Workshop 3:
OnLine HDF - the Easy Way to be Efficient

10th Fresenius Medical Care & EDTNA/ERCA

Middle East and Africa Renal Education Programme

12th – 14th Nov 2016, Barcelona, Spain

Treatment Options for People with

Chronic Kidney Failure

Stage 5d

Treatment Options for People with

Chronic Kidney Failure

Stage 5d

Haemodialysis Vascular Access

What do we mean by “vascular access” ?

Way in which we are able to remove and return blood to the patient

- ✓ **Internal vascular access**
  - Arteriovenous fistula(AVF)
  - Arteriovenous graft (AVG)
- ✓ **External vascular access**
  - Intrajugular catheter
  - Subclavian catheter
  - Femoral catheter

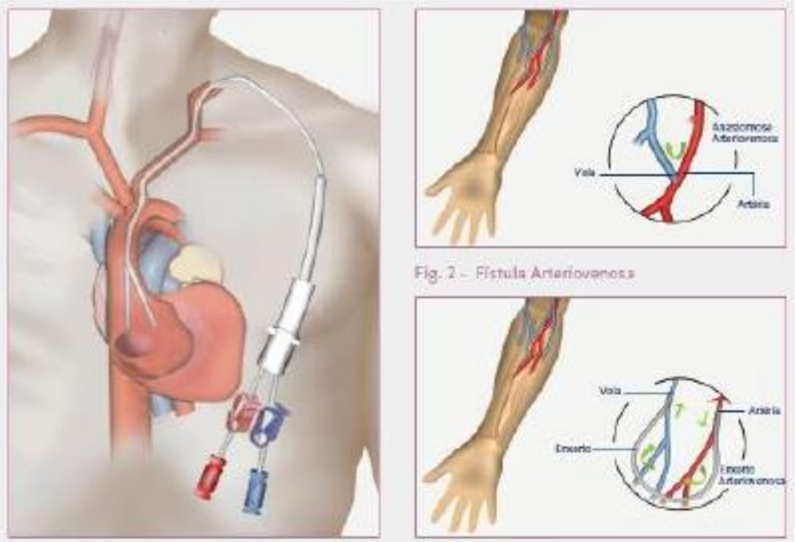


Fig. 1 - Cateter de Longa Duração

Fig. 2 - Fístula Arteriovenosa

Fig. 3 - Prótese Arteriovenosa

Haemodialysis Treatment

How is haemodialysis performed?

Haemodialysis uses a filter as a semipermeable membrane (dialyzer)

- ✓ **Dialyzer contains hollow fibres**
  - Hollow fibres are constructed of a semipermeable membrane
- ✓ **Blood passes through inside of hollow fibre**
- ✓ **Dialysate flows around outside of hollow fibre**
  - Chemical processes allow removal of wastes
  - Physical processes allow removal of excess fluid

Haemodialysis Treatment

Where can a haemodialysis treatment be done?

- ✓ At a dialysis centre
- ✓ At home
- ✓ At the hospital

Haemodialysis Treatment

How often is haemodialysis performed?

- ✓ Treatment is prescribed by the physician
- ✓ At least three times a week in most patients
- ✓ Treatments are usually 4 to 5 hours in duration

Haemodialysis Treatment

Pros

- Quickly stabilizes patient
- Treatment outcomes are generally predictable
- Time-efficient

Cons

- Expensive & technically complex
- Trained personnel required
- Vascular access required
- Complications (mechanical & technical) can be serious
- Anticoagulation generally necessary

Haemodialysis Treatment

Side effects

Caused by rapid changes in fluids and chemicals during treatment

Side effects include

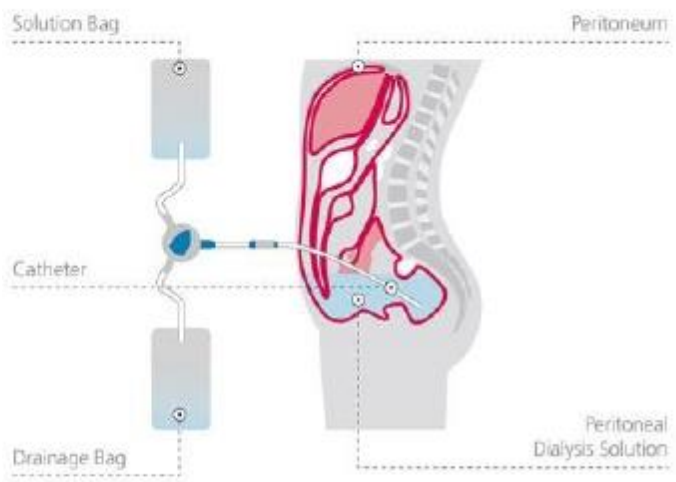
- ✓ **Blood pressure changes**
- ✓ **Cramping**
- ✓ **Nausea**
- ✓ **Weakness, dizziness**

Peritoneal Dialysis

Definition: peritoneal membrane

It is a thin membrane in the abdomen

- ✓ **Covers the abdominal organs**
- ✓ **Lines the abdominal wall**



Properties

Very thin

Highly vascular (many blood vessels)

Peritoneal Dialysis

How does it work ?

A solution, prescribed by physician, fills the peritoneal space between the membranes

The peritoneal membrane serves as filter

- ✓ **Performs function similar to the hollow fibres in the dialyzers**
- ✓ **Membrane thin enough to allow passage of fluid and molecules from bloodstream into dialysis fluid**

Peritoneal Dialysis

PD vocabulary

Inflow = Process where fresh dialysate solution flows into the abdomen

Dwell = Period of time when the dialysate solution remains in the peritoneum

- ✓ **This allows toxins, excess fluid to pass into the dialysate solution**

Outflow (drain) = Toxins, excess fluid and dialysate solution are drained from the abdomen

Exchange = Word used to describe the entire inflow-dwell-outflow cycle

Peritoneal Dialysis

Pros

- More liberal diet & fluid intake
- More stable lab values
- Can be done at home
  - ✓ Can also be done at work, on holiday, etc.
- Patient administers own treatment
- No needles needed

Cons

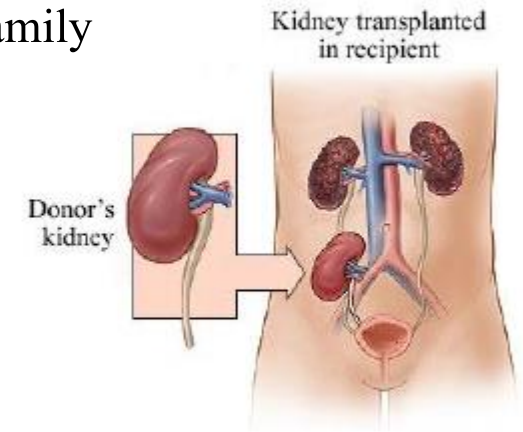
- Catheter in abdomen
  - ✓ Self image issues
  - ✓ Route for infection
- Requires skills
- Requires storage space in home
- Treatment needs to be done every day

Transplantation

3 types

Living - related

- ✓ Kidney donated by member of patient's immediate family



Living – non-related

- ✓ Kidney donated by friend, spouse, etc.

Cadaveric

- ✓ Kidney "harvested" from person whose brain function has ceased
- ✓ Kidney "harvested" from cadaver

Transplantation

Considerations

- It results in the patient having the most normal laboratory values
- Donor & patient’s tissues need to match as closely as possible
- Patient must be very compliant with anti-rejection drugs

Haemodialysis

Definitions

Hemo = Blood

Dialysis= Pass through or filter

Haemodialysis = Removal of waste products and excess fluid

Uraemia = Nitrogen-containing waste products in blood normally excreted by the healthy kidney

- ✓ From the Latin: “ure-” = referring to urine & “emia” referring to blood ⇒ “urine in blood”

Haemodialysis

Indications

- Why haemodialysis should be done

Renal insufficiency

- Volume overload (too much fluid)
- Hyperkalemia (too much potassium in blood)
- Metabolic acidosis (blood too acidic)
  - ✓ Serum bicarbonate < 15 mEq/L
- Uraemic intoxication
- Electrolyte imbalances
- Removal of substances
  - ✓ Poisons
  - ✓ Drugs

Goals of Haemodialysis

- **Management of some of the various conditions that are a result of renal failure**
  - ✓ Uraemia
  - ✓ Fluid overload
  - ✓ Electrolyte imbalance

Components of the Haemodialysis System

- **The delivery system (machine & dialysate)**
- **The extracorporeal (outside the body) circuit**
  - ✓ Fistula needles
  - ✓ Arterial bloodline
  - ✓ Venous bloodline
  - ✓ Dialyzer (artificial kidney)
- **Vascular access**

Principles of Haemodialysis

Definitions

Semipermeable = allows passage of some (but not all) substances and fluids

Solutes = Molecules and electrolytes (particles) suspended in fluid **-** the solids in a solution

