Vasovagal reactions in high school students: findings relative to race, risk factor synergism, female sex, and non-high school particpants

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BACKGROUND: High school (HS) students have a high incidence of vasovagal reactions and are a good population for the study of vasovagal reactions.
STUDY DESIGN AND METHODS: Data from 1076 Caucasian students, 226 African-American students, and 157 nonstudents from HS blood drives in 2001 were entered into a database. Race, high-risk-factor synergism, the phenomenon of "survivorship," and female sex were evaluated. In addition, non-HS student participants were described.
RESULTS: Vasovagal reactions were 84 percent lower in African-American HS students than in Caucasian HS students (3 of 226 vs. 88 of 1076; 1.3 vs. 8.2 percent; $p = 0.0001$; relative risk, 6.2). In Caucasian HS students, first-time donor status increased the vasovagal reaction rate to 9.4 percent (vs. 3.6% in repeat donors, $p < 0.004$). Low weight ($\leq$ 130 lb) increased the reaction rate to 13.6 percent (vs. 3.3% in weight > 81.2 kg, $p < 0.001$). Together they increased the reaction rate to 16.0 percent (vs. 3.2%, $p < 0.0001$). Females had more reactions than males (11.3 vs. 4.8%, $p < 0.001$), but the reaction rates equalized when donors under 150 lb were excluded (5.7 vs. 4.6%, $p = 0.66$).
CONCLUSION: African-American HS students had a significantly lower vasovagal reaction rate than Caucasian HS students. There was synergy among high-risk factors in Caucasian HS students. Female and male vasovagal reaction rates were similar when low-weight donors were excluded.

High school (HS) blood donors are young, frequently donate for the first time, and have a high incidence of vasovagal reactions. The high vasovagal reaction rate, which ranges from 8 percent to 11 percent,[1] makes them a unique population in which to study vasovagal reactions.

The following issues or questions were addressed in the present study. 1) Past studies have alluded to the possibility that African-American blood donors have fewer vasovagal reactions than Caucasians.[2,3] This study quantified the risk of a vasovagal reaction in Caucasian and African-American HS students. 2) Several measurable risk factors such as youth, low weight, and first-time donation status are associated with an increase in vasovagal reactions.[4-7] This study measured these risks and evaluated the degree to which they are additive. 3) Two recent studies reached different conclusions as to whether female sex increased the vasovagal reaction rate. One study found that confounding factors such as lower weight explained the higher vasovagal reaction rate in females,[7] while another study, although unpublished, found that female sex by itself was a risk factor (N.R. Haley, written communication, September 2000). This study addressed this question by evaluating female and male vasovagal reactions in four weight groups, which in a stepwise fashion eliminated lower weight donors. In addition to addressing these issues or questions, the study also evaluated non-HS participants to determine the extent of their participation, their demographics, and their vasovagal reaction rate.

ABBREVIATIONS: HS = high school; RR(s) = relative risk(s).

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MATERIALS AND METHODS

Phlebotomy

HS blood donations were collected on-site at Detroit metropolitan high schools. The donors were screened using a 40-question questionnaire, a mini-physical exam consisting mainly of vital signs, and a Hb-screening test. Accepted blood donors were subjected to a whole blood phlebotomy and collection of additional blood samples, which together did not exceed 535 mL. Blood donors rested on the donor bed after donation and were advised to spend 10 minutes at the refreshment site. All vasovagal reactions were recorded on the blood donor record, and an additional report was submitted if syncope occurred.

Data collection

Data from 1076 Caucasian HS students, 226 African-American HS students, and 157 nonstudent participants taken from randomly chosen Caucasian and African-American HS blood drives in 2001 were entered into a database (Excel 1997; Microsoft Corporation, Seattle, WA). The data entered consisted of the donor's age, race, sex, self-reported weight, blood donation status (first-time or repeat donation), a unique unit whole blood number, and the donor's reaction status. In addition, blood pressure results from 100 randomly selected Caucasian students were compared with 100 randomly selected African-American students.

Statistical analysis

Two-by-two contingency tables and a two-tailed Fisher Exact test were used to determine p values and relative risks (RRs) with 95 percent CIs. $p < 0.05$ was considered to be significant.

