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'Meat or wheat for the next millennium?'
Plenary Lecture

Animal- and plant-food-based diets and iron status: benefits and costs

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Fe seems to be the only nutrient deficiency that industrialized and low-income countries have in common. Thus, Fe is one of the most critical nutrition requirements to be met in most diets in human subjects. Fe deficiency is caused not only by too low an intake, but is also the result of low bioavailability, as well as an increased Fe requirement due to physiological variables or clinical problems which are not met by an increased dietary intake of Fe. In low-income countries poor dietary quality rather than Fe intake seems to be the key determinant of impaired Fe status. Sometimes the Fe intake even exceeds that in populations of industrialized countries. The interaction of all enhancers (e.g. ascorbic acid and meat), as well as inhibitors (such as bran, polyphenols, egg yolk, soyabean products, Ca, $Ca_3(PO_4)_2$ and phytic acid (or phytate)) is what determines the bioavailability of non-haem-Fe in the meal. Dietary composition seems to be particularly important when Fe reserves are low, or in the presence of Fe deficiency. Furthermore, the development of anaemia as a result of Fe deficiency, secondary to Fe-stress situations, is dependent on the Fe balance in the host. With respect to the dietary intake of Fe, other products in the food consumed as well as previous treatment of the product (e.g. heat treatment and processing) may also influence bioavailability. Despite all efforts to counteract Fe deficiency it still represents one of the dominant problems in the micronutrient sphere. It is apparent that there is no simple solution to the problem, and the fact that Fe deficiency still occurs in affluent societies consuming a mixed diet speaks for itself; a more holistic view of total dietary composition and the role of enhancers and inhibitors is needed.

Iron deficiency: Anaemia: Bioavailability

Fe deficiency is a nutrient deficiency of great and general interest for many reasons. Fe seems to be the only nutrient deficiency that industrialized and low-income countries have in common. Since dietary habits and food availability are quite different in these two extreme types of communities, it is apparent that Fe is one of the most critical nutritional requirements to be met in most diets in human subjects. However, it may also illustrate indirectly that Fe deficiency might not only be a question of Fe intake *per se*. A number of factors in addition to the dietary content of Fe can also result in Fe deficiency. Thus, we have to distinguish whether the deficiency is due to an inadequate dietary intake of Fe (primary Fe deficiency) or to an increased demand for Fe secondary to various physiological and pathological conditions, which is not met by the dietary intake (secondary Fe deficiency). A primary Fe deficiency may be due not only to an inadequate intake, but also to poor dietary quality leading to a low bioavailability, i.e. there are both quantitative and qualitative aspects of primary Fe deficiency.

A secondary Fe deficiency may be related to physiological variables, i.e. increased blood volume secondary to low O_2 tension at high altitudes, an increase in muscle mass as a result of extreme training, and menstrual losses and repeated pregnancies, or to various clinical problems, i.e. increased blood losses secondary to surgical trauma, tumours and parasitic infestations.

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Body Fe comprises two parts: metabolically-active Fe which essentially occurs in the form of haemoglobin, constituting about 70 % of the total body Fe, and also as myoglobin and various enzymes; storage Fe, which occurs as ferritin and haemosiderin, and constitutes about 12 % of the total body Fe. The less Fe that is stored, the more sensitive the individual is to developing Fe-deficiency anaemia in Fe-stress situations. An analysis of the total body Fe status in populations in low-income countries (Pawlowski *et al*. 1991) illustrates clearly why an extra demand on Fe balance secondary to hookworm infestations or malaria is deleterious, especially in females (Table 1). Obviously, in most diets the intake of Fe is on the borderline of the requirements, which quickly results in depletion of Fe stores when extra needs for Fe occur. Furthermore, the development of anaemia as a result of Fe deficiency, secondary to a parasitic infestation or other Fe-stress situations, is dependent on the Fe balance of the host, i.e. body Fe stores, as well as the qualitative and quantitative dietary Fe intake, absorption of Fe, and physiological factors influencing Fe requirement (Cook, 1990).

When dietary intake is low, just a few hookworms active over a short period of time may be sufficient to cause Fe-deficiency anaemia in individuals who are potentially Fe deficient, i.e. women and children. However, on the other hand, even a 'normal' dietary Fe intake will not protect against anaemia in the presence of a high hookworm load (Pawlowski *et al*. 1991). Thus, some conditions which cause extra Fe stress may necessitate extra Fe supplementation if the dietary supply is inadequate, irrespective of whether the Fe is derived from animal or vegetable sources.

For an updated review of the nutritional and physiological significance of Fe, the reader is referred to a recent publication by the British Nutrition Foundation (1995).

