Occurrence, risk factors and prevention of fainting during or after blood collection: French hemovigilance data and results from a prospective randomized trial

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Etablissement Français du Sang: The french transfusion public service

17 Regional Blood Banks.
• 14 in metropolitan France.
• 3 in overseas territories (Guadeloupe-French Guyana, Martinique, Island of la Reunion-Mayotte)

Yearly:
• 3 million blood donations
• 1.7 million blood donors of which 360,000 first-time donors
• 9,800 employees
• 153 blood collection centers, 40,000 mobile blood collection operations
• A budget of €846 million

Blood products delivered in 2014:
• Red blood cell concentrates: 3 084 611
• Platelets concentrates: 302 698
  - Apheresis platelets concentrates: 143 266
  - Whole blood derived platelets: 159 432
• Plasma : 353 977
Incidence of donor adverse events in France, 2014
186 / 100,000 blood donations

Incidence of adverse events in France, 2012-2014

ANSM (French drug agency) report, 2014

<table>
<thead>
<tr>
<th>Gravité</th>
<th>Score d'imputabilité</th>
<th>Total</th>
<th>Pourcentage</th>
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<td>1</td>
<td>2</td>
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<tr>
<td>Grade 2</td>
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<tr>
<td>Grade 3</td>
<td>14</td>
<td>71</td>
<td>458</td>
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<tr>
<td>Grade 4</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Total</td>
<td>22</td>
<td>137</td>
<td>1356</td>
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</table>
# Frequency of vasovagal reactions, 2012

**Incidence per 100 000 donations**

<table>
<thead>
<tr>
<th>Immediate vasovagal reactions</th>
<th>99,9</th>
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<tr>
<td>Whole Blood</td>
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<tr>
<td>Apheresis</td>
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<td>Delayed vasovagal reactions</td>
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<tr>
<td>Whole Blood</td>
<td>12,0</td>
</tr>
<tr>
<td>Apheresis</td>
<td>12,8</td>
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</tbody>
</table>

| Donor 18<=30 years old        | 191,0|
| Donor > 30 years old          | 28,4 |
| Male donors                   | 85,1 |
| Female donors                 | 117,4|
| New                           | 288,4|
| Repeat                        | 68,2 |
| Donor 18<=30 years old        | 13,9 |
| Donor > 30 years old          | 7,5  |
| Male donors                   | 3,6  |
| Female donors                 | 22,2 |
| New                           | 18,8 |
| Repeat                        | 11,0 |
## Donor adverse events, 2014

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>n=</th>
<th>%</th>
<th>Incidence per 100 000 donation</th>
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<tbody>
<tr>
<td></td>
<td>Whole Blood</td>
<td>Apheresis</td>
<td>Total</td>
</tr>
<tr>
<td>Immediat vasovagal reactions</td>
<td>3442</td>
<td>476</td>
<td>3918</td>
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<tr>
<td>Hematoma</td>
<td>277</td>
<td>203</td>
<td>480</td>
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<tr>
<td>Delayed vasovagal reactions</td>
<td>346</td>
<td>34</td>
<td>380</td>
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<tr>
<td>Arterial ponction</td>
<td>165</td>
<td>7</td>
<td>172</td>
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<tr>
<td>Citrate toxicity</td>
<td>0</td>
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<td>73</td>
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<tr>
<td>Neurological injury at site of venipuncture</td>
<td>39</td>
<td>5</td>
<td>44</td>
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</tbody>
</table>
Mechanisms of vasovagal reactions (VVR) (syncope / near-syncope) in blood donors

- Direct effects of removal of whole blood
- Psychological stress of instrumentation and giving blood (i.e., fear of needles, pain, and the sight of blood)
- Orthostatic effects superimposed on a hypovolemic state after the donation

- In humans, tolerance to orthostasis requires the successful integration of multiple elements of cardiovascular control.
- Syncope or near-syncope may occur when there is an abnormally large postural decrease in central blood volume, cardiac filling pressure, stroke volume, and cardiac output or inadequate (or inappropriate) neurohumoral reflex responses to orthostasis, primarily tachycardia and vasoconstriction
THE RELATIVE IMPORTANCE OF RISK FACTORS ACROSS THE TIME OF DONATION: CASE-CONTROL STUDIES OF IMMEDIATE AND DELAYED VASOVAGAL REACTIONS EVENTS

NARBEY D.¹, FILLET AM.¹, JBILOU S.¹, TIBERGHIEN P.¹², DJOUDI R.¹
¹EFS Medical Department, La Plaine Saint-Denis; ² University of Franche-Comté, Besançon, France

• Retrospective, multicenter case-control study
• Cohort of 8 834 214 donations from 2 889 632 different donors, 2011 to 2013 French haemovigilance data
• Vasovagal reactions (VVR) defined as immediate when occurring at the transfusion site, and as delayed when occurring outside the transfusion site and within the 24 hours following donation.
• Adverse events with a high imputability only
THE RELATIVE IMPORTANCE OF RISK FACTORS ACROSS THE TIME OF DONATION: CASE-CONTROL STUDIES OF IMMEDIATE AND DELAYED VASOVAGAL REACTIONS EVENTS

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• Controls drawn at random from the donor population (1 control by case) among healthy subjects free of VVR, matched on the collection site and day.
• Primary outcome: presence of an immediate and delayed VVR.
• Studied variables: sex (binary variable: man / woman), age (categorical variable: 18-24 years, 25-60 years, 61-70 years), BMI (Body Mass Index, categorical variable: underweight, normal, overweight, obesity), donor status (binary variable: repeat donor / first-time) and collection type (binary variable: whole blood / apheresis).
In summary

