



Physiology

Apheresis



Program

- ECV
- Fluid compartments
- Replacement of collected volume
- Calcium / Magnesium metabolism
- Use of citrate / heparine

ECV

Extra corporeal volume

“Volume of blood removed from the donor at any time. It includes all blood and plasma in collection packs and contained within the machine harness....”

- Collected component
- Blood in harness
- Blood taken for tests

ECV

- Important to know:
 - Volume disposable (also disposable blood warmer)
 - Volume to collect
 - TBV patient / donor
- Maximally 2% of TBV

Total blood volume

- 5 liter



ECV and apheresis

- **Europe:** maximal 20%.
- **USA:** No limits.
- **UK Red Book:** “During apheresis procedures the ECV should not exceed 15% TBV (excluding anticoagulant).”



ECV and apheresis

- Most patients without significant cardiovascular or pulmonary disease will tolerate an ECV and an ERCV of up to 15%.
- If the ECV or ERCV of a standard procedure will exceed 15%, or if the patient has significant cardiovascular disease, measures such as priming the circuit with a colloid or red cells should be considered.



Bruce C. McLeod: Apheresis Principles and Practice, 3rd edition, 2010

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Guide (standards)

- The collection volume (excluding anticoagulant) for each apheresis procedure must not exceed 16% of the estimated total blood volume. The total blood volume must be calculated on the basis of gender, height and weight.
- The volume of plasma (excluding anticoagulant) collected on each occasion must not exceed 750 mL



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15% ECV and Plasmapheresis

Female donor 1.70 m

- 750 mL
 - 650 mL
 - 550 mL
 - 450 mL
- TBV $\geq 6,667$ mL \rightarrow > 138 kg
 - TBV $\geq 6,000$ mL \rightarrow > 118 kg
 - TBV $\geq 5,333$ mL \rightarrow > 98 kg
 - TBV $\geq 4,667$ mL \rightarrow > 78 kg

Male donor 1.80 m

- 750 mL
 - 650 mL
 - 550 mL
- TBV $\geq 6,667$ mL \rightarrow > 122 kg
 - TBV $\geq 6,000$ mL \rightarrow > 102 kg
 - TBV $\geq 5,333$ mL \rightarrow > 82 kg

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TBV in children

Rule of thumb:

- Premature infant, at birth
 - Term new born infant
 - Children (>3 months)
- 90-105 mL/kg
 - 80-90 mL/kg
 - 70-75 mL/kg

