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JAMA. 2008;299(19):2279-2286 (doi:10.1001/jama.299.19.2279)

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Adverse Reactions to Allogeneic Whole Blood Donation by 16- and 17-Year-Olds

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THE UNREMITTING NEED AND INCREASING demand for blood components constantly challenges blood centers to maintain a safe and adequate blood supply from a decreasing pool of eligible donors that is now estimated at only 38% of the US adult population.^{1,2} Between 2001 and 2004, the National Blood Collection and Utilization Survey documented a 0.2% decrease in whole blood and apheresis red blood cell unit collections, during a time when transfusions increased by 2%, implying a diminished reserve and a greater likelihood of episodic shortages.³ In addition, the incremental restrictions imposed on donor eligibility in recent years, such as geographic deferrals for proven or perceived risk of transfusion-transmitted malaria and bovine spongiform encephalopathy, and the introduction of additional infectious disease tests, including those for Chagas disease and West Nile virus, further diminish the number of eligible blood donors and available screened blood units.⁴⁻⁷

In this environment, blood centers have endeavored to recruit more eligible donors by targeting appeals to underrepresented racial groups, streamlining donor history screening, eliminating unnecessary questions, obtain-

See also Patient Page.

Context Donations by minors (16- and 17-year-olds) now account for approximately 8% of the whole blood collected by the American Red Cross, but young age and first-time donation status are known to be independent risk factors for donation-related complications.

Objective To evaluate adverse reactions to allogeneic whole blood donation by 16- and 17-year-olds compared with older donors in American Red Cross blood centers.

Design, Setting, and Participants Prospective documentation of adverse events among 16- and 17-year-old donors using standardized collection protocols, definitions, and reporting methods in 2006. Data were from 9 American Red Cross blood centers that routinely collect from 16- and 17-year-olds, a population that provides 80% of its donations at high school blood drives.

Main Outcome Measures Rate of systemic (syncope-type) and phlebotomy-related donor complications per 10 000 collections.

Results In 2006, 9 American Red Cross regions collected 145 678 whole blood donations from 16- and 17-year-olds, 113 307 from 18- and 19-year-olds, and 1 517 460 from donors aged 20 years or older. Complications were recorded in 15 632 (10.7%), 9359 (8.3%), and 42 987 (2.8%) donations in each corresponding age group. In a multivariate logistic regression model, young age had the strongest association with complications (odds ratio [OR], 3.05; 95% confidence interval [CI], 2.52-3.69; $P < .001$), followed by first-time donation status (OR, 2.63; 95% CI, 2.24-3.09; $P < .001$) and female sex (OR, 1.87; 95% CI, 1.62-2.16; $P < .001$). Infrequent but medically relevant complications, in particular physical injury from syncope-related falls, were significantly more likely in 16- and 17-year-old donors (86 events; 5.9/10 000 collections) compared with 18- and 19-year-old donors (27 events; 2.4/10 000 collections; OR, 2.48; 95% CI, 1.61-3.82) or adults aged 20 years or older (62 events; 0.4/10 000 collections; OR, 14.46; 95% CI, 10.43-20.04). Sixteen-year-old donors who experienced even a minor complication were less likely to return to donate within 12 months than 16-year-olds who experienced uncomplicated donations (52% vs 73% return rate; OR, 0.40; 95% CI, 0.36-0.44).

Conclusions A higher incidence of donation-related complications and injury occurs among 16- and 17-year-old blood donors compared with older donors. The increasing dependence on recruiting and retaining young blood donors requires a committed approach to donor safety, especially at high school blood drives.

JAMA. 2008;299(19):2279-2286

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ing variances from US Food and Drug Administration regulations to collect blood from individuals with hereditary hemochromatosis, relaxing the upper and lower age limitations for blood donation, and advocating for state legislation to collect blood from 16- and 17-year-old high school students.⁸⁻¹¹ In the American Red Cross system be-

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tween 1996 and 2005, blood collection from young donors aged 16 to 19 years increased and now accounts for 14.5% of annual donations, whereas blood donation by older individuals declined.¹²

Most state regulations allow blood collection from 17-year-old donors without parental consent, although 5 states maintain this requirement. At the time of this publication, 22 states or US territories allow donation by 16-year-olds with parental consent, either through adoption of legislation or the granting of variances (Alabama, Alaska, Arizona, California, Georgia, Illinois, Iowa, Kentucky, Maine, Maryland, Michigan, Minnesota, Missouri, New York, Pennsylvania, Puerto Rico, South Carolina, Tennessee, Virginia, Virgin Islands, Washington State, and Wisconsin), and 2 states allow donation by 16-year-olds without parental consent (Kansas and Oregon). California also allows donation by 15-year-olds with written permission of a parent or guardian, plus the written authorization of a physician or surgeon. The American Red Cross requires parental consent for all 16-year-old donors, does not collect from 15-year-olds, and follows state regulations or variances applicable to parental consent for collection from 17-year-old donors.

