Preventing the risk of fainting in plasma donors

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Université Marie et Louis Pasteur, Besançon
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Conflict of interest: Employed by Etablissement Français du Sang (EFS), the public blood establishment responsible in France for the collection, qualification, and supply of plasma for transfusion purposes or for fractionation.

Is fainting really a sweet pleasure?

Eva Wiseman: 'What sweet pleasure comes with succumbing to a long faint.' Photograph: Getty

The Gardian, 2014

Drama avoided in Macon (France): “he” crosses the high school parking lot after losing consciousness…

… *30 minutes after a whole blood donation*

Drame évi … un malaise

Laurent BOLLET – 17 dé

01 / 03

C'est un miracle car le parking est souvent bondé, à quelques minutes près. Photo Laurent BOLLET

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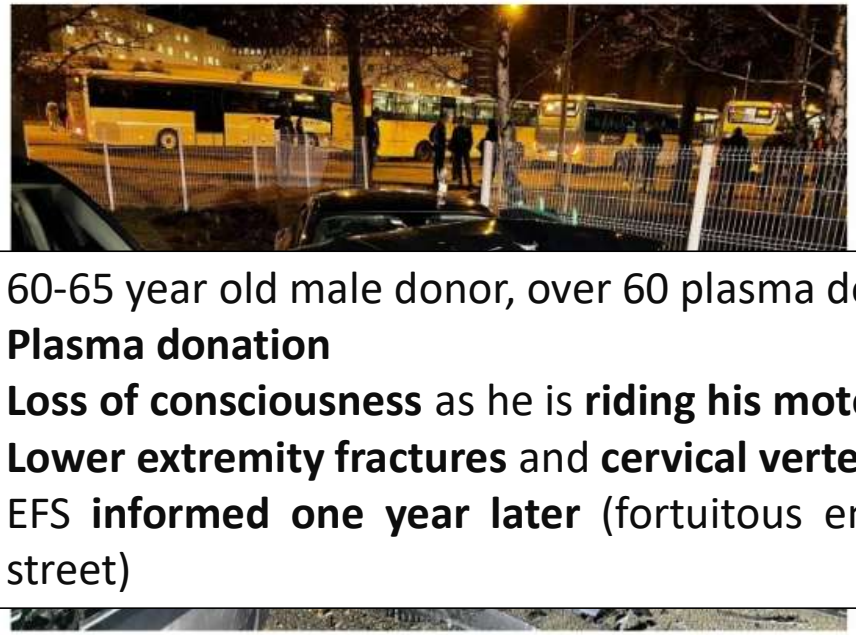

01 / 03 C'est un miracle car le parking est souvent bondé, à quelques minutes près. Photo Laurent BOLLET

- 60-65 year old male donor, over 60 plasma donations
- **Plasma donation**
- **Loss of consciousness** as he is **riding his motorcycle** back home.
- **Lower extremity fractures** and **cervical vertebra fracture with spinal cord injury**.
- EFS **informed one year later** (fortuitous encounter with an EFS employee in the street)

Frequency of fainting reactions in the Evasion study

Morand et al, Transfusion, 2016

Fainting reactions:

- At the donation unit: the need to lie down in the "Trendelenburg" position.
- After leaving the donation unit: the need to sit or lie down, up to 48 hours after donation

All participants were interviewed by phone to assess fainting reactions and fatigue 7 days after donation

Fainting reactions	All donors (n=4576)	Female donors (n=2302)	Male donors (n=2274)	OR
Overall	5,5% (n=253)	8,1% (n=187)	2,9% (n=66)	3,0 p<0,01
On-site	3,0% (n=136)	3,7% (n=86)	2,2% (n=50)	1,7 p<0,01
Off-site	3,0% (n=137)	5,1% (n=117)	0,9% (n=20)	6,0 p<0,01
Both on-site and off-site	0,4% (n=20)	0,7% (n=16)	0,2% (n=4)	4,0 p=0,014

Case–control study of immediate and delayed vasovagal reactions in blood donors

Narbey et al, Vox Sanguinis, 2016

- French hemovigilance data, 2011 to 2013
- 8410 immediate vasovagal reactions (VVRs) and 833 delayed VVRs among 8834214 donations (0,09% and 0,009%, respectively)

		Univariate analysis		Multivariate analysis	
		Odds ratio (95%CI)	p	Odds ratio (95%CI)	p
Immediate (on-site) VVR	**Whole Blood**	1	0,009	1	< 0,001
	Apheresis	0,89 (0,82-0,97)		1,53 (1,38-1,70)	
Delayed (off-site) VVR	**Whole Blood**	1	0,56	1	< 0,001
	Apheresis	0,92 (0,69-1,22)		1,61 (1,11-2,32)	

One control/case was drawn randomly from among donors without VVR. Explanatory variables (sex, age, body mass index (BMI), donation status), matching variables (donation region, date) and the interaction term (sex and BMI) were integrated into the multivariate model.

