間を調査し、回復時間の遷延の有無を確認しておくことも必要であろう。

血液比重による採血適否判定とHb簡易測定値との関係についてであるが、血液比重測定法と簡易Hb測定法はともに、手技を正しく行えば採血基準に従った適否判定に有用な手法と言える。H17年に実施された簡易Hb測定機器評価試験で、検査課自動血球計数装置の測定値と比較して平均値がやや低いことが確認されている。今回の検討は、同一検体を24～32時間後に検査課機器**で測定したHb値であるが、簡易Hb値は平均値で男性0.4、女性0.3 g/dLそれぞれ低い値を示していた。簡易Hb測定機器の誤差は±0.3 g/dLとされており、採血基準を下回る献血者からの採血が防止できる設定である。

Hb測定法への切り替えに伴い、現行基準値は健常男性のHb値と比較して低いことから、基準値を12.5から13.0 g/dLにひき上げた場合の採血予測を行ったところ、比重測定値1.053以上の判定時に比べ1.04%の減少が予測された。女性ではHbを現行基準と同じ12.5 g/dLと設定し、比重測定による判定と比較すると1.44%の減少が予測された。女性において、簡易Hb測定機器導入で献血者予測が減少する理由として、測定機器が本来のHb値よりやや低めに表示するよう設定されていることも影響していると思われる。

200mL採血数は減少傾向（H18年：200mL 26%、400mL 74%）にある。受血者にとり供血者数は少ないほうが望ましく、200mL採血は小児の輸血用に限定して採血している施設もある。200mLの採血基準を400mLと同一基準にひきあげた場合、200mL採血比率の低い九州地区ではほとんど影響がないと思われる。しかし、400mL確保に苦慮している地域では、冬季の献血者減少時期など採血計画の変更が必要となる可能性がある。Hb基準値の引き上げについては、今後予期しない感染症の流行や、供血者選択に新たな制限が加わる事態発生時などの血液確保も考慮して、検討されるべきであろう。

血液比重測定法は、基準値を満たすかどうかに限定した判定であるが、簡易Hb測定法では基準をはずれた献血申し込み者に対し、個々の状態に応じた健康指導が可能となる。Hb簡易測定機器導入後は、この利点を生かした健康指導体制も望まれる。

医学生の献血に対する意識調査であるが、今回の調査では35.1%（95%信頼区間29.9～40.7%）が献血をしたことがあるという結果となった。過去に行われた調査によると、19～29歳で献血経験のある人の割合は42.8%であり、この数値と比較すると本学医学生の献血経験者率は有意に低いことがわかる（$p<0.05$）。年齢が上がるにつれて献血経験の機会が増えると考えると、本学医学生の献血経験者率の低さは、回答者の平均年齢が22.3歳と若いことによるものだと推測できる。

一方、1年間の献血率（最近1年間に献血した人数を母集団の人数で除した数値）は15.2%（95%信頼区間11.6～19.7%）であった。日本赤十字社によると平成18年度の20～29歳の献血率は7.6%であり[1]、平成19年度もこの数値が維持されると仮定すると、医学生の献血率は一般の献血率に対して有意に高いと言える（$p<0.05$）。

また、今後の献血状況に関しては、「1年に以内に絶対献血する」と回答した10.7%（95%信頼区間7.6～14.8%）の人が必ず献血すると仮定し、平成18年度の20～29歳の献血率が平成20年度も維持されると仮定すると、平成20年度も本学医学生の献血率は一般よりも有意に高くなると考えられる（$p<0.05$）。

では、本学医学生の献血率が高い理由は何なのであろうか。調査票の分析の結果、最近1年間に献血した45名のうち19名（42%）が初めて献血をしており、この19名のうち14名（73.7%）が主な献血場所として「大学の献血バス」と回答していることや、最近1年間に献血した45名のうち17名（37.8%）が「1年以内に絶対献血する」、16名（35.5%）が「1年以内に献血するつもりでいる」と回答していることが分かった。これらのことから、本学医学生の献血率の高さは、献血経験者が継続的に献血することに加え、毎年10月に開催される大学祭での献血バスの活動による初回献血者確保によって維持されていると推測することができる。

これまでの考察から、本学医学生は「献血経験者率は低いが献血意志は高く、1度献血すると継続する可能性

が高い」という特徴を持つ集団であり、新規の献血者確保のための重要なターゲットとなり得ると結論づけることができる。

今後実際に医学生に対して献血のプロモーションを行う場合には、今回の調査結果で作成した献血意志関連モデルを参考にすると良い。未経験者のモデルでは、「あなたにとって、献血は義務の１つですか」、「近年、献血者数は増加していると思いますか、減少していると思いますか」が「規範意識」、「呼びかけられても献血しなかったとき、そのことを後悔することが多いですか」が「献血に対する態度」、「問 25. 仮に献血する気持ちになった場合、確実に実行できると思いますか」が「統制感」とそれぞれのカテゴリーに入っており、TRA あるいは TPB の理論が当てはまることがわかる。一方、経験者のモデルは TRA や TPB の理論とは一致せず、「継続的に献血をしており、前回の献血でネガティブなイメージを持たず、特に阻害要因がなければ献血経験者は継続的に献血を行う」という構造になっていることがわかる。

よって、未経験者に対しては TRA および TPB の理論に基づいた戦略を、経験者に対しては「毎回の献血で悪いイメージを持たせないこと」を念頭においた戦略を採ると良い結果が得られると考えられる。また、初回献血者の確保に関しては献血バスが大きな効果を持っていることも考慮すべきである。

E. まとめ

年齢基準の見直しで多くの献血者の増加が見込まれることから、血小板成分献血の上限年令(現行 54 歳)の見直しを第一優先のテーマとして検討を進めるべきである。次に 17 歳女性 400ml 全血献血でのデータ収集が今後の課題となる。全血献血の上限年令の見直しについては、増加が見込まれる献血者数は少なく、60 歳以上で比重落ち率が増加していることを考慮すると、研究の優先順位は低いと考えられる。

献血経験や意識に関する医学生調査では、献血経験者率は低いものの、献血率・献血意志は高い集団であり、献血プロモーションによる効果は十分得られることが示唆された。また、プロモーションの際には献血経験の有無によって異なる戦略を採ることが望ましいことも明らかにされた。

F. 健康危険情報

特になし

G. 研究発表

1. 論文発表

予定あり

2. 学会発表

予定あり

H. 知的財産権の出願・登録状況

(予定を含む)

1. 特許取得

特になし

2. 実用新案登録

特になし

3. その他

特になし

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

B.H. Newman

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 (≤ 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.

