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Management of Young Blood Donors

Bruce H. Newman

American Red Cross Blood Services, Southeastern Michigan Region, Detroit, MI, USA

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Summary
The emphasis on high-school blood drives and acceptance of 16-year-old blood donors led to more research on physiologic and psychological ways to decrease vasovagal reaction rates in young blood donors and to increase donor retention. Research on how to accomplish this has been advantageous for the blood collection industry and blood donors. This review discussed the current situation and what can be done psychologically, physiologically, and via process improvements to decrease vasovagal reaction rates and increase donor retention. The donation process can be significantly improved. Future interventions may include more dietary salt, a shorter muscle tension program to make it more feasible, recommendations for post-donation muscle tension / squatting / laying down for lightheadedness, more donor education by the staff at the collection site, more staff attention to donors with fear or higher risk for a vasovagal reaction (e.g. estimated blood volume near 3.5 l, first-time donor), and a more focused donation process to ensure a pleasant and safer procedure.

Introduction

Young blood donors are defined as donors under the age of 23 years. This group had 54% of all vasovagal reactions [1]. Many high-school donors are donating for the first time, and therefore they are uncertain of the process and outcomes; and they are willing to read presented materials and learn in comparison to experienced donors [2]. Their blood donation experience needs to be optimized for donor safety and to achieve the best blood donor return rates [3–5]. Many articles have evaluated the blood donation experience and stated the reasons for blood donation and barriers to blood donation [6–11]. The goals of management of young blood donors are to provide an excellent experience for the donor at every step in the donation process, to minimize the duration of the total donation process, to minimize vasovagal reaction rates, to protect against donor injury in those who sustain a reaction, and to maximize donor retention.

Vasovagal Reactions – New Findings on Risk Factors

Vasovagal reactions consist of symptoms like dizziness, sweating, pallor, and anxiety. Vasovagal reactions are mainly physiologic reactions that relate to blood volume loss and therefore occur toward the end of the phlebotomy or after the phlebotomy. Many studies have studied or reviewed risk factors for vasovagal reactions, and the reader is referred to those studies for an extensive discussion on risk factors [12–14]. Youth is the main risk factor for a vasovagal reaction [14–21]. Body size, as measured by estimated blood volume (EBV) calculations and less well by body mass index or weight, is the second most important risk factor, and first-time donation history is also a significant risk factor [14, 16]. Black African-American blood donors innately have lower vasovagal reaction rates than Caucasian blood donors [14, 22, 23]. Women have higher vasovagal reaction rates than men because they are smaller in size. Reactions can also be potentiated or even solely due to the donor's fear or psychological makeup. Thus, donors who faint prior to any action, or after a finger stick, or upon seeing blood, or upon seeing other donors with a reaction ('epidemic fainting') are exhibiting a psychological reaction that is inherent to the donors' nature. Recent studies have concentrated on body size, phlebotomy duration, lack of sleep and 'fear'. Body size, phlebotomy duration, and lack of sleep are discussed below while fear is discussed under the intervention for fear.

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Bruce H. Newman, MD
American Red Cross Blood Services
Southeastern Michigan Region
100 E. Mack Avenue, Detroit, MI 48201, USA
bruce.newman@redcross.org

Body Size

Vasovagal reaction rates are directly proportional to the percent of blood volume collected. The AABB limits whole-blood collections to 15% of the EBV, and the Council of Europe recently changed their limit from 13 to 15% of EBV [24]. The EBV for the minimum allowed donor weight of 50 kg (110 lb) is 3.5 l (= 50 kg × 70 ml/kg), and a 15% collection volume of 3.5 l is 525 ml, which is the target collection volume for the American Red Cross (ARC). However, donor weight alone is inaccurate, as EBV is also a function of height and sex. The ARC and the Blood System Institute (BSI) therefore use the variables of weight, height, and sex to determine the most accurate EBV in younger blood donors. Younger blood donors with EBVs below 3.5 l are deferred in both systems, and this decreased the vasovagal reaction rates [19, 20] and delayed vasovagal reaction rate [19]. More than 99% of the young donors eliminated for an EBV less than 3.5 l are women [19, 25]. Other approaches to ensure appropriate minimum donor size are to require a higher donor weight (e.g. 115 lb), or to collect a smaller whole-blood unit (e.g. 450 ml). Two blood centers evaluated whether 450- or 500-ml whole-blood units had different vasovagal reaction rates in their general donor population and did not find a difference [26, 27], but these studies did not evaluate a high-risk population. A recent study from Hong Kong [28] analyzed the vasovagal reaction rate in 38,436, first-time, 16- to 18-year-old whole-blood donors. Donors weighing more than 50 kg could opt for a 350- or 450-ml unit. The vasovagal reaction rates in the women who opted for a 350-ml donation were reduced by 35–58%, depending on the weight group. The vasovagal reaction rates in the men who opted for a 350-ml donation were reduced by 41–45% in the two lower weight groups, but no difference was detected in the two heavier weight groups. Thus, collection of a smaller unit reduced the vasovagal reaction rate in young, first-time donors. A similar prediction was made by a mathematical model in a study of high-school donors [29].

Phlebotomy Duration

There is also new recognition that phlebotomy duration is a significant risk factor. A study in 126,195, first-time, 17-year-old, Caucasian donors from 2006 found that the vasovagal reaction rate directly increased with increasing phlebotomy durations between 4 and 9 min and then plateaued [30]. The vasovagal reaction rates in women or men changed from 7.1% or 4.3% at the 4-min duration to 14.0% or 9.0%, at the 9-min duration. A study of 5.45 million allogeneic whole-blood donations from 2006 found that both vasovagal and syncopal reaction rates increased significantly with phlebotomy duration [31]. Vasovagal or syncope rates changed from 1.2% or 0.05% at the 4-min duration to 4.6% or 0.15% at the 13-min duration, with a linear increase between these two durations. The findings were similar in 321,140 17-year-old donors [31]. Vasovagal reaction or syncope rates changed from 5.8% or 0.24% at the 4-min duration to 10.1% or 0.35% at the 13-min duration, with a linear increase between these two durations. Potential ways to decrease the phlebotomy duration include re-engineering the donor tubing to permit a faster flow rate [32] or use of flow rate pumps, which is done in Japan. Why phlebotomy duration affects vasovagal reaction rates is unknown. However, placement of arm needles in air force pilots [33] and children [34] subjected to orthostatic stress was associated with 4- to 5-fold increase in vasovagal reaction rates. Donation-related needle injuries were also associated with more syncope (adjusted OR 13; 95% CI 8–22) [35]. These studies suggest that arm discomfort and pain cause autonomic decompensation.

Sleep

A recent Japanese study compared 4,924 donations with a vasovagal reaction and 43,948 donations with no vasovagal reaction; 30% of the donors with a vasovagal reaction had less than 6 h of sleep in comparison to 13% of the donors with no vasovagal reaction ($p < 0.0001$) [36]. In a multivariate analysis, less than 6 h of sleep was compared to more than 8 h of sleep, and less than 6 h of sleep increased vasovagal reaction rates in women (OR 3.6; 95% CI 3.2–4.1) and in men (OR 5.1; 95% CI 4.5–5.9).

