Intraoperative Fluid Management

- The appropriate administration of intravenous fluids to maintain/achieve
  - Optimal intravascular volume and cardiac preload
  - Oxygen-carrying capacity
  - Coagulation status
  - Acid-base homeostasis
  - Electrolyte balance
- Intraoperative intravenous fluids
  - Composition
  - Volume
  - Timing of administration
- Influence of fluid management on postoperative outcome

Intraoperative Fluid Management: Outline

- Body fluid compartments
  - Volume
  - Composition
  - Capillary endothelial barrier
- Intravenous fluids
  - Crystalloids
  - Colloids
- Intraoperative fluid management

BODY FLUID COMPARTMENTS
Total Body Water (TBW) = 60% of Body Weight (BW)

Extracellular Volume (ECV) = 20% of BW

Intracellular Volume (ICV) = 40% of BW
(Includes RBCs)

\[
\begin{align*}
\text{Plasma Volume (PV)} & = \frac{1}{5} \\
\text{Interstitial Fluid Volume (IFV)} & = \frac{4}{5}
\end{align*}
\]

70 kg, 40 y old healthy male

Total Body Water: 42 L

Intracellular Volume = 28 L
Extracellular Volume = 14 L

Plasma Volume = 3 L

Interstial Fluid Volume = 11 L

% of Total Body Water

\[
\begin{array}{c|c|c|c}
\% \text{ of Total Body Water} & \% \text{ of Body Weight} & \text{Plasma} & \text{Interstitial fluid} \\
\hline
7 & 4 & 142 & 145 \\
4 & 16 & 10 \text{ mEq/L} & 10 \text{ mEq/L} \\
26 & 16 & 150 \text{ mEq/L} & 150 \text{ mEq/L} \\
67 & 40 & 40 \text{ mEq/L} & 40 \text{ mEq/L} \\
\end{array}
\]

CATIONS

[Na⁺] = 142 mEq/L
[K⁺] = 4 mEq/L
[Mg²⁺] = 2 mEq/L
[Ca²⁺] = 5 mEq/L
[Cl⁻] = 103 mEq/L
[HCO₃⁻] = 25 mEq/L
[HPO₄²⁻] = 2 mEq/L
[Proteins] = 17 mEq/L

ANIONS

[Cl⁻] = 145 mEq/L
[K⁺] = 4 mEq/L
[Mg²⁺] = 2 mEq/L
[Ca²⁺] = 5 mEq/L
[Cl⁻] = 117 mEq/L
[HCO₃⁻] = 27 mEq/L
[HPO₄²⁻] = 2 mEq/L
[Proteins] = 1 mEq/L

% of Body Weight

\[
\begin{array}{c|c|c|c}
\% \text{ of Body Weight} & \% \text{ of Total Body Water} & \text{Plasma} & \text{Interstitial fluid} \\
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\end{array}
\]
Body Fluid Compartments: Electrolyte Composition

- **Intracellular fluid**
  - Potassium is the major intracellular cation
  - Phosphate is the major intracellular anion

- **Extracellular fluids**
  - Electrolyte content of interstitial fluid and plasma is similar, except for the protein concentration
  - Sodium is the major extracellular cation
  - Chloride is the major extracellular anion

Plasma Osmolality

- Plasma osmolality: 280 – 290 mOsm/kg
- Osmolality is determined by the number of dissolved solutes in plasma
- $Na^+$ and its anions account for 90% of these solutes

\[
\text{Plasma osmolality} = (2 \times [Na^+]_{\text{plasma}}) + \frac{[\text{glucose}]}{18} + \frac{[\text{urea}]}{6}
\]

- Urea readily permeates the cell membrane

\[
\text{Effective plasma osmolality} = (2 \times [Na^+]_{\text{plasma}}) + \frac{[\text{glucose}]}{18}
\]

- There is an osmotic equilibrium between ICF and ECF

Intracellular – Extracellular Barrier

The cell membrane is the barrier between the intracellular and extracellular compartments
- ATP-dependent $Na^+/K^+$ pump exchanges 3 $Na^+$ for 2 $K^+$
  - Maintenance of the $[Na^+]$ and $[K^+]$ gradient

- Proteins (intracellular >> extracellular): no diffusion

Interstitial – Intravascular Barrier

- Electrolytes pass freely between plasma and interstitial fluid
- Proteins (plasma >> interstitial fluid concentration)
  - Intact capillary barrier: diffusion of proteins is very limited
  - Damaged capillary barrier: proteins diffuse between plasma and interstitial fluid
Interstitial – Intravascular Barrier

- Traditional model: Starling’s law of capillary filtration

\[ Q = kA \left( \frac{P_c - P_i}{\sigma} \right) \]

- Revised Starling model: Endothelial layer model (endothelial cells + glycocalyx)

- An endothelial layer, including endothelial cells and glycocalyx, acts as the vascular barrier and has an important role in the capillary fluid filtration

- (Endothelial glycocalyx: a glycoprotein and polysaccharide containing layer (0.5 – 3 µm) lining the luminal vascular endothelium)

- The interstitial colloid osmotic pressure has only a small role in fluid movements across the capillary endothelium

- The colloid osmotic pressure of fluid in the intercellular clefts (subglycocalyx) is the major determinant of the transcapillary flow

- Fluid movement from the intravascular to the interstitial space is possible

- Absorption of fluid into the intravascular space is not possible

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*Reitsma et al., Pflugers Arch – Eur J Physiol (2007) 454*  

Comparison of traditional and revised views of the endothelial semipermeable membrane and the forces acting on it.

(A) Traditional view of continuous endothelium as a semipermeable membrane.

(B) The glycocalyx-cleft model identifies glycocalyx as a semipermeable layer. Its underside is subjected to the COP of fluid high inside the intercellular cleft rather than ISF, with important functional consequences.