Several blood centers have demonstrated that complications, deferrals, and first-time donation rates are highest in young donors.¹³⁻¹⁹ Recent escalation in blood donation by 16- and 17-year-olds prompted us to analyze data from the American Red Cross hemovigilance program regarding adverse events in 16- and 17-year-olds following allogeneic whole blood donation in 9 regional American Red Cross blood centers. These data comprise an extensive experience (>1.5 million whole blood donations in a 12-month time frame) and provide a detailed classification of the specific complications, as well as a quantitative estimate of the uncommon but medically more serious complications of blood donation in the youngest eligible blood donors.

METHODS

Data Origin and Collection

The American Red Cross hemovigilance program prospectively evaluates reports of complications and injuries, including cases referred for outside medical care, after allogeneic whole blood and automated (apheresis) collection procedures in 35 blood services regions.¹⁹ Collection staff in all American Red Cross regions receive standardized training, follow standard collection procedures, and use common definitions to recognize, manage, and document adverse reactions following blood collection. All major reactions that occur at the collection site and any reaction reported back to the centers are reviewed by a physician serving that center's region and tracked by the American Red Cross hemovigilance program; all cases involving outside medical care are also reviewed by the national medical director of the program.

Nine American Red Cross blood services regions were selected for this analysis because each had more than 1000 allogeneic whole blood registrations from volunteer, nonremunerated donors who were 16 years old at the time of donation between January 1, 2006, and December 31, 2006. These 9 American Red Cross blood regions collected blood in 10 states or US territories (Georgia, Illinois, Iowa, Kansas, Maryland, Missouri, New York, Oregon, Washington state, and Puerto Rico), and each region required parental permission for 16-year-old donors. High school and all other drive types (eg, church, civic organization, business) were included in the analysis.

Autologous, therapeutic, and automated collections were excluded from the analysis. Other reasons for exclusion were complications experienced by whole blood donors before phlebotomy or unrelated to phlebotomy (eg, injuries caused by other incidents at the site), or donations that were miscoded as for age, sex, or reaction category (eg, 15 citrate reactions recorded after whole blood donation).

Classification Scheme for Donor Complications

The American Red Cross hemovigilance program classifies complications into defined categories, with severity ratings (minor or major) for certain reaction types.¹⁹ Presyncopal (minor) symptoms include pallor, diaphoresis, or lightheadedness without the loss of consciousness. Short loss of consciousness (minor) is defined as lasting less than 1 minute. Long loss of consciousness (major) is defined as lasting 1 minute or more or complicated by loss of bowel or bladder control, seizures, or convulsions. Prolonged recovery is defined as presyncopal symptoms, with or without loss of consciousness, that do not resolve within 30 minutes. Small (<25.8 cm²) and large (≥25.8 cm²) hematomas include bruises or infiltration and "true" hematomas with a palpable mass. Reactions classified as "other" did not otherwise fit into established reaction categories and include such reactions as hyperventilation (minor) and chest pain (major). Allergic (minor, major) reactions were recorded in the system but are not included in the analysis because of their extreme rarity (19 total reactions); only 4 allergic reactions were classified as major (eg, shortness of breath, facial edema, severe allergic symptoms) and all occurred in donors older than aged 20 years.

Complications in each category were further classified depending on whether the donor received outside medical care. Outside medical care is defined as medical advice or treatment provided by someone other than American Red Cross staff and includes emergency medical personnel responding to 911 calls, visits to a primary health care physician or specialist, or interaction with any health care professional, whether further medical attention is sought independently by the donor or at the advice of American Red Cross staff.

Analysis of Complication and Return Donation Rates

Complication rates were calculated per 10 000 collections. The denominator includes the number of satisfactory and unsatisfactory (eg, quantity not sufficient) collections. There was a nonlinear rela-

relationship between donor age and overall rate of complications, such that reactions were disproportionately represented in donors younger than 20 years and fairly constant in age groups older than 20 years. Consequently, donor age groups were collapsed to specifically compare minor donors (16- and 17-year-olds) with young adults (18- and 19-year-olds) and adults (≥ 20 -year-olds).

The effect of a reaction on the return behavior of 16-year-old donors in the 9 American Red Cross centers was evaluated in a subanalysis by comparing cohorts of 16-year-old donors who experienced either a minor or a major complication to a randomly selected control group of 16-year-old donors who experienced uncomplicated donations. Eligible donors with a minor or major reaction event and concordant control donors without a recorded reaction provided a donation between March 2005 and February 2006. Donors from each group were then followed for 365 days for a subsequent presentation event, including those that may have led to deferral.

