Hemodiafiltration online, high efficiency hemodiafiltration (high convective volume)
what, who, when

Fischbach Michel
Pediatric Dialysis Unit
University hospital Strasbourg France
July 1981
Start of HDF
STRASBOURG

1) HDF with bags
2) water treatment: individual bedside reverse osmosis
3) Conventional heparin
4) heating of the substitution fluid
5) membranes...
Hemodiafiltration in children, a history

1) HDF with bags, July 1981: reverse osmosis at bedside, tolerance, « blood uremic detoxification »

2) HDF on line, November 1989: purity of the dialysis fluids (germ free; « no » endotoxins)

3) daily OL-HDF, September 2002: less cachexia

4) high efficiency (autosub + technology) and daily hemodiafiltration (BCM; on-line diffusive plasmatic sodium): volume control, cardiovascular preservation, normal growth
Until the 1980’s, HD was only prescribed as twice weekly dialysis sessions lasting 4 to 6 hours at one time: often poorly tolerated, only offering “survival”, without quality of life.

This led to changes in the dialysis regime over the 1990’s: twice weekly sessions were replaced by procedures performed three times a week.

Nevertheless, despite decades of experience and technical improvements in performing three times a week in-center HD (3x4.5 hours), patients/children treated by this conventional hemodialysis regime still have:

✓ an increased risk of cardiovascular morbidity/mortality,
✓ malnutrition due to protein wasting, impaired growth and
✓ bad volume control (overhydration; high BP; LVH)
As a result, there is a growing interest in the delivery of more intensive hemodialysis, that is:

✓ From HD to HDF (the addition of HF to HD, that is HDF, a complete dialysis dose) to OL-HDF (purity of the dialysis fluids),

✓ high efficiency HDF (hydraulic permeability of the membranes “Cordiax”; autosub+: viscosity control): impact of the achieved convective volume, “high efficiency HDF”

✓ titrating treatment length (4.5 hours ?; reduction in UF demands per dialysis session; UF rate< 1.25%/h BW; IDWG<4%; Cooling $T_D=36°$; Euvolemia ?)

✓ daily “optimyzed” dialysis (floating dry weight; BCM®; diffusible Napl on-line; Kt/V on-line; BVM®; BTM®)
From adequate to intensified dialysis

• « adequacy » assessment:
  outcomes (morbidity/mortality/cachexia/growth) and surrogates like urea kinetics (diffusion process) and more (β2 microglobuline or convective volume for convection mass transport?),

• How to improve conventional HD:
  ✓ high flux membrane for « all »
  ✓ biocompatibility/purity of the dialysis fluids (endotoxin’s level),
  ✓ volume control (dry weight/BP/LVH): interest of an objective assessment (bioimpedancemetry, BCM), reduction in UF demands per dialysis session
  ✓ should HDF become the standard for in center dialysis?

• More dialysis, more frequent/longer sessions: « daily » dialysis, daily in center high efficiency hemodiafiltration
Uremic toxins: which to dose?

Urea Kt/V as surrogate for the diffusion process and β2 microglobulin for the convective volume as surrogate for the convective mass transport?

Focusing on middle molecules...Convective dialysis dose

Small water soluble solutes
- Asymmetric dimethylarginine
- Benzylalcohol
- β-Guanidinopropionic acid
- β-Lipotropin
- Creatinine
- Cysteine
- Guanidine
- Guanidinoacetic acid
- Guanidinosuccinic acid
- Hypoxanthine
- Malondialdehyde
- Methyguanidine
- Myo-inositol
- Orotic acid
- Orotidine
- Oxalate
- Pseudouridine
- Symmetric dimethylarginine
- Urea
- Uric acid
- Xanthine

Protein-bound solutes
- 3-Deoxyglucosone
- CMPF
- Fructoseislyse
- Glyoxal
- Hippuric acid
- Homocysteine
- Hydroquinone
- Indole-3-acetic acid
- Indoxyl sulfate
- Kinurenine
- Kynurenic acid
- Methylglyoxal
- N-carboxymethyllysine
- P-cresol
- Pentaosidine
- Phenol
- P-OHhippuric acid
- Quinolinic acid
- Spermidine
- Spermine