Effects of Vasovagal Reactions on Blood Donors

Vasovagal reactions are uncomfortable and decrease blood donor retention rates [15, 37–40]. Pre-syncope reactions (no loss of consciousness) and syncope reactions (loss of consciousness) decreased blood donor return rates by 29–37% and 58–78%, respectively, in comparison to donors who did not have a vasovagal reaction [15, 37, 38, 40]. Syncope occurs in approximately 4–5% of vasovagal reactions [1] and in 0.12–0.27% [1, 21, 42] of allogeneic whole blood donations. 60–73% of the syncope reactions occur after the donor leaves the bed due to gravity, and 10–12% of the reactions occur after the donor leaves the blood collection site [41, 42]. Studies show that women, and especially smaller women, are more susceptible to gravity-precipitated syncope, and almost all syncope reactions that occurred after leaving the blood collection site occurred in women [41]. Syncope is an issue because many donors suddenly fall, and 4–9% sustain an injury [1, 41]. Overwhelmingly, the injuries are minor [42], but severe injuries such as fractures, lacerations, and closed-head injuries can occur [15]. While donor injury rates are very low in two very large organizations – ARC (0.011%) [1] and BSI (0.014%) [41] –, they are 3- to 6-fold higher in younger donors, being 0.037%, 0.052% and 0.065% in 18-, 17- and 16-year-old donors, respectively [43]. It seems intuitive that all blood donors should have the same risk of donor injury after syncope, but in a study in 30.2 million allogeneic ARC donations, the donor injury rate after syncope was much higher in younger than in older donors. Relative risks increased by 72%, 96% and 125% in 18-, 17- and 16-year-old donors in comparison to 43- to 57-year-old donors, who were the group with the lowest risk for injury after syncope [43]. It is unknown as to why younger donors have a disproportionate donor injury rate after syncope in comparison to older donors.

Tools to Evaluate Vasovagal Reactions

The main tool to identify and study vasovagal reactions is observation and recording of reactions by the collection staff. The reaction's occurrence, the location of the reaction's occurrence, the donor's demographics, the symptoms and signs, the presence of syncope, prolonged recovery, presence of injury, and applied interventions to prevent reactions are variables that can be captured and studied. Vasovagal reactions can be sorted by these factors and studied as uni-, bi-, or tri-variables, or via multivariable analysis. The last method is best because donors have multiple and often related risk factors (e.g. youth and first-time donation). The AABB National Donor Biovigilance Committee and the International Society of Blood Transfusion's Committee developed objective and useful categories; so data can be understood and compared. However, a limitation is that mild reactions may not be obvious or recorded. Donor interviews and written self-assessments can provide more accurate assessments of donor reactions. Thus, interviews 3 weeks later [44] or other post-donation surveys [45–47] detected much higher vasovagal reaction rates in the general donor population. The Blood Donor Reaction Inventory (BDRI) is a useful self-survey technique to obtain more detailed data directly from the donor, either before and/or after the donation, to evaluate vasovagal reactions [48]. A change from an 11-question BDRI into a 4-question BDRI was shown to be a better fit with observed vasovagal reactions [49]. The BDRI allows to obtain more detailed data from a small group of donations for analysis and to do research with hundreds of donations versus the thousands or tens of thousands of donations that need to be observed for reactions. Such studies can suggest the need for larger observation-based studies, and large observation studies can be more conclusive and relevant [50, 51].

Reducing Vasovagal Reactions and Increasing Donor Retention

An AABB working group was given the mission to reduce vasovagal reactions and injuries in adolescent blood donors, and they identified five parts to the donation process [52]. A slightly modified version is: i) pre-donation education; ii) drive set-up and environment; iii) staff supervision and skills; iv) interventions; and v) post-reaction treatment and instructions. Another approach is to divide the experience into: i) improving the donor psychologically to prevent vasovagal reactions and increase donor retention; ii) improving the donor physiologically to prevent vasovagal reactions and increase donor retention; and iii) improving the donor's attitude and making process improvements to prevent vasovagal reactions and increase donor retention.

Improving the Donor Psychologically to Prevent Vasovagal Reactions and Increase Donor Retention

'Fear'

'Anxiety' is identified in many older studies as being associated with vasovagal reaction rates [53–57]. A talkative phlebotomist [58], phlebotomists with good interactive skills [59, 60], a donor social support person during the donation process [61], and distraction [62, 63] all reduced anxiety and decreased vasovagal rates to some extent. There is concern that a fear question might discourage blood donations or even cause more donor reactions. Two donor fear questions were evaluated in 982 experienced donors, ages 16–92 years, with 4% being first-time donors [64]. Vasovagal reactions were evaluated using a 4-question BDRI (faintness, dizziness, weakness, or lightheadedness) because the group had very few observed reactions. 15% of those asked the fear questions expressed fear. Those asked the fear question (n = 488) did not have more reactions than those not asked the fear questions (n = 494) (22% positive BDRIs vs. 28% positive BDRIs; $p < 0.05$). A similar but larger study was done by the same blood center in 3,407 high-school students [65]. All donors were young, 50% were first-time donors, and reaction rates were based on phlebotomists' recorded observations. The donors' pre-donation brochure emphasized muscle tension if needed, and donors were given water after the health screen and prior to the donation. Half of the donors (n = 1,715) were asked a single fear question ('How afraid are you of having blood drawn from your arm?'), and the other half (n = 1,692) were not. The fear question was rated from zero (no fear) to 4 (extreme fear). Donors asked the fear question had the same vasovagal reaction rate as donors not asked the fear question (17.2% vs. 17.7%; $p = 0.68$). Thus, asking about fear did not increase the vasovagal reaction rate in a general donor population or in high-school donors. 44% of the donors (755/1,715) in the high school were afraid, and most had low or moderate amounts of fear. The proportion with fear was higher in first-time donors (495/855 (58%)) than in repeat donors (260/860 (30%)), but both groups had higher fear rate proportions than the general donor population (15%) [64, 65].

Those who expressed fear in the study of experienced donors had a higher percentage of positive BDRIs than those who did not express fear (48 vs. 18%; $p < 0.002$) [64]. In logistical regression analysis, fear was found to be a strong predictor for a positive reaction using BDRIs. In the high-school study, high-school donors who expressed fear had twice the vasovagal reaction rate as donors who did not express fear (187/755 (24.8%) vs. 108/960 (11.3%); OR 2.60, 95% CI 2.00–3.37) [65]. The same findings were found in first-time donors (125/495 (25.3%) vs. 47/360 (13.1%)), and in repeat donors (62/260 (23.8%) vs. 61/600 (10.1%)). Stronger fear was associated with a higher vasovagal reaction rate. When a binomial logistic regression analysis with forced entry of all significant individual predictors was conducted, donor fear was found to be the strongest individual predictor of a vasovagal reaction. When the logistic regression eliminated fear and body size (EBV) as factors, men, surprisingly, were more likely to have a vasovagal reaction than women. The two studies suggest that a 'fear' question be added to the donor questionnaire. The staff could then identify such donors and mitigate their fear through compassionate interactions, through suggestion of coping strategies, and by giving more attention to 'fearful' donors during the phlebotomy process.

A third study using the same 1,715 donors followed blood donor return rates over a 2-year period [66]. Fear decreased the blood donor return rate from 55% (no fear) to 45% (fear), but fear also affected the vasovagal reaction rate, and vasovagal reactions decreased the blood donor return rate from 56 to 36%. The study suggests that mitigation of fear would improve blood donor retention based on a double effect – on the effect of fear itself and on its effect on the vasovagal reaction rate. Dealing more directly with fear could decrease the vasovagal reaction rate and improve donor retention.

Other Techniques to Decrease Fear and Enhance the Donor's Experience

Researchers also improved communications to donors through an enhanced donor recruitment brochure [63, 67], use of a video [68], or through a better website [69]. The goals for each of these improvements were to reduce fear, decrease vasovagal reaction rates, and increase blood donor retention. An enhanced brochure more specifically and directly reviewed common donor concerns and barriers such as fear of pain, arm injury, being weak, and the possibility of a vasovagal reaction. It suggested validated empirical actions to cope with vasovagal reactions that included fluid loading, muscle tension, and distraction techniques. The effects of the brochure on 183 college students were objectively measured and compared to a standard brochure or a non-relevant brochure [67]. The new brochure improved the subject's confidence in their ability to successfully donate ($p < 0.001$) and intention to donate ($p = 0.003$). In a later study in 345 college students (253 women), subjects reading the new brochure showed the same findings and continued to show benefits 1 week later [63]. There was greater confidence in their willingness to donate blood (self-efficacy). Those reading the new brochure were more willing to donate blood (57%) than those reading the standard brochure (40%; $p < 0.05$), and a higher percentage of them scheduled a donation (43% vs. 30%; $p < 0.05$).