Levick and Michel, Cardiovasc Res 2010; 87: 198-210
Capillary Endothelial Glycocalyx

- The capillary endothelial glycocalyx has a role in:
  - Vascular permeability
  - Mechanotransduction (shear-stress sensing) → regulation of vasodilation
  - Blood – endothelial cell interactions
  - Control of the micro-environment affecting molecules involved in coagulation and inflammation
- Glycocalyx degradation can be caused by:
  - Inflammation
  - Sepsis
  - Ischemia / reperfusion injury
  - Diabetes mellitus (acute hyperglycemia)
  - Hypovolemia
  - ANP-mediated
    - Avoid inadequate IV volume administration ("preloading") in a normovolemic patient
    - Micovascular dysfunction, increased capillary permeability and tissue edema

INTRA VENOUS FLUIDS

Crystalloid Intravenous Solutions

- Aqueous solution (sterile) + low molecular weight molecules
  - Electrolytes
  - Glucose
- Pass freely across a semi-permeable membrane
  - Intravascular – interstitial barrier is permeable for solutes in crystalloids
  - Rapid distribution and equilibration within the extracellular fluid compartment
  - Isotonic, hypertonic, or hypotonic
  - No allergic reactions
  - Inexpensive

Intravenous fluid = Medication

- Indications
- Contraindications
- Side effects
**Colloid Intravenous Solutions**

- Crystalloid + high molecular weight molecules
  - NaCl 0.9% or balanced electrolyte solution
  - Macromolecules
  - Human albumin
  - (semi-)Synthetic: starches, gelatins, dextrans
- Do not pass freely across a semi-permeable membrane
  - Intravascular – interstitial barrier: semi-permeable for macromolecules
- Initial volume of distribution: equivalent to plasma volume
- Colloids maintain plasma colloid oncotic pressure
- Colloids remain longer in the intravascular space than crystalloids
- Used as plasma volume expanders
- Isotonic, Hypertonic
- Adverse reactions
- More expensive than crystalloids

**Intravenous Fluids: Osmolality and Tonicity**

- **Osmolality**
  - Determined by the number of particles dissolved per kilogram of an aqueous solution
  - Plasma osmolality ≈ 295 mOsm/kg
- **Tonicity**
  - "Effective osmolality"
  - Cell membrane permeable for the solutes in an iv fluid (e.g. glucose)
    - No redistribution of water between EC and IC
  - Solute in iv fluid do not move freely across cell membrane (e.g. sodium, chloride)
    - Redistribution of water between EC and IC is possible depending on the osmolality of the iv fluid
      - Osmolarity of iv fluid = osmolality of plasma → no redistribution of water (isotonic iv fluid)
      - Osmolarity of iv fluid > osmolality of plasma → redistribution of water
        - Hypotonic iv fluid (< plasma osmolality): water moves from extracellular to intracellular
        - Hypertonic iv fluid (> plasma osmolality): water moves from intracellular to extracellular

**Intravenous Fluids: Distribution**

- The distribution of iv fluids depends on
  - Composition of the iv fluid
  - Integrity of the glycocalyx (barrier between the EC and IC compartment)
  - Intravascular volume status
- Tonicity of iv fluid determines distribution between EC and IC compartment
  - Isotonic: no effect on cell volume (no movement of water between EC and IC compartment)
    - Osmolarity EC compartment = osmolality IC compartment
  - Hypotonic: cell swelling (water moves from EC to IC compartment)
    - Osmolarity EC compartment < osmolality IC compartment
  - Hypertonic: cell shrinking (water moves from IC to EC compartment)
    - Osmolarity EC compartment > osmolality IC compartment

### Solution Table

<table>
<thead>
<tr>
<th>Solution</th>
<th>Osmolarity (mOsm/L)</th>
<th>Na+ (mEq/L)</th>
<th>Cl⁻ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
<th>Ca²⁺ (mEq/L)</th>
<th>Mg²⁺ (mEq/L)</th>
<th>Glucose (g/L)</th>
<th>Lactate (mEq/L)</th>
<th>Acetate (mEq/L)</th>
<th>Gluconate (mEq/L)</th>
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</thead>
<tbody>
<tr>
<td>D₂W</td>
<td>278</td>
<td>154</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NaCl 0.9%</td>
<td>308</td>
<td>154</td>
<td>154</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>D₂O₃NaCl 0.3%</td>
<td>285</td>
<td>51</td>
<td>33</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Lactated Ringer’s</td>
<td>273</td>
<td>130</td>
<td>109</td>
<td>4</td>
<td>3</td>
<td>28</td>
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<td></td>
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</tr>
<tr>
<td>D₅L</td>
<td>555</td>
<td>130</td>
<td>109</td>
<td>4</td>
<td>3</td>
<td>50</td>
<td>28</td>
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<tr>
<td>Plasmalyte A</td>
<td>295</td>
<td>140</td>
<td>98</td>
<td>5</td>
<td>3</td>
<td>27</td>
<td>23</td>
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<tr>
<td>1.4% NaHCO₃</td>
<td>333</td>
<td>167</td>
<td>167</td>
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<tr>
<td>8.4% NaHCO₃</td>
<td>2000</td>
<td>1000</td>
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</tbody>
</table>
**Intravenous Fluids: Initial Volume of Distribution**

<table>
<thead>
<tr>
<th>Plasma</th>
<th>Interstitial space</th>
<th>Intracellular space</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dextrose 5 %</td>
<td></td>
</tr>
<tr>
<td>Lactated Ringer’s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NaCl 0.9 %, Plasmalyte</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HES</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NaCl 0.9 % (Normal Saline)**

- 308 mOsm/kg: slightly hypertonic
- Composition differs significantly from plasma
  - $[\text{Na}^+] = 154 \text{ mEq/L} = [\text{Cl}^-] > \text{ excess } \text{Cl}^- (+50 \% \text{ vs plasma}) > \text{ excess } \text{Na}^+ (+10 \% \text{ vs plasma})$
- Risk of hyperchloremic metabolic acidosis (Stewart approach)
  - SID of NaCl 0.9 % = 0
  - Large volumes of NaCl 0.9 % $\rightarrow$ SID of plasma decreases $\rightarrow$ Metabolic acidosis
- Clinical implications of hyperchloremia are unclear
  - Renal dysfunction?
    - Renal vasoconstriction, decreased renal perfusion, reduced GFR
    - Increased risk of contrast nephropathy?
    - Reduced gastric blood flow, impaired gastric emptying?
    - Reduced cardiac contractility?