Iron deficiency: a global problem of public health importance

It has been estimated that 1400 million people are affected by Fe deficiency and that more than 700 million have Fe-deficiency anaemia (DeMayer *et al*. 1989). Thus, Fe-deficiency anaemia is only the tip of the iceberg, and the prevalence of Fe deficiency represents about 2–2·5 times that of Fe-deficiency anaemia, even when malaria is not endemic and haemoglobinopathies are not widespread. On the other hand, of 1600 million people suffering from anaemia more than 50 % of the cases are attributable to Fe deficiency. WHO (World Health Organization/United Nations Children's Fund/United Nations University, cited by Viteri, 1998) data indicate that in low-income countries Fe-deficiency anaemia is present in 51 % of children 0–4 years of age, 46 % of school-age children, 42 % of women, 26 % of men.

Fe deficiency is much more prevalent in low-income countries than in the industrialized world, i.e. 1400 million of 3800 million people (38 %) *v*. 100 million of 1200 million people (8 %) respectively (DeMayer *et al*. 1989). The US NHANES II survey (Department of Health and Human Services, 1981) reports that 7 % of women have Fe-deficiency anaemia, but these cases are unevenly distributed within society, such that minority and poverty groups are over-represented. Interestingly, in an affluent society with less-pronounced socio-economic differences, such as Sweden, Hallberg & Hultén (1996) have reported a prevalence of Fe deficiency in women corresponding to 30 %, which indicates about the same prevalence of Fe deficiency anaemia as that in the USA, i.e. 8–10 % (based on the assumption that Fe deficiency is considered to be 2–2·5 times the rate of Fe-deficiency anaemia; Viteri, 1998).

Dietary iron: types and usual intakes

Fe appears in the food in two major forms: inorganic, as Fe^{3+} and Fe^{2+}, and organic, mostly as haem-Fe. While inorganic Fe, which is the dominant form of Fe in all diets, is derived from vegetable sources, organic Fe in the form of haem-Fe is derived from haemoglobin and myoglobin, primarily from meat, fish and poultry. In affluent societies with a high relative intake of animal products haem-Fe constitutes about 40 % of the dietary Fe intake, whereas it can constitute a very small proportion in low-income countries with a vegetable-based staple diet. In the present discussion, however, we should not forget the contribution of Fe through contamination, not only from soil and dust, but also from water, as well as from Fe pots during food preparation. The latter will be of importance in low-income countries where long periods of cooking are common.

There are two ways of describing the dietary content of Fe, in absolute amounts per 24 h or in relation to the energy content of the diet, i.e. the nutrient density concept. It is often found that food Fe is present in most diets in the proportion of about 6 mg/4·2 MJ (1000 kcal). However, the requirement for Fe is not related to energy turnover but depends on age and sex, and consequently it is given as mg Fe/d.

Table 2 shows the characteristics of Fe intake for various countries, expressed *per capita* and in relation to energy intake. The data show that the intake of Fe in absolute amounts appears to meet the requirements in many low-income countries (18 mg *per capita* per d for females; Food and Agriculture Organization/World Health Organization,

Table 1. Examples of body iron status in adults in low-income countries (From Pawlowski *et al.* 1991)

	Body Fe concentration (mg/kg)		Total body Fe (mg)	
Type of Fe	Men	Women	Man (60 kg)	Woman (50 kg)
Metabolic Fe	37	33	2220	1650
Storage Fe	13	5	780	250
Total body Fe	50	38	3000	1900

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Table 2. Estimates of iron intakes in various populations (From World Health Organization, 1970; Food and Agriculture Organization/World Health Organization, 1988; Becker, 1994; Ministry of Agriculture, Fisheries and Food, 1994)

Country	Fe intake	
	mg/person per d	mg/4·2 MJ (1000 kcal)
Bangladesh	23	12
Cameroon	10	
India:		
Adult women	23–30	
Men	28–35	
Kenya	16·8	
Latin America	16	8
Philippines	11	6
Senegal	12·6–36·4	
Sweden, 1989:		
Women 15–74 years	12	2·6
Men 15–74 years	16	4·2
UK, 1993	10	5

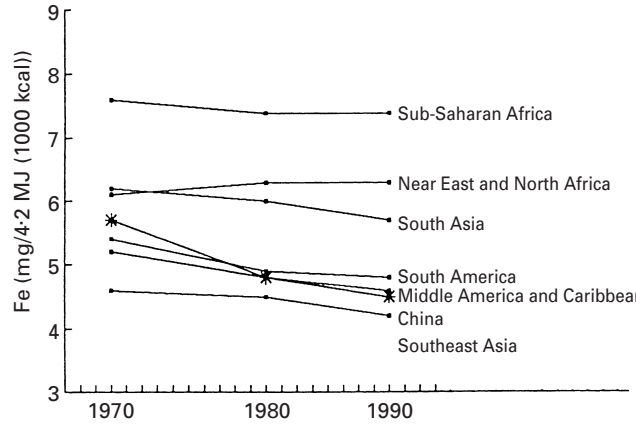

Fig. 1. The changes in nutrient density with respect to iron (mg/4·2 MJ (1000 kcal)) in various regions during 1970–1989 (From Administrative Committee on Coordination/Sub-committee on Nutrition, 1992 based; on data from Food and Agriculture Organization, 1990).

