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

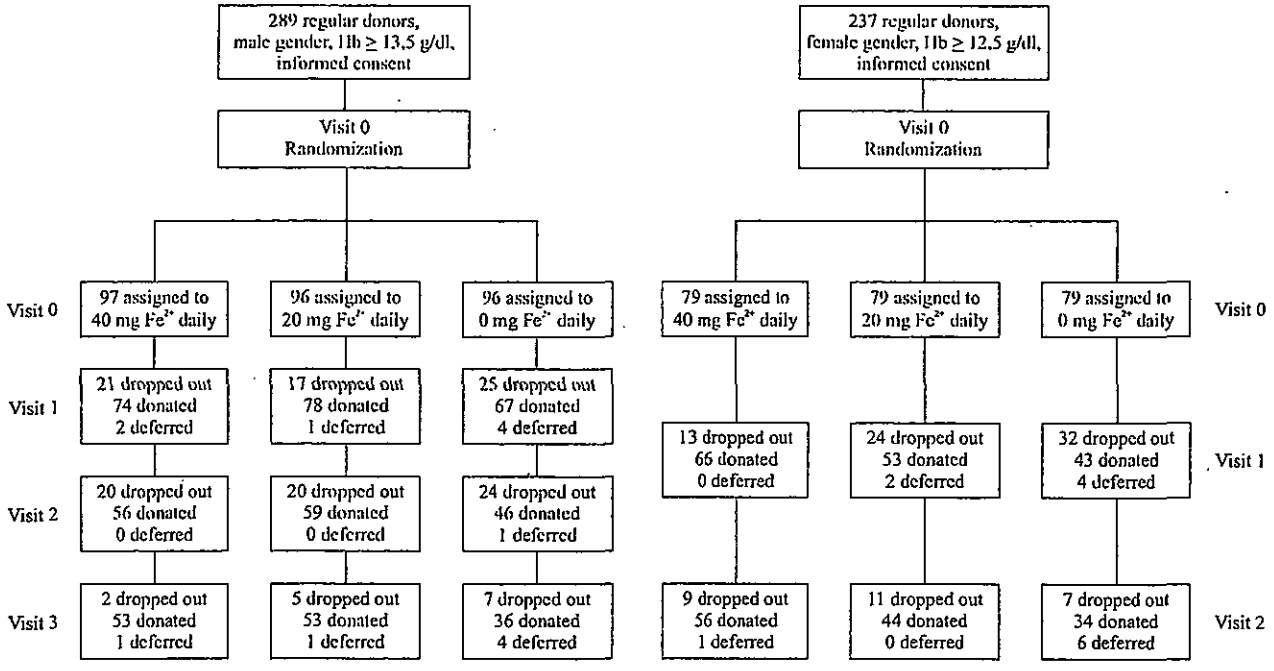

Fig. 1. Flow of participants during study.

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

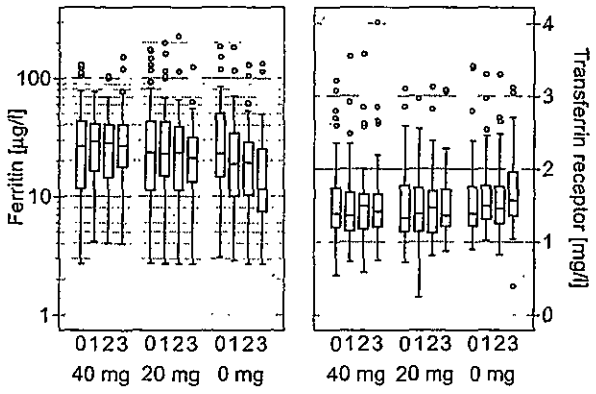

Fig. 2. Box-plot for the concentration of serum ferritin and soluble transferrin receptor in male donors.

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

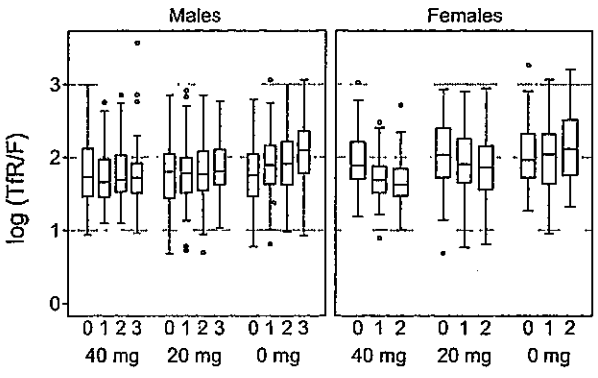

Fig. 3. Box-plots for the logarithm of the ratio of soluble transferrin receptor to ferritin concentration in male and female donors.

(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

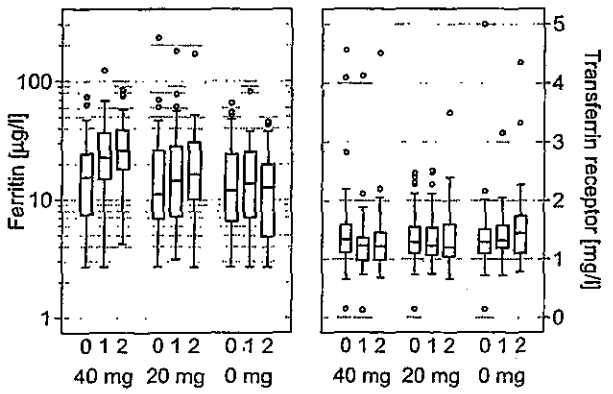

Fig. 4. Box-plot for the concentration of serum ferritin and soluble transferrin receptor in female donors.

