Physiologic strategies to prevent fainting responses during or after whole blood donation

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Vasovagal syncope (VVS) is a consistent, but infrequent (0.1%-0.3%) complication of volunteer, whole blood donation. Given the large number of blood donations, a significant number of donors is involved. Syncope occasionally leads to injury. Recent rigorous data collection and analysis have led to the association of a small number of donor and donation factors with the risk of syncope. An analysis of the time course of syncope reactions among approximately 500,000 whole blood donors suggests that there are three distinct periods of risk for vasovagal reactions before, during, and after phlebotomy. This review examines the physiologic mechanisms that contribute to these periods of increased risk including the direct effects of removal of approximately 500 mL of whole blood, the psychological stress of instrumentation and giving blood (i.e., fear of needles, pain, and the sight of blood), and the orthostatic effects superimposed on a hypovolemic state after the donation. Specifically, we describe interventions that have been useful in controlling VVS in patients with fainting syndromes and we examine the potential of these interventions in the blood donation context, based on the physiologic principles involved. Finally, we propose an intervention (dietary replacement of salt lost with blood donation) that has not been applied in transfusion medicine previously but which has the potential to reduce risk.

W hile whole blood donation is very safe, some donors experience vasovagal reactions during or after donation. The frequency of vasovagal syncope (VVS) is low, 0.1%-0.3%, but given the large number of blood donations (27 million in Europe and the United States annually [W. de Kort, Sanquin Blood Supply Foundation, The Netherlands, personal communication, 2011]), a significant number of donors are involved, as many as 27,000 to 81,000. In addition to the possible injuries experienced by reacting donors, these reactions if severe are highly disruptive and lead to fewer donations from reacting donors and probably from their immediate circle of contacts. Prevention of vasovagal reactions in blood donors is thereby an important issue.

The mechanisms underlying VVS in blood donors are thought to include the direct effects of removal of about 500 mL of whole blood, the psychological stress of instrumentation and giving blood (i.e., fear of needles, pain, and the sight of blood), and the orthostatic effects superimposed on a hypovolemic state after the donation. Recent studies have shed some light on the timing of vasovagal

**ABBREVIATIONS:** BDRI = Blood Donation Reactions Inventory; VVS = vasovagal syncope.

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TRANSFUSION **,** **
reactions in donors and physical characteristics of donors that predict vasovagal reactions, and prospective studies on potential interventions to further reduce the risk of syncope and injury are being performed.

Lower-body muscle tensing, plasma volume expansion, and water drinking have been applied as physiologic strategies to prevent syncope in patients with orthostatic intolerance, but it is not well known how these strategies should be applied or combined before, during, and after whole blood donation. The aim of this review is to describe the application of these three physiologic strategies in the light of the recently published time course of vasovagal reactions in the setting of whole blood donation. The focus will be on the physiology of the prevention of full VVS with complete whole blood donation.

**TIME COURSE OF VASOVAGAL REACTIONS DURING BLOOD DONATIONS**

We will use the term VVS for blood donation-associated transient loss of consciousness. VVS is associated with arterial hypotension and/or bradycardia. Clinically, these episodes are preceded by various symptoms including lightheadedness, dizziness, yawning, nausea, sweating, pallor, unclear thinking, and visual disturbances. However, in the absence of simultaneous hemodynamic measurements, isolated symptoms of lightheadedness or pallor during blood donation are not a proof of an impending syncope but may also result from anxiety. Since blood pressure measurements are lacking in the regular blood donation setting, these symptoms without loss of consciousness (often labeled as "presyncope" or "mild adverse events") will not be discussed in our review.

**VVS before venipuncture**

Between arriving at the donation site and the venipuncture, the fainting rate is extremely low (0.004%). Factors associated with VVS before venipuncture are donor’s young age and inexperience, that is, first-time status.

**VVS during donation (venipuncture to stand up)**

A complete blood donation typically takes 7 to 9 minutes during which the donor is in a recumbent or semirecumbent position. During the first 4 minutes after introduction of the needle the fainting rate continues to be very low (Fig. 1). Thus, immediate VVS due to the psychological stress of introduction of the needle alone is a very rare event in blood donors.