Frequency of faint

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- At the don
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- After leavi
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Multivariate analysis	
Odds ratio (95%CI)	p
1	
1,53 (1,38-1,70)	< 0,001
1	
1,61 (1,11-2,32)	< 0,001

t VVR. Explanatory variables
bles (donation region, date)
ultivariate model.

Adjusting the volume of collected plasma

France, regulated by ANSM

- Collected volume, excluding anticoagulant and sample tubes: **≤ 16% of the donor's total blood volume**
- Collected volume, excluding anticoagulant and sample tubes: ≤ 750 mL
- Extracorporeal volume, at any time during the procedure: ≤ 20% of the donor's total blood volume
- Plasma collection volumes determined according to the **Gilcher rule/scale** (weight and height, to account for the influence of body mass index on total blood volume)

3.1 Femmes

T / P	150	155	160	165	170	175	180	185	≥ 190
50	475	505	535	535					
52	490	520	550	585	585				
54	505	535	565	600	600				
55	515	540	575	610	645	645			
56	520	550	580	615	650	650			
58	535	565	600	630	670	705	705		
60	550	580	615	650	685	720	720		
62	570	600	630	665	700	740	780	780	
64	580	615	645	680	715	755	795	795	
66	600	630	660	695	730	770	805	840	840
68	600	645	680	710	750	785	820	850	850
70		660	695	725	765	800	830	850	850
72		660	710	740	780	810	840	850	850
74			725	760	795	825	850	850	850
76			725	775	805	835	850	850	850
78				790	820	845	850	850	850
80				805	830	850	850	850	850
82				805	840	850	850	850	850
≥ 84					850	850	850	850	850

3.2 Hommes

T / P	150	155	160	165	170	175	180	185	≥ 190
50	580	610	645	645					
52	595	625	660	695	695				
54	610	640	675	710	710				
56	625	660	690	725	765	765			
58	640	675	705	740	780	810	810		
60	660	690	720	760	795	825	825		
62	675	705	740	775	805	835	855	855	
64	690	720	755	790	815	845	855	855	
66	705	735	770	800	830	855	855	855	855
68	705	750	785	810	840	855	855	855	855
70		765	795	825	850	855	855	855	855
72		765	810	835	855	855	855	855	855
74			820	845	855	855	855	855	855
≥ 76			820	855	855	855	855	855	855

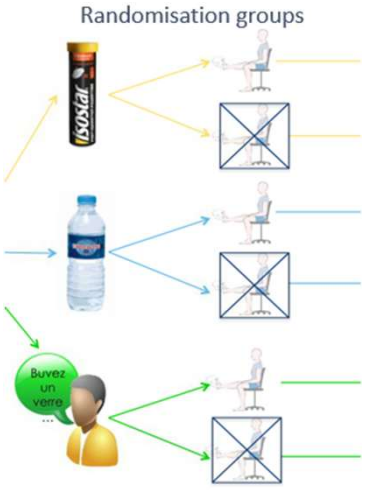
Hydration and muscle tension exercises have been shown to be associated with a reduced frequency of vasovagal/fainting reactions in blood donors

