zealand women with and without mild iron deficiency*

Characteristic	MID present	MID absent
Menstrual blood loss (BLU)	38	34†
Length of period (days)	5.2	4.9‡
Donates blood (%)	32	25
Has nose bleeds (%)	28	18†
Oral contraceptive agent use (%)	28	40†

*Modified from Heath *et al.* (haemoglobin = 120 g/L and serum ferritin < 20 μg/L).[6]

†$P < 0.05$.

‡$P = 0.09$.

BLU, blood loss units; MID, mild iron deficiency.

height velocity, and consequent earlier onset of menarche, rather than to any differences in socioeconomic status, menstrual blood loss or dietary intake (I Jones, pers. comm. 1996; M Skeaff, unpubl. data, 1994).

The USA EAR are based on the assumption that both iron and zinc in US diets are relatively highly available, ranging from an upper level of 18% for iron to 40% for zinc per day for the adolescent age group.[2] If diets contain very little animal protein, however, absorption of iron and zinc may be as low as 4% and 15%, respectively, thus theoretically increasing the EAR to 36 and 20.1 mg/day. Indeed, in Australia, the recommended dietary intake (RDI) for iron ranges from 10 to 13 mg/day, depending on whether an omnivorous or vegetarian diet is consumed.[32]

Excessive losses

Basal losses of iron and zinc in adolescent females are attributed to losses via exfoliation of epithelial cells largely from the gastrointestinal tract, but also from skin; losses via sweat and hair; and for iron, menstruation.[2] Losses of iron in urine are negligible. For zinc, a major portion of the intestinal losses are endogenous pancreatic and intestinal cell secretions. These losses are proportionately greater per unit body weight in children than adults.[33]

Menstrual blood loss (both 'heaviness' and duration) is a major determinant of iron (but not zinc) status in young women of child-bearing age.[17] Several studies, including some in Australia[10] and NZ[6] have reported an inverse association between serum ferritin levels and menstrual blood loss. Two other types of blood loss have also been implicated in NZ young women: recency of blood donation, and nose bleeds (Table 4).[6] Intense physical activity may also compromise both iron and zinc status of some adolescent athletes, as a result of increased turnover rates of red cell iron and whole-body iron,[34] and higher zinc losses in urine and sweat.[7] Excessive blood losses of iron may also arise from abnormal bleeding at delivery, and occult bleeding induced by regular use of aspirin or other non-steroidal anti-inflammatory agents.[35]

Inadequate supply of iron and zinc in the diet

The adequacy of iron and zinc intake depends on their amount and bioavailability in the diet. Many female adolescents have intakes of iron and zinc that may fail to meet their needs (Table 5). In the NZ National Nutrition Survey, 45%

of adolescent girls aged 15–19 years[11] were at risk of low intakes of dietary iron compared to 28% of 15-year-old girls in the earlier Australian National Diet Survey.[36] Similar findings have been reported for adolescents in the USA and Canada.[14,37,38] For intakes of zinc, the same trend is apparent. More than 60% of adolescents in the USA,[39] and 46% in Ontario, Canada[38] had inadequate intakes, although only 2.4% were at risk in the NZ National Nutrition Survey when the lower UK EAR for zinc was applied.[40] Some of these apparent discrepancies in prevalence estimates for inadequate intakes obviously arise, in part, from differences in EAR, although biases from subject selection, dietary methods used, and dietary under-reporting may also play a role.[16,41] Such dietary inadequacies have also been attributed to restrictions in energy intake arising from concerns about body weight, coupled with a sedentary lifestyle among this age group.[42]

Changes in food selection patterns may also play a role in compromising the adequacy of iron and zinc intakes. This trend was noted in the 1990 CSIRO Victorian Survey of adults.[43] Declines in the per capita consumption of red meat, a rich source of readily available haem iron and zinc, have been reported in NZ[44] and Australia,[45] concomitant with an increase in intakes of unrefined cereals, nuts and legumes. Such trends among Australian young women appear to be related to health and animal welfare concerns.[46] Hence, it is not surprising that the contribution of meat, poultry and fish to dietary intakes of iron and zinc has decreased in recent years in this age group. In the recent national surveys in Australia[47] and NZ[9] flesh foods contributed 21 and 22% of the iron, and 36 and 29% of the zinc for adolescent women, respectively. An earlier NZ study of young women found that flesh food contributed 40% of the zinc in their diet.[48] These national surveys found that cereals with and without fortified iron provided 46 and 48% of the iron and 25 and 32% of the zinc in Australian and NZ adolescent diets, respectively.