Middle molecules
- Adrenomedullin
- Atrial natriuretic peptide
- β2 Microglobulin
- B-Endorphin
- Cholecystokinin
- Clara cell protein
- Complement factor D

β2 - Microglobulin
- C1q
- C2b
- C3c
- Interleukin 1β
- Interleukin 6
- Kappa-lg light chain
- Lambda-lg light chain
- Leptin
- Methionine-encephalin
- Neuropeptide Y
- Parathyroid hormone
- Retinal binding protein
- Tumor necrosis factor alpha

Dialysis dose and growth
(Surface area normalized standard Kt/V: SAN)

Could be Kt/Vurea a marker of dialysis adequacy? A surrogate+++

Figure 6. Estimated SAN-stdKt/V versus age in two studies in which increased growth rates were linked to intensified dialysis regimens, one with hemodialysis treatments given 3 times/wk by Tom et al. (10) and one using 6-times/wk hemodiafiltration by Fischbach et al. (11).
Adequacy of dialysis in children: does small solute clearance really matter?
Goldstein SL. Pediatr Nephrol 19: 1-5, 2004

Dialysis and outcome: dialysis dose, dialysis time, specific impact of convection

- A minimum Kt/V urea (equilibrated) level of 1.2-1.4 (URR 65 to 75 %) is thought to be desirable
- Only « small solute urea clearance » prescription? *Dialysis prescription should be not only a « urea dialysis dose »*: phosphate and $\beta$2 microglobuline clearances +++ (convective flow)
- Dialysis and residual renal small-solute clearance are not equivalent

Optimal Hemodialysis Prescription: Do children need more than a urea dialysis dose?


*Kt/V urea (diffusion) and a “high” effective convective volume (HDF)*
Do we need indicators of dialysis adequacy based on middle molecule removal?


- From urea to MMW toxins purification: major importance of the convective flow/volume (HDF)
- At present, the most valid candidate is \( \beta_2 \) microglobulin, a threshold of < 27.5 mg/l (predialysis) might be proposed
- Phosphate should be considered as a MMW uremic toxin in terms of dialysis purification: water molecular environment
- The need for high flux membranes and the importance of a high convective volume (HDF)
From adequate to optimal dialysis

- « adequacy » assessment: outcomes
  (morbidity/mortality/cachexia/growth) or surrogates like urea kinetics (diffusion process) and more (β2 microglobuline or convective volume?),

- How to improve conventional HD:
  - high flux membrane for « all » (a low, « not determined » convective volume)
  - biocompatibility/purity of the dialysis fluids (endotoxin’s level),
  - volume control (dry weight/BP/LVH): interest of an objective assessment (bioimpedancemetry, BCM), reduction in UF demands per dialysis session
  - should HDF become the standard for in center dialysis?

- More dialysis, more frequent/longer sessions: « daily » dialysis, daily in center high efficiency hemodiafiltration
Membrane permeability:
diffusion process (urea) - convective flow ($\beta_2$-microglobulin)
low flux/high flux membranes, molecular permeability, from urea to other uremic toxins

![Graph showing sieving coefficient (S) vs. log molecular weight/size]

- **low-flux membrane**
- **high-flux membrane**
- **glomerular basement membrane**

- Urea: 60
- $\beta_2$-microglobulin: 12,800
- Albumin: 68,000
High-flux or low-flux dialysis? High-flux membranes recommended for all patients


Guideline 2.1 (EBPG, 2002): synthetic, high-flux membranes should be considered to delay long-term complications of HD therapy.

Specific indications include: to reduce dialysis-related amyloidosis (III); to improve control of hyperphosphataemia (II); to reduce the increased cardiovascular risk (II); to improve control of anaemia (III).

Guideline 2.1 (ERBP Advisory Board, 2010): synthetic, high-flux membranes should be used to delay long-term complications of HD therapy in patients at high risk (alb<40 g/L) (level 1A: strong recommendation based on high-quality evidence).