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[4]。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。

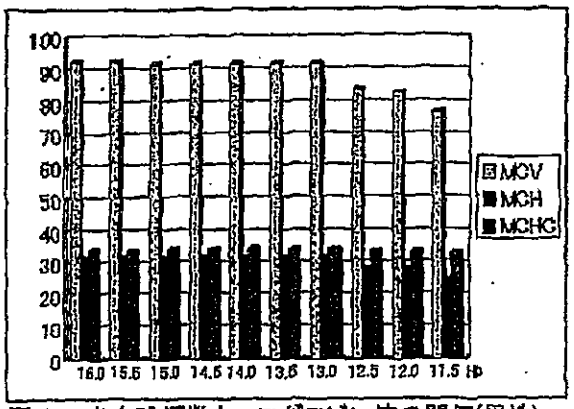

図1　赤血球恒数とヘモグロビン値の関係(男性)

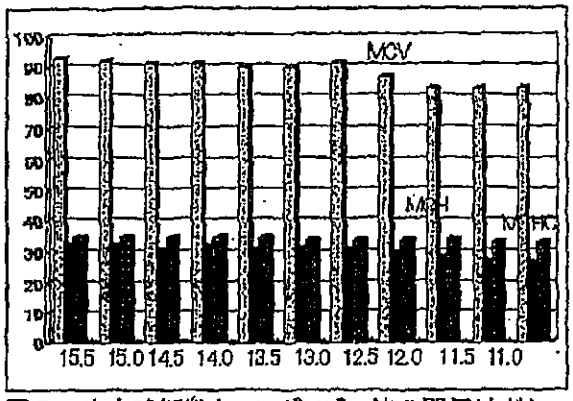

図2　赤血球恒数とヘモグロビン値の関係(女性)

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

Mid-America Division
Badger-Hawkeye Region
Heart of America Region
Midwest Region
North Central Region

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

American Red Cross Biomedical Services	Doc No 14.4.frm005	Version 1.2

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

Informed Parental Consent for Persons Not of a Legal Majority

Information

This form must be completed by a parent or legal guardian for blood donations by any person who has not yet reached the age of legal majority as defined by the laws of the state in which the donor makes the blood donation.

Questions or concerns about the blood donation process should be directed to

Department: **Donor Health Consultants**

Phone Number: **(800) 448-3543 (Press Option 6)**

Hours of operation: **M-F: 8am-9pm, Sat: 9am-1pm, Sun 4-8pm**

Parental Consent

I have received and read a copy of "What You Must Know Before Giving Blood" describing the overall blood donation process.

I have received and read a copy of "What You Must Know About NAT- A New Blood Test" describing additional test procedures and any research-related attachments.

I understand that in the event it becomes necessary to notify my son, daughter, or ward of test results, the American Red Cross will send those results directly to my son, daughter, or ward.

I understand the information provided to me and have had an opportunity to ask questions about the information it contains. I hereby give permission for my son, daughter, or ward, to make a voluntary donation of blood to the American Red Cross during his or her legal minority.

A signed consent from the Parent/Guardian will be required for each donation until the donor reaches the age of majority.

Donor Name [son, daughter, or ward] (print) _____

Parent/Guardian Name (print) _____

Parent/Guardian *Signature* _____ **Date:** / /

WBN/DIN → [ ]

American Red Cross Blood Services Washington, DC 20006	American Red Cross

WHAT YOU MUST KNOW ABOUT NAT

Possible Use of Donor Information and Blood Samples in Medical Research

The American Red Cross Blood Services mission is to provide a safe and effective blood supply for patients who need blood transfusions. As part of this mission, the American Red Cross may conduct research. Some research is conducted with other institutions, such as academic centers and biomedical companies.

Some examples of the types of research are:

- Studies relating to testing, storing, collecting and processing blood to increase the safety of the blood supply.
- Studies of new test methods for infectious agents carried in the blood, like Nucleic Acid Testing (NAT).
- Studies of ways to recruit blood donors and to evaluate donor eligibility.

Participation does not require additional blood to be collected or additional time.

By signing your Blood Donation Record, you are giving consent to allow us to use a portion of your blood donation and donor information for research like that listed above. Donor information for research will not include anything that would identify you as the donor, such as your name or Social Security Number (SSN).

Confidentiality

American Red Cross policy requires protection of the confidentiality of your donor identifying information, results of tests on your blood samples and information collected at the time of donation. Strict procedures are observed at all blood collection facilities to maintain the confidentiality of donor information.

Your donor identifying information will not be released to other institutions for research purposes without your consent. Your age, gender, general geographic location, and test results may be used to evaluate important information about disease or donor recruitment, but this information is combined with information about other donors and not identified with you.

While study results may be published, donor names and other identifying information will not be revealed, except as required by law. Records are kept, as required by State and Federal Laws. The Food and Drug Administration (FDA) may need to review and copy donor records in order to verify study data. The FDA, however, is committed to protection of the confidentiality of donor identity.

Testing and Storage

Blood samples used by researchers are coded. This means that your donor identifying information, including name and SSN, is not used in connection with research. Coded samples can be linked to information about donors' identity only by authorized Red Cross personnel who are required to follow Red Cross procedures to maintain confidentiality.

Some of your sample or information may be saved for future research on viruses or other agents that may be carried in blood. Samples linked to your identifying information may be used, either

now or in the future, for infectious disease testing, as described in What You Must Know Before Giving Blood or in other information about a specific research study that is being conducted today. Your identified sample and information will not be used for genetic testing or for research unrelated to blood safety without your consent.