Nadler's formula is not usable

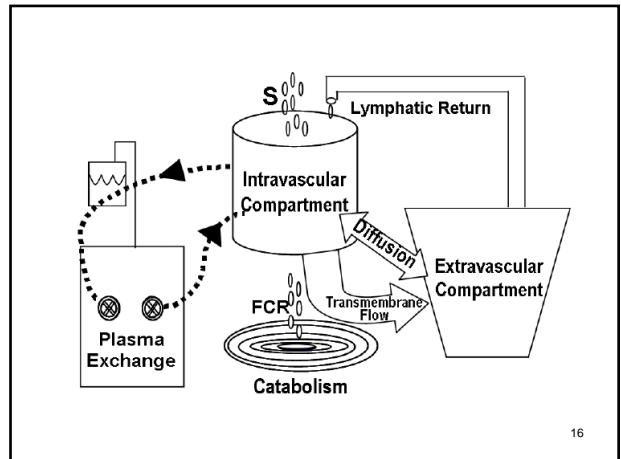
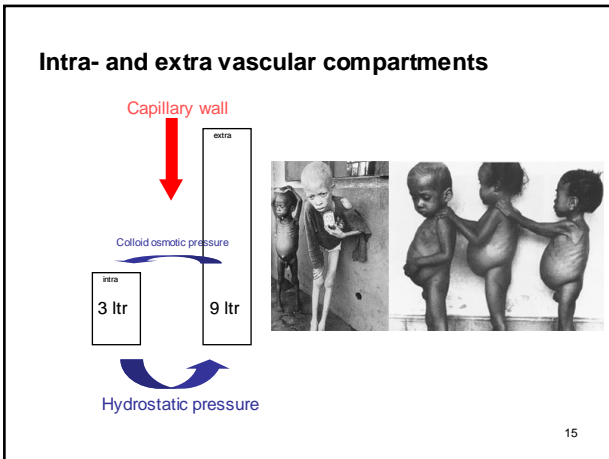
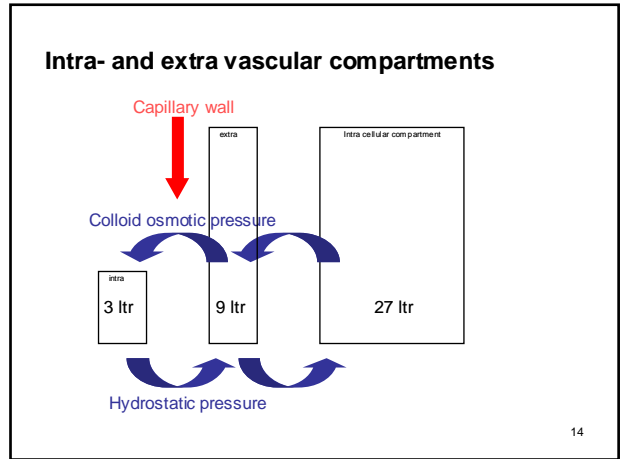
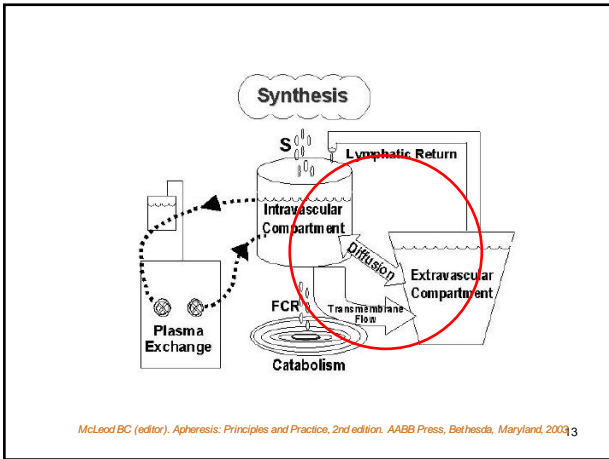
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ECV in children

- Volume disposable 150 – 250 mL
- Less variance in ECV in case of continuous systems
- (RBC) priming needed:
 - Depletion of >15% because of filling disposable
 - In case threatening the oxygen-carrying capacity by reduction of RBC volume
 - Usually if bodyweight is <20 kg

Note: if you prime..... Don't rinseback!!

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Therapeutic apheresis procedures

- Collection volume 1000 – 5000 mL
 - considerable volume of this is anticoagulant

COMPENSATION / REPLACEMENT IS NEEDED

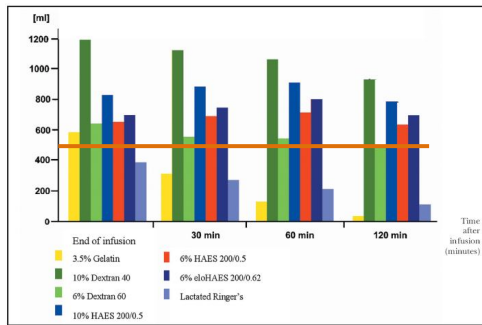
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Replacement fluids

- Crystalloids
 - Solutions of mineral salts or other water-soluble molecules, e.g. NaCl 0.9%
- Colloids
 - Fluids with larger insoluble molecules, e.g. starches, gelatins, albumin, plasma

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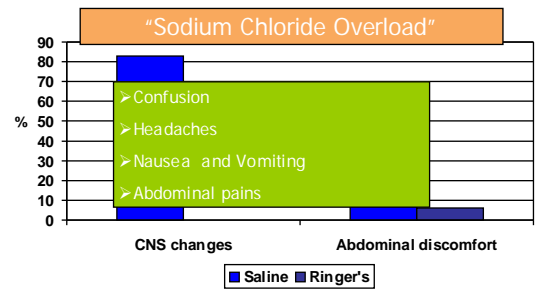
Replacement fluids



Van Zundert, et al. CPD Anaesthesia, 2006;8:131-149.

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Saline 0.9% vs Lactated Ringer's in Volunteers



Williams et al. Anesthesia and Analgesia, 1999.

