表2　C群およびD群の患者背景と採血前検査値

		C群 (n=5)		D群 (n=42)
男女比	(男:女)	2 : 3		11 : 31
年齢	(歳)	24.2±11.4		23.6±4.6
身長	(cm)	164.6±8.0		162.8±9.9
体重	(kg)	56.6±4.4		55.8±11.5
血清鉄	(μg/dl)	106.0±46.2	*	84.0±26.0
フェリチン	(ng/ml)	65.2±41.4		48.9±49.9
総鉄結合能(TIBC)	(μg/dl)	278.8±45.6		285.9±33.8
不飽和鉄結合能(UIBC)	(μg/dl)	172.8±86.3	*	202.7±41.0
血漿総蛋白量(TP)	(g/dl)	7.0±0.4		7.1±0.4
血小板数	($\times 10^4/\mu l$)	20.2±8.1		22.8±5.1
白血球数	($\times 10^2/\mu l$)	49.8±11.0		59.5±13.4
採血前Hb値	(g/dl)	13.2±1.8		13.9±1.3

* $p<0.05$　(Mean±SD)

C群：βが1以上であった患者
D群：βが1未満であった患者

有意差は認められなかったが，採血前Hb値はA群で有意に低い値を示した（表1）。しかし，採血前Hb値とβの相関関係については，決定係数（0.069），相関係数（－0.093）と共に低く，相関関係は認められなかった。

次に，採血後2週間の術直前Hb値が採血前Hb値以上に増加したC群（$\beta \geqq 1$）とそれ以下にしか回復しなかったD群（$\beta < 1$）に分配し，比較検討した。C群は5名，D群は42名であった。両群間の患者背景に有意差は認められなかったが，血清鉄およびUIBCに有意差を認めた（表2）。しかし，採血前Hb値を含むその他の採血前検査値に差は認められなかった。血清鉄およびUIBCとβとの相関を見ると，相関係数はそれぞれ0.356，－0.359と低く，両者の間には，弱い相関関係しか認められなかった（表3）。

表3　患者背景および採血前検査値とβとの相関関係

	相関係数	p値
年齢	- 0.199	0.226
身長	0.235	0.150
体重	0.135	0.414
血清鉄	0.356	0.026
フェリチン	0.227	0. 166
総鉄結合能(TIBC)	- 0.207	0. 208
不飽和鉄結合能(UIBC)	- 0.359	0. 024
血漿総蛋白量(TP)	- 0.047	0. 780
血小板数	- 0.096	0. 564
白血球数	- 0.301	0. 062
採血前Hb値	- 0.093	0. 574

考察

上下顎同時移動術時には輸血が必要となるような出血が起こる場合があり，患者のQOLを考慮すると有効かつ安全な自己血輸血が望まれる。当院における本術式の出血量は，大部分の症例で600～800 mlであるが，1,000 ml以上出血する症例もあるため[1]，確実に同種血輸血を回避するために

は自己血貯血は必須である。我々は，本法に対して400 mlの自己血貯血を行っているが，他施設においても術前の貯血量は400 mlが主流となっている[6]。800 ml以上の貯血を行わないとエリスロポエチンは健康保険の適応外となるため使用できず，採血による貧血を回復させるためには，十分な期間をとる必要性がある。顎矯正外科手術は待機手術であり，大部分の患者は若く，健康状態は良好であるため外来採血が可能で，通常は比較的長く術前貯血期間をとることができるが，患者の時間的な都合や手術日の決定が遅延することなどにより期間を短縮せざるをえない場合もある。他領域の手術においては術前貯血量が800 ml以上必要となるような症例ではエリスロポエチンを併用して手術1週間前まで採血を行い，Hb値の低下もほとんど認められなかったという報告がある[7]。一方で，多少の貧血があっても術前400 ml貯血をした胃全摘術において100 %術中の同種血輸血が回避できたという報告[8]もあり，上下顎同時移動術を受ける患者では400 mlの貯血と術前貯血期間を十分とることで同種血回避率100 %をより確実に維持できると考えられる。

幹細胞の分化が始まって末梢血中に網状球として出現するのに要する期間は，約8日であり[9]，健康成人の生理的赤血球産生量は，全血量に換算すると1日30～40 mlである[10]。さらに，有効な造血刺激が加わると赤血球産生予備能は最大5～6倍まで亢進する[11]。これらのことからは，2週間の貯血期間は貧血回復には十分な期間であるように考えられる。しかし，今回検討した47例中400 ml採血後2週間で完全に元のHb値に回復したものは5例のみであったことから，臨床的には，採血から手術までの期間が2週間以上あることが望ましいと考えられる。症例数が少なかったこともあり，予測因子を明確にすることはできなかったが，採血前のHb値の低い症例の方がβが高かったことから，採血前Hb値が低いほど赤血球造血能が亢進する可能性が示唆された。これは，鉄欠乏性貧血患者は，貯血開始1～2週の早期から著明な造血能の亢進がみられるという新名主らの報告[12]と一致する。この理由として貧血患者では，貧血のない患者と比較して採血後の内因性エリスロポエチン濃度が高い[11]ことが考えられる。しかし，造血には，エリスロポエチンとともに材料となる鉄が必要である。C群の5症例は，D群の42症例と比較して，採血前Hb値には差がなく，血清鉄およびUIBCに有意差を認めた。フェリチン値には有意差は認められなかったが，その平均値はD群が48.9 ng/mlであったのに対しC群では65.2 ng/mlと高い傾向にあった。これは，貧血患者の方が早期のHb値の回復は速いが，完全に回復するためには貯蔵鉄量が関係する可能性がある。採血後全症例に量的には十分な鉄剤を投与しているので，採血前の貯蔵鉄量が関係する可能性は少ないように思われるが，鉄の吸収には個人差があり，採血前に貯蔵鉄量の多い患者の方が鉄の吸収度が高かったことが要因の一つとして考えられる。また，C群の採血前Hb値はD群のそれと有意差がなく，貯蔵鉄量は多かったことから考えて鉄を有効にHb生成に利用できている可能性が考えられる。しかし，今回は鉄剤投与後の貯蔵鉄量を測定していないため明らかにはできなかった。さらに検討を進めることで，顎矯正外科手術に対するより有効な術前貯血を行うことが可能となるものと考える。