1988), while the nutrient density with regard to Fe is essentially lower in the more affluent societies.

Iron deficiency: a result of deficient iron intake only?

It has been assumed that in low-income countries it is essentially poor dietary quality rather than Fe intake that is the key determinant of impaired Fe status (Bothwell *et al*. 1989; World Bank, 1994). Thus, total Fe intake in populations that are dependent on vegetable-based diets may reach the dietary recommendations from the quantitative point of view, and sometimes even exceed those in populations of industrialized countries which are consuming more animal products (Food and Agriculture Organization/World Health Organization, 1988; Baynes & Bothwell, 1990; Murphy *et al*. 1992).

On the other hand, in affluent societies with a high intake of animal-based products containing Fe sources of high bioavailability, Fe deficiency is still showing a high prevalence, although at a lower level (British Nutrition Foundation, 1995; Allen & Ahluwalia, 1997). Thus it is apparent that the occurrence of Fe deficiency and how to deal with the problem is far more complicated than just a question of increasing Fe intake via the diet *per se*, nor is it related only to the source of dietary Fe, i.e. from plant or animal products. It is apparent, therefore, that a high bioavailability can only compensate for a low nutrient density to a certain extent.

The changes in nutrient density with respect to Fe, expressed on a per 4·2 MJ (1000 kcal) basis, during 1970–1989 are shown in Fig. 1 (Administrative Committee on Coordination/Sub-committee on Nutrition, 1992). This figure illustrates that there is some deterioration in the diet quality in terms of Fe content, except in Near East and North Africa. In the latter case this might be due to increased consumption of animal and vegetable sources, while in Sub-Saharan Africa the deterioration is assumed to be secondary to decreased animal sources in the diet. In South Asia reduced pulse production has been suggested to be the cause. In Middle America and the Caribbean it is presumed that animal sources are increasing, although vegetable sources are decreasing. Finally, in South America the Fe intake is decreasing, although animal sources in the diet are relatively high (Table 3).

A similar situation is reported from the UK, the Fe nutrient density is almost unchanged or slightly increasing, while that of total Fe is slightly decreasing (Ministry of Agriculture, Fisheries and Food, 1994). Thus, it is not clear what impact the use of vegetable *v*. animal sources really has on the Fe balance. It might be that this situation illustrates that it is essential not only to differentiate between plant and animal sources of Fe, but also between animal sources of Fe (e.g. poultry and fish *v*. red meat), and finally to establish possible interactions between nutrients (e.g. Ca and Fe intake).

Table 3. Regional trends in iron availability and anaemia 1970–1990 (Administrative Committee on Coordination/Sub-committee on Nutrition, 1992)

Region	Trends in dietary Fe supply	Trends in anaemia (non-pregnant women)
Sub-Saharan Africa	Down slightly, especially from animal sources	Up
Near East and North Africa	Up from both animal and vegetable sources	Probably down (36 % 1975–80, 28 % 1985–90)
South Asia	Down, due to reduced pulse production	High and increasing
Southeast Asia	Down slightly, especially vegetable sources from 1980	Probably up (40 % 1970–80, 57 % 1980–90)
Middle America and Caribbean	Down vegetable sources, but animal sources up	Probably up (20 % 1970–80, 30 % 1980–90)
South America	Down, but animal sources relatively high	Probably down (24 % 1970–80, 20 % 1980–90)

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Iron absorption

Although the mechanism of Fe absorption and its regulation is still unknown, it is assumed that it includes essentially three steps: (1) uptake from intestinal lumen to the mucosal cells; (2) transit through the mucosal cells; (3) release from the cells to the body. After digestion, the dietary Fe enters a pool of either haem-Fe or non-haem-Fe. This two-pool model was suggested by Bothwell *et al.* (1989). There is a common availability from non-haem-Fe as well as from haem-Fe which will equilibrate with either of the two pools. There are, however, some exceptions regarding certain forms of dietary Fe, e.g. ferritin, haemosiderin and contaminant Fe, which due to a lower solubility than most non-haem-Fe sources only partially enter the non-haem-Fe pool (Martinez-Torres *et al.* 1976).

