Iron fortification: an update[1-3]

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ABSTRACT Iron fortification is the optimal approach to reducing the high prevalence of iron deficiency in developing countries. Selection of the iron source entails a compromise between the use of inert compounds which are poorly absorbed and chemically reactive forms with high bioavailability. Although the vehicle and fortification compound must be chosen in tandem because most iron compounds cause discoloration or rancidity, the emphasis in this review is on the food vehicle. Technology for fortifying wheat flour and bread is well established and the use of these vehicles has probably had a significant impact on iron status in Western countries. Recent studies in India indicate that the fortification of common salt is technically feasible and field trials have shown a good hematological response. Similar success has been achieved by fortifying refined sugar with NaFeEDTA in Guatemala. Rice has advantages as a vehicle in those areas where it is the staple food but the technology requires further development. Fish-based condiments have been successfully fortified with NaFeEDTA and show promise as a vehicle in East Asian countries. The fortification of infant foods poses no technical problems and should be encouraged. Additional work is needed to identify other fortification options and to develop targeted fortification programs that will direct iron to those segments of a population in greatest need. *Am J Clin Nutr* 1983;38:648–659.

KEY WORDS Iron fortification, iron deficiency

Introduction

Nutritional iron deficiency is a major health problem in developing countries. The only proven way it can be alleviated is to increase iron intake, either by providing medicinal iron (supplementation) or by adding iron to the diet (fortification) (1). Iron supplementation has the advantage of producing rapid changes in iron status and of directing iron to those segments of a population in greatest need. However, its effectiveness is limited because of the gastrointestinal side effects of oral iron and the difficulty in sustaining motivation of the participants. Moreover, iron supplementation requires an effective system of health delivery and is costly to maintain.

Fortification is generally considered the best long-term approach for combatting iron deficiency. It reaches all segments of the population and does not require the cooperation of the individual. The initial cost is modest and the maintenance expense is far less than that of supplementation. However, there are many technical difficulties in fortifying the diet with iron, the most important being the identification of a form of iron that is adequately absorbed and yet does not alter the appearance or taste of the food vehicle. Because no single fortification strategy is suitable for world-wide use, reducing the global prevalence of a nutritional anemia will require the development of several op-

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tions from which a given country or region can select. The purpose of this report is to review current information on iron fortification with particular emphasis on the choice of the food vehicle.

Iron compounds

The success of iron fortification depends as much on the fortification compound as on the food vehicle. Fortification with iron is technically more difficult than with other nutrients because bioavailable forms of iron are chemically reactive and often produce undesirable effects when added into the diet. Since the population will seldom accept the fortified vehicle if the added iron can be detected, inert iron compounds are commonly used, but these are poorly absorbed and have little effect on iron status. A critical step in the design of an iron fortification program is the selection of an iron compound that is both unobtrusive and well absorbed.

Ideally, bioavailability of fortification iron should be determined by labeling the product isotopically and measuring its absorption from the diet in human subjects. However, because of the complexity of isotopic measurements in humans, bioavailability of iron compounds is often based on animal studies such as the Hb repletion method (2, 3). In this approach, Hb response to graded iron doses is measured in iron-deficient rats and compared to that observed with ferrous sulfate, the accepted standard in iron availability studies. Since even animal assays are too cumbersome for routine monitoring of bioavailability of different commercial iron sources, simple in vitro techniques such as particle size, dissolution rate in hydrochloric acid, or reactive surface area are commonly employed; the latter appear to be better predictors of iron absorption than particle size (4). A major concern with both animal and physical measurements of bioavailability is that their precise relationship to absorption in humans has not been adequately defined.

Bioavailable sources of iron pose serious problems to the food manufacturer. Soluble ferrous salts often produce color changes by forming complexes with sulfur compounds, tannins, polyphenols, and other food substances; discoloration is a particular problem when fortifying white foods such as refined sugar, rice, and salt. In addition, reactive iron compounds catalyze oxidative reactions resulting in undesirable odors and flavors. When these organoleptic problems develop slowly, the shelf-life of packaged food vehicles such as flour and processed cereals is reduced.