**NaCl 0.9 % (Normal Saline)**

- Avoid large volumes of NaCl 0.9 % intraoperatively
  - Usually there is no indication for NaCl 0.9 % intraoperatively
  - Postoperative excretion of a high sodium load and free water can be problematic
    - Stress response to surgery $\rightarrow$ retention of sodium and water
  - In spite of this, it is still widely used……
- Limited indications
  - Hyponatremia
  - Hypochloricemic metabolic alkalosis
    - E.g. persistent vomiting

**Balanced Electrolyte Solutions**

<table>
<thead>
<tr>
<th></th>
<th>NaCl (mEq/L)</th>
<th>Ca (mEq/L)</th>
<th>Mg (mEq/L)</th>
<th>K (mEq/L)</th>
<th>Cl (mEq/L)</th>
<th>HCO₃ (mEq/L)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>230</td>
<td>142</td>
<td>103</td>
<td>4.5</td>
<td>5</td>
<td>3/4</td>
<td>7.3</td>
</tr>
<tr>
<td>Lact. Ringer’s</td>
<td>273</td>
<td>130</td>
<td>109</td>
<td>4</td>
<td>3</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Plasma-Lyte A</td>
<td>295</td>
<td>140</td>
<td>98</td>
<td>5</td>
<td>3</td>
<td>27/23</td>
<td></td>
</tr>
</tbody>
</table>

- Electrolyte composition similar to that of extracellular fluid
- Balanced electrolyte solutions contain a buffer
  - Lactate, acetate, gluconate
  - In vivo metabolized to generate HCO₃⁻ (and CO₂)
**Lactated Ringer’s (Hartmann)**

- Slightly hypotonic
  - 273 mOsm/L → slightly hypo-osmotic compared to plasma
  - 100 mL free water/L
  - Avoid large volumes in brain surgery
- Contains Ca\(^{2+}\) (3 mEq/L)
- Buffer: Lactate
  - Converted to bicarbonate (liver, kidneys)
  - Increase of plasma glucose (clinically not significant)

### Table: Lactated Ringer’s vs Plasma

<table>
<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>Lact. Ringer’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolality (mOsm/L)</td>
<td>290</td>
<td>273</td>
</tr>
<tr>
<td>Na(^{+}) (mEq/L)</td>
<td>142</td>
<td>130</td>
</tr>
<tr>
<td>K(^{+}) (mEq/L)</td>
<td>103</td>
<td>109</td>
</tr>
<tr>
<td>CO(_2) (mEq/L)</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>HCO(_3) (mEq/L)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>1.3</td>
<td>28</td>
</tr>
</tbody>
</table>

**Plasma-Lyte A**

- Isotonic
  - 295 mOsm/L → iso-osmotic with plasma
  - Isotonic (no free water)
- Contains Mg\(^{2+}\) (3 mEq/L)
- Buffers
  - Acetate: converted to HCO\(_3\) (extrahepatic metabolism, in most tissues)
  - Gluconate: metabolised to CO\(_2\) and H\(_2\)O but alkalinizing effect is weak

### Table: Plasma-Lyte A vs Plasma

<table>
<thead>
<tr>
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<th>Plasma-Lyte A</th>
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<td>Glucose (mg/dL)</td>
<td>27</td>
<td>23</td>
</tr>
</tbody>
</table>

**Dextrose 5 % (1)**

- Glucose 50 g/L
- 278 mOsm/L → almost iso-osmotic with plasma
- Hypotonic because glucose is rapidly metabolized → free water
  - Distributes over total body water (EC + IC)
- Healthy volunteers: elimination half-life = 15 min
  - Elimination: insulin-dependent uptake by the body cells
  - Diabetes mellitus: slower elimination
  - Prolonged elimination during surgery: e.g. laparoscopic cholecystectomy = 30 min
- Intraoperative stress response → Risk of hyperglycemia
  - Aggravation of ischemic neurologic injury
  - Wound edema (plasma glucose > 180 mg/dL)
  - Osmotic diuresis
  - Increased morbidity and mortality in critically ill patients
  - Use glucose-containing solutions only for specific indications, not for routine maintenance or resuscitation

**Dextrose 5 % (2)**

- Indications for intraoperative glucose administration
  - Neonates and infants (< 6 months): at risk for hypoglycemia
  - Basal infusion rate (risk of hypokalemia)
  - Insulin-dependent diabetics
  - Patients receiving total parenteral nutrition before surgery
  - Rebound hypoglycemia
  - Pathology-related indications, including:
    - Insulinoma
    - Prolonged fasting
    - Specific metabolic syndromes (e.g. methylmalonic acidemia)
    - Hypokalemic hypotremia
    - Hyperkalemia
  - ±/− insulin
### Colloids