Since Fe excretion is limited and essentially unregulated, the absorption of Fe is the only regulatory point for total body Fe status. However, the extent to which Fe is absorbed from a meal is not only dependent on the sources of Fe in the meals, but also other factors in the diet which might interfere with its bioavailability, as well as on the Fe status of the individual and his/her requirements. Haem-Fe is considered as having a high bioavailability (15–35 %), and is not exposed to inhibitory factors as it is 'hidden' in the porphyrin ring. Non-haem-Fe, however, only shows a low bioavailability, which varies between 2 and 20 %, and is greatly dependent on the presence of inhibitory ligands. A special situation is also reported with respect to the lactoferrin-bound Fe in breast-milk, which has been reported to have an extremely high bioavailability; this factor could partly explain why, despite the low Fe content in breast-milk, Fe deficiency is not reported in breast-fed infants during the first 4–6 months (see British Nutrition Foundation, 1995).

Regulation at the site of absorption, which mostly occurs in the duodenum, is such that haem-Fe enters mucosal cells intact and Fe is then dissociated from the porphyrin ring. There appear to be special receptors in the brush-border membrane and two different re-absorption mechanisms seem to be included: (1) an energy-requiring carrier-mediated process which involves a transmembrane protein transporter and which seems to be adaptive to the Fe requirements; (2) a fatty acid-related complex with a limited adaptation response. Also, two different microvillus carriers have been reported for non-haem-Fe, and Fe^{3+} is probably reduced to Fe^{2+} before absorption. However, earlier assumptions of a role for an apotransferrin in the mucosal cells do not seem to have been verified (see British Nutrition Foundation, 1995).

An updated review on Fe absorption and bioavailability was published recently by Benito & Miller (1998).

Bioavailability

Bioavailability is usually defined as the proportion of a given nutrient in a given food or diet which the body can actually utilize. Thus, bioavailability includes the absorption and transport of a nutrient to the relevant body tissue as well as the conversion into physiologically-active compounds (Benito & Miller, 1998). Many studies so far have focused on the dietary factors influencing Fe bioavailability. However, much less is known about the physiological factors affecting absorption. This makes it difficult to compare results obtained using different methodologies.

The possibility of evaluating the potential of various Fe sources in the diet is further complicated by the fact that a large number of factors unrelated to the characteristics of the foodstuff are likely to influence the proportion of a nutrient absorbed from a particular food, e.g. the Fe status of the individual, the gastric acid production, gut transit time and gastric emptying, which might be difficult to separate from factors such as pH, the efficiency of digestion, previous intake of the nutrient, and the presence of gastrointestinal disorder or disease.

With respect to the dietary intake of Fe, other components in the food consumed, as well as previous treatment of the food (e.g. heat treatment and processing) may also influence Fe bioavailability. Among the dietary factors that affect Fe bioavailability are those that enhance the bioavailability of non-haem-Fe, e.g. ascorbic acid and meat, and those that inhibit the Fe absorption such as bran, polyphenols, egg yolk, soyabean products, Ca, $Ca_3(PO_4)_2$ and phytic acid (Benito & Miller, 1998). The interaction of all these enhancers as well as inhibitors is what determines the bioavailability of non-haem-Fe in the meal. Dietary composition seems to be particularly important when Fe reserves are low, or in the presence of Fe deficiency. The downward regulation of Fe absorption, however, seems to be very effective, thus development of Fe overload from dietary Fe intake in normal individuals is highly improbable.

Cook (1990) has summarized the importance of Fe nutritional status on the haem-Fe and non-haem-Fe absorption from a single meal, as indicated in Table 4, where values are expressed as the percentage dietary Fe which is absorbed.

For practical reasons, diets have been classified as being of high (15 %), intermediate (10 %) and low (5 %) Fe bioavailability, depending on the proportion of haem-Fe, and the presence of inhibitors and enhancers of non-haem-Fe absorption (Food and Agriculture Organization, 1988; DeMeyer *et al.* 1989). This variation in bioavailability has also led to a diversification of the recommended intakes of Fe (Table 5).

A low-bioavailability diet is characterized as a monotonous diet based on cereals and root vegetables with negligible quantities of fish, meat and ascorbic acid-rich foods. An intermediate-bioavailability diet is also based on cereals and root vegetables but contains ascorbic acid-rich food items and meat. A high-bioavailability diet is a diverse diet containing generous amounts of meat, poultry, fish and high amounts of ascorbic acid. This type of diet can easily become an intermediate-type diet if there is a regular

Table 4. Impact of iron nutritional status on the haem- and non-haem-iron absorption (% dietary iron absorbed) in a single meal (Cook, 1990)

Source of Fe	Normal men	Normal women	Fe-deficient subject
Haem	20	31	47
Non-haem	2·5	7·5	21

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Table 5. Recommended iron intakes (mg/d) for diets with different bioavailabilities (DeMayer *et al.* 1989)

Age (years) and sex	Type of diet with reference to bioavailability (classified according to % Fe absorbed): Very low (< 5)	Low (5–10)	Intermediate (11–18)	High (> 18
2–5	17	9	5	3
12–16: Girls	50	27	13	9
Boys	45	24	12	8
Adults: Females*	59	32	16	11
Males	28	15	8	5

* Menstruating.

consumption of inhibitors, e.g. tea, cereal fibres, beans and high-Ca foods.