Common iron sources and their relative costs are presented in **Table 1.** The *soluble* compounds are both the best absorbed and the most chemically reactive. Because of the high bioavailability of ferrous sulfate, it is used extensively to fortify foods such as bread and bakery products which are stored for only short periods of time. Ferrous fumarate is used to fortify corn-soy-milk, a protein supplement and weaning food supplied by the USA in international food assistance programs. The absorption of ferrous fumarate is comparable to ferrous sulfate when given at therapeutic levels without food (5, 6), but is apparently less when added to food (Hallberg L, personal communication). Ferrous lactate and ferrous gluconate are well absorbed but their cost generally limits their use to milk and soy-based for-

TABLE 1
Iron compounds used for fortification

	Relative cost*
I. Soluble	
1. Ferrous sulfate	1
2. Ferrous fumarate	5
3. Ferrous lactate	7
4. Ferrous gluconate	11
5. Ferric ammonium citrate	7
II. Phosphate	
1. Ferric orthophosphate	6
2. Sodium ferric pyrophosphate	17
3. Ferric pyrophosphate	
II. Elemental	
1. Reduced iron (hydrogen, CO)	1.5
2. Electrolytic	1.5
3. Carbonyl	1.5
IV. Complex	
1. NaFeEDTA	11
2. Hb	

* Incorporates purchase price, percentage iron, and bioavailability. Values expressed relative to ferrous sulfate.

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mulas. Ferric ammonium citrate is used commonly in infant formulas and has been used in the UK for fortification of wheat flour. Absorption of this iron source was reported to be poor in human subjects when baked into bread (7) or added to wheat chapatti (8), but comparable to that of ferrous sulfate in anemic rats (9); there is apparently considerable variation in bioavailability between different commercial products.

Phosphate compounds are at the opposite end of the spectrum in regard to bioavailability and organoleptic problems. Ferric orthophosphate and sodium pyrophosphate were used extensively for flour and cereal fortification in the USA because of their low cost and low vehicle reactivity, but their use declined when isotopic studies in human subjects showed absorption to be far less than that of ferrous sulfate (10, 11). Ferric orthophosphate is still in use but its relative biological value (absorption relative to ferrous sulfate) is highly variable, ranging from 5 to over 60 depending on the commercial batch (12–14). The relative cost of these iron forms is high because of poor availability.

Elemental iron powders, which occupy an intermediate position between the soluble and phosphate groups in regard to absorption and reactivity, have been used extensively for fortification of flour and bread in the USA and Europe. Surface area, bioavailability, and cost are lowest for hydrogen and CO-reduced iron, intermediate for electrolytic iron, and highest for carbonyl iron, but the differences are not pronounced (3). Segregation of these high density iron products may be a problem with some vehicles, and highly purified and finely powdered iron is pyrophoric (15). The physical properties and bioavailability of food grade elemental iron powders have been reviewed in detail elsewhere (16, 17).

A *complex* in which iron is tightly bound might minimize adverse reactions with a food vehicle but, unfortunately, most iron chelating substances compete with the intestinal mucosa for iron. One exception is EDTA which impairs absorption in high concentrations (18) but may actually enhance absorption when added in equimolar concentrations as in the case of sodium iron EDTA (NaFeEDTA) (19, 20). NaFeEDTA minimizes the problem of iron precipitation that occurs when fish sauce is fortified with iron (21) and when fortified sugar is added to tea (22). Another organic complex, dried Hb, has exceptionally high bioavailability but imparts an intense color to food and requires a continuing supply of animal blood.

Some of the technical problems that occur with food iron fortification might be circumvented by using a relatively inert form of iron in combination with a substance that enhances absorption such as ascorbic acid. The combination of a stabilizing agent to reduce the reactivity of iron during storage and an acidifying agent to enhance availability at the time of ingestion has been used to advantage in the fortification of common salt. Fortification with ascorbic acid alone may improve iron nutriture but the cost of adding it to the food supply of an entire nation would be prohibitive.

