Bulletin of the World Health Organization, **57** (6): 947-954 (1979)

An analysis of factors leading to a reduction in iron deficiency in Swedish women *

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The prevalence of iron deficiency anaemia among Swedish women of child-bearing age has fallen markedly since the mid-1960s. At that time, population studies in Göteborg and Uppsala showed that iron deficiency anaemia was present in about 25–30% of women. Later, in population studies in Göteborg in 1968–69 and 1974–75, the prevalence in the same age group was found to have fallen to 6–7%. Several factors may explain the improved iron status. The level of iron fortification of flour was increased from 30 mg/kg of flour in 1943 to 65 mg in 1970, this increase adjusting the iron intake to compensate for the lower energy requirement and expenditure of present-day living habits. There has also been a marked increase in the intake of iron tablets and of tablets containing ascorbic acid.

An analysis of various factors indicates that the 20–25% improvement in iron status can be accounted for by increased use of oral contraceptives (3–4%), the impact of increased iron fortification (7–8%), the widespread use of ascorbic acid supplements (3%), and greater prescribing of iron tablets (10%).

This analysis of the factors leading to the marked reduction in the prevalence of iron deficiency anaemia among Swedish women may be useful to public health planners in other countries with similar problems. Our results indicate that several factors need to be considered when planning controlled field trials and evaluating the results obtained. The methods used to analyse the impact of different factors on the reduction in iron deficiency can also be used to predict the effects of various public health measures on the iron status of a population.

Iron deficiency is one of the commonest deficiency diseases in the world. Awareness of its importance has increased, not least because of its negative effects on physical working capacity (*1, 2*) and the fact that in the countries in which iron deficiency anaemia is most widespread, the human body is the most important "machine" in both industrial production and agriculture.

In Sweden, the prevalence of iron deficiency in women was investigated in the mid-1960s in two population studies, one in Göteborg (*3*) and the other in Uppsala (*4, 5*). These two studies showed a high, and approximately equal, prevalence of anaemia. They also showed that the anaemia was due mainly to iron deficiency. In the Göteborg study, the iron deficiency was established by examination of bone marrow smears for stainable iron, while in Uppsala the response to treatment with iron or placebo was studied.

Since the mid-1960s several changes have occurred that might influence the incidence of iron deficiency among women in Sweden. For example, oral contraceptives have now become widely available and it is known that they generally reduce menstrual losses of iron; on the other hand, intrauterine devices increase menstrual losses. In addition, iron fortification of flour has increased in the past decade. More recently, a new group of women from the population of Göteborg was studied, first in 1968–69 (*6, 7*) and again in 1974–75 (*8*). These

* This research was supported by Swedish Medical Research Council (MFR) Project B78-19X-04721-03A and Project B75-27X-4578-01.

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studies showed a dramatic reduction in the frequency of anaemia. Although evaluation of the data has not yet been completed, this report will summarize some of the results so far available, particularly in respect to the prevalence of anaemia. Possible reasons for the marked reduction in iron deficiency will be discussed.

THE 1963–64 STUDY IN GÖTEBORG

In this study, women aged between 15 and 75 years, born on certain days in certain years were selected at random from the census register. In this report, only data from women of child-bearing age will be discussed and the emphasis will be placed on age groups that are of interest for comparison with the later studies in 1968–69 and 1974–75.

In the 1963–64 study, a thorough case history was recorded and the women were subjected to a complete clinical examination and extensive laboratory tests. In most women, this included a detailed dietary history, a gynaecological examination, measurement of menstrual losses, anthropometric measurements, and a bone marrow puncture, which was examined for stainable iron. The results of these investigations have been presented in several previous reports (*3, 9–15*). The prevalence of anaemia in the age-groups 35, 40, and 45 years is shown in Table 1. Anaemia was defined as haemoglobin (Hb) <120 g/litre. The mean prevalence was 24.6%.

THE 1966 STUDY IN UPPSALA

This study involved 5683 women aged between 16 and 46 years. The sample was derived from a general health study carried out in the County of Uppsala in 1966 (*4*). Over 70% of the population participated. Haematocrit was measured (duplicate determinations).