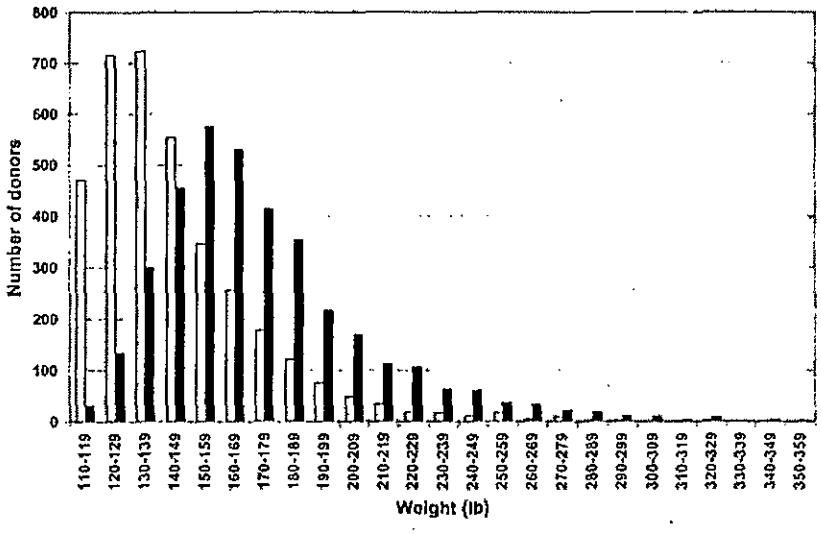

Fig. 1. Weights of first-time Caucasian high-school donors. (□) Female donors; (■) male donors.

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

	Weight (lb)						
Donor sex	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

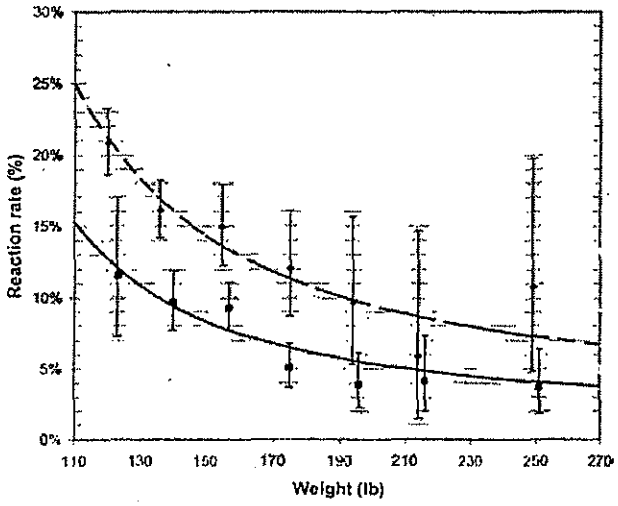

Fig. 2. Donor reaction rates in first-time Caucasian high-school students. Collections for each sex were grouped into 20-lb weight intervals for donor weights from 110 through 229 lb and a single interval for weights of 230 lb or more. The x coordinate of each group is the median weight, and the y coordinate 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)

	Blood-unit volume (mL)						
Sex	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*

	Blood-unit volume change (mL)		
Sex	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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The American Red Cross donor hemovigilance program: complications of blood donation reported in 2006

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BACKGROUND: The American Red Cross (ARC) initiated a comprehensive donor hemovigilance program in 2003. We provide an overview of reported complications after whole blood (WB), apheresis platelet (PLT), or automated red cell (R2) donation and analyze factors contributing to the variability in reported complication rates in our national program.

STUDY DESIGN AND METHODS: Complications recorded at the collection site or reported after allogeneic WB, apheresis PLT, and R2 donation procedures in 36 regional blood centers in 2006 were analyzed by univariate and multivariate logistic regression.

RESULTS: Complications after 6,014,472 WB, 449,594 PLT, and 228,183 R2 procedures totaled 209,815, 25,966, and 12,282 (348.9, 577.5, and 538.3 per 10,000 donations), respectively, the vast majority of which were minor presyncopal reactions and small hematomas. Regional center, donor age, sex, and donation status were independently associated with complication rates after WB, PLT, and R2 donation. Seasonal variability in complications rates after WB and R2 donation correlated with the proportion of donors under 20 years old. Excluding large hematomas, the overall rate of major complications was 7.4, 5.2, and 3.3 per 10,000 collections for WB, PLT, and R2 procedures, respectively. Outside medical care was recorded at similar rates for both WB and automated collections (3.2 vs. 2.9 per 10,000 donations, respectively).

CONCLUSION: The ARC data describe the current risks of blood donation in a model multicenter hemovigilance system using standardized definitions and reporting protocols. Reported reaction rates varied by regional center independently of donor demographics, limiting direct comparison of different regional blood centers.

Blood donation by healthy volunteers assures the availability of blood components for transfusion, which is a central tenet of modern health care. Accrediting and regulatory agencies (e.g., Joint Commission on Accreditation of Healthcare Organizations, Food and Drug Administration [FDA]) identify blood transfusion as a core function essential to quality medical care and promulgate specific requirements for appropriate use of blood components. Scientific efforts to improve blood safety have duly focused on the patient-recipient of blood transfusion and have substantially reduced the risk of infectious disease transmission. Similar scrutiny has not been applied to reducing the risk of blood donation, even though the infrequent occurrence of serious injury after blood donation may arguably now rival the residual risk of transfusion-transmitted infection.

ABBREVIATIONS: ARC = American Red Cross; LOC = loss of consciousness; R2 = automated red cell (donation).