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**Overall Vasovagal Syncope Rate in Allogeneic WB Intended Donations, 2007**

![Graph](image)

Fig. 1. Time course of VVS among whole blood donors. The overall VVS rate in men and women attempting to give whole blood expressed as a rate per time period from 10 minutes before the end of phlebotomy until 265 minutes after the end of phlebotomy. The authors of this study assumed that most donors stood up approximately 4 minutes after needle withdrawal and that the 5-minute peak in loss of consciousness reactions was related to this change in position. Collection staff support this assumption based on experience. WB = whole blood.
The very low fainting rate in the first few minutes increases toward the end of the donation with a sharp peak around the period of removal of the needle (Fig. 1). Approximately 10% of the total number of VVS associated with complete blood donations occurs during the 1 minute around the removal of the needle (Fig. 2).\(^{15}\)

After removal of the needle, donors to Blood Systems, Inc. (Scottsdale, AZ; from which organization the data provided in Figs. 1, 2, and 3 come) are requested to sit with their feet hanging over the side of the donation chair or bed before standing up. This transition step to the upright position is not required by the Food and Drug Administration (FDA) and it is unlikely that there is uniformity in this procedure in the United States. Subjects remain in the sitting position for approximately 1 to 3 minutes. The Blood Systems, Inc. standard operating procedure does not require the documentation of the time the donor assumes the upright posture so the time must be estimated and one must assume that it varies from donor to donor. The number of VVS episodes before the donor stands up amounts to approximately 40% of the total number of VVS episodes during and after complete whole blood donation (Fig. 3). In this period, VVS is associated with donor’s small blood volume and inexperience.\(^{1}\)

The amount of blood removed during a whole blood donation (540 mL)\(^{1,15}\) is about the same as the amount of blood pooled downward rapidly during standing up from a supine position (300-800 mL)\(^{18}\). Previous studies have consistently documented that intravascular instrumentation during orthostatic stress results in a very pronounced increase in VVS responses in subjects without a clinical history or tendency for VVS.\(^{19,20}\) In the classical study by Stevens\(^{19}\) performed in healthy young adult United States Air Force pilots and navigators the increase was fivefold with approximately 50% of the subjects experiencing VVS. In the study by de Jong-de Vos van Steenwijk\(^{20}\) in healthy 6- to 16-year-old subjects a fainting rate of 10% during standing increased to 40% after introduction of a venous line. Thus the effect of progressive volume depletion induced by removal of 540 mL of blood during donation in combination with the psychological stress of the instrumentation (i.e., fear of needles, pain, and the sight of blood)\(^{21-24}\) is a likely explanation for the peak fainting rate around the time of removal of the needle. Unex-
VVS Onset Time Distribution in Complete and Incomplete WB Donations, 2007

Cumulative

Fig. 3. Time course of VVS reactions among male and female donors giving complete and partial units of whole blood expressed as a percentage of the total reactions by sex that occurred in each time period. The figure includes incomplete (<450 mL) and complete donations. Donations are terminated before the desired volume is collected because of slow blood flow, pain at venipuncture site, vasovagal reactions, and other causes. Cumulative plots are presented. WB = whole blood.

Off-site VVS

Approximately 10% of VVS in the data set occurred after the donor left the donation site. The last VVS in the studies mentioned above occurred less than 5 hours after needle removal. It should be realized that the prevalence of off-site syncope may be underestimated, because from departure, there is no active follow-up of the donors: the off-site VVS rate is dependent on reactions voluntarily reported by donors. Off-site reactions are more common in females and in donors who have given a higher percentage of their estimated blood volume. These reactions are important since they are more often associated with injuries than on-site reactions.