Conversion of haematocrit values to haemoglobin concentration was based on a separate study of the relationship between Hb and haematocrit in women (Hb in g/litre = 4.02 × haematocrit value (%) − 31.0). The prevalence of anaemia (Hb <120 g/litre, corresponding to haematocrit <38%) for all the subjects studied was 31%.

THE 1968–69 AND 1974–75 STUDIES IN GÖTEBORG

The prevalence of anaemia was studied in five age groups in 1968–69 (38, 46, 50, and 60 years). Conventional haematological investigations were performed in all subjects (haemoglobin concentration, haematocrit, red cell count, red cell indices, plasma iron, transferrin saturation). In addition, more extensive investigations were carried out in the 38-year-old women; these included measurement of menstrual losses, a bone marrow evaluation, and studies of the women's capacity to absorb iron using a whole-body counter. The prevalence of anaemia in 1968–69 was markedly lower than in 1963–64; on the average, it was 6.6% for women in the 38- and 46-year age groups.

Table 1. Prevalence of anaemia (Hb < 120 g/litre) in Swedish women in three population studies in Göteborg

Year of study	Prevalence of anaemia(%) in women in age groups (years):		
	35	38–40[a]	44–46[b]
1963–64	17.6	30.8	25.2
1968–69	–	5.1	7.7
1974–75	–	–	7.4

[a] The women's ages were 40 years in the 1963–64 study and 38 years in the 1968–69 study.

[b] The women's ages were 45 years in the 1963–64 study, 46 years in the 1968-69 study, and 44 years in the 1974–75 study.

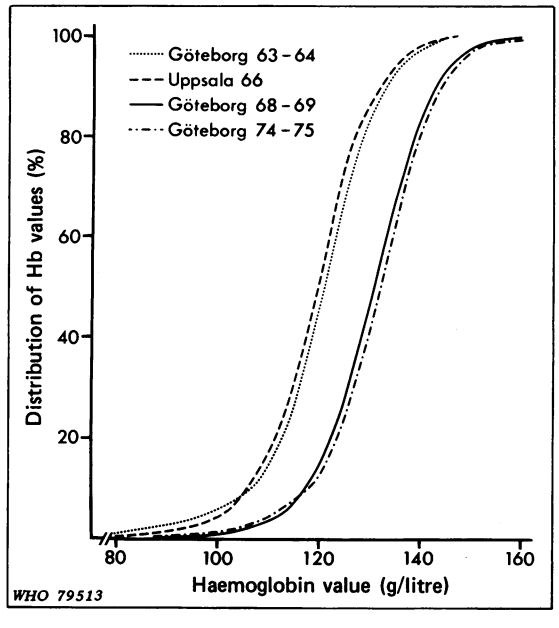

Fig. 1 Cumulative distribution of haemoglobin values in Swedish women in 4 population studies in Sweden: Göteborg 1963–64 (age groups 35, 40, and 45 years), Uppsala 1966 (16–46 years), Göteborg 1968–69 (38 and 46 years) and Göteborg 1974–75 (44 years).

Table 2. Mean haemoglobin values and prevalence of anaemia (Hb < 120 g/litre) in four population studies of women in Sweden

Place	Year	Age	Number of subjects	Haemoglobin (g/litre)	
				Mean value	%<120 g/litre
Göteborg	1963-64	35	91	127	17.6
		40	91	123	30.8
		45	107	124	25.2
		total	289	125	24.6
Uppsala[a]	1966	32-36	1014	125	–
		37-41	1015	125	–
		42-46	1023	125	–
		16-46	5683	125	31
Göteborg	1968-69	38	372	135	5.1
		46	431	135	7.7
		total	803	135	6.5
Göteborg	1974-75	44	326	136	7.4

[a] In the Uppsala study, no information is available about the prevalence of anaemia in separate age groups.

In 1974–75, these same women were recalled for a further study. The same haematological investigations were done and again the prevalence of anaemia (Hb<120 g/litre) was low; in the 44-year-old subjects, who were aged 38 years at the time of the previous study, the prevalence was 7.4%.

