Haemodialysis

DIASAFE®*plus*

Fresenius Polysulfone® Dialysis Fluid Filter

Fresenius Medical Care

Cardioprotective Haemodialysis

Despite significant improvements in the quality and efficacy of haemodialysis therapy in recent years, cardiovascular disease (CVD) remains the leading cause of death for dialysis patients. Today, almost every other dialysis patient dies from cardiovascular complications.

Fresenius Medical Care is supporting nephrologists world-wide in reducing their patients' risks for cardiovascular morbidity and mortality.

Innovative membranes like Fresenius Polysulfone® and Helixone®, modern monitoring devices like the Blood Volume Monitor, the Blood Temperature Monitor and Online Clearance Monitoring (OCM®), ultra-pure dialysis fluid prepared with DIASAFE®*plus* and modern ONLINE haemodiafiltration systems support the reduction of CVD risk factors.

Moreover, one of our major goals in coming years is the development and implementation of innovative new therapies and products that further improve the cardiovascular prognosis of dialysis patients.

The Dialysis Fluid Filter DIASAFE®*plus*

The quality and purity of the dialysis fluid are of major concern in modern-day renal replacement therapies, as large volumes of dialysis fluid come into contact with the patient's bloodstream during each treatment.

Bacterial endotoxins present in contaminated dialysis fluid may elicit undesirable acute reactions and influence the long-term outcome of patients on chronic haemodialysis.

Although water used for the production of dialysis fluid is treated by a series of purification steps, it still may not meet the stringent requirements on bacterial contamination levels laid down by various regulatory bodies.

By the application of special filters that are highly efficient in retaining bacterial contaminations, the required purity grades of dialysis fluid can be achieved easily.

The DIASAFE®*plus* filter, located at the end of the water treatment chain, ensures the safe production of ultrapure dialysis fluid. This is attributed to the excellent endotoxin-retention capabilities of its Fresenius Polysulfone® fibres.

Fresenius Polysulfone®

DIASAFE®*plus* is an integral part of contemporary dialysis machines. Only three handling steps are necessary to install or exchange DIASAFE®*plus* (Fig. 1):

- Open the locks of the filter holder
- Slide DIASAFE®*plus* filter into the guide grooves
- Close the locks – DIASAFE®*plus* is ready to use

Fig. 1: DIASAFE®plus can be connected with 3 rapid handling steps only. The DIAFIX™ lock system ensures a safe and hygienic connection.

The use of DIASAFE®*plus* is a key step towards Good Dialysis Practice.

Dialysis Fluid Purity

Dialysis fluids may contain microbial impurities such as endotoxins derived from bacterial fragments. Endotoxins are known to cause acute adverse reactions and promote long-term complications in haemodialysis patients [1, 2].

The toxic properties of endotoxins can be ascribed mainly to their lipid A component, which is not exposed by intact bacteria, but released only during growth or lysis of gram-negative bacteria [3, 4].

Endotoxin fragments may have molecular weights well below 2000 Da. These fragments are small enough to pass across both, low- and high-flux haemodialysis membranes into the patient's blood-stream (Fig. 2).

With respect to endotoxin permeability, significant differences exist between the various types of dialysis membranes, thereby offering variable degrees of safety during haemodialysis [3].

In order to avoid endotoxin-related complications during routine haemodialysis, the European Best Practice Guidelines for Haemodialysis (EBPG) [5] advise the usage of water having a purity level in compliance with the recommendations of the European Pharmacopoeia. However, the usage of ultrapure water for conventional high-flux dialysis is strongly recommended by the EBPG (Table 1).

Ultrapure water or dialysis fluid can easily be achieved through the application of special dialysis fluid filters – such as DIASAFE®*plus*.

	Pure water	Ultrapure water
Microbial contaminations (CFU/mL)	≤ 100	< 0.1
Bacterial endotoxins (IU/mL)	< 0.25	< 0.03

Table 1: The different purity levels of pure and ultrapure water according to the EBPG.