Food vehicles

Although the iron fortificant and food vehicle must be chosen in tandem, the latter is more important. In selecting the vehicle, consideration must be given to both the pattern of its consumption and the technical feasibility of its fortification (**Table 2**). The vehicle must reach a high proportion of the vulnerable population and be consumed evenly throughout the region or country. Any economic bias in vehicle consumption should favor low income groups in which

TABLE 2
Considerations for selection of food vehicle

Consumption
High proportion of population
Minimal regional variation
Unrelated to socioeconomic status
Minimal variation between individuals
Low potential for excessive intake
Contained in all meals
Linked to caloric intake
Technical
Centrally processed
Few production facilities
Good masking qualities
Low cost
Minimal segregation
Limited storage time
High bioavailability
No nutrient interactions

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nutritional anemia is more prevalent. It is important that the supply of iron be relatively constant to both the household and the individual and that there be little chance of some people consuming large amounts of the fortified vehicle as might occur with soft drinks or snack foods. Ideally, the vehicle should be a component of all meals because percentage absorption varies inversely with the iron content of the meal.

There are also several technical considerations in selecting a vehicle. It must be centrally processed to permit an entry point for iron, a factor that limits the use of home grown foods. The fewer the number of production facilities, the easier the task of monitoring the fortification process. Food vehicles that are dark in color or have a strong taste or odor permit the use of more reactive iron compounds. The vehicle should not be expensive nor should fortification greatly increase the purchase price. Segregation of iron during mixing or storage can occur with some vehicles, and organoleptic problems are lessened with vehicles that do not require prolonged storage, particularly if the climate is hot and humid. Substances that inhibit iron absorption, such as coffee (23), would not be suitable vehicles. Ideally, the vehicle should not contain other nutrients such as iodide that are affected by the added iron. Obviously, many trade-offs are involved in selecting vehicles for iron fortification.

Wheat

Wheat flour and bakery products deserve careful consideration because of the technical success of their fortification in Europe and North America. Fortification iron in wheat flour and bread account for about 20% of the iron intake in the USA and nearly twice this amount in Sweden. Although the efficacy of fortifying bread with iron has not been firmly established, the high level of iron added to the Swedish diet is considered an important factor in the marked reduction in the prevalence of anemia during the past 10 to 15 yr (24). The questionable efficacy of flour fortification in the UK (25) may relate to the use of poorly absorbed forms of iron. In developing countries where wheat is a staple food, it is an attractive vehicle because it reaches all segments of the population, provides a relatively even meal distribution of the added iron, and furnishes a reasonably constant iron supply to each individual. For example, based on food consumption data in Canadian women, it was predicted that with increased bread and wheat fortification, the difference between the 10th and 90th percentile in individual iron intake would be less than 2-fold (26). Another advantage of using wheat and bread as vehicles is that the bioavailability of iron added to high extraction wheat flour is several times greater than that added to other staple foods such as maize and rice (27). This is less important with large meals but could be an advantage with snacks in which most of the calories are derived from wheat flour.

The problem of reduced shelf-life is of little concern when fortifying bread and bakery products because they are consumed promptly. In fact, pilot studies have indicated that there would be little difficulty in tripling the current level of bread fortification in the USA using highly available ferrous sulfate (28). When flour is fortified with soluble iron sources changes in color, odor, and taste occur, a problem that has been largely eliminated by using elemental iron. This form of iron may segregate when flour is handled in bulk with pneumatic conveying systems and may be extracted by the magnets used to remove contaminants during milling. Wheat flour and wheat products appear to be the best vehicles for iron in regions such as Egypt and the Caribbean where wheat is the staple food. A drawback in many Third World countries is that most of the wheat flour is imported and consumption usually favors the higher income segments of the population. Unfortunately, wheat is not a staple food in many areas of the world where nutritional anemia is highly prevalent.