結語

術前2週間に400 mlの採血を行った症例においてHb値回復に影響をおよぼす因子について検索した。採血前Hb値と貯蔵鉄量がHb値回復程度に影響を与えている可能性が示唆された。

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Daily doses of 20 mg of elemental iron compensate for iron loss in regular blood donors: a randomized, double-blind, placebo-controlled study

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BACKGROUND: A considerable number of regular blood donors develops an iron deficiency, and the exact amount of iron required to compensate for the iron loss from whole-blood donation in males and females is still unknown.

STUDY DESIGN AND METHODS: A total of 526 regular blood donors (289 male and 237 female) were randomly assigned to treatment with either 40 mg, 20 mg, or 0 mg per day of elemental iron as ferrous gluconate for a period of 6 months, during which one unit of whole blood was collected on four occasions (males) or three occasions (females). Hemoglobin level, serum ferritin, and soluble transferrin receptor levels were measured before each donation.

RESULTS: Daily doses of either 40 mg or 20 mg of elemental iron adequately compensated for iron loss in males, who gave blood at 2-month intervals, but did not result in a positive iron balance or an increase in storage iron as reflected by the logarithm of the ratio of transferrin receptor to ferritin concentration. In females, who donated at 3-month intervals, the same daily doses not only restored the iron balance but also led to an increase in storage iron. The number of gastrointestinal side effects due to iron supplementation (12%) was only slightly higher in both iron groups than in the placebo group.

CONCLUSION: The results of this study indicate that 20 mg of elemental iron per day can adequately compensate for iron loss in males and females who donate whole blood up to four (females) or six times per year (males).

The major side effect of whole-blood donation is iron depletion. In Germany, men are generally allowed to donate whole blood every 8 weeks and women every 12 weeks. However, the normal diet is usually unable to compensate for the resulting iron loss.[1,2] Consequently, a considerable number of regular blood donors develops a negative iron balance that may eventually progress to iron deficiency anemia.[3-7] Menstruating female donors are at a particularly high risk for chronic iron deficiency. Although this is well-known, only a few controlled, double-blind studies have dealt with the question of whether iron supplementation can prevent iron depletion in menstruating female blood donors.[8-11] There is evidence suggesting that daily doses of 40 mg of elemental iron as ferrous sulfate can sufficiently compensate for iron loss resulting from whole-blood donation and can improve iron status.[10,11] However, the question of whether a lower dose of iron is sufficient to compensate for iron loss in female donors is still open. In addition, controlled studies on iron supplementation in male donors are lacking. Most importantly, no valid measure of iron storage was used in early studies.[12,13] Today, serum ferritin and soluble transferrin receptor levels can be routinely measured and iron status can be much better assessed than previously.[14-17] The logarithm of the ratio of

ABBREVIATIONS: Fe^{2+} = elemental iron as ferrous gluconate; log(TfR/F) = logarithm of ratio of the soluble transferrin receptor to ferritin concentration.

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the soluble transferrin receptor to ferritin concentration (log[TfR/F]), which was shown to have a highly linear correlation to body storage iron, is currently the most precise measure of body storage iron available.[14,15] Here, we present the results of a double-blind study in which we randomly assigned regular male and female blood donors to treatment with 40 mg, 20 mg, or 0 mg (placebo) per day of elemental iron for 6 months.

MATERIALS AND METHODS

Selection of donors and study design

A total of 526 regular blood donors (289 male and 237 female) were enrolled in this study, which was approved by the Ethics Committee of Charité University Medical Center. Written informed consent was obtained from all volunteers. In accordance with the German guidelines for blood donor selection, all donors were determined to be healthy based on their history and had hemoglobin (Hb) concentrations of no less than 13.5 g per dL (males) or 12.5 g per dL (females). The investigational products consisted of identical capsules in blister packs containing 1.5 mg pyridoxal-phosphate, 2.25 µg cyanocobalamine, 400 mg ascorbic acid, 200 µg folic acid, and 75 µg biotin without (placebo) or with 20 mg of elemental iron as ferrous gluconate (Fe^{2+}) (Phyt-Immun GmbH, Homburg, Germany). Ascorbic acid was added to enhance iron absorption. Because most people believe in beneficial effects of vitamin supplements, the other selected vitamins were added for improved compliance. The form of iron used meets the European Community criteria for dietary foods for special medical purposes. The participants were randomized to one of three groups receiving either 40 mg Fe^{2+}, 20 mg Fe^{2+}, or 0 mg Fe^{2+} in two capsules once daily for 6 months. Hb, serum ferritin, and soluble transferrin receptor levels were determined before blood collection at each initial and follow-up visit. Each male volunteer was scheduled for a total of four visits, including a randomization visit before the first donation at Week 0 and three subsequent predonation visits at 2-month intervals. The females were scheduled for a total of three visits: a randomization visit at Week 0 and two predonation visits at 3-month intervals (Fig. 1). The intervals were chosen in accordance to the German guidelines, which allow six donations per year for male and four donation per year for female volunteers. Volunteers with hemoglobin concentration less than 13.5 g per dL (males) or 12.5 g per dL (females) were deferred, but not excluded from study. Compliance, which was defined as the ingestion of at least 90 percent of the capsules as prescribed, was checked by counting the returned capsules between blood donations.