STRATEGIES TO PREVENT FAINTING REACTIONS

Physical counterpressure maneuvers: evidence for effectiveness to combat orthostatic and emotional VVS

In the past decade, patients with a tendency for vasovagal fainted have successfully implemented physical counter-pressure maneuvers like leg crossing and tensing of leg and abdominal muscles to combat orthostatic intolerance. The mechanism underlying the effectiveness of these maneuvers is a static contraction of the skeletal muscles in the legs, buttocks, pelvic region, and abdomi-
nal wall resulting in emptying of large capacitance veins and thereby in an increase in central blood volume, cardiac filling pressures, stroke volume, and cardiac output. Different investigators have used slightly different maneuvers (leg crossing, leg and abdominal muscle tensing, leg crossing combined with lower body muscle tensing, buttock clenching). Interventions that are effective have in common that they involve tensing of leg and abdominal muscles. In the following we will use the term lower-body muscle tensing. Arm tensing has also been applied but this maneuver only is effective because it is typically accompanied by strong leg and abdominal muscle tension. Arm tensing alone does not translocate a large amount of blood centrally, because the venous volume in the arms is small.

The effectiveness of lower body muscle tensing in combating orthostatic vasovagal fainting has been demonstrated in physiologic studies and clinical trials. Physical counterpressure maneuvers are effective almost instantaneously. The minimal delay (2-3 sec) between the onset of muscle tensing and the start of the increase in blood pressure (Fig. 5) is accounted for by the transfer time of the blood between the right and the left ventricle (approx. 4-5 heart beats).

Physical counterpressure maneuvers have also been used successfully by psychologists to decondition blood injection injury phobias (emotional faints), but the physiologic effects involved have hardly been studied. An example of the impressive effects of leg crossing combined with lower-body muscle tensing in the semisitting position.
position on arterial blood pressure in a medical student during a session of deconditioning of a blood injection injury phobia is given in Fig. 6.41 Note again that the effects of muscle tensing are almost instantaneous. Physical counterpressure maneuvers are thereby of prime importance as a strategy to prevent, abort, and/or enhance recovery of vasovagal fainting in blood donors.

Physical counterpressure maneuver in the context of whole blood donations

Ditto and colleagues36 published the first study that examined physical counterpressure maneuvers in the context of whole blood donations. In a small pilot study, these investigators randomized relatively inexperienced blood donors to either standard donation or donation after video instruction in muscle tensing. The 2-minute video taught donors to repeatedly tense the muscles of their arms, legs, and abdomen at 5-second intervals while maintaining a normal breathing pattern. Results indicated that predonation video instruction was associated with an attenuation of donor reports of reactions on the Blood Donation Reactions Inventory (BDRI, a subjective measure of pre-faint symptoms). These findings were later confirmed and extended in studies using larger numbers of donors and a placebo-controlled comparison group.12,42-44 The results of muscle tensing studies in blood donation context are given in Table 1. Although an attenuation of donor reports of reactions on the BDRI support the notion that muscle tensing reduces subjective reports of presyncopal reactions, additional studies in large samples of donors are required to determine level of effectiveness in preventing full VVS in the blood donation setting.

Two recent studies have addressed directly the hemodynamic effects of muscle tensing during whole blood donation. Ditto and coworkers37 reported higher levels of heart rate, cardiac output, and blood pressure during whole-body applied tension. In another study, Kowalsky and coworkers45 demonstrated that donors who engaged in repeated lower-body muscle tensing during donation show significantly higher levels of cerebral oxygenation compared to those who engaged in a minimal foot movement designed as a distraction control condition. As can be seen in Fig. 7, those who engaged in muscle tensing maintained cerebral oxygenation levels above predonation baseline levels despite their loss of blood volume.

Advice to apply physical counterpressure maneuvers during and after donation should be as simple and specific as possible to keep donors interested. Taking the time course of vasovagal reactions during blood donation (Fig. 1) and the instantaneous effect of physical counterpressure maneuvers on blood pressure (Figs. 5 and 6) into account, we propose the use of lower-body muscle tensing in the following way.