Clearance = Removal of specific solutes

Solvent = Fluid in which solutes are suspended

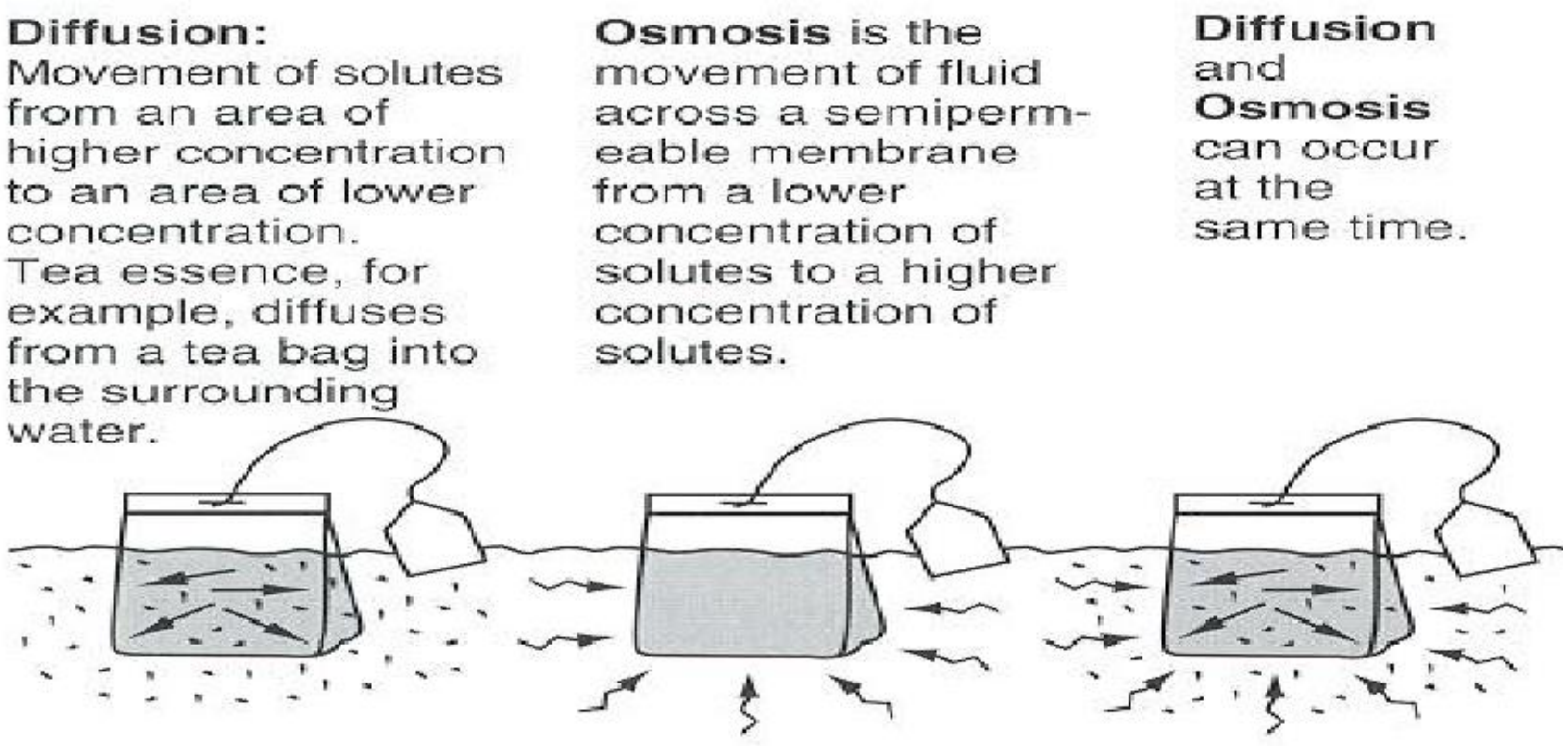
Principles of Haemodialysis

Definitions (cont.)

Osmosis = movement of **fluid** from area of lesser concentration of solutes to area of greater concentration of solutes, through a semipermeable membrane

Diffusion = movement of **solutes** from an area of greater concentration to an area of lesser concentration

Principles of Haemodialysis



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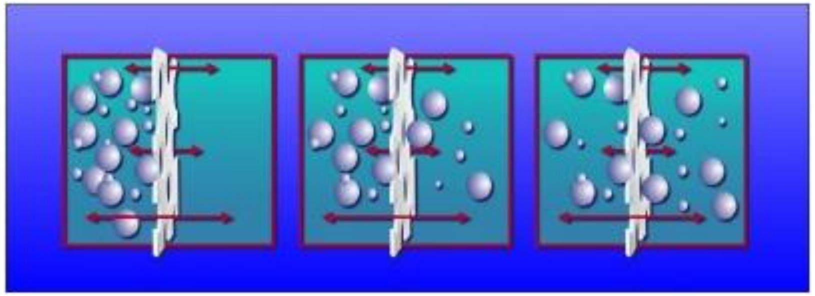
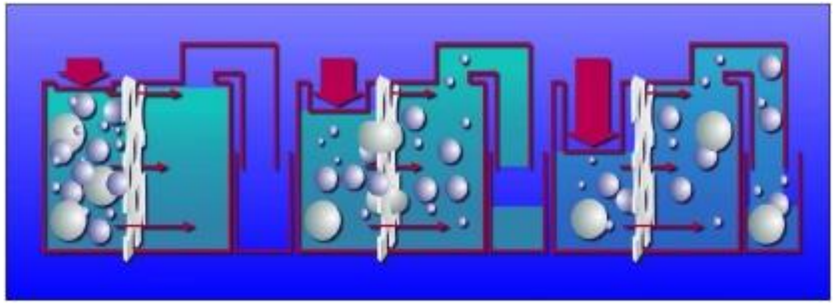
Principles of Haemodialysis

Diffusion



Random movement of molecules along a concentration gradient.

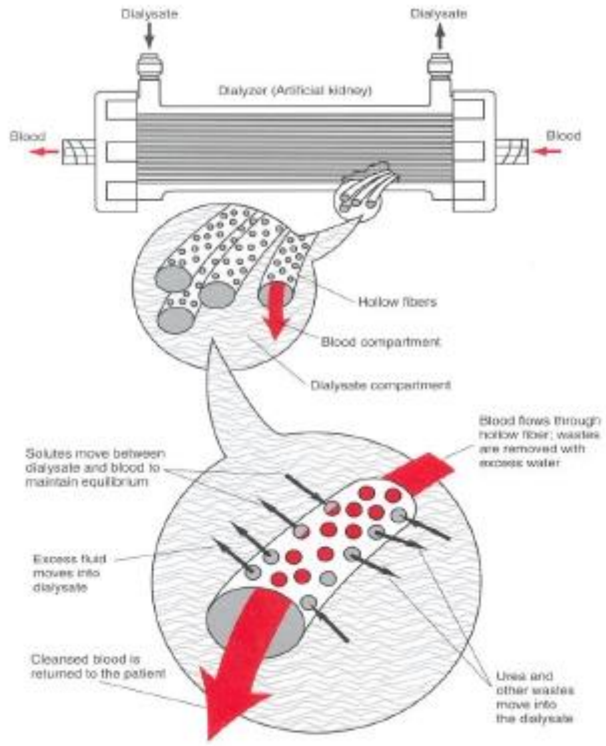
Convection



Exertion of pressure results in filtration of water & solutes across the membrane.

Principles of Haemodialysis

The following 2 slides are portions of the illustration at right, adapted to improve visibility. This is an excellent representation that there is a two-way movement of solutes through the membrane.



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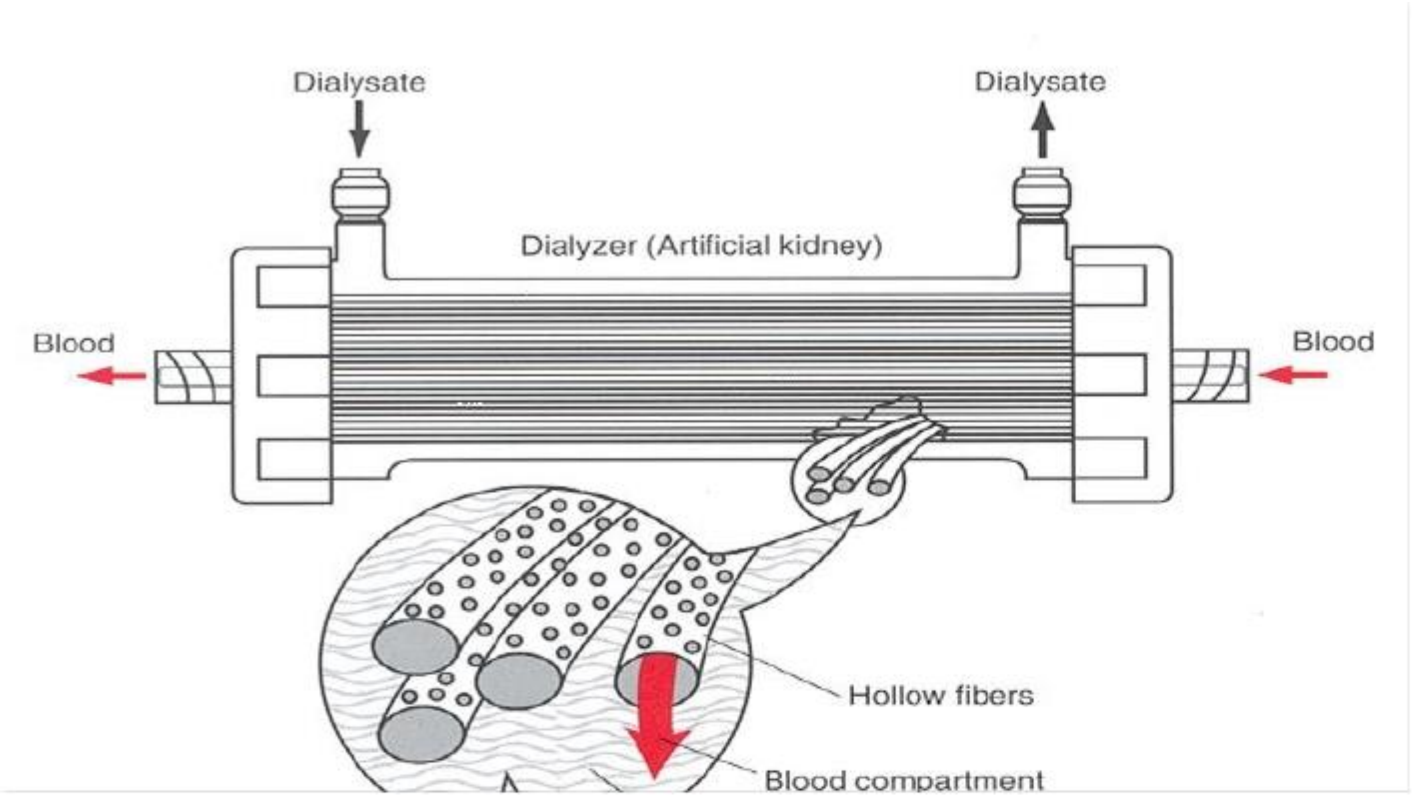
Principles of Haemodialysis