Salt

The use of salt as a vehicle for iodide has been successful in eradicating endemic goiter and it may be the optimal vehicle for iron fortification in many countries. Refined salt provides a relatively constant intake for each individual, has little potential for excessive intake, is consumed by most of the population, and is not limited to the higher income segments. It is the only iron vehicle

that is feasible in India because it is one of the few dietary items that is centrally processed. However, in certain coastal regions salt is obtained locally by solar evaporation of sea water and bypasses industrial processing. In the Philippines, fortification of refined salt is considered impractical because intake favors the higher socioeconomic strata.

The fortification of salt is beset by formidable technical problems. The overriding difficulty is that bioavailable forms of iron produce unacceptable changes in color, especially with less refined cooking salts because of their high moisture content. In hot, humid climates the iron may actually gravitate to the bottom of the storage container, leaving the upper layer of the vehicle iron-free and the lower layer with potentially harmful quantities (29). Salt fortification has been studied in India for several years. Iron absorption measurements have shown that fortification with sodium iron pyrophosphate, ferric orthophosphate, or ferric pyrophosphate is unacceptable because of low bioavailability (30). Efforts have therefore focused on the use of one of these inert iron compounds in combination with substances that promote absorption. South African workers have shown that the combination of ferric orthophosphate, starch, and ascorbic acid is technically feasible and ensures adequate assimilation, although the cost of ascorbic acid may be prohibitive (31, 32). The combination of ferrous sulfate, sodium hexametasulfate (stabilizer), and sodium acid sulfate (enhancer) is also technically feasible but again the cost is relatively high (33, 34). Ferrous sulfate and orthophosphoric acid are adequately absorbed, but some deterioration of bioavailability occurs during storage due to the formation of insoluble iron phosphates (35). NaFeEDTA provides adequate amounts of iron but it discolors refined salt and is relatively expensive.

The combination of ferric orthophosphate and sodium acid sulfate has recently been reported to produce acceptable long-term bioavailability of the added iron with only slight discoloration, even under adverse storage conditions (36). The cost of this strategy can be reduced further by using ferrous sulfate, orthophosphoric acid (color stabilizer), and sodium acid sulfate (enhancer). In recent field trials in India, common salt was fortified in this manner to a level that provided an additional iron intake in adults of 10 to 15 mg/day (37). The salt was fortified by crushing to a coarse powder and batch mixing it with the three chemicals to achieve an iron content of 1 mg/g. Discoloration was minimal except when poor quality salt with a moisture content above 10% was used. Ordinary gunny sacks used for packaging and transportation proved unworkable because of the corrosive nature of the added chemicals but this problem was eliminated by using unlaminated high-density polyethylene. The product was tested for 12 to 18 months in one urban and three rural areas, and was well accepted except in some areas where the population was not accustomed to using crushed salt. Where the prevalence of anemia was high, a gratifying improvement in Hb levels was observed. The cost of fortification, which increased the cost of salt by about 20%, was estimated at about US $0.07/person/yr. These findings indicate that common salt merits strong consideration as a vehicle for iron.

Sugar

Sugar, which has been used successfully for vitamin A fortification, has been proposed as a vehicle for iron (38–41) because its intake is relatively constant for each individual and it reaches a high proportion of the population. Pilot fortification studies have used highly refined sugar because industrial grade sugar has a greater potential for idiosyncratic consumption. Iron added to sugar would be well absorbed, especially if consumed in citrus drinks, although a high proportion of sugar intake in adults is with tea and coffee which impair iron absorption. Sugar is an attractive vehicle in regions such as the Caribbean and Central America where it is produced, but in many developing countries refined sugar consumption favors the middle and upper economic segments of the population (42). As with salt, the main technical drawback to using sugar is in selecting an available form of iron that does not darken the product. Additional problems include segregation, which may reduce the shelf-life of less refined products with high moisture content, and the immediate dis-

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coloration that occurs when iron fortified sugar is added to tea.