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The blood supply depends entirely on the daily commitment of altruistic volunteers, who ostensibly gain little personal benefit from blood donation but are exposed to potential risk of discomfort, complications, and in rare cases, injury resulting from the collection procedure. Approximately 2 to 6 percent of all presenting donors experience a complication, most of which previously have been classified as light, mild, or minor reactions that resolve promptly but are still unpleasant for the donor.[1-9] Serious injury occurs infrequently, but typically results from a loss of consciousness (LOC), either at the donation site or after leaving the premises. Donor characteristics that correlate with higher syncopal complication rates after whole blood (WB) donation include young age, first-time donation status, low weight or total blood volume, female sex, and Caucasian race, although these may not all be independent predictors of reactions.[6-10] Changing population and donor demographics during the period 1996 through 2005 revealed that blood collection from young donors, aged 16 to 19 years, was increasing whereas blood donation rates by older individuals was declining.[11]

In light of these demographic trends, blood centers should continuously strive to improve the donation experience for all donors and should have an effective and comprehensive program to monitor donor complications as the keystone of a donor safety program. The importance of donor adverse reactions has been highlighted in the recent efforts by the AABB to initiate a US biovigilance program.[12] Our experience now provides a model system to assess the advantages and limitations of a national donor hemovigilance program.

Each year, the American Red Cross (ARC) has nearly 7 million encounters with individuals who present to donate WB or apheresis components to provide more than 40 percent of the US blood supply. The ARC established a national hemovigilance program to systematically analyze donor complications at its 36 blood regions. We describe annual hemovigilance data from 2006 and analyze factors contributing to variability in reported overall reaction rates in our system, which may serve as a basis for further improvements in hemovigilance efforts to protect healthy, volunteer blood donors.

MATERIALS AND METHODS

In 2003, ARC initiated a comprehensive hemovigilance program that prospectively collects data on events that occur at the time of donation, or that are reported later, including reports of donors receiving outside medical care. In mid-2005, the event definitions (Table 1) were modified to include citrate reactions for automated collections and the national reporting system was updated and fully implemented. This report describes data gathered in the first full calendar year of the modified program.

Collection site procedures

The 36 regional blood regions follow standard procedures for WB and automated collections from volunteer, allogeneic donors. WB is collected into 500-mL collection sets (Fenwal, Inc., Round Lake, IL; Pall Medical, Inc., East Hills, NY). The mean volume of collection is 517 ± 10 mL with trip scales and 524 ± 10 mL with electronic scales. Apheresis platelets (PLTs) are collected with one of three apheresis devices: Amicus (Baxter Healthcare, Round Lake, IL), Spectra (Gambro BCT, Lakewood, CO), or Trima (Gambro BCT). Automated red cell (R2) procedures for 2-unit red cell (RBC) collections are performed with Alyx (Fenwal, Inc.), Trima (Gambro BCT), or Haemonetics MCS+ 8150 (Haemonetics, Braintree, MA) systems. PLT procedures included plateletpheresis and plateletpheresis with infrequent plasma collection. PLT/plasma/RBC collections, plasma/RBC collections, and automated plasma and plasma/RBC collections were excluded from the analysis.

All adverse reactions occurring at the collection site are managed by collection staff, documented on the blood donation record according to the classification scheme (Table 1), and captured in a central electronic database. All donors are also instructed to contact the regional blood center if they experience problems or have concerns about their health after donation. Donor reactions or injuries reported by the donor or third parties after the donation event are managed by standard procedures, reviewed by a facility physician, and reported to the national hemovigilance program.

Classification scheme for donor complications

The standardized classification system for donor complications defines 15 reaction categories (Table 1). The scheme incorporates a severity rating (minor, major) for reaction types in most categories, and every category is further divided into whether or not the donor received outside medical care. Minor complications typically resolve within a short period of time (e.g., 30 min), and the donor recovers completely at the donation site and/or is managed solely by giving the donor instructions for care after an injury (e.g., hematoma) occurs. Major reactions typically require follow-up with the donor and review by ARC staff, either because they may be medically more serious or they may be more of a concern to donors (e.g., loss of bowel or bladder control during a short LOC), even if the reaction is not more medically significant than a minor complication. Presyncope defines a variety of symptoms (e.g., pallor, lightheadedness, dizziness, nausea) that may be related to vasovagal reactions, hypovolemia, or anxiety but do not progress to LOC. The small and large hematomas include true hematomas (e.g., a palpable mass), bruises, and infiltration at the venipuncture site. Reactions classified as "other" comprise a variety of

TABLE 1. Definitions of donor complications*

Complication	Brief description: Minor category	Brief description: Major category
Systemic (syncopal-type):		
Symptomatic (presyncopal, prefaint)	Pallor, weakness, light-headedness, dizziness, diaphoresis, nausea/vomiting, no LOC.	
LOC	Short LOC: lasting less than 1 min.	Long LOC: lasting 1 min or more or complicated by seizures or convulsions or loss of bladder or bowel control.
Presyncopal or LOC with injury		Injury (e.g., head injury, fractures, abrasions, lacerations) associated with symptoms of prefaint or LOC.
Prolonged recovery		Symptoms of prefaint or LOC or other reaction that do not resolve within approx. 30 min.
Phlebotomy-related		
Hematoma	Small: involved area measures 2 × 2 in. or less.	Large: involved area measures more than 2 × 2 in.
Nerve irritation		Suggested by pain, tingling, numbness, or sharp shooting pains after phlebotomy.
Suspected arterial puncture		Suggested by rapid (<3 min) bleed time, pulsatile flow, and/or bright red blood.
Systemic (other)		
Citrate (automated procedures only)	Citrate reactions that persist despite intervention or are accompanied by additional symptoms such as nausea, muscle tightness, or cramping. Citrate reactions that involve perioral or peripheral tingling or numbness that resolves with reduced flow rate or calcium are not captured.	Symptoms of minor citrate plus prolonged or exaggerated muscle spasm (tetany), vomiting, chest tightness.
Allergic	Hives, itching, rash, or redness of skin.	Symptoms of minor allergic reactions, plus swelling of the face, neck, or throat; wheezing; or respiratory difficulty.
Other reaction	Symptom profile different from established categories (e.g., anxiousness, hyperventilation, headache).	Symptom profile different from established categories (e.g., chest pain, thrombophlebitis).