<table>
<thead>
<tr>
<th>Solution</th>
<th>Osmolarity (mOsm/L)</th>
<th>In vitro COP (mmHg)</th>
<th>Initial volume effect (%)</th>
<th>Na⁺ (mEq/L)</th>
<th>Cl⁻ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
<th>Ca²⁺ (mEq/L)</th>
<th>Mg²⁺ (mEq/L)</th>
<th>Other</th>
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<td>Plasma</td>
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<td>142</td>
<td>103</td>
<td>4.5</td>
<td>5</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin 4 or 5 %</td>
<td>300</td>
<td>19</td>
<td>80 - 90</td>
<td>130 - 160</td>
<td>128</td>
<td>0 - 2</td>
<td></td>
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</tbody>
</table>

**Indications are limited**

### Albumin (4 or 5 %)

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</table>

**Indications are limited**

- Derived from pooled human blood or plasma
- Heat-treated to minimize risk of virally transmitted diseases
- High cost
- Limited supply
- Reimbursed for specific indications only

### Albumin (4 or 5 %)

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<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Indications are limited**

- Isotonic and iso-oncotic compared to plasma
- Initial plasma volume expansion ≈ 80 % of the infused volume
- Plasma volume expansion ≈ 2.5 h (healthy volunteers)
- Low incidence of allergic reactions
- No advantages in terms of mortality in ICU patients
- SAFE study: albumin 4 % associated with higher mortality than NaCl 0.9 % (33 % vs 20 %) in patients with head injury
Hydroxyethyl Starch (HES) (1)

- Amylopectin derivative produced from maize or potato starch
- Hydroxyethyl substitution at positions C2, C3 or C6 of glucose molecule (majority at C2)
- Hydrolysis to obtain the required molecular weight (MW)

<table>
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<tr>
<th>Solution</th>
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<td>142</td>
<td>103</td>
<td>4.5</td>
<td>5</td>
<td>3</td>
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<tr>
<td>Tetraspan® (6 % HES 130/0.42)</td>
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<td>36</td>
<td>~ 100</td>
<td>140</td>
<td>118</td>
<td>4</td>
<td>2.5</td>
<td>1</td>
<td>Starch</td>
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<tr>
<td>Volulyte® (6 % HES 130/0.40)</td>
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<td>36</td>
<td>~ 100</td>
<td>137</td>
<td>110</td>
<td>4</td>
<td>1.5</td>
<td>Starch</td>
<td></td>
</tr>
</tbody>
</table>

Hydroxyethyl Starch (HES) (2)

- HES is mixed in NaCl 0.9 % or a balanced electrolyte solution
  - NaCl 0.9 %: risk of hyperchloremic metabolic acidosis
- Plasma volume expansion
  - Initial plasma volume effect ≈ 100 %
  - Duration of volume expansion: 4 – 6 h
  - Volume effect is greater during anesthesia-induced hypotension
  - Volume effect lasts longer when given to replace hemorrhage

Hydroxyethyl Starch (HES) (3)

- HES molecules / solutions differ in physicochemical properties
  - Concentration
  - In vitro MW (average, range)
  - Degree of hydroxyethyl substitution: determines resistance to degradation
  - C2:C6 ratio: refers to site of substitution and is a measure of half-life
  - Extent and range of metabolism: In vivo molecular weight distribution over time
  - Different clinical effects and side effects
- Elimination of HES molecules is complex
  - Renal excretion:
    - Smallest molecules (< 60-70 kDa) are quickly eliminated
    - Larger molecules require cleavage by alpha-amylase into smaller fragments before being excreted
  - Phagocytosis by the reticuloendothelial system
    - Remnants may be found in liver and spleen after years
  - After 72 hrs, ~ 60 % of the molecules in urine
- Intravascular volume effect is much shorter than the half-life of HES molecules

Hydroxyethyl Starch (HES) (4)

- Side effects
  - Deposits in skin, liver, muscle, spleen, endothelial cells, kidneys
  - Pruritus (in up to 22% of patients)
  - Coagulation disturbances:
    - Interference with von Willebrand factor, factor VIII
    - Platelet dysfunction
  - Anaphylactic / anaphylactoid reactions
  - Renal toxicity:
    - ICU: increased incidence of renal dysfunction, renal replacement therapy
    - Increased mortality in patients with sepsis
Hydroxyethyl-starch solutions (HES) no longer to be used in patients with sepsis or burn injuries or in critically ill patients

HES will be available in restricted patient populations

Increased risk of renal dysfunction and mortality

HES: Guidelines for Clinical Use (1)

- HES should not be used in critically ill patients, in patients with sepsis or burn injuries
  - Increased risk of mortality, renal dysfunction, coagulopathy
  - Clinical studies (ICU patients)
    - "CRISTAL" trial (JAMA 2013; 310: 1809-17)
- Avoid HES if any contraindication is present

HES: Guidelines for Clinical Use (2)

- HES can be used in acute blood loss with hypovolemia if colloids are insufficient under the following conditions:
  - Confirmed hypovolemia due to acute blood loss
  - Acute situation (< 6 h of onset of blood loss)
  - Lowest effective dose for the shortest period of time
    - Guided by hemodynamic monitoring
    - Not longer than 24 h
    - Only last-generation HES solutions
    - Maximum dose (for 6% HES 130/0.4): 30 mL/kg
    - Absence of any contraindication
    - Monitoring of kidney function
- Avoid the use of HES in children
  - Insufficient safety data

