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ORIGINAL ARTICLE

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Iron status in Danes updated 1994. I: Prevalence of iron deficiency and iron overload in 1332 men aged 40–70 years. Influence of blood donation, alcohol intake, and iron supplementation

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Abstract Iron status, S-ferritin, and hemoglobin (Hb) were assessed in a population survey in 1994 (DAN-MONICA 10) comprising 1332 Caucasian Danish men equally distributed in age cohorts of 40, 50, 60 and 70 years. Blood donors ($n=186$) had lower S-ferritin, median 76 μg/l, than nondonors, median 169 μg/l ($p<0.0001$). S-ferritin in donors was inversely correlated with the number of phlebotomies ($r_s=-0.57$, $p<0.0001$). S-ferritin in nondonors ($n=1146$) was similar in men 40–60 years of age, median 176 μg/l, and subsequently decreased at 70 years of age to a median of 146 μg/l ($p=0.01$). In the entire series, the prevalence of small iron stores (S-ferritin 16–32 μg/l) was 2.7%, that of depleted iron stores (S-ferritin <16 μg/l) 0.45%, and that of iron deficiency anemia (S-ferritin <13 μg/l and Hb <129 g/l) 0.15%. Among nondonors, the prevalence of iron overload (S-ferritin >300 μg/l) was 20%. S-ferritin in nondonors correlated with body mass index ($r_s=0.19$, $p=0.0001$) and with alcohol intake ($r_s=0.26$, $p=0.0001$). In the entire series, 28% of the subjects took supplemental iron (median 14 mg ferrous iron daily). Iron supplements had no influence on iron status. Nondonors ($n=170$) treated with acetylsalicylic acid had lower S-ferritin, median 136 μg/l, than nontreated, median 169 μg/l ($p<0.001$) and those treated with H_2-receptor antagonists ($n=30$) had lower S-ferritin, median 142 μg/l, than nontreated, median 171 μg/l ($p<0.04$). Compared with the DAN-MONICA 1 iron status survey of Danish men in 1984, the prevalences of iron depletion and iron deficiency anemia are unchanged whereas the prevalence of iron overload has increased significantly. In Denmark, iron fortification of flour was abolished in 1987. This apparently had no negative effect on iron status in men.

Key words Ferritin · Iron deficiency · Iron fortification · Iron metabolism · Iron overload · Men

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Introduction

For the planning of iron fortification programs, it is necessary to perform regular monitoring of iron status of populations and population subgroups. Assessment of iron status in Danish men was previously performed in the DAN-MONICA 1 and DAN-MONICA 5 surveys in 1984 and 1988 [1, 2]. The results showed that iron depletion and iron deficiency anemia occurred with low frequencies, whereas moderate iron overload was reported in a relatively high fraction of the men. In January 1987, the mandatory fortification of flour with iron in Denmark ceased [3].

The present study was initiated in order to update iron status in a population of Danish men. Special attention was paid to whether the prevalence of iron deficiency or of iron overload might have changed since the abolition of food iron fortification.

Subjects and methods

Men

The selection of the participants is summarized in Table 1. A World Health Organization (WHO)-initiated survey for the "Monitoring of Trends and Determinants in Cardiovascular Disease" (DAN-MONICA 1) was conducted at the Center for Prevention of Disease in Glostrup, in Copenhagen County, in

Table 1 Selection of Danish male participants in the MONICA 10 Iron Status Survey in Copenhagen County 1993–1994

Age in years mean (range)	No. of Danish men invited	No. of men who attended	No. of men examined in iron status survey	Percent of invited men examined
41.7 (41.0–42.8)	539	347	347	64.4
51.8 (51.1–52.8)	537	376	376	70.0
61.7 (61.0–62.9)	479	347	346	72.2
71.7 (71.0–72.8)	423	263	263	62.2
Total	1978	1333	1332	67.3

