How to define and quantify Haemodiafiltration

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What uraemic toxins?

<table>
<thead>
<tr>
<th>Compound</th>
<th>MW</th>
<th>Compound</th>
<th>MW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitric oxide</td>
<td>30</td>
<td>Guanidinoacetate</td>
<td>177</td>
</tr>
<tr>
<td>Urea</td>
<td>60</td>
<td>Hippurate</td>
<td>179</td>
</tr>
<tr>
<td>Methylguanidine</td>
<td>73</td>
<td>myo-Inositol</td>
<td>180</td>
</tr>
<tr>
<td>Phenol</td>
<td>94</td>
<td>ADMA/SDMA</td>
<td>202</td>
</tr>
<tr>
<td>Phosphate</td>
<td>96</td>
<td>Dimethylarginine</td>
<td>202</td>
</tr>
<tr>
<td>p-Cresol</td>
<td>108</td>
<td>Spermine</td>
<td>202</td>
</tr>
<tr>
<td>Creatinine</td>
<td>113</td>
<td>CMPF</td>
<td>240</td>
</tr>
<tr>
<td>Hypoxanthine</td>
<td>136</td>
<td>Pseudouridine</td>
<td>244</td>
</tr>
<tr>
<td>Spermidine</td>
<td>145</td>
<td>Indoxyl sulfate</td>
<td>251</td>
</tr>
<tr>
<td>Xanthine</td>
<td>152</td>
<td>Phenylacetylglutamine</td>
<td>264</td>
</tr>
<tr>
<td>Urate</td>
<td>168</td>
<td>β-Endorphin</td>
<td>2465</td>
</tr>
<tr>
<td>Guanidinosuccinate</td>
<td>175</td>
<td>Parathormone</td>
<td>9425</td>
</tr>
<tr>
<td>Indole-acetate</td>
<td>175</td>
<td>β2-Microglobulin</td>
<td>11818</td>
</tr>
</tbody>
</table>

CMPF, carboxymethylpropylfuranpropionic acid; ADMA, asymmetric dimethylarginine; SDMA, symmetric dimethylarginine.
RR (%, mean ± SD, n = 14) of the water-soluble compounds (A: urea, B: uric acid), protein-bound solutes (C: hippuric acid, D: indole acetic acid, E: indoxylsulphate, F: p-cresylsulphate) and LMWPs (G: b2-microglobulin, H: cystatin C, I: myoglobin, J: retinol-binding protein) in HD, pre-HDF and post-HDF.
Box-plot representation of reduction percentages in kappa (KL) and lambda (LL) FLC after correction for fluid removal, for HD and HDF treatment groups.
Serum FLC reduction percentage corrected for fluid removal (a) and clearance (b) as a function of substitution volume in post-dilution HDF. Corrected reduction percentages show a linear correlation, both for $\kappa$ ($r = 0.61; P = 0.04$) and $\lambda$ ($r = 0.58; P < 0.05$) FLC, while clearances show a trend in the same direction without reaching statistical significance ($\kappa$, $r =$...
Serum phosphate in hemodialysis and hemodiafiltration cohorts.


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HEMO study, infections mortality
**Fig. 3.** Kaplan–Meier analysis of all-cause mortality of 490 haemodialysis patients, classified according to lower (<32.2 mg/L, n = 245) and higher (≥32.2 mg/L, n = 245) β2-microglobulin (β2-M) concentrations. Patients with higher β2-M concentrations (thick line) exhibited a significantly higher death rate compared to those with lower β2-M concentrations (thin line) (log-rank test, P < 0.001).
Mortality risk for patients receiving hemodiafiltration versus hemodialysis: European results from the DOPPS

B Canaud, JL Bragg-Gresham, MR Marshall, S Desmeules, BW Gillespie, T Depner, P Klassen and FK Port

1Department of Nephrology, Lapeyronie University Hospital, Montpellier, France; 2DOPPS, URREA, Ann Arbor, Michigan, USA; 3Department of Renal Medicine, Middlemore Hospital, Otahuhu, Auckland, New Zealand; 4Department of Nephrology, CHUQ-Ho tel Dieu de Que bec, Que bec, Canada; 5Department of Biostatistics, University of Michigan, Ann Arbor, Michigan, USA; 6Department of Medicine, University of California, Davis, Sacramento, California, USA and 7Department of Clinical Research, Amgen, Inc., Thousand Oaks, California, USA

Kidney International - 2006
HDF and survival

### Table 4. Risk of all-cause mortality and fatal and nonfatal cardiovascular events by achieved convection volume in liters per treatment