Supine

To promote arm blood flow during the period the blood is taken, the donors are instructed to periodically squeeze a small rubber ball with the donating arm. Rhythmic squeezing a small ball will not have an important effect as far as translocation of a large amount of venous blood from the arm centrally (see before). However, squeezing a ball may have a reflex influence on preventing VVS by...
increasing heart rate, cardiac contractility, and sympathetic outflow (exercise pressor response). In addition to arm squeezing, we suggest instructing donors to apply lower-body muscle tensing whenever they experience lightheadedness. Increasing intrathoracic pressure by straining (Valsalva maneuver) during lower-body muscle tensing should be avoided, because it impedes venous return to the heart and thereby reduces the effectiveness of the maneuver. The optimal duration and frequency of muscle contractions and relaxation remain to be established. For the time being, in response to perceived lightheadedness, we advise lower-body muscle tensing with or without the legs crossed with a duration of 5 to 10 seconds for contractions and a frequency of three times per minute (Fig. 6) during the first part of the phlebotomy.

All donors should be advised to apply lower-body tensing when the bag is nearly full and especially around the time the tubing is clamped and the needle is removed, because this period is accompanied by a sharp increase in vasovagal responses (Fig. 1). The collection staff may wish to signal the need to perform the increased muscle tensing as the bag fills, by asking the donor to switch the ball from the venipuncture arm to the contralateral arm and to perform lower-body muscle tensing. During the period directly after removal of the needle, with the donors sitting up with their feet hanging over the side of the donation chair or bed, leg crossing and lower-body tensing is advised especially in case of symptoms.

**Upright**
All donors should be advised to apply lower-body muscle tensions on arising after donation. They should also be instructed regarding the usefulness of leg crossing with muscle tensing as a preventive measure if they stand while they are in the refreshment area and for the first hour after donation. In case of symptoms of an impending vasovagal faint, they should be advised to tense their lower-body muscles maximally. Further, they should be instructed that if this intervention is ineffective, they should immediately squat, kneel down, or lay flat on their backs. Squatting (to sit in a crouching position with the knees bent and the buttocks on or near the heels) is an emergency measure that is about as effective as lying down to increase cardiac filling and reduce the risk of loss of consciousness. On arising from the squatting position lower-body muscle tension should again be applied to prevent a transient arterial blood pressure decrease. While there are currently no data on the use of muscle tension after donation, the physiologic data supporting the utility of these interventions in patients with fainting disorders and the data from blood donors during donation justify a study to assess its effectiveness.

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**Table 1. A summary of findings from randomized controlled trials that have examined the effect of muscle tensing on BDRI scores**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Comparison</th>
<th>Was BDRI reduced?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ditto et al.</td>
<td>n = 605</td>
<td>Placebo vs. standard donation</td>
<td>Yes, in women</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Muscle tensing vs. placebo</td>
<td>Yes, in women</td>
</tr>
<tr>
<td>Ditto et al.</td>
<td>n = 467</td>
<td>Muscle tensing vs. standard donation</td>
<td>Yes</td>
</tr>
<tr>
<td>Ditto and France</td>
<td>n = 467</td>
<td>Placebo vs. standard donation</td>
<td>Yes</td>
</tr>
<tr>
<td>Ditto et al.</td>
<td>n = 178</td>
<td>Muscle tensing vs. standard donation</td>
<td>Yes, in those with &lt;3 prior donations</td>
</tr>
<tr>
<td>Ditto et al.</td>
<td>n = 1209</td>
<td>Muscle tensing vs. placebo</td>
<td>Yes</td>
</tr>
<tr>
<td>Ditto and France</td>
<td>n = 467</td>
<td>Upper-body tension (arms only) vs. standard donation</td>
<td>Yes</td>
</tr>
<tr>
<td>Ditto et al.</td>
<td>n = 1209</td>
<td>Lower-body tension (legs/abdomen) vs. standard donation</td>
<td>Yes</td>
</tr>
<tr>
<td>Ditto et al.</td>
<td>n = 1209</td>
<td>Full-body tension vs. standard donation</td>
<td>Yes</td>
</tr>
<tr>
<td>Ditto et al.</td>
<td>n = 1209</td>
<td>Upper-body tension (arms only) plus distraction vs. standard donation</td>
<td>Yes</td>
</tr>
<tr>
<td>France et al.</td>
<td>n = 414</td>
<td>Placebo vs. standard donation</td>
<td>Yes, in women</td>
</tr>
<tr>
<td>France et al.</td>
<td>n = 414</td>
<td>Water vs. placebo</td>
<td>Yes, in women</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Water plus leg lift vs. standard</td>
<td></td>
</tr>
</tbody>
</table>