Laboratory methods

Hemoglobin concentrations in fingerstick blood samples were determined by the acid methemoglobin method using a photometer (HemoCue B-Hemoglobin photometer, HemoCue, Großostheim, Germany). Ferritin and soluble transferrin receptor concentrations in serum were

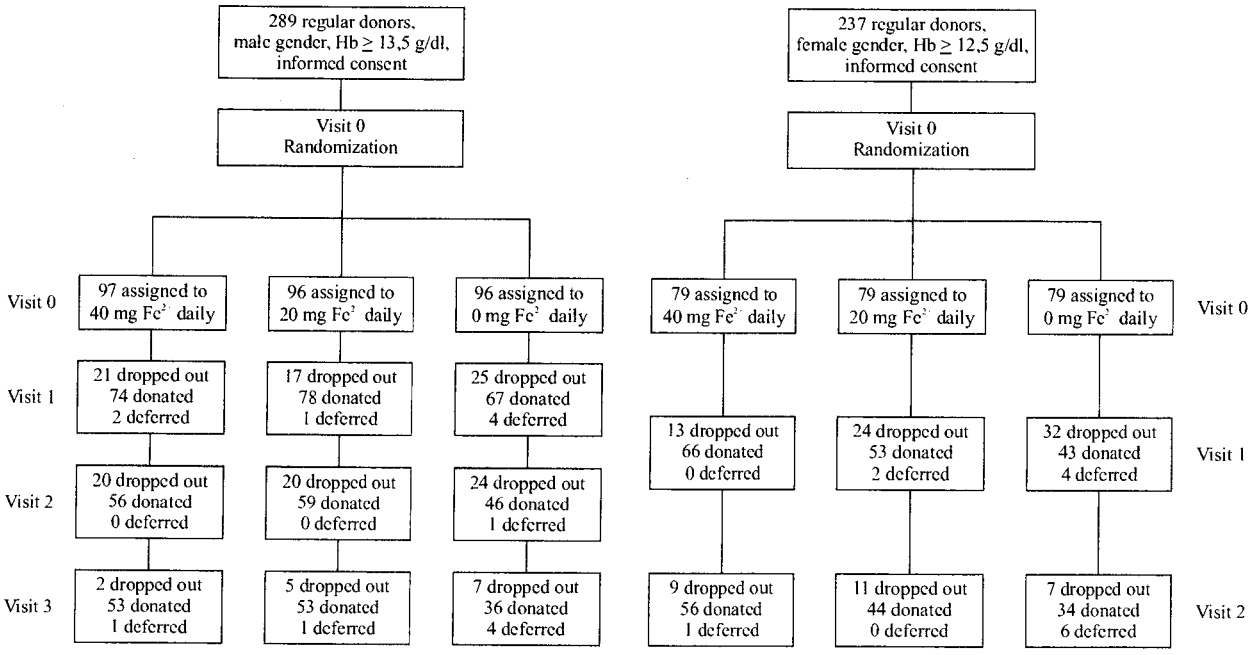

Fig. 1. Flow of participants during study.

determined by nephelometry using an automatic analyzer (BN Prospec, Dade Behring, Marburg, Germany).

Statistics

Sample-size calculation, randomization, and statistical analyses were performed using software (Stata for Windows, Stata Corp., College Station, TX). Based on the serum ferritin concentration, the required sample size was determined to be 49 males and 40 females per group, assuming a power of 0.9, a significance level of 0.0167 (Bonferroni adjustment for three groups), a smallest meaningful ferritin difference of 10 µg per L between groups, three (males) or two (females) follow-up measurements, a within-subject correlation coefficient of 0.8, and a standard deviation (SD) of 26 µg per L (males) or 22 µg per L (female) for serum ferritin. Assuming a dropout rate of 50 percent, we arrived at a final sample size of 98 males and 80 females per group.

The randomization plan was generated using block randomization with variable block length. Statistical analyses were performed as an intent-to-treat analysis for all participants coming for more than one visit using a linear regression model for longitudinal data (cross-sectional time-series regression model with generalized estimating equation analysis).[18] The logarithm of the ratio of transferrin receptor to ferritin concentration, an accepted measure of storage iron, was used as the outcome variable. To model the change in storage iron over time, we applied the difference values for log(TfR/F) and included the iron supplement as the predictor variable.

RESULTS

Males

Of the 289 male volunteers (age range, 19-67 years) enrolled in the study, 141 (49%) dropped out, yielding a dropout rate of 44 percent in the 40 mg of Fe^{2+} group, 44 percent in the 20 mg of Fe^{2+} group, and 58 percent in the placebo group (p = 0.075; Fisher's exact test). A total of 63 (45%) of the male dropouts withdrew before their second visit (Table 1). The mean interval between visits was 60 days. Deferral from donation because of unacceptable hemoglobin concentration values (<13.5 mg/dL) occurred in 14 of 825 visits (1.7%). This was more frequently the case in the placebo group than in the 20 mg and 40 mg iron groups (n = 9 vs. 2 vs. 3, p = 0.022; Fisher's exact test). Compliance was poor in roughly one-third of the male participants.