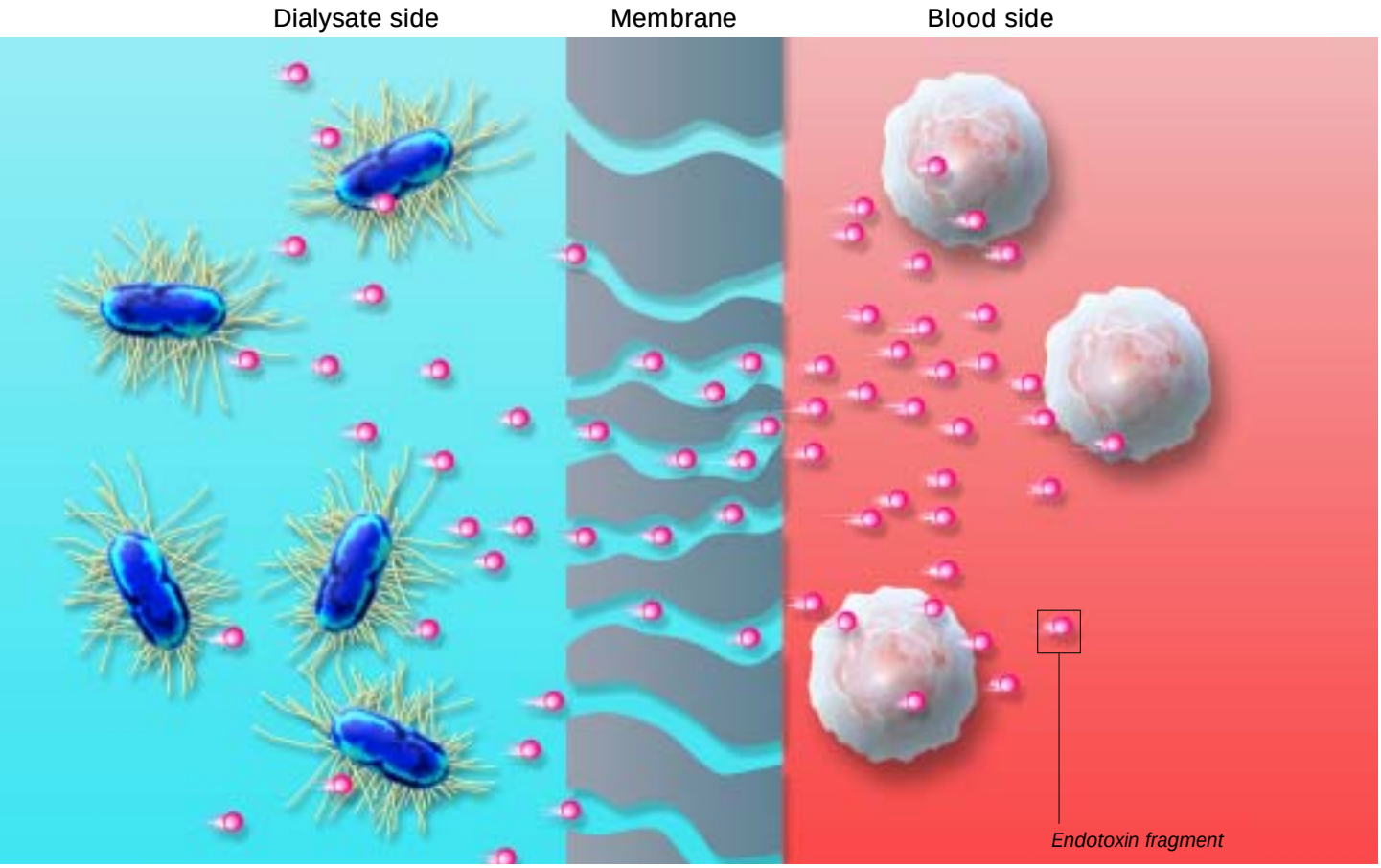

Fig. 2: Fragments of bacterial endotoxins enter the patient's blood-stream and activate leucocytes, thereby leading to acute and chronic complications in haemodialysis patients.

Clinical Advantages of Using Ultrapure Dialysis Fluid

Endotoxins can activate immune-competent cells in a number of ways, thereby contributing to chronic inflammation that is present in all haemodialysis patients [6] (Fig. 3). Recent evidence demonstrates that chronic inflammation is a major risk-factor for progressive atherosclerotic cardiovascular disease (CVD) [7].