Gelatins

<table>
<thead>
<tr>
<th>Solution</th>
<th>Osmolarity (mOsm/L)</th>
<th>In vitro COP (mEq/L)</th>
<th>Initial volume effect (%)</th>
<th>Na⁺ (mEq/L)</th>
<th>Cl⁻ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
<th>Ca²⁺ (mEq/L)</th>
<th>Mg²⁺ (mEq/L)</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>295</td>
<td>142</td>
<td>103</td>
<td>4.5</td>
<td>5</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isogel® (4% gelatin)</td>
<td>284</td>
<td>100</td>
<td>151</td>
<td>103</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>Gelatin</td>
<td></td>
</tr>
<tr>
<td>Gelofusine® (4% gelatin)</td>
<td>274</td>
<td>33</td>
<td>70-90</td>
<td>154</td>
<td>120</td>
<td></td>
<td></td>
<td>Gelatin</td>
<td></td>
</tr>
</tbody>
</table>
Gelatin: Isogelo® (Gelatin 4 %)

- Composition
  - Succinylated gelatin 40 g/L (from bovine collagen)
  - Na⁺ = 154 mEq/L, Cl⁻ = 120 mEq/L
- Average molecular weight: 26 500 Da
- Plasma volume expansion
  - Initial effect ~ 100 %
  - Duration of volume expansion: 4 – 5 hrs
- Minimal effect on coagulation
- Anaphylactic / anaphylactoid reactions
  - Severe reactions: 0.05 – 0.1 % of patients

Gelatins and anesthesia UZ Leuven: adhere to the guidelines for HES

Balanced Electrolyte Solutions: Pharmacokinetics in Healthy Volunteers

- Distribution clearance: Distribution of fluid from plasma to interstitial space
  - Distribution half-life = 8 min
  - Within 25 – 30 min equilibration is complete
    - ~ 33 % of the infused fluid is retained intravascularly (disregarding excretion)
    - ~ 20 % of the infused fluid is retained intravascularly (some excretion is present)
  - Hypotension: reduced distribution clearance
- Elimination clearance: Balanced electrolyte solutions are eliminated rapidly (kidneys)
  - Half-life \( T_{1/2} \) = Time required for elimination of 50 % of the infused volume
  - \( T_{1/2} \) varies for different crystalloids
    - Median \( T_{1/2} \): 
      - NaCl 0.9 %: 110 min
      - Ringer’s lactate: 50 min
    - 50 – 80 % of 2 L of lactated Ringer’s is eliminated within 2 h
Longer elimination half-life: increased volume expansion of plasma and interstitial fluid

Balanced Electrolyte Solutions during Anesthesia and Surgery (1)

- General anesthesia with mechanical ventilation and surgery: retarded elimination of crystalloids
  - $T_{1/2}$ is significantly increased
  - 10 – 20% of 2 L of lactated Ringer’s is eliminated within 2 h
    - Awake volunteers: 50 - 80% 
    - Activation of renin-angiotensin axis, vasodilation, lower blood pressure
    - Facilitates edema formation (retained fluid distributes in plasma and interstitial space)
- Anesthesia without mechanical ventilation and without surgery does not affect $T_{1/2}$ when MAP is maintained
- Hypotension: 100% volume effect
  - MAP decrease of ≥ 20%
  - SAP decrease of ≥ 30%

Balanced Electrolyte Solutions during Anesthesia and Surgery (1)

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  - MAP decrease of ≥ 20%
  - SAP decrease of ≥ 30%
- Replacement of intraoperative blood loss
  - Volume blood loss: balanced electrolyte solution ≈ 1:1 - 2
Plasma volume relative to baseline when Ringer’s acetate solution is infused according to the 3 : 1 rule over 30 min after 900 ml of blood has been withdrawn from male volunteers weighing 76 kg (A). To reach normovolemia, a much smaller amount of Ringer should be infused. Titration is necessary to maintain normovolemia (B).

Half-Life of Colloids

- **$T_{1/2}$** for plasma volume expansion
  - Hydroxyethyl starch 130/0.4: 110 (103 – 166) min (median, 25th – 75th percentile range)
  - Albumin 5 %: 110 (79 – 348) min
  - The same during anesthesia and surgery without hypotension as in healthy volunteers
  - Hypotension (anesthesia-induced): $T_{1/2}$ for plasma volume expansion increases
  - Hypovolemia: $T_{1/2}$ for plasma volume expansion increases
  - Longer-lasting than for crystalloids

- **$T_{1/2}$** for the rate of elimination of oncotic macromolecules
  - Hydroxyethyl starch 130/0.4: 12 hrs
  - Albumin 12 – 16 hrs
  - Macromolecules persist for many hours outside the bloodstream

Surgery and Interstitial Fluid Accumulation

- Prolonged elimination $T_{1/2}$
  - Longer duration of plasma expansion
  - Interstitial fluid accumulation (lasting several days)
- Postoperative period
  - Fast return to normal $T_{1/2}$ for crystalloids (elective surgery)
  - Trauma and emergency surgery: prolonged $T_{1/2}$ in the postoperative period?
  - Postoperatively fluid will move from the interstitium into the plasma
  - Distribution of colloids into the interstitium
    - No detailed studies
    - Macromolecules in the interstitium
    - Refractive edema? Insufficient data
  - Inflammation and sepsis: Disruption of the endothelial glycocalyx
    - Colloids: leakage of macromolecules into the interstitium → increasing edema

Crystalloids versus Colloids

- Heavily debated for years
- Meta-analyses show no difference in mortality, except for subgroups of patients
  - A randomized trial in critically ill patients comparing 4% albumin with NaCl 0.9% indicated a higher mortality rate in a subset of patients with traumatic brain injury
  - Clinical data show a significantly increased mortality, a higher need for renal replacement therapy and a higher rate of severe bleeding in septic patients receiving hydroxyethyl starch for acute volume resuscitation in comparison with crystalloids
- Generally there is no outcome benefit for colloids over crystalloids
Crystalloids – Colloids: General Remarks

- Crystalloids, when given in sufficient amounts, are just as effective as colloids in restoring intravascular volume.
- Replacing an intravascular volume deficit with crystalloids generally requires two times the volume needed when using colloids.
  - Severe intravascular fluid deficits can be more rapidly corrected when using colloid solutions.
- The rapid administration of large amounts of crystalloids (> 4 - 5 L) is more frequently associated with tissue edema.
- Outcome data show no advantage for colloids in comparison with crystalloids.
  - One colloid is not superior over another.