In view of underlying practical considerations, and the observation of a reduction of an intermediate marker (β₂-microglobulin), synthetic, high-flux membranes should be recommended even in low-risk patients (level 2B: weak recommendation, low quality evidence).
The clinical benefits of high-performance (HPM) dialyzers have often been reported since the advent of the synthetic polyacrylonitrile dialysis membrane.

HPMs, which have high permeability, eliminate a wide spectrum of uremic toxins and offer excellent biocompatibility, are now essential for hemodialysis, hemofiltration, and hemodiafiltration.

For HPMs whose mean pore size is enlarged to allow better dialysis membrane performance, however, the dialyzing fluid must be **highly purified** to prevent endotoxins contamination.
Masakane Ikuto ASN 2008:  
*mortality risk and dialysis fluids purity*

1) Endotoxines in the dialysat < 0.05 UI/ml in 93.6% dialysis center from Japan

2) Mortality risk correlate to the endotoxin level in the dialysate:
   - RR 1 if < 0.001 ET/ml versus RR 1.48 if 0.1 à 0.25 ET/ml
### Recommandations for a « standard » dialysate

<table>
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<tbody>
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<td>JAPON</td>
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### Recommandations for an « ultrapur » dialysate

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<td>JAPON</td>
<td>&lt; 0.001 UI / ml</td>
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### Recommandations for the substitution fluid (convective volume)

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1) If economically feasible, high-flux membranes should be used in combination with ultrapure disposable dialysate, but small convective volume that is backfiltration risks, and low efficiency HDF…for the same price!

2) High efficiency Hemodiafiltration (high convective volume), is a safe routine replacement therapy: a “complete” use of a high flux membrane, with a large determined convective volume (no more cost, but more efficiency)
High-flux membrane dialysis: limitations

1) not determined, low-dose convective volume (UF and backfiltration)
2) purity of the dialysate?

Not determined and internal convective flow (« push/pull »), that is « internal » hemodiafiltration compensate by backfiltration, from dialysate (purity, endotoxines free?)

Ref: Ledebo, NDT Plus, 2010
From HDF to OL-HDF: double filtered dialysate allows for ultrapure substitution fluid production

HDF is the addition of a determined, high convective volume to HD. The convective flow (HF) requires ultrafiltration (UF) of the plasma. *If the convective flow exceeds the desired weight loss, the fluid balance is maintained by an infusion of replacement fluid, as applied in HF or HDF.*

On line substitution fluid production is obtained *by cold sterilization that is ultrafiltrated ultrapure dialysate*
On line HDF: substitution fluid is produced on line from the filtered dialysate.

On-line HDF

blood

ultrapure dialysis fluids

controllable and measurable convective removal

Principles of fluid preparation for on-line HDF

Gambro system
AK 190/200 ULTRA
AAMI water
Infusion
 dialysis fluid

Fresenius system
2008/4008 on-line
ultrapure water
Infusion
 dialysis fluid

From: Ledebo, ARR 1999
High-flux membrane dialysis or secured OL-HDF (a complete dialysis dose)

- **High-flux HD**
  - Uncontrolled and unknown convective removal
  - UF = (weight loss) +/- backfiltration

- **On-line HDF**
  - Determined and high convective flow = « no » backfiltration
  - Filtered / pure dialysate
  - UF = (weight loss) + convective flow
  - No backfiltration
  - Controllable and measurable convective removal

The effect of on-line hemodiafiltration on improving the cardiovascular function parameters in children on regular dialysis

Converting from HD to OL-HDF predilution, there was:

- a significant decrease in hs-CRP (from 7.9 ± 8.9 to 3.4 ± 3 µg/mL) (P=0.01)
- a significant decrease in frequency of diastolic dysfunction (P=0.04), while systolic function (FS and EF) improved significantly (P=0.007 and 0.05, respectively),
- but LVMI and MBPI pre or post dialysis did not change
From adequate to optimal dialysis

« adequacy » assessment: outcomes (morbidity/mortality/cachexia/growth) or surrogates like urea kinetics (diffusion process) and more (β2 microglobuline or convective volume?),

- **How to improve conventional HD:**
  - high flux membrane for « all »
  - biocompatibility/purity of the dialysis fluids (endotoxin’s level),
  - volume control (dry weight/BP/LVH): interest of an objective assessment (bioimpedancemetry, BCM), **reduction in UF demands per dialysis session**
  - should HDF become the standard for in center dialysis?