COMPARISON BETWEEN DIFFERENT YEARS

The distributions of haemoglobin values in women aged 35–45 years in Göteborg in 1963–64 and in women aged 16–46 years in Uppsala in 1965 were practically identical (Fig. 1). The bone marrow studies done in Göteborg (*3*) and studies using iron supplementation in Uppsala (*5*) clearly show that this anaemia was primarily due to iron deficiency. As shown in Fig. 1 and Table 1, the 1968–69 and 1974–75 studies showed a distinctly lower prevalence of anaemia (Hb<120 g/litre). The mean values for haemoglobin are also significantly different from those obtained in 1963–64 (Table 2). The mean heamoglobin value had increased by about 10 g/litre.

REASONS FOR OBSERVED DECREASE IN IRON DEFICIENCY ANAEMIA

In analysing various possible explanations for the reduction in iron deficiency anaemia, various factors have to be considered (Table 3).

Table 3. Theoretical causes of observed reduction in prevalence of anaemia in Sweden

*Observed difference **not true**:*
- *Systematic errors* related to
  - sampling of subjects
  - measurement of haemoglobin
    - sampling of blood
    - analytical errors (standardization)

*Observed difference **true**:*
- *A reduction in iron losses*
  - reduction in menstrual iron losses (due to oral contraceptives)
  - reduction in number of pregnancies
- *An increase in iron absorption*
  - a better composition of the diet (e.g., more meat, fish, etc.)
  - an increased level of efficacy of iron fortification
  - increased use of pharmaceutical iron
  - other factors (e.g., increased intake of ascorbic acid)

Methodological errors

A systematic sampling error is unlikely since the subjects were selected at random from the total population (subjects born on certain days were drawn from the census register) and the drop-out from the original sample was low (less than 10% in all studies in Göteborg). Furthermore, the comparison is made between women of similar age groups, obviously an important aspect of any haematological study in women.

Another potential source of error could be the determination of haemoglobin concentration, which could involve both sampling errors and analytical errors. In the Göteborg studies, the same laboratory was used on each occasion and the manner of blood

sampling was uniform with regard to position of the patient, avoidance of prolonged blood stasis, and use a wide-bore needle. The measurements were made using the International Haemiglobincyanide Reference Preparation. It therefore seems very improbable that methodological errors could account for the observed reduction in anaemia.

Reduced iron losses

Menstrual losses. All oral contraceptives used in Sweden today reduce the menstrual iron losses by about 50%. In the 1963–64 study, only 1 woman in the 30-year age group was using oral contraceptives. In 1968–69, 11.7% of 38-year-old women and 1.7% of the 46-year-olds were using oral contraceptives. These numbers increased by 12.7% and 5.8% respectively if any previous use of contraceptives was included. In 1974–75, about 8% of the 44-year-old women were taking oral contraceptives.

Table 4. Average consumption of foodstuffs per capita per day, energy content, and iron content in the diet in 1960, 1965 and 1973[a]

	1960	1965	1973
Consumption (g per person per day)			
Vegetables	43	60	74
Fruit	211	211	205
Meat	128	132	131
Fish	51	51	49
Bread, flour, cereals	198	188	176
Total energy content in the diet (MJ/day)	12.4	12.5	12.2
Iron content in the diet (mg/day)			
Native	11	12	11
Fortification iron	3	5	8
Total iron content of diet	14	17	19
Correction for 50% bioavailability of most fortification iron used	−1.5	−2.5	−4
Total bioavailable iron	12.5	14.5	15
Nutrient density of iron (mg/4 MJ)			
Uncorrected	4.5	5.4	6.2
Corrected for biovailability of fortification iron	4.0	4.6	4.9

[a] Based on information from the National Swedish Agricultural Marketing Board (sales statistics) and on studies on bioavailability of fortification iron (*19*).

Some women had been given the pill because of menorrhagia, but in most instances the administration was unrelated to the size of the menstrual loss. It can thus be calculated that out of the 30 women per 100 who were iron deficient in the late 1960s, 3–4 were subsequently on the pill and this may have accounted for a reduction in their menstrual iron losses.

Intrauterine devices (IUDs) increase menstrual losses by about 50%. The effect of the gradually increasing use of IUDs has not been considered in the present analysis.

