



ABO Blood Donor Safety Issues White Paper

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EXECUTIVE SUMMARY, WHITE PAPER ON DONOR SAFETY ISSUES

Blood donation is associated with little acute risk for the vast majority of donors. However, a small proportion of donors may suffer harm that rarely leads to permanent disability or injury. These adverse reactions may lead to the loss of the current donation, reduce the likelihood that a donor will return to donate again, create adverse publicity for the donation program and carry legal liability. Short-term reactions include vasovagal reactions that may lead to syncopal episodes and physical harm due to falls, and local injury to blood vessels, nerves and tissues. A small proportion of donors require outside medical care after blood donation with attendant costs. This white paper will focus on vasovagal reactions in whole blood donors. Iron deficiency is a major long-term complication that may be addressed in a separate white paper.

Recommendations:

ABO centers should have active programs to manage, document and investigate adverse reactions that occur at the donation site or are later reported to the center.

ABO centers should have active hemovigilance programs in place to monitor donor adverse events over time. The classification of reactions in each center should permit international comparisons among ABO members to facilitate benchmarking of donor reaction frequencies, donor safety measures, and efforts to prevent reactions and reduce donor injuries associated with reactions.

Since there are unknowns about prevention of vasovagal reactions, ABO centers are encouraged to participate in studies of the efficacy of possible risk mitigating strategies.

Centers should have active programs to prevent the occurrence of adverse events:

- Centers should ensure pre- and post-donation donor education regarding the risks of donation and steps that may be taken to minimize the risk.
- Younger, first time donors are at highest risk for vasovagal reactions. Therefore, additional measures are warranted to reduce reactions in this group.
 - Young donors should not be permitted to donate $\geq 15\%$ of their estimated blood volume. The donor's blood volume can be easily estimated using the donor's self-reported height and weight in the Nadler formula. Implementation of more stringent criteria for younger donors with a low estimated blood volume has clearly resulted in a reduction in vasovagal reactions.
- Most injuries associated with vasovagal reactions occur if the donor faints when standing up some time after the blood donation. Therefore interventions to reduce donor injury should be aimed at preventing the reactions which occur after the donor leaves the donor

- Chair. There is evidence that reactions occurring after the donor leaves the chair are associated with donor difficulty in compensating for orthostatic drop in blood pressure.
 - Centers should provide donors with instructions on preventing loss of consciousness and injury after they leave the donor chair.
- Centers should encourage face-to-face staff interaction with donors and promote donor distraction during donation. Centers should consider additional collection staff training so that donors are effectively monitored and distracted during donation and in the refreshment area.
- Centers should design their donation sites to minimize the opportunity for harm from falling. Centers should improve supervision of donors during their stay in the refreshment area after completing the donation.
- There is good evidence that programs of fluid and salt preloading prevent orthostatic loss of consciousness in patients with fainting syndromes. These same manoeuvres should work to reduce donor injury. More effort is necessary to determine the most effective educational interventions to encourage donors to participate in programs of salt and fluid loading pre-donation and replenishment post-donation.
- There is good evidence that applied muscle tension (AMT) training increases cerebral blood flow by increasing cardiac filling. When applied by patients with dysautonomia AMT decreases the incidence of loss of consciousness. Because fainting in blood donors is also associated with decreased cerebral blood flow, muscle tensing is likely to reduce risk if performed properly by donors. Better educational interventions are necessary to engage donors in becoming skilled at preventing dizziness and loss of consciousness though tensing the large muscles of their buttocks and thighs.

BACKGROUND

Blood donation is very safe for the vast majority of donors.^{1,2} However, a small number of donors experience adverse effects at the time of or shortly after donation. These include phlebotomy related complications (bruising, nerve injury) and systemic reactions (faint or pre-faint reactions, termed vasovagal reactions). Rarely, these reactions may result in permanent disability or injury to the donor. The loss of consciousness reactions which occur after the donation are most frequently associated with donor injury.³ A reaction at the time of collection may also lead to cessation of collection and loss of the donation. It has been demonstrated that donors who experience an adverse reaction are less likely to return to donate. Donor reactions resulting in injury may lead to legal claims against the blood centre. Finally, donors who have a negative donation experience are unlikely to encourage those in their social circle to become blood donors.