* Donor complications are classified according to type and severity (minor, major); cases in each minor and major complication category are further subclassified with respect to the need for outside medical care.

reactions or symptoms that do not otherwise fit into the established categories, including suspected thrombophlebitis and chest pain as major, other reactions. For every complication category, outside medical care is defined as medical advice or treatment provided by someone other than ARC staff (e.g., emergency medical services, a primary health care physician or specialist, or any health care professional), whether sought independently by the donor or at the advice of ARC staff. Donors may seek outside medical care for reactions that are common and self-limiting (e.g., large hematomas), as well as those that are medically more relevant to their well-being (e.g., syncope-related injuries).

National hemovigilance program

Every month, the hemovigilance program at the ARC National Headquarters Medical Office compiles and analyzes data on donor complications following WB and automated procedures that are either documented by collections staff at the time of donation or reported by the donor or a third party after the donation event, including cases that receive outside medical care. All major reactions (Table 1) that occur at the donation site and all reactions that are reported to the blood center after the donor leaves the site are captured on a standard case report form, investigated, and reviewed by the blood center physician and reported in a tally on a monthly basis to the National Medical Office. If a donor is referred for outside medical care by staff or later reports that he or she sought or received care from any outside health care provider, the complete blood donation record is reviewed by the National Medical Office and is maintained in a separate database. In this report, the actual medical care provided is not further differentiated and varies considerably from simple reassurance or advice to apply warm packs for the resolution of hematoma to administration of intravenous fluids and hospitalization.

Complications associated with allogeneic WB, apheresis PLT, and R2 procedures in 36 regions from January 1, 2006, to December 31, 2006, were analyzed; autologous and therapeutic collections were excluded. The analysis

also excluded 49 WB collection events in which a citrate reaction was recorded because these records most likely represent miscoding or misclassification of complications after WB donation, as well as 43 PLT donations and 45 R2 donations recorded for 16-year-old donors. Donor age was not recorded for 94 WB and 2 PLT donations.

Complications experienced by donors before the donation process or unrelated to phlebotomy (e.g., injuries caused by other accidents at the site) or experienced by individuals who did not donate blood (e.g., canteen volunteers) were excluded from the analysis. The denominator for the number of donations of each procedure type was the number of satisfactory collections plus the number of incomplete ("quantity not sufficient") collections. Donor complication rates were calculated per 10,000 collections for minor and major complications and for cases receiving outside medical care for different donor age groups.

Statistical analysis

Complication rates for different procedure types and among different age groups were compared by calculating odds ratios (ORs) and 95 percent confidence intervals (CIs; Instat, GraphPad, Inc., San Diego, CA). Linear regression and analysis of variance for the correlation between the proportion of young donors and monthly complications rates was performed with computer software (SAS Version 9.1.3, SAS Institute, Inc., Cary, NC).

A multivariate logistic regression analysis was performed to identify demographic variables that were independently associated with complications after WB, R2, or PLT donations using software (SAS STAT, SAS Institute, Inc.). There was an inverse and nonlinear relationship between donor age and the rate of complications, and complications were disproportionately represented in donors under age 20 and fairly constant above age 20. Consequently, the multivariate analysis considered the donors in the age groups as 16-year-olds, 17-year-olds, young adults (18- and 19-year-olds), and adults in each subsequent decade (e.g., 20-29, 30-39, up to 80+). A "STEPWISE" selection method was used to determine which effects entered the logistic regression model and also which effects remained in the model. A significance level of not greater than 0.05 was necessary for an effect to enter into the model and a significance level of not greater than 0.05 was necessary for an effect to remain in the model at any iteration step. The regression analyses for WB, PLT, and R2 procedures evaluated the independent variables (regional blood center, donor age, sex, donation status) and the dependent outcome (any complication). Outlier regions that performed fewer than 150 procedures in 2006 were not reported (three regions) in the R2 model. The ARC Institutional Review Board determined that the research was exempt under 45CFR46, 21CFR50.

RESULTS

Donations and donor complications at regional blood centers

In 2006, the donor hemovigilance program analyzed a total of 6,014,472 WB, 449,594 PLT, and 228,183 R2 collections, which were associated with 209,815, 25,966, and 12,282 adverse reactions (348.9, 577.5, and 538.3 per 10,000 donation), respectively. Minor symptomatic (presyncopal) reactions accounted for the majority of complications (258.3 per 10,000 collections) for WB, and small hematomas, for PLT and R2 donations (377.0 and 217.9 per 10,000 collections, respectively; Table 2). Excluding large hematomas, the overall rates of major complications were 7.4, 5.2, and 3.3 per 10,000 collections for WB, PLT, and R2 procedures, respectively (Table 2).

Regional and monthly variability in complications after WB donation

The complication rates observed for WB donation in the 36 regions demonstrated considerable regional and monthly variability; the systemwide mean was 348.9 ± 140.7 (range, 145.9-679.5) complications per 10,000 donations (Fig. 1). The overall WB complication rates in the 36 regions were normally distributed and 24 regions were within 1 standard deviation (SD) of the mean, and 34 regions were within 2 SDs of the mean (data not shown). For adverse reactions recorded by collection staff, mean monthly rates of reactions at the donation site varied over a wider range for the small- and medium-sized regions (approx. 57,000-207,000 WB collections per year) compared to the largest regions (with >208,000 WB collections per year).

Complication rates across the system demonstrated seasonal variation that was most pronounced for WB donation and strongly correlated with donor age. Specifically the rates of systemic (syncopal-type) complications (i.e., presyncope, LOC, injury, prolonged recovery) and the proportion of young donors (16-19 years old) for WB and R2 donations were higher in the spring and autumn compared to the winter and summer, whereas the rates of phlebotomy-related complications remained constant throughout the year (Fig. 2A). Systemic (syncopal-type) complications after WB donation correlated strongly with the proportion of donors less than 20 years old ($R^2 = 0.96$) and logistic regression demonstrated that the model explains a significant portion of the variation in the data ($F = 248.00$; $p < 0.0001$). Monthly variation was substantially less pronounced for systemic (syncopal-type) complications after automated collections (Fig. 2B) and did not correlate as strongly with the proportion of donors less than 20 years old as observed for WB ($R^2 = 0.58$; $p = 0.004$); no correlation was observed for PLT donations ($R^2 = 0.03$; $p = 0.58$).