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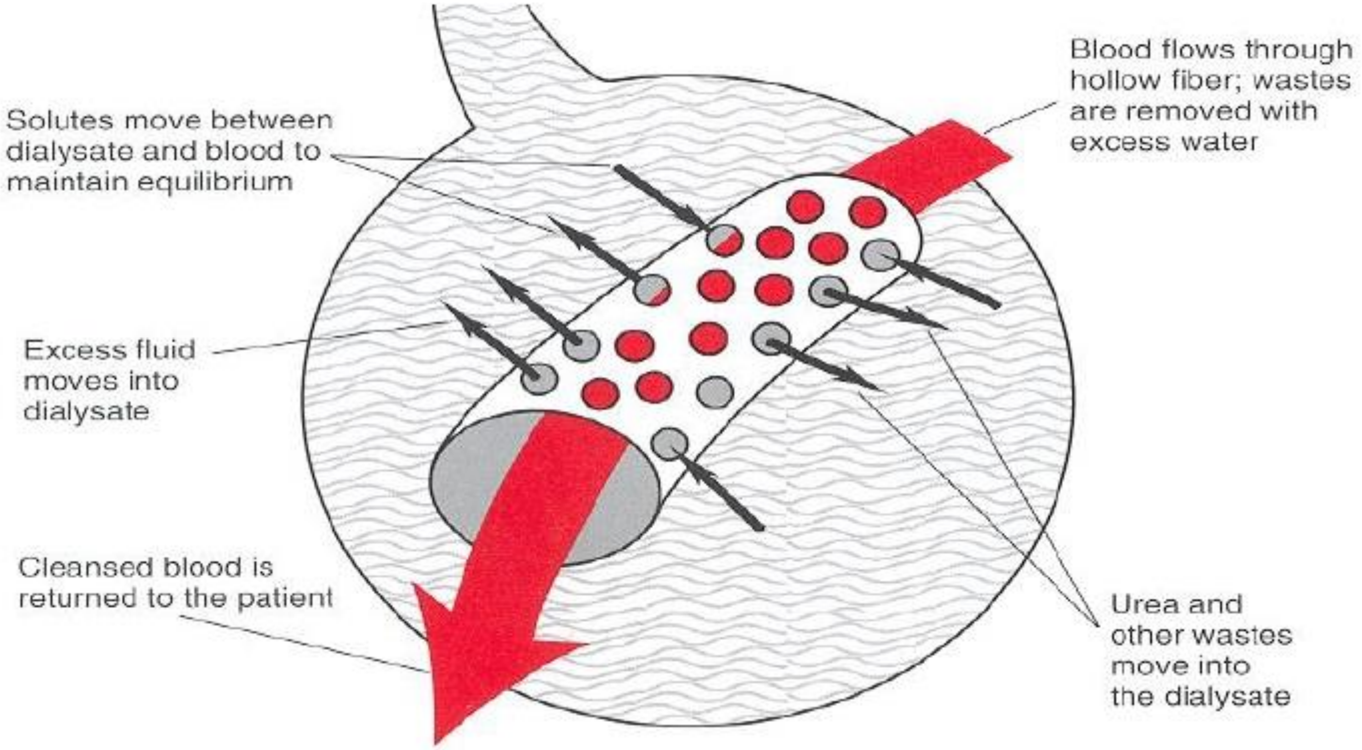
Principles of Haemodialysis



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Principles of Haemodialysis

Factors affecting removal of toxins

- Dialysate flow rate (DFR or Qd)
- Blood flow rate (BFR or Qb)
- Dialyzer membrane characteristics

Principles of Haemodialysis

Factors affecting removal of toxins

Concentration gradients

- Differences between concentration of a given solute in patient's blood compared to fresh dialysate
- Differences in concentration of solutes between intercellular, extracellular and vascular fluids

Molecular weight of solute

- Small molecules move faster than large molecules

Principles of Haemodialysis

Dialyzer membranes

Semipermeable

Hollow fibres made with microscopic pores

- ✓ Pores are too small to allow passage of RBCs
- ✓ Pores are large enough to allow passage of fluid
- ✓ Pores are large enough to allow passage of smaller molecules and electrolytes
- ✓ Pores allow passage of some medications and not others (depends on the size of the molecule)

Principles of Haemodialysis

Dialyzer membrane characteristics

Membrane surface area

- ✓ Amount of membrane in contact with blood & dialysate

Permeability

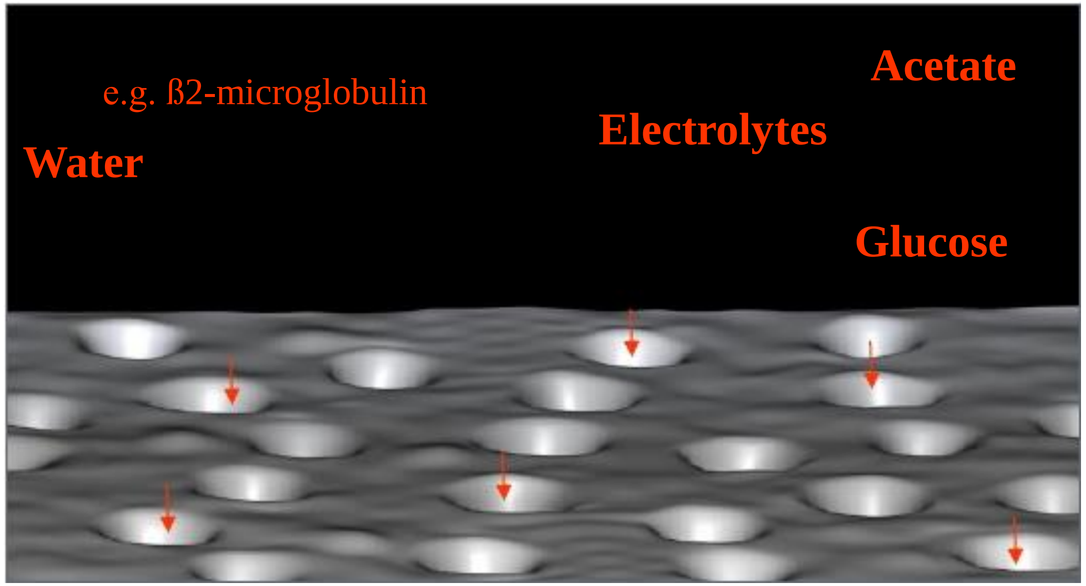
- ✓ Pore size, pore number, thickness, design

Resistance factors

- ✓ Blood film, dialysate film, membrane

Membrane

Blood



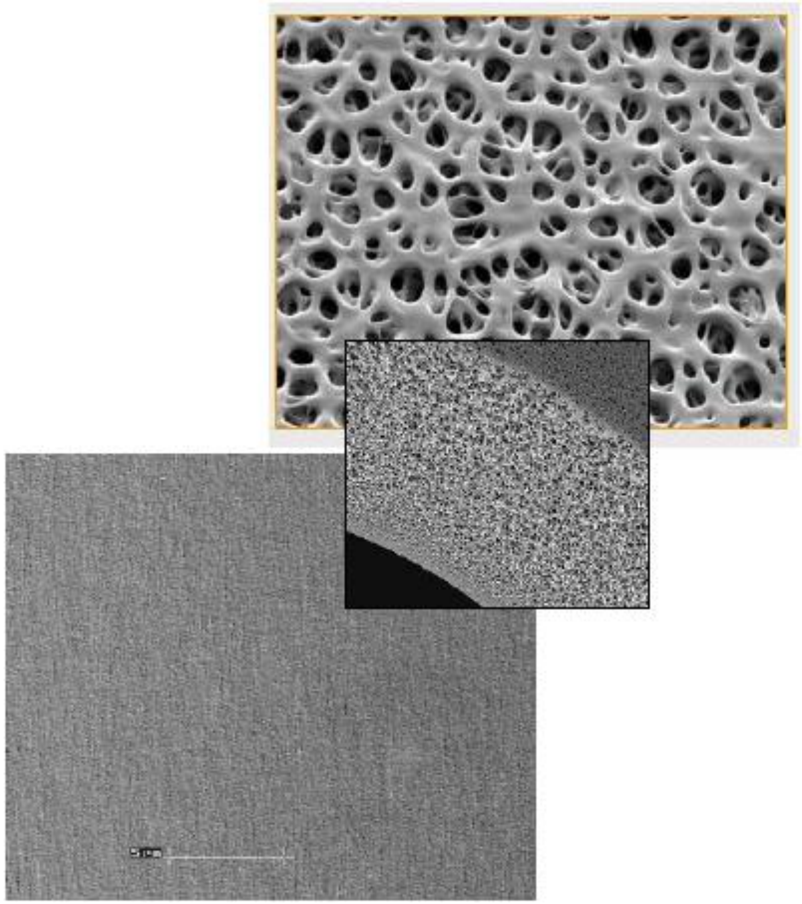
The membrane functions similarly to a sieve!

Electrolytes Bicarbonate Bacterial fragments

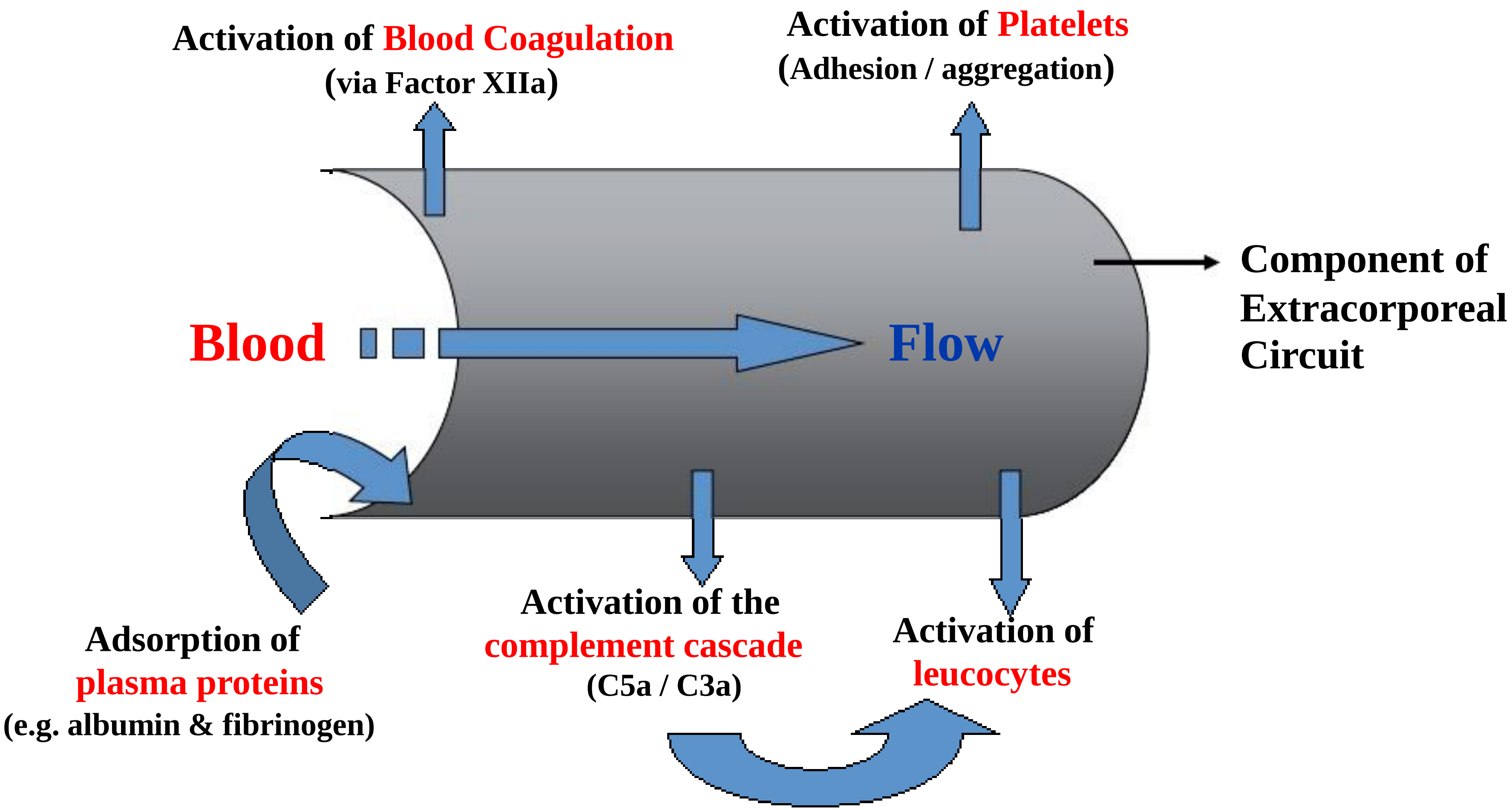
Dialysis Fluid

Dialyzer Membrane Characteristics

Synthetic:



Several pathways triggered simultaneously by blood-material interactions:



Dialysis Adequacy

Definition

- ✓ Dialysis treatment achieves the following goals:
- ✓ Reduction of uraemic toxins to acceptable levels
- ✓ Removal of excess fluid
- ✓ Bringing serum electrolytes into prescribed ranges

Dialysis Adequacy (cont.)

Factors affecting adequacy

Blood flow rate (BFR or Qb)

- Part of the physician's prescription
  - ✓ Can range from 250 - 500 ml/min
  - ✓ (Higher flow rates are preferable but not always achievable)

Dialysate flow rate (DFR or Qd)

- Part of the physician's prescription
  - ✓ 500 ml/min or using Autoflow

Dialysis Adequacy (cont.)

Another factor affecting clearance

Counter-current flow

- ✓ Dialysate flows through dialyzer in opposite direction from blood flow

Dialysis Adequacy (cont.)

Choice of dialyzer

Conventional = slowest, lowest clearance

High efficiency = greater solute clearance than conventional but not as great

as …

High flux = Highest clearances available with current membranes

Dialysis Adequacy (cont.)

What can you do to ensure adequacy?

- Prepare dialyzer according to proper procedure
    - ✓ Ensures maximum performance of the dialyzer
- Set blood flow according to prescription
- Set dialysate flow according to prescription
- Make sure supervisor is aware of deviations from prescription

Fluid Removal

Definitions

Ultrafiltration = Filtration under pressure

✓ In haemodialysis, ultrafiltration = fluid removal under pressure

Positive pressure = pressure exerted by the blood flowing through the dialyzer

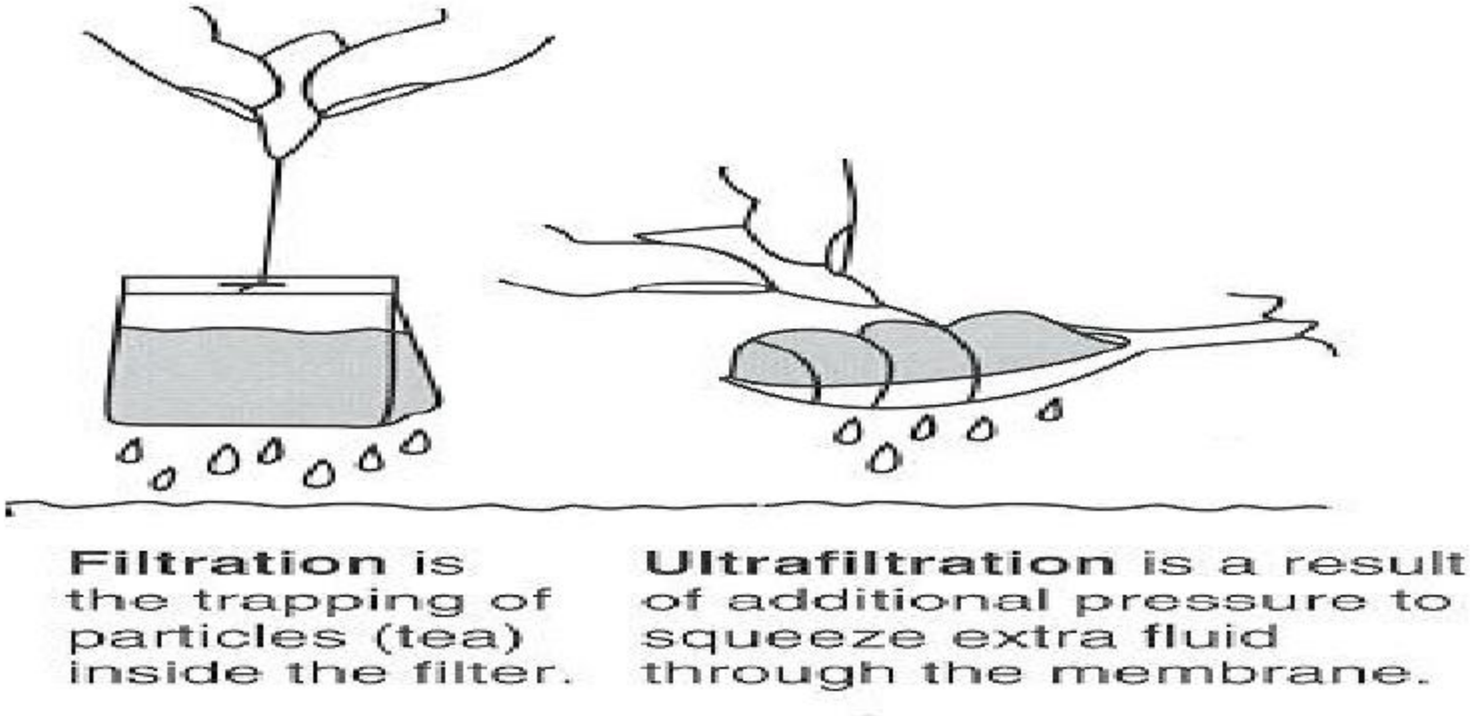
✓ Results from blood being pushed by blood pump

Negative pressure = pressure applied to the dialysate side by the machine

✓ Pulls excess fluid from blood compartment to dialysate compartment → drain

Transmembrane pressure = sum of positive plus negative pressures at membrane level

Fluid Removal



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Fluid Removal

Transmembrane Pressure (TMP) = Positive pressure + Negative pressure

Ultrafiltration Coefficient (KUF)

- A value that indicates ml of fluid pulled across the membrane in an hour when 1 mmHg of TMP is applied

HDF milestones

Fig. 1.2 LW Henderson and the first hemo(dia)filtration machine (Reprinted from Henderson et al. [7]. With permission from Elsevier)

M.J. Nublé et al. (eds.), *Hemodiafiltration: Theory, Technology and Clinical Practice,* DOI 10.1007/978-3-319-23332-1_2

HDF milestones

Blood Purification

Blood Purif 2013;35:55–62
DOI: 10.1159/000345175

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Emerging Clinical Evidence on Online Hemodiafiltration: Does Volume of Ultrafiltration Matter?

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Abstract

Online hemodiafiltration (OL-HDF), first described in 1985, is today a widely prescribed treatment modality for end-stage chronic kidney disease (CKD) patients. Other than in the United States, prescription of the treatment modality is widespread with a steady increase since its inception. Indeed, in Western Europe, more CKD patients receive OL-HDF than peritoneal dialysis, hitherto the second most prescribed therapy after conventional hemodialysis. The rise and success of OL-HDF can be attributed to diverse clinical advantages that have been documented over the last two decades. Numerous publications attest to the beneficial effects of OL-HDF in terms of removal of a broad spectrum of uremic toxin, anemia control, phosphate reduction, increased hemodynamic stability and blood pressure control and less dialysis-related amyloidosis, to mention just a few. Significantly, the improvement in these conditions is considered to contribute to improved patient outcomes. Despite the extended worldwide clinical experience, elaborate scientific validation of the principles of the therapy and technical innovations that facilitate its prescription, a point of contention is whether OL-HDF leads to a reduction of mortality rates. A number of observational and retrospective analyses have indicated a survival benefit, while prospective investigations involving small numbers of patients but nevertheless specifically addressing survival have further supplied evidence of improved survival with OL-HDF. The quest for large-scale, multicenter prospective randomized controlled trials examining patient survival led to the CONTRAST and the Turkish OL-HDF trials. Both trials have been concluded and published recently. In this chapter, we document and assess the key investigations that have examined the impact of OL-HDF on patient outcome and survival. Based on the findings of previous analyses and of the two recently concluded trials, it appears that the volume of convection appears to be decisive towards the survival benefit accredited to OL-HDF. We consider the implications of this new evidence.