Assessment of Intravascular Volume Status

- Clinical signs and symptoms of dehydration (tachycardia, hypotension, oliguria):
  - Not sensitive
  - Not specific
  - Do not allow an accurate assessment of a patient’s fluid status.
- Laboratory results:
  - Not specific
  - Do not allow an accurate assessment of a patient’s fluid status.
- Hemodynamic measurements:
  - Static hemodynamic parameters are not a reflection of fluid status.
  - Functional hemodynamic parameters: assessment of fluid responsiveness.
- Fluid responsiveness: Need for iv fluids.

All measurements should be interpreted in view of the clinical setting.
Fluid Loss: Laboratory Changes

Laboratory signs of dehydration include:
- Rising hematocrit
- Progressive metabolic acidosis
- Lactate
- Urinary specific gravity > 1.010
- Urinary sodium < 10 mEq/L
- Urinary osmolality > 450 mOsm/kg
- Hypernatremia
- BUN to creatinine ratio > 10:1

Hemodynamic Parameters

- Static “volume” parameters: no good correlation with intravascular volume status
  - Central venous pressure
  - (Swan-Ganz catheter: no routine use)
- Functional hemodynamic parameters: serial measurements to assess fluid responsiveness
  - Transesophageal echocardiography
  - Esophageal Doppler
  - Various minimally invasive systems to monitor changes in stroke volume / cardiac output

Algorithms for preoperative / intraoperative hemodynamic optimization (goal-directed fluid therapy)

Perioperative Fluid Losses

- Preoperative fluid deficit
  - Preoperative fasting
  - Bowel preparation
  - Pathology-related fluid losses
- Intraoperative fluid losses
  - Basal fluid losses
  - Surgical blood loss
  - (Redistribution of extracellular fluid, “Third space loss”?)
- Postoperative fluid losses
  - Basal fluid losses
  - Surgery-related fluid losses
  - Pathology-related fluid losses

Preoperative Fluid Deficit (1)

- Preoperative fasting
  - Routine preoperative fasting causes no significant intravascular fluid deficit
  - Theoretically: basal fluid loss/h x hours npo
  - Prolonged periods of fasting may cause an intravascular fluid deficit
  - Generally no correction necessary
- Mechanical bowel preparation
  - Significant fluid losses (1 – 3 L) are possible
    - Electrolyte disturbances: hypokalemia, hyperphosphatemia, hypocalcemia, hyponatremia or hypernatremia, hypomagnesemia
  - Avoid if possible
    - Start IV balanced electrolyte solution the night before surgery
- Pathology-related fluid (and electrolyte) losses / deficits
Preoperative Fluid Deficit (2)

- Preoperative fasting
- Mechanical bowel preparation
- Pathology-related fluid (and electrolyte) losses / deficits
  - E.g. GI losses, wound and burn edema, pleural effusion, ascites
  - Volume and composition varies according to the etiology
  - Balanced electrolyte solution +/- additional electrolytes
  - Albumin 5% may be indicated (e.g. ascites)
  - Assess intravascular volume status

Anesthesia and Vasodilation

- General anesthesia
- Neuraxial anesthesia
  - Decreased sympathetic tone
  - Avoid giving fluids to compensate for vasodilation induced by anesthesia
  - There is no real fluid loss
  - Hemodynamic changes are temporary
  - R/ Vasopressor

---

### Volume and Composition of Gastrointestinal Fluids

<table>
<thead>
<tr>
<th>Fluid source</th>
<th>24-h volume (mL)</th>
<th>Na⁺ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
<th>Cl⁻ (mEq/L)</th>
<th>HCO₃⁻ (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saliva</td>
<td>500 - 2000</td>
<td>2 - 10</td>
<td>20 - 30</td>
<td>8 - 18</td>
<td>30</td>
</tr>
<tr>
<td>Stomach</td>
<td>1000 - 2000</td>
<td>60 - 100</td>
<td>10 - 20</td>
<td>100 - 130</td>
<td>0</td>
</tr>
<tr>
<td>Pancreas</td>
<td>300 - 800</td>
<td>135 - 145</td>
<td>5 - 10</td>
<td>70 - 90</td>
<td>95 - 120</td>
</tr>
<tr>
<td>Bile</td>
<td>300 - 600</td>
<td>135 - 145</td>
<td>5 - 10</td>
<td>90 - 130</td>
<td>30 - 40</td>
</tr>
<tr>
<td>Jejunum</td>
<td>2000 - 4000</td>
<td>120 - 140</td>
<td>5 - 10</td>
<td>90 - 140</td>
<td>30 - 40</td>
</tr>
<tr>
<td>Ileum</td>
<td>1000 - 2000</td>
<td>80 - 150</td>
<td>2 - 8</td>
<td>45 - 140</td>
<td>30</td>
</tr>
<tr>
<td>Colon</td>
<td>-</td>
<td>60</td>
<td>30</td>
<td>40</td>
<td>-</td>
</tr>
</tbody>
</table>

Intraoperative Fluid Losses / Shifts

- Basal fluid losses
- Surgical blood loss
- Fluid shift from surgical trauma and inflammation: ‘Third space fluid losses’?
Basal water losses parallel energy expenditure

