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Sources of Iron: Diet, Supplemental, and Environmental

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Keywords

Hemoglobin · Anemia · Iron deficiency · Iron fortification · Animal-based foods · Dietary diversification

Animal-based foods have traditionally played an important role in combating iron deficiency, because of the high bioavailability of heme iron. However, with the urgent need to change to more sustainable and durable diets, greatly increasing meat consumption to reach recommended daily intakes of iron is not desirable in the present context. Therefore, alternative, more sustainable sources of dietary iron need to be identified, such as fish or insects. Also, plant-based foods can be good sources of dietary iron, such as soybeans and lentils. Algae, seaweeds, and mushrooms are other foods that can provide important amounts of iron, but are often underutilized.

Iron fortification and supplementation are interventions aimed at either specific population groups (pregnant and lactating women, children between 6 and 24 months) or at the general population (e.g., iron fortification of staple foods). These interventions are often implemented in combination with other micronutrients (e.g., folic acid). Bio-fortification aims to increase iron content of foods by breeding techniques and even genetic modification approaches.

Non-intentional increases of iron in the diet can arise from contamination, either during the processing (e.g., milling) or during the preparation (e.g., brewing) of foods or drinks. Also drinking water can contain high amounts of iron, and even though having a low bioavailability, this iron can contribute to overall iron status of populations, resulting in iron nutrition being better than expected based on dietary assessment in some populations.

To improve iron status of populations vulnerable for iron deficiency, it is not only important to identify potential iron-rich food sources, but also take into account acceptability and cultural habits. In many countries, food taboos play an important role in the etiology of iron deficiency and anemia. Finally, affordability and iron bioavailability of the foods identified need to be considered too. Designing sustainable, acceptable, affordable, and durable diets that provide enough

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C. D. Karakochuk et al. (eds.), *Nutritional Anemia*, Nutrition and Health,
https://doi.org/10.1007/978-3-031-14521-6_10

iron (and other vitamins and minerals) for populations, especially those with a high demand for iron such as pregnant and lactating women and young children, will be a major challenge the coming years.

Introduction

The paradox of iron deficiency in humans is well-known: While iron is one of the most abundant minerals on earth, an estimated two billion people are iron deficient [1]. But most forms of iron present in the earth's crust, such as hematite (Fe_2O_3), are not bioavailable for humans and, hence, cannot serve as source of iron for human metabolism. Thus, for centuries, humans have depended on relatively costly or rare iron-rich foods and more or less bioavailable iron compounds in efforts to improve health. Hippocrates, in the fourth century B.C., has been credited of using watercress, a vegetable rich in iron, as part of his treatments [2]. But it would take almost six centuries before the nutritional importance of iron itself for human health was described by Boussingault [1]. Amazingly, Jean-Baptiste Boussingault was not medically trained but a geologist, who also, for example, reported on the role of minerals in soil in plant growth or nitrogen balance in animals [1]. And it took a further 50 years, until 1928, before the role of iron in treating nutritional anemia was clearly demonstrated by Mackay [2]. And even though the role of iron in treating nutritional anemia is known for almost a century now and iron deficiency is probably the most prevalent micronutrient deficiency globally, most efforts in the last decades to reduce the prevalence of anemia and iron deficiency have not been altogether successful, and thus the prevalence of anemia and iron deficiency continues to remain high.

Before discussing in more detail different potential dietary and non-dietary sources of iron, it should be made clear in advance that there is a huge difference in the bioavailability of different iron compounds. Dietary iron occurs mainly in three forms: elemental iron, either as ferrous iron (Fe2+) or as ferric iron (Fe3+), and heme iron, that is, Fe2+ chelated into a heme complex as found in hemoglobin or myoglobin. Heme iron (with dietary sources obviously coming from animal-source foods) has a much higher bioavailability (in the range of 10–40%) than ferric iron (bioavailability in the range of 5–15%) coming from plant-based foods, as ferric iron first needs to be reduced to its ferrous state before it can be absorbed [3]. Hence, whether iron, ingested through the mouth, ends up being absorbed in the duodenum and becomes part of human metabolism or, as is the case for most of the iron consumed, leaves the gut with the stools is for an important part determined by its chemical form. When iron comes from foods and diets, it is obvious that in addition to iron, other (micro)nutrients are also ingested and these can induce, depending on their interactions (see Chap. 20), promoting or inhibiting effects on the absorption and bioavailability of iron. Furthermore, specific conditions in the gut itself such as acidity, enzymatic activity, microbiome composition, and parasite infestation are not constant and can vary according to age, health, and populations and affect iron bioavailability directly or indirectly (such as through inflammation and microbial metabolism). As iron bioavailability is covered extensively in Chap. 10, the current chapter will focus mainly on the potential sources of iron available to humans, rather than the intricate details of absorption itself for each compound or food. However, where needed, the bioavailability and wider context of certain iron formulations will be discussed.