Complication rates in donor groups stratified for age, donation status (first-time vs repeat donation to the American Red Cross), and sex were compared by calculating the 95% confidence intervals (CIs) for the proportion or by calculating odds ratios (ORs) and 95% CIs (InStat by Graphpad Inc, San Diego, California). Multivariate, stepwise logistic regression analyses were performed using SAS STAT statistical software version 8.2 (SAS Institute Inc, Cary, North Carolina). The regression analyses evaluated the independent variables (donor age, sex, donation status, drive type, region) and the dependent outcome (any complication excluding small hematoma and presyncope). 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 $\leq .05$ was necessary for an effect to enter into the model and a significance level of $\leq .05$ was necessary for an effect to remain in the model at any iteration step.

Informed consent was obtained from all donors at the time of whole blood collection, and parental permission for donation was obtained for all 16-year-old donors and for 17-year-old donors if required by state law. The American Red Cross institutional review board determined that the research satisfied criteria for exemption.²⁰

RESULTS

Donations

During the study period, the 9 American Red Cross blood centers performed 44 305 and 101 373 whole blood collections from 16- and 17-year-old donors, respectively, along with 113 307 collections from 18- and 19-year-olds, and 1 517 460 from donors aged 20 years and older. As a percentage of donations, 16- and 17-year-olds provided 8.2% of donations (2.5% from 16-year-olds; 5.7% from 17-year-olds) within the 9 centers under study, and 7.5% (450 317 of 6 014 472 collections) over the entire American Red Cross system. Among the 9 centers, the contribution that 16- and 17-year-old donors made to the total collections in a region varied from 4.2% to 11.2%. The overall proportion of female donors ranged from 35% to 53%; and the overall proportion of first-time donations ranged from 12% to 29%. Eighty percent of collections from 16- and 17-year-old donors in the 9 American Red Cross regions occurred at high schools, 14% at civic/community drives, 3% at churches, and 3% at other or nonspecified drive types.

Complications

In 2006, the 9 American Red Cross regions recorded 67 978 complications after whole blood donation in all reaction categories, for an overall rate of 382.7 per 10 000 or 3.8% of all collections. Complications occurred after 15 632 (10.7%) donations by 16- and 17-year-olds, 9359 (8.3%) by 18- and 19-year-olds, and 42 987 (2.8%) by donors aged 20 years or older. The most frequent complications in donors aged 16 and 17 years, 18 and 19 years, and 20 years and older were symptomatic

presyncope reactions (894.8, 683.1, and 198.7/10 000, respectively), and small hematomas (118.3, 105.0, 74.6/10 000, respectively; TABLE 1). The rates of loss of consciousness and major systemic (syncopal-type) complications were inversely related to donor age and more common among younger donors (FIGURE 1). Sixteen- and 17-year-olds were significantly more likely to experience any loss of consciousness and major systemic (syncopal-type) complications (53.1/10 000 collections) than 18- and 19-year-old donors (33.4 complications/10 000 collections; OR, 1.59; 95% CI, 1.41-1.80), or donors aged 20 years or older (8.0 complications/10 000 collections; OR, 6.65; 95% CI, 6.08-7.28) (Table 1). Most notably, injuries related to syncope were more common among 16- and 17-year-old donors (5.9/10 000) compared with 18- and 19-year-olds (2.4 injuries/10 000 collections; OR, 2.48; 95% CI, 1.61-3.82) or compared with donors aged 20 years or older (0.4 injuries/10 000 collections; OR, 14.46; 95% CI, 10.43-20.04) (Table 1). Excluding small hematomas, the rate of phlebotomy-related complications was not different among 16- and 17-year-olds (4.4/10 000) compared with 18- and 19-year-olds (2.9 complications/10 000 collections; OR, 1.51; 95% CI, 0.99-2.30) but was statistically significant compared with donors aged 20 years or older (1.5 complications/10 000 collections; OR, 2.87; 95% CI, 2.18-3.79) (Table 1).

A secondary analysis of donation-related complications compared 16-year-olds to 17-year-olds. The rate of presyncopal reactions was statistically but only marginally higher in 16-year-olds (961.5/10 000) compared with 17-year-olds (865.6 reactions/10 000 collections; OR, 1.12; 95% CI, 1.08-1.17). Among first-time donations, 16-year-olds had statistically higher presyncopal complication rates than 17-year-olds (1015 vs 971/10 000; OR, 1.05; 95% CI, 1.01-1.10). Differences between 16- and 17-year-olds in the other reaction categories did not reach statistical significance (data not shown).