RESULTS

Demographics

Table 1 identifies the demographics of Caucasian and African-American HS students and nonstudent participants. Caucasian and African-American HS students were similar for mean donor age, percentage of females, percentage of first-time donors, and percentage of donors who weighed no more than 130 lb, but African-American HS students weighed slightly more (166 vs. 157 lb).

Nonstudent participants were 10.8 percent of the total number of participants. In comparison to HS students, they were significantly older (mean age, 44 vs. 17 years), had a lower first-time donor rate (9 vs. 79%-82%), weighed significantly more (180 vs. 157-166 lb), and had a lower percentage of donors under who weighed no more than 130 lb (10 vs. 22%–24%).

Comparison of vasovagal reaction rates

The vasovagal reaction rate was 8.2 percent (88 of 1076) in Caucasian HS students versus 1.3 percent (3 of 226) in African-American HS students ($p = 0.0001$; RR, 6.2; 95 percent CI, 2.0-19.3) versus 1.3 percent (2 of 157) in nonstudent participants ($p < 0.0004$). Eight syncopal reactions occurred in the Caucasian HS students, and none occurred in the other two groups ($p = 0.34$ with African-American students). Blood pressure results in Caucasian and African-American HS students were compared as a potential cause for the vasovagal reaction rate difference between the two groups. Table 2 shows a comparison of blood pressures in 100 randomly selected Caucasian HS students and 100 randomly selected African-American HS students. The differences were not significant.

Additive effects of high-risk factors in Caucasian HS students

The additive effects of risk factors could only be evaluated in the Caucasian HS students because the other two groups had very few reactions. Table 3 shows the effect of different risk factors. A first-time donor had a vasovagal reaction rate of 9.4 versus 3.8 percent in a repeat donor ($p < 0.002$; RR, 2.6). A low-weight donor ($\leq$ 130 lb) had a 13.6 percent vasovagal reaction rate versus 3.3 percent in a high-weight donor ($\geq$ 180 lb) ($p < 0.0001$; RR, 4.0). Adding both risk factors together increased the reaction rate to 16.0 versus 3.2 percent in donors who lacked these factors ($p < 0.004$; RR, 5.0). Since 45 percent of the Caucasian females weighed no more than 130 lb and only 5 percent of the males weighed no more than 130 lb, female sex was added last because of the confounding factor of low weight. The four factors increased the reaction percentage to 16.4 versus 3.8 percent in those who lacked these factors ($p < 0.01$; RR, 5.0).

TABLE 1. Blood donor demographics in Caucasian, African-American, and nonstudent participants

Population	Number	Mean age (years)	Females percentage	First-time donor percentage	Mean weight (lb)*	Percentage weighing no more than 130 lb
Caucasian HS students	1076	17	49	79	157 (150)	24
African-American HS students	226	17	47	83	166 (160)	22
Nonstudent participants	157	44	52	9	180 (180)	10

* Number in parentheses is median.

Repeat Caucasian donations (the "survival" phenomenon)

Repeat donors weighed more than first-time donors (163 vs. 155 lb), but the percentage of males and the percentage of females weighing no more than 59.0 kg in the two groups were statistically the same. Eighty-four percent of the repeat donors donated their second lifetime unit and 16 percent donated their third lifetime unit, based on a random sample of 50 HS blood donors. Repeat donors had a 60 percent reduction (3.8 vs. 9.4%) in their vasovagal reaction rate, but there was no synergistic benefit when additional factors such as "high weight" (weight ≥ 81.7 kg) or "male sex" or "both" were added to repeat donor status.

Vasovagal reactions in females

Table 4 shows the vasovagal reaction rate in Caucasian girls and boys at four different weight scenarios. Vasovagal reactions were higher in females than males when all donors were included (11.3 vs. 4.8%, p = 0.002) or when donors under 130 lb were excluded (9.4 vs. 5.0%, p = 0.018). Vasovagal reactions in females and males were similar when donors under 150 lb were excluded (5.7 vs. 4.6%, p = 0.66).