Iron Sources

Iron can come from many different sources, and these sources can be consumed unwittingly of the iron content or specifically sought out to increase iron intake. In this chapter, we have divided iron sources into three different categories:

I. Common dietary sources of iron: iron in everyday foods and diets.
II. Intentionally increased iron intake (dietary and non-dietary).
III. Non-intentionally increased iron intake.

In the first category, the common dietary sources, iron intake is discussed in the context of typical examples of regular foods and ordinary diets worldwide, as well as the impact of dietary restrictions on iron intake is covered. Furthermore, the increased iron requirements in pregnancy and lactation in relation to dietary iron sources are examined. Under intentionally enhanced intake of iron, we discuss fortification and biofortification of staple foods and specific food items with iron as well as iron supplementation. In addition, iron-specific dietary diversification and food-based interventions are also considered, including interventions targeting food processing and cooking techniques. Finally, under the nonintentional sources of iron, contamination of foods with environmental iron including iron-rich drinking water is discussed.

Common Dietary Iron Sources

Dietary patterns around the world differ widely, and as the iron content of foods consumed also ranges widely, the contribution of diet to overall iron intake ranges from negligible to excessive intakes. Surprisingly perhaps, there is no clear consensus on the amount of iron that needs to be consumed on a daily basis. Different recommendations, with different physiological bases, are in common use. For example, the estimated average requirement (EAR), set by the Institute of Medicine (IOM, USA), estimates the average intake needed in a given population, whereas the recommended dietary allowance (RDA) or recommended dietary intake (RDI) gives the amount of iron needed to assure that 97.5% of a population achieves the requirements for that nutrient. The IOM assumes a bioavailability of iron of 18%, whereas the FAO/WHO have made recommendations based on diets with different bioavailability, some of them as low as 5% (Table 10.1). As a result, recommended dietary intakes of iron range from 3 mg/day to >50 mg/day, and perhaps even more perplexing to non-nutritionists is that some recommended intakes from FAO/WHO are higher than the upper limits set by the IOM.

Table 10.1 FAO/WHO and IOM recommended daily intake recommendations for iron (mg/day), by age group

	FAO/WHO recommended nutrient intakes[b]			Institute of Medicine[c] Dietary reference Intakes		
	Estimated bioavailability					
Age (years)[a]	5%	10%	15%	EAR	RDA	UL[d]
0.5–1	18.6	9.3	6.2	6.9	11	40
1–3	11.6	5.8	3.9	3.0	7.0	40
4–6	12.6	6.3	4.2	4.1	10	40
7–8	17.8	8.9	5.9	4.1	10	40
9–10	17.8	8.9	5.9	5.7–5.9	8	40
11–13 male	29.2	14.6	9.7	5.9	8	40
11–13 female (pre-menarche)	28.0	14.0	9.3	5.7	8	40
11–13 female (post-menarche)	65.4	32.7	21.8	–	–	40
14–17 male	37.6	18.8	12.5	7.7	11	45
14–17 female	62.0	31.0	20.7	7.9	15	45
Male (>18 years)	27.4	18.8	9.1	6	8.0	45
Female (18–50 years)	58.8	29.4	19.6	8.1	18	45
Female lactating (>18 years)	30	15	10	6.5	9	45
Pregnant women (>18 years)[e]	–	–	–	22	27	45
Female post-menopausal	22.6	11.3	7.5	5	8	45

[a] The age categories of the FAO/WHO and Institute of Medicine recommendations differ slightly

[b] Vitamin and mineral requirements in human nutrition: 2nd edition. WHO/FAO. 2004

[c] Dietary references intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Institute of Medicine, 2001. *EAR* estimated average requirement; *FAO* Food and Agricultural Organization of the United Nations; *IOM* Institute of Medicine; *RDA* Recommended Dietary Allowance; *UL* tolerable upper intake levels; *WHO* World Health Organization

[d] UL or tolerable upper intake levels were determined on appearance of gastrointestinal side effects when iron was consumed on an empty stomach