Besides the application of haemodialysis membranes with a high biocompatibility, the usage of ultrapure dialysis fluid, in particular, has been shown to reduce markers of chronic inflammation in haemodialysis patients [8]. Therefore, it is suggestive that ultrapure dialysis fluid has a beneficial effect on inflammatory diseases such as atherosclerotic CVD [9].

Moreover, oxidative stress – a situation, in which the normal balance between production of reactive oxygen species (ROS) and antioxidant activity is tilted in favour of ROS – is increased by several treatment-related stimuli, including bacterial endotoxins derived from the dialysis fluid [10, 11].

As oxidative stress is associated with the progression of malnutrition, anaemia and inflammatory diseases such as atherosclerosis, it appears desirable to reduce dialysis-induced oxidative mechanisms, e. g. through the usage of biocompatible membranes and ultrapure dialysis fluid [10, 11].

The importance of ultrapure dialysis fluid in routine haemodialysis treatments is emphasized by the finding that endotoxins act in synergy with advanced glycation end-products (AGE), which enhance inflammation and oxidative stress [12]. Furthermore, the use of ultrapure dialysis fluid has been shown to reduce the plasma levels of the AGE compound pentosidine [13].

Finally, ultrapure dialysis fluid has also been shown to improve iron utilization and the response to erythropoietin; thus, ultrapure dialysis fluid could be beneficial for anaemia treatment allowing for a reduction in erythropoietin dosage, while maintaining optimal haemoglobin levels [14, 15].

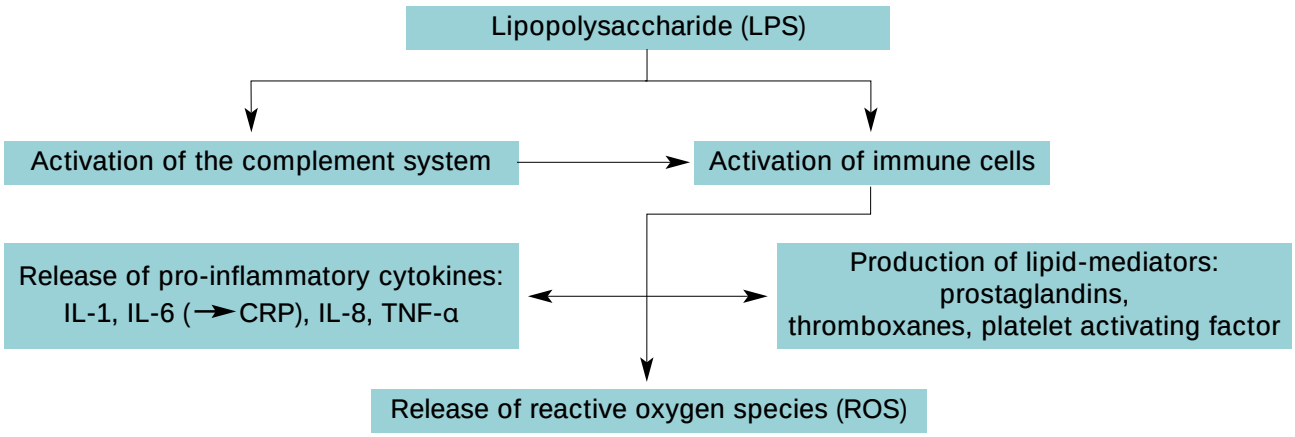

Fig. 3: Endotoxins (LPS) stimulate the release of pro-inflammatory cytokines, reactive oxygen species and lipid-mediators from immune-competent cells.

DIASAFE®*plus* in the ONLINE*plus*™ System

Ultrapure dialysis fluid prepared with the DIASAFE®*plus* dialysis fluid filter, together with haemodialysers containing endotoxin-retaining membranes (Fresenius Polysulfone® or Helixone®) are the main building blocks for a high-quality haemodialysis treatment.

The ONLINE*plus*™ system takes the quality standards of convective treatment modalities as haemodiafiltration/haemofiltration (HDF/HF) one step further: using two DIASAFE®*plus* dialysis fluid filters in series, an extremely high microbiological safety is achieved by double filtration of the substitution fluids used in ONLINE HDF/HF therapies [16].