Most of our knowledge today about Fe bioavailability in human subjects is based on studies using the extrinsic-tag radioFe technique with ^{55}Fe and ^{59}Fe (Cook *et al*. 1972; Hallberg & Björn-Rasmusson, 1972) for intrinsically- and extrinsically-labelled single meals. This ingenious methodology has been used almost to perfection by several authors, who in a series of studies have analysed the interaction between various Fe sources in the food and enhancers and inhibitors in normal mixed diets. Although this technique seems to represent a reasonable approach to the analysis of relative bioavailability in single foods and meals, the method has been criticized for not reflecting normal conditions, as the single meals tested usually are given as the first meal of the day after an overnight fast (Hurrell, 1997; Benita & Miller, 1998). Thus, Cook *et al*. (1991) introduced a method of labelling the complete diet during a 2-week period. Their results indicated a less pronounced effect (2·5-fold) of the most enhancing diet when compared with inhibitory diets, while a 6-fold difference was observed between the two diets using the single-meal technique. Results reported by Tidehag *et al*. (1996) as well as by Hallberg *et al*. (1997) also supported the proposal that all meals of the day should be labelled. Thus, results from the single-meal technique may exaggerate the interaction of enhancers and inhibitors.

Iron deficiency and excess: a public health dilemma?

A classical example of the dilemma between benefits and costs of Fe deficiency and excess is illustrated by the debate regarding Fe medication in subjects with malaria. Murray *et al*. (1975, 1978) reported that Fe medication could be a health risk in patients with malaria, as it seems to aggravate the disease. This possibility might be related to the increased release of reticulocytes in the blood as a result of increased erythropoesis, and a large increase in serum Fe from Fe supplementation which enhanced Fe availability to the plasmodium.

Another example of the dilemma of Fe balance is illustrated by the interaction between Fe deficiency and Fe excess and the immunological response (Brock, 1995). Since Fe represents a reactive nutrient which interferes with free-radical formation, both deficiency and excess could have an effect. While Fe deficiency might enhance the resistance to malaria and decrease the microbicidal activity in the neutrophils, it also depresses cell-mediated immunity (Chandra, 1975). Fe overload, on the other hand, seems to enhance the susceptibility to some infections and impair the phagocytic uptake of neutrophils, and saturation of neutrophil lactoferrin reduces their bactericidal activity (De Sousa, 1989). This finding is in agreement with the observation that Fe saturation of lactoferrin in milk reduces its bactericidal effect (Reiter, 1978; Hambraeus & Lönnerdal, 1994). Fe overload is also reported to affect the T-cell subsets and reduce tumouricidal activity (British Nutrition Foundation, 1995). However, there is much more to be learned about Fe and its involvement in immunological activities.

Iron excess: a public health risk?

There have been objections to the strategy of Fe fortification for public health reasons, based on the potential risk of inducing Fe excess and overload conditions leading to possible involvement in cancer and heart disease. However, this should not be an issue against Fe fortification in low-income countries where the risk of Fe deficiency is a dominant public health problem (Administrative Committee on Coordination/Sub-committee on Nutrition, 1997). Fortification might have further significance in affluent societies, where Fe medication could be a relevant alternative, since haemochromatosis is particularly prevalent, e.g. in central Sweden and northeast Italy, and certain groups in the USA. In these cases Fe fortification might lead to liver cirrhosis, increased rate of liver cancer and also myocardial dysfunction; diabetes has also been reported, although as a rare consequence. Fe fortification is still a matter for controversy (Lynch, 1995). Interestingly, nevertheless, in Sweden discussion of potential risks of Fe excess partly led to the withdrawal in 1994 of the general Fe fortification of wheat flour.

The cost of iron deficiency

Any efforts to counteract the development of Fe deficiency could be analysed in relation to gain in lifespan and productivity, the so-called disability-adjusted life year. The costs in life years gained from reduction in mortality and a life free of illness and disability, expressed as disability-adjusted life years, show that Fe fortification costs 4 US$ per disability-adjusted life year saved and Fe supplementation of pregnant women costs 13 US$ per disability-adjusted life year gained (World Bank, 1994; Viteri, 1998). Fe fortification could also be analysed in a short-term perspective, where the number of disability-adjusted life years is multiplied by the average annual income of the population that benefits from a fortification programme, and divided by the estimated cost of intervention, resulting in a benefit:cost value of 81 with respect to Fe-deficiency anaemia (Viteri, 1998; World Health Organization/United Nations Children's Fund/United Nations University, 1998).