[e] WHO recommends supplementation of 30–60 mg elemental iron per day for pregnant women

It is estimated that today >40% of the world population has an inadequate intake of iron, with diets in Asia and sub-Saharan Africa especially lacking in iron [23]. Milman, using data from 49 dietary intake surveys in 29 European countries, reported median intakes in Europe varying from 7.6 mg of total iron/day (Bosnia) to 18.5 mg total iron/day (Lithuania and Slovakia) [4]. Interestingly, 19 out of these 29 countries reported daily iron intakes for nonpregnant women of reproductive age (WRA) of <11 mg/day, and in almost all countries, >50% of women had a daily intake of <15 mg/day, the most commonly used RDA for WRA. Dietary iron intake in several African countries was even more variable, ranging from 3.8 mg/day in South Africa to >50 mg/day in Ethiopia [5]. Iron intakes in WRA were inadequate in 34% of women in Kenya, to 100% of women in South Africa. In contrast, dietary iron intake in WRA in Ethiopia was inadequate in <12% of the women [5]. Ferguson et al. used linear programming to identify for which nutrients the recommended nutrient intakes (RNIs) were likely not to be met in five Southeast Asian countries [6]. They found that realistic ordinary diets were unlikely to provide the RNI for iron in infants in Cambodia, Indonesia, Laos, Thailand, and Vietnam and for WRA in Cambodia and Vietnam, even when including two servings of chicken liver/week.

Iron in Animal-Based Foods

Increasing intake of iron-rich foods to allow individuals to meet daily iron requirements is often considered synonymous to increasing intake of animal-source foods. Common foods associated with a high iron content are often also animal-source foods, such as liver and blood-containing products. As animal-source foods contain heme iron, the bioavailability of the iron is also high. Chicken liver, for example, contains ~10 mg of iron/100 g [7], while sausages containing blood are reported to have from ~7 mg of iron/100 g (Scottish black pudding) to up to 30–50 mg iron/100 g (Spanish and Peruvian blood sausages) [3]. In several Asian countries, so-called blood curd is popular either as a snack or added to soups. Blood curd contains ~25 mg iron/100 g [8]. However, these products are almost never consumed daily and more often restricted to special occasions. Contrary to popular belief, other forms of animal products contain considerably less iron, even though highly bioavailable, with chicken or beef meat containing only ~1.0–4.0 mg iron/100 g. Eggs are also not a good source of iron, containing on average 1.8 mg iron/100 g, which is mainly concentrated in the egg yolk. Moreover, egg white appears to inhibit the absorption of non-heme iron [9]. Cow’s milk is a disappointingly poor iron source (0.5 mg iron/L), and cow’s milk consumption in early childhood is even associated with iron deficiency [10].

However, at the same time, the EAT-Lancet commission report on sustainable and healthy diets promotes a sharp shift towards eating less animal-source foods derived from animal husbandry. Indeed, this report acknowledges the delicate balance between increasing nutrient intake and decreasing the impact on climate change in many low- and middle-income countries while estimating that, by 2050, only 13 g of protein from animal-source foods per day is available for sub-Saharan Africa [11]. Hence, alternative dietary sources of iron with a lower carbon footprint need to be identified (e.g., fish, shellfish) and preferentially introduced into local diets. Several species of fish are rich in micronutrients, including iron that is mainly in the form of heme iron and high molecular complex-bound non-heme iron, both of which have a higher bioavailability than non-heme iron from plant sources [12]. Studies from Bangladesh and Cambodia report iron content of small freshwater fish ranging from 0.6 to 14.4 mg total iron/100 g raw edible freshwater fish and from 0.3 to 3.3 mg total iron/100 g for marine fish [13–15]. In Bangladesh, 3 out of 25 species of fish had a high iron content (>5.0 mg/100 g), with heme iron ranging from 0.4 to 4.9 mg. In Cambodia, over 50% (9 out of 16) of the fish species analyzed had a high iron content, with heme iron ranging from 1.3 to 5.4 mg/100 g [16]. Interestingly, the fish *Esomus longimanus*, which is found in rice fields in Cambodia, contained 45.1 mg iron per 100 g edible parts, of which 36.0 mg was heme iron. One serving of traditional Cambodian sour soup made with this species of fish would supply ~45% and ~ 42% of the daily requirement of iron in WRA and children, respectively. Shrimp and prawns were reported to have total iron concentrations ranging from 0.6 to 14.3 mg/100 g, with the percentage of heme iron ranging from 18% to 93% of total iron (0.4–4.9 mg/100 g). Adding small dried fish to plant-based diets can substantially enhance the content (and bioavailability) of iron in the diet, as well as increase the amount of other minerals, such as zinc and calcium. Consumption of fish in the world has quadrupled in the last 40 years, and in many countries, especially in South and Southeast Asia, fish represents ~28–75% of animal protein consumption, with the lowest-income households spending more money on fish than on other animal-source products [12]. This underscores the potential value of fish as a source of dietary iron among vulnerable groups [17] and the relevance of initiatives such as improving aquaculture and marine practices to safeguard and increase their potential as a sustainable food source. This would thereby contribute to more sustainable diets and could reduce the impact of food systems on climate change [18].