TABLE 2. Rates of complications after WB and automated collections per 10,000 donations

Complications	WB (6,014,472)	Apheresis PLTs (449,594)	R2 (228,183)
Systemic (syncopal-type) complications			
Presyncopal (symptomatic, prefaint)	258.3	61.3	195.2
Short LOC	7.9	2.1	6.5
Major			
Long LOC	1.8	0.5	0.9
Prolonged recovery	2.4	0.8	1.0
Injury	1.1	0.3	0.1
Systemic (other) complications			
Citrate			
Minor		121.4	112.8
Major		2.2	0.4
Allergic (minor, major)	0.1	0.4	0.2
Other (minor, major)	0.6	1.0	1.0
All systemic			
Rate	272.1	190.1	317.9
Number of events	163,663	8,546	7,255
OR* (95% CI)	1.00	0.69 (0.68-0.71)	1.17 (1.15-1.20)
Phlebotomy-related complications			
Small hematoma	74.5	377.0	217.9
Major			
Large hematoma	0.4	9.4	1.9
Suspected nerve irritation	0.7	0.8	0.1
Suspected arterial puncture	1.1	0.2	0.4
Phlebotomy-related			
Rate	76.7	387.5	220.3
Number of events	46,152	17,420	5,027
OR (95% CI)	1.00	5.21 (5.12-5.31)	2.91 (2.83-3.00)
All reactions			
Rate	348.9	577.5	538.3
Number of events	209,815	25,966	12,282
OR (95% CI)	1.00	1.70 (1.67-1.72)	1.57 (1.54-1.60)
Major reactions			
Rate†	7.4	5.2	3.3
Number of events	4,443	232	76
OR (95% CI)	1.00	0.70 (0.61-0.80)	0.45 (0.36-0.57)
Outside medical care			
Rate	3.2	2.9	2.9
Number of events	1,903	132	66
OR (95% CI)	1.00	0.93 (0.78-1.11)	0.91 (0.72-1.17)

* ORs shown for univariate analyses compared to the rate for WB collections.
† Excluding large hematoma; univariate comparison of donation types.

Allogeneic WB donation and complications

The most common complications associated with allogeneic WB collections were systemic (syncopal-type) reactions (272.1 per 10,000 donations), most of which were mild symptomatic (presyncopal, prefaint) reactions that occurred at an overall rate of 258.3 per 10,000 donations (2.5%; Table 2). Of the major reaction categories, the most frequently reported was prolonged recovery (2.4 per 10,000 donations) or LOC for more than 1 minute (1.8 per 10,000 donations). The overall complication rate decreased with increasing donor age (Fig. 3) for both first-time and repeat donors (data not shown).

Young donors (<20 years old) accounted for 874,922 (14.5%) WB donations in 2006 and had a significantly higher reaction rate than older donors (Fig. 3). An analysis of complications in these young donors is presented elsewhere.[10] Multivariate analysis confirmed that regional blood center, age, sex, and first-time donation status are independent correlates for adverse events (Table 3). Donor age was the strongest independent predictor of complications; the effect of age effectively leveled off above age 40, although the differences between age groups was still significant. Other variables, including donor race, height, and weight, were not available on all donations for inclusion in this analysis. The overall complication rate was lower but the proportion of small hematomas was higher in the older age group (>60 years) compared to younger age groups (Fig. 3).

Overall, 1,903 WB donors had outside medical care documented after a complication, for a rate of 3.2 per 10,000 collections. Forty-six of these donors reported hospitalization after donation. The observed rate of reported outside medical care after WB donation was higher after first-time (5.7 per 10,000) compared to repeat (2.6 per 10,000) donations (OR, 2.2; 95% CI, 2.0-2.4). Major

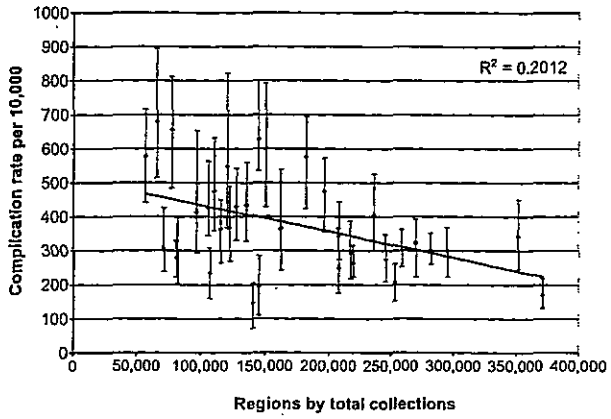


Fig. 1. Variability in rate of complications among ARC blood centers. The 36 regional blood centers are ordered by total collections in 2006 and plotted against their mean monthly overall complication rate per 10,000 collections. Bars show the maximum and minimum monthly complication rate for each center.