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Dietary diversification, changes in food preparation or food supplementation?

It is a challenge to improve the Fe status of the world population in order to control Fe deficiency from a global perspective. Such improvement will require investigation of a number of different approaches, including anything from nutrition education to Fe fortification, Fe supplementation and reduction of parasitic infestations, as well as active public health programmes (Yip, 1997). However, there does not seem to be any single approach which could function as a golden standard.

As mentioned previously, it has been assumed that Fe deficiency in low-income countries is more a result of low bioavailability of dietary Fe than of low Fe intake *per se* (Bothwell *et al*. 1989). Thus, any actions to change dietary habits in favour of increasing Fe bioavailability in the diet are recommended (World Bank, 1994). However, such action requires changes in dietary habits leading to an increased intake of ascorbic acid, increased consumption of animal products, and/or changes in food preparation in order to reduce the content of inhibitors, e.g. phytic acid in wholemeal flour. This type of change is in agreement with the general principle supported by most nutritionists that nutrient deficiencies should be solved primarily by changes in the dietary habits. However, such actions involve costs which cannot always be met, or are unrealistic in low-income countries as they require increased food availability for the population as well as better nutrition education programmes. This approach necessitates an active national or even international food and nutrition policy, and governmental actions which may involve considerable socio-economic costs. Furthermore, all these actions may only give results in a long-term perspective, which might be too long term for those low-income countries where Fe deficiency represents a great public health problem.

Thus, in a short-term perspective there might not be any other solution than the use of Fe supplementation, in some cases in combination with deworming in order to reduce the stress on Fe status from intestinal parasites. This approach has been tested in a number of low-income countries and it was found that the direct costs of distributing nutrients as supplements or as fortified foods are relatively low, 0·12 US$ per person in 1994 (at the US$ value of that year; World Bank, 1994).

The complex situation regarding the outcome of prevention of Fe deficiency may also be illustrated from the experience gained throughout this century in an affluent society such as Sweden. In the 1920s Fe deficiency in preschool children and schoolchildren in northern Sweden was much more prevalent than it is today when Fe-deficiency disease is rare among children in this region (Samuelson & Sjölin, 1972). However, the extent to which this outcome is a result of better dietary habits, better socio-economic conditions or Fe fortification of infant foods and gruel is unknown.

Fe fortification of cereals, especially wheat flour, which has an extraction rate of 70 % in Sweden, was introduced in the 1940s. It then continued until January 1994 when, after some discussion, it was ended. Nevertheless, Fe deficiency has been reported to occur in about 30 % of females of reproductive age (Hallberg & Hultén, 1986). There is little if any difference when compared with the situation in other Nordic countries, e.g. Norway, which has not had any Fe fortification of wheat flour, but has had very similar dietary habits. It has been argued that this negative finding in Sweden is a result of using an Fe supplement which has too low a bioavailability (Hallberg *et al*. 1986). Another reason could be that the vehicle used, wheat flour, does not represent the optimal vehicle to reach the target group. We are now following with great interest the possible changes in Fe status of the Swedish population after the cessation of Fe fortification of wheat flour. The only preliminary findings so far obtained indicate that at least there has been less need for bleeding of individuals with haemochromatosis and polycythemia vera during the last few years (Olssen *et al*. 1997). This might at least indicate that the bioavailability of the fortification Fe was not as low as suggested.

There is, however, a need for a holistic view of the nutritional problem which is illustrated in the case of Ca–Fe interaction. The interpretation of interaction between inhibitors such as Ca and Fe bioavailability might lead us into another dilemma. A high Ca intake is common in societies with a high consumption of dairy products, i.e. in the industrialized countries. From the Fe point of view, single-meal studies seem to indicate that consumption of dairy products should be decreased as Ca affects the bioavailability of Fe. However, decreasing consumption of dairy products might lead to increased problems of osteoporosis in old age, which at present represents a very acute public health problem of increasing importance in affluent societies, and requires increased rather than decreased consumption of Ca-rich food items, at least in the first two to three decades of life. Studies using totally mixed meals over a period of days seem to indicate that the practical implications of this Ca–Fe interaction have been somewhat overestimated, which of course has great practical implications for dietary counselling.

It is still an open question as to which is the most appropriate approach to deal with these two predominant nutritional problems in an affluent society: Fe fortification and/or supplementation for those in need, or reduced consumption of dairy products, which has then to be compensated for by Ca supplementation. The long-term effect of a lower optimal Ca intake on osteoporosis *v.* the acute effect of Ca as an inhibitor of Fe bioavailability has to be carefully evaluated.