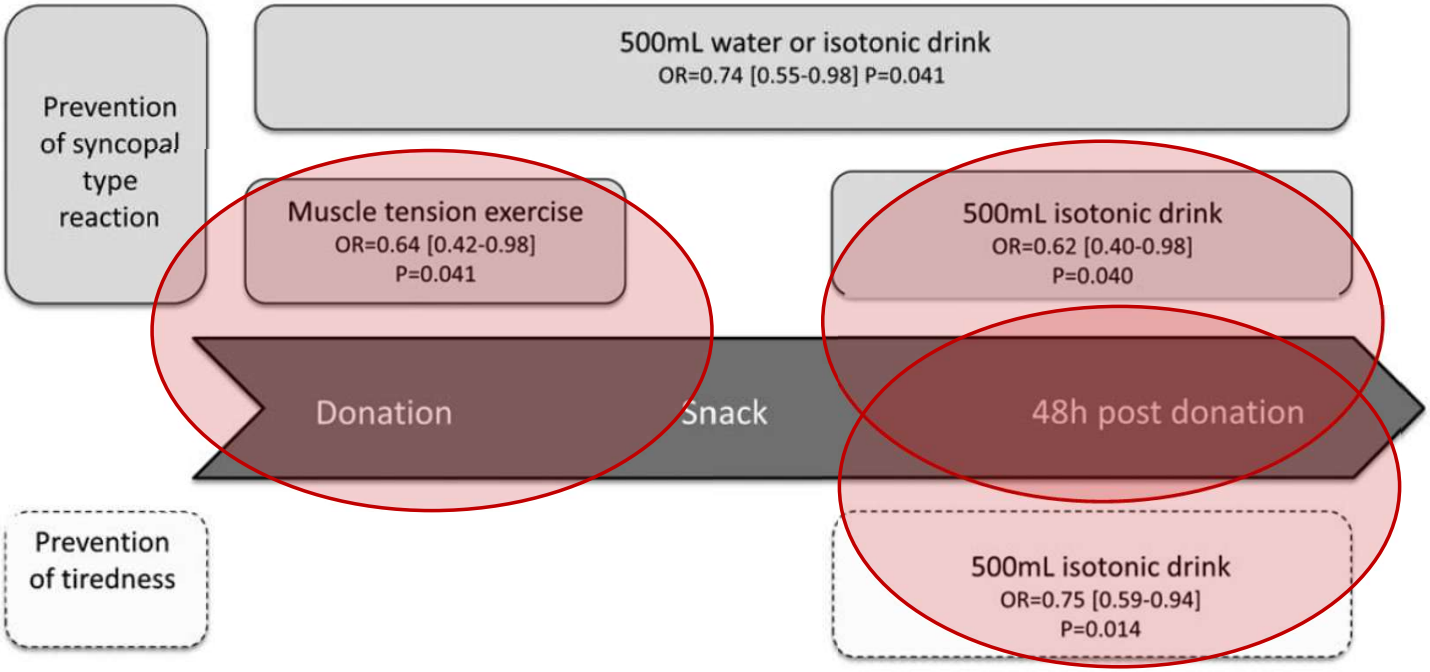
Ditto et al, Vox Sang 2010; Ando et al, Transfusion 2009; France et al, Transfusion 2010; Kowalsky, Transfusion 2011; Newman et al, Transfusion, 2007; Tomasulo et al, Transfusion 2011, Holly et al, Ann Behav Med, 2012, Thijsen et al, Transfusion, 2018; Menitto et al, Transfusion, 2018; Wierum-Oselton et al, Transfusion, 2019; Jia et al, Chin J Blood Transfusion, 2020; Goldman et al, Transfusion, 2021; Lewin et al, Transfusion, 2022

Evasion Study

Morand et al, Tranfusion, 2016

- Factorial design, cluster randomization
- 4576 whole blood donors
- All donors were interviewed 7 days after





Summary of the interventions and the phases of blood donation where they appear to have a beneficial effect.