Recently, there has been increasing awareness of the effect of blood donation on donor iron stores. Ongoing iron depletion results in iron deficiency without anemia and eventually in donor deferral due to failed hemoglobin screen. However, the donor may experience adverse effects related to iron deficiency alone, while passing the hemoglobin screen. Several studies are underway to further characterize the negative impact of non-anemic iron deficiency alone on otherwise healthy blood donors.

The ABO medical group is well placed to summarize current knowledge regarding donor safety issues. Physicians in our group are actively involved in both the ISBT Hemovigilance Working Party, donor vigilance subgroup, as well as the AABB Donor Hemovigilance Working Group. Studies evaluating the risk factors for vasovagal reactions, interventional trials to reduce reactions, and large observational studies on the impact of mitigating actions have all been done in ABO member organizations.³⁻⁸ Members of the group have been active not only in performing these studies, but also in publishing original articles and summaries of the literature on this topic. ABO members have also been actively involved in the AABB Younger Donors Adverse Reaction Working Group and the AABB Inter-organizational Task Force on Donor Hemoglobin and Iron, both of which have resulted in the publication of Association Bulletins.⁹

This initial section of the White Paper will discuss the classification of acute reactions associated with whole blood donation, and factors related to vasovagal reactions. This includes risk factors for vasovagal reactions, interventional studies on mitigating strategies, and post-implementation observational studies.

DONOR VIGILANCE

Clear definitions of donor reactions are important to each blood operator in order to establish baseline rates of various types of reactions in their particular donor population. Evaluation of the risk factors for reactions requires knowledge about donation characteristics and characteristics in both donors having reactions and the entire donor base (numerator data and denominator data). Following the rates of reactions over time allows blood operators to assess the potential impact of changes in donor eligibility criteria, collection methods and the effectiveness of strategies implemented to mitigate reactions. Internationally, the use of comparable definitions may allow for comparison and benchmarking among blood systems. Using consistent terms and definitions allows comparison as more is learned about the adverse events associated with transfusion. Ideally one should document what happened to a donor in a descriptive way without using any

categories. This will provide the most flexibility for accurate comparison of data. Information about donor eligibility criteria, demographics, methods of blood donation, amount of blood donated, data capture, and scope of the vigilance system are also necessary to perform valid comparisons between blood operators.

It has been difficult to compare acute reaction rates between various ABO members, because of differing definitions and terms in use. Some members have been following the AABB donor hemovigilance scheme definitions, while others have been following ISBT definitions or national definitions, since at this time there is no accepted format for the various analyses that are necessary for donor vigilance. The ISBT has created hemovigilance software (ISTARE) which is not used by the majority of member countries, and does not facilitate analysis of donor reaction data. The AABB, working with a research /software firm (Knowledge Based Systems, Inc. – KBSI), has designed a data system which can accept data from blood systems with varying sophistication in data capture and still preserve the possibility of performing some analysis and some high level comparisons.¹⁰ American blood centers have the capacity to enter data using their present definitions and, as they migrate to the AABB definitions, continue to enter data and avail themselves of more opportunities for analysis and comparison. At the present time, a minority of American centers are participating in the system. Members of the ABO medical group are actively involved in a revision of the ISBT donor reactions definitions to allow analysis of reaction data and comparison with the AABB donor hemovigilance scheme. An initial meeting was held at the ISBT meeting in Amsterdam and at the AABB meeting in Denver, and a second draft of the revised classification system has been circulated to members of the ISBT Hemovigilance Working Group for comment. The definitions, minimum denominator data, and basic information regarding the blood system are all being developed. In addition, the AABB hemovigilance group is considering a modification to their computer application, Donor Hemovigilance Analysis and Reporting Tool (DonorHART), to simplify data entry and permit other blood operators to add aggregate data to the system. Our group will continue working on this process and will make a recommendation to ABO about the best path for ABO members to proceed.