Such trends in food selection patterns may have a major impact on the bioavailability of iron and zinc from adolescent diets, and thus biochemical indices of iron and zinc status. Flesh foods are a rich source of readily available haem iron and zinc, whereas cereals often have a high content of phytic acid (myo-inositol hexaphosphate), a strong inhibitor of iron and zinc absorption.[2] Certainly, in a recent study of young NZ women, those who excluded red meat from their diets were more likely to have low serum zinc (i.e. < 10.71 μmol/L; 21% cf. 12%) and ferritin values (i.e. < 20 μg/L; 41% cf. 21%) than those who ate red meat.[17] As well, the phytate : zinc ([Phy]:[Zn]) molar ratios of their diets had a significant negative association with serum zinc values, a finding consistent with that observed earlier for Canadian adolescents.[5,17] Elevated dietary [Phy]:[Zn] molar ratios (i.e. > 15) have been associated with suboptimal zinc status in several other studies.[49–52]

Interestingly, vegetarianism per se is not necessarily a significant predictor of suboptimal iron and zinc status. In a Canadian adolescent study, semi-vegetarians who excluded red meat had lower serum ferritin and plasma zinc levels than either vegetarians or omnivores, suggesting that a poorly planned diet rather than vegetarianism itself may increase risk of iron and zinc deficiency.[5]

Table 5. Intake and prevalence of inadequate intake of iron and zinc in adolescent girls

Country (year)	Age (years)	*n*	Fe intake (mg/day)*	% At risk to inadequate intakes†	Zn intake (mg/day)*	% At risk to inadequate intakes†
Australia NDS[36] (1985)	15	395	10.8	28‡	9.2	48
Australia NNS[47] (1995)	12–15	304	10.5§	?	8.6	?
Australia NNS[47] (1995)	16–18	218	10.1§	?	8.7	?
NZ NNS[9,11] (1997)	15–19	163	10.0§	45	–	–
NZ NNS[9,11] (1997)	15–18	137	–	–	9.8	42¶; 2.4**
NZ‡‡ (1993)	13–15	248	9.8	?	8.1	61‡
USA NHANES III[37] (1991)	11–18	1692	–	–	8.6	61†,¶
USA NHANES III[37] (1991)	12–15	373	10.2§	?	–	–
Canada[38] (1994)	14–19	111	11.2	33††	7	46††
UK NDS[21] (2000)	11–14	238	9.1	?	5.9	?
UK NDS[21] (2000)	15–18	210	8.9	?	6.1	?

*Mean unless stated otherwise.

†Based on probability approach unless otherwise stated.

‡< 70% RDI.

§ Median (Australian RDI Fe: 10–13 mg/day; RDI Zn: 12 mg/day).

¶Based on US 1989 RDA 12 mg/day.

**Based on UK EAR 5.5 mg.

††Based on Canadian RNI 12 mg/day.

‡‡M Skeaff, unpubl. data, 1994.

EAR, estimated average requirements; NDS, National Diet Survey; NHANES, National Health and Nutrition Examination Survey; NNS, National Nutrition Survey; RDA, recommended daily allowance; RDI, recommended daily intake; RNI, recommended nutrient intake.

An additional diet-related factor known to have an antagonistic interaction with zinc, and hence with the potential to lower the biochemical zinc status of adolescents, is the consumption of high doses of iron supplements.[53,54] Pregnant adolescents may be especially at risk if they are routinely supplemented with prenatal iron supplements.[14,54] In a recent NZ study, a small group of women (n = 8) taking a very high daily dose of iron-only supplements (i.e. 105 mg/day) had a mean hair zinc value that was significantly lower compared to those not taking any iron-only supplements.[17] A similar adverse effect on serum zinc levels has been reported for pregnant women in NZ taking iron prenatal supplements and USA adolescents.[54,55] In the recent NZ National Nutrition Survey, however, less than 10% of women (15–49 years) reported taking an iron supplement in the year before their 24 h recall interview,[9] compared to 23% in the 1986 US National Health Interview Survey.[56] Therefore, unless adolescents are being treated for IDA with high dose iron supplements, use of iron supplements is unlikely to impair zinc absorption in this population.