You will be notified in person, by phone, or by letter, about any test results that may impact your health. You will receive information about how these test results may affect your health and future eligibility as a blood donor.

Possible Participation in a Follow Up Study
If your test results are positive or unexpected, Red Cross staff may ask you to participate in a follow up study. Participation is voluntary and of no cost to you.

Benefits
By using new infectious disease tests like NAT, you may find out sooner if you are infected by one of the agents being tested. This may be important to your health.

Risks
There is a very low chance that your blood sample may give a false positive or true positive infectious disease result. If this happens, the blood that you donate will not be used for transfusion and there is the likelihood that you may not be able to donate again. If you are donating for a specific patient and have a positive test result, your blood donation will not be available for that patient. If you are donating blood for yourself and have a positive result, your blood donation may not be available to you.

Your Right Not To Participate
You may refuse to participate now or at any time during the donation process. If you decide that you do not want your donation or donor information to be used for possible research like that listed above, you will not be able to donate today. It is very important to include all donors in such research in order to provide a safe and effective blood supply.

If you decide not to participate at this time, your decision will not change your future relationship with the Red Cross.

If you begin donating and then decide that you do not want to participate, you must notify the blood collection staff before you leave the collection site. If you decide to withdraw in the future, contact the Scientific Support Office at (301) 212-2801. However, test information collected before your withdrawal may still be used or disclosed after your withdrawal.

Questions
If you have any questions about your donation, please feel free to ask the ARC staff member performing your confidential health history interview. If you have questions later, you can contact the Blood Center at 1-800-652-9742.

If you have scientific questions, you can call the Scientific Support Office at (301)212-2801. If you have any questions about your rights as a research participant, call the American Red Cross Institutional Review Board Administrator at (301)738-0630.

You have been given this information sheet to read and will be offered a copy to keep.

American Red Cross Blood Services
Washington, DC 20006

What You Must Know Before Giving Blood

Thank you for coming in today!

This information sheet explains how **YOU** can help us make the donation process safe for yourself and patients who might receive your blood. **PLEASE READ THIS INFORMATION BEFORE YOU DONATE!** You will be asked to sign a statement that says you understand and have read this information today. **If you have any questions now or anytime during the screening process, please ask blood center staff.**

Accuracy And Honesty Are Essential

Your **complete honesty** in answering all questions is very important for the safety of patients who receive your blood. We will ask you for identification each time you try to donate. Please register using the same identifying information each time you donate (name, date of birth, etc.). **All information you provide is confidential.** Although your interview will be private, it may require more than one American Red Cross employee to participate in or be present at your health history and blood donation.

What happens when you give blood

To determine if you are eligible to donate we will:

- ask questions about your health, travel, and medicines
- ask questions to see if you might be at risk for hepatitis, HIV, or AIDS
- take your blood pressure, temperature, and pulse, and
- take a small blood sample to make sure you are not anemic.

If you are able to donate we will:

- cleanse your arm with an antiseptic. **(If you are allergic to Iodine, please tell us!),** and
- use a new, sterile, disposable needle to collect your blood.

While you are donating: (the donation usually takes about 10 minutes)

- you may feel a brief "sting" from the needle at the beginning.

After donating we will give you

- a form with post-donation instructions, and
- a number to call if you have any problems or decide after you leave that your blood may <u>not</u> be safe to give to another person.

What to expect after donating

Although most people feel fine before and after donating blood, a small number of people may have a(n)

- lightheaded or dizzy feeling
- upset stomach
- black and blue mark, redness, or pain where the needle was, and
- very rarely, loss of consciousness, or nerve or artery damage.

We will give you a number to call to report any problems or concerns you may have following your donation.

Why we ask questions about sexual contact

Sexual contact may cause contagious diseases like HIV to get into the bloodstream and be spread through transfusions to someone else.

Definition of "sexual contact":

The words "have sexual contact with" and "sex" are used in some of the questions we will ask you, and apply to any of the following activities, whether or not a condom or other protection was used:

- vaginal sex (contact between penis and vagina)
- oral sex (mouth or tongue on someone's vagina, penis, or anus), and
- anal sex (contact between penis and anus).

Continued on back

American Red Cross Blood Services
Washington, DC 20006

What You Must Know Before Giving Blood, Continued

Persons who should not donate

You should not give blood if you

- had hepatitis on or after the age of 11
- had malaria in the past 3 years
- met any of the conditions listed in the CJD Information Sheet
- were held in a correctional facility (including jail, lock up, prison, or juvenile detention center) for more than 72 straight hours in the last 12 months.
- have had sexual contact in the past 12 months with anyone who is sick with hepatitis or AIDS
- had or were treated for syphilis or gonorrhea or tested positive for syphilis in the last 12 months
- were raped in the last 12 months
- **have AIDS or have ever had a positive HIV test**
  AIDS is caused by HIV. HIV is spread mainly through sexual contact with an infected person, or by sharing needles or syringes used for injecting drugs.
- **done something that puts you at risk for becoming infected with HIV**
  You are at risk for getting infected if you
  - have ever used needles to take drugs, steroids, or anything not prescribed by your doctor
  - are a male who has had sexual contact with another male, even once, since 1977
  - have ever taken money, drugs, or other payment for sex since 1977
  - have had sexual contact in the past 12 months with anyone described above
  - received clotting factor concentrates for a bleeding disorder such as hemophilia
  - were born in, or lived in, Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria, since 1977.
  - since 1977, received a blood transfusion or medical treatment with a blood product in any of these countries, or
  - had sex with anyone who, since 1977, was born in or lived in any of these countries.
- have any of the following conditions that can be signs or symptoms of HIV/AIDS
  - unexplained weight loss (10 pounds or more in less than 2 months)
  - night sweats
  - blue or purple spots in your mouth or skin
  - white spots or unusual sores in your mouth
  - lumps in your neck, armpits, or groin, lasting longer than one month
  - diarrhea that won't go away
  - cough that won't go away and shortness of breath, or
  - fever higher than 100.5 F lasting more than 10 days.