Pregnancy. A full-term pregnancy has a profound influence on the woman's iron balance and iron supplementation is therefore recommended as a routine in Sweden. The number of pregnancies, previous or recent, was about the same in the age range 35–46 years, the group that was used in the detailed comparative analysis. A change in the frequency of pregnancy is therefore unlikely to have had any significant influence on the prevalence of anaemia. There was no difference in the frequency of abortions.

Increased absorption of iron

Dietary habits. There is no evidence that dietary habits have improved during the last 10–15 years in respect of iron nutrition. As shown in Table 4, there has not been any increase in the intake of fish, meat, or fruits that might have increased the absorption of iron from the diet. Table 4 shows that the increased intake of iron via food is due entirely to increased iron fortification. The haem iron intake is close to 1.5 mg, of which 0.5 mg is derived from blood sausage.

Iron fortification of foodstuffs. Sweden was one of the first countries to adopt iron fortification. Fortification of wheat flour with iron was introduced in 1944. The enrichment level was then 30 mg per kg of flour. In 1963, when the first population study was carried out, the level was raised to 50 mg and enrichment was extended to all sifted flours, including ryé flour. In 1970, the level was raised to 65 mg per kg of sifted flour. The fraction of the total daily iron intake that comes from fortification iron has increased from 21% (1960) to 42% (1973). It has been possible to calculate that about 50% of the fortification iron used at present (mainly reduced carbonyl iron) is bioavailable (*19*). Using this figure, the proportion of "effective" fortification iron has increased from almost 12% to about 27% of the total daily intake of available iron. Fortification iron

thus forms an important part of the iron on the diet (Table 4). This increase in "effective" daily iron intake of 2.5 mg over the period 1960–73 would correspond to an increase in iron absorption of about 0.3 mg in subjects on the borderline between normality and iron deficiency. From the known distribution of iron requirements in women, it can be calculated that increased absorption could account for improvement in 7–8% of the original 30% of iron deficient women in Sweden in the mid-1960s. (For the principles underlying these calculations see Hallberg, *16*.)

Use of iron tablets. The high prevalence of iron deficiency among Swedish women in the mid-1960s was rapidly brought to the attention of the medical profession. The interest of the general public was also awakened by factual information provided by the mass media. Owing to the availability of reliable sales statistics for pharmaceutical products, it has been possible to study retrospectively the distribution of oral iron products. The statistics cover only the period from 1965, however.

As will be seen from Table 5 the sales of iron products, expressed as kilograms of iron, increased greatly during the study period. The figures represent all pharmaceutical products containing iron, including combination drugs. The iron intake per day per capita is high but it is not evenly distributed over all individuals in the community. It is relatively low in children and the elderly and is substantially higher in women than in men. The use of iron tablets is particularly high in young women of child-bearing age (15–30 years). The daily intake of iron per capita is higher in Sweden than it is in the United Kingdom, Federal Republic of Germany, and France. We have not been able to discover whether the statistical methods for measuring consumption of drugs differ or whether there is a true difference in consumption.

Table 5. Sale of oral preparations containing iron in Sweden[a] and countries of western Europe

Year		Total sales (kg)	Fe intake (mg per day per capita)
1965		8 314	2.9
1970		13 595	4.7
1974		17 269	5.8
1975[b]	England		1.0
	Federal Republic of Germany		0.7
	France		0.7

[a] From Swedish Drug Market (SDM).
[b] From International Medical Statistics Ltd (IMS).

The intake of iron tablets has also been ascertained in the population studies done in Göteborg by means of interviews.[a] As shown in Table 6 the proportion of women who had taken iron during the last 12 months increased by about 10%. This information is important since increased sales need not necessarily mean an increased consumption. However, the increase in sales between 1963–64 and 1968–69 (63%) is in good agreement with the increased proportion of women who have taken iron (67%, see Table 6). The fact that iron sales increased until 1974, although the proportion of women using iron stayed constant, suggests an increase in either the dose of iron or the duration of treatment. Increased use of iron by other groups, e.g., blood donors, must also be considered. A market analysis carried out in 1975 showed that about 60% of the sales of pharmaceutical iron-containing products were on prescription.