Insects are drawing increased attention as a potentially nutrient-rich food source in human diets. More than 2000 insect species are edible and are consumed frequently in tropical regions. Several insect species (e.g., crickets, palm weevils, termites, and caterpillars) are especially rich in zinc and iron [19]. In Thailand, the iron content of edible parts from four different insects obtained from supermarkets of street hawkers ranged from 2.8 mg iron/100 g for the mulberry silkworm (*Bombyx mori L.*) to 9.1 mg iron/100 for the scarab beetle (*Holotrichia* sp.) [20]. A study comparing four commonly consumed insects with sirloin beef showed that cricket and sirloin beef had comparable high levels of iron, higher than grasshopper or buffalo worms. However, iron solubility was higher from insects than beef, and the in vitro iron bioavailability in buffalo worms and sirloin was comparable to that of ferrous sulfate ($FeSO_4$) [21]. However, there are also some disadvantages to insect consumption, as they contain anti-nutrient components (e.g., chitin and chitosan) and also may contain allergens and toxic bioactive compounds, host parasites, and pathogenic bacteria. Lastly, insects may potentially be contaminated with pesticides and heavy metals from the environment [20, 22].

Iron in Plant-Based Foods

Plant-based foods have the potential to be iron-rich, even more than animal-source foods, but iron bioavailability is much lower. However, the largest component of most diets is generally plant-based foods, rather than animal-source foods, as they are more affordable, more accessible, and, in some cases, more acceptable, than animal-source foods. For example, legumes, including beans, peas, and lentils, are good sources of iron. Soybeans contain around 7.8 mg iron/100 g, and fermented soybean products can provide from 1.8–2.1 mg iron/100 g of tofu or tempeh up to 12 mg iron/100 g for Japanese natto. Lentils are another iron-rich food, providing 7 mg iron/100 g. White, lima, red kidney and navy beans, chickpeas, and black-eyed peas provide 3.5–5.2 mg iron per 100 g of cooked product. Nuts and seeds are also iron-rich plant-based foods. Seeds that are richest in iron include pumpkin, sesame, hemp, and flaxseeds, containing ~12–42 mg iron/100 g. Nuts, including almond, cashews, pine, and macadamia nuts, contain ~3.5–5.6 mg iron/100 g. Some types of vegetables also contain high concentrations of iron and are often also rich in vitamin C, a nutrient that can enhance iron absorption. Leafy greens, such as spinach, kale, swiss chard, collard, and beet greens, contain ~2–5 mg iron/100 g of cooked product. Other vegetables, such as broccoli, cabbage, and brussels sprouts, contain ~0.6–1.4 mg iron/100 g of cooked product. Whole grains, such as amaranth, spelt, oats, and quinoa, contain ~2.2–4.1 mg iron/100 g of cooked product. However, phytates, fibers, and plant matrix effects may significantly reduce iron bioavailability in these foods as well as, albeit often to a lesser extent, in all plant-based foods.