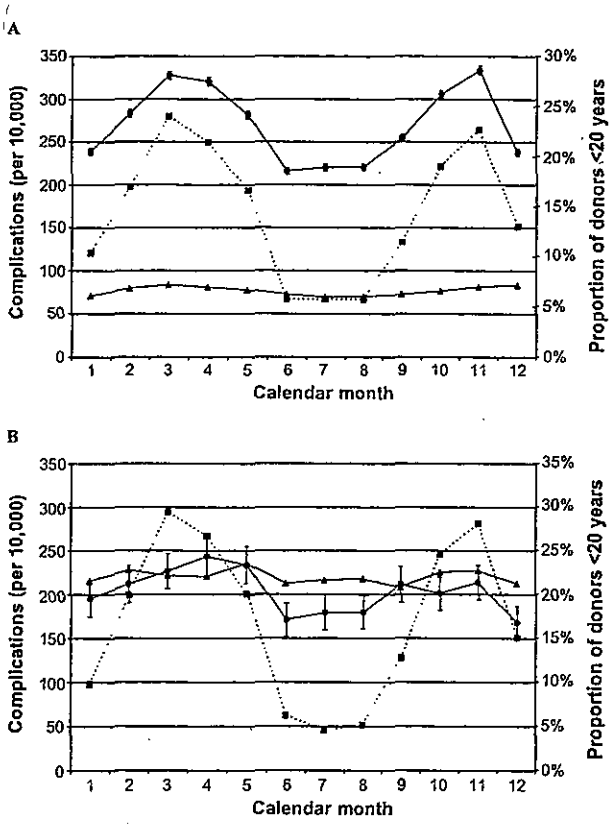


Fig. 2. Seasonal variability in donation-related complications correlates with the proportion of young donors. (A) WB; (B) R2. (●) Systemic (syncopal-type) complications; (▲) phlebotomy-related complications; (■, dotted line) proportion of donors less than 20 years old.

syncopal-type reactions (long LOC, LOC or presyncope with injury, prolonged recovery) accounted for approximately half (46%) of all reactions associated with outside medical care (Fig. 6A).

Automated collection procedures and donor complications

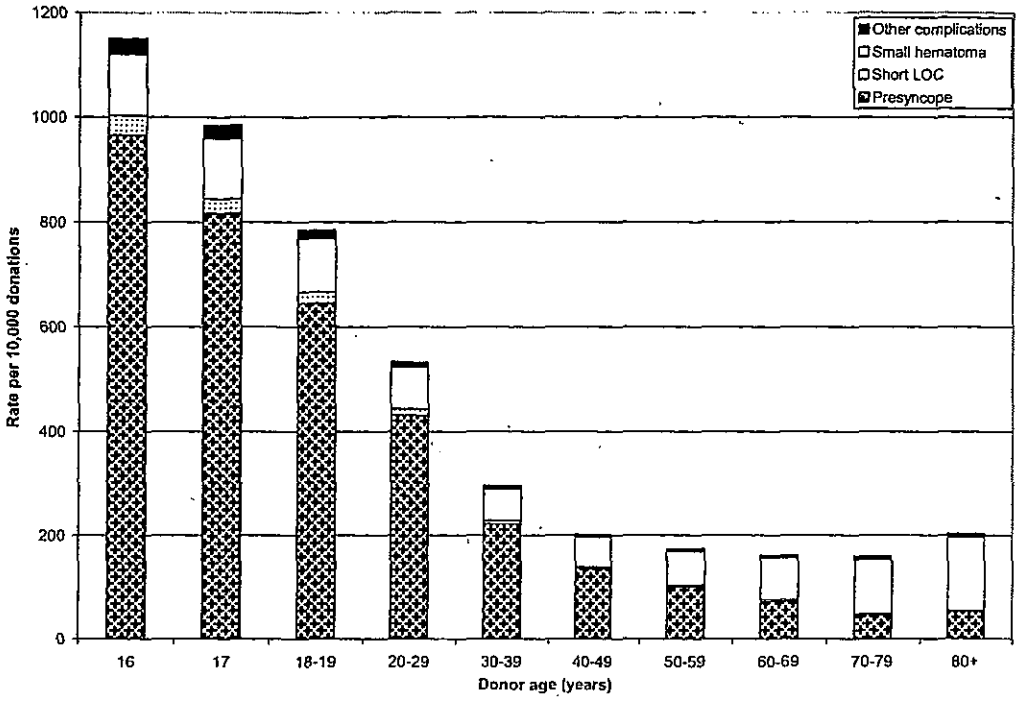
The most common complications associated with PLT and R2 donations were hematomas, followed by systemic citrate and syncopal-type reactions (Table 2). The rate of systemic reactions was lower for PLT donations (OR, 0.69; 95% CI, 0.68-0.71) and slightly but significantly higher for R2 donations (OR, 1.17; 95% CI, 1.15-1.20) compared to WB collections in a pairwise, univariate analysis (Table 2). The rate of major reactions, however, was significantly lower for both PLT (OR, 0.70; 95% CI, 0.61-0.80) and R2 (OR, 0.45; 95% CI, 0.36-0.57) collections. The rate of outside medical care was not significantly different for PLT, and R2 (2.9 per 10,000) collections compared to WB (3.2 per 10,000) collections (Table 2).

As with WB donation, younger donors were more likely to experience complications after PLT (Fig. 4) and R2 (Fig. 5) collection, but the influence of age on the rate of donor complications was considerably less pronounced. Multivariate analysis confirmed that regional blood center, age, sex, and first-time donation status are independent correlates for adverse events (Table 3). Age was a strong independent predictor of complications, but there were no differences in complication rates in age groups above age 50 for R2 and above age 30 for PLT donation. Significant differences were observed among regional blood centers.

The observed rate of reported outside medical care was not different for WB (3.2 per 10,000) compared to automated procedures (2.9 per 10,000), but the composition of reaction types differed. Phlebotomy-related complications (large hematoma, possible nerve irritation) accounted for 39 percent of outside medical care reported after automated collections (Fig. 6B). Eight of these 198 donors reported hospitalization after donation.

DISCUSSION

A safe and adequate blood supply encompasses efforts to minimize the risk to the blood donor as well as the transfusion recipient. The present analysis represents the first report of the comprehensive ARC donor hemovigilance program. The data confirm the overall safety of blood donation and provide an estimate of risk currently associated with allogeneic WB and automated collection procedures. We have used the data internally for program and procedure development and have shared the data externally with various organizations to evaluate the impact of regulatory guidance and inform public policy. For



Donor age (years)	16	17	18-19	20-29	30-39	40-49	50-59	60-69	70-79	80+
Total donations	46,274	404,033	424,615	812,190	822,429	1,319,311	1,314,912	616,876	223,185	30,553

Fig. 3. Rates of donor complications associated with allogeneic WB donation. The overall rates are significantly ($p < 0.05$) different between each successive age group, except between the 60- to 69- and 70- to 79-year age groups.