Diffusion

Diffusion

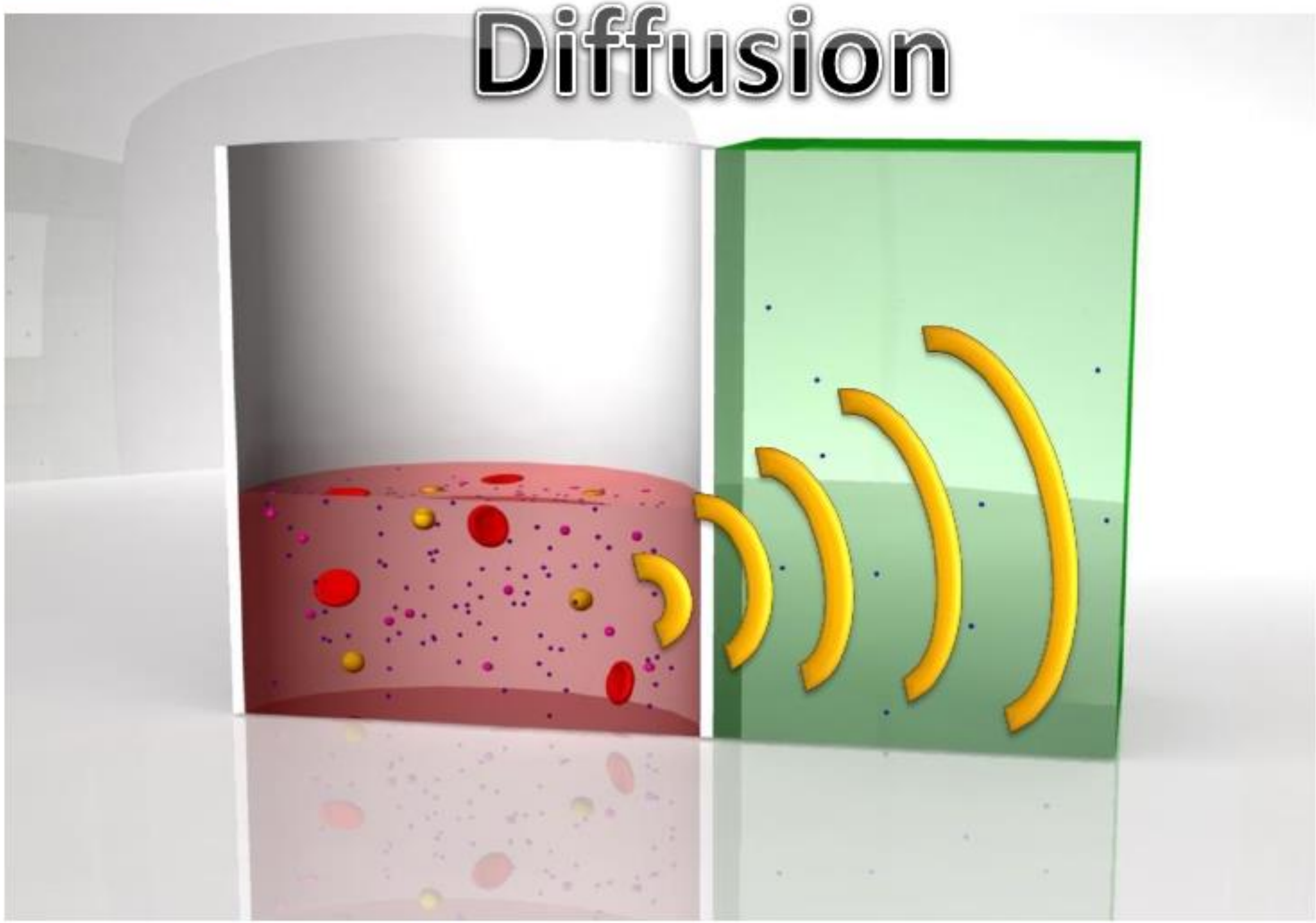
Diffusion is the main transport mechanism of small molecular size solutes also in mixed convective-diffusive therapies. Solute diffusion follows a trans-membrane concentration gradient between blood and dialysis fluid according to a first-order kinetics and the process is represented mathematically by the Fick's law:

$$J_D / A = -K_o * dc / dx \qquad (2.7)$$

M.J. Nublé et al. (eds.), *Hemodiafiltration: Theory, Technology and Clinical Practice,* DOI 10.1007/978-3-319-23332-1_2

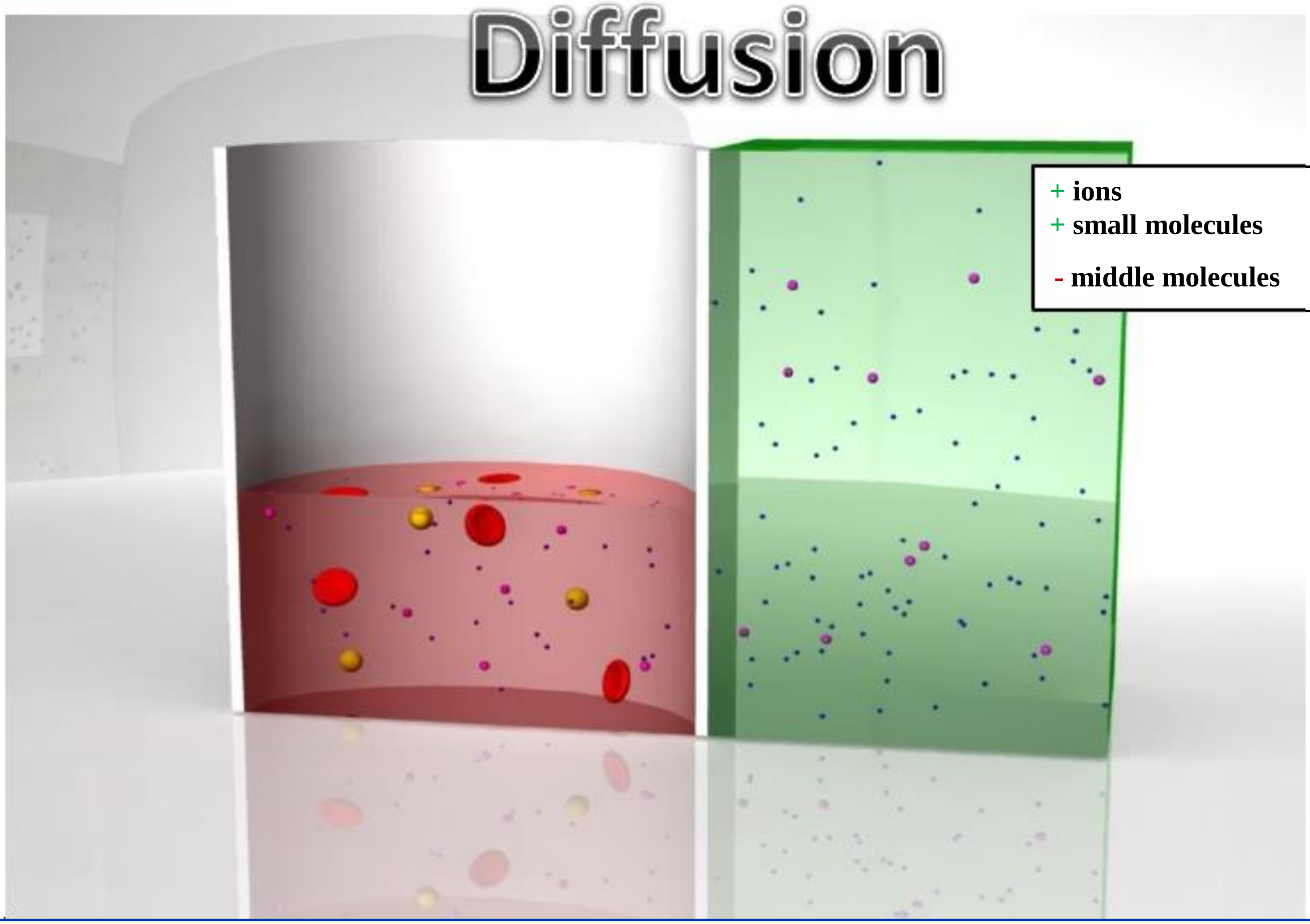
Online HDF - Physical principles of dialytic techniques

Haemodialysis



Online HDF - Physical principles of dialytic techniques

Haemodialysis



+ ions
+ small molecules
- middle molecules

Convection

Convection

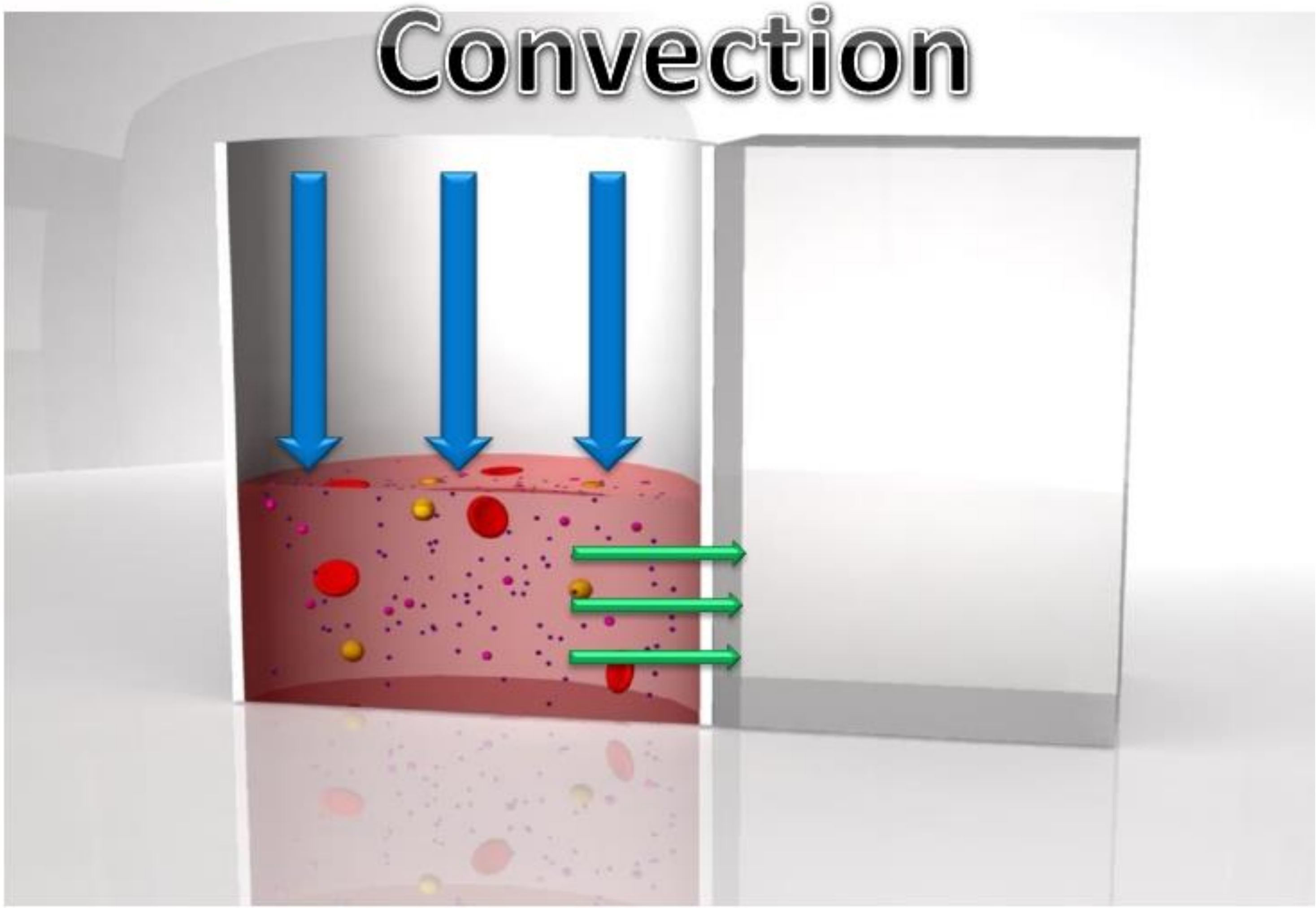
Convection is the main transport mechanism of middle molecular size solutes in mixed convective-diffusive therapies. Convective solute removal is the result of the bulk movement of the solvent (plasma water) across the membrane driven by the hydrostatic pressure gradient between blood and dialysate compartments. Convective transport is constant over a wide range of molecular weight solutes but decreases as the hydrated molecular size approaches that of the pores of the membrane. In general, the degree to which convection increases total solute removal is proportional to Q_{UF} and to the molecular weight of the solute [12]. The membrane characteristics (electro-chemical properties and structure, pore radius and conformation) also play an important role [13–16]. The ability of a membrane to remove a specific solute from plasma by convection is determined by its sieving properties and expressed mathematically with an index, the sieving coefficient (S_C, dimensionless), unique for that solute and that membrane. Sc, measured in vitro in a defined experimental setting and in the absence of diffusion, is the ratio between the solute concentration detected in the UF (C_{uf}) and its average plasma concentration within the dialyzer [6]:

$$S_c = 2C_{uf} / \left(C_{in} + C_{out}\right) \qquad (2.5)$$

M.J. Nublé et al. (eds.), *Hemodiafiltration: Theory, Technology and Clinical Practice,* DOI 10.1007/978-3-319-23332-1_2