Algae and seaweed are also micronutrient-rich (including iron), although the nutritional composition of brown, red, and green seaweeds varies between species, season, and ecology of the harvesting location [23]. In Venezuela, four species of marine algae (*Ulva* sp., *Sargassum* sp., *Porphyra* sp., *and Gracilariopsis* sp.) were shown to be good sources of ascorbic acid and (bioavailable) iron, with iron concentrations ranging from 15.5 mg (*Prophyra* sp.) to 196 mg/100 g of dry weight (*Gracilariopsis* sp.) [24]. All algae, added as a dose between ~10 and 20 g to a rice-based meal, significantly increased iron absorption, up to fivefold of the absorption value of the rice-based meal alone, probably due to both the high vitamin C concentration and a low or non-existent phytate content (an antinutrient that can reduce iron absorption). Samples of edible algae *Porphyra vietnamensis* growing along different localities of the West Coast of India had iron concentrations in a range of ~33–298 mg iron/100 g of dry weight [25]. However, edible seaweed can also contain significant heavy metal concentrations, even though intake is generally below toxic levels, unless there is regular and sizeable consumption of seaweed. Bioaccumulation of arsenic is a risk, and more studies of heavy metal toxicokinetics are needed before any recommendations can be made [23]. For *P. vietnamensis*, the recommended daily intake was 1.3 g/day to avoid any risk of arsenic toxicity. Spirulina, a cyanobacteria or blue-green algae that has received a lot of attention in the last 20 years, could also be a good source of iron and other micronutrients, as iron content ranges between 58 and 180 mg/100 g of dry weight [26]. Finally, a potential source of iron is mushrooms. A study on the iron content of 30 edible mushrooms in Turkey found an average content of 36 mg iron/100 g of edible parts (ranging from 5 to 84 mg iron/100 g) [27]. However, in general, mushrooms are not normally consumed on a daily basis, and more research is warranted in this area.

Iron Intake in Specific Cases: Dietary Restrictions and Increased Requirements

Certain individuals or population groups abstain from consuming certain food groups because of religious beliefs or cultural taboos. For examples, some individuals follow vegan or vegetarian diets, which lack animal-source foods. These diets are often associated with an increased risk for both iron deficiency and anemia [28]. However, Clarys et al. showed that the overall dietary iron intakes of vegans in Belgium were at least as high as those of their peers who were consuming an omnivorous diet (23 vs. 17 mg iron/day); hence, differences in iron status are most likely due to the lower bioavailability of iron from plant-based diets [29]. Food taboos are another factor that can influence iron intakes, but are often ignored or not well-documented. In many cultures, food taboos exist—especially for pregnant and lactating women—often resulting in a lower intake of essential nutrients. For example, in North Laos, up to 80% of women adhered to postpartum food restrictions, which included eating only rice in the postpartum month(s). In a study in Addis Ababa, Ethiopia, almost 20% of pregnant women avoided certain foods during pregnancy, including organ meat and dark green leafy vegetables. Women avoiding these food groups had a significant higher risk for anemia [30]. Dietary restrictions can also arise from traditional and social hierarchic food distribution patterns within the household, often allocating expensive, animal-source foods to the adult men, resulting in restricted access to high-iron foods by women and children. Many traditional beliefs and practices also restrict infant diets, often withholding animal-source foods during the first year or beyond. In Thailand, a common belief is that a child should not be given fish, before she/he can say “Pla” (meaning fish in Thai), to avoid the risk of choking on the bones.

Nutritional status of the mother during pregnancy and lactation is an important determinant of the nutritional status of the newborn, but most iron is already transferred to the infant during the last trimester of pregnancy and during delivery, with maternal iron preferentially being transferred to the fetus, as long as maternal iron status permits [31]. Indeed, the amount of iron in human breastmilk is low, ~0.6 mg/L during the first month of lactation and declining to around 0.2–0.3 mg/L at 6 months postpartum, with apparently no correlation between maternal iron status and breastmilk iron concentration [32]. Iron in human breastmilk is present as lactoferrin, which has a very high bioavailability (~50%) [33]. Lactoferrin serves both as an iron-carrier and chelator, thereby potentially having bacteriostatic activities. Yet, despite the high bioavailability of lactoferrin, concern exists over the iron intake of fully breastfed infants after 4 months, with iron deficiency being more prevalent in infants exclusively breastmilk for 6 months [34]. Iron intake in the second half of infancy should come mainly from complementary foods, with recommended intakes of iron ranging from 6 to 18 mg/day depending on the bioavailability of iron in the diet (Table 10.1). Unfortunately, most traditional complementary foods, especially in low- and middle-income countries (LMIC), have a low nutrient density, and when they contain iron, this is often found in combination with fiber and phytic acid, which may reduce nutrient absorption [35]. Concomitantly, infants and young children require high nutrient intakes and absorption to support their high growth velocity. As a result, many infants and young children in LMIC become iron deficient during the first 2 years of life, as dietary iron intakes are low and bioavailability of ingested iron is low as well. Moreover, boy infants appear to be at an even higher risk for anemia and iron deficiency than girls [36, 37]. One possible explanation for these sex-specific differences may be the higher growth rate of male infants, as compared to females, leading to increased iron requirements in males. We estimated that daily iron intake of male infants should be almost 1 mg/day higher than that of female infants to achieve similar iron body stores [36].