- **More dialysis, more frequent/longer sessions:** « daily » dialysis, daily in center high efficiency hemodiafiltration
1) Highly permeable membranes for « all »

2) One should consider, as a new standard in HD, *that the minimal treatment time of 270 min = 4.5 h*, depending on the patient’s weight or V, be delivered and an UF rate of no >10 ml/h/kg applied for patients treated as a thrice weekly schedule (Movelli E et al. NDT 2007)

3) Assessing and correcting underlying chronic inflammation: purity of the dialysis fluids, the Japanese experience (Endotoxin <0.001 U/ml)

4) The volume of substitution, a surrogate of the convective dialysis dose, should be considered as a critical factor for patient survival.

5) Technological improvement will never replace neither the expertise of caregivers or individualized care.
Association between high ultrafiltration rates and mortality in uraemic patients on regular haemodialysis. A 5-year prospective observational multicentre study

E. Movilli et al. NDT 2007; 22:3547-3552

- From 65% to less than 20% survival at 5 years if BW loss per hour (UF rate) was over 12mL/H/kgBW
- Importance of dialysis time
- Reduction in UF demands per hour/session
UF rate< 1.25%/h BW (floating dry weight)
IDWG<4% ? Euvolemia ? Cooling T_D=36°

M Fischbach et al Pediatr Nephrol 2015


Longer dialysis session length is associated with better intermediate outcomes and survival among patients on in-center three times per week hemodialysis: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS) F. Tentori, J. Zhang, Yun Li et al. NDT 2012; 4180-88

Combined effects of longer treatment time and improved dialysate purity: the « Japanese » experience

Fig. 4. Association between prescribed TT and mortality by region. Interaction between TT and region (P < 0.0001). Longer TT was associated with lower mortality in Eur/ANZ [HR = 0.94 (95% CI: 0.91–0.97) per 30 min TT, P = 0.0002] and Japan [HR = 0.75 (95% CI: 0.69–0.81), P < 0.0001] but not in North America [HR = 0.98 (95% CI: 0.95–1.02), P = 0.28]. Model was adjusted for age, sex, race, time on dialysis, BMI, 13 summary comorbid conditions, residual kidney function, prescribed blood flow rate and catheter use, stratified by study phase and accounted for facility clustering. The chosen reference category was for North American patients with prescribed TT at 240 min.
From adequate to optimal dialysis

• « adequacy » assessment : outcomes (morbidity/mortality/cachexia/growth) or surrogates like urea kinetics (diffusion process) and more (β2 microglobuline or convective volume?),

• How to improve conventional HD:
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  ✓ should HDF become the standard for in center dialysis ?

• More dialysis, more frequent/longer sessions: « daily » dialysis, daily in center high efficiency hemodiafiltration
Hémodiafiltration modalities

If the convective flow exceeds the desired weight loss, the fluid balance is maintained by an infusion of replacement fluid (bags, dialysate, on-line substitution), as applied in HF or HDF

- **Conventional, classical, historical HDF**: substitution fluid (bags/costs+++ ) with « balanced » compensation (1978)

- **High flux hemodialysis i.e. internal HDF**: highly permeable membranes with retrofiltration due to the high hydraulic permeability coefficient (dialysate backfiltration risks)

- **Online HDF**: substitution fluid produced from the « ultrafiltered ultrapur dialysate » (1987)
Different forms of HDF: internal HDF, classical HDF (with bags), on-line HDF
On line HDF: substitution fluid is produced on line from the double filtration of the dialysate.
Hemodiafiltration, HD and HF

The convective transport (HF) requires ultrafiltration (UF) of the plasma, i.e. the convective flow. *If the convective flow exceeds the desired weight loss, the fluid balance is maintained by an infusion of replacement fluid, as applied in HF or HDF.*

In HDF addition of substitution solution can be made before the filter called *predilution* mode, after the filter, *postdilution* mode, or mixed.
Principles of blood purification