DISCUSSION

Caucasian HS students have a high predisposition toward blood donation-related vasovagal reactions because of their youth, high percentage of first-time donations, and lower weight.[4-7] Other studies have also shown that history of syncope and psychological factors can also increase vasovagal syncopal reaction rates.[8] The percentage of vasovagal reactions in first-time, mainly Caucasian HS donors has been reported to be as high as 8.7 times greater than in experienced blood donors.[1] Thus, Caucasian HS students represent an excellent population in which to study vasovagal reactions.

Two studies provided some evidence that African-Americans might have a lower predisposition for blood donation-related vasovagal reactions than Caucasians.[2,3] The present study is the first to quantify and compare the risk in two relatively equal groups of Caucasian and African-American HS students. African-American HS students have a vasovagal donor reaction that is 84 percent lower than Caucasian HS students (1.3 vs. 8.2%, p < 0.0001), and none of the eight syncopal vasovagal reactions occurred in the African-American group (0 vs. 0.74%, p = 0.34), although the differences in syncope between the two groups did not reach significance. Several studies have shown that elevated systolic blood pressure is protective against vasovagal reactions.[5-7] This potential explanation was studied but did not account for the differences between African-American and Caucasian vasovagal reaction rates (see Table 2).

Several studies have also demonstrated synergy among risk factors.[2,5,7] Graham[2] studied 352 Caucasian blood donors in 1957 (published 1961) in a hospital setting. The risk of a vasovagal reaction in his setting was

TABLE 2. Comparison of blood pressures in randomly selected Caucasian and African-American HS students

	Caucasian students	African-American students	p value*
Number	100	100	NA
Male percentage	61	52	0.2538
First-time percentage	73	85	0.0554
Mean BP†	115.6/71.3	117.4/71.6	0.36/0.84
Median BP	114/70	117/70	NA
Systolic BP ≤100 (%)	16	15	1.000
Systolic BP ≥140 (%)	7	13	0.2381
Diastolic BP ≤60 (%)	16	15	1.000
Diastolic BP ≥80 (%)	24	28	0.6289
Mean BP (females)	111.2/69.5	115/71.2	0.24/0.46
Mean BP (males)	118.4/72.5	119.6/72.5	0.62/0.71

* p < 0.05 is clinically significant.
† BP = blood pressure.

TABLE 3. Additive effects of risk factors in Caucasian HS students

Risk factor(s)	Vasovagal reaction rate (%)	p value*	RR (95% CI)
HS student	88/1076 (8.2)		
HS student; FT† donor (A1)	80/853 (9.4)	0.002	2.6 (1.3-5.3)
HS student; weight ≤130 lb (B1)	36/264 (13.6)	<0.0001	4.1 (1.9-8.6)
HS student; FT donor; weight ≤130 lb (C1)	35/219 (16.0)	<0.004	5.0 (1.2-20.4)
HS student; FT donor; weight ≤130 lb; female (D1)	32/195 (16.4)	<0.01	4.3 (1.1-17.6)
HS student; repeat donor (A2)	8/223 (3.6)		
HS student, weight ≥180 lb (B2)	8/239 (3.3)		
HS student; repeat donor; weight ≥180 lb (C2)	2/63 (3.2)		
HS student; repeat donor; weight ≥180 lb, male (D2)	2/53 (3.8)		

* Comparisons were made between A1 and A2, B1 and B2, etc.
† FT = first-time.

TABLE 4. Comparison of vasovagal reaction rates for females and males for four different weight groups

	Females*	Males*	p value†
≥110 lb			
All	51/523 (11.3)	27/553 (4.8)	0.002
First-time	55/422 (13.0)	25/433 (5.8)	0.0004
Repeat	4/101 (4.0)	2/120 (1.7)	1.000
≥130 lb			
All	32/341 (9.4)	27/537 (5.0)	0.018
First-time	29/266 (10.9)	23/417 (5.5)	0.011
Repeat	3/75 (4.0)	4/120 (3.3)	1.000
≥150 lb			
All	8/141 (5.7)	19/415 (4.6)	0.660
First-time	7/109 (6.4)	16/323 (5.0)	0.633
Repeat	1/32 (3.1)	3/92 (1.6)	1.000
≥180 lb			
All	1/44 (2.3)	7/191 (3.7)	1.0
First-time	1/34 (2.9)	5/138 (3.6)	1.0
Repeat	0/10 (0)	2/53 (3.8)	1.000