Besides improving hygiene and safety of convective therapy modalities, the ONLINE*plus*™ option also offers additional treatment features and adds to ease of handling.

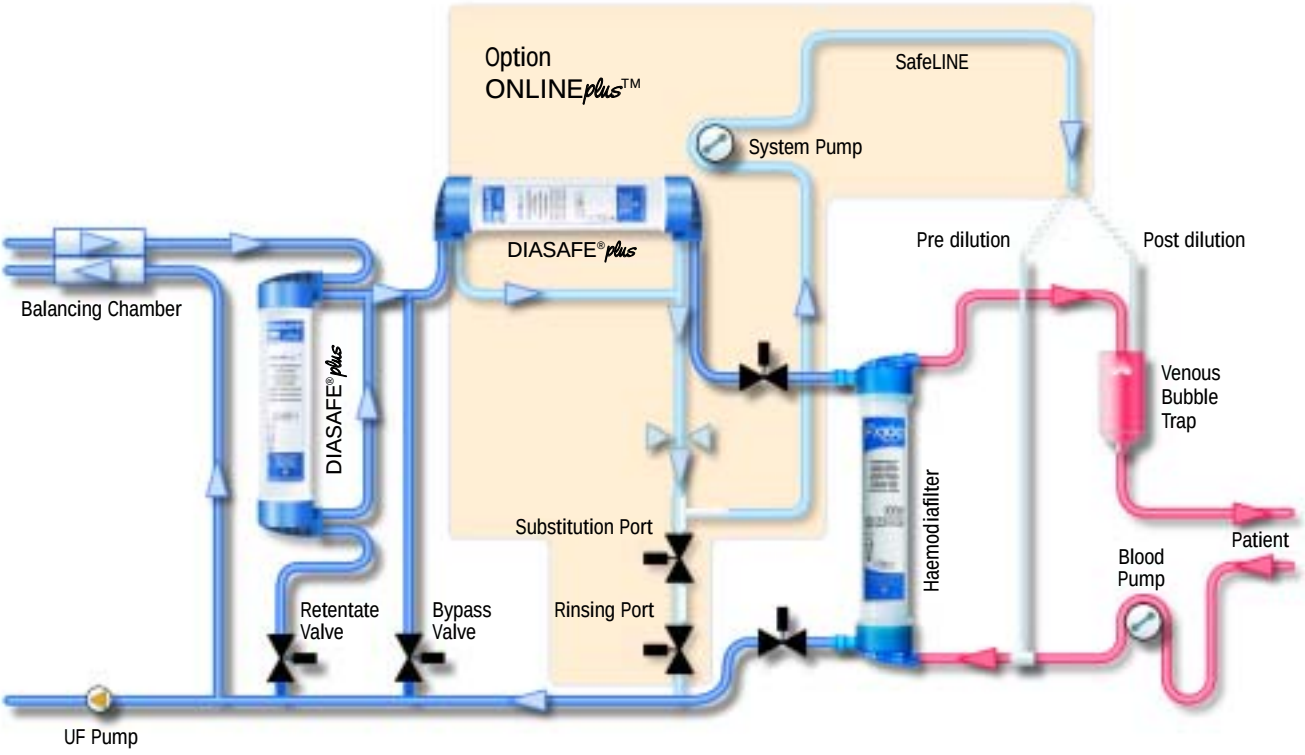

Fig. 4: Schematic flow chart of ONLINE haemodiafiltration with the ONLINEplus™ system

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Technical Data

Membrane material	Fresenius Polysulfone®
Effective Surface (m^2)	2.2
Weight (g)	170
Housing material	Polypropylene
Potting material	Polyurethane
Sealings	Silicone
Connection to machine	DIAFIX™ Lock System
Filtration rate	5 mL/min mm HG (3.75 L/min bar; max. 2 bar)
Operating time	Standard HD: max. 12 weeks ONLINE HF/HDF, ONLINE priming/rinsing: max. 12 weeks or 100 treatments
Disinfection	Puristeril® 340 or Puristeril® *plus* (peracetic acid) Diasteril® (hydroxyacetic acid) or Citrosteril® (citric acid) Sporotal® 100 (sodium hypochlorite) max. 11 times
Article number	500 820 1

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