VASOVAGAL REACTIONS-FREQUENCY, MECHANISMS AND RISK FACTORS

Frequency of vasovagal reactions

Approximately 2 to 5% of all whole blood donors experience some form of mild vasovagal reaction, or presyncope, including dizziness, light-headedness, pallor, or other symptoms that usually resolve promptly but contribute to an unpleasant donation experience.^{1,4,5} Syncope (loss of consciousness) occurs in approximately 4 in 1,000 donations, and donors are injured from vasovagal reactions in approximately 6 per 10,000 donations. Injury is more likely to occur in reactions occurring once the donor has left the donation chair. If donors are questioned about symptoms several weeks after donation or at the time of next donation, the actual rate of reactions is considerably higher than that determined by staff at the time of donation.⁸

Mechanisms and risk factors

A good understanding of the mechanisms of vasovagal reactions permits the development of mitigation strategies. Unfortunately, the mechanisms for vasovagal reactions are multifactorial and the risk of injury varies significantly from the time the donor enters the donation site until 4

+ hours after the donation.^{1,11} It is clear that several mechanisms are involved. These include the direct effect of acute hypovolemia, psychologic stress, and changes in vasovagal tone or orthostatic blood pressure after donation. Analysis based only on rates has not been adequate to generate ideas for continuous improvement.

Risk factors identified in large observational studies

Large observational studies done at ARC and Blood Systems using multivariate regression analysis have delineated risk factors for both presyncopal and syncopal reactions summarized in Table 1.³⁻⁷ Major independent predictors include first time donation status, younger age, and low estimated blood volume (EBV). Without any mitigating actions, small, female, 16-year-old blood donors are the most likely to experience reactions. Donors in slightly older age cohorts also have an increased reaction rate, when compared to donors over age 25. Older age (donors over age 65) was not found to be a risk factor for increased reactions. Since the average blood draw, including samples, in the US and Canada is approximately 540 mL, donors with an EBV of less than 3,500 mL are losing over 15% of their blood volume in a whole blood donation. In some studies, the rate of vasovagal reactions decreases as the EBV increases, with donors having an EBV over 5,000 mL having the lowest reaction rate. EBV is calculated based on height, weight, and gender. It is unclear if lower weight alone is an independent predictor of increased reaction risk. Similar risk factors were found for reactions occurring on the clinic site and delayed reactions, which are more likely to be associated with injury.^{3,8} Female gender and low EBV were particularly important factors for delayed reactions.

Underlying medical illnesses

In large observational studies, the presence of underlying medical illnesses, such as diabetes or hypertension and the use of medications, such as hypoglycemic agents and antihypertensives, were not shown to be risk factors for vasovagal reactions. However, these risk factors are difficult to assess in large observational studies of the entire donor population, since eligibility criteria varies between blood operators and the denominator may be small for some of these specific risk categories.

General hydration, nutrition, and physical activity

There is lack of data about the influence of general hydration and nutrition on the day of donation and the level of physical activity post-donation on the frequency of reactions. General advice given to donors about hydration, nutrition, and physical activity is more based on “common sense” than any actual study data.

Psychological variables

More recently, there has been interest in determining psychological variables that might be predictors for vasovagal reactions. Fear has been found to be an important contributor to the risk of syncopal and pre-syncopal reactions in blood donors. Investigators have demonstrated that those donors who answer positively to simple questions related to fear of blood donation prior to donation are at higher risk of vasovagal reactions. In the study, volunteer blood donors completed a predonation survey which consisted of two items: “How afraid are you of having blood drawn from your arm?” and “How afraid are you of seeing blood drawn from someone else’s arm”. Each question was rated on a 5-point scale (0, not afraid to 5, extremely afraid). Donors answering yes to the fear questions (nearly half the donors) were more likely to report



presyncopal symptoms on a survey.¹² Important, the study demonstrated that asking the questions did not increase the risk of syncopal or presyncopal symptoms. A similar study was also completed in 17 and 18 year old high school students who were donating blood at a high school blood drive.¹³ Consistent with the previous study, fear was a significant independent predictor of donor reactions. These two studies suggest that the standard pre-donation screening process could be modified to identify that 40% of the donor population which is at highest risk of presyncope. Donors identified as being at highest risk might be provided with additional resources to help prevent adverse reactions. Although these results are intriguing, these studies were led by one group of investigators, involve a small number of selected donors, and use mainly surrogate end-points for actual moderate or severe complications. Therefore, further corroboration from other groups is necessary.