Conclusion

Fe deficiency is still one of the dominant nutrient deficiencies from a global perspective. Analysis of data seems to indicate that it is always due to some form of insufficient intake of Fe, which does not meet normal or increased Fe requirements as result of increased Fe turnover.

It is obvious that the bioavailability of Fe in the diet is of utmost importance. Thus, in the long-term, dietary modification through increased consumption of specific foods which contain Fe with high bioavailability, or changes in food preparation procedures such as fermentation, can be beneficial. Consumption of components that enhance the

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bioavailability of non-haem-Fe should also be recommended. However, since Fe deficiency is still of relevance in affluent societies with an abundance of food and high intake of animal foods, it seems that this approach is not the only solution. Fortification may still be beneficial. As overconsumption of fortified foods may be a potential problem, there is a need for guidelines for monitoring food fortification. A better understanding of the physiological regulation of Fe absorption and bioavailability is urgently needed.

Most of the world population base their diet on vegetable sources, and the Fe intake *per se* from vegetable sources may be adequate. Nevertheless, the dietary intake of Fe may not satisfy the Fe requirements of a large percentage of menstruating women due to the low bioavailability. This situation seems to be valid for populations in both low-income countries and certain population groups in affluent societies.

Despite all efforts to counteract Fe deficiency, it still represents one of the predominant problems in the micronutrient sphere. Obviously there is no simple solution to the problem, and the fact that Fe deficiency still occurs in affluent societies consuming a mixed diet with no real problems of food availability speaks for itself. A more holistic view of total dietary composition and the role of enhancers and inhibitors, and of physiological regulation are needed before we can draw any conclusions regarding the role of meat or wheat in the Fe status of man.

References

Administrative Committee on Coordination/Sub-committee on Nutrition (1992) *Second Report on the World Nutrition Situation*, vol. 1, *Global and Regional Results*. New York: ACC/SCN.

Administrative Committee on Coordination/Sub-committee on Nutrition (1997) *Major Issues in Developing Effective Approaches for the Prevention and Control of Iron Deficiency*. New York: UNICEF.

Allen LH & Ahluwalia N (1997) *Improving Iron Status Through Diet. The Application of Knowledge Concerning Dietary Iron Bioavailability in Human Populations. John Snow Inc/OMNI Project.* Washington, DC: USAID.

Baynes RD & Bothwell TH (1990) Iron deficiency. *Annual Review of Nutrition* **10**, 133–148.

Becker W (1994) *Befolkningens Kostvanor och Näringsintag i Sverige 1989 (Food Consumption and Nutrient Intake in Sweden 1989)*. Uppsala: Statens Livsmedelsverk.

Benito P & Miller D (1998) Iron absorption and bioavailability. An updated review. *Nutrition Research* **8**, 561–603.

Bothwell TH, Baynes RD, MacFarlane BJ & MacPhail AP (1989) Nutritional iron requirements and food iron absorption. *Journal of Internal Medicine* **226**, 357–365.

British Nutrition Foundation (1995) *Iron. Nutritional and Physiological Significance. The Report of the British Nutrition Foundation's Task Force.* London: Chapman & Hall.

Brock JH (1995) Iron in infection and immunity. In Iron Nutritional and Physiological Significance, pp. 58–64 [British Nutrition Foundation, editors]. London: Chapman & Hall.

Chandra RJ (1975) Impaired immunocompetence associated with iron deficiency. *Journal of Pediatrics* **86**, 899–902.

Cook JD (1990) Adaptation in iron metabolism. *American Journal of Clinical Nutrition* **51**, 301–308.

Cook JD, Dassenko SA & Lynch SR (1991) Assessment of the role of non-heme iron availability in iron balance. *American Journal of Clinical Nutrition* **54**, 717–722.

Cook JD, Layrisse M, Martinez-Torres L, Walker R, Monsen E & Finch CA (1972) Food iron absorption measured by an extrinsic tag. *Journal of Clinical Investigation* **51**, 805–815.

DeMayer EM, Dallman P, Gurney JM, Hallberg L, Sood SK & Srikantia SG (1989) *Preventing and Controlling Iron Deficiency Anaemia Through Primary Health Care. A Guide for Health Administrators and Programme Managers.* Geneva: WHO.

Department of Health and Human Services (1981) *NHANES II (National Health and Nutrition Examination Survey, Second, 1976–1980). Haematology and Biochemistry, Age 6 months–74 years*. Hyattsville, MD: US Department of Health and Human Services, National Center for Health Statistics.

De Sousa M (1989) Immune cell function in iron overload. *Clinical and Experimental Immunology* **75**, 1–6.

Food and Agriculture Organization (1990) *Food Production Yearbook*. Rome: FAO.