* Data presented as n (%).
† $p < 0.05$ is different.

quite high (15%), and a combination of factors increased the risk to 35 percent to 71 percent in some scenarios. Tomasulo et al.[5] and Kasprisin et al.[6] in blood center studies showed much lower risks. The risks in those two studies did not exceed 6.4 percent, even when risks were combined. The present study evaluated low-weight (≤ 59.0 kg) and first-time donation status in Caucasian HS students and found that low weight was a more significant factor than first-time donation status based on RRs (4.0 vs. 2.6) (see Table 3). Trouern-Trend et al.[7] found the same pattern in a study of vasovagal syncopal reactions. When low-weight and first-time donation status were combined, the risk was even greater (RR, 5.0). However, female sex barely affected the risk, when it was added as a fourth "risk" factor (RR, 4.3) because most of the "low-weight" individuals (< 130 lb) had already been excluded.

Repeat blood donors had a 60 percent decrease in vasovagal reactions (3.8 vs. 9.5%, $p < 0.004$) and adding other positive factors such as "high weight," "male," or "both" did not provide any additional benefit. Thus, repeat blood donation status alone is a good predictor for a low vasovagal reaction rate in HS students.

Female sex as a risk factor was evaluated by observing the vasovagal reaction rate in a stepwise fashion as lower weight donors were removed. The pattern clearly showed that lower weight (≤ 130 lb), which is much more common in females than in males (45 vs. 5%), was a major factor for increased vasovagal reactions in females. However, when donors under 150 lb were excluded, there were no differences between female and male vasovagal reaction rates. Thus, low weight is the main factor that causes a high reaction rate in females.

One limitation in this study was the low number of repeat donors. This influenced the RR ratios by increasing variability and decreasing precision. A second limitation was the size of the African-American population studied. It was too small to evaluate the causes of vasovagal reactions in the population.

In summary, this study showed that African-American HS students have a significantly lower vasovagal reaction rate than Caucasian HS students. There is synergy among high-risk factors and low weight is a more significant risk factor than first-time donor status. Although females have more vasovagal reactions than males, this is mainly due to lower weight, and the differences disappeared when donors under 150 lb were excluded. Repeat HS blood donors have 60 percent fewer vasovagal reactions, and a successful first-time donation is a good predictor of future success.

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Donor reactions in high-school donors: the effects of sex, weight, and collection volume

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BACKGROUND: The high incidence of donor reactions in first-time, 17-year-old Caucasian whole-blood donors makes this group ideal for the study of donor reactions.
STUDY DESIGN AND METHODS: Donor reaction rates were retrospectively evaluated in 7274 first-time, 17-year-old Caucasian whole-blood donors based on observations recorded at the collection sites. The effect of sex and weight on donor reactions was determined. In addition, a model was developed to estimate how different blood collection volumes would affect donor reaction rates.
RESULTS: The donor reaction rate was 12.0 percent (870/7274). Female donors overall had a higher donor reaction rate than male donors (16.7% vs. 7.3%) and also had a higher donor reaction rate than male donors at each 20-lb weight interval in the range from 110 to 189 lb. A model suggested that a change in the blood-unit volume from 450 to 500 mL would increase donor reaction rates by 18 percent in either female or male donors, whereas a reduction in the blood-unit volume from 500 to 400 mL would decrease donor reaction rates by 29 and 27 percent in female and male donors, respectively.
CONCLUSION: First-time, 17-year-old Caucasian female donors had a higher donor reaction rate than male donors overall and at equivalent donor weights. In the range of present US blood-unit volumes, a change in collection of as little as 50 mL could have a significant impact on blood donor reaction rates in high-school students.