Comparison of the prevalence of inadequate intakes of iron and zinc (Table 5) with the prevalence estimates for suboptimal iron (based on serum ferritin) and zinc status (based on serum zinc) among adolescents reveals some inconsistencies (Tables 1,2). There are several factors to do with the collection and interpretation of both intake and status data that may be responsible for this apparent lack of congruence. Data on the prevalence of inadequate intakes may be influenced by under-reporting of food intake. It is also possible that the bioavailability factors used to calculate the dietary requirement estimates overestimate absorption from adolescent diets because of differences between adolescent and adult food selection patterns. Absorption of iron and zinc also depends on the iron and zinc status of an individual, which vary widely among adolescents because their requirements are so dependent on the timing of puberty and the onset of menarche. Likewise, the factorial model used to estimate iron and zinc requirements may be incorrect. Certainly adult NZ women may have lower requirements for iron than adolescents because so many use oral contraceptive agents (i.e. 50–60%).[57] Oral contraceptive agents are associated with a 60% reduction in menstrual iron losses.[58] Data on the prevalence of low iron and zinc status are likely to be influenced by the methods used for subject recruitment, and the collection, separation, and analysis of the blood samples, which vary among studies.[15,59] Further, although confounding factors, such as, infection, type of contraception used, stage of sexual maturation, and cigarette smoking all impact on biochemical indices of iron and/or zinc,[6,17,20,45,58,60,61] they may not have been taken into account in the prevalence estimates summarised in Tables 1,2.

Potential adverse health consequences of iron and zinc deficiency among adolescents

The many similarities between the adverse health consequences of both iron and zinc deficiency are emphasised in Table 6. Of the disturbances listed, those of particular significance for iron are impaired work performance, developmental delay, cognitive impairment, and adverse pregnancy outcomes. Such functional consequences are known to occur when there is a measurable decrease in haemoglobin concentrations,[2] but the extent to which they are also associated with iron deficiency without any clinical or biological evidence of anaemia is less certain. To our knowledge, there are no published accounts of double-blind randomly controlled trials in Australia and NZ that have examined the functional consequences of ID and IDA in adolescents.

Haas and Brownlie have reviewed studies investigating the relationship between iron deficiency and reduced work capacity.[62] Results from both human and animal studies have shown that when haemoglobin iron is lacking, physical work performance is reduced via a decrease in oxygen transport to exercising muscles, whereas endurance performance at reduced exercise intensities appears to be more closely related to tissue iron concentrations through reduced cellular oxidative capacity. In a NZ study, iron deficiency and anaemia were reportedly more common in high school adolescent females with low aerobic fitness, as indicated by submaximal estimation of VO_2max.[12]

The effect of iron deficiency on cognitive development in children has been rigorously reviewed by Grantham-McGregor and Ani.[63] Few trials have been carried out in the adolescent age group. For prepubertal children with IDA, treatment with iron appears to have a beneficial effect on cognition, based on the evidence from randomised clinical trials (RCT). Nevertheless, causal inferences cannot be made. There has been one RCT conducted on US adolescents with iron deficiency in the absence of anaemia, in which treatment with iron significantly improved memory.[64] Three other trials on much younger children with iron deficiency, but not anaemia, did not show any treatment effect on cognitive function, but their sample sizes were smaller.[65–68] Hence, it is still not clear at what level of iron deficiency cognition becomes affected, whether the effect is age-dependent, and the extent to which the changes observed are reversible across different stages of growth and development.