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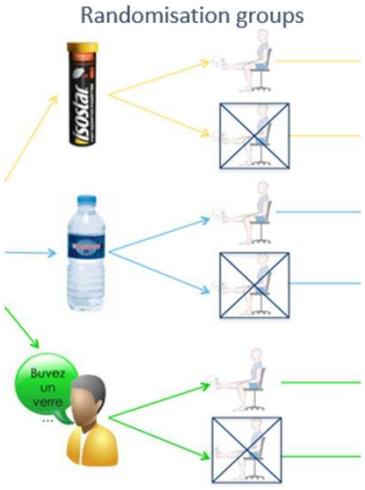
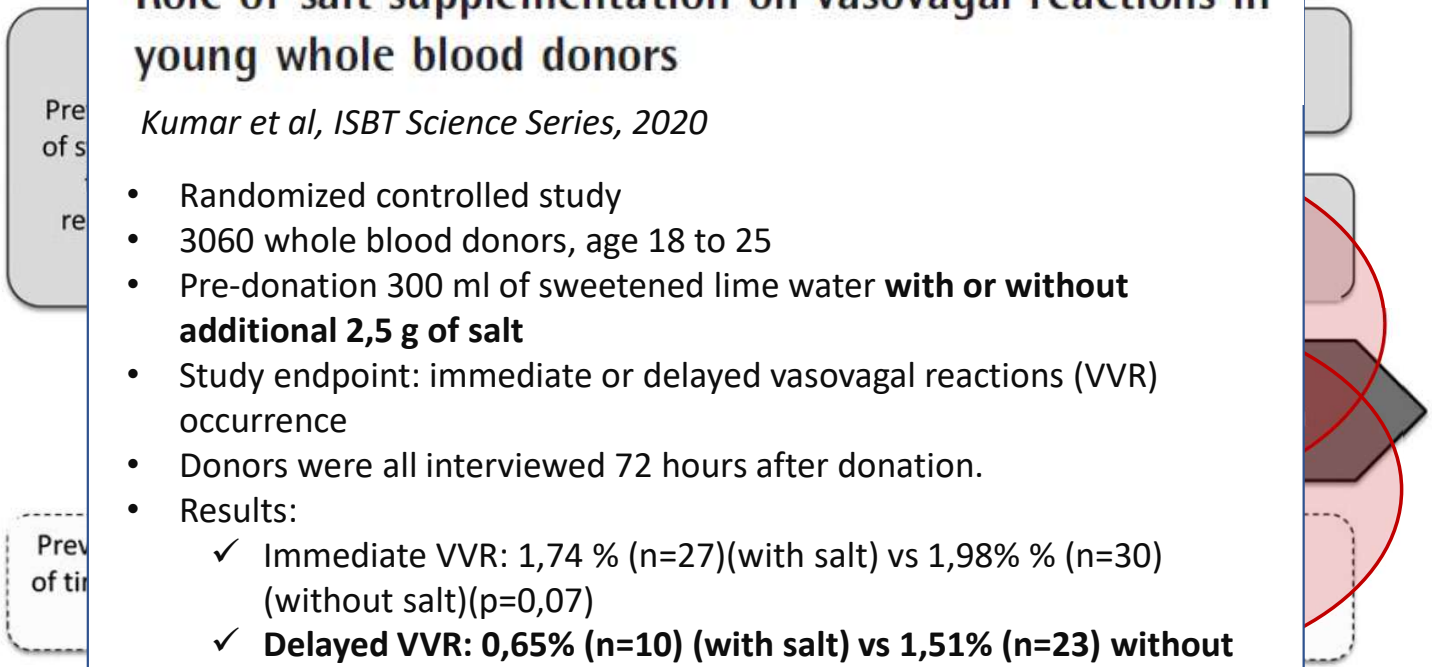


Role of salt supplementation on vasovagal reactions in young whole blood donors

Kumar et al, ISBT Science Series, 2020

- Randomized controlled study
- 3060 whole blood donors, age 18 to 25
- Pre-donation 300 ml of sweetened lime water **with or without additional 2,5 g of salt**
- Study endpoint: immediate or delayed vasovagal reactions (VVR) occurrence
- Donors were all interviewed 72 hours after donation.
- Results:
  - ✓ Immediate VVR: 1,74 % (n=27)(with salt) vs 1,98% % (n=30) (without salt)(p=0,07)
  - ✓ **Delayed VVR: 0,65% (n=10) (with salt) vs 1,51% (n=23) without salt (p=0,02)**



Summary of the interventions and the phases of blood donation where they appear to have a beneficial effect.

Preventive interventions for vasovagal reactions in whole blood donors: a cluster-randomised, stepped-wedge, crossover trial of 73 sites involving 1·4 million donors England

Kaptoge et al, Lancet Haematol, 2026

- Cluster-randomised, stepped-wedge, crossover trial involving 73 blood donation sites (clusters) across England
- Interventions:
  - 500 mL pre-donation isotonic drink (*vs* standard 500 mL plain water)
  - Extended 3-minute post-donation rest on the donation chair (*vs* standard 2-minute rest)
  - Modified applied muscle tension (AMT) exercise (*vs* current AMT practice)
  - Psychosocial intervention using preparatory materials (*vs* no materials).
- Primary outcome: in-session vasovagal reaction (VVR) with loss of consciousness (LOC).
- Among the secondary outcomes:
  - All in-session VVR
  - Delayed VVR with LOC
  - All delayed VVR
- No systematic donor interview at distance of blood donation