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Clinical studies have evaluated the incidence of blood donor reactions[1] and have studied the correlation of donor characteristics such as weight,[2-6] age,[3-6] first-time or repeat donor status,[3-6] race,[6-8] and sex[3,4,6] to donor reaction rates. This study evaluated first-time, 17-year-old, Caucasian high-school students because these donors have a very high donor reaction rate of approximately 9 to 11 percent,[6,9] which is seven to nine times higher than the donor reaction rate in an experienced, general donor population.[2] We evaluated two nonfixed variables (sex, weight), but three variables (donor status, age, race) were fixed. We also developed a model for donor reaction rates as a function of sex and the ratio of whole-blood collection volume per donor weight, which allowed us to estimate the effects of various whole-blood collection volumes.

MATERIALS AND METHODS

Blood donor suitability and phlebotomy

High-school blood donors met acceptability criteria before being subjected to phlebotomy. The donors then lay in a supine position, and a 525-mL phlebotomy was performed in the antecubital fossa of the arm with a 16-gauge needle. The blood collection volume included 481 mL in a whole-blood unit, 33 mL in tubes for post-donation tests, and 11 mL trapped in the plastic tubing. Blood donor reactions observed at the collection site were recorded. A "donor reaction" was defined as the presence of any of the following symptoms or signs during or shortly after whole-blood donation: dizziness, diaphoresis (sweating), sudden weakness, hypotension, bradycardia, and syncope (faint). Approximately 97 percent of the reactions were nonsyncopal reactions.

Blood donor selection and data analysis

All high-school blood drive donor history records from 77 blood drives between October 1, 2003, and March 23, 2004, were reviewed. Donor selection was limited to 17-year-old, first-time, Caucasian donors who successfully donated a whole-blood unit. Studies have shown that African-American donors have a considerably lower donor

rate than Caucasian donors, so African-American donors were excluded from the study.[6,7] The decision to use successful donations and exclude unsuccessful donations was an arbitrary one. A total of 7274 donor history records were deemed suitable for evaluation.

Statistical analysis

Confidence intervals (CIs) for reaction rates were calculated as minimum-length intervals by integration of the Bayesian posterior with diffuse priors[10] with the assistance of computer software (the Solver tool in Microsoft Excel 2002, Microsoft Corp., Redmond, WA). Logistic regression was performed with Epi Info.[11] Proportion comparisons were done with the Fisher Exact test.

RESULTS

Donor weight distribution

Figure 1 shows a bell-shaped curve for male donors, with some skewing toward higher weights. In contrast, the curve for female donors appears truncated, suggesting that many Caucasian high-school female donors weighed less than 110 lb and could not donate blood.

Donor reaction rates in 17-year-old, first-time Caucasian blood donors

Table 1 shows the donor reaction rate for the total population and for each sex in 20-lb incremental weight groups. The donor reaction rate for the total population was 12.0 percent. Female donors had a 2.3-fold higher donor reaction rate than male donors, 16.7 percent versus 7.3 percent, and female donors had higher donor reaction rates within equivalent weight groups. Female donor reaction rates were 61 to 149 percent greater than male donor reaction rates, depending on the weight group. Figure 2 shows the donor reaction rates versus weight for female and male donors. Donor reaction rates appeared to decrease asymptotically as donor weights increased. Thus, logistic regression of reaction rate against a linear function of coded sex, reciprocal weight, and the product of coded sex and reciprocal weight—representing an interaction between sex and weight—was performed. The model was

$$\ln\left(\frac{r}{1-r}\right)=a+bs+\frac{c}{w}+\frac{ds}{w}, \quad (1)$$

where r is proportion of donors of coded sex s and weight w having a reaction; s = 0 if donor is male or 1 if donor is female; w is donor weight (lb); and a, b, c, and d are constants.

The coefficient d of the term representing sex–weight interaction was not significantly different from zero ($p = 0.09$ by a two-tailed test), so this term was omitted from the model. The remaining constants were found to have the following values: $a = -4.2941$, $b = 0.6120$, and $c = 284.1776$. All were significantly different from zero ($p < 0.0001$ by a two-tailed test). These constants yield the following formulas, which are plotted in Fig. 2.

$$\ln\left(\frac{r}{1-r}\right)=-4.2941+\frac{284.1776}{w} \text{ for male donors} \quad (2)$$

$$\ln\left(\frac{r}{1-r}\right)=-3.6821+\frac{284.1776}{w} \text{ for female donors.} \quad (3)$$

These formulas were used to give estimates of donor reaction rates at infinite weight, which were 2.5 percent for female donors and 1.3 percent for male donors. In a more practical context, the estimated donor reaction rates at 300 lb were 6.1 percent for female donors and 3.4 percent for male donors.