In the male placebo group, the mean serum ferritin concentration decreased from 35 µg per L at baseline to 21 µg per L at the final visit, the number of males with depleted iron stores (ferritin <12 µg/L) increased from 20 percent to 54 percent, and the mean concentration of soluble transferrin receptors rose slightly from 1.6 mg per L to 1.7 mg per L (Table 2, Fig. 2). In the male 20 mg iron group, serum ferritin decreased from 35 µg per L to 25 µg per L, whereas the median ferritin value changed only slightly (Table 2, Fig. 2); both the number of males with depleted iron stores (25%) and the transferrin receptor concentration (1.5 mg/L) remained nearly constant. In the male 40 mg iron group, the ferritin (33 µg/L) and transferrin receptor levels (1.5 mg/L) remained constant, whereas the number of individuals with iron depletion dropped from 26 percent to 13 percent.

The log(TfR/F) remained nearly constant in both iron groups, but rose continuously in the placebo group

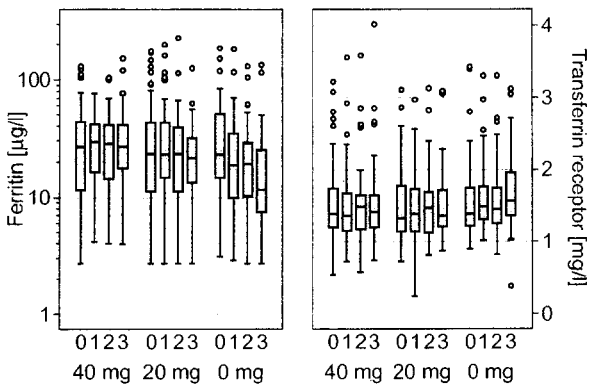

Fig. 2. Box-plot for the concentration of serum ferritin and soluble transferrin receptor in male donors.

TABLE 1. Reasons and numbers of dropouts during study

	Unknown		Gastrointestinal complaints		Poor compliance		Other	
Reason	(%)	(n/total)	(%)	(n/total)	(%)	(n/total)	(%)	(n/total)
Male donors								
40 mg iron	15.5	15/97	5.2	5/97	12.4	12/97	13.4	13/97
20 mg iron	18.8	18/96	6.3	6/96	16.7	16/96	3.1	3/96
0 mg iron (placebo)	20.8	20/96	6.3	6/96	21.9	21/96	11.5	11/96
Female donors								
40 mg iron	8.9	7/79	2.5	2/79	10.1	8/79	6.3	5/79
20 mg iron	20.3	16/79	6.3	5/79	11.4	9/79	6.3	5/79
0 mg iron (placebo)	24.1	19/79	3.8	3/79	10.1	8/79	11.4	9/79

TABLE 2. Serum ferritin concentration, number of donors with depleted iron stores (ferritin concentration <12 µg/L), and logarithm of the ratio of transferrin receptor to ferritin concentration (log[TfR/F]) for all donors with at least one follow-up visit

Visit number	Ferritin (µg/L) (mean ± SD)	Depleted iron stores (%)	Depleted iron stores (n/total)	log(TfR/F) (mean ± SD)
Male donors				
40 mg iron				
0	32.7 ± 27.5	26.3	20/76	1.54 ± 0.51
1	31.4 ± 18.8	16.2	12/74	1.47 ± 0.49
2	30.2 ± 20.8	17.9	10/56	1.50 ± 0.51
3	33.2 ± 26.7	13.0	7/54	1.52 ± 0.55
20 mg iron				
0	34.7 ± 36.3	25.3	20/79	1.48 ± 0.48
1	33.1 ± 33.3	21.8	17/78	1.46 ± 0.44
2	30.2 ± 32.7	25.4	15/59	1.47 ± 0.45
3	25.0 ± 19.8	24.5	13/53	1.52 ± 0.47
0 mg iron (placebo)				
0	35.1 ± 32.4	19.7	14/71	1.55 ± 0.50
1	27.5 ± 27.9	30.9	21/68	1.61 ± 0.45
2	24.9 ± 24.7	29.8	14/47	1.60 ± 0.52
3	21.4 ± 27.5	53.9	21/39	1.67 ± 0.53
Female donors				
40 mg iron				
0	19.3 ± 15.0	39.4	26/66	1.43 ± 0.65
1	28.5 ± 19.8	15.2	10/66	1.26 ± 0.49
2	31.4 ± 19.4	14.0	8/57	1.29 ± 0.54
20 mg iron				
0	20.0 ± 32.3	54.6	30/55	1.38 ± 0.46
1	23.3 ± 27.9	45.1	23/51	1.36 ± 0.42
2	23.5 ± 26.1	34.1	15/44	1.35 ± 0.49
0 mg iron (placebo)				
0	17.7 ± 15.0	48.9	23/47	1.39 ± 0.65
1	17.6 ± 14.5	44.2	19/43	1.40 ± 0.42
2	15.1 ± 12.3	48.7	19/39	1.55 ± 0.66

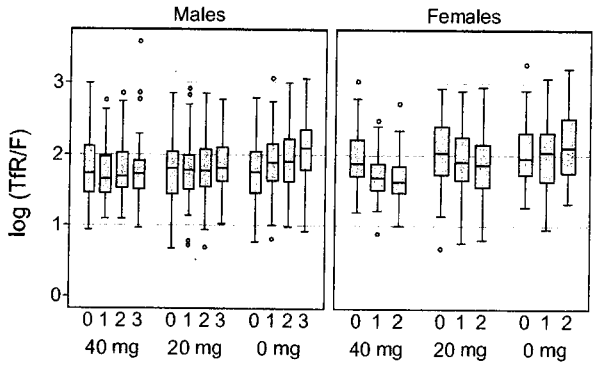

Fig. 3. Box-plots for the logarithm of the ratio of soluble transferrin receptor to ferritin concentration in male and female donors.