1982–1984; 2280 Caucasian Danish men in age cohorts of approximately 30, 40, 50, and 60 years were chosen at random from the Census Register and invited to participate in the survey. The intention was to reinvite these men to a follow-up survey in 1993–1994 (DAN-MONICA 10), but only 2010 men could be located, and 32 of these were deceased, i.e., 1978 men were candidates for a reinvitation. Of these, 268 had moved to other parts of the country. Another 206 men refused to participate, but accepted a telephone interview, and a further 171 men refused both participation and a telephone interview. The demographic variables did not differ significantly between nonparticipants and participants. Of the 1978 candidates, 1333 men participated in the survey, and blood samples were available from 1332 of these for analysis of iron status. The mean age in the four cohorts was 42, 52, 62, and 72 years (Table 1), in the following termed "40", "50", "60" and "70" years.

The sample comprised individuals with widely different socioeconomic backgrounds. The majority of the participants were fit and healthy, and, according to the questionnaires, only a few may suffer from diseases (inflammatory disease, liver disease, malignancy) which can cause an inappropriate elevation of serum ferritin.

Methods

The participants gave a detailed social and medical history, including blood donation activity within the preceding 5 years, and were requested to present all their medicine as well as vitamin and mineral supplements to the investigator. The use and amount of iron supplements were recorded. Alcohol intake was recorded in a questionnaire and converted into drinks/week. In Denmark a drink contains approximately 12 g ethanol. Coffee and tea consumption were likewise recorded in a questionnaire as cups/day. Body mass index (BMI) was calculated as body weight in kilograms divided by body height in $(m)^2$.

Blood samples were collected by venipuncture between 10:00 a.m. and 12:00 a.m. Ninety-five percent of the participants were fasting. Hemoglobin (Hb) was measured on Technicon-H2 (Hb in mmol/l × 16.115 = Hb in g/l; Hb in g/l × 0.062054 = Hb in mmol/l). Serum was stored at –25 °C until analysis of ferritin was performed in 1994. Serum ferritin was measured by a competitive radioimmunoassay (Ferritin RIA Amersham, Cardiff, UK) [4]. In the concentration range of 13–40 μg/l, the within-assay reproducibility (coefficient of variation) is 5.6% and the between-assay variation (total assay variation) 12.0% [4]. The kit is calibrated closely to the WHO International Human Liver Ferritin Standard 80/602 [5]. Ferritin RIA Amersham values of 13, 16, 20, and 32 μg/l correspond to WHO ferritin standard values of 12, 15, 19, and 30 μg/l [5]. The results are described using three different critical serum ferritin values,. <13 μg/l, <16 μg/l, and <20 μg/l (corresponding to WHO standard ferritin values of 12, 15, and 19 μg/l), as indicators of small or absent iron stores. As suggested by Cook and Skikne [6], a ferritin cut-off value of <12 μg/l was considered to indicate absent iron stores. Likewise, as proposed by Worwood [7], small or absent body iron reserves were considered present at serum ferritin values <15 μg/l. As proposed earlier [2], a cut-off value of <20 μg/l was also used.

The cut-off value for low hemoglobin in men (130 g/l) was defined according to the WHO recommendation [8]. As hemoglobin was measured in mmol/l, we chose a cut-off value of <8.0 mmol/l, corresponding to <128.92 g/l. Furthermore, we used the age-specific 5th percentiles for hemoglobin in iron-replete men with serum ferritin >32 μg/l as cut-off values. The 5th percentile for hemoglobin was 135 g/l (8.4 mmol/l), 137 g/l (8.5 mmol/l), and 131 g/l (8.1 mmol/l) in men aged 40, 50–60, and 70 years, respectively.

Serum ferritin of <13 μg/l and hemoglobin below 129 g/l or below the age specific 5th percentile were considered to indicate iron-deficiency anemia. A serum ferritin value of ≤32 μg/l was considered to indicate the absence of stainable hemosiderin bone marrow iron, whereas a value of >32 μg/l was considered to reflect "replete" iron stores [9, 10].