Methodological limitations also apply to some of the investigations of low iron status and symptoms of depression.[11,69,70] Of the two RCT on adolescent girls, an improvement in mood with iron supplementation was only reported in those whose iron status ranged from anaemia to iron sufficiency, but not among those with non-anaemic iron deficiency only.[64,71]

Table 6. Adverse health consequences of iron and zinc deficiency

Impaired immune competence
Impaired cognitive function
Poor appetite
Impaired mood
Impaired growth
Poor pregnancy outcome: low birth weight; prematurity

Although both animal studies and *in vitro* tests have shown that iron deficiency is associated with impaired immunity,[72] the clinical relevance of these findings to humans is uncertain. Only one study has reported a significant reduction in morbidity of school children with iron deficiency anaemia after treatment with oral iron supplements.[73] No studies on adolescent girls have been reported.[74]

Despite the well-recognised effects of zinc deficiency in relation to immunity, growth, morbidity, and survival of children in developing countries,[75] its effect on growth and function among adolescents in industrialised countries is uncertain. In two NZ and one Canadian adolescent study, no relationship was observed between biochemical zinc indices and height percentiles, but adolescents with low hair or serum zinc concentrations were heavier, fatter, and/or had higher body mass indices than their peers with high hair or serum zinc values (I Jones, pers. comm. 1996).[5,76] Our current understanding of the mechanisms by which zinc nutriture influences body composition is incomplete. It is possible that zinc deficiency, by changing the energy cost of weight gain, may be responsible for the increasing prevalence of short fat children in emerging countries, such as, Latin America.[77] Animal studies have suggested that these changes may be mediated by an interaction of zinc with insulin activity and thyroid hormone conversion.[78–81]

Slower skeletal growth, maturation, and reduced bone mineralization may also occur with marginal zinc nutriture during adolescence.[3,82] This is of significance because nearly one-third of total skeletal mineral is accumulated in the 3–4 year period immediately after the onset of puberty.[83] Therefore, if adolescents fail to accrue bone mineral normally because of reduced bone mineralization induced by zinc deficiency, permanent deficits in bone mineral density may occur, leading to an increased risk of osteoporosis in later adulthood. Hence, promoting the intake of foods rich in zinc as well as other nutrients to achieve peak bone mass in adolescence and thereby reduce the risk of osteoporosis in later life is important.[3]

The few human studies that have investigated the relationship between zinc status and cognition and behaviour have been reviewed by Penland.[84] Findings have been inconsistent, despite the animal studies that clearly indicate that deficiencies of zinc can affect cognition. More research on zinc and cognition is required to identify possible biological mechanisms, and well-designed human RCT need to be conducted on high-risk subgroups, such as, adolescent vegetarians to confirm that zinc deficiency has a negative impact on cognition. Finally, in some studies both IDA and zinc deficiency during pregnancy have been associated with premature delivery, low birth weight infants, and increased perinatal infant mortality.[85–87] In some cases, low serum ferritin in the absence of anaemia has also been associated with premature labour.[87]

Treatment and prevention of iron and zinc deficiency in female adolescents

The recommended treatment for iron deficiency anaemia is iron supplementation, preferably with slow release ferrous sulphate or an equivalent to minimise side-effects, for at least 6 months to 1 year. Ferrous gluconate (hydrated) or ferrous fumarate are also used. These preparations contain 18–106 mg elemental iron. However, compliance to such regimens, especially among adolescents, is often low. This has been attributed in part to gastrointestinal symptoms, such as, abdominal discomfort, nausea, and constipation. Gadowsky *et al.* concluded that Canadian pregnant adolescents consumed prescribed prenatal supplements more sporadically than their adult counterparts, so that no correlation was observed between iron supplements taken and iron status.[14] Cromer *et al.* summarise some strategies that could be used to enhance compliance of adolescents to iron supplements, which include initiating home pill counts, enlisting a supportive parent to remind the adolescent of the medication schedule, and informing the patient of any side-effects associated with the proposed therapeutic regimen.[88]

The recommended treatment for clinical zinc deficiency, like IDA, is supplementation.[89] Zinc supplements can be given alone, but it is preferable for the zinc to be combined with multimicronutrient supplements or prenatal iron and folate supplements.[90] Uncertainty still exists about the dose and the best type of zinc salt to use in relation to its bioavailability and side-effects. The recommended level for pregnant women is 15 mg/day. In general, water-soluble preparations (e.g. zinc sulphate, zinc acetate, or amino acid chelates) are better absorbed than insoluble compounds, such as, zinc oxide, especially in persons with achlorhydria.[91] In Canadian pregnant adolescents receiving prenatal supplements, only those receiving supplements in which zinc was in the sulphate rather than the oxide form, had plasma zinc levels that were significantly elevated compared to their non-zinc supplemented counterparts.[92] More research is needed on the mechanisms underlying absorption and utilization of zinc to identify the most effective dietary zinc supplement.