- **Diffusive Process (HD):** low MW uremic toxins removal i.e. urea

- **Convective mass transport (HF):** middle Mw uremic toxins removal i.e. phosphate

- **Membrane adsorption (+++/PMMA/Torray ?)**
Blood purification dialysis modalities: diffusion versus convection

**Diffusive Process**
(hemodialysis)

- Membrane area
- Mass transport coefficient
- Concentration gradient
- Blood flow x extraction coefficient

\[ K_{HD} = Q_B \times \frac{c_i - c_o}{c_i} \]

\( i, o \): in outlet solute concentrations

**Convective mass transport**
(hemofiltration)

- Ultrafiltrate flow \( Q_{UF} \)
- Hydraulic permeability
- Transmembrane pressure (TMP; mmHg)
- Sieving coefficient \( S \)* Molecular permeability

\[ S = \frac{2 \times C_{UF}}{c_i + c_o} \]

\( C_{UF} \): ultrafiltrate solute concentration

\[ K_{HF} = Q_{UF} \times S \quad \text{(postdilution)} \]

\[ Q_{UF} < \frac{1}{3} Q_B \quad \text{(in practice)} \]
Simultaneous purification: diffusion process and convection mass transport i.e. hemodiafiltration

**one minute of dialysis « is equal» to two minutes of purification, one of HD and another one of HF**

\[
K_{HDF} = K_{HD} + x Q_{UF} \times 0.46
\]

\[
K_{HDF} = K_{HD} (1 - Q_{UF} \times S/Q_B) + K_{HF} \text{ (Granger)}
\]

with \( Q_{UF} \times S = K_{HF} \) and \( Q_B = K_{max} \)

\[
K_{HDF} = K_{HD} + K_{HF} - \frac{K_{HD} \times K_{HF}}{K_{max}}
\]

If \( K_{HD} \) is equal to \( K_{max} \) then \( Q_{HDF} = K_{HD} \)
Uremic toxins

Vanholder R et al. KI 2003; 1934-43

The small water soluble compounds (prototype urea): < 500D
The protein-bound compounds (prototype p-cresol)
The larger “middle molecules” (prototype β₂-microglobulin): > 500D

<table>
<thead>
<tr>
<th>Low MW</th>
<th>Middle large MW</th>
<th>Protein bound compounds</th>
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<tr>
<td>&lt; 500 D²</td>
<td>&gt;500</td>
<td></td>
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<tr>
<td>&lt;60 000</td>
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- Urea
- β₂ m
- Paracresol
- Guanidine
- Leptine
- Indoxyl sulfate
- Phosphate
- AGE
- Acide urique
- Interleukines, TNFα
- Oxalate
- Ig light chain
- Homocysteine
- PTH
- Acide urique
- Ig light chain
- Homocysteine
- PTH
- Acide urique
- Ig light chain
- Homocysteine
- PTH
- Acide urique
- Ig light chain
- Homocysteine
- PTH
HDF allows an optimal blood purification not only for urea, but also for the middlemolecular weight compounds (Babb theory).

*From M Fischbach et al. Contr Nephrol 1985*
Hyperphosphatemia, a « silent killer »
(FGF23; Klotho) of patients with renal failure

17 young adult patients with childhood onset of CRF (median 26 years at screening time): coronary calcifications were found in 7 out of 17 patients

Premature atherosclerosis in young adults and childhood onset chronic renal failure
The effect of dialysis modality on phosphate control: HD compared to HDF.
The Pan Thames Renal Audit
A. Davenport et al. Nephrol Dial Transplant 2010; 25:897-901

- HDF offers improved phosphate control compared to standard intermittent HD

![Graph showing serum phosphate levels in hemodialysis and hemodiafiltration cohorts.](image1)

**Fig. 1.** Serum phosphate in hemodialysis and hemodiafiltration cohorts. Data expressed as mean (SEM). ***P < 0.001.

![Histogram showing frequency distribution of phosphate levels.](image2)

**Fig. 2.** Frequency distribution curves of the pre-dialysis midweek serum phosphate concentrations in the haemodialysis patients (black bars) and haemodiafiltration patients (white bars).
Impact of convective flow on phosphorus removal in maintenance haemodialysis patients


This study revealed a higher phosphorus removal and phosphorus reduction rate with postdilutional on-line HDF compared to high-flux HD. Long-term use of on-line HDF therefore may have a positive impact on the cardiovascular status of the patients.