Some of these obstacles have been surmounted by using NaFeEDTA as the fortifying agent (20). This iron compound imparts a very slight yellowish tinge to refined sugar and greatly retards discoloration when the fortified product is added to tea. Segregation has not been a problem with white sugar because NaFeEDTA sticks to the crystal when moisture content is above 1%. A key advantage of NaFeEDTA is its high bioavailability. Absorption from this complex is 1.5 to 2 times higher than from native dietary iron in a cereal meal and may actually facilitate absorption of nonheme iron in meals of low bioavailability. On the other hand, NaFeEDTA reduces the facilitating effect of ascorbic acid on iron absorption and does not fully escape the action of strong inhibitors such as tea (19).

Preliminary analysis of an extensive field study with NaFeEDTA-fortified sugar in Guatemala has shown significant improvement in iron status (41). Fortification was found to be technically feasible and acceptance by the population was good. No adverse effects of this chelate on other divalent cation nutrients such zinc, copper, and manganese have been seen and there are no unfavorable interactions when sugar is fortified simultaneously with encapsulated vitamin A and iron. However, NaFeEDTA is somewhat more costly than other fortification strategies. The addition of sufficient iron to sugar to increase iron intake in an adult woman by about 5 mg iron daily (13 mg iron/100 g sugar) would cost approximately US $0.10/person/yr although the cost of the vehicle itself would be increased by only about 1 to 2%. Attempts are underway in other countries to fortify sugar with less expensive iron sources.

Rice

Rice is a logical vehicle for iron fortification because it is a staple food for more than half the world's population and the main component of the diet in many countries where nutritional anemia is highly prevalent. Early studies using biosynthetically labeled rice showed low absorption of its intrinsic iron (43), but more recent measurements with an extrinsic tag have shown absorption to be comparable to other cereals and grains (27). Where rice is the staple food, its intake is closely tied to caloric intake and varies little with respect to income. In some areas home milling may be a drawback with this vehicle but in most countries it is milled commercially. Government control of the fortification process would be difficult in countries such as the Philippines where there is a large number of small mills.

The usual approach to fortifying rice is to prepare a premix of rice grains coated with iron and other nutrients which is then mixed with common rice in a ratio of 1:99–1:199 (44, 45). As with other food vehicles, the poor masking property of rice poses a technical problem because even a few discolored grains may make the product unacceptable. This can be solved by using an inert form of iron such as ferric orthophosphate or ferric phosphate but these iron sources are not likely to improve iron status. In a study conducted in 1949 in Bataan, Philippines (44), fortified rice was said to reduce the prevalence of anemia, but efficacy has not been adequately evaluated. Rice fortification has been required by law in the Philippines since 1950 but this has never been enforced.

The focus of recent studies has been to coat rice with a more available form of iron such as ferrous sulfate and to mask color changes in the fortified grain with a coating agent such as talc. One possible approach is to seal the iron with an edible polymer which would resist both washing and cooking and yet rapidly disintegrate in the intestinal tract (46). However, it is generally assumed that the enriched rice should be coated in a manner that would minimize iron loss during washing but ensure complete release during cooking. In this case, cooking water and eluted iron must be reabsorbed by the rice grain to minimize nutrient loss.

We have recently prepared a rice premix using ferrous sulfate and an intermittent shellacking process (Morck TA, Lynch SR, Cook JD, unpublished observations). The premix was fortified to a level that would provide 8 to 10 mg iron daily (3 mg iron/100 mg rice) at a 1:99 dilution with common rice. The fortified grains were whitened with talc and were barely detectable when mixed into unfortified rice. The iron coat was resistant to washing in a conventional rinse

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test but isotopic studies showed absorption of less than 50% as compared to iron in other foods eaten simultaneously, apparently because the iron was not fully released from the coated grain.