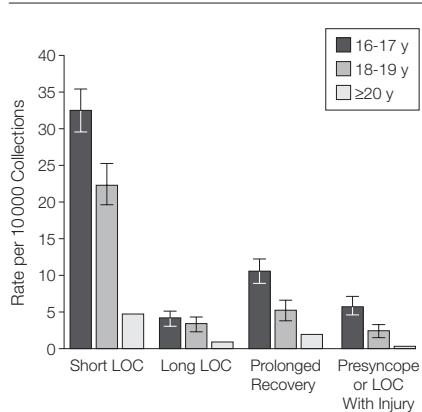
Table 1. Complication Rates of Allogeneic Whole Blood Donation

Complication	No. of Donor Complication Events (Rate per 10 000 Collections), by Donor Age, y			OR (95% CI), by Donor Age, y	
	16-17	18-19	≥20	16-17 vs 18-19	16-17 vs ≥20
No. of donations	145 678	113 307	1 517 460		
Systemic (syncopal-type)					
Presyncope	13 035 (894.8)	7740 (683.1)	30 151 (198.7)	1.34 (1.30-1.38)	4.85 (4.75-4.95)
Short LOC ^a	473 (32.5)	253 (22.3)	713 (4.7)	1.46 (1.25-1.70)	6.93 (6.17-7.78)
Long LOC (major) ^a	61 (4.2)	39 (3.4)	154 (1.0)	1.22 (0.81-1.82)	4.13 (3.07-5.55)
Prolonged recovery (major) ^a	154 (10.6)	60 (5.3)	289 (1.9)	2.00 (1.48-2.69)	5.56 (4.57-6.76)
Presyncope or LOC with injury (major) ^a	86 (5.9)	27 (2.4)	62 (0.4)	2.48 (1.61-3.82)	14.46 (10.43-20.04)
Subtotal, excluding presyncope	774 (53.1)	379 (33.4)	1218 (8.0)	1.59 (1.41-1.80)	6.65 (6.08-7.28)
Phlebotomy-related complications					
Small hematoma ^a	1724 (118.3)	1190 (105.0)	11 327 (74.6)	1.13 (1.05-1.22)	1.59 (1.51-1.68)
Large hematoma (major) ^a	16 (1.1)	9 (0.8)	44 (0.3)	1.38 (0.61-3.13)	3.79 (2.14-6.71)
Nerve irritation (major) ^a	20 (1.4)	8 (0.7)	77 (0.5)	1.94 (0.86-4.42)	2.71 (1.65-4.43)
Arterial puncture (major) ^a	28 (1.9)	16 (1.4)	111 (0.7)	1.36 (0.74-2.52)	2.63 (1.74-3.98)
Subtotal, excluding small hematoma	64 (4.4)	33 (2.9)	232 (1.5)	1.51 (0.99-2.30)	2.87 (2.18-3.79)
Other (major, minor) ^{a,b}	35 (2.4)	17 (1.5)	59 (0.4)	1.60 (0.90-2.86)	6.18 (4.07-9.39)
Overall	15 632 (1073.1)	9359 (826.0)	42 987 (283.3)	1.34 (1.30-1.37)	4.12 (4.04-4.20)

Abbreviations: CI, confidence interval; LOC, loss of consciousness; OR, odds ratio.

^aSee "Classification Scheme for Donor Complications" section for descriptions of complications.

^bOther includes reactions that do not fit into other categories. Allergic reactions were not included in the analysis because of their rarity (19 total; 3, 1 and 15 in 16-17-y-olds, 18-19-y-olds, ≥20 years, respectively).

Figure 1. Complication Rates of Loss of Consciousness and Major Systemic (Syncopal-Type) Complications by Donor Age

LOC indicates loss of consciousness. The rate of LOC, prolonged recovery, and syncope-related injury as a function of donor age is shown with error bars denoting 95% confidence intervals. Variability was plotted for donors aged 20 years or older but error bars for 95% confidence intervals are very small (the rate for short LOC: 4.7 [95% CI, 4.4-5.0]; for long LOC: 1.0 [95% CI, 0.9-1.2]; for prolonged recovery: 1.9 [95% CI, 1.7-2.1]; and for presyncope or LOC with injury: 0.4 [95% CI, 0.3-0.5]).

A stratified analysis evaluated the systemic (syncopal-type) complication rates in comparable donor subgroups with respect to age, donation status, and sex.

Within each corresponding donor subgroup, the complication rate was inversely related to donor age when sorted for donation status and sex (FIGURE 2). Among first-time donations by female donors, the rate of systemic (syncopal-type) complications in 16- and 17-year-olds (1214/10 000) was significantly higher compared with the corresponding subgroup of 18- and 19-year-olds (1004 complications/10 000 collections; OR, 1.24; 95% CI, 1.18-1.30) or donors aged 20 years or older (689 complications/10 000 collections; OR, 1.87; 95% CI, 1.80-1.94) (TABLE 2). Similarly, the highest systemic (syncopal-type) reaction rate was observed in the youngest donor group (16- and 17-year-olds) in each donor stratum (female/repeat donors, male/first-time donors, and male/repeat donors) (Figure 2).