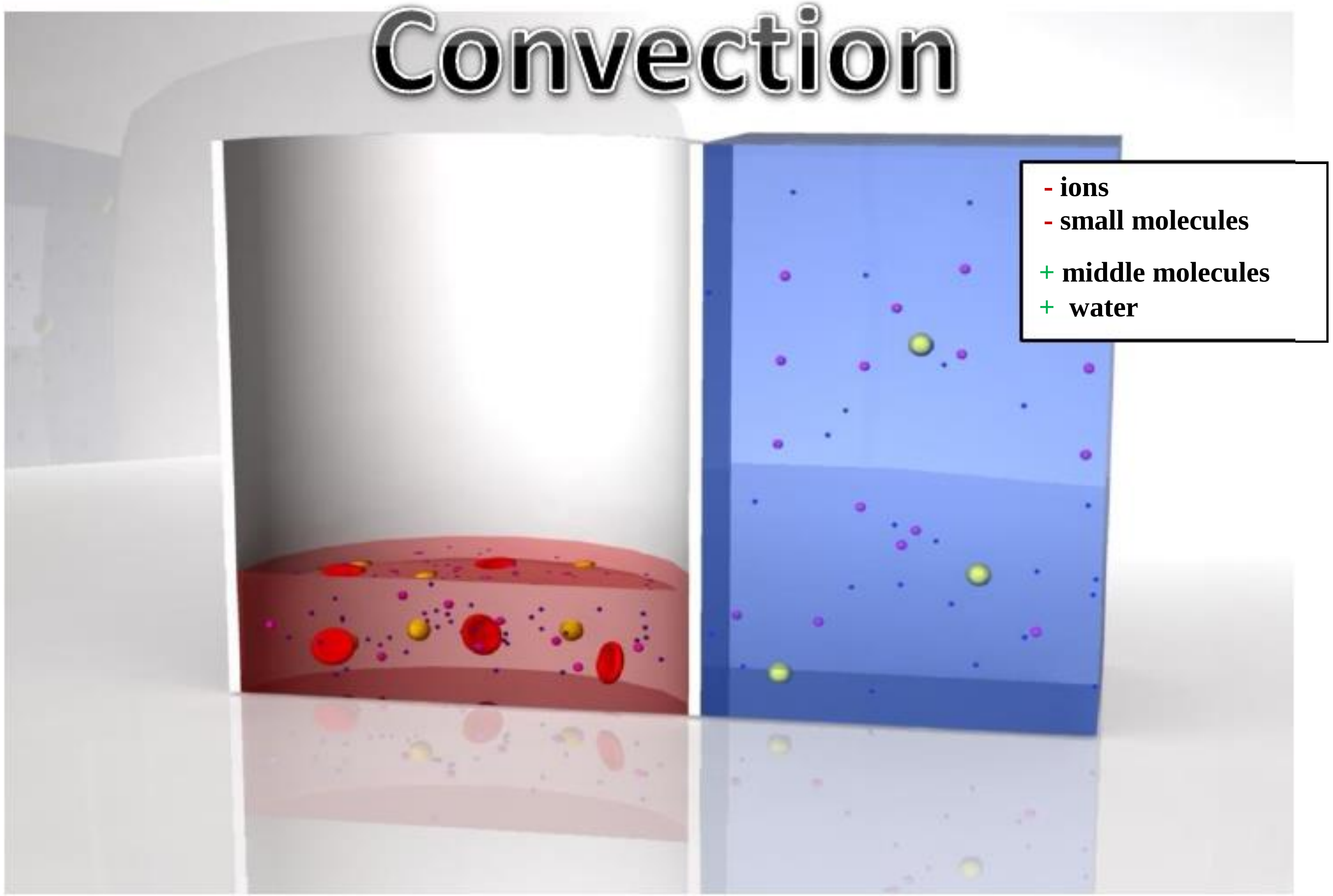
Online HDF - Physical principles of dialytic techniques

Hemofiltration



Online HDF - Physical principles of dialytic techniques

Hemofiltration



Convection

Interactions Diffusion-Convection

Interactions Between Diffusion and Convection

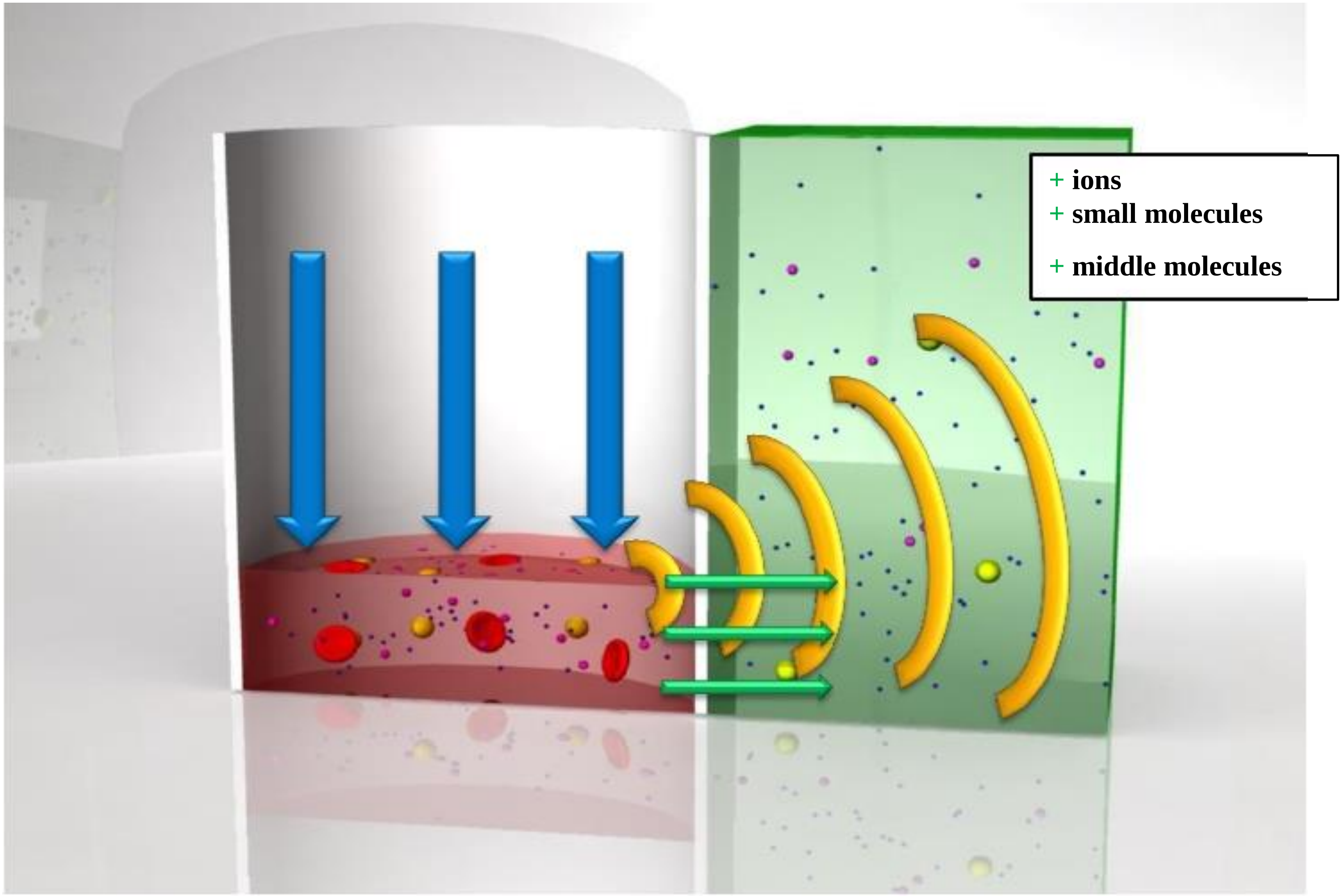
Convection and diffusion act simultaneously as solute transport mechanisms in HDF, even if to a different extent according to the molecular weight of the removed solute. However, the overall mass transport is not the sum of the two separate components because of an interaction between them, which is more prominent at the high Q_{UF} of HDF. Their effects cannot be distinguished from each other, but some mathematical models have attempted to quantify their combined effect in term of solute removal. The simplest model is described by the equation [23]:

$$K_{HDF} = K_D + Q_{UF} * T \qquad (2.9)$$

M.J. Nublé et al. (eds.), *Hemodiafiltration: Theory, Technology and Clinical Practice,* DOI 10.1007/978-3-319-23332-1_2

Online HDF - Physical principles of dialytic techniques

HD + HF = HDF (Hemodiafiltration)



HDF - Technical aspects

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BACKGROUND — Conventional hemodialysis clears uremic toxins mostly by diffusion driven by the thermal energy of the uremic toxin molecule. Clearance of the toxin by diffusion is inversely proportional to the radius of the toxin molecule. As a result, conventional hemodialysis clears larger toxin molecules less effectively than smaller ones. Clearance of larger toxins is limited by their low rate of diffusion, even if they can easily pass through the pores in the dialyzer membrane.