(Fig. 3), as was clearly demonstrated in the regression analysis (Table 3). The log(TfR/F) value increased by nearly 0.09 per donation in the placebo group, but changed only marginally in the two iron groups. Both iron groups differed significantly from the placebo group with respect to log(TfR/F).

Females

Of the 237 female volunteers (age range, 19-65 years) enrolled in the study, 96 (41%) dropped out, yielding a dropout rate of 28 percent in the 40 mg iron group, 44 percent in the 20 mg iron group, and 49 percent in the placebo group ($p = 0.015$; Fisher's exact test). A total of 69 (72%) of the female dropouts withdrew before their second visit (Table 1). The mean interval between visits was 88 days. Deferral from donation because of unacceptable dropout concentration values (<12.5 mg/dL) occurred in 13 of 546 visits (2.4%). This was the case more frequently in the placebo group than in the 20 mg and 40 mg iron groups (n = 10 vs. 2 vs. 1, $p = 0.001$; Fisher's exact test). Compliance was poor in roughly one-quarter of the female participants.

In the female placebo group, the mean concentration of serum ferritin decreased from 18 µg per L at baseline to 15 µg per L at the final visit, the number of females with depleted iron stores (ferritin <12 µg/L) remained constant (49%), and the mean soluble transferrin receptor concentration rose from 1.4 mg per L to 1.6 mg per L (Table 2, Fig. 4). In the female 20 mg iron group, serum ferritin increased from 20 µg per L to 24 µg per L, the number of individuals with depleted iron stores decreased from 55 percent to 34 percent, and the transferrin receptor concentration remained nearly constant (1.4 mg/L). In the female 40 mg iron group, ferritin concentration rose from 19 µg per L to 31 µg per L, transferrin receptor level fell slightly from 1.4 mg per L to 1.3 mg per L, and the number of individuals with iron depletion decreased from 39 percent to 14 percent.

The log(TfR/F) dropped in both iron groups, but rose continuously in the placebo group (Table 2, Fig. 3), as demonstrated by the regression analysis. The log(TfR/F) value increased by nearly 0.09 per donation in the placebo group (Table 3), but decreased by roughly 0.06 and 0.12, respectively, in the 20 mg and the 40 mg iron groups.

Side effects

Most donors (approx. 60%) did not report any side effects. There was no significant difference in the incidence of adverse effects between the three groups. In particular, the frequency of gastrointestinal complaints was low (11% in the 40 mg iron group, 13% in the 20 mg iron group, and 11% in the placebo group).

TABLE 3. Regression models for the change in log(TfR/F)

Predictor	Coefficient	95-percent confidence interval	p value
Male donors			
20 mg Fe^{2+}	−0.074	−0.121 to −0.028	0.002
40 mg Fe^{2+}	−0.118	−0.168 to −0.068	<0.001
Constant	0.091	0.058 to 0.123	<0.001
Female donors			
20 mg Fe^{2+}	−0.150	−0.238 to −0.061	0.001
40 mg Fe^{2+}	−0.209	−0.292 to −0.127	<0.001
Constant	0.086	0.018 to 0.153	0.012

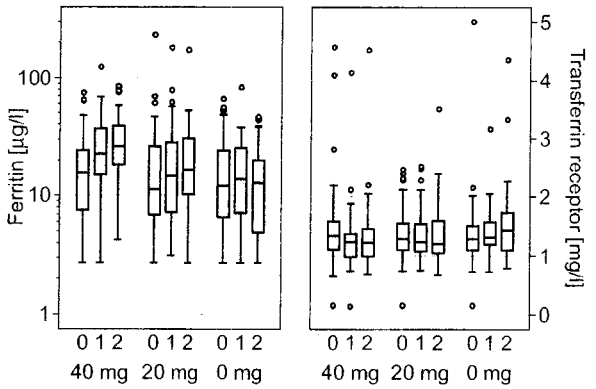

Fig. 4. Box-plot for the concentration of serum ferritin and soluble transferrin receptor in female donors.

DISCUSSION

Regular blood donation frequently leads to iron depletion, and it has been shown that iron supplementation can prevent this complication.[8,10,11] However, the exact dose needed to compensate for this type of iron loss remains unclear, and there is uncertainty as to whether iron supplementation is required in both male and female donors. Attempting to elucidate this complex issue more precisely, we monitored the logarithm of the TfR/F ratio as a measure of body storage iron in regular male and female whole-blood donors. The donors were randomly assigned to receive daily supplements containing selected vitamins plus 40 mg, 20 mg, or 0 mg of elemental iron. Dropout rates were marginally (male) or significantly (female) higher in the placebo group than in both iron groups. The reason for this finding is obscure.

Daily doses of 40 mg and 20 mg of elemental iron resulted in both a positive iron balance and an increase in storage iron in female donors and compensated for iron loss in males. This indicates that 20 mg of elemental iron per day is indeed sufficient to compensate for iron loss in both males and females. The differences in storage iron responses may be due to the shorter donation intervals in males (every 2 months) compared to females (every 3 months). It is likely that the ascorbic acid in the capsules may have increased the iron absorption by roughly 50 percent.[19] The question of whether the other vitamins may play any role in this context is speculative. The only reason for including these vitamins in the investigational products was our desire to improve the compliance rate.