In a stepwise logistic regression analysis of correlates of complications (loss of consciousness and major systemic [syncopal-type] plus major phlebotomy-related complications), young age demonstrated the strongest association (OR, 3.05; 95% CI, 2.52-3.69; $P < .001$), followed by first-time donation status (OR, 2.63; 95% CI, 2.24-3.09; $P < .001$), and female sex (OR, 1.87; 95% CI, 1.62-

2.16; $P < .001$) (TABLE 3). There were significant but lesser effects in reaction rates when smaller regions were compared with the largest one (Table 3). The drive type (high school drives compared with other drive types, eg, church, civic) was not significantly associated with donor complications in the multivariate analysis.

Requirement for Outside Medical Care After Blood Donation

Among all donors, 583 were referred by collection staff or reported as receiving outside medical care for adverse events related to whole blood donation in 2006, for an overall rate of 3.3 per 10 000 donations. Eighty-five 16- and 17-year-olds (5.8 individuals/10 000 donations) received outside medical care, which was significantly more frequent than the rate observed in adults aged 20 years or older (433 events; 2.9 individuals/10 000 donations; OR, 2.05; 95% CI, 1.62-2.58) but not different from that observed for 18- and 19-year-old donors (65 events; 5.7 individuals/10 000 donations; OR, 1.02; 95% CI, 0.74-1.40) (TABLE 4). Among 16- and 17-year-olds, systemic (syncopal-type) complications accounted for 66% of cases of

outside medical care, and phlebotomy-related complications accounted for the remainder. The most common reason for outside medical care was syncope-related injury, especially in donors aged 16 to 19 years. Thirty-two 16- and 17-year-old donors received outside medical care after syncope-related falls: 25 with head injuries (eg, contusion, concussion, laceration); 3 with facial lacerations requiring sutures; 3 with dental injuries; and 1 with a broken jaw. Twenty-two of 32 injured donors (69%) who received outside medical care weighed 59 kg or more; only 4 of 32 (12.5%) weighed less than 54 kg. The injuries to young donors usually occurred soon after donation in the canteen area (17 events; 53%); in the restroom (5 events; 16%); or in another area of the school (9 events; 28%); and 1 event occurred outside the school (3%).

Return Behavior

Fifty-two percent (1861 of 3559) of 16-year-old donors who experienced a minor complication returned to donate in the next year compared with 73% (2613 of 3559) who had an uncomplicated donation (OR, 0.40; 95% CI, 0.36-0.44). Return donation was even less likely among 16-year-old donors if they experienced a major complication (31%; 30 of 98) compared with the no complication group (81%; 79 of 98; OR, 0.11; 95% CI, 0.05-0.21) (TABLE 5).

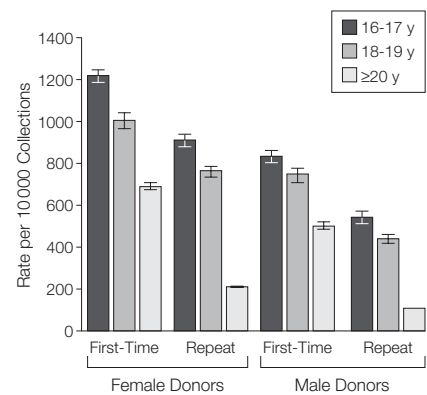
COMMENT

Blood centers have a dual responsibility to provide an adequate supply of blood components to the communities they serve and to protect the safety of their volunteer donors. With the increasing collection of whole blood from minors aged 16 and 17 years in recent years, we sought to describe and quantify the adverse reactions experienced by these donors compared with 18- and 19-year-olds, and compared with adults aged 20 years and older. This analysis demonstrates that most donors in all age groups had uncomplicated donations, but young age had the strongest association with complications followed by first-time donation status and female sex; there was also some variation between regional blood centers.

The most common systemic and phlebotomy-related complications of blood donation (ie, presyncope, small hematoma), although uncomfortable for the donor, are medically inconsequential. The significance of these minor complications, however, lies primarily in the observation that any complication, even a minor one, reduces the likelihood of return donation, as does any temporary deferral for other reasons.²¹ In addition, minor complications may be an indirect measure of more serious complications, although this is difficult to assess because of infrequent occurrence. Although the absolute differences in

complication rates between the age groups are relatively small in this study, they are statistically significant and remain a potential medical concern: the risk of syncope-related injury was 2.5 times more likely in 16- and 17-year-old donors (5.9/10 000) compared with 18- and 19-year-olds (2.4 injuries/10 000 donations), and 14 times more likely compared with donors aged 20 years or older (0.4 injuries/10 000 do-

Figure 2. Total Systemic (Syncope-Type) Complication Rates by Age, Sex, and Donation Status



The rate of presyncope and systemic (syncope-type) complications in stratified donor subgroups with respect to age, sex, and donation status are shown with error bars denoting 95% confidence intervals. Variability was plotted for donors aged 20 years or older but error bars for 95% confidence intervals are very small (the rate for repeat females: 214 [95% CI, 210-217]; and for repeat males: 106 [95% CI, 104-108]).