In another study, the authors explored the use of the same brochure, a video, or a combination of new brochure and video to increase donor recruitment in 599 college students (62% women, 49% never donated) [68]. Both the new brochure and video improved anxiety, attitude, donation confidence, and donation intention to the same degree. The video provided another option for those who preferred watching a video, but one could do either with the same effect. There was no synergy from doing both. An improved web-based approach was evaluated in 673 college students, 60% of whom were non-donors [69]. In non-donors, the authors' website produced greater changes in donor attitude, confidence, and intention than the standard website and the control website, and in donors, the authors' website produced greater changes in donor confidence than the standard website and control website. In summary, improvements can be made in audiovisual media to decrease donor fear and improve donor recruitment.

Evaluation of Adverse Events and Psychological Factors on Donor Retention

Veldhuizen et al. [45] in the Netherlands evaluated 12,051 whole-blood donations in 2008 via a post-donation survey of experienced donors and evaluated the effects of vasovagal reaction and adverse arm events on blood donor-return rates over a 2-year period. They also evaluated the effects of psychological variables such as intention, self-efficacy, cognitive attitude, and affective attitude on blood donor decisions to return or not. Thus, both donor adverse events and psychological factors were evaluated. Women had more vasovagal reactions (4.1% vs. 0.9%) and more arm injuries (7% vs. 2%) than men, for a total of 11% versus 3%, but women were less likely to stop donating blood after a vasovagal reaction than men (OR 1.8 vs. OR 3.9). High levels of self-efficacy (OR 0.53), cognitive attitude (OR 0.75), and affective attitude (OR 0.75) in women reduced their probability to stop future blood donations, and the same was true in men with high levels of self-efficacy (OR 0.66) and cognitive attitude (OR 0.79). The study shows that donor attitudes affect their blood donation return rate after an adverse event, and self-efficacy (confidence) appears to be the most important psychological factor. This is another study that shows the importance of the psychological approach to blood donors.

Improving the Donor Physiologically to Prevent Vasovagal Reactions and Increase Donor Retention

Two Large Intervention Studies to Prevent Vasovagal Reactions

Two studies from two large organizations evaluated the interventions of donor selection (≥ 3.5 l EBV required), 16-oz (473 ml) water fluid preloading within 30 min of the phlebotomy, and muscle tension in young whole-blood donors [19, 20]. The ARC study compared 754,000 and 711,000 whole-blood donations from 16- to 18-year-old donors in the 2008 and 2009 school years, respectively, to a baseline of 2.02 million donors of the same age from 2005–2007 [20]. Several actions were taken in the 2008 school year (new pre-donation materials for high school students and their parents, standard work guidance for staffing levels, elimination of the view of the venipuncture area from the waiting area, encouraging each donor to drink 16 oz (473 ml) of water before phlebotomy and to perform leg lifting as a form of muscle tension), and in the 2009 school year, 16- to 18-year-old donors had to have an EBV of at least 3.5 l to donate. The vasovagal reactions rates in 16- to 18-year-old donors were 8.78% in the baseline years (2005–2007), 8.01% in the 2008 school year, and 7.06% in the 2009 school year. The decrease in the vasovagal reaction rate was 1.72% or 20% (1.72/8.78%). The decrease in the pre-syncope reaction rate was inversely proportional to age, with 18%, 25% and 33% reductions in 18-, 17- and 16-year-old donors, respectively, in comparison to the baseline years. Overall, there was 6% decrease in the syncope rate in 16- to 18-year-old donors in comparison to the baseline years. The decrease in the syncope rate was inversely proportional to age, with 3%, 5% and 14% reductions in 18-, 17- and 16-year old donors, respectively, in comparison to the baseline years. There was no change in the donor injury rate for any age group. Researchers from the same group also evaluated a 16-oz (473 ml) water drink via a survey of 21,237 high-school donors in the last 4 months of 2009 [70]. There was a statistical difference between female first-time donors who drank all of the water and female first-time donors who did not drink the water (8.9% vs. 10.8%; OR 0.81, 95% CI 0.66–0.91). Male first-time donors who drank all of the water also showed an 18% difference when compared with male first-time donors who did not drink the water (4.6% vs. 5.5%; OR 0.82, 95% CI 0.62–1.09), but it did not reach a statistical difference. That male first-time donors do benefit from drinking 16 oz of water is consistent with the decrease in vasovagal reactions rates in all ARC male, high-school, first-time donors in 2008 [20], in the study by Tomasulo et al. [19] that showed a 21% reduction in men with EBVs greater than 3.5 l, and in data from 8,894 high-school donors in 2004 and 2005 [51].

BSI performed a similar comparison of vasovagal reaction rates in 17- to 22-year-old donors for two time periods [19]. There were no interventions for the 99,859 donations in calendar year 2007, which was used as the baseline. For the 113,172 donations between August 1, 2008 and July 31, 2009, the three interventions used were the offer of a 473–500 ml water drink to each donor; encouraging donors to apply muscle tension in the lower legs and buttocks for 5 s alternating with 5 s of relaxation, starting at the beginning of phlebotomy; and elimination of donors with EBVs of less than 3.5 l. Overall, there was a 24% reduction in the vasovagal reaction rate and a 22% reduction in the syncope rate. In women, there was 20% reduction in the vasovagal reaction rate, a 21% reduction in the syncope rate, a 21% reduction in the delayed syncope reaction rate (more than 4 min after the phlebotomy ended), and a 40% reduction in off-site syncope rate. This last fact is important because donors with off-site syncope reactions are more frequently injured and sent to hospital emergency rooms than donors with similar reactions that occur at the collection site [18]. The combined effects of water and muscle tension were compared in the pre- and post-intervention groups in donors that had EBVs that exceeded 3.5 l. The comparisons showed a 12% decrease in vasovagal reaction rates in women ($p < 0.0001$) and a trend toward an 11% decrease in syncope rates in women ($p = 0.066$). In men, there was a 21% decrease in vasovagal reaction rates ($p < 0.0001$) but no significant change in syncope rates. The three interventions together had no effect on fall (donor injury) rates. In sum, BSI's interventions reduced the vasovagal reaction rate by 24% and the syncope rate by 22% but had no effect on the donor fall (donor injury) rate [19]. The outcomes at ARC and BSI were similar except BSI reported a greater reduction in the syncope rate (22 vs. 6%).

Compliance with the Interventions

The BSI reduced the proportion of donors with EBVs below 3.5 l by 96%, and the ARC probably had a similar rate. The use of water and muscle tension in both studies was incomplete. A recent editorial stated that compliance should be improved for these two measures [71]. A recent South African study had a compliance rate of 81% for young donors drinking all of the water where 75% were repeat donors [72]. In the study by Newman et al. [51], the donor refusal rate was 1.4%. Two other situations that occurred in this study were that some nurses failed to participate in the study (3.8% of the water not given) and logistical support failed to deliver sufficient water for the blood drive (6.0% of the water not given). These latter situations are correctable with good supervision and close attention to logistical support to ensure that sufficient water is present at the blood drive. These statistics suggest that one should be able to get compliance for drinking 16 oz (473 ml) of water to the 90–95% range in a young donor population, if every donor is encouraged to drink the water. An ARC survey found that just 22% of the young donors were willing to do muscle tension as prescribed (alternate leg raising every 10 s during the entire phlebotomy) [20, 70]. Lower-body muscle tension should be made more feasible by limiting the exercise to just the last 3 or 4 min of the phlebotomy and by decreasing the number of 5-second tensions to just 3 or 4 per minute [71]. Muscle tension is also a form of distraction. The benefit of muscle tension data is supported by small trials that used BDRI evaluations to show differences [73–75], but there are no large observation trials.

Mechanisms for Interventions

The mechanism of lower-body muscle tension is to empty the blood from large capacity veins into the heart, thus increasing stroke volume and cardiac output [76–78]. The effect is almost immediate, occurring after 2–3 s [79, 80]. Lower-body muscle tension can be used prophylactically during the donation to prevent a vasovagal reaction [76–78]. Alternatively, it can also be used as treatment for a donor that becomes dizzy on the bed [65]. Wieling et al. [81] suggested that lower-body muscle tension should also be used by the donor before leaving the bed to increase blood flow into the heart and post-donation if lightheadedness or dizziness develops. If it fails for lightheadedness while standing, the donor should squat since it also increases the blood supply to the heart, and if immediate relief does not occur, the donor should move to a laying position because it eliminates the risk of a traumatic injury from a fall. These maneuvers require that the donor receives some impending warning like lightheadedness or dizziness. It is possible that younger donors do not receive or recognize the same impending warnings as older donors because they have a much higher donor injury rate after syncope.