Ineligible donors

We maintain a confidential list of people who may be at risk for spreading transfusion-transmitted diseases. By continuing this process, you consent to be entered in this confidential list of deferred donors if you are at risk for spreading such diseases. When required, we report donor information, including test results, to health departments, military medical commands, and regulatory agencies. Donation information may also be used confidentially for medical studies.

If you decide not to give blood

If you decide that you should not give blood, you may leave now.

Testing your blood

Your blood will be tested for hepatitis, HIV (the virus that causes AIDS), syphilis, and other factors. (There are unusual circumstances in which these tests cannot be performed.) You will be notified about test results that may disqualify you from donating blood in the future or that may show you are unhealthy. Your blood will not be used if it could make someone sick. (A sample of your blood or a portion of your donation might be used now or in the future for additional tests or other medical studies. Please tell us if you object.)

Though the tests we use are very good, they are not perfect. HIV antibodies may take weeks to develop after infection with the virus. If you were infected recently, you might have a negative test result, yet be able to infect someone. That is why you must not give blood if you are at risk of getting AIDS or other infectious diseases. **If you think you may be at risk for HIV/AIDS or want an HIV/AIDS test, please ask for information about other testing facilities. Please do not donate to get tested for HIV, hepatitis, or any other infections!**

Travel to or birth in other countries	Blood donor tests may not be available for some contagious diseases that are found only in certain countries. If you were born in, have lived in, or visited certain countries, you may not be eligible to donate.

American Red Cross Biomedical Services	Doc No ARC F6628CJD	Version 05/08
Form: **CJD Information Sheet**		

What this form is about

This form explains Creutzfeldt-Jakob disease to the donor.

Who should use this form

This form applies to collections staff.

Revision History

Revision Number	Summary of Revisions
07/04	Developed and released prior to revision history requirement
05/08	• Removed watermark so sheet can be printed from eDOCs or eBinder • Revised American Red Cross Logo • Placed into System 3 Document template

CJD Information Sheet

American Red Cross

Please do not donate if you—

- Since January 1, 1980 through December 31, 1996—
  - -Spent a total time that adds up to 3 months or more in any country(ies) in the United Kingdom (UK).
  - -The UK includes any of the countries listed in Table 1 below.
- Were a member of the U.S. military, a civilian military employee, or a dependent of a member of the U.S. military that spent a total time of 6 months on or associated with a military base in any of the following areas during the specified time frames—
  - -From 1980 through 1990 - Belgium, the Netherlands (Holland), or Germany
  - -From 1980 through 1996 - Spain, Portugal, Turkey, Italy, or Greece
- Since January 1, 1980 to present—
  - -Spent a total time that adds up to 5 years or more in Europe (includes time spent in the UK from -1980 through 1996 and time associated with the military bases in Europe as outlined above).
  - -The European countries that are affected are listed below in **Table 1** and **Table 2**.
  - -Received a blood transfusion in any country(ies) listed in **Table 1** below.
  - -Received an injection of bovine (beef) insulin made in any of the countries listed below.
- Ever received—
  - -A dura mater (or brain covering) transplant during head or brain surgery.
  - -Human pituitary growth hormone (brain extract).
- Any blood relative has had Creutzfeldt-Jakob disease. A blood relative is your mother/father, grandparent, sibling, aunt/uncle, or children.
- Have been told that your family is at risk for Creutzfeldt-Jakob disease.

If any of these apply to you, your donation cannot be accepted. If you have any questions, please ask us. We sincerely appreciate your support.

Table 1

United Kingdom			
♦ Channel Islands	♦ Falkland Islands	♦ Isle of Man	♦ Scotland
♦ England	♦ Gibraltar	♦ Northern Ireland	♦ Wales

Table 2

Europe		
♦ Albania	♦ Hungary	♦ Poland
♦ Austria	♦ Ireland (Republic of)	♦ Portugal
♦ Belgium	♦ Italy	♦ Romania
♦ Bosnia/Herzegovina	♦ Kosovo (Federal Republic of Yugoslavia)	♦ Serbia (Federal Republic of Yugoslavia)
♦ Bulgaria	♦ Liechtenstein	♦ Slovak Republic (Slovakia)
♦ Croatia	♦ Luxembourg	♦ Slovenia
♦ Czech Republic	♦ Macedonia	♦ Spain
♦ Denmark	♦ Montenegro (Federal Republic of Yugoslavia)	♦ Sweden
♦ Finland	♦ Netherlands (Holland)	♦ Switzerland
♦ France	♦ Norway	♦ Turkey
♦ Germany		♦ Yugoslavia (Federal Republic includes Kosovo, Montenegro, and Serbia)
♦ Greece		

###

American Red Cross Biomedical Services	Doc No 14.4.ja021	Version 1.1
Job Aid: **Medication Deferral List**	Approved by Quality Assurance	
	Approval date 05.04.06	

Please tell us if you are now taking or if you have EVER taken any of these medications:

- ☐ **Proscar® (finasteride) – usually given for prostate gland enlargement**
- ☐ **Avodart® (dutasteride) – usually given for prostate enlargement**
- ☐ **Propecia® (finasteride) – usually given for baldness**
- ☐ **Accutane®, Amnesteem®, Claravis®, or Sotret®, (isotretinoin) – usually given for severe acne**
- ☐ **Soriatane® (acitretin) – usually given for severe psoriasis**
- ☐ **Tegison® (etretinate) – usually given for severe psoriasis**
- ☐ **Growth Hormone from Human Pituitary Glands – used only until 1985, usually for children with delayed or impaired growth**
- ☐ **Insulin from Cows (Bovine, or Beef, Insulin) – used to treat diabetes**
- ☐ **Hepatitis B Immune Globulin – given following an exposure to hepatitis B**

  Note: This is different from the hepatitis B vaccine which is a series of 3 injections given over a 6 month period to prevent future infection from exposures to hepatitis B.

- ☐ **Unlicensed Vaccine – usually associated with a research protocol**

Please tell us if you are now taking or if you have taken any of these medications in the last 7 days:

- Clopidogrel
- Coumadin (warfarin)
- Heparin
- Plavix
- Ticlid
- Ticlopidine

IF YOU WOULD LIKE TO KNOW WHY THESE MEDICINES AFFECT YOU AS A BLOOD DONOR, PLEASE KEEP READING:

- If you have taken or are taking **Proscar, Avodart, Propecia, Accutane, Amnesteem, Claravis, Sotret, Soriatane, or Tegison,** these medications can cause birth defects. Your donated blood could contain high enough levels to damage the unborn baby if transfused to a pregnant woman. Once the medication has been cleared from your blood, you may donate again. Following the last dose, the deferral period is one month for **Proscar, Propecia, Accutane, Amnesteem, Claravis** or **Sotret**, six months for **Avodart** and three years for **Soriatane**. Tegison is a permanent deferral.
- **Growth hormone from human pituitary glands** was prescribed until 1985 for children with delayed or impaired growth. The hormone was obtained from human pituitary glands, which are found in the brain. Some people who took this hormone developed a rare nervous system condition called Creutzfeldt-Jakob Disease (CJD, for short). The deferral is permanent. CJD has not been associated with growth hormone preparations available since 1985.
- CJD has been reported in extremely rare cases in Australian women who took **gonadotropin from human pituitary glands** for treatment for infertility. Gonadotropin from human pituitary glands was manufactured and distributed outside the United States and was never marketed in the United States to treat infertility. Human chorionic gonadotropin which is used for fertility treatments in the United States is not derived from human pituitary glands and is not a cause for deferral.
- **Insulin from cows (bovine, or beef, insulin)** is an injected material used to treat diabetes. If this insulin was imported into the US from countries in which "Mad Cow Disease" has been found, it could contain material from infected cattle. There is concern that "Mad Cow Disease" is transmitted by transfusion. The deferral is indefinite.
- **Hepatitis B Immune Globulin (HBIG)** is an injected material used to prevent infection following an exposure to hepatitis B. HBIG does not prevent hepatitis B infection in every case, therefore persons who have received HBIG must wait 12 months to donate blood to be sure they were not infected since hepatitis B can be transmitted through transfusion to a patient.
- **Unlicensed Vaccine** is usually associated with a research protocol and the effect on blood transmission is unknown. The deferral is for one year.
- If you have taken **Clopidogrel, Plavix Ticlid, or Ticlopidine in the last 7 days,** these medications affect the portion of your blood called platelets. If you are donating platelets, your donated blood could contain high enough levels of the medications that it could affect the quality of the platelets that you give. Once the medication has been cleared from your blood, you may donate platelets again. Following the last dose, the deferral period is 7 days.
- If you have taken **Coumadin (Warfarin) or Heparin in the last 7 days,** these medications can affect the blood's ability to clot, which might cause excessive bruising or bleeding when you donate. Therefore, we ask that you be off of these drugs for 7 days prior to giving blood. Following the last dose, the deferral period is 7 days.

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American Red Cross Biomedical Services Washington, DC 20006	**Controlled Documents Approval**	

SECTION 1: Document Package Information

Transmittal Sheet Title: Revised health History Tables and Related Douments Number: 2522
Version: 1.0

Document Title: Time Period: May 2006

List Documents Here:	14.4.ja041, v-1.1	14.4.tbl010, v-1.4
14.3.019, v-1.3	14.4.ja049, v-1.2	14.4.tbl011, v-1.2
14.3.070, v-1.2	14.4.tbl001, v-1.3	14.4.tbl012, v-1.2
14.3.092, v-1.2	14.4.tbl002, v-1.3	14.4.tbl016, v-1.3
14.3.094, v-1.2	14.4.tbl003, v-1.4	14.4.tbl021, v-1.2
14.4.ja021, v-1.1	14.4.tbl004, v-1.4	14.4.tbl023, v-1.3
14.4.ja028, v-1.2	14.4.tbl005, v-1.2	14.4.tbl024, v-1.3
14.4.ja029, v-1.4	14.4.tbl006, v-1.3	14.4.tbl025, v-1.2
14.4.ja031, v-1.3	14.4.tbl008, v-1.2	14.4.tbl026, v-1.2
14.4.ja032, v-1.1	14.4.tbl009, v-1.3	
List Documents Here (continued):		
14.4.tbl027, v-1.2	14.4.tbl039, v-1.3	
14.4.tbl028, v-1.2	14.4.tbl044, v-1.3	
14.4.tbl029, v-1.4	14.4.tbl045, v-13.	
14.4.tbl030, v-1.2	14.4.tbl046, v-1.3	
14.4.tbl031, v-1.3	14.4.tbl047, v-1.3	
14.4.tbl033, v-1.2	14.4.tbl048, v-1.3	
14.4.tbl034, v-1.4	14.4.tbl201, v-1.1	
14.4.tbl035, v-1.2	14.4.tbl202, v-1.1	
14.4.tbl036, v-1.2	14.4.tbl208, v-1.1	

American Red Cross Biomedical Services Washington, DC 20006	**Controlled Documents Approval**	

SECTION 2: Approvals

Your approval signifies that you have reviewed the documents according to the requirements for your functional area.