Table 1. Predictors of presyncopal symptoms and syncopal reactions (refs 3-7, 12)

Risk factor	Risk of reactions, adjusted odds ratio	Comments
<u>Donation status</u> First donation	1.95-2.80	
<u>Physiologic and demographic variables</u> Age		
16-18	3.89	Older donors (>65) examined in some studies and not at higher risk
17-20	2.75 - 4.01	
19-24	2.37	
Female gender	1.20 - 2.52	May be particular important risk factor for delayed reactions
Weight 110-120 lbs. (50-54 kg)	2.11- 2.52	May not be independent of EBV
EBV ¹ <3500 ml	2.45 - 2.88	In some studies continuous variable, with EBV >5000 ml having lowest rate
<u>Psychological variables</u> Fear of donation	2.6 ²	Donors reporting fear on a predonation survey 2.6 time more likely to experience presyncopal reactions

¹ EBV = estimated blood volume

² unadjusted odds ratio



DONOR INJURY FROM VASOVAGAL REACTIONS

Studies performed at Blood Systems have shown that it is useful to divide the whole blood donation process into 4 periods.¹⁴ Period 1 begins when the donor enters the donation site and ends with the venipuncture. Period 2 begins with the venipuncture and ends when the donor stands up for the first time after the donation process, approximately 5 minutes after the needle withdrawal. Period 3 begins when the donor stands up after the donation, and is divided into 3A (donor remains on-site) and 3B (after donor leaves the donation site). This division exposes the fact that more than 90% of injuries associated with vasovagal reactions occur from syncopal reactions, the majority of which occur during periods 3A and 3B. Fainting is very rare during Period 1 and injuries are rare from reaction occurring during Periods 1 and 2. There is a peak in the rate of syncope just at the time that the donor stands up. Bravo further analyzed the risk factors associated with syncopal reactions in each of the periods and showed that while first time donor status and youth remain risk factors, the greatest risk of loss of consciousness (and thus injury) is associated with female gender and low EBV. All these observations provide solid evidence for the long-held view that the relative hypovolemia which occurs after blood donation decreases the capacity to compensate for orthostatic changes in blood pressure. Those donors who because of their gender and cardiac physiology or their EBV are limited in their capacity to raise blood pressure and control cerebral perfusion with orthostatic changes are most at risk for syncope and injury.

To summarize, the most frequent donor injuries related to vasovagal reactions occur from reactions occurring after the donor stands up during period 3 and these injuries and reactions are caused by a failure to compensate for orthostatic changes in blood pressure due to relative hypovolemia or slower cardiac filling. The best way to prevent the injuries related to this adverse event is to help the donor restore capacity to compensate for orthostatic changes in blood pressure.

MITIGATING ACTIONS FOR VASOVAGAL REACTIONS

Application of interventions in large scale observational trials

Both ARC and Blood Systems independently made operational changes to their standard practices in an effort to reduce syncopal reactions among young whole blood donors. These interventions were based both on the predictors of presyncopal symptoms and syncopal reactions (first time donation status, younger age, and EBV below 3,500 ml) discussed above, and smaller interventional studies on the use of water loading and muscle tension, discussed below. Both studies compared the reactions in the time before and after introduction of several measures. The study description, reaction rates, and effect on reactions are summarized in Table 2.^{15,16}

Although several interventions were introduced at the same time, compliance with pre-donation water loading and muscle tensing exercises was poor. It was therefore felt by both organizations that the data supported the benefit of the selection criteria for EBV to mitigate reactions among young donors, largely to the extent predicted by statistical models. It was difficult to assess the provision of water and use of applied muscle tension, partly due to inconsistent or incomplete application.

Table 2. Observational studies to reduce reactions among allogeneic whole blood young donors (ref 15, 16)

Study	Study Description	Reaction Rates at Collection Sites	Effect on Reactions
Tomasulo et al ¹⁵	213,031 donations from 17-23 year olds before and after implementing: <ol style="list-style-type: none"> 1. selection of donors with EBV \geq3500 ml 2. predonation water 3. muscle tensing exercises⁺ 	Female donors, 17-23 yr Before: 4.3% After: 3.2%	Before vs After: -20%
Eder et al ¹⁶	>600,000 donations from 16-18 year olds (including 143,948 16-year-old donors) in 9-month school years, comparison to baseline period after implementing: Transition: predonation education, staff supervision, standard drive guidance, including predonation water (16 oz) and muscle tension advice (alternate, repetitive leg lifting) Study (full implementation) period: selection of donors with EBV \geq 3500 ml	All donors 16-18 yr: Baseline: 8.8% Transition: 8.0% Study: 7.1% Female donors, 16 yr: Baseline: 13.4% Transition: 11.0% Study: 9.5%	Study vs baseline: -20% -29%

⁺ Donors were instructed to tense the major muscles in the legs and buttocks and sustain the tension for 5-second intervals at the beginning of phlebotomy while alternating with 5 seconds of relaxation.