16 oz (473 ml) of hypotonic water can reduce vasovagal reaction rates by 16–21% in high-school donors that drink all of the water [20, 51, 70], but the effects of hypotonic water are limited to 45–60 min. The differences in rates between 16% and 21% may be due to whether the study was done prior to implementation of interventions (21% [51]) or after implementation of interventions (16%, e.g. muscle tension, EBV < 3.5 l [70]). There are two possible explanations for the water-load mechanism – one is gastric distension [82, 83] and the other is due to osmoreceptors in the portal circulation [84–86]. Gastric stretching causes a sympathetic discharge that causes peripheral vasoconstriction, which leads to less blood flow to the arms and legs and more central blood flow [82–84]. It maintains a person's blood pressure when blood flow to the gastrointestinal tract is increased to absorb food. A water load is limited by the fact that half of the water leaves the stomach within 20 min [86]. The osmoreceptors in the portal circulation respond to a hypotonic water solution involving anti-diuretic hormone and the kidneys [84–86]. The study of Newman et al. [51] suggested the former mechanism because the time duration between drink and phlebotomy had an effect on vasovagal reaction rates and suggested that gastric filling was the mechanism of action. Individual response to water and timing of the water relative to the phlebotomy to achieve the best response need further study.

Potential from Isotonic Drinks

Wieling et al. [81] suggested the use of two isotonic drinks (sports drinks) that equal 500 ml in volume and contain 0.4 g of sodium. They believe that isotonic drinks before the blood donation and immediately after the blood donation and 1.2 g of sodium-containing food (e.g. 2 oz of pretzels at the refreshment table (0.7 g of sodium)) to replace the sodium salt content lost from the blood donation will facilitate more rapid replenishment of the blood volume. A higher ingestion content of 2.4 g of sodium would be preferred. Theoretically, a more rapid replenishment of the blood volume through increased dietary sodium content would protect all blood donors, including young blood donors, from reactions after the blood collection and after they leave the collection site [81, 87]. Increases in dietary sodium have been shown to be useful in patients with orthostatic hypotension due to autonomic failure [88], in healthy subjects with orthostatic intolerance [89], in dehydrated athletes [90, 91], and in deconditioned astronauts returning to earth [92]. Approximately half of the sodium salt remains within the body for 24 h due to slow excretion. Dietary sodium replacement requires action on the donor's part, which may or may not occur. No clinical trial has yet tested whether dietary sodium is effective in the blood donation setting. The purpose of an isotonic drink instead of water is to extend the effect beyond 1 h. Isotonic fluids would work equally well to hypotonic water during the donation if the mechanism of action is gastric filling and wall stretching. However, an isotonic drink would not work if the mechanism of action is absorption of hypotonic fluid via the portal vein because it is not hypotonic. Testing of a 500-ml isotonic preloading solution on vasovagal reaction rates is needed so it can be compared with hypotonic water.

Automated 2-RBC Unit Collections

Another approach to reduce vasovagal and syncope rates is the use of automated 2RBC-unit blood collections. There are several machines including the MCS+ 8150TM (Haemonetics, Braintree, MA, USA), AlyxTM (Fenwal, Inc., Lake Zurich, IL, USA), and TrimaTM (Terumo Caridian BCT, Lakewood, CO, USA) that can be used for these collections. Donors need to be larger in size with higher minimum weights, the total blood volume collected is smaller than in manual one-unit whole-blood collections (445 ml vs. 525 ml), and the donor's blood volume is partially replaced with a 0.9% intravenous saline solution. All of these factors lead to reduced vasovagal reaction and syncope rates in younger blood donors. In addition, the donor's hemoglobin needs to be higher, 13.3 g/dl or hematocrit of 40%. In the study of Benjamin et al. [93] comparing 206,570 2RBC donations with 4,348,686 whole-blood donations in 2007, approximately 7% of the high-school students were collected for 2RBC units. 92% of the procedures were in men. In a comparison with whole-blood donations, the following were reduced: presyncopal vasovagal reaction rate (1.86% vs. 2.77%; OR 0.67, 95% CI 0.64–0.68); syncope rate (<1 min) (0.073% vs. 0.098%; OR 0.74, 95% CI 0.63–0.87); prolonged recovery rate (0.009% vs. 0.019%; OR 0.48 , 95% CI 0.30–0.75); and donor injury rate (0.001% vs. 0.010%; OR 0.14, 95% CI 0.05–0.45 [93]. In another large study, Wiltbank and Giordano [94] reported similar findings. In their study, 249,154 2RBC collections were compared against 1,023,682 whole-blood donations. The moderate and complex reactions were less common in the 2RBC collections (0.16% vs. 0.47%; $p < 0.0001$). 2RBC units are a good option but it is limited mainly to men and one must be a larger-sized person with the right blood group to be done.

Phlebotomy Duration

In addition to currently used interventions, our preliminary data (unpublished) suggest that shortening the phlebotomy duration from 7 to 5 min might have a positive impact on both vasovagal reaction and syncope rates in donors, including younger donors [31]. Based on 2006 data, changing the phlebotomy duration from a mean of 7 to 5 min in 17-year-old donors reduced the vasovagal reaction and syncope rates by 30% and 27%, respectively. Further analysis in a post-intervention period would provide better data as to its potential current effects. A feasible method to decrease the phlebotomy duration and a clinical trial to evaluate its effects on vasovagal reaction rates would be needed before consideration of this intervention.

Studies on Syncope and Related Injuries

Kamel et al. [18] and Bravo et al. [41] studied the timing of syncope during the whole-blood donation process in 2007 (n = 554,534) in all age groups, and Wieling et al. [81] suggested further interventions. The timing of syncope was divided into four periods: 1) pre-donation; 2) during the phlebotomy and for 4 min after the phlebotomy, which assumes the donor is still on the bed; 3a) after the phlebotomy but still at the blood drive site; and 3b) after the phlebotomy and after donor has left the blood drive site. There were 1,563 syncopal events (0.28% of donations), and the relative incidence for syncope for periods 1, 2, 3A and 3B was 3%, 38%, 49% and 10%, respectively [41]. Syncope in period 1 (prior to donation) was a rare event (0.004%). Based on multivariable risk factor analysis, the risk factors during this period were youth (OR 11.1, 95% CI 4.6–27.3) and first-time donation (OR 4.3, 95% CI 2.1–8.8). During period 2 (donor on the bed), the risk factors were EBV < 3.5 l (OR 3.2, 95% CI 2.2–4.8), first-time donation (OR 2.5, 95% CI 2.1–3.1), and youth (OR 2.1, 95% CI 1.7–2.6). Women had a lower risk of syncope during this period than men (OR 0.6, 95% CI 0.5–0.8). During period 3A (after leaving the bed but still on-site), the risk factors were EBV < 3.5 l (OR 4.6, 95% CI 3.5–6.0), youth (OR 3.9, 95% CI 3.2–4.7), and first-time donation (OR 1.9, 95% CI 1.6–2.3). During period 3B (donor left the blood drive site), the risk factors were EBV < 3.5 l (OR 14.1, 95% CI 5.1–39.0), female sex (OR 2.9, 95% CI 1.2–7.4), and youth (OR 2.5, 95% CI 1.7–3.8). 95% (147/155) of the donors, with syncope during period 3B were women. There were 75 donor injuries in 1,563 syncopal events (4.8%). 84% (63/75) of the injuries occurred during period 3, and 71% (53/75) occurred in women. All of the injuries during period 3B (donors offsite) occurred in women (16/16). There were 165 cases of outside medical care in the 1,563 donors with syncope (10.6%). 76% of the outside care were from syncope during period 3, and 81% (133/165) were in women. 89% of the outside medical care cases in period 3B were in women (40/45) [32].