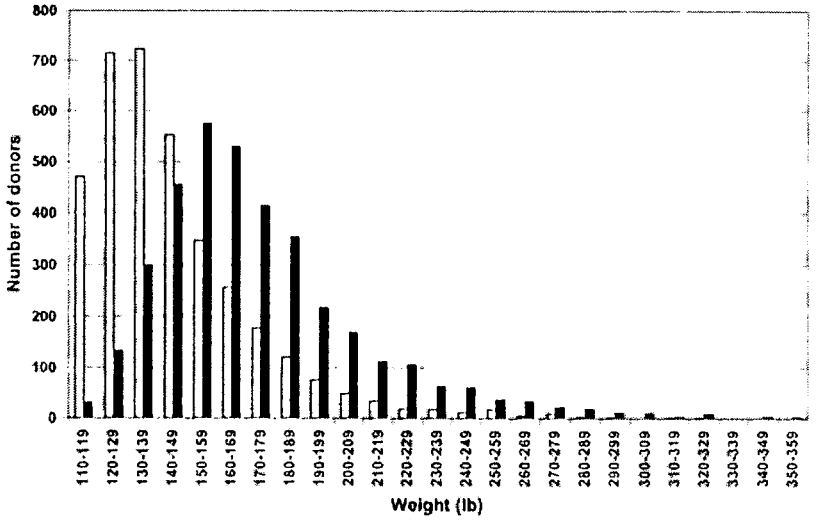

Fig. 1. Weights of first-time Caucasian high-school donors. (□) Female donors; (■) male donors.

Model for the effect of different blood-unit volumes on blood donor reaction rates

There is evidence that lower blood collection volumes are associated with lower reaction rates (see Discussion). We propose a unifying hypothesis that, for 17-year-old, first-time Caucasian donors, the donor reaction rate is a function of sex and the ratio of whole-blood collection volume to donor weight. Using the fact that Equations 2 and 3 were based on data obtained using a collection volume of 525 mL,

TABLE 1. Donor reaction rates in first-time, Caucasian high-school students

Donor sex	Weight (lb) 110-129	130-149	150-169	170-189	190-209	210+	Total
Female							
Number of reactions/number of donations	248/1187	206/1278	90/602	36/298	12/124	10/116	602/3605
Percent reactions	20.9	16.1	15.0	12.1	9.7	8.6	16.7
Male							
Number of reactions/number of donations	19/164	73/754	103/1108	39/768	15/386	19/489	268/3669
Percent reactions	11.6	9.7	9.3	5.1	3.9	3.9	7.3
Total							
Number of reactions/number of donations	267/1351	279/2032	193/1710	75/1066	27/510	29/605	870/7274
Percent reactions	19.8	13.7	11.3	7.0	5.3	4.8	12.0

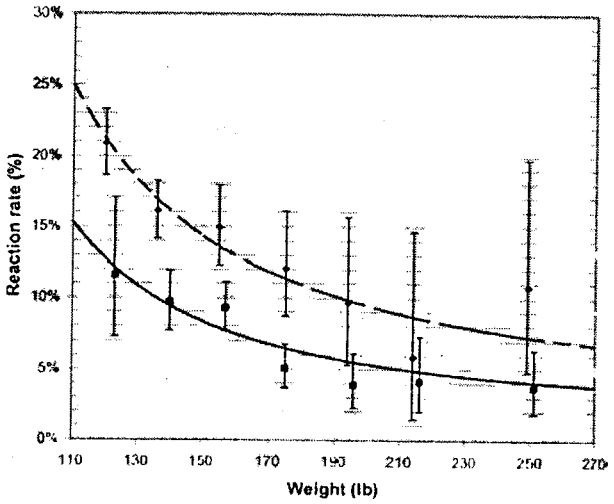

Fig. 2. Donor reaction rates in first-time Caucasian high-school students. Collections for each sex were grouped into 20-lb weight intervals for donor weights from 110 through 229 lb and a single interval for weights of 230 lb or more. The x coordinate of each group is the median weight, and the y coordinate is the reaction rate and its 95 percent CI. Curves were derived by logistic regression, as described under Materials and Methods. (◆) 95 percent CI, female donors; (■) 95 percent, male donors; (– –) model, female donors; (—) model, male donors.