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Exchange fluids and volume effects

		Initial volume effects (%)	Duration (hrs)
Crystalloids	NaCl 0.9%	20%	0-1
Colloids	HES 130 6%	100%	3-6
	HES 200 6%	100%	3-4
	HES 200 10%	145%	3-4
	Gelofusin®	70-80%	2-3
	Geloplasma®	60-80%	2-3
	Haemacel®	70%	2-3
	Dextran 5%	100%	2-4
	Dextran 10%	200%	2-4
	Dextran 6%	120%	6-8
	Albumin 20%	300%	2-8

Adapted from: van Zundert, et al. CPD Anaesthesia, 2006;8:131-149.

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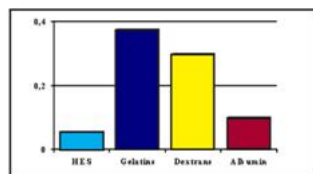
Replacement fluids can have side effects

CAVE RBC transfusion (risk of augmenting hyperviscosity)

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Replacement fluids

- Plasma
- Albumin
- Crystalloids
- Colloids



Van Zundert, et al. CPD Anaesthesia, 2007;9:43-57.

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Calcium



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Calcium

- 99% in the bones → calcium phosphate (± 24,500 mmol)

Extra cellular fluid: 22.5 mmol → 9 mmol in plasma (2.2 – 2.6 mmol/L)



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Plasma calcium

Total calcium 2.2 – 2.6 mmol/L (9 - 10.5 mg/dL)

- Ionized (free) calcium 1.1 – 1.4 mmol/L (4.5 – 5.6 mg/dL)
- Remainder bound mainly to albumen (± 50%)

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Calcium metabolism

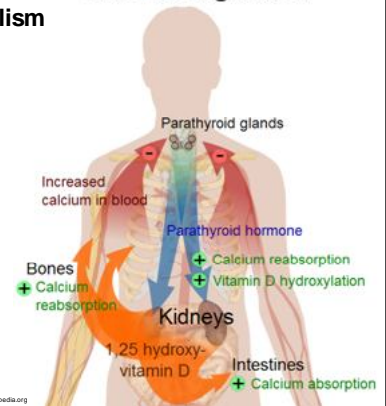
- Active intake by intestines
- Excretion via Kidney:
 - 250 mmol/day in pre-urine
 - Reabsorption of 245 mmol/day
- Exchange blood – bone

→ parathyroid hormone (PTH)

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Calcium metabolism

Calcium regulation



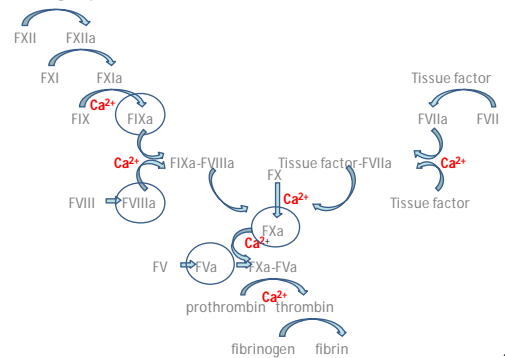
<http://www.ankipedia.org>

Function of Calcium

- Structural function → bones
- Signaling function → messenger for some hormones
- Enzymatic function → co-enzyme for clotting factors
- Function in transmission of nerve impulse
- Function in the contraction of muscles

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Clotting system



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Prevention of blood clotting by citrate



Luis Agote

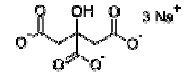
1914



Albert Hustin

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Citrate



- Trisodiumcitrate
 - Flavoring and buffering agent in drinks / food
 - Prevention of blood clotting in disposable / machine
 - Laxans
 - WHO "oral rehydration solution"



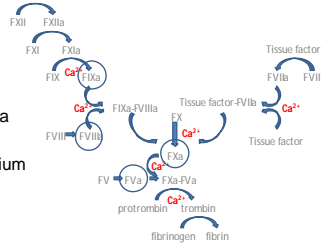
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Citrate

- Completely dissolved in plasma
- No binding to cells
- Chelates calcium and magnesium
- Prevents coagulation

Neutralized by:

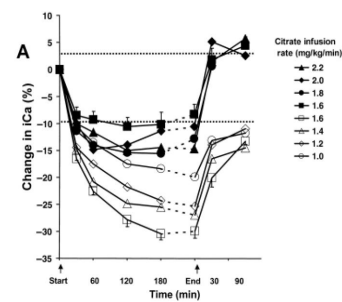
- Distribution throughout extra cellular fluid
- Rapid metabolism by the kidneys, liver and skeletal muscle



Jeff Winters, AABB Oct. 2007

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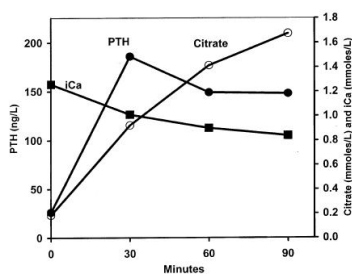
Serum calcium & citrate infusion



Bolin, Transfusion 2002

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Serum PTH, iCa and citrate during plt apheresis



McLeod BC, Szczepiorkowski JM, Wainstein R, Winters JL, eds. Apheresis: Principles and Practice, 3rd edition. Bethesda, MD: AABB Press, 2010

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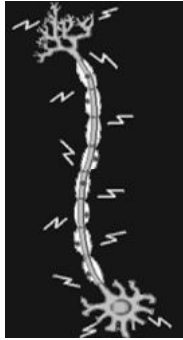
Function of calcium

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- Function in the contraction of muscles

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Hypocalcaemia by citrate

- Decrease in ionized calcium results in increased excitability of neurons to the point of spontaneous depolarization.



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Symptoms of hypocalcaemia

1. **Minor:** metallic taste and (peri-oral) tingling
Actions: Slow rate of infusion, return speed↓ / Increase the blood to citrate ratio
2. **Moderate:** metallic taste, (peri-oral) tingling, nausea, shivering, light-headedness, paraesthesia and tremors, hypotension
Actions: stop apheresis procedure keep needle in situ, Calcium tablets

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Symptoms of hypocalcaemia

3. **Severe:** metallic taste, tingling, nausea, shivering, light-headedness, paraesthesia and tremors, hypotension, carpedal spasm, muscle cramps + laryngeal spasm, complaints with swallowing, positive Chvostek's and Trousseau's sign, arrhythmia (longer QT interval)
Actions: stop apheresis procedure keep needle in situ: 10 mL calcium i.v.

Long term effects?

Comparison of bone density of 45 donors >100 PLT-apheresis with 40 donors <50 procedures.
35% of >100 procedures donors showed significant osteopenia.

Detke J. Clin Apheresis 2003

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Hypocalcaemia during apheresis

Therapy

- Return speed
- AC – WB ratio
- Milk products
- Oral calcium
- I.V. calcium
 - Bolus
 - Continuously

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Citrate → Metabolic Alkalosis & Hypokalemia

Additional factors to consider

- Presence of citrate in replacement fluids (e.g. FFP for TTP)
- Large volume PBSC collections (average drop Ca^{2+} of $11.3 \pm 7\%$)
- Renal disease preventing the excretion of bicarbonate
→ symptoms of hypocalcaemia ↑, suppression of respiratory rate
→ **Metabolic alkalosis**
- Metabolic alkalosis results in potassium uptake in cells → hypokalemia
Decrease in potassium and cardiac arrhythmia

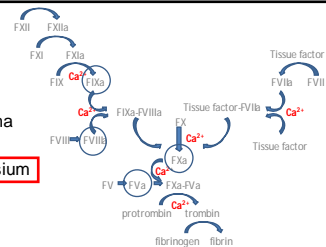
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Citrate

- Completely dissolved in plasma
- No binding to cells
- **Chelates calcium and magnesium**
- Prevents coagulation

Neutralized by:

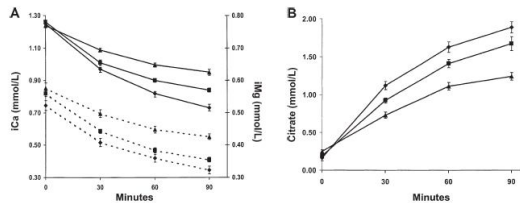
- Distribution throughout extra cellular fluid
- Rapid metabolism by the kidneys, liver and skeletal muscle