Eder et al. [15] evaluated 86 donor injuries in 145,678 whole-blood donations (0.059%) in 16- and 17-year-olds in 2006 at the ARC. Donor injury was 14 times more likely in 16- to 17-year-olds than in donors older than 20 years. This is consistent with higher syncope rates in younger donors and higher donor injury rates per syncope in younger donors than in older donors [43]. 32 donors received outside medical care. 25 had head injuries (e.g., contusion, concussion, laceration), 3 had facial lacerations, 3 had dental injuries, and 1 had a fractured jaw. 17 injuries (53%) occurred on site, 5 (16%) occurred in the bathroom, 9 (28%) occurred in another part of the school, and 1 (3%) occurred outside of the school [15].

Wieling et al. [81] stated that syncope is due to the blood volume removed (525 ml), the psychological stress from the needle and process, and orthostatic changes after leaving the bed. Standing up causes immediate pooling of 300–800 ml of blood [95]. The 525-ml blood volume loss, the pooling of the blood in the lower extremities, and the 10–15 min in a supine position, which inhibits rapid adjustment to volume changes upon standing, all cause a decrease in the central blood volume and can lead to exaggerated dizziness or syncope if the body cannot rapidly adjust to it. A peak in syncope found just after the phlebotomy may be due to this initial blood pressure drop when standing. After the body adjusts, there may still be orthostatic tachycardia or vasovagal syncope due to the blood volume loss. A second peak in syncope occurred 9 min after the phlebotomy ended, and then syncope slowly disappeared over time. Being a woman and a low EBV were the main predictors for delayed and off-site syncopal reactions. A study showed that women had less responsiveness than men to increase blood pressure when undergoing an orthostatic challenge [18, 96]. Fu et al. [97] showed that women had less orthostatic tolerance when hypovolemic, predominantly due to less cardiac filling and a smaller stroke volume.

Effects of Interventions on Blood Donor Return Rates

Several small studies did not show substantially better blood donor return rates among blood donors with intervention-reduced vasovagal reaction rates. A randomized study of 421 donors [66] did not show a 2-year return rate difference between college donors given water and muscle tension (9.9% vasovagal reaction rate) versus no interventions (17.9% vasovagal reaction rate). The return rates were 35% or 34%. A further analysis showed the importance of anxiety and its direct negative effect on donor intention, and its negative effect through causing more needle and vasovagal reaction reports, which also decrease donor retention. The study suggested that the psychological handling of donors plays a corollary role or perhaps even more important role in donor retention than reduction of reactions. Several small trials that used muscle tension showed variable results for donor retention [73–75]. These variable results suggest minimal benefits from muscle tension in terms of blood donor retention.

Improving the Donor's Attitude and Making Process Improvements to Prevent Vasovagal Reactions and Increase Donor Retention

The prevention of vasovagal reactions and maximizing of donor retention is not just based on mechanisms to reduce vasovagal reaction rates but also on establishing self-efficacy (confidence) and providing a good blood donation experience. Half of the young donors are first-time donors; therefore, they lack knowledge about the process. First-time donors, in contrast to repeat donors, are more willing to carefully read the pre-donation material (76 vs. 28%) [9]. They want more explanation and more attention because the blood donation process is unknown to them. If suggested, they will drink the 16 oz (473 ml) of water and do the lower-body muscle tension procedure during the donation. As previously noted, the refusal rate for water in almost 9,000 high-school students (78% first-time donors) was less than 2% [51]. In contrast repeat donors have experience and develop confidence because of that experience. 72% skimmed the pre-donation reading material [9], and they do not listen to advice because they feel their risk is low [2]. They may provide 88% of the blood and have a lower risk for a reaction, but they still have slightly more than half of the vasovagal reactions [16]. Experienced donors are as likely as first-time donors to not return if they experience a vasovagal reaction [37]. Masser [2] suggested reaching experienced donors in a stealth and indirect manner. For example, give special reading materials to the young donors; the experienced donors will ask, if they are interested. Give a checklist to all donors to optimize their donation against vasovagal reactions and state that this checklist is especially for our 'first-time donors'. The material especially becomes relevant when one experiences a vasovagal reaction.

Blood centers encourage increased hydration within 24 h to improve the presence of good veins and better blood flow rates (no studies), that donors follow their normal eating pattern, and that donors get a good night's sleep. As previously noted, a good night's sleep reduced the vasovagal reaction rate [36]. The blood donation process begins by recognizing that each donor is the most important person in the room and all focus should be on the donor. Each donor, by choosing to donate blood, choose to help others. Therefore, the receptionist should thank each donor for coming and should confidently explain the preliminary donation process to each donor and ensure that each donor keeps his or her place in line according to order of arrival. The donor needs to be thanked two more times – by the phlebotomist and by the refreshment coordinator. The pre-donation material at the blood drive site should explain the blood donation procedure, answer the donor's basic questions, adequately address the fears that are important to the donor, provide deferral information so the donor can self-defer, and address other issues such as post-donation blood tests and confidentiality. Excellent material, with additional access to a video or internet site, can effectively give the donor critical information and increase accessibility through audiovisual media. These pieces can also be used to communicate with parents, school administration, and school nurses. However, it should be recognized that donors may not engage with the pre-donation materials, and the health historian and phlebotomist need to interact with donors to ensure that donors have adequate knowledge to make the right intervention choices.

It is important that the staffing level be consistent with the blood drive's goal. This eliminates or minimizes donor wait times. Staff needs to be on time and ready to start when the blood drive starts. Any delay at the start-time will carry forward and delay donor flow. Staffing levels should also take into account breaks and meals. Donors and sponsors are upset when the donor-wait time is related to insufficient collection staff. The collection staff, however, is not responsible for uneven donor flow because of recruitment practices. The blood center recruitment coordinator should work with the company coordinator(s) to ensure an even flow. Otherwise, it may make sense to stop walk-in traffic or move donors to later times to ensure a good experience for each blood donor. Staffing levels are critical as the wait time may be one of the most important factors for donors and sponsors judging the blood drive's success, and lack of staff may decrease blood donor return rates [3–6]. The donors when waiting to see a health historian should be shielded from seeing blood donor reactions because they can cause psychological vasovagal reactions.

As previously noted, it is important to address 'fear' during the donation history via a written question, and almost 60% of the first-time young donors will answer positively [65]. Fear, if present, will need to be mitigated by the health historian and phlebotomist through compassionate and informative interactions, having the donor read additional written materials, encouragement of coping mechanisms, and by spending more time with the donor during the phlebotomy. The same is true for donors with low EBVs. Donors appreciate staff that is professional, interactive, and compassionate. The blood collection industry is just beginning to recognize that the donor's psychological makeup and experience and the blood center's staffing level and care can make a difference in vasovagal reaction rates and blood donor retention. Further work will need to be done to quantify the effects of a good process.