Statistics

Serum ferritin values were log-normally distributed, for which reason medians and geometric means are quoted. The significance of differences was assessed using the Mann-Whitney and Kruskall-Wallis rank sum tests, as well as the χ^2-test with Yates' correction. Correlations were calculated using Spearman's correlation coefficient (r_s) corrected for ties.

Results

Serum ferritin

The average rate of participation was 67.3%, being highest among 50- and 60-year-old men (Table 1). The serum ferritin values in the various age-groups are shown in Tables 2 and 3 and in Fig. 1. Serum ferritin in the entire male series displayed a discrete but significant increase from 40 to 60 years of age ($p = 0.03$), and a slight but significant decrease from 60 to 70 years of age ($p = 0.01$) (Table 2). Among nondonors, 40-, 50-,

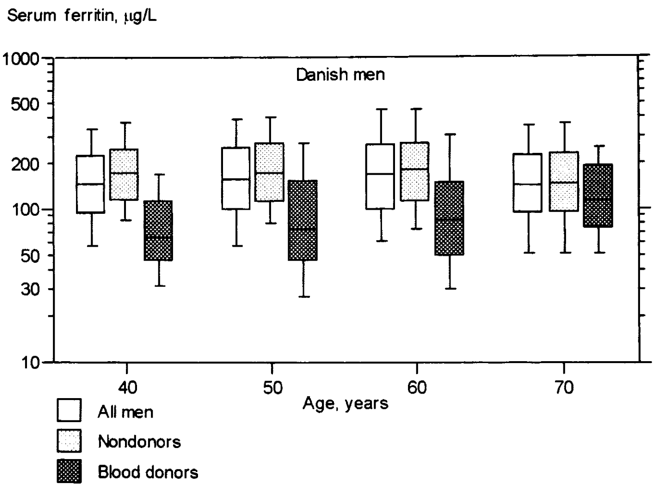

Fig. 1 Serum ferritin in 1332 Danish men according to age and blood donation. *Box plots* indicate 10th, 25th, 50th, 75th and 90th percentiles

Table 2 Serum ferritin in 1332 Danish men according to age and blood donation activity. Copenhagen MONICA 10 Iron Status Survey 1994

	All men			Nondonors			Blood donors		
Age (years)	40–60	70	p*	40–60	70	p*	40–60	70	p*
Men (n)	1069	263		899	247		170	16	
Serum ferritin (μg/l)									
Geometric mean	155	140		175	142		81	122	
Median	158	143	0.06	177	147	0.0002	74	113	0.02
5–95th percentile	44–503	37–459		60–524	31–594		22–344		
23–97.5th percentile	31–660	31–588		48–675	37–486		21–522		
Observed range	10–2375	9–1365		10–2170	9–1365		15–2375	48–447	

* Differences between age-groups: Mann-Whitney test

Table 3 Distribution of serum ferritin values in 1332 Danish men according to age and blood donation activity. Figures indicate percentage of subjects (read vertically) in each age-group. Copenhagen MONICA 10 Iron Status Survey 1994

	All men			Nondonors			Blood donors		
Age (years)	40–60	70	p*	40–60	70	p*	40–60	70	p*
Men n	1069	263		899	247		170	16	
Serum ferritin (μg/l)				% of men					
<13[a]	0.19	0.38	0.5	0.22	0.41	0.5	0	0	
<16[a]	0.47	0.38	0.9	0.33	0.41	0.9	1.18	0	
<20[a]	0.75	1.14	0.5	0.56	1.22	0.4	1.76	0	
16–32	2.62	3.04		0.89	3.25		11.8	0	
33–100	22.4	25.1		17.1	24.0		50.6	37.5	
101–200	37.7	41.8	0.3	40.1	41.9	0.001	24.7	43.8	0.2
201–300	19.2	14.4		22.0	14.6		4.71	12.5	
>300	17.7	15.2		19.6	15.9		7.06	6.25	
Total (%)	100	100		100	100		100	100	

[a] Ferritin values of 13, 16, and 20 μg/l correspond to WHO standard ferritin values of 12, 15, and 19 μg/l
* χ^2-test.

and 60-year-old men had serum ferritin values which were not significantly different ($p = 0.5$), whereas 70-year-old men still had significantly lower values than 60-year-old men ($p = 0.002$) (Table 2).