In the present study, we monitored ferritin and soluble transferrin receptor levels as well as the logarithm of the TfR/F ratio. The latter variable, which was shown to have a highly linear correlation with body storage iron, is the most precise measure of body storage iron available.[14,15] Until now, body iron of blood donors was assessed mainly by measuring serum ferritin.[1,3,5-7] However, this variable is somewhat unspecific and may give false-high results in the presence of various underlying diseases.[2] In fact, if ferritin had been the only variable used for assessment of body storage iron, the effects of 20 mg elemental iron in males would have been underestimated in our study.

Interestingly, the number of side effects in the two groups treated with iron(II)-gluconate was only slightly higher than the number observed in the placebo group. In particular, the incidence of gastrointestinal side effects in the iron groups was very low (12%). Due to the slight risk of poisoning in children, iron capsules should be delivered in individual packages. Elemental iron preparations like carbonyl iron are preferred as an alternative by many experts due to the much higher lethal doses.[9,10,20,21] However, carbonyl iron is not available in the European countries. In comparison, bioavailabity of carbonyl iron is slightly lower than that of ferrous salts,[21] but side effects seem to be comparable: The incidence of gastrointestinal complaints for both preparations was reported much higher in two previous studies, probably due to the supplementation with higher doses of iron.[9,21] The utility of iron supplements for prevention of iron deficiency in menstruating female blood donors is currently being discussed.[20,22] However, others and we prefer a supplementation of iron for a short-term period after blood donation but not in general.

In conclusion, our results indicate that daily doses of 20 mg Fe^{2+} can adequately compensate for iron loss resulting from whole-blood donation in males who donate up to six times a year and in females who donate up to four times a year.

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2. 貧血と採血基準を考える
～血液学的立場から～

香川県赤十字血液センター
内田 立身

1．貧血の定義

貧血の定義について血液学の代表的な教科書をみると、①a reduction below normal in the concentration of hemoglobin or red blood cells in the blood[1] ②anemia is functionally best characterized by a hemoglobin concentration below normal[2] などの記載があり、健常人のヘモグロビンの下限値から判断するのが一般的である。米国人においては表1のような数字が用いられている[1) 2) 3) 4)]。この際、健常人として選ばれる対象のうち特に鉄欠乏状態の多い女性では血液学的に正常でない人が含まれ、下限域が低く算定される可能性があった。

表1 米国健常人のヘモグロビン(g/dL)下限値

	男性	女性	文献番号
WHO	13.0	12.0	3
Beutler E	14.0	12.3	1
Lee GR	13.2	11.6	2
NHANESⅢ	13.5	12.0	4

最近、Beutlerら[5] は米国人の貧血の定義としてNHANES-Ⅲ(The Third US National Health and Nutrition Examination Survey)[4] が行なったように、トランスフェリン飽和率16%以上、血清フェリチン10ng/mL以上の人を健常人として正常域の5%値未満を貧血としている(表2)。血液学的な貧血の定義として妥当な決め方である。

日本人の貧血の頻度について、私たちは「1981年～1991年」までの鉄欠乏の頻度を検索したことがあるが[6]、このデータをもとに鉄欠乏のない健常人を対象としてヘモグロビン値を求めたところ表3のとおりとなった。同じ方法で求められた斎藤ら[7] の成績とあわせると、鉄欠乏のない日本人のヘモグロビン下限値は男性12.8～13.2g/dL、女性11.8～12.1g/dLとなり、日本人成人の貧血の定義は男性13.0g/dL未満、女性12.0g/dL未満が妥当と考えられた。最近の日本人については鉄欠乏に関する正確なデータがなく、厚生労働省が行なっている「国民健康・栄養調査報告」などから鉄欠乏のない健常人のヘモグロビン値を求め、日本人の貧血の定義を定める必要がある。

表2 健常米国人のヘモグロビン(g/dL)下限値
(Beutler, 2006)

	男性(20～59歳)	女性(20～49歳)
白 人	13.7 (6,907人)	12.1 (2,966人)
アフリカ系	12.8 (434人)	11.1 (205人)

表3 鉄欠乏のない健常日本人のヘモグロビン値

	平均ヘモグロビン値	1標準偏差	5%正常分布値	文献
男性(284例)	14.8	1.0	12.8	6
女性(390例)	13.9	0.9	12.1	
男性 (26例)	15.0	0.9	13.2	7
女性(134例)	13.4	0.8	11.8	

2．日本人の貧血の頻度

私たちは、1981～1991年にかけて3,015名の女性で貧血の調査を行なった。その成績は、健常者43.6%、貯蔵鉄欠乏33.4%、潜在性鉄欠乏8.4%、鉄欠乏性貧血8.5%、その他6.5%

表4　日本人の貧血の頻度(%)（平成16年度国民健康・栄養調査報告から）

年齢	男性			女性		
	平均Hb±SD	Fr<10(%)	Hb下限値	平均Hb±SD	Fr<10(%)	Hb下限値
20～29	15.1±1.0	1.6	13.1	12.9±1.0	30.5	10.9
30～39	15.1±0.8	1.2	13.5	12.7±1.2	36.5	10.3
40～49	15.2±1.0	1.2	13.2	12.5±1.6	37.5	9.3
50～59	14.9±1.2	1.8	12.5	13.2±1.1	10.0	11.0
60～69	14.5±1.4	2.5	11.7	13.1±1.0	3.9	11.1
70≦	14.0±1.5	2.8	11.0	12.6±1.2	5.6	10.2
計	14.6±1.4	2.1	11.8	12.9±1.2	17.3	10.5