• VVRs reported among 8,834,214 donations: 0.09% immediate VVR and 0.009% delayed VVR
• First-time donation (OR 3.72; 95%CI: 3.36-4.12) and age group 18-24 years (OR 3.30; 95%CI: 2.81-3.87) are strongly associated with immediate VVR
• Compared to men with similar weight status, women with a normal BMI, overweight or obese experience a higher incidence of delayed VVR (OR 7.31; 95%CI: 4.96-10.77; OR 7.89; 95%CI: 4.84-12.87; OR 3.72; 95%CI: 1.42-9.38, respectively)
• Compared to men with a normal BMI, underweight men experience a higher incidence of delayed VVR (OR 6.39; 95%CI: 1.56-26.13)
• Compared to whole blood donation, apheresis is associated with a higher risk incidence of immediate (OR 1.26; 95%CI: 1.12-1.41) or delayed VVRs’ (OR 1.70; 95%CI: 1.23-2.34) occurrence.
The high school boys would class and do it so they about how
more such delicate flower!

apparently
One fatality following whole blood donation
Causal relationship between the donation and subsequent death of the donor

“The individual initially complained of lightheadedness after donating a unit of whole blood and was managed conservatively with rest and oral hydration. Subsequently, after walking a short distance in the donation area, the person knelt down, and after getting back up to a standing position, fell backward. The traumatic brain injury with intracerebral and subdural hematoma that was sustained in this fall ultimately led to the donor’s death”

There were no conditions detected during pre-donation screening that would have contraindicated donation, or that signaled unusual risk.
Interventions to reduce fainting

Isotonic water:
- An isotonic drink (vs no water, or plan water) facilitates the intravascular volume restoration and electrolyte replacement, leading to faster homeostasis, which might reduce syncopal-like reactions and tiredness after blood donation.
- 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, in dehydrated athletes, and in deconditioned astronauts returning to earth.

Wieling W et al, Transfusion, 2011
Interventions to reduce fainting

Muscle tensing

- Patients with a tendency for vasovagal faints have successfully implemented physical counterpressure 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 abdominal 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.

- Interventions that are effective have in common that they involve tensing of leg and abdominal muscles.

- 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.

Wieling W et al, Transfusion, 2011
Prevention of Fainting Reactions after Whole Blood Donation:

A Cluster Randomized Trial to Assess the Efficiency of Hydration with Isotonic Solution, Water and Applied Muscle Tension

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Evasion study

- Prospective study
- Factorial design
- Comparison of 3 strategies regarding hydration (500mL of an isotonic drink, 500mL of a slightly mineralized water or an advice to drink a glass of water or fruit juice) in combination with or without muscle tensing exercises
- Cluster randomization (1 cluster = 1 blood donation unit)
- Donor phone interview one week after donation.
Evasion study: measured outcomes

- The main outcome measure was the **cumulated incidence of presyncope and syncope during blood donation and within 48 hours afterwards**.
  - At the donation unit, presyncope (feeling faint) and syncope (fainting) were defined as reactions that required the donor to lie down in the “Trendelenburg” position.
  - After leaving the donation unit, syncope-type reactions were defined as the need to sit or lie down.
- Secondary outcomes were
  - (i) syncope-type reactions during each of the three donation periods, during blood collection, immediately post-donation and within 48h after leaving the donation unit
  - (ii) the impact of blood donation on normal daily activities and donor tiredness during the 48h after leaving the unit.
Study compliance:

- **Isotonic water**: 71.4% of donors drank all 500 mL and 94.8% at least half.
- **Plain water**: 66% of donors drank all 500 mL and 90.7% at least half.
- **Muscle tensing exercises**: 88.3% of donors performed all proposed exercises and 98.0% performed at least half.
Donnez et pensez à vous...

Activez le retour de votre sang veineux de vos jambes vers votre cœur.

Ces exercices simples sont à répéter pendant tout le prélèvement sanguin, chacun par série de 10 en alternant les 3 types d'exercices.

**EXERCICE 1**

**RESPIRATION ABDOMINALE**
Soufflez par la bouche en pinçant les lèvres comme pour souffler sur une bougie.

**EXERCICE 2**

**ORIGINE DES ORTEILS**
Serrez vos orteils fortement comme pour attraper un objet.

**EXERCICE 3**

**FLEXION/EXTENSION DE CHEVILLE**
Pointez du pied, jambe tendue et relevez-le vers vous par des mouvements de la cheville.

Evasion study findings

- Vasovagal reactions occurrence during blood donation can be reduced by muscle tensing exercises (30% reduction when compared to no exercises)
- Vasovagal reactions occurrence after blood donation (off site) can be reduced by isotonic hydration during donation (30% reduction when compared to « advised to drink »)
- Unusual tiredness occurrence can be reduced by isotonic hydration during blood donation (25% reduction compared to « advised to drink »)

Pending question:
- Do the observed reductions in vasovagal reactions apply to severe reactions as well?
- Muscle tensing during blood donation is being generalized in France
- Isotonic water hydration for all donors or a subset of donors with a high(er) risk profile (women, first-time, and young donors): decisions pending

More needs to be done!
Fainting and resulting complications are not acceptable

We owe this to our donors, to you

Thank you for your precious gift