It is important to explain the phlebotomy process to first-time donors and engage with all donors during the phlebotomy process, or offer the possibility of more engagement if desired. No donor should feel abandoned. As previously noted, muscle tension toward the end of the phlebotomy process should be encouraged and could also be beneficial as a means of distraction. Post donation, the donor's arm is bandaged, and the phlebotomist should thank the donor for donating blood and explain the importance of the donation for the community and for patients. The donor is usually happy with the achievement, and the added boost adds to the donor's

Table 1. Summary on reduction of the vasovagal reaction rate in young blood donors and making the experience more pleasant

Psychologically improve the donor
Deal more directly with donor fear
Improve donor recruitment brochure
Improve on-site brochure
Video/internet options
Ask donors a question about 'fear'
Health historian interaction / push coping strategies for at-risk donors (fear, low EBV)
Explain procedure at every step to first-time donors
Spend sufficient time with donors during phlebotomy
Encourage or provide distraction
Interaction during phlebotomy
Muscle tension at end of phlebotomy
Improve donor confidence
Education / optimize behaviors for preparation for donation
Achieve successful donations
Physiologically improve the donor
Require EBV > 3.5 l in young blood donors
Alternatively, smaller collection volume
Alternatively, require higher EBV in young donors (e.g. EBV > 4.0 l, 4.5 l)
Preload 473–500 ml water drink close to phlebotomy in young blood donors
Encourage prophylactic lower-body muscle tension for young blood donors
Use shorter, more feasible method at end of phlebotomy
Alternative is to use lower-body muscle tension for onset of symptoms on the bed
Use before release from the bed
Use for lightheadedness after release from the bed
– Squat/lay down if above is not successful
Encourage predonation behaviors that may help
Eat normal meal prior to donation
Increase salt content the day before the donation
Good hydration within 24 h of the donation
Good night's sleep before the donation (6.5–9 h)
Donor is stable in sitting position with legs overhanging the bed before being allowed to go to the refreshment table
If food given at bed, then above applies to leaving the bed
Make sure first-time donors are stable when leaving the bed
2RBC collections in qualified candidates
Process Improvements
Provide sufficient staff for collection goal, including time for meals/breaks
No wait time / minimal wait time (critical issue)
Even donor flow scheduling or compensatory measures
Communications to school/parents
Health historian should deal with the 'fear' issue
Provide card during phlebotomy to first-time donors that explains how to optimize preparation for next donation
Thank the donor 3 times (receptionist, phlebotomist, refreshment coordinator)
Phlebotomist should emphasize the value of the donation for the community and for the patients
Good post donation information
Optimize management of syncope / donor injury
Give salty food at refreshment table
Encourage 15 min at refreshment table / close observation of donors

pleasure and satisfaction. As previously noted, the donor should be put in a sitting position with legs hanging over the side of the bed for at least a couple of minutes, and the donor should be asked if he or she feels well before being allowed to leave the bed. The donor should be strongly encouraged to use lower-leg muscle tension before leaving the bed, and the phlebotomist should observe the donor for steadiness. As previously noted, the donor should also use muscle tension if he or she becomes dizzy, and if muscle tension does not work, then the donor should use a squat position. If that does not immediately work, the donor should move to a laying position to prevent traumatic injury from a sudden fall. Resources are inadequate to walk the donor to the refreshment site. It is also unclear if a helper could stop a donor from a sudden fall, and a helper might sustain a back injury while trying to stop a donor from falling.

The refreshment coordinator should also thank the donor, ask the donor how he or she did, and meet the donor's needs for fluids and 2 oz of pretzels. The donor should be encouraged to stay in the refreshment area for 15 min, and the donor should be closely observed for a vasovagal reaction. The refreshment coordinator should notify collection staff immediately if one occurs. Table 1 provides a summary of potential actions during the blood donation process that can improve donor safety and make the blood donation process a more pleasant experience.

Managing Donor Syncope and Injury

Although the goal is to prevent donor syncope and subsequent donor injury, current documented efforts have achieved no more than a 22% reduction in syncope and no reduction in donor injuries. Therefore, collection staff needs to be prepared for syncope. 27–40% of syncope events occurs on the bed, and they occur more commonly in men than women [41, 86]. In such donors, the needle should be removed because a significant percentage may have convulsions/tetany [42]; legs should be elevated; and the donor should not be allowed to fall from the bed. Oxygen, medications, and intravenous fluids are not necessary. The donor spontaneously revives and should be monitored with vital signs, for mental status, and for general condition until the donor feels well enough to leave. It is difficult to get compliance with how to sit at the table to prevent injury because syncope in the worst case scenario occurs in just 0.6% of the blood donors. Prevention of a fall is ideal but is often not possible. Donors with syncope should be evaluated for donor injury and should be placed on an emergency cot and monitored until recovered. Donor injury needs to be treated appropriately. The overwhelming majority presented minor injuries, but serious injuries like significant head injury, laceration, bone fracture, or tooth injury should be referred for outside medical care. Donors who do not recover well or have the reaction at the end of the blood drive may need to be referred to an emergency room. Overnight hospitalizations are rare. Donors who develop offsite syncope may be referred back to the blood drive site, if the site is open. Otherwise, witnesses often telephone 911 for emergency service, and donors may be taken to an emergency room. In rare instances, lay persons may not feel a donor pulse that is present and may inappropriately start cardiopulmonary resuscitation, which can lead to injury. In sum, blood center collection staffs do the utmost to protect the donor, but they are limited by the nature and location of the fall.

Summary on Appropriate Actions

The emphasis on high-school blood drives and acceptance of 16-year-old blood donors led to more research on physiologic and psychological ways to decrease vasovagal reaction rates in young blood donors and to increase donor retention. This review discussed the current situation and what can be done psychologically, physiologically, and via process improvements to decrease vasovagal reaction rates and increase donor retention. The donation process can be significantly improved. Future interventions may include more dietary salt, a shorter muscle tension program to make it more feasible, recommendations for post-donation muscle tension / squatting / laying down for lightheadedness, more donor education by the staff at the collection site, more staff attention to donors with fear or higher risk for a vasovagal reaction (e.g. EBV near 3.5 l, first-time donor), and a more focused donation process to ensure a pleasant and safer procedure.

Disclosure Statement

Conflict of interest none.

References

1 American Red Cross Regional Blood Centers: American Red Cross Whole-Blood Donation Database; July 1, 2005 to June 30, 2010.
2 Masser B: Experienced donors, adverse events, and retention (editorial). Transfusion 2012;52:1844–1848.
3 Nguyen DD, Devita DA, Hirschler NV, Murphy EL: Blood donor satisfaction and intention of future donation. Transfusion 2008;48:742–748.
4 Schlumpf KS, Glynn SA, Schreiber GB, Wright DJ, Randolph Steele W, Tu Y, Hermansen S, Higgins MJ, Garratty G, Murphy EL: National Heart, Lung and Blood Institute Retrovirus Epidemiology Donor Study. Factors influencing donor return. Transfusion 2008;48:264–272.
5 Germain M, Glynn SA, Schreiber GB, Gelinas S, King M, Jones M, Bethel J, Tu Y: Determinants of return behavior: a comparison of current and lapsed donors. Transfusion 2007;47:1862–1870.
6 Thomsen RA, Bethel J, Lo AY, Ownby HE, Nass CC, Williams AE: Retention of 'safe' blood donors. Transfusion 1998;38:359–367.
7 Ferguson E. Bibby PA: Predicting future blood donor returns; past behavior, intentions, and observer effects. Health Psychol 2002;21:513–518.
8 Gillespie TW, Hillyer CD: Blood donors and factors impacting the blood donation decision. Transfus Med Rev 2002;16:115–130.
9 Rugege-Hakiza SE, Glyn SA, Hutching ST, Bethel J, Nass CC, McEntire RL, Hirschler NV, Campbell JG, Ladavac A, Schreiber GB: Do blood donors read and understand screening educational materials. Transfusion 2003;43:1075–1083.
10 McVittie C, Harris L, Tilopoulos N: 'I intend to donate but …': non-donors' view of blood donation in the UK. Psychol Health Med 2006;11:1–6.
11 Schreiber GB, Schlumpf KS, Glynn SA, et al: Convenience, the bane of our existence, and other barriers to donating. Transfusion 2006;46:545–553.
12 Newman B: Donor reactions and injuries from whole blood donations. Transf Med Rev 1997;11:64–75.
13 Trouern-Trend JJ, Cable RG, Badon SJ, Newman BH, Popovsky MA: A case-controlled multicenter study of vasovagal reactions in blood donors: influence of sex, age, donation status, weight, blood pressure, and pulse. Transfusion 1999;39:316–320.
14 Wiltbank TB, Giordano GF, Kamel H, Tomasulo P, Custer B: Faint and prefaint reactions in whole-blood donors; an analysis of predonation measurement and their predictive value. Transfusion 2008; 48:1799–1808.