example, the lower rates of serious reactions with automated PLT collections compared to WB collections served as the basis for a response to the FDA draft guidance on collection of PLTs by automated methods[13] to demonstrate that additional requirements for medical supervision at the collection site were unwarranted and would unnecessarily restrict PLT collection and availability. These data support the conclusions reached by others that plateletpheresis is associated with the lowest rate of systemic reactions compared to other collection procedures.[14]

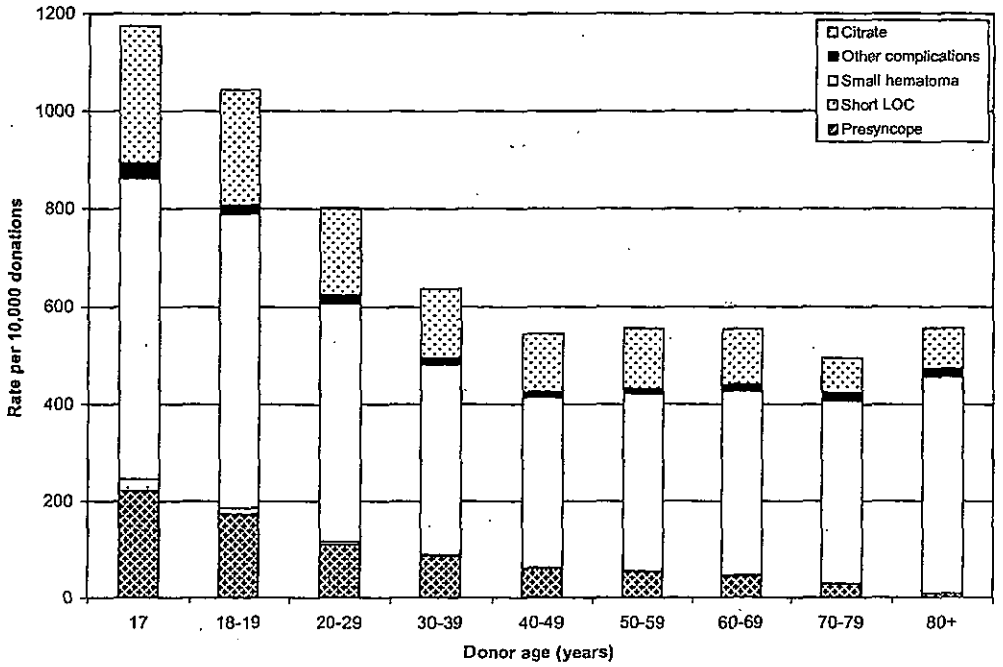
The AABB has proposed the establishment of a national biovigilance program that would include a donor adverse reaction component.[12] The national collection of donor complication data is currently constrained by the different definitions of reactions and data collection procedures in use by blood centers in the United States, which prevents direct comparisons between the complication rates reported by various blood collection agencies. We now demonstrate that even in a large multicenter system utilizing standardized protocols, considerable variability is apparent in reported reaction rates among different regional blood centers. Reaction rates are known to vary with donor age, gender, race, weight, and first-time donation status.[6-10] A major source of the variability we observed between regions relates to donor demographics, as evident by the strong correlation of higher reaction rates with the higher proportion of young donors in spring and fall compared to summer and winter. Nevertheless, we show that the blood region was also independently associated with complications separate from donor characteristics (age, donation status, and sex), suggesting that regional practices may affect the likelihood of reactions or the recognition and reporting of those reactions. Regional variability likely cannot be eliminated because of the inherent subjectivity in evaluating and recording donor complications. Any comparison of complication rates between different regional centers, for example, to evaluate staff performance or compare collection equipment, could be misleading. Despite the variability among regions, data from an individual region or a small subset of regions in a more controlled operational trial have proven useful to evaluate donor complications associated with implementation of new collection procedures or new equipment (data not shown). Further analysis of the regional variability may provide insight into practices consistently associated with lower complication rates.