In contrast, hemodiafiltration (HDF) increases the clearance of larger toxins by large-volume ultrafiltration. Ultrafiltration carries toxins through the membrane pores by fluid flow, also known as convection. As long as the toxin molecule can easily pass through the membrane pores, the rate of transfer is independent of the molecule size.

HDF requires the infusion of significant amounts (at least 15 to 20 and up to 150 L) of infusate to replace the ultrafiltrate. This infusate fluid must be sterile and pyrogen free since it is infused directly into the blood. In addition, the rate of infusion must be accurately controlled so that fluid balance errors do not occur.

The infusate is either provided from the manufacturer in bags or generated by filtering the dialysis fluid within the dialysis machine. Continuous HDF, such as is used for treatments in intensive care units, utilizes fluid provided in bags by the manufacturer. When infusate is administered from bags, the rate of infusion is regulated independently from the rate of ultrafiltration, which increases the complexity of the dialysis procedure.

For chronic renal replacement therapy, infusate is usually generated by the dialysis machine, which is much less expensive than using bagged fluid. The infusate can be used for priming, washback, and, in heparin-free dialysis, for periodic flushing.

The infusate is drawn from the main dialysis fluid flow, downstream of the flow-balancing and control systems (figure 1) [1]. The resulting reduction in volume in the dialysis fluid compartment drives additional ultrafiltration at exactly the same rate as the infusate flow. In this way, there is no effect on the patient's overall fluid balance and no need for additional fluid-balancing systems. This process is known as online HDF.

HDF *online* - Technical aspects

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ONLINE HDF — As noted above, in online hemodiafiltration (HDF), the infusate is drawn from the main dialysis fluid flow, which obviates the need for additional fluid-balancing systems.

Components and technology — The dialyzer used in online HDF is the same as in high-flux dialysis. The machine must be capable of producing ultrapure dialysis fluid, and the technology is based on that for standard high-flux dialysis. The ultrapure fluid is produced by ultrafiltration of the dialysis fluid after the concentrates have been added. The ultrafilters are reused between treatments and disinfected as part of the machine's normal disinfection process.

For HDF, the majority of the ultrapure fluid is delivered to the dialyzer as usual. An additional pump diverts some of this fluid into the blood lines via additional filters in order to render it sufficiently pure for infusion. These additional infusate filters are disposable in some equipment and may be reused in others. If they are reused, the filters are disinfected and tested automatically by the machine before use (figure 1).

The control systems within the dialysis machine monitor the disinfection process and the integrity of the filters and fluid pathway. The infusate generated by the HDF system can be used for priming, wash-back, and flushing, which may offset the cost of the filters.

Infusion of replacement fluid — The infusate may be delivered into the tubing upstream of the dialyzer (pre-dilution), downstream of the dialyzer (post-dilution), both upstream and downstream (mixed dilution), or into the middle of the dialyzer blood pathway (mid-dilution) (figure 1).

HDF - Technical aspects

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- **Post-dilution -** Post-dilution is used in the majority of HDF treatments. This is because it is more efficient in terms of maximizing clearance for a given volume of infusate.

  However, post-dilution infusion often results in clotting and protein deposition (fouling) of the dialysis membrane surface. Clotting and fouling are related to the marked increases in hematocrit and protein concentrations within the dialyzer, caused by the high rates of ultrafiltration used in HDF. Clotting and membrane fouling increase transmembrane pressure (TMP) and reduce clearance by diffusion by restricting pore area and increasing the length of the diffusion pathways.

  Fouling may be reversed by temporarily reducing ultrafiltration rate. Clotting, on the other hand, once established, is irreversible and requires a filter change or termination of the treatment.

  The risk of clotting and fouling is increased with ultrafiltration rates greater than 20 to 25 percent of blood flow rate. However, ultrafiltration rates up to 30 percent can be achieved with systems that continuously control TMP based on measurements of ultrafiltration rate. Generally, all HDF systems have the hardware to run in TMP-controlled mode, although a software update may be required.

  The probability of fouling and clotting is increased when blood flow is interrupted. For that reason, a reliable vascular access is required. In intermittent treatments, extracorporeal blood flow rates of at least 350 mL/min in adults and 5 to 8 mL/min/kg body weight or 150 to 240 mL/min/m^2 body surface area in children are recommended [2]. HDF also requires adequate anticoagulation throughout the procedure and the absence of any condition that increases blood viscosity (such as high hematocrit, cryoglobulinemia, gammopathies).

- **Pre-dilution -** For patients who cannot undergo post-dilution HDF, pre-dilution or mixed-dilution HDF combined with feedback control of TMP may be used [3].

  In pre-dilution HDF, the upstream infusion dilutes the blood components before ultrafiltration takes place. This reduces the risk of fouling and clotting and allows much higher ultrafiltration rates, approaching or even exceeding the blood flow rate. Pre-dilution does not completely remove the risk of fouling and clotting, as higher ultrafiltration rates are generally used. The risk of clotting may also be increased, compared with conventional dialysis, since anticoagulant concentrations in the dialyzer are reduced by the dilution.

  Despite higher ultrafiltration rates, clearance rates may be lower with pre-dilution HDF compared with post-dilution. This is because solute concentrations in blood and ultrafiltrate are reduced by the upstream infusion, which decreases the drivers for clearance by diffusion or convection. Infusion rates have to be much higher in pre-dilution HDF compared with post-dilution to achieve the same clearance rate. Typically, infusion rates of over 60 percent of blood flow rate are used in pre-dilution HDF.

- **Mixed dilution -** In mixed-dilution HDF, a standard high-flux dialyzer is used. The infusate is delivered into the blood via two lines, one upstream and one downstream of the dialyzer. This combines the effects of both pre- and post-dilution to optimize the clearance rate. The system may vary the rates of ultrafiltration, upstream, and downstream infusions, depending on measurements of pressure at various points to achieve maximum clearance without clotting or excessive pore blockage.

- **Mid-dilution -** In mid-dilution HDF, special dialyzers are used. Infusion fluid enters the blood through an additional port in the dialyzer halfway down the dialyzer blood pathway. This system has been proposed to combine the benefits of both pre- and post-dilution.

HDF - Technical aspects

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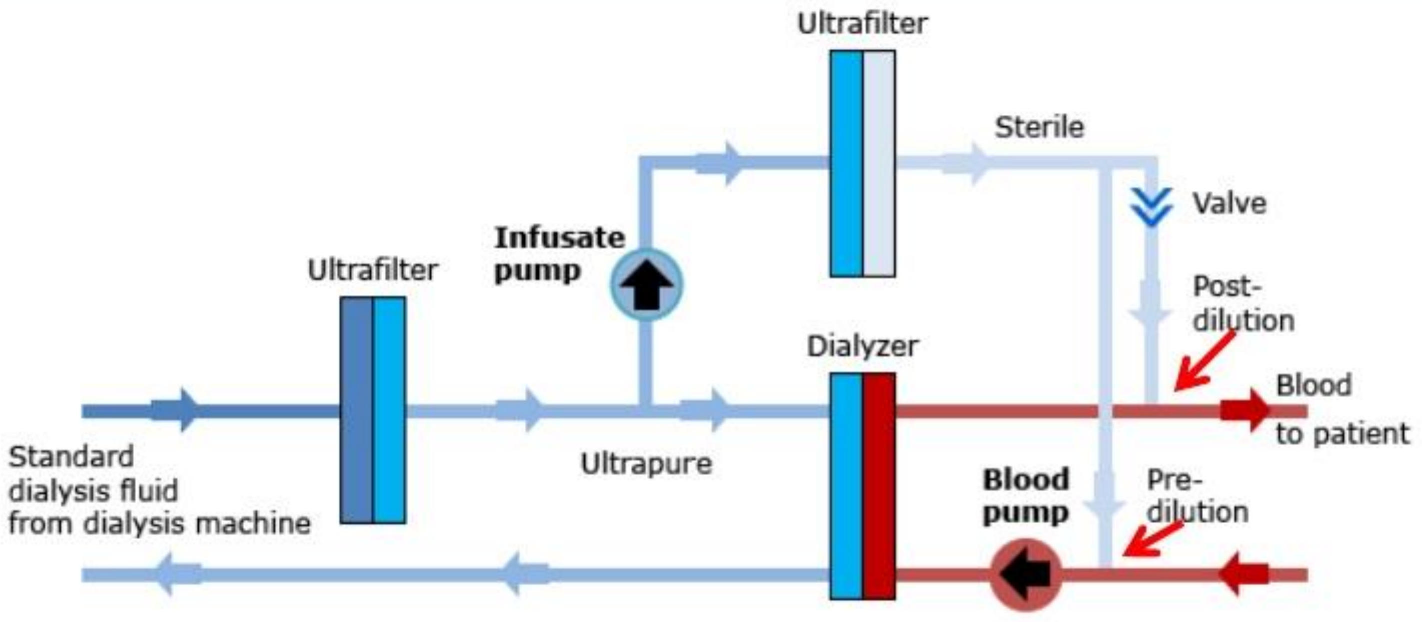
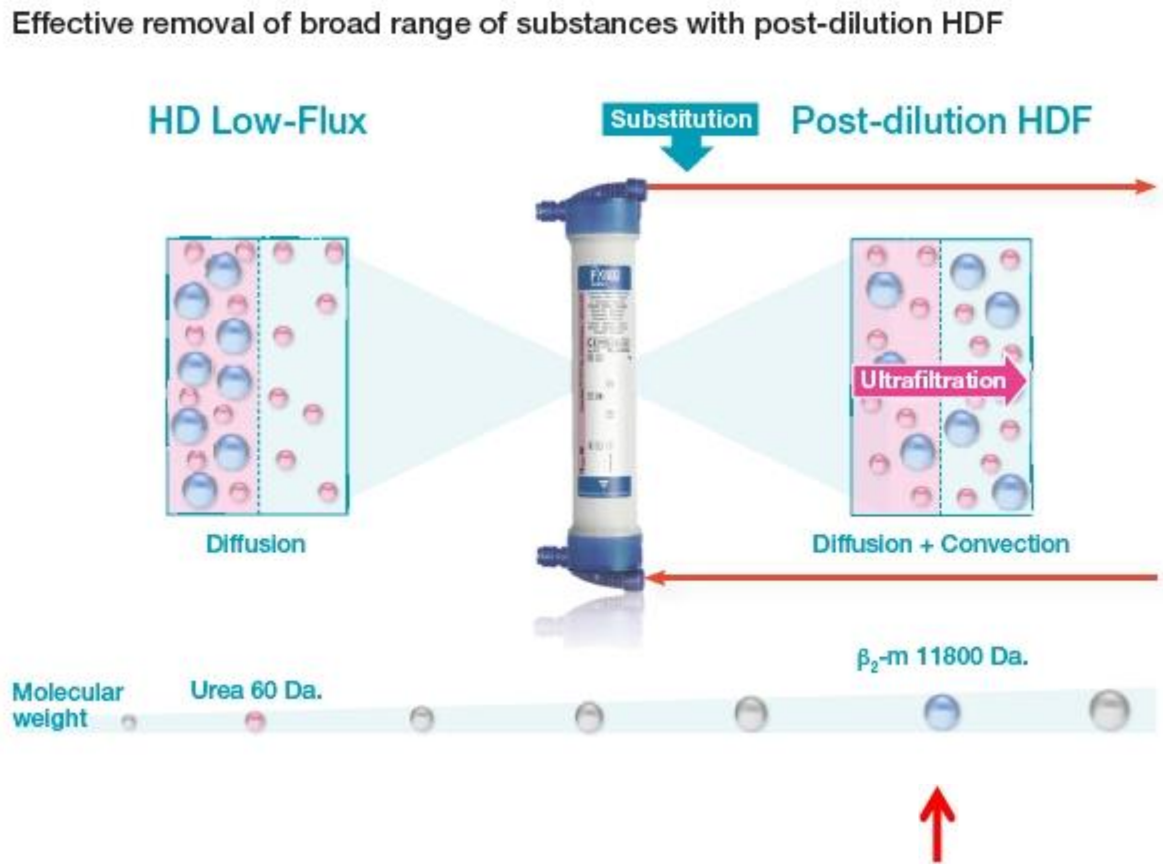
Blood and dialysis fluid pathways in hemodiafiltration