Serum ferritin and blood donation

Tables 2 and 3 show that blood donors in all age-groups had significantly lower serum ferritin compared with nondonors ($p < 0.0001$). Serum ferritin levels in donors were inversely correlated with both the total number of phlebotomies and the number of phlebotomies within the preceding 2–5 years, as demonstrated in Table 4.

Serum ferritin and body weight

In the entire series ($n = 1332$), significant positive correlations existed between serum ferritin and body weight ($r_s = 0.15$, $p = 0.0001$) and BMI ($r_s = 0.17$, $p = 0.0001$). Among nondonors ($n = 1146$), the correlation between serum ferritin, body weight, and BMI was slightly higher: $r_s = 0.19$, $p = 0.0001$.

Serum ferritin vs. alcohol intake

There was no significant difference in alcohol intake between blood donors and nondonors ($p = 0.3$). Table 5 shows the relationship between alcohol intake and serum ferritin in nondonors. In donors there was a similar correlation between alcohol intake and serum ferritin ($r_s = 0.24$, $p = 0.002$).

Serum ferritin vs. coffee and tea consumption

Of all the men, 93% were coffee drinkers (median five cups/day, 5–95th percentile 1–12 cups/day) and 37% were tea drinkers (median two cups/day, 5–95th percentile 1–7 cups/day). There was a significant inverse correlation between serum ferritin and the number of cups (coffee and tea) consumed per day ($r_s = –0. 16$, $p = 0.0001$).

Iron deficiency

The prevalence of low serum ferritin values in the entire series is shown in Table 3. Of the 40- to 60-year-old

Table 4 Influence of blood donation patternon serum ferritin in 186 Danish male blood donors aged 40–70 years. Copenhagen MONICA 10 Iron Status Survey 1994

No. of phlebotomies*	No. of male blood donors	Phlebotomy vs. S-ferritin, Spearman's (r_s)	*p*-value
≤2 years: 4 (0– 8)	180	–0.57	0.0001
≤5 years: 10 (0–20)	177	–0.55	0.0001
Total: 33 (4–99)	169	–0.32	0.0001

* Median (5–95th percentile)

Table 5 Alcohol intake and the association with serum ferritin in 1119 Danish male nondonors. Copenhagen MONICA 10 Iron Status Survey 1994

Age (years)	Men (*n*)	Alcohol* (no. of drinks/week)	S-ferritin* (μg/l)	Spearman's (r_s)	*p*-value[a]
40	281	10 (0–44) NS	173 NS	0.21	0.001
50	309	10 (0–40) NS	173 NS	0.25	0.0001
60	294	11 (0–42), 0.0001	183 0.001	0.28	0.0001
70	235	4 (0–30)	146	0.22	0.001

* Median (5–95th percentile)
[a] Mann-Whitney test

men, 0.47% had serum ferritin levels <16 μg/l, i.e., absent iron stores, similar to the prevalence of iron deficiency of 0.38% in 70-year-old men. As shown in Table 3, donation of blood had no substantial influence on the prevalence of iron deficiency.

Iron-deficiency anemia

Two nondonors, a 60- and a 70-year-old man, corresponding to 0.15% of the entire series, fulfilled the criteria for iron-deficiency anemia (i.e., serum ferritin <13 μg/l and hemoglobin <129 g/l as well as <5th percentile for age). One man was treated with low-dose acetylsalicylic acid, and neither took H_2-receptor antagonists, antacids, coumarin anticoagulants, or iron supplements.

Small iron stores

Serum ferritin values of 16–32 μg/l, i.e., small iron stores, were present in 1.73–3.46% of the men in the various age-groups (Table 3). The frequency was significantly lower among 40- to 60-year-old nondonors than among donors ($p = 0.01$).