男性1,537名、女性2,634名の調査。

で40歳台前半では17.2％の鉄欠乏性貧血がみられた[6]。

その後、日本人についての詳細なデータがなく、特に女性の鉄欠乏性貧血の頻度をみるには毎年厚生労働省が行なっている国民健康・栄養調査から類推するのがよいと思われる[8]。表4はその成績である。高齢者を除くと男性の貧血は5.8％以下、鉄欠乏の頻度も2.5％以下であるが、女性は16.8％が貧血であり血清フェリチン低値(鉄欠乏)の頻度も高率であることから、ほとんどが鉄欠乏性貧血である。40歳台では25.0％に貧血があり同年代の半数（47.5％）が鉄欠乏状態にある。

また、香川県赤十字血液センターにおいて平成17年度に400mL献血を申し込んだ女性のうちヘモグロビン不足(Hb12.5g/dL未満)で献血ができなかった女性の比率[9]を表5に示すが、30～40歳台女性の約35％が献血できていない。また、日本赤十字社による全国的な調査によると[10]、平成17年に比重不足で献血できなかった人は485,746人で、これは東京都で1年間に献血できた人の数407,235人をはるかに凌駕するほどである。

表5　ヘモグロビン不足で献血できない女性の割合
（平成17年：香川県赤十字血液センター）

年齢	Hb<12.5g/dL
16～19	28.6%
20～29	32.6%
30～39	35.6%
40～49	35.3%
50～59	18.9%
60～69	17.5%
全体平均	19.4%（申込者数 9,963人）

わが国の女性の貧血の頻度は欧米に比して高い。米国の国民健康・栄養調査報告によると、20～40歳台の女性の鉄欠乏性貧血の頻度は5％、鉄欠乏状態は11％[11]、米国24血液銀行における2003年度の女性ヘモグロビン不足(12.5g/dL未満)の割合は平均で6.6％(1.3～13％)、Wisconsin州において17～49歳では21～23％である[12]。わが国のこれに対応する成績は400ml献血ができなかった女性が該当し、16～19歳で28.6％、20～29歳で32.6％、30～39歳で35.6％、40～49歳で35.3％であり[13]、どの調査をみても頻度は高いといわざるを得ない。

わが国で鉄欠乏の多い原因は鉄摂取量の不足にある。平成16年国民健康・栄養調査によると、男性の1日平均鉄摂取量は8.1mg、女性の1日平均は7.7mg（20～39歳で6.9～7.0mg)で必要量に比して少ない[8]。日本人の必要鉄摂取量は男性10mg、月経のある女性12mgであるが、その差2mgは全血にして10～12mLにしか相当せず、平均的月経量を30～40mLとして外国並に15～18mgは必要であろう。となるとわが国の月経のある女性は必要量の半分の鉄しか摂取していない。しかも鉄摂取量は過去の上記の調査によると年々減少してきている。

他方、米国における調査によると、白人男性で1日あたり17.2±0.3mg、女性で13.4±0.4mgで相当の開きがある[8]。採血基準を考える際には、以上のようなわが国の事情を勘案して決める必要がある。

3．採血基準をどう決めるか

日本の現状を踏まえて、わが国の採血基準をどう決めたらよいかについて以下に私見をまじえて述べたい。

代表的な国の採血基準を表6に示す。このうちEU諸国とオーストラリアは男女差があるが、米国とわが国は男女差がない。わが国の採血基準は1986年に改定され、200mL献血と400mL献血に分け、比重法かヘモグロビン法で判定するようになっている。現在、貧血の定義はヘモグロビンで記載されており、わが国の医療機関のすべてがヘモグロビン法で貧血を診断しているので、ヘモグロビン法に統一することが望ましい。また献血も400mL献血が主流になりつつあるので諸外国に倣い200mL、400mLを一本化して表記するのがよいと考えられる。

表6　各国の採血基準（400mL相当）

	男性	女性
Council of EU	13.5	12.5
Australia	13.0	12.0
U.S.A	12.5	12.5
日本	12.5	12.5

1)　ヘモグロビンの正常範囲から決める

鉄欠乏のない健常者から正常分布域を定め、5％正常値を求めると男性13.0g/dL、女性12.0g/dLとなり、これ以上を採血基準とする方法はわかりやすく貧血の定義とも一致する。

2)　貧血状態にない人から採血する

赤血球は鉄欠乏の進展に伴い、小赤血球化、低色素性化する。図1、図2は男性および女性におけるヘモグロビンと赤血球恒数との関係で、MCV・MCHが低下するのは男性で12.5g/dL、女性で12.0～12.5g/dLである[14]。また、鉄欠乏性貧血82例の私達の検討から、ヘモグロビンの分布域の上限は13.0g/dLであることをみると、現行の米国やわが国の基準である12.5g/dLは矛盾しない数字となってくる。

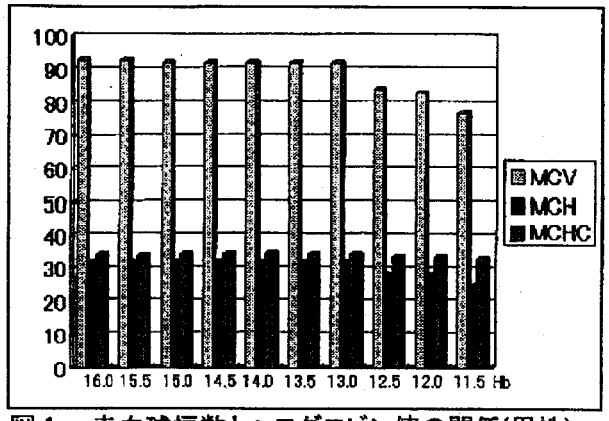

図1　赤血球恒数とヘモグロビン値の関係(男性)