Signatory Name	Role	Signature	Date
Please print or type name here Pat Demaris Anne Eder	*Check role* Process Owner ☒ CEO/ Division VP ☐ None ☐ Medical Office ☒ None ☐ Executive QA ☒ System QA ☐ BIT-QRM ☐ Testing Support QA ☐ Facility Quality Director ☐	Pat Demaris Anne Eder	05/05/06 05/05/06 05.05.06

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平成１５年度　厚生労働科学研究費補助金（医薬品等医療技術リスク評価研究事業）
分担研究報告書

４．採血により献血者に起こる副作用・合併症の解析

―平成14年の全国データから―

分担研究者
佐竹　正博　（東京都赤十字血液センター）
中村　榮一　（東京都赤十字血液センター）

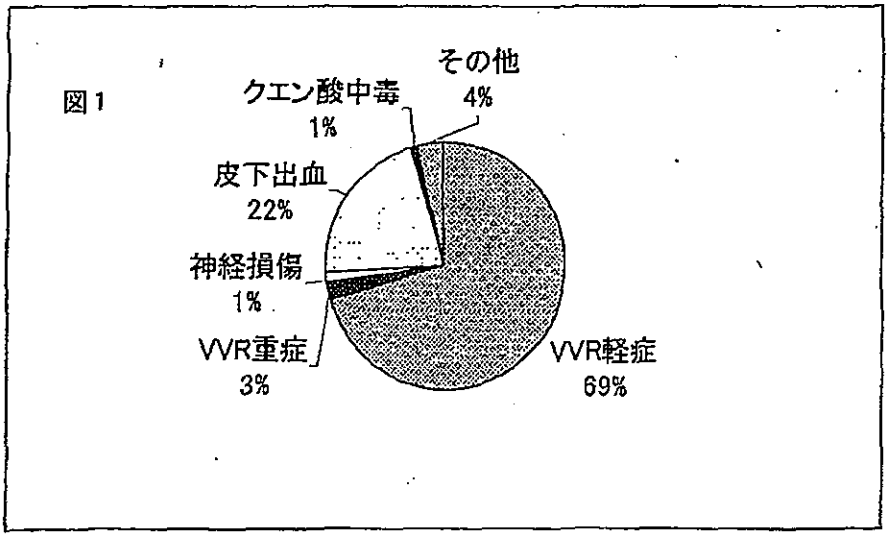
日本赤十字社では、献血時の採血によって献血者に起こる副作用や合併症のデータを集積しているが、ここでは全国の血液センターから集められた平成14年のデータをもとに解析を試みた。

まず、すべての採血種における全献血者の副作用の頻度を表に示した。

	VVR 軽症	VVR 重症	神経損傷	皮下出血	クエン酸中毒	その他	合計
%	0.73	0.026	0.011	0.23	0.011	0.039	1.04

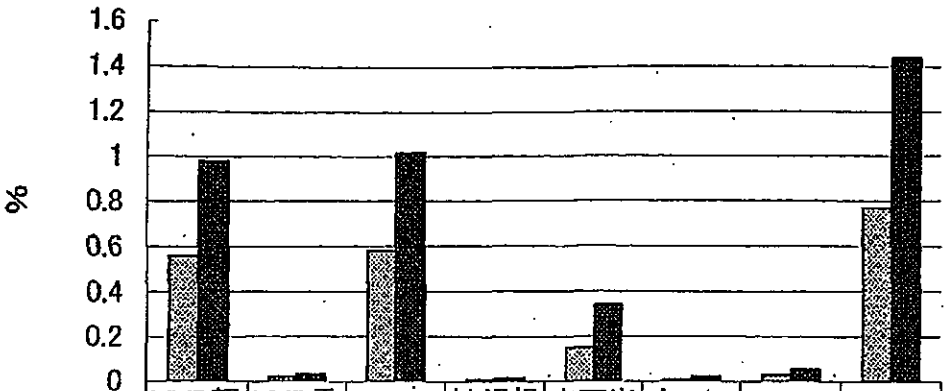
全献血者の約1%に何らかの副作用が起こっており、その73%はVVR（vasovagal reaction、血管迷走神経反応）である。献血者に長期にわたる愁訴・運動障害などを起こす可能性のある神経損傷が1万人に1.1人の確率で起こることは重大である。副作用の割合を示したのが図1である。VVRに次いで、皮下出血が22%を占めている。