In another preliminary study in the Philippines, a rice premix designed for 1:200 dilution with common rice was coated with sufficient ferrous sulfate to provide the full recommended daily allowance for iron (18 mg), assuming a per capita intake of 300 g raw rice daily (42). This premix was coated by dispersing anhydrous ferrous sulfate in an isopropyl-chloroform coating solution and the suspension was mixed with raw rice in a rotary pan until the grains were uniformly coated. The premix was air dried at room temperature for 1 h, then packed and stored in polyethylene bags. Although less than 10% of the added iron was lost during rinsing, the iron content of the premix was reduced by 25% after 8 wk storage at room temperature and by over 50% after 8 wk accelerated storage at 50°C. Periodic sensory evaluation of the enriched rice showed acceptable results after 12 wk storage at room temperature but both the color and flavor were affected by storage at 50°C. These recent observations suggest that the technical problems in coating rice with an available form of iron are by no means insurmountable.

Condiments

Problems with color, taste, and odor of an iron fortified vehicle can be minimized by using a highly flavored substance such as fish sauce or fish paste, condiments which are used in place of salt in certain East Asian countries. Fish sauce is a colored, strongly flavored extract of marine fish with a high salt content. In Thailand, fish sauce (nam-pla) is produced through fermentation by hundreds of small companies and sold through local stores and street vendors. Most forms of iron are rapidly precipitated when added to this product but this has been circumvented by using NaFeEDTA which does not cause storage problems or changes in appearance or taste and is not detectable by the consumer (21). In a 12-month field trial using fish sauce fortified to a level of 1 mg/ml, a good Hb response was observed in iron-deficient women and children (21). Another large field trial with this fortification strategy is in progress in Thailand. One constraint to using fish sauce as an iron vehicle is that it is not used in all regions of the country although its consumption is progressively increasing.

Fish-based condiments have also been proposed as vehicles in the Philippines where there are two common products, fish sauce (patis) and fish paste (bagoong). These condiments are prepared by mixing one part salt to three parts fish or shrimp, packing the mixture in wooden vats or concrete tanks, and allowing it to ferment for 6 to 18 months. Fish sauce is a clear, amber-colored extract specified to contain no less than 10% protein and 25% salt by weight. It is a high quality product consumed only by the upper income segments of the population. Fish paste is a similar fermented product of lower quality which is consumed by the majority of individuals in the low socioeconomic segment of the population. Fish paste could be fortified by adding NaFeEDTA directly or by using a highly fortified premix of fish sauce which is used to prime the fermentation of fish paste.

Maize

Maize has desirable properties as a vehicle for iron but it is a staple food in relatively few areas of the world. Corn meal and corn grits have been fortified with iron in the USA for many years (47) and present no major technical problems. When these dry-milled products were fortified to a level of 40 mg iron/lb with reduced iron, little or no segregation occurred and no adverse odors or flavors were encountered after 56 days of accelerated storage (48). On the other hand, stabilized ferrous sulfate at this level caused some deterioration in flavor and odor. Maize has not been evaluated as a primary vehicle for iron in any developing country; one reason may be that the food is commonly processed in the home in rural areas.

Milk products

Attention in this review has been given to vehicles that would be consumed by most of the population in a given geographic region. While this does not apply to milk products,

they are considered here because of their potential importance as vehicles for iron during childhood, particularly the 1st yr of life (49, 50). The infant's relatively generous endowment of iron at birth disappears rapidly during the first few months as body size increases. Although the iron content of human milk is relatively low, it can meet iron requirements through much of infancy (51–53); from the standpoint of iron nutrition, breast-feeding is strongly advised for at least 6 months and preferably longer. If breast-feeding is discontinued, sufficient iron can be provided in infant formulas to prevent the development of iron deficiency. Absorption of added iron is comparable from cows' milk, pasteurized milk, condensed milk, evaporated milk, reconstituted powder, and milk-based formulas with added carbohydrates and fat (54). As a vehicle for iron, infant formula has the advantage that it can be fortified with highly available iron sources such as ferrous sulfate, ferrous gluconate, or ferrous lactate. Moreover, because of the limited amount of the vehicle that must be fortified, ascorbic acid can be included to enhance bioavailability at reasonable cost.