Maintenance fluids (hospitalized pts): 100 ml/100 kcal

From Holliday MA and Segar WE, Pediatrics (1957), 19

Computed need for average hospital patients

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Rate (mL/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>For the first 10 kg</td>
<td>4 mL/kg/hr</td>
</tr>
<tr>
<td>For the next 10 kg</td>
<td>40 mL/hr + 2 mL/kg/hr</td>
</tr>
<tr>
<td>For weight &gt; 20 kg</td>
<td>40 mL/hr + 20 mL/hr + 1 mL/kg/hr</td>
</tr>
</tbody>
</table>

Daily Maintenance Fluid Requirements for a 70 kg Adult

<table>
<thead>
<tr>
<th>Water (mL/24 hr)</th>
<th>Electrolytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Insensible Perspiration</td>
<td>400</td>
</tr>
<tr>
<td>Lungs Insensible</td>
<td>400</td>
</tr>
<tr>
<td>Kidneys Urine</td>
<td>1500</td>
</tr>
<tr>
<td>GI tract Feces</td>
<td>100</td>
</tr>
<tr>
<td>Total / 24 hr</td>
<td>2500 mL</td>
</tr>
</tbody>
</table>

Intraoperative Basal Fluid Losses

- Increased insensible fluid losses?
  - Generally overestimated in the past
- $1 = 1.5 \text{ mL/kg/hr of a balanced electrolyte solution}$

- 4 – 2 – 1 rule

<table>
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<tr>
<th>Weight (kg)</th>
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<tr>
<td>For the next 10 kg</td>
<td>40 mL/hr + 2 mL/kg/hr</td>
</tr>
<tr>
<td>For weight &gt; 20 kg</td>
<td>40 mL/hr + 20 mL/hr + 1 mL/kg/hr</td>
</tr>
</tbody>
</table>

Surgical Blood Loss

- Continuous estimation of blood loss is necessary
  - Visual estimate, weighing of sponges, measuring level in suction containers
  - Hemoglobin concentration or hematocrit do not necessarily reflect blood loss
  - Volume compensation during bleeding is necessary

- Maintenance of circulatory volume
  - Volume blood loss:colloid = 1:1
  - Volume blood loss:crystalloid = 1:2
- Transfusion guidelines
  - Cfr. les "Hemodilutie en transfusie"
  - Blood products should not be used for volume resuscitation per se
Surgery-Related Fluid Losses: Extravascular Fluid Shifts

- Perceived redistribution (intravascular → interstitial) and sequestration of extracellular fluid during surgery
  - So-called “Third space fluid losses”
  - Highly overestimated in the past (Non-existent?)
- Fluid losses from the intravascular to the interstitial space → Tissue edema
  - Intact vascular barrier: almost protein-free fluid and electrolytes
  - There always is some (limited) shifting out of the intravascular space
  - Damaged vascular barrier: protein-containing fluid
- Causes of fluid shifts:
  - Acute hypervolemia
  - Surgical trauma
  - Inflammation
  - Ischemia-reperfusion injury
  - Endotoxin exposure

Surgery-Related Fluid and Electrolyte Disturbances

- Specific to the type of surgery
  - Gastrointestinal surgery
    - Possible losses of large amounts of water and electrolytes
    - Electrolytes: vary according to the source of the losses
  - Hepatic surgery
    - Hyperaldosteronism, sodium and water retention
  - Lung surgery
    - Risk of pulmonary edema
  - Neurosurgery
    - Diabetes insipidus, cerebral salt wasting
    - SIADH
  - Burns
    - Large losses of extracellular fluid

Perioperative Fluid Therapy: Choices

1. Choice of IV fluid during surgery?
   - Too little → hypoperfusion
   - Too much → edema

2. How much IV fluid during surgery?
   - Fluid load versus complications (modified from Bellamy): Both hypovolemia and hypervolemia can lead to organ dysfunction and adverse outcomes. The challenge is to keep patients at all times in the optimal zone.

Choice of IV Fluid during Surgery?

- Balanced electrolyte solution = generally the fluid of choice
  - Plasma-Lyte A, Lactated Ringer’s (Hartmann)
  - NaCl 0.9 %: avoid large volumes
    - Hyperchloremic metabolic acidosis
  - D5W: specific indications
    - Risk of hyperglycemia
- Colloids: guidelines
  - Albumin: reimbursed for specific indications only
  - (Semi-)synthetic colloids: guidelines
  - Contraindications
- Blood products: guidelines
How much IV Fluid during Surgery?

Just the right amount of fluid for an individual patient undergoing a specific procedure
- Procedure-dependent
- Timing of fluid administration may be important
  - No “preloading”
  - Substitution of actual fluid losses
- Intraoperative intravenous fluid volume strategies
  - Restrictive fluid management
  - Goal-directed fluid therapy (GDFT)
  - Zero fluid balance
  - Difficult to evaluate clinically during major surgery

Restrictive Fluid Management

Restrictive vs liberal fluid management: Conflicting clinical data
- Lack of a uniform definition of restrictive or liberal fluid therapy
  - Big differences in fluid management within control groups and within study groups
- Fact: uncontrolled large fluid volumes should be avoided (major abdominal or thoracic surgery)
  - No compensation for preoperative fasting, for vasodilating effects of anesthesia, for presumed third space losses, and for diuresis
  - Compensate
    - Basal fluid losses (1 - 3 mL/kg/hr)
    - Blood loss (crystalloids 1:2, colloids 1:1)
  - Beneficial effects on postoperative outcome
    - Fewer overall complications
    - Earlier return of bowel function
    - Shorter length of hospital stay

Goal-Directed Fluid Therapy

- Individualized optimization of fluid and hemodynamic status to improve postoperative outcome
  - Optimization/maximization of stroke volume (SV) and cardiac output (CO)
  - Fluid bolus (200 – 250 mL) as an assessment of fluid status: SV increase > 10 % = fluid responsive
  - Assessment of SVV or PPV (goal: < 10 %)

Frank–Starling-based stroke volume optimization

When a patient is hypovolemic and on the steeper ascending part of the Frank–Starling curve, an intravenous fluid challenge (VC1) will lead to a > 10 % increase in SV. Such a patient has “recruitable” SV, and is in a fluid-responsive state.