Studies of individual interventions

Performance of trials on individual interventions to reduce reactions and injuries in blood donors has been difficult. Moderate and severe reactions are relatively rare; therefore very large studies are needed to achieve statistical significance. Since reactions are multifactorial, there may be confounding factors influencing study results. Donor compliance with recommendations to eat a recommended amount of salt, quaff a recommended amount of fluid, or perform (rather odd) muscle tensing exercises may be poor. Finally, as demonstrated in the large interventional studies outlined above, from a practical perspective, organisations often implement several measures at once in a concerted effort to reduce donor reactions, making it difficult to tease out the efficacy of each specific intervention.

There are no controlled trials available which prove that any of the individual interventions listed below, such as increasing salt and/or water intake, or performing muscle tensing excises, reduce donor injuries. However, known cardiovascular physiology, and the success of these methods in other clinical situations, suggests that some of these interventions will reduce the rate of loss of consciousness reactions and resulting injury, especially among our younger donors.¹¹ These interventions are of great interest for future studies by ABO members. An additional challenge is educating and empowering donors to increase compliance with these measures.

i) Expanding and restoring blood volume through dietary salt intake

The sodium content of the diet determines the body's extracellular volume, plasma volume and thereby the blood volume. Having a normal blood volume is critical for maintaining perfusion of the brain in adjusting to standing up. Increasing salt intake improves capacity to maintain blood pressure with orthostatic changes in patients with diseases of the involuntary nervous systems, in astronauts on the day they return to the earth and in dehydrated athletes.

A whole blood donation leads to the loss of 475 to 540 mL of intravascular volume and about 2.5 to 3 grams of salt (1.2 grams of sodium). Most people on a Western diet eat 3-4 grams of salt each day. If blood donors arrive at the donation site having taken in extra salt, such as having had a cup of soup and a pepperoni pizza the night before the blood donation, they may be partially protected from vasovagal reactions when compared to donors who have not had a salty meal. If donors eat 3 grams of salt and drink a pint of fluid immediately before, during or immediately after a blood donation, they may be less likely to faint and be injured when they stand up after a blood donation. This amount of salt corresponds to the salt lost in the donation so it is a healthy (not harmful) amount of salt, but in fact it is difficult to eat 3 grams of salt in the form of pretzels or potato chips. A bottle of endurance Gatorade contains about 30% of the fluid necessary to compensate for a blood donation and about 15% of the salt needed to restore the salt lost in a blood donation. Therefore a bottle of endurance Gatorade and bag of pretzels right before or immediately after a whole blood donation may be a good start on restoring the blood lost in a blood donation.

ii) Drinking water alone

There is some evidence that drinking 500 ml of water alone (without a salty snack) within 30 minutes of blood donation reduces the reaction rate. The largest study, done in close to 9,000 high school students, showed a reduction in overall reaction rates from 12.5% in the control group to 9.9% in donors given water. There was no categorisation of reactions by severity. A small study done in first time donors demonstrated a decrease in mild reactions but was not

adequately powered to evaluate more severe reactions, while a study from South Africa showed no difference in reactions, but a very low overall reaction rate, possibly because of the reduced frequency of syncopal reactions in Black donors.^{18,19} Although drinking water alone does not increase the blood volume (salt is required to do that), it may increase the donor's blood pressure slightly and transiently (for less than an hour) through a reflex which leads to the constriction of the peripheral blood vessels (gastrovascular reflex). However, the effect is transient, and drinking water alone later may lead to diuresis, actually decreasing the donor's blood volume. Drinking water alone before the blood donation may have an immediate effect on blood pressure but it is not likely to decrease the injuries associated with reactions occurring more than 30 minutes after the blood donation.

iii) Applied muscle tension (AMT)

Although applied muscle tension exists in many forms, it typically involves repeated rhythmic contraction of the large muscles of the buttocks and legs. AMT has been used for years to treat patients with syncope related to autonomic nervous system dysfunction, blood and needle phobia and other causes of vasovagal syncope.¹¹ Clinical and laboratory studies document that contraction of the skeletal muscles in the thighs and buttocks forces blood in the large capacitance vessels into the thorax which increases cardiac filling pressure, stroke volume and cardiac output. Blood pressure is increased within 3-4 seconds. AMT helps prevent syncopal and presyncopal reactions by increasing blood pressure which improves cerebral blood flow and oxygenation. Upper body contraction is not as effective as thigh and buttock contraction.