If it is assumed that about 30% of the iron purchased is not taken, the average daily iron intake, via tablets, in women of child-bearing age rose from about 10 mg in 1965 to 15 mg in 1970 and 20 mg in 1974. Since not all women take iron, and since those who take iron generally do so periodically, e.g., 3–6 months per year, the dose actually used may be calculated to be of the order of 100–300 mg per day, which is consistent with the commonly recommended dosage of iron in Sweden.

Table 6. Intake of iron tablets: proportion of women in Göteborg who had taken iron tablets during the 12 months preceding the examination

Year	Age (years)	Women taking iron tablets (%)	Index
1963–64	35–45	16.9	100
1968–69	38–46	28.2	167
1974–75	44	25.7	150

Intake of ascorbic acid. A further factor to consider is the intake of ascorbic acid. There has been a very marked increase in the intake of tablets containing ascorbic acid, either as multivitamin tablets or as ascorbic acid alone, often in large doses. In Sweden, 233 million doses are now taken yearly.

[a] The data are based on a market study carried out by SEMKA AB in May, 1975.

This might mean that 10% of the population over 14 years of age consume 35 mg or more of ascorbic acid each day in tablet form. However, since ascorbic acid is usually taken during certain periods of the year, principally in the winter, it could be that about 40% of the population take it for 3 months of each year.

From what is known of the potential effect of vitamin C on iron absorption, it is possible to calculate that this could imply a 4.3-fold increase in the weighted mean absorption of iron. Dividing this figure by 10 (10% of the population) and by a factor of 3 (as ascorbic acid is generally taken with only 1 of 3 meals) the average increase in absorption of iron in the total population would be 10–15%. In the adult female population this would give an average increase in iron absorption of about 0.2 mg/day. From the known distribution of iron requirements, this means that it might reduce the prevalence of iron deficiency in women of fertile age by 5% in Sweden. This calculation assumes an even distribution in the whole population for the intake of ascorbic acid tablets. As this is undoubtedly not true, the real effect is probably much less than 5%, perhaps more realistically 3%.

RELATIVE IMPORTANCE OF VARIOUS FACTORS IN EXPLAINING THE REDUCTION IN PREVALENCE OF ANAEMIA

The actual reduction in prevalence of anaemia is from about 25–30% to 6–7%, i.e., about 20%. Fig. 2 summarizes the calculated contribution of the different factors discussed. Adding together the expected effects of contraceptive pills (3–4%), the benefits of increased iron fortification of flour (7–8%), and the effects of increased intake of ascorbic acid tablets (3%) would account for about half the reduction in prevalence and the remaining 10% would be due to the increased intake of iron tablets, which would thus have the greatest single impact.

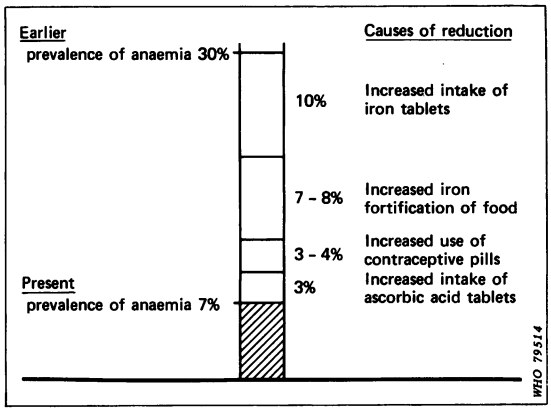

Fig. 2. Factorial analysis of causes of reduction in prevalence of anaemia in Swedish women of fertile age.

Although there are strong indications that iron tablets are often taken for the right indication, we do not know how many women take iron tablets unnecessarily. Nor do we know with certainly how many women in need of extra iron do not take iron tablets.

DISCUSSION

Since the prevalence of iron deficiency anaemia in Swedish women is still about 7% it is necessary to continue stressing the importance of good dietary habits, to pursue efforts to make iron fortification more effective, and to prescribe iron products for the right therapeutic and prophylactic indications. If these measures were to be neglected, there would be a great risk of the prevalence rising once more.

Knowledge about the negative effects of iron deficiency is incomplete. During the last few years research in this field had been intensified. It seems quite clear that chronic iron deficiency anaemia reduces the individual's physical working capacity (*1, 2*).