Extensive work with fortified milk formulas has been conducted in Chile (49) where powdered milk is distributed by the government to over 80% of infants and lactating mothers. About 3 kg milk powder is given monthly from birth to 6 months of age and 2 kg from 6 to 12 months. Mean duration of breast-feeding is about 3 months and solids are introduced at about 4 months of age. In an initial fortification trial, low fat milk powder was fortified with ferrous sulfate to provide 15 mg iron/l reconstituted milk. Although the prevalence of anemia was reduced substantially when this fortified product was given from 3 to 15 months of age, some of the milk was consumed by other family members and the amount of absorbed iron was too small to prevent iron deficiency in a significant proportion of the infants. In a subsequent trial, the product was acidified to discourage family consumption and ascorbic acid (100 mg/l) was added to facilitate absorption. This fortified milk reduced the prevalence of anemia at 15 months of age to less than 2% as compared to 28% in infants receiving unfortified formula. These findings clearly demonstrate the efficacy of infant formula as an iron vehicle.

Processed cereals

Iron-fortified infant cereals can also satisfy the high growth requirements for iron after 3 months of age and are suitable for use in the breast-fed infant (54). The technical problems are similar to those encountered with flour. Ferrous sulfate is an unsuitable iron source because of its tendency to cause rancidity with prolonged storage. High iron levels can be achieved with less available forms of iron such as ferric orthophosphate or sodium iron pyrophosphate but efficacy is a concern. This has led to extensive use of elemental iron powders of small particle size, particularly electrolytic iron, for the fortification of proprietary dry cereals in North America. Bioavailability is believed to be adequate, but again there is a need for a simple method to monitor bioavailability of these iron forms.

Blended food supplements make up an important subgroup of processed cereals. Corn-soy-milk which consists of 59% maize meal, 17% soy flour, and 15% nonfat milk, and 5% soybean oil (27), is fortified with 16 mg iron as ferrous fumarate and 40 mg ascorbic acid/100 g dry cereal, giving a molar ratio of ascorbic acid:iron of about 0.7. Although the effect on iron status of this particular product has not been evaluated in a field setting, there is little doubt that if a bioavailable form of iron is used and adequate amounts of ascorbic acid are added (55), these foods would have a major impact on iron nutrition in the most vulnerable segment of a population (27).

Other

Several other food vehicles for iron have been proposed but these have not been adequately studied or cover only limited population groups. Because of their excellent masking properties, dried fish products might be suitable in fish-consuming populations such as Southeast Asia. In a recent study in Japan, 30 to 80 mg iron/day was added to the diet by fortifying boiled and dried anchovies (tsukudani) with ferrous sulfate (56). No technical problems were en-

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countered and some improvement in hemoglobin levels was observed during a 3-month field trial. Curry mix (masala) has been proposed as an iron vehicle in an Indian population living in Durban, South Africa (57). A significant increase in absorbed iron occurred when this product was fortified with NaFeEDTA, and the vehicle has the added advantage that it promotes iron absorption even without iron, presumably by stimulating gastric acid secretion.

Because of the exceptionally high absorption of heme iron, dried Hb, which is extracted from slaughter house blood, has been proposed for fortification. The most advanced work in this area has been conducted in Chile where chocolate cookies have been prepared with 6% Hb (58). These cookies are presently distributed to 750,000 children as part of a school lunch program. Each child receives 30 g of cookies daily which contain 1.8 g Hb or 5 mg heme iron and provide about 1 mg absorbed iron daily. The program requires 16 tons of dried Hb monthly, or about 125,000 l of whole blood; the cost of the program is US $0.54/child/6-month school year. A gratifying improvement in Hb levels has been observed in pilot studies.

The options for fortifying commercially available food products in developed countries are numerous. In the USA, a variety of foods such as dried breakfast cereals and reconstituted beverages are fortified with iron and often promoted commercially on this basis. For example, soft drinks have been proposed as vehicles (39, 59) and there is currently a fruit-flavored beverage marketed in Scotland called "Irn Bru" that is fortified with ferric ammonium citrate. However, there are legitimate concerns with this haphazard approach to iron fortification. It is virtually impossible to ascertain the effect of any one product on iron balance in the population and it is difficult to regulate the level of iron supplied to the population as a whole. The most important concern is that individuals who have an inherited defect in the ability to regulate iron absorption from the gastrointestinal tract may consume excessive amounts of the fortified product and thereby accelerate the rate of tissue iron loading.