To date, six small studies, all involving the same research group, have been published on the effects of applied muscle tension on blood donor reactions (Table 3).²⁰⁻²⁵ The main study outcome measured was performance on a survey and patterns of return to donate. One small study demonstrated that donors who engaged in repeated lower body muscle tensing showed higher levels of cerebral oxygenation as compared to those who engaged in minimal foot movement. Nevertheless each of these studies demonstrated the expected benefit of muscle tensing. As previously mentioned, two large interventional studies have been performed utilizing the instruction to perform muscle tension (BSI and ARC).^{15,16} In both these studies, multiple interventions were utilized simultaneously and it was not possible to determine the impact of applied muscle tensing. Both studies indicated that compliance with the instructions to perform muscle tensing was poor.

Patients with fainting syndromes have used muscle tensing very successfully to prevent fainting from an orthostatic challenge.^{26,27} These patients are highly motivated because their syndromes can prevent them from holding jobs or leading normal lives. Learning to prevent fainting through muscle tensing (actually voluntarily doing what the autonomic nervous system normally does involuntarily) is an important life skill for these highly motivated patients and they have demonstrated that the exercises are effective against orthostatic fainting. To date, it has been difficult to establish the same motivation among blood donors, especially young blood donors who are most susceptible to vasovagal reactions involving loss of consciousness. Educational and instructional interventions which resonate with blood donors should be sought in an effort to reduce the current rate of donor injury.

Table 3. Randomized studies of applied muscle tension (AMT) (ref 20-25)

Study	Study Description	AMT	Control	Design	Conclusion
Ditto 2003, Journal of Behavioral Medicine	2 minute video to teach AMT prior to donation (174 total donors)	37 ≤2x donors	47 >2x donors 94 ≤2x donors	AMT donors randomly selected based on availability of computer for video. Selection of controls not described	Fewer presyncopal reactions (faintness, dizziness, weakness) following donation
Ditto 2003, Transfusion	2 minute video to teach AMT prior to donation (605 total donors)	216 from sitting in chair to completion of donation	189 AMT control from sitting to needle insertion 200 placebo control	RCT in groups of 15- 20 consecutive donors	Beneficial effect for female donors – less presyncopal reactions, fewer donor chair reclines and greater successful donations
Ditto 2006, Health Psychology	2 minute video to teach AMT prior to donation (467 total donors)	172 from sitting in chair to completion of donation	140 AMT control from sitting to insertion of needle 155 no treatment control	RCT	Both male and female donors had less presyncopal reactions
Ditto 2007, Transfusion	2 minute video with 5 different forms of muscle tensing (1209 total donors)	Full AMT–203 Lower body - 208 Upper body - 200 Upper body w/distraction - 200	204 – no treatment control	RCT of six conditions involving tension of different muscle groups or donation as usual	Full and lower body AMT had less presyncopal reactions. Legs and lower abdomen important components of AMT
Ditto, 2009 Transfusion	Follow-up from 4th study. 1059 of the 1209 donors. Number of subsequent donations	Fully body AMT 181/203 Lower body AMT 188/208 Upper body AMT 170/200 Upper body w/distraction 172/200	No treatment controls 180/204	Follow up of subjects in RCT of Ditto 2007, Transfusion	Women assigned to AMT significantly more likely to return 67% vs. 55%. No significant difference in men.
Kowalsky, 2011 Transfusion	Effect of AMT on cerebral oxygenation during blood donation - 72 experienced female donors	34	38 "distraction" controls	RCT on mobile blood drives	Significant difference in regional cerebral oxygenation with AMT. No impact on presyncopal symptoms in an experienced donor group



iv) Drive set-up and environment

There have been no randomised trials of the drive set up and environment examining the effect on donor adverse events; indeed there is an overall scarcity of published literature in this aspect of blood collection. There is some evidence in large blood systems that the collection center is an independent variable for vasovagal reactions, and that collection sites such as mobile buses are associated with higher rates of fainting. This suggests that variables related to the collection set up may influence reaction rates.