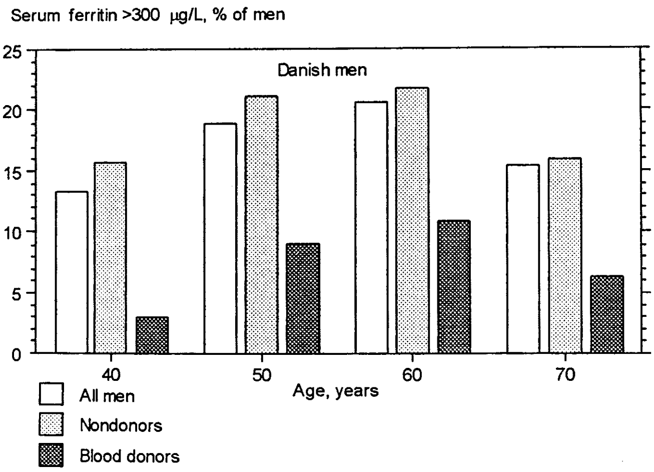

Fig. 2 Prevalence of iron overload (serum ferritin >300 μg/l) in 1332 Danish men according to age and blood donation

Iron overload

The prevalence of high serum ferritin values >300 μg/l, indicating iron overload, increased with age in 40- to 60-year-old men (Fig. 2). In all men in the series aged 40–60 years the prevalence rose from 13.2 to 20.8%, being 17.7% on the average (Table 3). In nondonors the prevalence rose from 15.7 to 22.0% with an average of 19.6%, and in donors from 3.0 to 10.8% with an average of 7.06%. Seventy-year-old men had a lower prevalence of iron overload, i.e., 15.2% for the entire series and 15.9% for nondonors.

Serum ferritin values of 301–700 μg/l, indicating a moderate iron load, was present in 15.5% of all men, in 17.0% of nondonors, and in 5.9% of donors. A heavy iron load defined as serum ferritin >700 μg/l was observed in 1.73% of all men, in 1.83% of nondonors, and in 1.08% of donors.

Serum ferritin and iron supplements

In the entire series, 370/1332 men (27.8%) took ferrous iron supplements. Information about the amount of iron supplement was available for 295 men. Median iron supplement was 14 mg/day, 5–95th percentile 8–26 mg/day. Information about the frequency of supplement was available for 326 men. Supplement was taken a median of 30 days/month, 5–95th percentile 10–31 days. Supplementary iron was most frequently taken as combined multivitamin-mineral tablets containing 10–20 mg of ferrous iron. In nondonors, serum ferritin levels were not significantly different compared with nonsupplemented men ($p = 0.5$) (Table 6). Likewise, the prevalences of iron deficiency (serum ferritin <16 μg/l), small iron stores (serum ferritin ≤32 μg/l), and iron overload (serum ferritin >300 μg/l) were not significantly different in iron supplemented and nonsupplemented men (Table 6).

Table 6 Relation between serum ferritin and the use of iron supplements in 1332 Danish men aged 40–70 years, according to blood donation activity. Copenhagen MONICA 10 Iron Status Survey 1994

	Iron supplement	Iron (mg/day)	Men (*n*)	Serum ferritin				
				Median (μg/l)	5–95%-tile (μg/l)	<16 μg/l (%)	≤32 μg/l (%)	>300 μg/l (%)
Nondonors	Yes	14 (6–18)	308	178	55–443	0	0.97	19.5
	p-value			0.5*		0.5**	0.3**	0.8**
	No		838	168	52–554	0.48	2.0	18.6
Blood donors	Yes	14 (14–69)	62	74	31–364	0	11.3	6.5
	p-value			0.5*		0.6**	0.7**	0.8**
	No		124	78	22–345	1.6	12.1	7.3

[a] Median (5–95th percentile)
* Mann-Whitney test
** χ^2-test

In blood donors there was no significant influence of iron supplementation on serum ferritin levels (Table 6). There was no correlation between serum ferritin and the monthly amount of iron supplement in either of the groups.