図1



これを男女別にみたのが次の図2である。

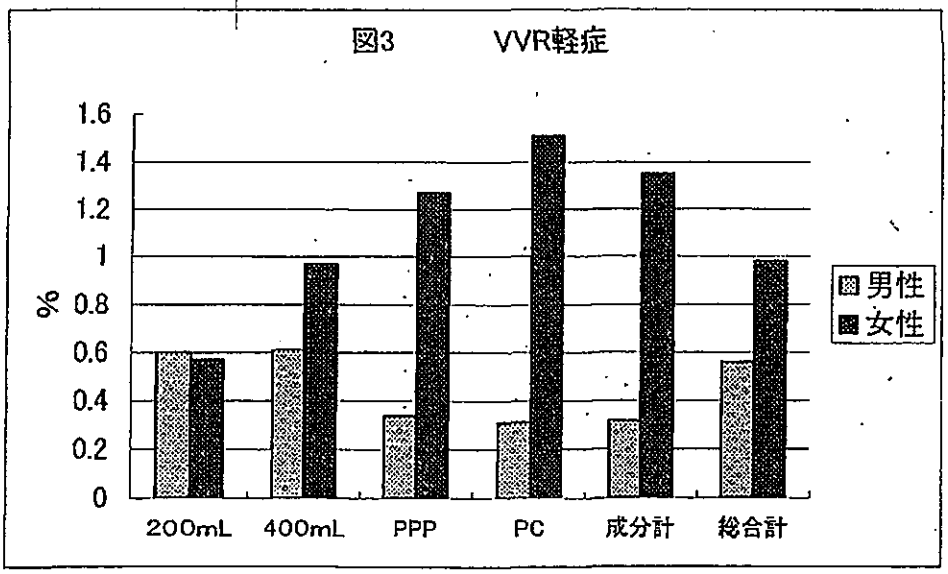
図2　　全ての採血



	VVR軽症	VVR重症	VVR計	神経損傷	皮下出血	クエン酸中毒	その他	合計
男性	0.56	0.021	0.58	0.0093	0.15	0.0051	0.029	0.77
女性	0.98	0.035	1.02	0.014	0.34	0.02	0.054	1.44

男女別でとくにパターンの大きな変化はないが、すべての副作用において女性のほうがその頻度が高い。しかしながら、これを採血種別にみていくと男女間でかなり大きな差があることがわかる。図 3 は比較的軽症の VVR の発生頻度を採血種別にみたものである。

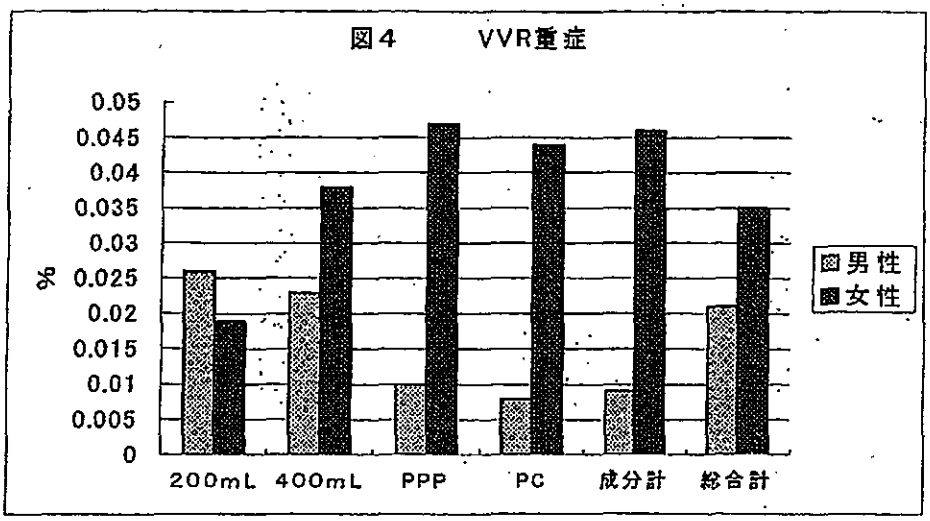
図3　　VVR軽症



200mL 採血では男女ほぼ同じ頻度で VVR が起こっているが、400mL になると女性のほうが有意に多くなる。これは、女性のほうが一般に循環血液量が少なく、血管内の volume loss による症状が現れやすく、それが VVR に加算されて頻度が高くなったものと思われる。PC や PPP の成分採血になると、男性ではむしろ VVR が少なくなっているのに対し、女性ではさらに頻度が高くなっている。女性で多くなるのは、前述のように血漿採取量の増加の影響が出ているものと思われるが、男性でかえって少なくなる理由は不明である。男性の場合、血漿採取量が循環血液量に影響を及ぼさない範囲では、専用椅子に 1 時間近くゆっくり座って採血を受ける成分採血の方が心理

的に余裕があり、VVR が起こりにくいこともあるのではないかと想像される。

重症の VVR では図 4 にように 200mL 採血ではむしろ男性の方が多い。成分採血では女性は男性の 5 倍ほど重大



な転帰をとりやすい。男女とも 200mL 採血では循環血液量に影響が出ることはほとんど考えられないので、この採血において男女の VVR の頻度がほぼ同じであることは、純粋に神経学的な機序のみで起こる VVR の頻度に性差はあまりないことを示すものといえる。図 5 は軽症と重症を合わせた全 VVR の頻度である。