It is common practice for all operators to assess the venue or drive and clear it for suitability, however evidence of what constitutes best practice for a site is lacking and many venues are used because of historical reasons and/or their physical site. Some operators use different set ups for high schools and universities. The AABB Association Bulletin “Strategies to reduce adverse reactions and injuries in younger donors” appendix 1 notes that in a survey of 26 blood centers nine responded that the drive set-up for high school drives differed from the set up for regular drives however the detail is not clear on how this differs.¹⁰ In university sessions in England an additional nurse is rostered.

The AABB Younger Donors Adverse Reaction Working Group recommended that blood centers should consider the following aspects of drive set up that may mitigate adverse reactions at high school blood drives:

- Procedures for site selection
- Controlled donor flow and adequate staff or volunteer availability
- Progressive recovery strategies
- Escorting donors through the process
- Predonation canteen table for fluid and food
- Postdonation canteen/refreshment area
- Adequate time in the canteen (about 15 minutes)
- Placing donors on gym mats on floor during recovery and refreshment periods after donation to minimize orthostatic fainting and the vertical fall if fainting occurs
- Staff with enhanced training to recognize presyncopal signs and symptoms can be assigned to the refreshment area
- Areas for recovery should have mobile screens and wheel-chairs available to prevent nonreacting donors from seeing reactions, and for transport of reacting donors when required.

Most operators will consider the majority of these for all sessions rather than just for those where adolescent donors predominate. It is widely accepted that sites should have sufficient room to be able to conduct blood collection efficiently and, in addition, for staff to be able to safely manage any donors who faint. Despite the lack of evidence in the literature there is intuitively sense in staff being able to identify and follow through vulnerable donors, having staff trained in early recognition of presyncopal symptoms and in having donors stay in the refreshment area postdonation for a suitable time. The length of stay required and the definition of particularly vulnerable donors, however, is variable between centres.

There is limited evidence that a targeted strategy which includes the set up and environment in high school and university drives reduces the rates of donor vasovagal reactions. Eder et al describe a standard work guidance that included standard work for staffing, materials, equipment and work sequence specifically including outlined layouts for the drive set-up, and moving the waiting area from in front of the venipuncture area. This resulted in a significant decrease in the rates of presyncopal reactions among 16 and 17 year old donors in three of four regions where it was implemented.²⁸ Similar results were seen in the UK where implementation of 'Points of Care' resulted in a significant reduction in the rates of pre-syncopal and syncopal reactions in both public and university clinics.^{29,30} Several measures were implemented to reduce syncopal reactions, including giving the donor a pre-donation 500ml drink of water, controlling donation and recovery positions, adjusting the clinic environment to have donors facing away from the donation area, and promoting professional staff behaviours to reduce uncertainty and anxiety. An individualised approach to donors recognising their history, defining high risk and vulnerable donors and recognising individual coping strategies were also encouraged. Whilst these authors describe strategies that have had a beneficial impact on the rates of presyncope and syncope, the improvements are multifactorial and the relative contribution of the change in the drive set up and environments is not known.

v) Donor education

Predonation education, particularly of younger first time donors, may be an important tool in enhancing donor understanding of the physiology of donation in a lay person's terms. With the appropriate knowledge and development of simple skills the donor can hopefully decrease the risk of fainting and injury, learn techniques that can treat dizziness and decrease the level of fear associated with blood donation. The challenge to donor education is the sheer volume of information, mostly related to recipient safety and infectious disease testing, that must be included in the mandatory donor pamphlet given to each donor immediately prior to donation. Additionally, several studies have shown that most donors only skim this pamphlet.

Education attempts to prevent reactions have mainly been directed at additional brochures or messages conveyed through electronic media such as the blood centre website. These educational materials are obviously highly variable, and unlike most of the donation process, and not regulated or standardized. France and colleagues have evaluated recruitment material in different written or audio-visual formats in randomized controlled studies of young blood donors.³¹⁻³⁷ These studies provided donors with information that addresses concerns about fear, pain, and potential complications and gives specific instructions about preventive measures such as fluid loading and muscle tension exercises. The authors concluded that the enhanced educational material improved donors' attitudes, willingness to donate blood, and intent to return to donate.