General Considerations on Dietary Sources of Iron

Unfortunately, data on the iron status of a population or data on the iron content of foods is not always available, and many iron-rich foods are underutilized. In many cases, iron deficiency prevalence is estimated from anemia prevalence, which is inaccurate as anemia is caused by a myriad of causes, which may comprise of both nutritional and non-nutritional causes. It is also important to evaluate diets that are actually and realistically consumed, especially in the most at-risk populations. In LMICs, where nutritional anemia is often a serious public health problem, the risk of iron deficiency is often higher in young children and in WRA, especially in pregnant and lactating women. And as prevalence of iron deficiency is higher in lower socioeconomic status groups, the dietary iron sources that are affordable and available are often limited. It is thus crucial for approaches that aim to improve dietary diversity to consider specific situations and constraints to assess how the local food basket can realistically contribute to covering nutrient requirements, especially iron requirements in this case.

Intentionally Increased Iron Intake (Dietary and Non-dietary)

The intentional enhancement of iron intakes can be roughly divided into dietary strategies and non-dietary strategies. Dietary strategies encompass dietary diversification, bio-fortification, and fortification of staple foods, whereas non-dietary strategies include supplementation, as well adaptation of food processing techniques. Dietary strategies and supplementation are covered under other chapters in this book (see Chaps. 26 and 27). Therefore, only a brief summary is provided and some examples are given in Table 10.2.

Supplementation is regarded as the most straightforward intervention to improve dietary iron intakes, although it is often considered as a short- to medium-term solution to fight iron deficiency. However, supplementation programs, such as iron and folic acid (IFA) supplements for pregnant and lactating women, have been in place for decades. The World Health Organization recommends IFA supplements for pregnant women at risk for iron deficiency, with supplements providing 30–60 mg of elemental iron/tablet, and women typically receive 90–180 tablets, to be taken during pregnancy and during the first months of lactation. Recommended iron intake in

Table 10.2 Examples of interventions to intentionally increase dietary iron intake

	Intervention strategies to increase dietary iron intake			
Target group	Supplementation	Fortification	Bio-fortification	Dietary diversification
Pregnant and lactating women	IFA supplements, containing 30–60 mg of iron	Iron-fortified drinks [48] Iron-fortified foods [48]		
Women of reproductive age	Weekly IFA supplements [49]	Iron-fortified drinks [48]		
Adolescent girls (10–19 years)	Intermittent IFA supplements	Fortified drinks [50]		
Young children (6–23 months)	Home fortification with micronutrient powders [51]			
Whole population	–	(Mandatory) fortification of rice, wheat, or maize flour, condiments [52]	Rice (genetically modified or conventional breeding), sweet potato, cassava root, wheat [53]	Increased intake of legumes [54]

IFA iron and folic acid

pregnancy is high (>20 mg/day, Table 10.1), whereas the tolerable upper intake level (UL) set by the IOM is 45 mg/d, giving a narrow window, and indeed complaints on gastrointestinal side effects are not uncommon. A Cochrane review on daily IFA supplements showed that this strategy is effective, with iron deficiency at term reduced by 57% [38]. Moreover, limited evidence suggests that improving iron status of women before conception through weekly IFA supplements can have a positive impact on birth weight [39]. However, the long-term sustainability of providing iron supplements is questionable, as well as that there is a potential negative interaction with infectious diseases, with, for example, a study from Tanzania showing an increase in morbidity and mortality in children receiving iron and folic acid supplements, not only due to malaria but also to other infectious diseases [40]. A specialized type of supplementation is home fortification with micronutrient powders (MNPs), which could be regarded as a method of delivery "in-between" supplementation and fortification. The purpose of home fortification with MNPs is to increase micronutrient intake of children between 6 months and 2 years of age, by adding the MNP to the meal of a child, thereby providing ~12.5 mg of elemental iron. The use of MNP reduces the risk for anemia and iron deficiency by an estimated 18% and 53%, respectively [41]. However, some studies have reported an increase in diarrheal disease with the use MNPs, and there is also a concern for increased gut inflammation and negative effects on the child's intestinal microbiome due to the high iron content [42]. In view of the serious potential drawbacks and the many implementation and uptake challenges of the existing supplementation strategies, new iron supplementation approaches are needed, with new formulations that provide a lower overall dose of iron, but with a higher bioavailability, as extensively described in Chap. 26.