Phosphate should be considered as a MMW uremic toxin in terms of dialysis purification: water molecular environment; importance of the convection (HDF)
Pre-dialysis $\beta_2m$ and treatment mode, the more convective flow (HDF) the lower plasma level of $\beta_2m$

<table>
<thead>
<tr>
<th>Study</th>
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# Uremic toxins

*Vanholder R et al. KI 2003; 1934-43*

The small water soluble compounds (prototype urea): < 500D
The protein-bound compounds (prototype p-cresol)
The larger “middle molecules” (prototype $\beta_2$-microglobulin): > 500D

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The gut-kidney axis: indoxyl sulfate, \( p\)-cresyl sulfate, endotoxins and CKD progression

Björn KI Meijers and Pieter Evenepoel.
Nephrol Dial Transplant 2011; 26:759-761

CKD: a systemic disease with cross talk between the gut and the “body” (CKD-MBD-CardioVascular)

- Uremic toxins production
- “leaky” gut (endotoxins)
P-cresol, a protein-bound uremic toxin impact on survival


14 patients treated with the same high-flux filter 2 weeks on each modality

N= 175 HD patients, prosp. obs. study

Improved survival

Log-rank P = 0.041

Free p-cresol < 1.97 mg/L

Free p-cresol ≥ 1.97 mg/L

Total solute removal (mg)

N= 175 HD patients, prosp. obs. study

14 patients treated with the same high-flux filter 2 weeks on each modality
On-line HDF: *a combination of solute removal, « purification » and dialysis fluids purity*


**HDF and blood purification impacts**
- Nutrition, uremic toxins and anorexia (leptin)
- Anemia, improved erythropoietin response
- Cardiovascular disease, AGE removal
- Infectious complications, complement factor D removal
- Joint pain, dialysis related amyloidosis

**HDF and ultrapure dialysis fluid impacts**
- Amyloidosis
- Anemia
- Nutrition
- Joint pain, dialysis related amyloidosis
HDF versus HD : advantages

• **Optimal blood purification capacities** both for urea and middle molecular weight compounds : high level dialysis dose easily achieved. A high dialysis dose usually induce a good nutrition status, especially with an increased caloric intake (apetite)

• **Hemodynamic stability over the session** : increased tolerance to weight loss and blood pression control improvement (hemofiltration effect) : osmotic stability, compartiment preservation, peripheral vascular resistances, myocardial contractility
HF and HDF predilution, reduce intradialytic hypotension in ESRD

Intradialytic symptomatic hypotension occurrence was reduced in on line predilution HF and HDF

This lower frequency of ISH was associated in HDF, with a significant increase in predialysis SBP values (from 137.3 to 141.3 mmHg)

Figure 2. 7.5% of all of the 28,950 sessions were complicated by ISH. In the evaluation period compared with the basal run-in, there was a statistically significant decrease of sessions with ISH in HF (9.8 to 8.0%, decrease of 18.4%; P = 0.011) and in HDF (10.6 to 5.2%, decrease of 50.9%; P < 0.001) compared with low-flux HD group (7.1 to 7.9%, increase of 9.9%).
Hemodiafiltration
with high permeable membranes in children

<table>
<thead>
<tr>
<th></th>
<th>HD</th>
<th>HDF</th>
<th>HDF</th>
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<tbody>
<tr>
<td></td>
<td>15 h/week</td>
<td>9 h/week</td>
<td>9 h/week</td>
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<tr>
<td></td>
<td>cuprophane</td>
<td>PAN</td>
<td>polysulfone</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
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<tr>
<td>TAc urea</td>
<td>28±4</td>
<td>18±3</td>
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<td>mmol/L</td>
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<td>PCRn g/kg/j</td>
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<td>1.8±0.3</td>
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<td>Phosphate</td>
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<td>1.34±0.15</td>
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<td>mmol/L</td>
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<tr>
<td>Aluminium</td>
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<td>0.5</td>
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<td>g/day</td>
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<tr>
<td>Hemoglobin g/dl</td>
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<tr>
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</table>

Hemodiafiltration with high permeable membranes in children
High-volume online haemodiafiltration improves erythropoiesis-stimulating agent (ESA) resistance in comparison with low-flux bicarbonate dialysis: results of the REDERT study


A significant reduction in hepcidine and β2microglobulin, and higher Kt/V

Is HDF more favourable than HD for treatment of renal anaemia?