these equations were generalized to be consistent with the hypothesis

$$\ln\left(\frac{r}{1-r}\right) = -4.2941 + 0.5412907\frac{v}{w} \text{ for male donors} \quad (4)$$

$$\ln\left(\frac{r}{1-r}\right) = -3.6821 + 0.5412907\frac{v}{w} \text{ for female donors,} \quad (5)$$

where v is the blood collection volume in mL. When v = 525, Equations 4 and 5 are simplified to Equations 2 and 3, respectively.

The collection volume is the blood-unit volume plus the volume of blood in collection-set tubing and samples for testing. As previously stated, the latter is estimated to be 44 mL. Table 2 uses this estimate, the above model, and this study's donor weight distribution to give expected donor reaction rates at various blood-unit volumes. Table 3 compares the expected rates at different blood-unit volumes. The model suggests that an increase in the whole-blood unit volume from 450 to 500 mL would cause a 1.2-2.7 percent absolute increase in the donor reaction rate and a 17.9 to 18.2 percent relative increase in the donor reaction rate in first-time, Caucasian, high-school donors. Female donors had a greater absolute increase in the donor reaction rate (2.7 reactions per 100 collections vs. 1.2), but both sexes had similar relative increases of approximately 18 percent. A decrease in the whole-blood collection volume from 500 to 400 mL would decrease the donor reaction rate by 27 to 29 percent. Female donors would have a greater absolute decrease in the donor reaction rate (5.1% vs. 2.1%), but female and male donors would have a similar relative decrease (29% vs. 27%).

TABLE 2. Expected donor reaction rates at other collection volumes (reactions per 100 collections)

Sex	Blood-unit volume (mL) 500	481	450	400	350	300	250
Female	17.8	16.7	15.1	12.7	10.7	8.9	7.4
Male	7.8	7.3	6.6	5.7	4.8	4.1	3.5

TABLE 3. Expected effects of blood-unit volume changes on donor reaction rates*

Sex	Blood-unit volume change (mL) 450 to 500	500 to 400	500 to 250
Female	+2.7 (+17.9%)	-5.1 (-28.7%)	-10.4 (-58.4%)
Male	+1.2 (+18.2%)	-2.1 (-26.9%)	-4.3 (-55.1%)

* Absolute change in reactions per 100 collections (relative change).

DISCUSSION

Donor reactions are common. In a recent study, 7.0 percent of 1000 randomly selected interviewed whole-

blood donors had a donor reaction.[2] The rate was 2.5 percent based on observation at the collection site, but an additional 4.5 percent were found after a donor interview 3 weeks later. Approximately 97 percent of the donors had mild reactions, meaning that the donors had symptoms and signs such as dizziness, diaphoresis, pallor, and sudden weakness but did not faint. A 1-year follow-up showed that donors who had a reaction were 34 percent less likely than asymptomatic donors to return and donate again within a 1-year period.[12] Studies show that the blood donation return rates are even lower when donors had syncope.[13-15] Therefore, it is clear that a non-syncopal donor reaction decreases a donor's return rate, and syncope further decreases the return rate. Donor reactions are also a donor safety issue. One study showed a 14 percent injury rate in donors who progressed to syncope.[16] These injuries were often to the head and were generally minor, but lacerations and fractures occasionally occur. Serious injuries such as a closed-head injury are very rare but possible.

Three key factors associated with the probability of a donor reaction are weight,[2-6] age,[3-6] and first-time or repeat donor status.[3-6] Weight and age are the most important factors, and first-time or repeat donor status has marginal importance.[17] High weight, high age, and repeat status all protect donors against donor reactions. Caucasian donors have more risk for a donor reaction than African-American donors have.[6-8] Several studies have shown that female donors have more donor reactions than male donors,[3,4,6] but this was thought to be due to the female donor's smaller size because when female and male high-school donors over 149 lb were compared, the donor reaction rates were the same.[6] In addition, in 850 first-time, Caucasian donors from the same study, there were no differences in donor reaction rates when female and male donors in equivalent 20-lb weight groups were compared.[6] This study evaluated 8.6-fold more donors (7274 vs. 850) and detected large differences between reaction rates of female and male first-time Caucasian donors of similar weight.