The body has extremely efficient and ingenious ways of maintaining homoeostasis and optimal function, including, at the haemoglobin level, a combination of mechanisms to ensure transport of oxygen to the tissues. Until the contrary is proved, it is reasonable to accept the appropriateness of this natural system and to take steps to enable the individual to maintain his or her optimal haemoglobin value. The measures taken must naturally be assessed in relation to the cost and possible risks.

In the USA, there is at present much discussion about the possible risks of increasing the enrichment level of flour to 88 mg/kg. As this paper shows, the iron intake in Sweden is considerably higher than would be achieved in the USA by increased fortification and it has been at this higher level for a long period—more than 10 years. Studies in Sweden to detect any ill effects of increased iron intake would therefore be of great international interest. In a certain area in northern Sweden, several cases of iron overload in men have been observed (*20*). The relationship between this and the increased level of

iron fortification in Sweden is unclear. In recent population surveys in other parts of Sweden and in our search during the last decades for patients with haemochromatosis, we have been able to trace only a few cases in western Sweden and there is no suggestion of a rising incidence of this disease. A more systematic search for iron overload in the Swedish male population seems warranted, however, especially as serum ferritin assays may be an accurate new screening device.

The balance of evidence indicates that during the last 50 years or more there has been a significant reduction in Sweden in energy expended in jobs and during leisure time. It has been shown that for decades there has been a linear relation between the daily energy intake (energy expenditure) and the intake of many nutrients, including protein, calcium, vitamin A, thiamine, and iron (*17, 18*). It would seem essential to change the nutrient density of the diet in such a way that requirements for specific nutrients, such as iron, can be met by an intake of 8.4 MJ rather than the 12.55 MJ previously necessary. The increase in the level of iron fortification in Sweden should thus be considered as an adjustment of the dietary composition to the change in living habits.

ACKNOWLEDGEMENTS

The authors wish to thank Juris Purens and Mikael Lindahl, AB Hässle, for obtaining and processing the sales statistics presented in this article.

RÉSUMÉ

ANALYSE DES FACTEURS À L'ORIGINE D'UNE DIMINUTION DE L'ANÉMIE FERRIPRIVE CHEZ LES FEMMES SUÉDOISES

La prévalence de l'anémie ferriprive chez les femmes suédoises d'âge fertile a diminué sensiblement depuis le milieu des années 60. A l'époque, des études faites dans la population à Göteborg et à Uppsala avaient montré qu'environ 25 à 30% des femmes souffraient d'anémie ferriprive. Par la suite, des études faites à Göteborg en 1968–1969 et en 1974-1975 ont montré que le taux de prévalence de l'anémie ferriprive dans le même groupe d'âge était tombé de 6 à 7%. Plusieurs facteurs peuvent expliquer l'amélioration de la situation à cet égard. Le degré d'enrichissement en fer de la farine a été porté de 30 mg/kg en 1943 à 65 mg/kg en 1970, cette augmentation de l'apport de fer constituant un ajustement à la diminution des besoins et des dépenses énergétiques résultant du mode de vie actuel. Il y a également eu une augmentation marquée de la consommation de comprimés contenant du fer ou de l'acide ascorbique.

Une analyse de divers facteurs indique que 20 à 25% de l'amélioration de la situation en ce qui concerne la teneur en fer du sang peut être attribuée à l'utilisation plus fréquente de contraceptifs oraux (3 à 4%), à l'effet d'un enrichissement accru en fer des aliments (7 à 8%), à la généralisation de l'utilisation de suppléments nutritifs contenant de l'acide ascorbique (3%) et à la prescription plus fréquente de comprimés contenant du fer (10%).

Une analyse des facteurs entraînant une diminution sensible de la prévalence de l'anémie ferriprive chez les femmes suédoises peut être utile aux planificateurs de la santé publique dans d'autres pays où des problèmes analogues se posent. Nos résultats montrent que plusieurs facteurs doivent être pris en considération lors de la planification d'épreuves de terrain contrôlées et de l'évaluation des résultats obtenus. Les méthodes utilisées pour analyser l'incidence de différents facteurs sur la diminution de l'anémie ferriprive peuvent également être employées pour prévoir les effets de diverses mesures de santé publique sur les carences en fer dans la population.

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