Vitamin supplements

In the entire series, 440/1332 men (33.0%) took vitamin, mineral, or vitamin-mineral supplements daily; 38.9% of men aged 40 years, 30.1% of men aged 50 years, 33.4% of men aged 60 years, and 28.9% of men aged 70 years took supplements. Among nondonors, 373/1146 (32.5%) took vitamin supplements. There was no significant difference between serum ferritin levels in supplement users vs. nonusers ($p=0.7$).

Medication

Among the 1146 nondonors, medicine relevant for this study was taken by the following number of participants: standard-dose acetylsalicylic acid (1–3 g/day), $n=97$; low-dose acetylsalicylic acid (150–300 mg/day), $n=73$; other nonsteroidal anti-inflammatory drugs (NSAIDs), $n=41$; H_2-receptor antagonists, $n=30$; antacids, $n=46$; coumarin anticoagulants, $n=9$.

Men treated with standard- and low-dose acetylsalicylic acid had lower serum ferritin levels ($p=0.04$ and $p=0.008$, respectively) than nontreated men. The entire group of nondonors treated with acetylsalicylic acid ($n=170$) had lower serum ferritin (median 136 μg/l, 5–95th percentile 41–503 μg/l) than nontreated men (169 μg/l, 54–515 μg/l) ($p=0.0005$). Treatment with other NSAIDs or coumarins had no significant influence on serum ferritin levels ($p=0.5$ and $p=0.7$, respectively).

Nondonors treated with H_2-receptor antagonists due to gastritis or peptic ulcer had lower serum ferritin levels (142 μg/l, 29–350 μg/l) than nontreated men (171 μg/l, 54–521 μg/l) ($p=0.036$). Treatment with antacids or coumarins had no significant influence on serum ferritin levels ($p=0.2$ and $p=0.7$, respectively).

Discussion

The aim of this epidemiologic survey was to assess iron status in a random sample of Danish men, being representative of the male population in Denmark with respect to social and other demographic factors. The majority of men were considered to be fit and healthy; a few among the men aged 60–70 years might have diseases which could influence serum ferritin levels in both a downward (occult bleeding) and an upward (inflammation or malignancy) direction.

The serum ferritin concentration is closely correlated with bone marrow hemosiderin iron and mobilizable body iron stores [9–11] and has been used for epidemiologic studies of iron status in populations since the 1970s. In adult men, each microgram of serum ferritin per liter corresponds to iron stores of approximately 7.5 mg [11].

Previous studies have shown that serum ferritin in boys is relatively stable from late childhood until adolescence [12–14]. When the adolescent growth spurt has ceased, there is a gradual increase in serum ferritin, i.e., body iron stores, from about 15–16 years of age until 30–35 years of age, when ferritin levels become stable [1, 2, 13, 14]. Subsequently, serum ferritin levels in healthy men remain relatively constant into old age [14]. In the entire series of men, median serum ferritin was 155 μg/l (5–95th percentile 41–498 μg/l), corresponding to estimated median body iron stores of approximately 1163 mg and 5–95th percentiles of 308–3735 mg. Nondonors had a median serum ferritin of 169 μg/l (5–95th percentile 54–515 μg/l), corresponding to estimated median iron stores of 1268 mg and 5–95th percentiles of 405–3863 mg. However, it should be noted that in states of inflammation and hepatic tissue injury, estimation of iron stores may be misleading due to an inappropriate elevation of serum ferritin. Among factors with a potential influence on iron status in men are: (a) blood donation; (b) alcohol intake; (c) treatment with acetylsalicylic acid inducing gastrointestinal blood loss; (d) gastrointestinal blood losses due to gastritis or peptic ulcer indicated by the use of H_2-receptor antagonists or antacids; (e) dietary iron intake and factors influencing the bioavailability of dietary iron, of which only coffee and tea were included in the present paper; (f) iron supplementation.