Table 2. Total Systemic (Syncope-Type) Complication Rates by Donor Age, Sex, and Donation Status^a

Donor Sex and Donation Status	16-17 y			18-19 y			≥20 y			OR (95% CI)	
	No. of Events	No. of Donations	Rate/10 000 Collections (95% CI)	No. of Events	No. of Donations	Rate/10 000 Collections (95% CI)	No. of Events	No. of Donations	Rate/10 000 Collections (95% CI)	16-17 y vs 18-19 y	16-17 y vs ≥20 y
Female											
First-time	6512	53 627	1214 (1187-1242)	2220	22 121	1004 (964-1043)	6331	91 830	689 (673-706)	1.24 (1.18-1.30)	1.87 (1.80-1.94)
Repeat	2767	30 458	909 (876-941)	3053	40 156	760 (734-786)	13 340	624 358	214 (210-217)	1.21 (1.15-1.28)	4.58 (4.39-4.78)
Male											
First-time	3412	41 020	832 (805-859)	1486	19 986	744 (707-780)	4070	80 741	504 (489-519)	1.13 (1.06-1.20)	1.71 (1.63-1.79)
Repeat	1118	20 573	543 (513-574)	1360	31 044	438 (415-461)	7627	720 521	106 (104-108)	1.25 (1.16-1.36)	5.37 (5.04-5.73)
Total	13 809	145 678	948 (933-963)	8119	113 307	717 (702-732)	31 368 ^b	1 517 450 ^b	207 (205-209)	1.36 (1.32-1.40)	4.96 (4.86-5.07)

Abbreviations: CI, confidence interval; OR, odds ratio.

^aTotal systemic (syncope-type) complications include presyncope, short loss of consciousness, long loss of consciousness, loss of consciousness with injury, and prolonged recovery.

^bThe total does include 6 first-time donations, 4 repeat donations, and 1 event of pre-faint reaction for which donor sex was not reported.

nations). Almost half of all injuries recorded by the collection staff in the 9 American Red Cross regions occurred in 16- and 17-year-old donors; and many (eg, concussion, laceration requiring stitches, dental injuries, broken jaw) were severe enough to require outside medical care. Finally, there is a strong correlation between even minor com-

plications and the failure to return to donate blood again among 16-year-olds. Consequently, any negative experience diminishes the likelihood of return blood donation, and increases the possibility that a short-term yield in donations incurs the ultimate expense of deterring future blood donation by young donors.

These findings are particularly pertinent at a time when blood centers are becoming increasingly reliant on young donors to maintain an adequate blood supply. Zou et al describe increasing recruitment of first-time donors in the 16- to 19-year-old age groups and declining rates of blood donation in older age groups.¹² The pressing need to expand the donor pool raises the inherent dilemma of putting minor-age donors at any degree of risk and the difficulty in defining a level of risk that may be reasonably tolerated. The recruitment of minors for blood donation provides a measurable benefit to the national blood supply in terms of both safety and availability. Young donors have lower prevalence and incidence of transfusion-transmitted infectious diseases compared with older donors,²² and 16- and 17-year-old donors contribute a significant proportion (approximately 8%) of the units

collected by the American Red Cross. If the practice of collecting blood from 16-year-olds was extended nationwide, others have estimated that an additional 200 000 additional units could be added to the nearly 15 million units collected annually in the United States.¹¹

Complication rates after allogeneic whole blood donation are known to be higher in young and first-time donors, and our results confirm and extend these observations to the youngest eligible donor group.¹³⁻¹⁹ The mechanisms responsible for the increased susceptibility to systemic (syncopal-type) complications following blood donation in young donors, however, are not clearly defined. Central thalamic pathways and peripheral and ventricular baroreceptor sensitivity may play a central role, and the age-dependent differences in responses to physical and emotional stress may underlie the observed differences in young donors compared with older donors.^{23,24} A psychological component to the propensity for reactions among young anxious donors has also been described, and the phenomenon of "epidemic fainting" or clusters of reactions among donors who witness a reaction at a blood drive is widely recognized although poorly studied.²⁵ In the cur-

Table 3. Multivariate Logistic Regression Model of Correlates of Systemic (Syncopal-Type) and Major Phlebotomy-Related Donation Complications

Risk Factor	Odds Ratio (95% Wald Confidence Limits)	P Value
Age group, y		
≥ 20	1.00 [Reference]	
16-17	3.05 (2.52-3.69)	<.001
18-19	2.55 (2.13-3.05)	<.001
Donation status		
Repeat	1.00 [Reference]	
First-time	2.63 (2.24-3.09)	<.001
Sex		
Male	1.00 [Reference]	
Female	1.87 (1.62-2.16)	<.001
Region in order of decreasing size ^a		
A	1.00 [Reference]	
B	0.72 (0.57-0.90)	.03
C	0.65 (0.49-0.85)	.009
D	0.46 (0.35-0.61)	<.001
E	1.41 (1.13-1.75)	<.001
F	0.95 (0.72-1.26)	.37
G	0.90 (0.66-1.22)	.75
H	1.82 (1.41-2.34)	<.001
I	0.56 (0.37-0.84)	.01

^aTotal collections range from 294 828 in region A to 77 646 in region I.