Fortification programs

While the selection of the food vehicle and iron source are primary considerations, there are other aspects to developing a fortification program. The full sequence of required steps is outlined in **Table 3.** Prevalence studies are needed at the outset to establish that iron deficiency is sufficiently widespread to warrant a national intervention program; iron deficiency limited to certain segments of a population can be dealt with more effectively by supplementation or targeted fortification. Having determined the need for fortification, dietary surveys are necessary to characterize the regional diet with respect to its content of heme and nonheme iron and factors that enhance or inhibit iron absorption. It is desirable to measure iron absorption from the regional diet in human subjects using the extrinsic radioiron tag method. These dietary surveys and isotopic studies are the basis for determining whether the major problem is limited iron intake, low bioavailability, or both, and for estimating the level of iron fortification that will be required to reduce the prevalence of iron deficiency.

One of the more costly and time-consuming steps in developing a national fortification policy is conducting field trials to establish efficacy. The need for a field trial is less critical if radioiron measurements are performed with the regional diet to measure the actual increase in absorbed iron that results from fortification. However, because a central issue with fortification is its long-term effectiveness, it is important to test the program under field conditions.

TABLE 3
Development of an iron fortification strategy

1. Determine prevalence of iron deficiency
2. Determine iron intake from dietary survey
3. Measure basal iron absorption from typical diet
4. Obtain consumption data for potential vehicles
5. Choose type and amount of iron fortificant
6. Develop fortification technology
7. Perform storage studies of fortified vehicle
8. Perform isotopic measurements to determine increment in absorption
9. Conduct field trial to determine efficacy
10. Implement a national strategy with continued evaluation

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TABLE 4
Causes of unsuccessful field trials

Fortification level too low
Low bioavailability of fortification iron
Inhibitory effect of regional diet
Poor consumer acceptance
Deficiencies in laboratory assessment of iron status
Duration of trial too short
Inadequate study design or statistical evaluation
Low initial prevalence of iron deficiency
Heavy parasitism
Other causes of anemia

Field studies may fail to demonstrate a beneficial effect of fortification for a variety of reasons (**Table 4**). The impact on iron status will obviously depend on the amount of added iron and the bioavailability of the iron source. In addition, basal absorption from the regional diet may be so low that increasing iron intake may have little effect. The trial may prove ineffective because the fortified product is not widely consumed or well accepted by the population. There are also pitfalls related to the design and conduct of the trial itself. Preliminary hematological surveys should always be performed in the region proposed for the field trial to ensure that there is in fact a high prevalence of iron deficiency. The ability to detect small changes in iron nutrition in a population has been greatly enhanced in recent years by using a battery of iron status measurements such as transferrin saturation, red cell protoporphyrin, and serum ferritin (1, 60, 61), but these must be carefully performed and adequately standardized. It is necessary to conduct the trial for an adequate period of time as iron status does not change rapidly with fortification. A field trial may also fail because of heavy parasitism or malabsorption in the target population and iron will not alleviate anemia due to other causes such as chronic infection.

A field trial is expensive and can take several years to design, conduct, and analyze. In countries where the cost of a preliminary field trial is prohibitive or where the high prevalence of iron deficiency anemia necessitates immediate action, it would be reasonable to forego the trial and proceed directly to a national fortification program. In this case the efficacy of fortification must be assessed by monitoring iron status in the population after implementation of the program. However, there are many factors that may contribute to a change in iron status in a given country over time and without field trials there can be no certainty as to the precise impact of the fortification policy per se. The more costly the fortification program and the more limited the economic resources of the developing country, the more important it is to avoid adopting a program of questionable benefit.

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