<table>
<thead>
<tr>
<th></th>
<th>Hemodialysis</th>
<th>Online Hemodiafiltration Convection Volume Tertiles</th>
<th>P for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;18.17 L</td>
<td>18.18–21.95 L</td>
</tr>
<tr>
<td>Total mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>crude</td>
<td>1.0</td>
<td>0.95 (0.66–1.38)</td>
<td>0.83 (0.57–1.22)</td>
</tr>
<tr>
<td>adjusted&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.0</td>
<td>0.79 (0.53–1.14)</td>
<td>0.77 (0.51–1.14)</td>
</tr>
<tr>
<td>adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.0</td>
<td>0.80 (0.52–1.24)</td>
<td>0.84 (0.54–1.29)</td>
</tr>
<tr>
<td>Fatal and nonfatal cardiovascular events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>crude</td>
<td>1.0</td>
<td>1.37 (0.94–1.98)</td>
<td>1.06 (0.72–1.56)</td>
</tr>
<tr>
<td>adjusted&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.0</td>
<td>1.41 (0.92–2.11)</td>
<td>0.93 (0.62–1.40)</td>
</tr>
<tr>
<td>adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.0</td>
<td>1.35 (0.86–2.11)</td>
<td>1.04 (0.66–1.62)</td>
</tr>
</tbody>
</table>
Diffusion
Convection / filtration
Temperature, velocity and energy

\[ E = \frac{Tk}{2} = \frac{mv^2}{2} \]

E = Average energy
T = Absolute temperature
m= mass
V = average velocity
K = Boltzmann’s constant
Einstein’s theory of diffusion

Albert Einstein considered diffusion to be a consequence of Brownian motion of solute molecules. The process could be predicted mathematically from temperature, radius of the molecule and the viscosity of the solute.

\[ x^2 = 2Dt = \frac{K_b T}{3\pi r \eta} t \]

Where \( x \) is the average distance travelled by a molecule in time \( t \), \( D \) is the diffusivity. \( K_b \) is Boltzmann’s constant linking temperature to kinetic energy, \( T \) is the absolute temperature, \( r \) is the effective radius of the molecule and \( \eta \) is the viscosity of the solution.
Brownian motion

\[ \text{ABS}(x) = \sqrt[2]{2tD} \]

Average absolute distance moved is proportional to the square root of time and diffusion coefficient
Urea and B-2-Microglobulin

- **B-2-M**
  - M.Wt = 12800
  - Diffusion 1 x

- **Urea**
  - M.Wt = 60
  - Diffusion 15 x
Diffusion

\[ \sqrt{\text{M.Wt}} \]
Sieving

SC=0.5
Convection / filtration
Pure convection
Convection + diffusion
Convection + diffusion
Jaffrin 1995

\[ K_t = K_0 + 0.43Qf + 0.0083Qf^2 \]
\[ K_t = K_0 + S \left( 1 - \frac{K_0}{Qb} \right) Qf \]
\[ K = Q_{Bi} \frac{1 - \frac{Q_{Do}}{Q_{Di}} \frac{Q_{Bo}}{Q_{Bi}} Z}{1 - \frac{Q_{Bo}}{Q_{Di}} Z} \]  \hspace{1cm} (18)

with

\[ Z = \left( 1 - \frac{Q_{u}}{Q_{Bi}} \right)^{(p/Q_{u})^{-1}} \left( 1 - \frac{Q_{u}}{Q_{Do}} \right)^{-\left(p/Q_{u}-1\right)} \]  \hspace{1cm} (19)

and \( p = PA + (1 - \sigma)(1 - f)Q_{u} \), where \( f \) is the function of the Peclet number, Eq. (6), or a constant \( F \), \( 0 \leq F \leq 1 \). Similar for-
Diffusion and convection

![Graph showing the comparison of diffusion and convection for urea, vitamin B₁₂, and inulin.](image)
High-flux backfiltration
Super-flux
Recommendation
Definitions

• HDF requires effective ultrafiltration at least 20% of blood flow rate.
• Effective ultrafiltration takes account of pre-dilution.
  – In pre-dilution HDF, UF rate needs to be 2-3 times greater compared to post-dilution.
• The HDF component is quantified as the total effective volume ultrafiltered.
Effective ultrafiltration

\[ Q_{pw} = Q_b \times (1-Hct) \times (1-Pct) \]

\[ DF = \frac{Q_{pw}}{Q_{pw} + Q_{inf}} \]

Effective UF = actual UF x DF
Out of scope

• Mid-dilution
• Internal filtration

For these modes, manufacturers should indicate effective ultrafiltration rates for range of likely flow conditions.

• How to normalize (surface area, urea distribution volume)
• “Adequate dose”.