The positive association between alcohol intake and serum ferritin levels confirm our results from the DAN-MONICA 1 survey and those from an Australian study [15, 16]. In the present survey, the influence on serum ferritin was unrelated to the type of alcohol consumed (beer, wine, spirits), as also reported by Leggett et al. [16]. Undoubtedly the majority of men had normal biochemical liver tests. Whether the elevation in serum ferritin actually reflects an increase in body iron stores or is merely a nonspecific elevation due to release of ferritin from damaged hepatocytes remains unknown.

Polyphenols are constituents of many plants and potent inhibitors of intestinal iron absorption [17]. Both coffee and tea contain polyphenols. Accordingly, there was an inverse relationship between the amount of coffee and tea consumed and serum ferritin.

Acetylsalicylic acid was used by 15% of nondonors, due either to its analgetic or anti-inflammatory effects or to its inhibition of platelet activity [18]. It appeared that acetylsalicylic acid, even in low doses, had a significant negative impact on serum ferritin levels. Acetylsalicylic acid is known to cause moderate gastrointestinal blood losses, even in otherwise healthy subjects without gastritis or peptic ulcer [19].

As in previous studies [20, 21], it appeared that blood donation had a profound negative influence on body iron status. The effect was associated with the donation pressure. Of the 1069 men aged 40–60 years, 16% were blood donors, and among the 70-year-old men, 6% were donors. Donors had a median ferritin of 76 μg/l (55–95th percentile 24–344 μg/l), corresponding to estimated median body iron stores of 570 mg and 5–95th percentiles of 180–2580 mg. Accordingly, the prevalences of small iron stores (serum ferritin 16–32 μg/l) were significantly higher ($p=0.001$) in donors compared with nondonors. However, the prevalence of iron deficiency and depleted iron stores (serum ferritin <13 μg/l and <16 μg/l, respectively) was similar in the two groups, which indicates that the Danish hematologic criteria for male donation of blood and postdonation iron treatment are adequate to protect the donor from iron depletion. Predonation hemoglobin must be ≥135 g/l (≥8.4 mmol/l) in order to allow donation [20]. This cut-off value corresponds to the 5th percentile for hemoglobin in the present and previous series [1] and is clearly high enough to prevent the occurrence of deficiency anemia in donors. It also appears that donation of blood was very effective in reducing the prevalence of iron overload from an average of 18% to 7% ($p=0.0001$).

From the point of view of deficiency, iron status was satisfactory in Danish adult male nondonors in 1994, only 0.35% of men presenting with iron deficiency and only 0.15% with iron-deficiency anemia. The DAN-MONICA 1 Iron Status Survey in 1984, which comprised 1044 Danish male nondonors aged 30–60 years [1], showed a prevalence of iron deficiency of 0.38% and of iron-deficiency anemia of 0.21%, i.e., figures similar to those obtained in the present study. The abolition of the iron fortification of flour in 1987 apparently had no impact on the prevalence of iron deficiency among middle-aged and elderly men.

For comparison, the NHANES III survey in the USA, 1988–1994, reported a prevalence of iron deficiency of <1% among men aged 20–49 years and of 2% among men aged 50–69 years [22]. Corresponding figures for iron deficiency anemia were <1% and 1%, respectively [22]. Iron deficiency was defined as abnormal values for at least two of the following three indicators: serum transferrin saturation <15%, serum ferritin <12 μg/l, erythrocyte protoporphyrin >1.24 μmol/l red blood cells. Iron-deficiency anemia was defined as an additional hemoglobin value <5th percentile for age (<137 g/l in men aged 20–49 years, <133 g/l in men aged 50–69 years) [22]. Thus in Western societies, the prevalence of iron deficiency in middle-aged and elderly men is low and does not constitute a nutritional problem.

From the point of view of overload, the prevalence of iron overload was high, 18.8% of nondonors having serum ferritin values >300 μg/l. The DAN-MONICA 1 Iron Status Survey in 1984 [1] showed a prevalence of iron overload of 10.4%; i.e., despite the absence of iron fortification there has been a marked increase in iron load in adult Danish men during the past decade. A similar tendency has been reported from the USA [22]. The reasons for the increase in iron stores are probably changes in nutritional habits during the last decade, with a higher intake of iron with good bioavailability, and an increased intake of alcohol.