15 Eder AF, Hillyer CD, Dy BA, Notair EP, Benjamin RJ: Adverse reactions to allogeneic whole-blood donation by 16- and 17-year-olds. JAMA 2008;299:2279–2286.
16 Eder AF, Dy BA, Kennedy JM, Notari EP, Strupp A, Wissel ME, Reddy R, Gibble J, Haimowitz MD, Newman BH, Chambers LA, Hillyer CD, Benjamin RJ: The American Red Cross donor hemovigilance program: complications of blood donation reported in 2006. Transfusion 2008;48:1809–1819.
17 Reiss RF, Harkin R, Lessig M, Mascari J: Rates of vaso-vagal reactions among first time teenaged whole blood, double red cell, and plateletpheresis donors. Ann Clin Lab Sci 2009;39:138–143.
18 Kamel H, Tomasulo P, Bravo M, Wiltbank T, Cusick R, James RC, Custer B: Delayed adverse reactions to blood donation. Transfusion 2010;50:556–565.
19 Tomasulo P, Kamel H, Bravo M, James RC, Custer B: Interventions to reduce the vasovagal reaction rate in young whole blood donors. Transfusion 2011;51:1511–1521.
20 Eder A, Dy B, Kennedy J, Perez J, Demaris P, Procaccio A, Benjamin RJ: Improved safety for young whole blood donors with new selection criteria for estimated blood volume. Transfusion 2011; 51:1522–1531.
21 Tomasulo P, Bravo M, Kamel H: Time course of vasovagal syncope with whole blood donation. ISBT Sci Ser 2010;5:52–58.
22 Newman BH: Vasovagal reactions in high school students: findings relative to race, risk factor synergism, female sex, and non-high school participants. Transfusion 2002;42:1557–1560.
23 Newman BH, Siegfried BA, Buchanan LA: Donor reactions among African-American and Caucasian first-time whole-blood donors (letter).Transfusion 2005;45:1398.
24 Guide to the Preparation, Use and Quality Assurance of Blood Components, 17th ed. Strasbourg, Council of Europe Publishing, 2013.
25 Rios JA, Fang J, Tu Y, Wright DJ, Spencer B, Hillyer CD, Hillyer KL, Eder AF, Benjamin RJ, NHLBI REDS-II: The potential impact of selective donor deferrals based on estimated blood volume on vasovagal reactions and donor deferral rates. Transfusion 2010;50:1265–1275.
26 Bianco C, Robins JL: Whole blood collection volumes and donor safety: equivalence between 450 mL and 500 mL collections (abstract). Transfusion 1994;34(suppl):15S.
27 Kakaiya RM, Burns S, Dausch D: Comparison of systemic reactions among blood donors with 450 mL and 500 mL whole blood donation (abstract). Transfusion 2005;45:(suppl):88A–89A.
28 Wong HK, Lee CK, Leung JN, Lee IY, Lin CK: Reduction in vasovagal reaction rate in young first-time blood donors by collecting 350 mL rather than 450 mL. Transfusion 2013;53:2763–2765.
29 Newman BH, Satz SL, Janowicz NM, Siegfried BA: Donor reactions in high-school donors; the effect of sex, weight, and collection volume. Transfusion 2006;46:284–288.
30 Newman B, Siegfried B, Buchanan BA: Are vasovagal reaction rates in blood donors related to the duration of the phlebotomy? (letter). Transfusion 2008;48:568–569.
31 Newman B, Siegfried B: Phlebotomy duration and vasovagal reaction rates in 5.4 million donations (abstract). Transfusion 2013;53(suppl):110A.
32 Van der Meer PF, de Korte D: Increase of blood donation speed by optimizing the needle-to-tubing connection: an application of donation software. Vox Sang 2009;97:21–25.
33 Stevens PM: Cardiovascular dynamics during orthostasis and the influence of intravascular cannulation. Am J Cardiol 1966;17:211–218.
34 De Jong-deVos van Steenwijk CC, Wieling W, Johannes JM, Harms MP, Kuis W, Wesseling KH: Incidence and hemodynamic characteristics of near-fainting in healthy 6- to 16-year old subjects. J Am Coll Cardiol 1995;25:1615–1621.
35 Custer B, Bravo M, Tomasulo PA, Kamel H: Donor adverse events: needle-relted injuries and vasovagal reactions are strongly associated (abstract). Vox Sang 2011;101(suppl 1):141–142 (P-157).
36 Takanashi M, Odajima T, Aota S, Sudoh M, Yamaga Y, Ono Y, Yoshinaga K, Motoji T, Matsuzaki K, Satake M, Sugimori H, Nakajima K: Risk factor analysis of vasovagal reaction from blood donation. Transfus Apher Sci 2012;47:319–325.
37 France CR, Rader A, Carlson B: Donors who react may not come back: analysis of repeat donation as a function of phlebotomist ratings of vasovagal reactions. Transfus Apher Sci 2005;33:99–106.
38 Newman BH, Newman DT, Ahmad R, Roth AJ: The effect of whole-blood donor adverse events on blood donor return rates. Transfusion 2006;46: 1374–1379.
39 Rader AW, France CR, Carlson B: Donor retention as a function of donor reactions to whole-blood and automated double red cell collections. Transfusion 2007;47:995–1001.
40 Custer B, Rios JA, Schlumpf K, Kakaiya RM, Gottschall JL, Wright DJ: Adverse reactions and other factors that impact subsequent blood donation visits. Transfusion 2012;52:118–126.
41 Bravo M, Kamel H, Custer B, Tomasulo P: Factors associated with fainting – before, during and after whole blood donation. Vox Sang 2011;101:303–312.
42 Newman BH, Graves SG: A study of 178 consecutive vasovagal syncopal reactions from the perspective of safety. Transfusion 2001;41:1475–1479.
43 Newman B, Siegfried B: Syncope after whole blood donation: factors associated with increased donor injury (letter). Transfusion 2012;52:210–212.
44 Newman BH, Pichette S, Pichette D, Dzaka E: Adverse effects in blood donors after whole-blood donation: a study of 1,000 blood donors interviewed 3 weeks after whole-blood donation. Transfusion 2003;43:598–603.
45 Veldhuizen I, Atsma F, van Dongen A, de Kort W: Adverse reactions, psychological factors, and the effect on donor retention in men and women. Transfusion 2012;52:1871–1879.
46 Goldman M, Osmond L, Qi-Long Y, Cameron-Choi K, O'Brien SE: Frequency and risk factors for donor reactions in an anonymous blood donor survey. Transfusion 2013;53:1979–1984.
47 Sojka P, Sojka BN: Adverse effects in blood donors after whole blood donation: You find what you look for! (letter). Transfusion 2004;44:135–136. Reply: Newman BH, Pichette S, Pichette D, Dzaka E: Transfusion 2004;44:136.
48 Meade MA, France CR, Peterson LM: Predicting vasovagal reactions in volunteer blood donors. J Psychosom Res 1996;40:495–501.
49 France CR, Ditto B, France JL, Himawan LK: Psychometric properties of the Blood Donation Reactions Inventory: a subjective measure of presyncopal reactions to blood donation. Transfusion 2008; 48:1820–1826.
50 Hanson SA, France CR: Predonation water ingestion attenuates negative reactions to blood donation. Transfusion 2004;44:924–928.
51 Newman B, Tommolino E, Andreozzi C, Joychan S, Pocedic J, Heringhausen J: The effect of a 473-mL (16-oz) water drink on vasovagal donor reaction rates in high-school students. Transfusion 2007;47:1524–1533.
52 Connor JD, Lipton KS: Association Bulletin #08–04: Strategies to Reduce Adverse Reactions and Injuries in Younger Donors. Bethesda, AABB, 2008. Available from: *www.aabb.org/resources/publications/bulletins/Pages/ab08–04.aspx*.
53 Brown H, McCormack P: An analysis of vasomotor phenomena (faints) occurring in blood donors. Br Med J 1942;1:1–5.
54 Graham DT: Prediction of fainting in blood donors. Circulation 1961;23:901–906.
55 Reutz PP, Johnson SA, Callahan R, Meade RC, Smith JJ: Fainting: a review of its mechanisms and a study in blood donors. Medicine (Baltimore) 1967;46:363–384.
56 Callahan R, Edelman EB, Smith MS, Smith J: Study of incidence and characteristics of blood donor 'reactors'. Transfusion 1963;3:76–82.
57 Moloney WC, Lonnergan LR, McClintock JK: Syncope in blood donors. N Engl J Med 1946;234: 114–118.
58 Ogata H, Iinuma N, Nagashima K, Akabane T: Vasovagal reactions in blood donors. Transfusion 1980;20:679–683.
59 Stewart KR, France CR, Rader AW, Stewart JC: Phlebotomist interpersonal skill predicts a reduction in reactions among volunteer blood donors. Transfusion 2006;46:1394–1401.
60 Williams GE: Syncopal reactions in blood donors: an investigation of 222 cases. Br Med J 1942;1:783–786.
61 Hanson SA, France CR: Social support attenuates presyncopal reactions to blood donation. Transfusion 2009;49:843–850.
62 Bonk VA, France CR, Taylor BK: Distraction reduces self-reported physiological reactions to blood donation in novice donors with a blunting coping style. Psychosom Med 2001;63:447–452.
63 France CR, France JL, Kowalsky JM, Cornett TL: Education in donation coping strategies encourages individuals to give blood: further evaluation of a donor recruitment brochure. Transfusion 2010; 50:85–91.
64 France CR, France JL, Kowalsky JM, Ellis GD, Copley DM, Geneser A, Frame-Brown T, Venable G, Graham D, Shipley P, Menitove JE: Assessment of donor fear enhances prediction of presyncopal symptoms among volunteer donors. Transfusion 2012;52:375–380.
65 France CR, France JL, Himawan LK, Yunuba Stephens K, Frame-Brown T, Venable G, Menitove JE: How afraid are you of having blood drawn from your arm? A simple fear question predicts vasovagal reactions without causing them among high school donors. Transfusion 2013;53:315–321.
66 France CF, France JL, Wissel ME, Ditto B, Dickert T, Himawan LK: Donor anxiety, needle pain, and syncopal reactions combine to determine retention: a path analysis of two-year donor return data. Transfusion 2013;53:1992–2000.
67 France CR, Roen M, France JL, Trost Z: Enhancing attitudes and intentions in prospective blood donors: evaluation of a new donor recruitment brochure. Transfusion 2008;48:526–530.
68 France CR, France JL, Wissel ME, Kowalsky JM, Bollinger EM, Huckins JL: Enhancing blood donation intentions using multimedia donor education materials. Transfusion 2011;51:1796–1801.