Mortality risk for patients receiving HDF versus HD: European results from the DOPPS

Canaud B et al. Kidney Int 2006

• The **relative risk of mortality** after adjustments for several variables (age, comorbid conditions, haemoglobin, Kt/V) was **significantly reduced by 35% for patients receiving high efficiency HDF** compared to low flux HD or high flux HD.

• Several explanations: HDF « package »
  - improved removal of small and larger molecules solutes (Phosphate), « surrogates » of the achieved convective volume
  - enhanced intradialytic hemodynamic stability
  - reduced inflammation due to better biocompatibility (β2 microglobulin
  - regulation of calcification inhibitors, like: fetuin-A, matrixGLA protein, osteoprotegrin
High-efficiency postdilution Ol-HDF (ESHOL) reduces all-cause mortality in dialysis patients


They found that high-efficiency OL-HDF (>24L/session) in patients with ESRD on hemodialysis was associated with a 30% reduction in all-cause mortality compared with conventional high-flux hemodialysis.
## Impact of high convective volume high efficiency hemodiafiltration

<table>
<thead>
<tr>
<th>Study name</th>
<th>Threshold volume for survival benefit (observational studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOPPS (Canaud) 2006</td>
<td>&gt; 15 L</td>
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<tr>
<td>Riscarid (Panichi) 2008</td>
<td>&gt; 23 L</td>
</tr>
<tr>
<td>Contrast (Grooteman) 2012</td>
<td>&gt; 21.95 L</td>
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<tr>
<td>Purkush (Ok) 2012</td>
<td>&gt; 17.4 L</td>
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<tr>
<td>ESHOL (Madrid) 2013</td>
<td>&gt; 23.1 L</td>
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<tr>
<td><strong>Minimal convective volume</strong>, post dilution</td>
<td>? 3 L/m²/h or 12-15L/m²/session</td>
</tr>
<tr>
<td>or predilution (easier to achieve?)</td>
<td>? 18-27 L/m²/session</td>
</tr>
</tbody>
</table>
HDF : substitution fluid optimization (convective volume), blood flow +++

- Pressure control (Gambro) : maximal efficient PTM assessed to obtain a gain of convective volume (PTM « pulses »)
- Filtration fraction (Fresenius; autosub+) : initially based on on line hematocrite (and historically on total proteins given by the medical prescription…), improved by viscosity on line assessment (autosub+)+++  
- Conclusion : importance of the total amount of water, not only related to the proteins (filtration fraction <50%) but also to the blood cells (hematocrite « outlet » <50%)
Adequate HDF prescription: « quality » of a high convective volume

importance of the membrane

- Hydraulic permeability: high convective volume
  (> 25 L in postdilution; > 60L in predilution)
- Molecular permeability: extraction coefficient
  (phosphate and $\beta_2$ m 80 %)
- Loss of albumine (< 5 gr)
- Purity of the dialysis fluids
HDF: a complete dialysis dose

- On-line Urea Kt/V > 1.4 (V « Morgenstern or BCM)
- High convective volume (autosub+) but need for a volume of « good quality » (impact of the membrane):
  - beta-2-microglobulin extraction coefficient >80%
  - myoglobin>65%
- Risk of « loss » in the dialysate and high convective volume (check for albumin; quality of the membrane)
- Dialysis fluids: purity, temperature control (« cooling »; BTM), NaD (on-line diffusive sodium), Ca++, HCO$_3$-
- More than purification, importance of the volume control (UF and sodium balance): BCM, BP, IDWG…