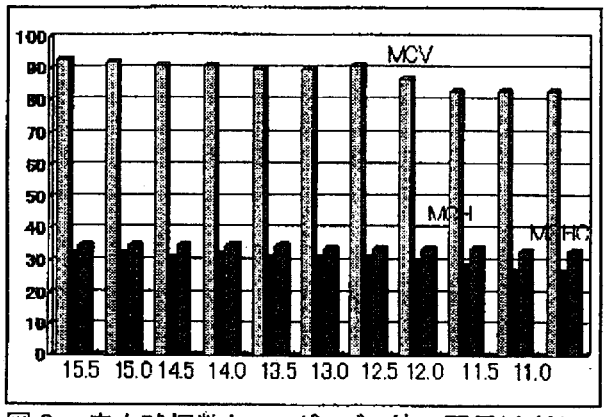

図2　赤血球恒数とヘモグロビン値の関係(女性)

3)　現在考えられる適切な採血基準は

上記を踏まえて採血基準について考察すると、わが国では鉄欠乏状態にある女性の頻度が高く、抜本的対策の見出せない現状では、貧血のない鉄欠乏からの採血をできるだけ避けるために女性の基準は12.0g/dLよりは12.5g/dLのほうが妥当と思われる。また、男性については貧血のない鉄欠乏はほとんどないが、12.5～13.0g/dLは貧血の人から採血することになり矛盾を生ずるので、13.0g/dLが妥当ではないかと思われる。

いずれにしても、採血基準の改定には正確なデータに基づく議論が必要である。それには、日本人の鉄欠乏性貧血、貧血のない鉄欠乏、鉄欠乏のない健常人の頻度（これは現行の国民健康・栄養調査の個々のデータから算出可能である）、献血申込者のヘモグロビン不足による男女別、年齢別不適格者の頻度などの解析によって決められるべきであろう。

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(17)

American Red Cross

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Dear Parent or Guardian,

Your 16-year-old has expressed an interest in donating blood at an upcoming American Red Cross blood drive. The states of Illinois, Iowa, Kansas, Nebraska, Minnesota, Missouri and Wisconsin allow 16-year-olds to donate blood with written parental/guardian consent. We are asking for your support by completing the attached consent form.

Please read the attached forms: "What You Must Know Before Giving Blood" and "What You Must Know About NAT – A New Blood Test." If you have any questions about the information contained in these documents, please call 1-800-448-3543 – M-F: 8 am - 9 pm, Sat: 9 am - 1 pm, Sun: 4 pm - 8 pm – and press Option 6 to speak to a Red Cross donor health consultant.

We support each student's willingness to give blood and ask that you offer your encouragement too. Much like voting and driving a car, the opportunity to donate blood and save a life has become a right of passage for thousands of high school students. Becoming a blood donor is a very personal decision, and we understand that parents and students may be somewhat apprehensive about taking this step. This is completely natural, so we want to provide you with some additional information about donating blood.

Blood donation is a safe procedure using single-use sterile needles and supplies. To ensure that your student has a positive experience, we recommend that they follow these guidelines:

- Get a good night's sleep before the blood drive.
- Eat well and drink plenty of fluids in the days leading up to the blood drive, especially the day of the drive.
- Drink at least 16 oz of caffeine free fluid (2 cups) 3-4 hours before the donation and after.
- Be honest and accurate about their weight (donors must weigh at least 110 lbs).

While the donation process is safe, reactions can occur. Most reactions are mild and can include fainting or small bruises. Our staff is fully trained to work with first-time and younger blood donors, and to respond to any reactions. We hope you will encourage your student to support our blood drive. Since one blood donation can be separated into three components, your student has the potential to save as many as three lives with a single donation.

Please note that the FDA requires that donors are asked specific questions about their health history. This information helps ensure the safety of the blood donor and the blood recipient. These questions are asked privately and are completely confidential.

You should be very proud of your son or daughter's decision to donate at the upcoming drive. *Please help support this act of generosity by completing the consent form prior to the drive.* If you are not currently a blood donor, please consider making an appointment for yourself. For more information call 1.800.GIVE.LIFE or visit our website at givebloodgivelife.org.

Sincerely,

David C. Mair MD

David C. Mair, M.D., Senior Medical Director

Form:
Informed Parental Consent for Persons Not of a Legal Majority

What this form is about

This form provides staff with a mechanism for documenting a parent or legal guardian's informed consent for someone not of legal majority to donate blood or blood components.

Who should use this form

This form applies to all staff who obtain informed special consent from donors or parent/legal guardian.

Instructions

- Ensure the region-identifying information is on the form.
- Instruct the parent/legal guardian to
  - Print the name of the son, daughter, or ward in the space provided.
  - Print his or her name.
  - Sign the consent form.
  - Date the consent form.
- Affix a Whole Blood Number/Donation Identification Number (WBN/DIN) to the form.

Revision History

Revision Number	Summary of Revisions
1.0	Initial version
1.1	Developed and released prior to revision history requirement
1.2	Revised instructions for completion of form Reformatted signature, date, and WBN lines