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Fig. 7. Mean (±SEM) change in cerebral oxygenation during whole blood donation for donors engaging in lower body applied muscle tension (O) or a distraction control involving gentle foot flexion (●). Because blood donation draw times vary across individuals, cerebral oxygenation data were averaged into three equal periods for all participants (i.e., first, second, and third interval of their donation).
Dietary salt supplement: evidence for effectiveness to combat orthostatic intolerance

The sodium content of dietary salt (NaCl) determines the volume of the extracellular fluid, including the plasma volume and thereby the blood volume. An increase in dietary salt will increase the plasma and blood volume. Adequacy of the blood volume, and in particular the amount of blood available for the cardiac ventricles (central blood volume), is a crucial factor in circulatory adjustment to an upright posture. Accordingly, beneficial effects of an increase in dietary sodium intake on the magnitude of the plasma volume and orthostatic tolerance are reported in patients with symptomatic orthostatic hypotension due to autonomic failure, in otherwise healthy subjects with orthostatic intolerance, and in dehydrated athletes and in deconditioned astronauts returning to earth.

El-Sayed and Hainsworth have documented that chronic plasma volume expansion induced by an increase in dietary salt impressively increases the time to faint during a combined tilt-body suction experiment. Specifically, the time to faint increased from approximately 20 minutes on a standard salt diet to 30 minutes on a high-salt diet. Astronauts are relatively hypovolemic from their zero-gravity exposure and many experience significant orthostatic hypotension soon after return to earth. As a countermeasure an acute isotonic fluid-loading procedure is performed on landing day. The standard procedure consists of the consumption of 1.0-g salt tablets (i.e., tablets with 17 mmol NaCl) per 125 mL of water with a total volume of 15 mL/kg body weight in 2 hours. For an astronaut with a body weight of 70 kg, the fluid loading amounts to the consumption of 70 × 15 = 1050 mL of water with 8.4 g of NaCl (143 mmol), that is, roughly the equivalent of 1 L of isotonic saline (0.9% NaCl). The 1 L of NaCl fluid loading will be distributed over the total extracellular fluid space (approx. 20% of the body weight). With a body weight of 70 kg the extracellular fluid volume expansion by consumption of 1 L of isotonic saline will amount to 1000/1400 = 70 mL per liter of extracellular fluid. The plasma volume is part of the extracellular fluid volume. With an estimated plasma volume of approximately 3 L in an astronaut of 70 kg, 1 L of isotonic saline will increase the plasma volume by approximately 200 mL.

Dietary salt supplement in blood donors

A donation of 540 mL of whole blood implies a loss of approximately 320 mL of plasma water and approximately 2.9 g of NaCl (i.e., almost 1.2 g of sodium). FDA food labels list grams (or milligrams) of sodium because there are usually other sodium-containing salts in food products (e.g., sodium citrate). In the following discussion about dietary salt supplement, we therefore will use sodium content.

A daily intake of fewer than 2.3 g of sodium is recommended, but most US citizens have a higher intake (approx. 3-4 g). The amount of extra salt needed (1.2 g NaCl) is within the fluctuations in intake that occur with normal diets occasionally in daily life.