The Danish nutrition survey in 1985 reported a median intake of dietary iron among men aged 35–74 years of 17 mg/day [23]. Since 1954, each kilogram of flour had been fortified with 30 mg carbonyl iron. This mandatory iron fortification was abolished in 1987, reducing the average iron content of the diet by 2.4 mg/10 MJ [2]. However, the "functional" decrease was smaller, about 0.4 mg/10 MJ, due to the low bioavailability of the fortification iron [2]. Accordingly, the subsequent nutrition survey in 1995 reported a median intake of dietary iron of 11.8 mg/day in men aged 35–74 years [24]. Although the total iron intake is lower, the intake of heme iron, having a high bioavailability, has increased [24]. Comparison of the surveys in 1985 and 1995 shows that the consumption of dairy products, eggs, fat, and tea, all of which impair intestinal iron absorption, has declined. At the same time, the consumption of meat and poultry as well as alcohol (beer, wine, spirits), all of which enhance iron absorption, has increased [24]. Furthermore, a large Danish survey has shown that the intake of alcohol in the age-group 40–70 years increased in the period from 1979 to 1992 [25].

In recent years there has been concern that iron overnutrition among otherwise healthy individuals may lead to increased risk of chronic disease, notably coronary heart disease [26] and cancer [27]. The concern was based on the ability of free iron to catalyze the formation of highly reactive radicals for superoxide and hydrogen peroxide [28]. However, at present findings in these areas are controversial, but they constitute a major argument against reintroducing a general iron fortification program.

The use of nutritional supplements (vitamin, mineral, or vitamin-mineral) is prevalent among Danish men and has been relatively constant during the past decade. In the DAN-MONICA 1 survey in 1983, 36% of the 1433 men aged 30–60 years took regular supplements [1], and in the DAN-MONICA 5 survey in 1988, 37% of the 1524 men aged 35–65 years took supplements [2], compared with 33% in the present survey. Most combined vitamin-mineral supplements contain 14–20 mg of ferrous iron. In the previous DAN-MONICA 1 survey there was no difference in overall serum ferritin levels between those men taking vitamin-mineral supplements and those not taking supplements [1]. However, in that survey we did not inquire specifically about whether the supplements contained iron. In the DAN-MONICA 5 survey, male participants were asked about the use of supplementary iron, but again there appeared to be no association between iron supplements and serum ferritin levels [2].

In the present survey the participants were requested to bring along their supplements, and the daily intake of ferrous iron was recorded. Iron supplementation had no appreciable impact on median body iron stores in either nondonors or blood donors. The prevalences of iron deficiency, small iron stores, and iron overload were similar in iron supplemented and non-supplemented men, and there was no correlation between serum ferritin and the monthly amount of iron supplements. These findings are in contrast to those reported in a study on young Danish women, showing that women with low ferritin values had a beneficial effect of iron supplementation [29]. The effect of supplementary iron must be considered in combination with the intake and bioavailability of dietary iron. These factors display a high interindividual variation that masks the association between the amount of supplementary iron and serum ferritin. In healthy iron-replete men with a stable iron balance, supplementary iron in amounts of 14–20 mg/day has a negligible impact on iron status, as iron absorption is regulated strictly according to body iron needs. Absorption is generally increased when body iron balance becomes negative and iron stores decline [17].

Hereditary hemochromatosis is characterized by an inappropriately high intestinal iron absorption [30], which is caused by a mutation in the *HFE*-gene on chromosome 6p [31]. The prevalence of homozygosity in the Danish population is 0.3–0.5%, that of heterozygosity 11–13% (N. Milman, unpublished). The penetration of the gene depends, among other factors, on the intake of iron, dietary as well as supplemental. The high prevalence of iron overload in Danish men and the widespread use of iron-containing vitamin-mineral supplements should encourage the producers to manufacture vitamin-mineral supplements without iron as well.

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