Jeff Winters, AABB Oct. 2007

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Serum magnesium during plateletapheresis



Bolan, et al. Transfusion 2001;41:1165-1171

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Plasma magnesium

Total magnesium 0.7 – 1.1 mmol/L (1.5 – 2.5 mg/dL)

- Ionized (free) magnesium 0.5 – 0.7 mmol/L (1.1 – 1.5 mg/dL)
- Remainder bound mainly to Albumen and globulins

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Magnesium

Involved in:

- Synthesis of nucleic acids
- Synthesis of proteins
- Intermediary metabolism
- Specific actions in
 - Neuromuscular systems
 - Cardiovascular systems

Mg²⁺ competes with Ca²⁺ for binding sites on proteins and membranes

Competitively inhibition of calcium

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Magnesium

Affects:

- Muscular contraction and relaxation including the heart and vascular muscles.
- Electrical activity of myocardial cells
- Stabilization of the axon
- The release of neurotransmitters

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Hypomagnesaemia

Caused by

- Redistribution of Mg
- Gastrointestinal
- Renal loss
- Renal disease
- Endocrinal
- Diabetes mellitus
- Alcoholism
- Miscellaneous
- Drugs
 - Diuretics
 - Cytotoxic drugs
 - Antibiotics
 - B adrenergic agents
 - Others

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Hypomagnesaemia

Citrate and hypocalcaemia

Electrolyte disturbance
• Hypokalaemia
• Hypocalcaemia
Neuromuscular and central nervous system
• Carpopedal spasm
• Convulsions
• Muscle cramps
• Muscle weakness, fasciculations, tremors
• Vertigo
• Nystagmus
• Depression, psychosis
• Athetoid movements & choreiform movements
Cardiovascular
• Atrial tachycardias, fibrillation
• Supraventricular arrhythmias
• Ventricular arrhythmias
• Torsade de pointes
• Digoxin sensitivity
Complications of magnesium deficiency
• Altered glucose homeostasis
• Atherosclerotic vascular disease
• Hypertension
• Myocardial infarction
• Osteoporosis
Miscellaneous
• Migraine
• Asthma
• Chronic fatigue syndrome
• Impaired athletic performance

Citrate → Hypomagnesemia

- Mg²⁺ also bound by citrate
- During plateletapheresis: 30% drop in magnesium levels
- Steeper decrease and recovers more slowly than calcium
- Muscle spasms & weakness
- Decreased vascular tonus (blood pressure) + abnormal cardiac contractility
- Interference with potassium and calcium homeostasis
- If suspected 8 mmol Mg²⁺ i.v. in 1 minute

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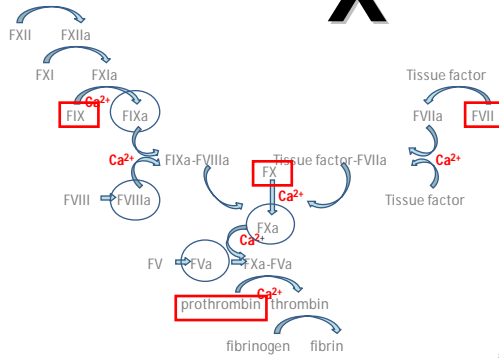
Apheresis procedures – Ca²⁺ / Mg²⁺

- Use of citrate
- AC – WB ratio
- Citrate in blood components transfused
- Albumen as substitution for collected volume

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Clotting system

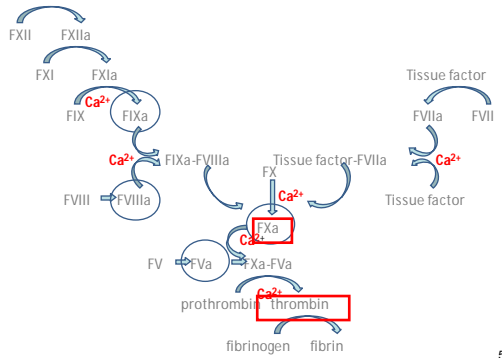
Ca²⁺



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Clotting system

Heparin?



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In summary

- ECV
- Fluid compartments
- Replacement of collected volume
- Calcium / Magnesium metabolism
- Use of citrate / heparine

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