Absorption of supplemental iron or zinc is enhanced if the supplements are taken in the fasting or post-absorptive state. However, to reduce the side-effects of iron supplements, the generally accepted recommendation is to take them shortly after meals.[93] If zinc is included with the iron (and folate), the supplements should be taken with meals, so that the presence of ligands in food minimises the inhibitory effect of supplemental iron on zinc absorption and vice versa.[94–96] It is essential that iron supplements are only taken by individuals with biochemical evidence of ID or IDA because of the relatively high prevalence of genotypes associated with hereditary haemochromatosis in populations of Northern European decent.

Antagonistic nutrient interactions may also occur between iron and copper, and zinc and copper, especially when these elements are given as a supplement.[97] The interaction between zinc and copper may arise with only modest increases in zinc intake if the zinc is taken independently of meals.[98] Current recommendations suggest that the zinc : copper molar ratio in supplements should be about 10:1, up to a maximum of 1 mg copper per day. The zinc : iron molar ratio in a combined supplement should be approximately 1:1 and should not

exceed 2:1.[89] When large doses of zinc are taken between meals (i.e. > 50 mg/day), some discomfort, such as, bloating, nausea and abdominal cramps may occur, together with evidence of biochemical copper deficiency.[99] Long-term use of large doses of zinc (i.e. 100–160 mg/day) in men and women may also decrease high-density-lipoprotein (HDL) cholesterol concentrations or possibly elevate levels of total serum cholesterol, low-density-lipoprotein cholesterol, and triglycerides.[100–103] Smaller doses (15–50 mg/day) may be sufficient to attenuate the exercise-induced increase in HDL.[104]

Treatment of non-anaemic ID and mild zinc deficiency

The treatment of non-anaemic iron deficiency is much more controversial. The Australian Iron Status Advisory Panel advises women to increase their dietary intake of bioavailable iron, as the first treatment option for non-anaemic iron deficiency (i.e. serum ferritin 10–15 µg/L). However, the efficacy of dietary intervention for the treatment of women who are iron deficient has recently been questioned, based on the results of two recent studies. In a NZ trial, young women with non-anaemic iron deficiency (serum ferritin < 20 µg/L and haemoglobin = 120 g/L) were randomly assigned to a placebo, supplement or diet group for 16 weeks.[105] The strategies that were practiced by the diet group were in keeping with the NZ Food and Nutrition Guidelines and based on the principles outlined in Table 7.[106]

Adherence to the dietary regimen was confirmed by the significant increases in intake of flesh foods, haem iron, vitamin C, and foods cooked using cast-iron cookware, and the decrease in intakes of phytate and calcium, as shown in Table 8.

These dietary changes were accompanied by a 26% increase in serum ferritin concentration ($P = 0.068$; geometric mean serum ferritin 10.3 µg/L at baseline, 14.0 µg/L at 16 weeks) in comparison to the non-anaemic iron deficient placebo group. Nevertheless, two individuals became anaemic during the study and were excluded. In a second study, young iron deficient Australian women were also advised to follow a diet high in absorbable iron for 12 weeks. However, in this study there was no increase in either haem or non-haem iron intake; nor were there any significant changes in intakes of vitamin C, meat, alcohol, phytate, calcium or tea. There was a slight increase in serum ferritin compared to baseline, at the end of the 12 week intervention. Six months after the end of the formal diet intervention, bioavailable iron intake was, if anything, lower than at baseline.[107] The results of these two studies, clearly highlight the difficulties faced by even highly motivated individuals who receive intensive dietary counselling to improve their iron status by dietary means. Further, they emphasise that supplementation is likely to be a more practical and effective option for most premenopausal women with mild iron deficiency. This may be particularly the case for adolescent girls who may be unwilling to adopt a dietary regimen that requires them to increase their intake of flesh foods, because of their animal welfare and/or health concerns.[46,108]