Table 4. Outside Medical Care

Complications	No. of Donor Complication Events Needing Outside Medical Care (Rate per 10 000 Collections) [95% CI], by Age, y			OR (95% CI), by Donor Age, y	
	16-17	18-19	≥20	16-17 vs 18-19	16-17 vs ≥20
No. of donations	145 678	113 307	1 517 460		
Systemic (syncopal-type) complications					
Presyncope	0	1 (0.1) [0.0-0.3]	4 (0) [0]		
Short LOC ^a	2 (0.1) [0.0-0.3]	3 (0.3) [0.0-0.6]	8 (0.05) [0.0-0.1]	0.52 (0.09-3.10)	2.60 (0.55-12.26)
Long LOC ^a	6 (0.4) [0.1-0.7]	6 (0.5) [0.1-1.0]	43 (0.3) [0.2-0.4]	0.78 (0.25-2.41)	1.45 (0.62-3.41)
Prolonged recovery	16 (1.1) [0.6-1.6]	12 (1.1) [0.5-1.7]	100 (0.7) [0.5-0.8]	1.04 (0.49-2.19)	1.67 (0.98-2.83)
Presyncope or LOC with injury	32 (2.2) [1.4-3.0]	15 (1.3) [0.7-2.0]	38 (0.3) [0.2-0.3]	1.66 (0.90-3.06)	8.77 (5.48-14.04)
Phlebotomy-related complications					
Small hematoma ^a	1 (0.1) [0.0-0.02]	2 (0.2) [0.0-0.4]	9 (0.1) [0.0-0.1]	0.39 (0.04-4.29)	1.16 (0.15-9.14)
Large hematoma ^a	13 (0.9) [0.4-1.4]	8 (0.7) [0.2-1.2]	95 (0.6) [0.5-0.8]	1.26 (0.52-3.05)	1.43 (0.80-2.55)
Nerve irritation	4 (0.3) [0.0-0.5]	5 (0.4) [0.1-0.8]	57 (0.4) [0.3-0.5]	0.62 (0.17-2.32)	0.73 (0.27-2.01)
Arterial puncture	5 (0.3) [0.0-0.6]	2 (0.2) [0.0-0.4]	16 (0.1) [0.1-0.2]	1.94 (0.38-10.02)	3.26 (1.19-8.89)
Other	6 (0.4) [0.1-0.7]	11 (1.0) [0.4-1.5]	63 (0.4) [0.3-0.5] ^b	0.42 (0.16-1.15)	0.99 (0.43-2.29)
Total, all categories of outside medical care	85 (5.8) [4.6-7.1]	65 (5.7) [4.5-7.3]	433 (2.9) [2.7-3.2]	1.02 (0.74-1.40)	2.05 (1.62-2.58)

Abbreviations: CI, confidence interval; LOC, loss of consciousness; OR, odds ratio.

^aSee "Classification Scheme for Donor Complications" section for descriptions of complications.

^bIncludes 6 allergic reactions.

Table 5. Effect of Complications on Return Rates of Blood Donation Among 16-Year-Old Donors

	Minor Complication ^a	No Complication	OR (95% CI)	Major Complication ^a	No Complication	OR (95% CI)
Returned, No. (%)	1861 (52)	2613 (73)		30 (31)	79 (81)	
Did not return, No. (%)	1698 (48)	946 (27)		68 (69)	19 (19)	
Total donors	3559	3559	0.40 (0.36-0.44)	98	98	0.11 (0.05-0.21)

Abbreviations: CI, confidence interval; OR, odds ratio.

^aSee "Classification Scheme for Donor Complications" section for descriptions of complications.

rent analysis, however, drive setting (high school vs other) was not an independent predictor of complications, which suggests that the drive environment does not contribute to the differences observed between age groups.