Food-based approaches include a wide range of different strategies such as dietary diversification, food fortification, and bio-fortification. Food-based approaches aim to deliver micronutrients through the diet, and these interventions are considered appropriate as medium- and long-term strategies, with good acceptability and sustainability. Dietary diversification aims to increase the number of food groups being consumed, thereby providing a wider variety and higher concentrations of nutrients in the diet. These interventions are discussed in detail in Chap. 27.

If the iron content of diets is low, bio-fortification or iron fortification of staple foods can be used to increase iron intakes, either as a parallel approach or as a transitional supportive approach until behavioral changes in dietary diversity come into effect. Indeed, iron fortification is feasible for a wide range of food vehicles, including rice, fish and soy sauce, salt, or bouillon cubes [43]. However, some strategies appear to be more effective than others [44, 45]. Also, there is concern about monitoring fortification programs, as many LMIC countries lack the resources for certifying appropriate levels of iron fortification. A recent estimate from four African countries showed that iron-fortified foods contributed to <15% of the RDI for WRA, mainly because iron fortification levels were below standard. If standards were met, iron-fortified foods could contribute up to 65% of the RNI for WRA [46]. Bio-fortification aims at increasing iron content of crops through breeding techniques or genetic engineering. However, pure conventional breeding techniques might sometimes be insufficient, for example, for rice, while genetic engineering of rice could potentially increase iron content of the rice kernel up to four times [47]. Food fortification and bio-fortification are described in detail in Chaps. 24 and 27.

Indirect Methods to Increase Dietary Iron Intake: Food Processing and Preparation

Food processing in its simplest forms includes milling, grinding, and cooking and has the potential to markedly increase the bioavailability of iron. The development of interventions to optimize food processing techniques to improve iron content and bioavailability may provide sustainable tools to improve dietary iron uptake at minimal cost. Examples are parboiling of rice, germination, limited washing of rice, absorption cooking, or the promotion of whole grain or partially milled grains. Parboiling is the process of heat treatment of rice after soaking. For example, by using iron-fortified water during the soaking process, the parboiled rice can obtain significantly higher iron concentrations than rice soaked with regular water. However, other processes are less straightforward, such as the germination of white sorghum, which not only reduced phytate content but also iron content; hence, overall effects on iron status remain to be investigated [55].

Another approach is using food processing techniques to improve the bioavailability of iron. For example, fermentation is one of the oldest food processing techniques known to mankind [56]. Fermentation of maize and of black-eyed peas (Vigna *unguiculata*) significantly increased iron uptake in Caco-2 cells [57, 58]. While most fermentation processes do not significantly increase the iron content of foods, they may have a positive impact on iron bioavailability by reducing the phytate content, breaking down the plant matrix, and sometimes increasing the content of iron absorption enhancing substances, such as vitamin C. A special case is the fermentation of complementary foods, mainly maize- or sorghum-based porridges in East and West Africa, either spontaneously with lactic acid bacilli or added yeast. Although most studies show increases in iron solubility after fermentation, the question remains whether there is a real impact on iron bioavailability as phytic acid-iron ratios remained high [59].

Over the last decades, other non-dietary interventions have been developed with the aim to increase the iron intake of populations. For example, the practice of cooking in iron pots, rather than in aluminum pots, was introduced as potential intervention to increase iron intake, as iron leaches into the food during cooking. A study conducted in Ethiopia showed a positive impact of the use of iron pots on iron status in young children. The authors estimated that cooking in iron pots resulted in 0.24 mg available elemental iron/100 g cooked food, compared to 0.05 mg available elemental iron/100 g cooked food from aluminum pots [60]. However, given the low amount of iron in the cooked food in relation to the RDA of iron and the low bioavailability of iron, whether this increase on iron status was clinically important is questionable. Harvey et al. reviewed the impact of non-food sources of iron, including iron of cooking pots, and concluded that any impact on iron status is highly uncertain [61], while a more recent review is relatively more positive on the potential impact of cooking in iron pots [62]. But in a well-conducted study in Benin, serum ferritin concentrations were lower, rather than higher, in children and women using iron pots for 6 months [63].

The consumption of traditional beers in Southern Africa has also been associated with higher iron status and has even been associated with iron overload [64]. Beer brewed in iron pots in South Africa contained between ~15 and 68 mg iron/L, and ~ 10% of the beer consumers had evidence of iron overload [65]. The long brewing process and the relative acidity of the home brew were factors that likely promoted the increased iron content and bioavailability.