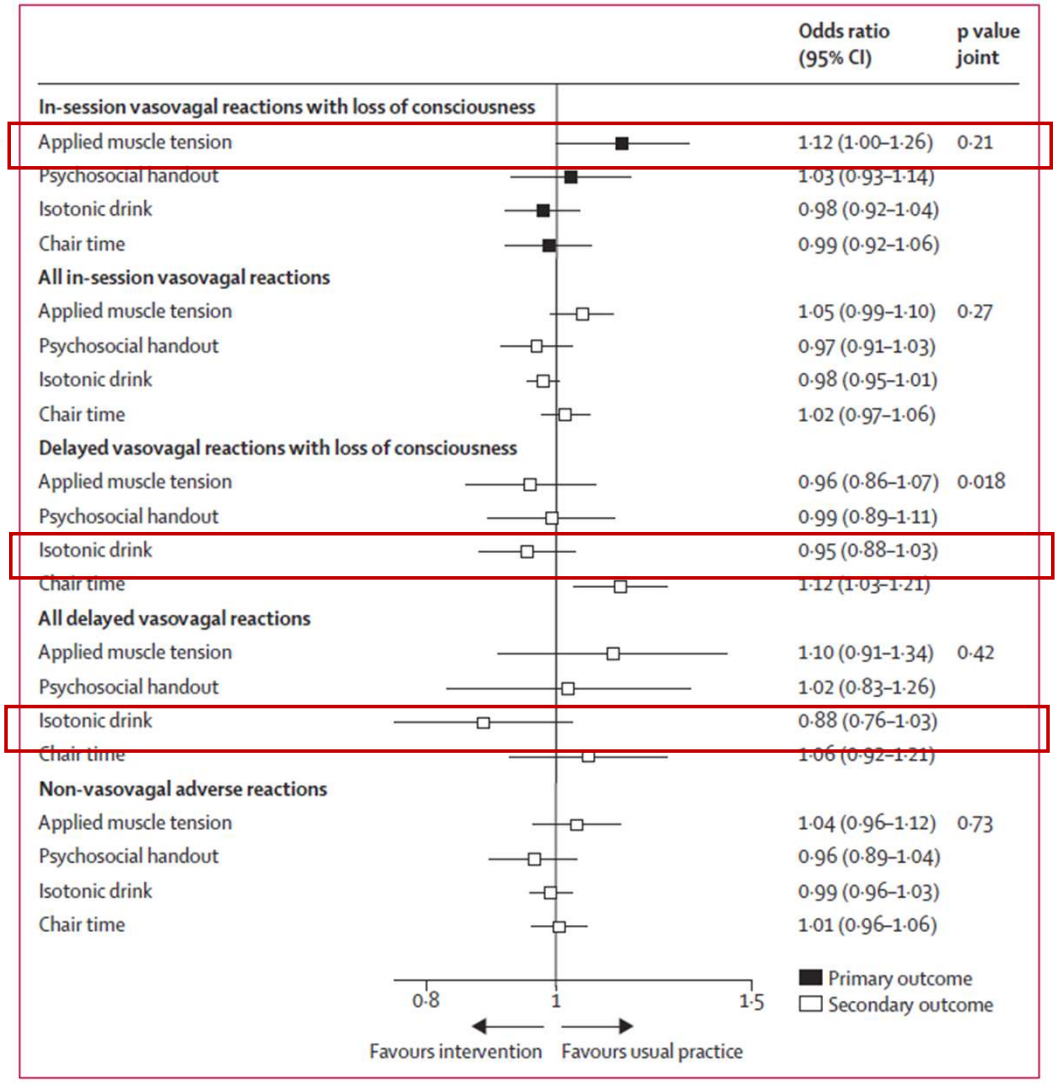


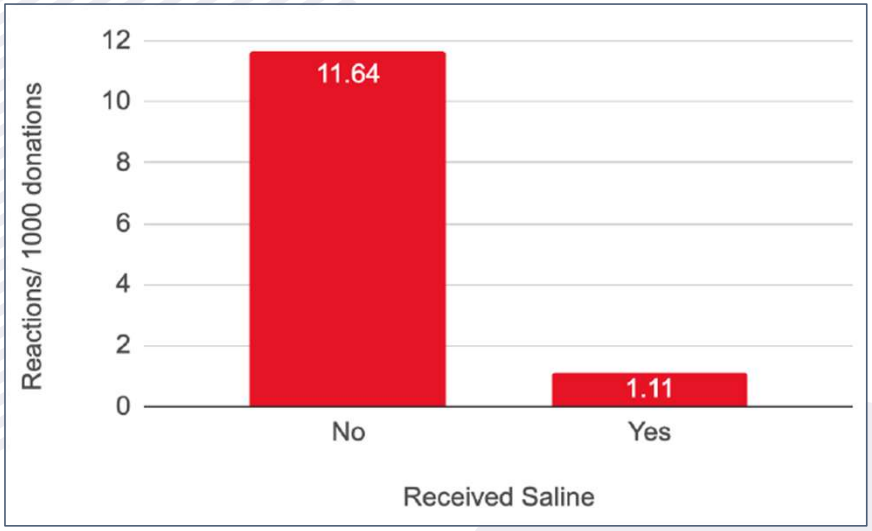
Figure 2: **Primary and secondary outcomes**
Statistical significance threshold was p<0·05 for the primary outcome and p<0·0125 for the four secondary outcomes.

Frequency of vasovagal reactions with large volume plasma donation in Canada

Khandelwal et al, AABB, 2023 and 2024

- Plasma donations between 1/6/2021 and 30/06/2024
- Progressive implementation of saline infusion if collection volume >562mL
- Variables examined: age, gender, height, weight, TBV, plasma volume, saline infusion, ..
- Descriptive analysis, logistic regression model
- Final model including variables independently associated with donor vasovagal reactions

Saline infusion	
Yes	157 (28.5%)
No	384 (69.7%)
Unknown	10 (1.8%)



- **VVR risk is higher when saline not infused *(p<0.0001*)**