When the patient is no longer hypovolemic (VC2), the same fluid challenge will result in a <10 % increase in SV. The patient is now not fluid responsive and will not benefit from a further fluid challenge.

Assessment of Stroke Volume Variation or Pulse Pressure Variation

**SVV - Stroke Volume Variation**

\[ SVV = \frac{(SV_{\text{max}} - SV_{\text{min}})}{SV_{\text{mean}}} \]

**PPV - Pulse Pressure Variation**

\[ PPV = \frac{(PP_{\text{max}} - PP_{\text{min}})}{PP_{\text{mean}}} \]

**Goal:** PPV or SVV < 10%

**Conditions:** Mechanical ventilation (TV ≥ 8 mL/kg IBW), Absence of arrhythmias, RV failure, open chest surgery, increased intraabdominal pressure

---

Goal-Directed Fluid Therapy

- Individualized optimization of fluid and hemodynamic status to improve postoperative outcome
  - Optimization/maximization of stroke volume (SV) and cardiac output (CO)
- Various technologies
  - Esophageal Doppler: SV, corrected flow time
  - Arterial waveform analysis: SV, CO, SVV, PPV
- Different algorithms → fluid administration and pharmacological therapy

---

NICE guideline algorithm (UK)

1. Measure stroke volume
2. 200-250 ml fluid over 5-10 minutes
3. Stroke volume increase >10%?
   - No
   - Yes: Monitor stroke volume for clinical signs of fluid loss
4. Stroke volume reduction >10%?
   - No
   - Yes: Simple algorithm
   - No assessment before fluid administration
   - No perfusion pressure parameters
   - No inotropes/vasopressors

---

Goal: SVV or PPV < 10%
**Goal-Directed Fluid Therapy**

- GDFT and postoperative outcome: conflicting clinical data
  - Recent trials do not consistently support beneficial effects demonstrated in earlier studies
  - Advances in surgical techniques and perioperative care?
    - Enhanced recovery protocols
- Sometimes larger total fluid volume with GDFT than with a restrictive fluid management
  - Fluid responsiveness does not equal need for fluids
  - Timing of fluid administration may be more important than total fluid volume, as long as overhydration is avoided
- Technical limitations
  - For selected procedures / patients
    - Major surgery
    - Surgery with large fluid shifts
    - Significant cardiopulmonary comorbidity

**Zero Fluid Balance**

Goal: minimal weight gain or loss

- Intraoperative compensation of fluid losses: fluid in = fluid out
  - “No (minimal) weight gain”
- Basal fluid losses + surgical fluid losses
- Problem: sometimes difficult to accurately assess intraoperative fluid losses
- Often part of an enhanced recovery program
- Clinical outcome data
  - Elective surgery: outcome data are comparable to GDFT
  - Problem: not easy to implement for surgery with major fluid shifts / blood loss

**Intraoperative Fluid Infusion Rate and Clinical Outcome: Minor / Moderate Surgery**

- In low risk patients undergoing short-lasting minor/moderate surgery a more liberal fluid strategy may be beneficial (20 – 30 mL/kg crystalloid extra)
  - Less PONV
  - Less pain
  - Reduced neurohumoral stress response
  - Improved postoperative sense of well-being and functioning
  - Improved postoperative pulmonary function

**Intraoperative Fluid Infusion Rate and Clinical Outcome: Major Intraabdominal Surgery**

- Some clinical studies indicate benefits for a restricted fluid management in comparison with a liberal fluid management
  - Fewer cardiopulmonary complications
  - Fewer wound healing complications
  - Faster return of gastrointestinal function
  - Shorter hospital stay
- Some but not all studies indicate that a GDFT (SV optimization) improves outcome
  - No difference with zero fluid balance strategy?
  - Beneficial for selected patient populations?
- Excessive fluid administration should be avoided during major intraabdominal surgery
- Some patients may benefit from GDFT
- Well-designed RCTs are necessary
Intraoperative Fluid Infusion Rate and Clinical Outcome: Thoracic Surgery

Restrictive fluid management has been widely adopted for thoracic surgery
• Reduction of pulmonary complications (acute lung injury, ARDS)
• High intraoperative fluid load → independent risk factor for postpneumonectomy pulmonary edema
• Increased risk of acute kidney injury?
  → No good evidence
  → Excessive fluid administration should be avoided during thoracic surgery
  → Well-designed RCTs are necessary to determine the optimal fluid volume strategy during thoracic surgery

Intraoperative Fluid Management: A Practical Approach

A normovolemic patient without comorbidity
• Basal intraoperative iv fluid infusion: 1 – 3 mL/kg/h
  → Balanced electrolyte solution
• Replace blood loss
  → Crystalloid 1:2 (balanced electrolyte solution)
  → Colloid 1:1 (guidelines)
  → Blood products (guidelines)
• Do not replace
  → Preoperative fasting deficit
  → "Third space losses"
  → Urine output
• Goal: no weight gain during surgery

A patient with cardiovascular or pulmonary co-morbidity or preoperative hypovolemia undergoing major surgery
• Basal intraoperative iv fluid infusion: 1 – 3 mL/kg/h
  → Balanced electrolyte solution
• Replace blood loss
  → Crystalloid 1:2 (balanced electrolyte solution)
  → Colloid 1:1 (guidelines)
  → Blood products (guidelines)
• Goal-directed fluid therapy
  → Predetermined algorithm (crystalloid bolus, vasopressor, inotropic) based on fluid responsiveness
  → Goal: optimization of stroke volume
  → Technical limitations