We recognize the limitations of the current analysis, which did not evaluate the relative contribution of some previously described donor characteristics to the risk of complications after whole blood donation, such as low weight or white race.^{8,17,18,26,27} However, our data show that low-weight donors (<59 kg) are not overrepresented in the cohort of more serious donation-related complications that received outside medical care. Another potential limitation is that the cases associated with outside medical care may be subject to reporting or treatment bias among 16- and 17-year-olds if their parents are more likely to be involved in the decision to seek medical assistance or if collection staff are more attentive to young donors. The increased occurrence of minor phlebotomy-related complications (eg, small hematomas) in the youngest donors suggests that reporting bias may exist because there is no physiologic basis or expectation that hematomas or bruises are more likely to occur in healthy 16- and 17-year-old donors compared with adults. Suspected arterial puncture, however, demonstrated a more significant increase among young (16- to 19-year-old) donors compared with adults, and has been previously postulated to reflect predisposing anatomical conditions in the younger donors.^{28,29} While we cannot control for increased staff or parental attention and possible reporting bias on high school drives, we have no evidence that collection staff are

more likely to report syncope-related injuries on high school drives than on other drive types.

Other blood centers use different classification schemes and have reported similar trends in the rates of mild, moderate, and severe complications among young donors.^{13-18,30} Direct comparison of blood centers, however, is not possible because of subjective differences in defining, recognizing, and reporting donor complications, as well as possible differences in donor demographics that contribute to variation in complication rates. Even within the American Red Cross, variability was seen in the reported donor complication rates among the 9 American Red Cross regions, and those that collected from more donors generally had lower complication rates than the smaller regions. We have not identified correlates of lower complication rates related to different practices among the regions, and these differences may instead be related to donor demographics and any combination of staff experience, attention, or reporting bias and are the focus of further study.

Several interventions (eg, having the donor drink 16 oz water shortly before donation, or using applied muscle tension, distraction, or behavior modification) have been demonstrated to marginally reduce donor complication rates,³¹⁻³³ but no single measure has been shown to prevent a majority of systemic reactions or to prevent the rare but more serious complications, such as syncope-related injury after whole blood donation. Reducing the relative proportion of blood loss by requiring a higher donor weight or by reducing the collection volume have also been proposed as safety measures. How-

ever, we show that over two-thirds (69%) of the injuries that required outside medical care in this cohort occurred in donors weighing more than 59 kg, and others have presented data suggesting that a switch to a larger collection set (500 mL vs 450 mL) had no effect on complication rates.^{34,35} Consequently, these data suggest that increasing the weight requirement or decreasing the collection volume would have marginal benefit, limited to a small subset of donors, and would have little effect on the incidence of more serious complications. Alternatively, the possibility that automated collection procedures with concurrent intravascular fluid replacement may reduce the incidence of severe complications is being further explored.

Conclusions

The current analysis demonstrates a significantly increased risk of minor and major complications of allogeneic whole blood donation by 16- and 17-year-old individuals compared with older donors that extends to an increased risk of syncope-related physical injury and complications requiring outside medical care. Although the absolute magnitudes of the differences between the age groups are relatively small, the differences are statistically significant; young age is the strongest correlate of major complications and 16- and 17-year-old donors accounted for almost half of the syncope-related injuries in this series.

These data on common and infrequent complications of blood donation should be considered when age limits are deliberated by state authorities. The relatively comparable reaction rates in 16- and 17-year-old donors, and their increased complication

rates compared with young adults and adults, suggest the need for a consistent approach. Blood centers have an obligation to constantly monitor risks of blood donation and to make a concerted and committed effort to achieve the lowest possible rate of complications. Although zero risk may not be attainable even in adults, the rate of complications in minors calls for ongoing attention to a sustained operational effort that is continually focused on donation safety.

Author Contributions: Drs Eder and Benjamin had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Eder, Benjamin.

Acquisition of data: Eder, Dy, Notari, Benjamin.

Analysis and interpretation of data: Eder, Hillyer, Dy, Notari, Benjamin.

Drafting of the manuscript: Eder, Hillyer, Benjamin.

Critical revision of the manuscript for important intellectual content: Eder, Hillyer, Dy, Notari.

Statistical analysis: Eder, Dy, Notari.

Administrative, technical, or material support: Benjamin.

Study supervision: Hillyer, Benjamin.

Financial Disclosures: The authors are employed by the American Red Cross and received no separate compensation for their role in the study.

Funding/Support: The American Red Cross hemovigilance program is an ongoing quality assurance function and as such is supported by the organization; however, there was no separate funding for this study.

Role of the Sponsor: The American Red Cross did not have a role in the design and conduct of the study; collection, management, and interpretation of the data; and preparation, review, or approval of the manuscript.

Disclaimer: The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the American Red Cross.

Additional Contributions: Jean Kennedy, BSN, serves as case coordinator, American Red Cross hemovigilance program, American Red Cross National Headquarters, Washington, DC. The authors acknowledge the physicians and staff in the 9 regional American Red Cross donor centers for their daily commitment to blood collection and caring for blood donors without whom this study would not be possible. None of these individuals was compensated for their role in this study.

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