To prevent VVS the 320 mL of plasma loss due to the donation of blood needs to be corrected as quickly as possible by oral intake of 1.2 g of sodium and extra water, ideally before or otherwise shortly after phlebotomy. The challenge is to devise a trial of a salt replacement strategy that is simple and effective. The time course of salt excretion after an oral load is a key factor in this strategy. Acute increases in sodium intake are excreted slowly by the body, with roughly 50% retained within 24 hours. A cup of soup (250 g) has a salt content of about 0.8 g NaCl. Thus, if on the evening before donation 3 cups of soup are consumed (2.4 g NaCl), more than 1.2 g of NaCl can be expected to be retained on the next day (i.e., enough to replace the donation-related loss). However, such a large extra intake of soup and/or sodium the day before donation is not feasible from the blood center and blood donor perspective. An extra sodium intake of approximately 1 g (with 0.5 g retained) may be a more realistic goal, and thus extra sodium intake on the day of donation is needed. If sodium intake is increased on the morning of a blood donation by drinking endurance sport drinks and eating salted snacks like pretzels or soup, almost all of the salt can be expected to be retained during the period the homeostatic mechanisms are trying to restore the effective circulating volume. Plasma water also must be restored and thus sufficient fluid intake is mandatory. A bottle of endurance sports drink (approx. 250 mL) contains 0.2 g NaCl and some glucose that will promote intestinal NaCl uptake. It is an isotonic solution that is rapidly absorbed. With two bottles of endurance sports drink (one bottle before and one after donation) the loss of plasma water (320 mL) will be restored and in addition approximately 0.4 g NaCl will be added leaving a NaCl deficit of about 0.8 g. A 1-oz bag of pretzels contains approximately 0.34 g of NaCl. Thus with two bottles of a sport drink and 2 oz of pretzels (or alternatively 2 cups of soup) the sodium deficit of 1.2 g can be corrected on the day of donation. It is important to note that, apart from an older study no studies have documented the beneficial effects of salt replacement on the tendency for VVS during and after whole blood donation.

One may argue that not only the plasma water, but also the volume of the red blood cell mass (with a whole blood donation of 540 mL approx. 220 mL) must be supplemented after donation by additional NaCl and water to restore the effective circulating volume. Thus, the calculated 1.2 g of NaCl supplement is a conservative estimate.
Pressor response to water drinking: evidence for increase in blood pressure and effectiveness to combat orthostatic intolerance in patients with autonomic failure and normal subjects with tendency for VVS

If one drinks 500 mL of water it will be distributed over the total body water (approx. 60% of body weight) and thereby will barely increase the plasma volume. Water drinking will result in a water diuresis due to its effect on plasma osmolality. In supine healthy subjects the water diuresis starts within 30 minutes after the intake of the water load (half-life of antidiuretic hormone is approx. 30 min) and is rapid. Most of a water load will be excreted in hours.\textsuperscript{50,59,60} Despite the negligible effects on plasma volume, rapid ingestion of 500 mL of water has been shown to be effective in combating orthostatic intolerance in patients with primary autonomic failure.\textsuperscript{60,61} The maximal effect occurs after 30 to 40 minutes. It amounts to an increase of 30 to 40 mmHg in systolic blood pressure and the effect lasts for approximately 1 hour. The blood pressure increase is caused by an increase in sympathetic nerve outflow, but the afferent signal for this sympathetic activation is unknown. Stretch of the stomach wall by the water load and induction of hypoosmolality in the portal venous system have been postulated. At present the latter mechanism seems to be the best explanation for the underlying mechanism in patients with autonomic failure.\textsuperscript{60}

Water drinking barely increases blood pressure in healthy young subjects, but preliminary data suggest that a water load of 500 mL can be applied to improve orthostatic tolerance in healthy subjects.\textsuperscript{62-64} Lu and coworkers\textsuperscript{63} have reported that drinking 500 mL of water 15 minutes before a tilt-body suction orthostatic stress test increases the standing time by approximately 5 minutes. Impressive as it is, this 5-minute increase in standing time is a transient effect. The best available evidence about the duration of a water load on sympathetic outflow comes from a study that recorded muscle sympathetic nerve activity after water load of 500 mL.\textsuperscript{55} The muscle sympathetic nerve activity increase lasted for 1 hour. In contrast, plasma volume expansion with Na and water has a very prolonged effect (>1 day).