Table 8. Impact of dietary intervention on intakes of selected dietary components during a 16 week period*

Dietary component	Baseline	Intervention
Meat/fish/poultry (g)	117.7	141.5
Total iron (mg)	10.5	12.4
Haem iron (mg)	1.4	1.9
Non-haem iron (mg)	9.4	11.0
Vitamin C (mg)	88.0	235.0
Phytate (mg)	1048.0	819.0
Calcium (mg)	697.0	625.0

*Modified from Heath *et al.*[105]

Table 7. Dietary strategies to enhance the content and bioavailability of dietary iron*

1. Increasing the intake of iron containing foods.
Participants were encouraged to eat at least one serving of high iron foods rich in haem iron (e.g. red meat, liver) and one serving of medium iron foods (e.g. processed meat, chicken, fish, legumes) each day. Vegetarians were advised to eat at least four servings of medium rich foods each day. In addition, participants were encouraged to increase their intake of foods with a high non-haem iron, fortificant iron or vitamin C content and to use a cast-iron fry pan, especially when cooking tomato-based sauces.

2. Increasing the intake of foods containing factors said to enhance non-haem iron absorption.
Participants were asked to consume foods and beverages containing at least 50 mg of vitamin C in each meal. Tables showing quantities of foods providing 50 mg vitamin C, recipes using vitamin C-rich foods and practical ideas for conserving the vitamin C content of fruit and vegetables were provided. Participants were also given ideas for adding meat, fish and chicken to composite dishes based on plant foods. The use of fermented soy sauce was also encouraged.

3. Decreasing the intake of foods containing factors believed to inhibit non-haem iron absorption.
Participants were given advice to decrease their intake of foods that are particularly high in phytates (e.g. wheat bran, nuts) and polyphenols (e.g. spinach). They were also asked to soak dried beans and discard the soaking water before cooking and to choose beans other than soybeans.

4. Modifying eating patterns so that enhancers of non-haem iron absorption were eaten with meals and potential inhibitors between meals.
Participants were advised to consume tea, coffee, red wine and port between meals, if at all, replacing them with vitamin C-rich foods with main meals. While participants were also asked to avoid large servings of calcium-rich foods with their main meals, care was taken to encourage adequate calcium intakes between meals to ensure that this advice did not compromise their calcium intake.

*Based on Heath *et al.*[105]

The supplemental dose recommended for treatment of IDA is unnecessarily high for treatment of iron deficiency without anaemia and could be reduced to 50 mg/day, a level that will minimise gastrointestinal discomfort and not adversely affect zinc status,[53] provided the adolescents take the supplement with meals.[94] Some experts have argued that all adolescent girls should be routinely supplemented with iron to build iron stores before they enter pregnancy, although such a strategy is unlikely to remove the need for iron supplementation during pregnancy unless the adolescents consume a diet rich in bioavailable iron throughout pregnancy.[109]

Prevention of iron and zinc deficiency during adolescence

Most of the dietary strategies listed in Table 7, if adopted, would enhance the content and bioavailability of both iron and zinc in adolescent diets. The only exception is the strategy related to increasing intakes of vitamin C with main meals. This recommendation is aimed at augmenting the absorption of non-haem iron (but not zinc), although the magnitude of its effect appears to be much less pronounced from the whole diet than from single meals.[110] The strategies that are especially beneficial for facilitating the absorption of zinc are those that aim to reduce phytate intakes (i.e. point 3) by avoiding the consumption of high phytate foods (e.g. wheat bran, oatmeal, nuts, unleavened bread), and/or using products in which phytate content has been reduced by microbial phytase enzymes (e.g. sprouted whole grain cereals and legumes, and yeast-leavened baked products), or diffusion of water soluble phytates by soaking (e.g. legumes).[111]

Adoption of such dietary strategies by adolescent females has two advantages. First, it should ensure they have adequate body iron stores and tissue zinc pools before they enter pregnancy. Second, consuming an habitual dietary pattern that is rich in highly bioavailable iron and zinc during pregnancy should help the adolescents to meet their increased iron and zinc needs, and thus prevent an adverse pregnancy outcome.

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