Food and Agriculture Organization/World Health Organization (1988) *Requirements of Vitamin A, Iron, Folate, and Vitamin B_{12}. Report of a Joint FAO/WHO Expert Consultation. FAO Food and Nutrition Series* no. 23. Rome: FAO.

Hallberg L & Björn-Rasmusson E (1972) Determination of iron absorption from the whole diet. A new two-pool method using two radioiron isotopes given as haem and non-haem iron. *Scandinavian Journal of Haematology* **9**, 193–197.

Hallberg L, Brune M & Rossander L (1986) Iron bioavailability of carbonyl iron in man: Studies on iron fortification of wheat flour. *American Journal of Clinical Nutrition* **43**, 59–67.

Hallberg L & Hultén L (1996) Iron requirements, iron balance and iron deficiency in menstruating and pregnant women. In *Iron Nutrition in Health and Disease. Swedish Nutrition Foundation 20th International Symposium*, pp. 165–181 [L Hallberg and N-G Asp, editors]. London: John Libbey & Co.

Hallberg L, Hultén L & Gramatkovski E (1997) Iron absorption from the whole diet in men: how effective is the regulation of iron absorption? *American Journal of Clinical Nutrition* **66**, 347–356.

Hambraeus L & Lönnerdal B (1994) The physiological role of lactoferrin. *Proceedings of the IDF Seminar on Indigenous Antimicrobial Agents of Milk–Recent Developments*, pp. 97–107. Brussels: International Dairy Federation.

Hurrell RF (1997) Bioavailability of iron. *European Journal of Clinical Nutrition* **51**, Suppl. 1, S4–S8.

Lynch SR (1995) Iron overload: Prevalence and impact on health. *Nutrition Reviews* **53**, 255–260.

Ministry of Agriculture, Fisheries and Food (1994) *National Food Survey 1993*. London: H. M. Stationery Office.

Martinez-Torres C, Renzi M & Layrisse M (1976) Iron absorption by humans from haemosiderin and ferritin. Further studies. *Journal of Nutrition* **106**, 128–135.

Murphy SP, Beaton GH & Calloway DH (1992) Estimated mineral intakes of toddlers: Predicted prevalence of inadequacy in village populations in Egypt, Kenya and Mexico. *American Journal of Clinical Nutrition* **56**, 565–572.

Murray MJ, Murray AB, Murray NJ & Murray MB (1975) Refeeding malaria and hyperferraemia. *Lancet* **i**, 653–654.

Murray MJ, Murray AB, Murray NJ & Murray MB (1978) The adverse effect of iron repletion on the course of certain infections. *British Medical Journal* **2**, 1113–1115.

Olssen KS, Väisänen M, Konar J & Bruce A (1997) The effect of withdrawal of food iron fortification in Sweden as studied with phlebotomy in subjects with genetic hemochromatosis. *European Journal of Clinical Nutrition* **51**, 782–786.

Pawlowski ZS, Schad GA & Stott GJ (1991) *Hookworm Infection and Anaemia. Approaches to Prevention and Control*. Geneva: WHO.

Reiter B (1978) Review of the progress of dairy science: antimicrobial systems in milk. *Journal of Dairy Research* **45**, 131–147.

Samuelson G & Sjölin S (1972) An epidemiological study on child health and nutrition in a Northern Swedish county. IV. Haematological investigation especially in regard to iron deficiency anaemia. *Acta Paediatrica Scandinavica* **61**, 63–73.

Tidehag P, Hallmans G, Wing K, Sjöström R, Ågren G, Lundin E & Zhang J (1996) A comparison of iron absorption from single meals and daily diets using radioFe (^{55}Fe^{59}Fe). *British Journal of Nutrition* **75**, 281–289.

Viteri FE (1998) Prevention of iron deficiency. In *Prevention of Micronutrient Deficiencies. Tools for Policymakers and Public Health Workers*, pp. 45–102 [CP Howson, ET Kennedy and A Horwitz, editors]. Washington, DC: National Academy Press.

World Bank (1994) *Enriching Lives. Overcoming Vitamin and Mineral Malnutrition in Developing Countries*. Washington, DC: World Bank.

World Health Organization (1970) *Requirements of Ascorbic Acid, Vitamin D, Vitamin B_{12}, Folate and Iron. Technical Report Series* no. 542. Geneva: WHO.

World Health Organization/United Nations Children's Fund/United Nations University (1998) *Consultation on Iron Deficiency: Indicators and Strategies for Iron Deficiency Control Programmes*. Geneva: WHO (In the Press).

Yip R (1997) The challenge of improving iron nutrition: limitations and potentials of major intervention approaches. *European Journal of Clinical Nutrition* **51**, S16–S24.

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