Water drinking in blood donors

To date, three studies have specifically examined the effects of predonation water loading on the experience of vasovagal reactions to blood donation. The first study to examine predonation water loading in the context of blood donation was conducted as a small, randomized controlled trial of college men and women who were donating for the first time.\textsuperscript{66} Donors were randomly assigned to drink either 0 or 500 mL of bottled water approximately 30 minutes before donation. Ratings of vasovagal reactions were obtained immediately after donation using the BDRI, and group comparisons revealed that water loading significantly reduced reactions relative to the no-water control group. This finding was later confirmed in a study of nearly 9000 high school donors who ingested either no water or 473 mL of water approximately 0 to 30+ minutes before donation.\textsuperscript{67} Based on phlebotomist reports, those who received water had a significantly lower reaction rate compared to those who did not (9.9 and 12.5%, respectively). Further analyses indicated that the benefit of water loading was most consistent among first-time donors and more likely to be evident when ingestion occurred closer to the time of actual donation. Most recently, Ando and colleagues\textsuperscript{68} reported that individuals with pulse rate increases of 15 or more beats per minute upon standing before donation were at elevated risk for vasovagal reactions to blood donation. Further, they noted that reactions among these high-risk donors (large postural increase indicates poor orthostatic tolerance) were significantly attenuated after ingestion of 300 mL of water 15 minutes before donation. These observations by Ando and colleagues do not come unexpectedly; postural tachycardia is a marker of orthostatic circulatory intolerance. For instance, it is very common after prolonged bed rest and after space flight. Water drinking has been shown to diminish postural tachycardia.\textsuperscript{69} In sum, although acute water ingestion appears to have a salutary effect on donation reactions, additional research is needed to address such issues as individual differences in response, ideal dose and timing of ingestion relative to blood draw, and the potential benefit of salt loading before or during the donation process. None of these studies examined the effect on vasovagal reactions that occurred after the donor left the donation site.

Salt and water versus water alone

There are no controlled trials available comparing the relative effectiveness of isotonic plasma volume expansion with a 1.2-g sodium supplementation plus extra water versus the consumption of 500 mL of water alone. The physiologic data as outlined above strongly argue for the isotonic salt approach, since the effects are prolonged for hours. The delayed reactions with injuries are most troublesome and they appear to be plasma volume dependent. Water drinking alone will not correct hypovolemia. On the other hand, the transient beneficial effect of water intake under hypovolemic conditions may be applied to diminish a tendency to faint during the actual period of blood donation. Further studies are clearly needed to document which approach is most effective. Advice should be as simple as possible and a similar fluid load before and after donation would be ideal. In addition the advice given should be acceptable to donors.
SYNTHESIS

Our review has provided a physiologic explanation for blood donor VVS at various times before, during, and after donation. In addition, we have analyzed some interventions that have been shown to reduce the rate of VVS and, where appropriate, provided a physiologic rationale for the success of these interventions. Finally, we have proposed that a new intervention, salt supplementation, should be rigorously assessed on the basis of the understanding of the important role dietary salt plays in controlling intravascular volume and the evidence of its efficacy in patients with orthostatic hypotension due to autonomic failure, patients with a tendency for vasovagal faints, dehydrated athletes, and deconditioned astronauts returning to earth. While we recognize that there are no data on salt replacement in blood donors, our proposal assumes that maintenance of blood volume or rapid restoration of blood volume after donation will help all donors and should reduce the rate of reactions and injuries regardless of age, sex, blood volume, and donation experience. It is known, however, that some reactions are more likely to be associated with injury than others. The higher risk reactions are those which occur when the donor is upright and when the donor is off site.1,8 In addition it is known that young donors, inexperienced donors, and donors with low estimated blood volume have a higher VVS rate than more experienced, mature, and larger donors.5,10 Female sex and low estimated blood volume are factors strongly associated with off-site and late VVS reactions.8 Therefore, rapid restoration of blood volume may be particularly valuable for these donors. A trial of salt supplementation should be initiated with a monitoring system that permits assessment of the impact on those donors most likely to react and most likely to be injured after a reaction.

While VVS reactions with loss of consciousness are those most likely to be associated with injury, ideally interventions selected to reduce fainting would also have the potential to reduce the more common, milder reactions that can reduce donor satisfaction and likelihood of return.6,70 It is known that there are no significant differences between the predictors of mild reactions and more severe reactions5,8,10 and a recently completed preliminary trial13 of three interventions (control of maximum percentage of blood volume to be donated, water drinking, and muscle tensing) showed that the beneficial impact of the interventions is similar on multiple reaction types. Thus, it seems reasonable to assume that a reduction in all reaction types could be achieved with an intervention primarily based on an understanding of VVS.

CONFLICT OF INTEREST

The author(s) certify that they have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in this manuscript.

REFERENCES