69 France CR, France JR, Kowalsky M, Copley DM, Lewis KN, Ellis GD, McGlone ST, Sinclair KS. A Web-based approach to blood donor preparation. Transfusion 2013;53:328–336.
70 Dy BA, Perez J, Kennedy JM, Easton T, Benjamin RJ, Procaccio A, Eder AF: Donor survey to assess water and muscle tension interventions on high school blood drives (abstract). Transfusion 2010; 50(suppl):33A.
71 Newman BH, Siegfried BA: The quest to reduce vasovagal reactions in young blood donors (editorial). Transfusion 2011;51:2061–2063.
72 van den Berg K, Lam J, Bruhn R, Custer B, Murphy EL: Water administration and the risk of syncope and presyncope during blood donation; a randomized clinical trial. Transfusion 2012;52:2577–2584.
73 Ditto B, France CR, Albert M, Byrne N, and Smyth-Laporte J: Effects of applied muscle tension on the likelihood of blood donor return. Transfusion 2009;49:858–862.
74 Ditto B, France CR, Holly C: Applied tension may help retain donors who are ambivalent about needles. Vox Sang 2010;98:e225–e230.
75 Ditto B, Gilchrist PT, Holly CD, Dubuc S, Delage G, France CR: The effects of leg crossing and applied tension on blood donor return. Vox Sang 2013;105:299–304.
76 Krediet CT, de Bruin IG, Ganzeboom KS, Linzer M, van Lieshout JJ, Wieling W: Leg crossing, muscle tensing, squatting, and the crash position are effective against vasovagal reaction solely through increases in cardiac output. J Appl Physiol 2005;99: 1697–1703.
77 Krediet CT, van Dijk N, Linzer M, van Lieshout JJ, Wieling W. Management of vasovagal syncope; controlling or aborting faints by leg crossing and muscle tensing. Circulation 2002;106:1684–9.
78 van Dijk N, de Bruin IG, Gisolf J, Bruin-Bon HA, Linzer M, van Lieshout JJ, Wieling W: Hemodynamic effects of leg crossing and skeletal muscle tensing during free standing in patients with vasovagal syncope. J Appl Physiol 2005;98:584–590.
79 Levine BD: Regulation of central blood volume and cardiac filling in endurance athletes: the Frank-Starling mechanism as a determinant of orthostatic tolerance. Med Sci Sports Exerc 1993;25:727–732.
80 Wieling W, Harms MP, Ten Harkel AD, van Lieshout JJ, Sprangers RL: Circulatory response evoked by a 3 s bout of dynamic leg exercise in humans. J Physiol 1996;494:601–611.
81 Wieling W, France CR, van Dijk N, Kamel H, Thijs RD, Tomasulo P: Physiologic strategies to prevent fainting responses during or after whole blood donation. Transfusion 2011;51:2727–2738.
82 Vacca G, Mary DA, Battaglia A, Grossini E, Molinari C: The effect of distention of the stomach on peripheral blood flow in anesthetized pigs. Exp Physiol 1996;81:385–396.
83 Rossi P, Andriesse GI, Oey PL, Wieneke GH, Roelofs JM, Akkermans LM: Stomach distension increases efferent muscle sympathetic nerve activity and blood pressure in healthy humans. J Neurol Sci 1998;161:148–155.
84 Haberich FJ: Osmoreception in the portal circulation. Fed Proc 1968;27:1137–1141.
85 Nakai M: Cardiovascular responses to gastric hypoosmolar stimulation in anesthetized dogs. Jpn J Physiol 1993:43:335–346.
86 May M, Jordan J. The osmopressor response to water drinking. Am J Physiol Regul Integr Comp Physiol 2011;300:R40–46.
87 Wieling W, van Lieshout JJ, Hainsworth R: Extracellular fluid volume expansion in patients with posturally related syncope. Clin Auton Res 2002; 12:242–249.
88 Mtinangi BL, Hainsworth R: Early effects of oral salt on plasma volume, orthostatic tolerance, and baroreceptor sensitivity in patients with syncope. Clin Auton Res 1998;8:231–235.
89 El-Sayed H, Hainsworth R: Salt supplement increases plasma volume and orthostatic tolerance in patients with unexplained syncope. Heart 1996; 75:134–140.
90 Merson SJ, Maughan RJ, Shirreffs SM: Rehydration with drinks differing in sodium concentration and recovery from moderate exercise-induced hypohydration in man. Eur J Appl Physiol 2008;103: 585–594.
91 Von Duvillard SP, Braun WA, Markofski M, Beneke R, Leithauser R: Fluids and hydration in prolonged endurance performance. Nutrition 2004; 20:651–656.
92 Waters WW, Platts SH, Mitchell BM, Whitson PA, Meck JV: Plasma volume restoration with salt tablets and water after bed rest prevents orthostatic hypotension and changes in supine hemodynamic and endocrine variables. Am J Physiol Heart Circ Physiol 2005;288:H839–847.
93 Benjamin RJ, Dy BA, Kennedy JM, Notari EP, Eder AE: The relative safety of automated two-unit red blood cell procedures and manual whole-blood collection in young donors. Transfusion 2009;49:1874–1883.
94 Wiltbank TB, Giordano GE: The safety profile of automated collections: an analysis of more than 1 million collections. Transfusion 2007;47:1002–1005.
95 Smit AA, Halliwill JR, Low PA, Wieling W: Pathophysiological basis of orthostatic hypotension in autonomic failure. J Physiol 1999;519:1–10.
96 Convertino VA: Gender differences in autonomic functions associated with blood pressure regulation. Am J Physiol 1998:275:R1909–1920.
97 Fu Q, Witkowski S, Okazaki K, Levine BD: Effects of gender and hypovolemia on sympathetic neural responses to orthostatic stress. Am J Physiol Regul Integ Comp Physiol 2005;289:R109–116.