Based on safety data for a 500 mL collection volume from a large blood center[18] and from the American Red Cross, most blood centers increased their whole-blood unit volume from 450 mL to a higher value. The American Red Cross collects 481 mL in each unit but 525 mL in total volume. This volume can be collected in any donor—even a donor with the lowest allowable weight, 110 lb (50 kg)—because it meets the AABB standard for a maximum whole-blood collection volume of 10.5 mL per kg of body weight.[19] Other blood centers collect two different whole-blood units—a 450-mL unit for low-weight donors and a 500-mL unit for donors weighing over approximately 120 lb.

A large blood center compared donor reaction rates in 282,000 donors who donated 450-mL whole-blood units and 547,000 donors who donated 500-mL whole-blood units.[18] The center did not detect a difference in donor reaction rates, which were 1.36 and 1.28 percent, respectively. But the subjects were from the general donor population, approximately 80 percent of whom were repeat donors and were much older and heavier than high-school students. A more sensitive study would have compared equivalent groups of very-high-risk donors such as the lower-weight female donors in this study, but this would have required entry of donor weight into the blood center's database, which is often not done.

In the donors studied here, the effect of two variables, sex and weight, on the reaction risk were determined. Three other variables, age, race, and first-time donor status, were fixed. It is probable but unproven that the bulk of the reactions in this group were caused by these five risk factors. Future studies could measure other factors that are thought to be associated with reactions such as a history of a donor reaction or being in the environment of a "group reaction." One could determine if there was an independent contribution from each variable by use of a logistics regression analysis, and such analysis could also quantify the contribution.

The model in this study, which relates the donor reaction rate in first-time, Caucasian high-school students to sex and the ratio of blood collection volume to donor weight, suggests that a 50-mL increase in whole-blood collection volume increased donor reaction rates by 18 percent. The model also suggests that a decrease in the blood-unit volume from 500 to 400 mL would decrease donor reaction rates by 29 percent in female donors and 27 percent in male donors, which is a very significant improvement. These lower rates are supported by Japanese data. The Japanese collect 400-mL (70% of collections) and 200-mL (30% of collections) units. They report a donor reaction rate of 0.6 to 0.7 percent based on 3.3 million whole-blood donations (H. Ikeda, Japanese Red Cross Society Central Blood Center, Japan; and M. Satake, Tokyo Red Cross Blood Center, Japan; written communications, 2003). Our data and model indicate that collecting 400-mL whole-blood units might be particularly effective in reducing donor reaction rates in young, low-weight, and first-time donors.

One limitation in this study was the lack of high-weight female donors. This made it difficult to show sex-related differences at high weights. A second limitation was that the data were based solely on observation of donors. In another study, a postdonation interview increased the number of reactions detected in a general donor population 2.3-fold, from 2.5 to 7.0 percent.[2] We do not believe that limiting the study to successful donations had an effect. The rate of unsuccessful donations in 4340 high-school students in the fall and winter of 2004 in our center was 5.0 percent (219/4340). It was 4.0 percent (21/525) in donors with a reaction and 5.2 percent (198/3815)

in donors with no reaction ($p = 0.21$). These data also challenge the perception that donor reactions are associated with more unsuccessful donations.

In conclusion, first-time, female Caucasian high-school students have a much higher donor reaction rate than male donors of equivalent weight. A model suggested that a change in the blood-unit volume from 450 to 500 mL would increase the donor reaction rate in this group by approximately 18 percent, and a decrease in the blood-unit volume from 500 to 400 mL would decrease the donor reaction rate by 27 to 29 percent. This kind of decrease in donor reaction rates would have a significant positive impact on safety and blood donor retention rates—particularly in first-time, lower-weight, high-school donors and other donors at high risk.

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