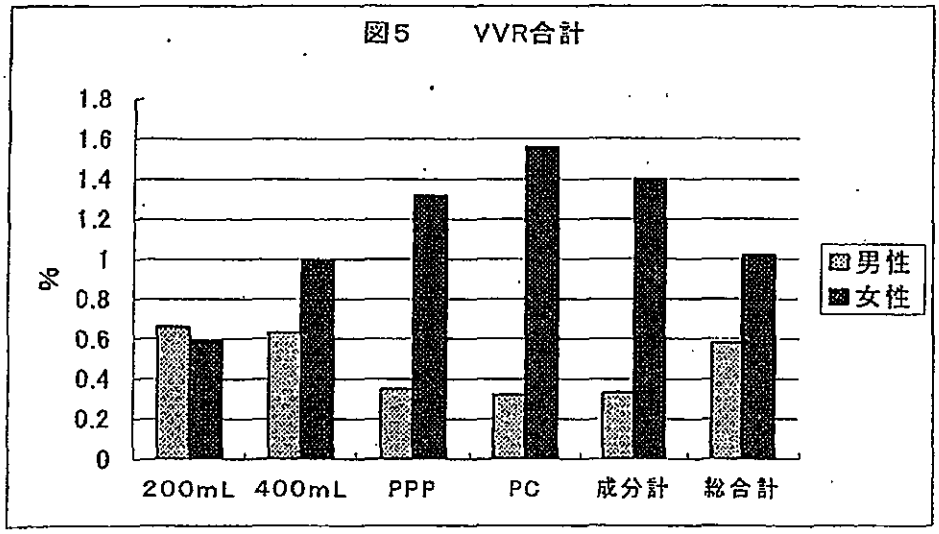
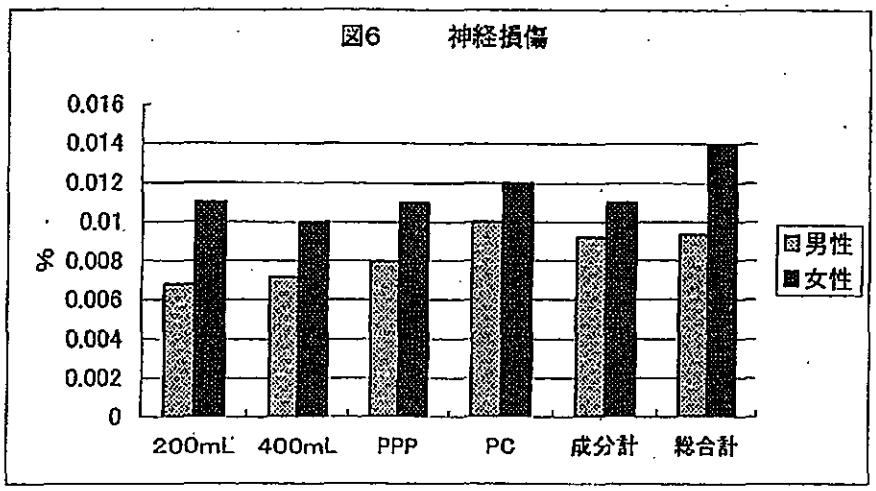
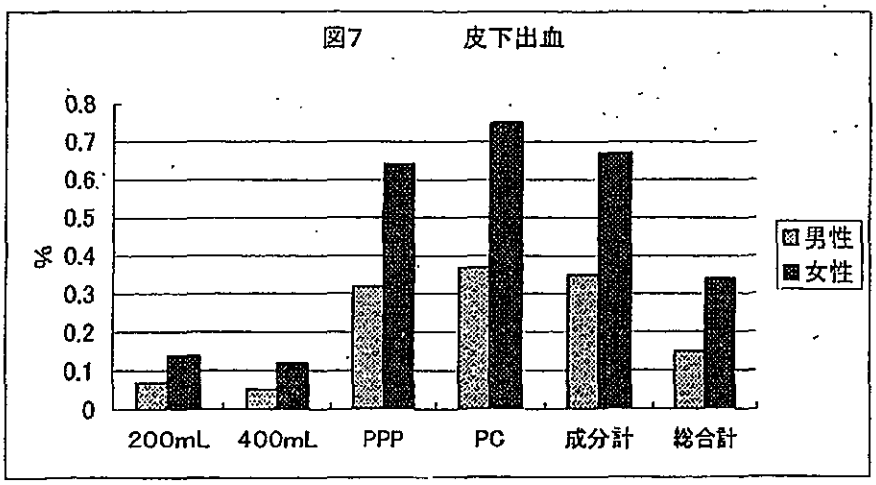


図6は神経損傷の頻度である。ここでは予想されるように採血種別による頻度の差はほとんどない。これはいっぽうでこのデータ収集が大きな片寄りのないものである事を示すものと思う。女性のほうがどの採血種別でも男性より頻度が高い。女性はより痛みに敏感であることが影響していると思われる。これは RSD(reflex



sympathetic dystrophy)などが女性に多いといわれる事などからも推察される。

図7は皮下出血の頻度である。特徴的なのは、200mL、400mL 採血ではどちらも同程度に頻度が低いのに対し、成分採血では約6倍ぐらい高いことである。これは、穿刺針が長時間静脈内に留置されている間に血管壁を傷つ



ける可能性が高いためであると考えられるが、さらに、長時間異物が挿入されていることにより、創傷の治癒機転が少なからず阻害される事もあるのではないかと考えられる。どの採血種でも女性は男性のちょうど2倍の報告がある。女性の方が美容上より気にしやすいこともあるだろうが、破綻血管からの止血について女性が本質的に弱点を持っている可能性はないだろうか。

図8はクエン酸中毒の頻度で、母集団は成分採血者のみとした。血漿採血（PPP）よりも血小板採血（PC）の方が遥かにクエン酸中毒を起こしやすい。これは採取血小板の凝集を防ぐために PC 採取の場合は ACD 輸注比を高く設定するためと、PC 採取の方が時間が長くかかるためと思われる。また、女性の方が圧倒的に頻度が高いのは、体格が小さいために循環血液量が少なく、クエン酸の血中濃度が高くなりやすいためと思われる。