Saline infusion	Adjusted Odds Ratio [OR,95%CI]	p-value
yes	ref	
no	10.296 [7.965 - 13.309]	*p<0.0001*

Differing mechanisms underlying fainting reactions associated with blood / plasma donation

- **Early-on**: neurocardiogenic (vasovagal) mechanism/reflex with **relative hypovolemia**
- **Later**: orthostatic intolerance in relation with **sustained intravascular volume deficit** (+/- secondary vasovagal response)

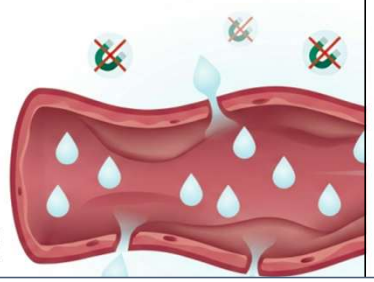
What is lost during plasma donation

Plasma Unit

=

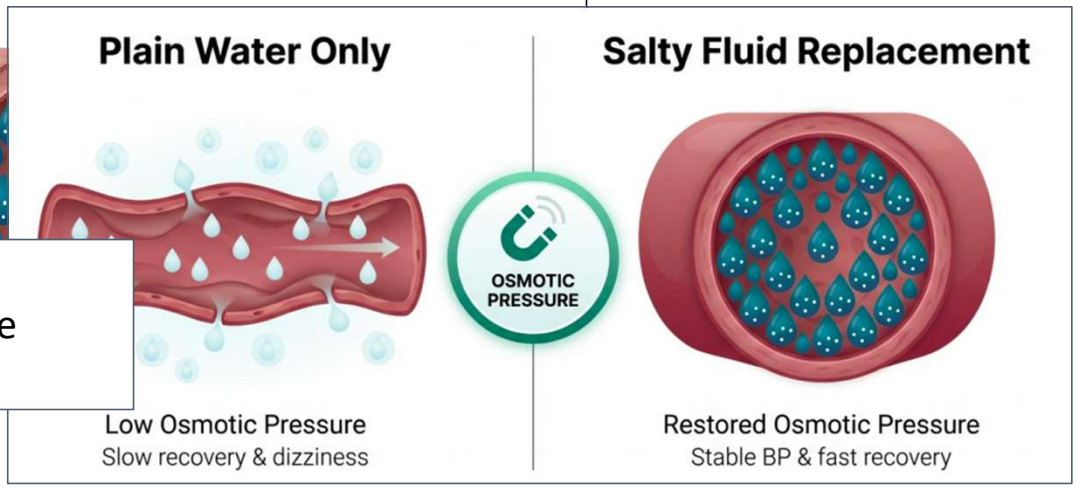
Osmotic Pressure: The Biological Magnet

The Effect of Drinking Plain Water Only



The Effect of Drinking or Infusing a

Sugar uptake slows fluid absorption, does not support intravascular volume expansion and may result in reactive hypoglycemia



How much salt is enough salt?