Courtesy of James Tattersall, MD, MRCP and Peter J Blankestijn, MD.

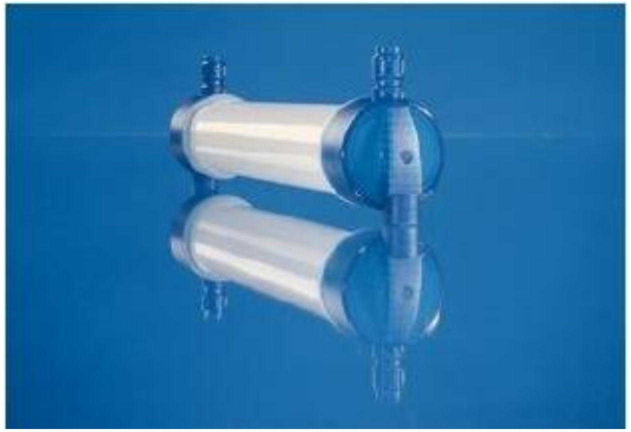
HDF - Technical aspects



The treated water

The "filter" for ultra-pure water – DIASAFE

The “filter” – Dialyzer



Dialyzer

The HD machines (TS5008) and the extracorporeal circuit (ECC)

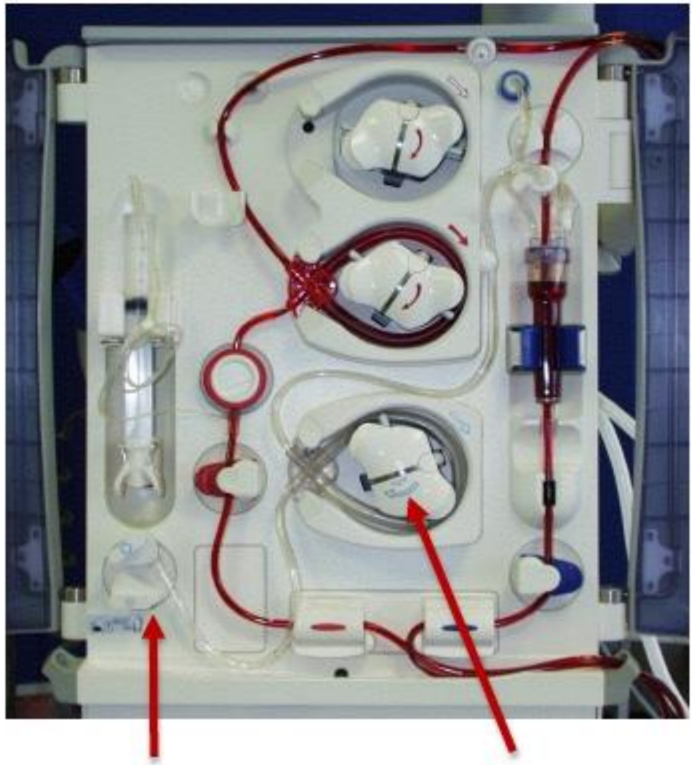
OnLine HDF - Simplicity and safety

- ✓ Online production of replacement fluid
- ✓ Online Priming, Bolus and Reinfusion
- ✓ No need for saline solutions
- ✓ HDF Online and HF Online

  (pre or post-dilution)
- ✓ Great simplicity

OnLine HDF - Simplicity and safety

- ✓ Versatile dialysis flow control allowing significant water and dialysate savings: **AutoFlow**
- ✓ Lets you do HDF with **no added costs**
- ✓ Automatic calculation of the substitution volume: **AutoSub**.



ONLINE*plus* Substitution door

ONLINE*plus*-H(D)F Pump

OnLine HDF - Physical principles of dialytic techniques

In hemodialysis many physical processes occur between the patient's blood and the dialysate, through the dialyzer.

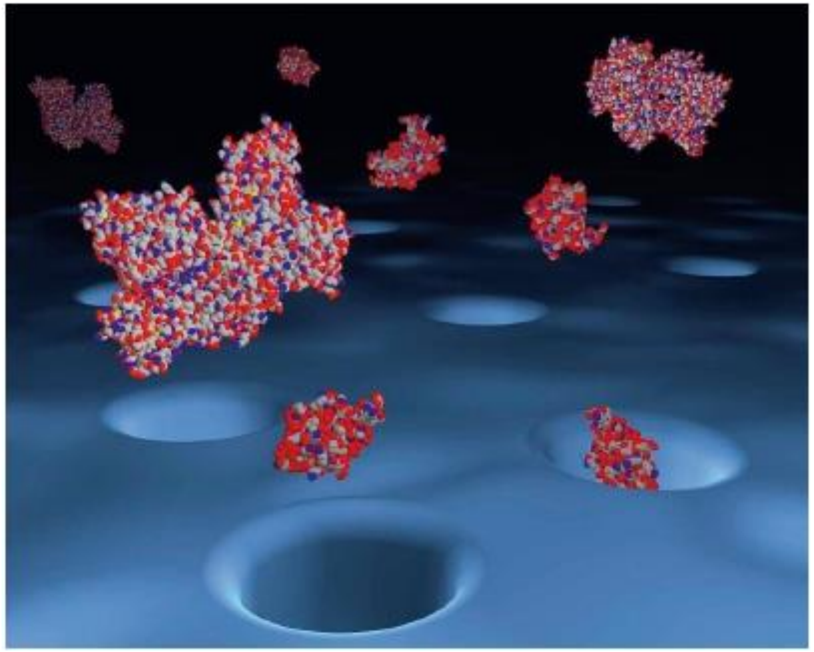
The dialyzer is a filter consisting of a semipermeable membrane.

On one side of the membrane passes the blood, on the other passes the dialysate.

Online HDF - Physical principles of dialytic techniques

Diffusion, convection, filtration and **osmosis** are processes that occur between the blood and the dialysate through the semipermeable membrane.

This is possible due to differences in concentration, hydrostatic pressures, osmotic pressures, and flow (blood or dialysate) changes.



High-Efficiency Postdilution Online Hemodiafiltration Reduces All-Cause Mortality in Hemodialysis Patients

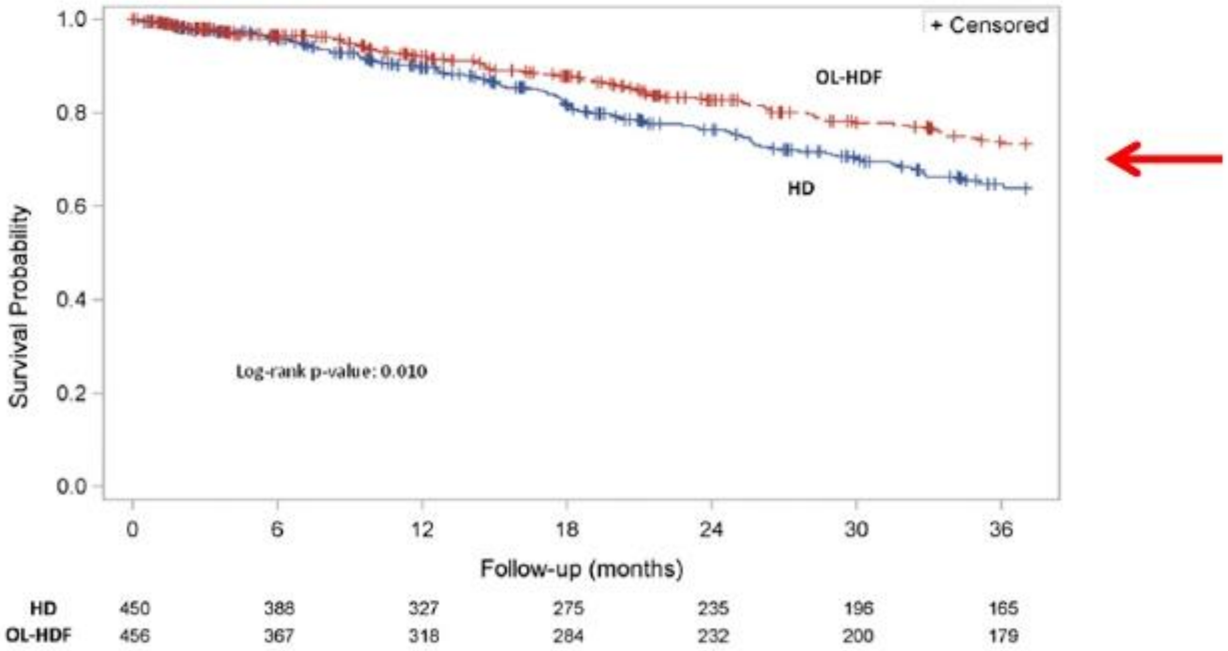


Figure 2. Kaplan–Meier curves for 36-month survival in the intention-to-treat population (P=0.01 by the log-rank test). HD, hemodialysis.

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HighVolumeHDF®

Doubts

Thank you very much for your attention!