Although these findings are promising, and it is logical to believe that approaches that reduce fear and increase their self-confidence might decrease syncopal reactions, such objective benefits have not yet been demonstrated in interventional trials. All studies to date have been led by one group of investigators, have involved rather small numbers of selected donors, and have focused primarily on surrogate endpoints (i.e., survey tools to assess anxiety, symptoms or intent to donate), rather than complication rates or actual number of subsequent donations.

The AABB Association Bulletin “Strategies to reduce adverse reactions and injuries in younger donors” recommends educational initiatives targeting high school students and their parents in advance of blood drives, in addition to training of recruitment and collection staff. Some ABO members have created educational modules for use by school nurses. Having presented these modules at the periodic meetings of school nurses allows the incorporation of appropriate material in high school health class curricula.

The optimal delivery method for donor education is unknown but may include brochures, an educational DVD podcast, downloadable eBook or similar application and the blood center’s website. A study compared the presentation of donor information material in an audio-visual format, a brochure, and a video found that all methods were equally effective in increasing donor confidence, decreasing donor anxiety and increasing the intent to donate.³⁴ A study looking at the effects of Web-based donor materials found that use of the study site reduced anxiety and enhanced blood donation attitudes, confidence, intentions, anticipated regret, and moral norm among donors and non-donors, compared to the standard blood center site.³¹

vi) Post-donation information

Donors may experience vasovagal reactions after leaving the clinic, and these are most likely to be associated with injury.^{1,2} A new AABB Standard requires that blood centres provide donors with written instructions about postphlebotomy care and adverse events that may occur after donation. Although this clearly may be important in fulfilling the blood centre’s obligation to the donor, there have been no studies assessing the actual utility of post-donation education on mitigating reactions occurring off the clinic site.

ADDITIONAL ACTIONS OR CRITERIA FOR DONORS WHO HAVE ALREADY HAD 1 REACTION

There is a paucity of literature regarding suggested management of donors after experiencing an immediate or delayed vasovagal reaction with blood donation. Practices vary amongst ABO members regarding deferral of donors who have had previous vasovagal reactions. In Australia, the practice is to permanently defer donors after one syncopal episode with significant injury such as a fracture or dislocation, 3 consecutive pre-syncopal episodes, or 3 non-consecutive syncopal episodes. At CBS, donors are permanently deferred if they have had two successive syncopal reactions, or one severe syncopal reaction with complications. At ARC and BSI, donors are not routinely deferred after syncopal reactions. Deferral practices are not necessarily evidence-based. All blood services require that all blood donors be informed about possible adverse reactions related to donation, and provides care and follow-up to those who experience an adverse reaction at the collection site. All adverse reactions are investigated and recorded, but there are no clear guidelines on the utility of specific additional measures at the time of subsequent donation for donors wishing to return after a vasovagal episode.

Eder *et al.* studied a cohort of over 1 million donors, 18 673 of whom were returning donors after an adverse reaction to whole blood donation.³⁸ Over 95% of these adverse events were vasovagal reactions. In the first instance, syncope after a first donation significantly reduced the

likelihood of return donation (18% return rate) compared with presyncopal episodes (27% return rate) or no reaction (35% return rate). Among those who did return, syncope was more frequent in those who experienced syncope as first time donors (FTD) (3.5%), and amongst those who had presyncope as FTD (0.6%) compared with those who had no reaction at all (0.3%). However, only 2% of all syncopal reactions in returning donors occurred in those with prior syncope, and the vast majority of donors with previous reactions had no reaction on subsequent donation. Hence the authors concluded that a first reaction had little value in predicting subsequent syncopal episodes during repeat donation, and that a single syncopal episode was not grounds to justify donor deferral.

A study of 208 patients with recurrent syncope showed that the best predictor of syncope recurrence is the number of syncopal events in the preceding year.³⁹ Subjects with no episodes of syncope in the preceding year had a 7% rate of syncope in the subsequent 12-month period; those with more than 6 episodes of syncope in the preceding year had a 69% likelihood of a syncopal episode in the subsequent year. This was not a study of syncope associated with blood donation.

Given the lack of large well-designed trials, it is difficult to write evidence-based guidelines on the management of donors following syncope and presyncope. From the limited literature available, it would seem that a single syncopal episode is not reason enough to permanently defer a donor. However if there is recurrent syncope, particularly in the prior 12 months, donors may be at significantly increased risk of further syncope. Centers should therefore develop a policy for donors with recurrent syncope.

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