The impact of the more recent, and excessively promoted, “Lucky Iron Fish” on iron status is in contrast highly questionable. These small iron ingots in the form of a fish are added to the water while cooking food, and iron is purportedly leached into the water (and into the cooked food). Depending on acidity, 3–80 mg iron/L is reported to be released [66]. But the surface of cast-iron cooking pots is much larger than of the ingot; hence, the biological plausibility of these small ingots leaching so much iron is questionable. Indeed, a randomized controlled trial in Cambodia did not find any impact of the Lucky Iron Fish on iron status [67], and furthermore, there are also concerns that heavy metals such as arsenic and lead could leach out of the iron ingot. More research on these products is needed to establish their safety and efficacy.

Non-intentionally Increased Iron Intake (Dietary and Non-dietary)

Finally, dietary iron intakes can be increased non-intentionally by inadvertent high iron concentrations in foods, or even non-foods, as a result of external or environmental factors.

Environmental Contaminants

Non-intentional enhancement of iron intake is most often the result of contamination of foods or drinks. A well-known example is the Ethiopian cereal teff, which when processed traditionally in small-scale iron grinding mills can lead to daily iron intakes of >200 mg [61]. However, studies report wide variations in the amount of iron that can be absorbed due to iron contamination of foods. In Senegal, the amount of iron in millet that came from contamination varied between 10 and 80% of the total iron content [68], and Greffeuille et al. reported that traditional milling of maize in Benin doubled or even tripled iron content [69]. An important question is how much of the contaminating iron is freely available for absorption. An extreme example of non-intentional non-dietary iron intake is pica. Pica is often defined as the craving for eating abnormal substances, such as earth, clay, or solid ice (in large amounts). Data from studies on pica suggests that most iron coming from soil is not bioavailable. Pica is often associated with iron deficiency, and one hypothesis on the etiology of geophagy (eating of earth) is that iron deficiency triggers geophagy, as a way to replenish iron stores [70]. However, even though soils and clays often contain large amounts of iron, in the order of 2–3 mg/g, bioavailability of the iron is very low. Indeed, addition of soils or clay to cooked white beans reduced iron uptake in Caco-2 cells, suggesting an inhibitory effect [71].

Iron in the Environment

Another non-intentional source of dietary iron intake can occur when drinking water or soil content is also high in iron. Karakochuk et al. analyzed groundwater from wells in Prey Veng province in Cambodia and reported that ~70% of samples exceeded the recommended maximum level for iron, with a mean concentration of 1.4 mg iron/L [72]. Indeed, iron coming from groundwater could explain the discrepancy between dietary iron content of foods in Cambodia [6] and biochemical data showing very low levels of iron deficiency in the population [73]. In a study in Bangladesh, iron in drinking water ranged from 0 to 79 mg iron/L, with iron content in some areas up to ~4 mg iron/L, contributing to a daily intake of ~11 mg/day. Pregnant women living in the high-iron areas had significant lower risk for iron deficiency and iron deficiency anemia [74]. Finally, iron soil content is associated with plant growth, and iron-deficient soils can lead to retarded plant growth and chlorosis. Increasing the iron content of soil can be done through application of ferrous sulfate (FeSO4) or organic fertilizers. The higher iron content of the cultivated plant can help to increase dietary iron intakes and thereby reduce the risk for iron deficiency populations consuming those plants [75].

To conclude, the first step to identify strategies to increase iron status in humans is to assess dietary iron intakes and sources. Dietary iron can come from many different food sources or can be consumed as a result of food contamination, food processing, or the environment. In addition, nondietary strategies, such as oral supplementation with iron tablets, are commonly used to increase iron intakes in individuals. But a high dietary iron intake is not equivalent to a high iron status, as iron bioavailability is a critical determinant of iron uptake and is affected by many factors. Furthermore, a fine balance is needed between improving iron status when needed, without unnecessary exposure to high amounts of (poorly absorbable) iron with potentially negative health effects, not even mentioning the potential toxicity of iron overload. Ultimately, a single golden bullet to solve the problem of iron deficiency does not exist. This is the lesson that needs to be drawn from all public health interventions in the last few decades aimed at reducing the prevalence of anemia and iron deficiency. Therefore, a wider perspective is needed, starting with comprehensive measurement of the prevalence of iron deficiency and/or anemia in a population; an extensive examination of the potential causes, underlying risk factors, and the groups most affected; and, finally, the determination of optimal approaches to address iron deficiency and/or anemia in the target population.

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