TABLE 3. Multivariate logistic regression analysis of donor complications

	WB		R2		Apheresis PLTs	
Effect	Point estimate	95% Wald CI	Point estimate	95% Wald CI	Point estimate	95% Wald CI
Age (years)						
16	3.42	3.14-3.73	NA	NA	NA	NA
17	3.33	3.07-3.62	2.94	1.56-5.55	1.77	1.37-2.28
18-19	3.11	2.87-3.37	3.02	1.60-5.70	1.69	1.37-2.08
20-29	2.25	2.07-2.44	2.83	1.50-5.33	1.30	1.08-1.56
30-39	1.33	1.22-1.44	2.30	1.22-4.33	1.06	0.88-1.28*
40-49	0.95	0.88-1.03*	1.95	1.04-3.67	0.90	0.75-1.08*
50-59	0.84	0.78-0.92	1.84	0.98-3.46*	0.92	0.77-1.11*
60-69	0.80	0.73-0.87	1.81	0.96-3.41*	0.95	0.79-1.14*
70-79	0.80	0.73-0.87	1.69	0.89-3.23*	0.84	0.70-1.02*
80+	1.00 (referent)		1.00 (referent)		1.00 (referent)	
Sex						
Male	0.56	0.55-0.56	0.64	0.60-0.68	0.53	0.52-0.55
Female	1.00 (referent)		1.00 (referent)		1.00 (referent)	
Donation status						
First	2.00	1.98-2.02	1.33	1.25-1.40	2.04	1.83-2.28
Repeat	1.00 (referent)		1.00 (referent)		1.00 (referent)	
Region						
A	0.90	0.86-0.94	3.61	2.72-4.80	1.99	1.75-2.26
B	2.00	1.90-2.10	1.18	0.16-8.83*	2.25	1.94-2.62
C	0.90	0.86-0.95	0.88	0.65-1.19*	0.98	0.85-1.13*
D	1.11	1.06-1.16	1.90	1.42-2.55	1.52	1.34-1.72
E	0.82	0.78-0.86	1.15	0.86-1.54*	1.83	1.61-2.08
F	2.12	2.01-2.24	5.34	3.72-7.68	1.58	1.34-1.85
G	2.46	2.35-2.58	3.52	2.60-4.77	2.48	2.18-2.83
H	0.84	0.80-0.88	1.00	0.72-1.38*	1.54	1.35-1.76
I	0.54	0.51-0.57	0.89	0.66-1.19*	2.12	1.87-2.40
J	0.85	0.81-0.90	1.18	0.87-1.60*	2.72	2.34-3.15
K	1.96	1.87-2.06	1.56	1.16-2.09	2.54	2.20-2.92
L	1.25	1.19-1.31	1.68	1.25-2.26	3.15	2.77-3.58
M	1.10	1.05-1.16	1.15	0.82-1.63*	1.68	1.45-1.96
N	0.44	0.42-0.47	0.26	0.18-0.36	2.13	1.82-2.48
O	0.82	0.78-0.86	NA	NA	0.75	0.64-0.88
P	1.40	1.33-1.46	NA	NA	1.37	1.20-1.57
Q	0.59	0.56-0.62	0.44	0.32-0.60	1.35	1.17-1.55
R	1.20	1.14-1.26	2.80	2.04-3.83	2.47	2.14-2.84
S	0.79	0.74-0.84	0.46	0.29-0.72	0.09	0.04-0.20
T	0.93	0.89-0.98	2.76	2.07-3.69	0.64	0.54-0.77
U	1.39	1.32-1.46	1.70	1.25-2.32	0.13	0.10-0.19
V	0.94	0.89-1.00	0.74	0.52-1.04*	2.98	2.55-3.48
W	1.98	1.89-2.07	2.00	1.49-2.67	1.84	1.61-2.10
X	0.62	0.59-0.66	0.24	0.16-0.37	2.29	1.95-2.68
Y	2.39	2.27-2.52	4.13	3.07-5.54	2.22	1.91-2.56
Z	1.24	1.17-1.30	1.91	1.39-2.63	0.81	0.70-0.94
AA	1.36	1.29-1.43	1.39	1.03-1.87	2.22	1.93-2.55
BB	1.33	1.27-1.40	4.53	3.37-6.08	2.69	2.35-3.09
CC	1.10	1.04-1.17	0.83	0.57-1.19*	0.44	0.34-0.56
DD	1.64	1.56-1.71	1.77	1.32-2.39	2.06	1.79-2.38
EE	1.30	1.24-1.37	1.01	0.70-1.45*	1.01	0.86-1.19*
FF	1.05	0.99-1.12*	1.24	0.91-1.70*	0.03	0.01-0.07
GG	1.10	1.05-1.15	1.81	1.35-2.43	1.44	1.26-1.63
HH	2.15	2.04-2.26	NA	NA	1.07	0.86-1.35
II	0.69	0.65-0.73	0.42	0.28-0.65	0.55	0.46-0.65
JJ	1.00 (referent)		1.00 (referent)		1.00 (referent)	

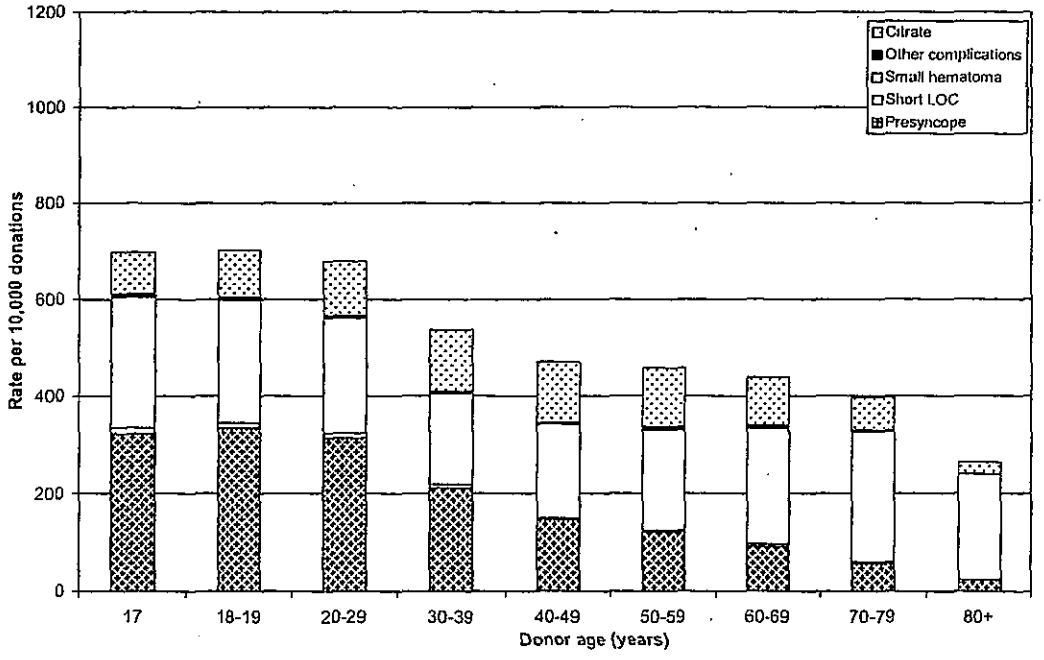
* Not significant.

Our experience also delineates the limitations of a national hemovigilance program and identifies opportunities for future improvement that may be tracked by the program. The approach to classify the type of complication rather than to capture specific signs or symptoms simplifies data collection, but we recognize that our definitions of donor complications are not mutually exclusive; for example, donors in the prolonged recovery category may also have had LOC as a feature of their reaction. This redundancy leads to having more than one code that can be used to describe a reaction; in addition, more than one type of reaction is possible. In both circumstances, staff is instructed to record the reaction based on the most severe symptoms. This subjectivity in evaluation and



Total donations	1,218	3,560	26,986	44,812	119,535	156,890	72,477	21,771	2,300

Fig. 4. Rates of donor complications associated with apheresis PLT donation. Differences in overall rates between successive age groups are different ($p < 0.05$) between 18- to 19-, 20-to 29-, and 30- to 39-year groups.



Total donations	18,578	20,814	29,580	30,392	51,141	50,291	21,747	5,178	417

Fig. 5. Rates of donor complications associated with R2 donation. Differences between overall rates between successive age groups are significant between the 20- to 29- and 30- to 39-year groups only.