- A whole blood donation of 540 mL implies a loss of ≈ 320 ml of plasma and ≈ **2.9 g NaCl** (i.e., almost 1.2 g Na).
- A plasma donation of 750 ml implies a loss of ≈ **6.75 g NaCl** (i.e. ≈ 2.77 g Na)
- *A daily intake of 2.0 to 2.3 g Na (equivalent ≈* ***5 g NaCl****) is recommended (in real life: 3 to 4 g Na / day).*

- 500 ml of a sports drink may contain ≈ 0.32 g Na (+ water and glucose)(**≈ 0.77 g NaCl**)
- A (28 g) bag of pretzels may contain ≈ 0.34 g Na (≈ **0.82 g NaCl**)
- 500 ml of saline contains **4,5 g NaCl**

Studies including NaCl loading: how much ?

- Poles et al (English military, 1942): **9 g NaCl** in 1000 ml iv (saline)
- Morand et al (France, Evasion study): **0.68 g NaCl** in 500 ml po
- Kumar et al (India): **2.5 g NaCl** in 300 ml po
- Goldman et al (Canada): 0.45 g NaCl in a bag of salty snacks
- Lewin et al (Canada): 0.45 g NaCl in a bag of salty snacks
- Khandelwal et al (Canada, apheresis): 4.5 g NaCl in 500 ml iv (saline) +a salty snack (0.45 g NaCl): **4.95 g NaCl**
- Kaptoge et al (UK, Stride study): 0.35 g Na (≈ **0.84 g NaCl**) in 500 ml po
- Poreau et al (France, Predonpsy study, ongoing): 0.5 g NaCl in a bag of salty snacks

Saline infusion in plasma donors: current practices

Industry

250 to 500 ml saline infusion, most often at the end of the procedure

INTERNATIONAL QUALITY PLASMA PROGRAM

The IQPP Donor Safety Standard: part of a series of standards developed by Plasma Protein Therapeutics Association (PPTA) IQPP Standards Working Group.

IQPP Donor Safety Standard

Version 1.0
Implemented April 1, 2025

IQPP: Global Standards for Plasma Safety & Quality - PPTA

"Donor fluid administration:

- Centers shall have in place a program to administer fluids as part of the donation process.
- Administer a minimum of 250 mL of 0.9% NaCl solution (saline) i.v. to donors as part of the automated plasmapheresis process (In the United States, industry practice is to use 500 mL of 0.9% NaCl when available)."

Not-for-profit blood establishments

A large variety of practices:

- 250 to 500 ml saline at the end of the procedure
- 200 ml to 300 ml saline, fractioned during the procedure
- No saline infusion

Preventing the risk of (delayed) fainting in plasma donors

- Measures to prevent fainting reactions in plasma donors comprise **adjusting collected plasma volume** to donor characteristics, **applied muscle tension** exercises**, hydration** and **increased salt intake**, p.o. or i.v. (saline infusion).
- **Data** regarding efficacy of **saline infusion** in the setting of plasma donation is unfortunately limited, less so in the setting of whole blood donation.
- **Physiopathology of delayed fainting** - dangerous, and notoriously undereported - after whole blood or plasma donation **strongly favors salt intake** as a preventive method.
- All currently available apheresis are designed to **accommodate saline infusion**. The use of **dedicated connectors** (keyed connectors) prevents accidental inversion between citrate and saline lines.
- Saline infusion also ensures **tubing rinsing** and return to the donor of residual red blood cells, thus contributing to the **prevention of iron deficiency**.
- Saline infusion probably also **decreases fatigue** after plasma donation, and therefore **facilitates donor return**.

My (personal) take: if not in place, think about it!

And to all: Contribute to a high quality randomized trial assessing the impact of saline infusion on delayed fainting, fatigue, iron depletion and return rate in plasma donors.