Water treatment For Dialysis

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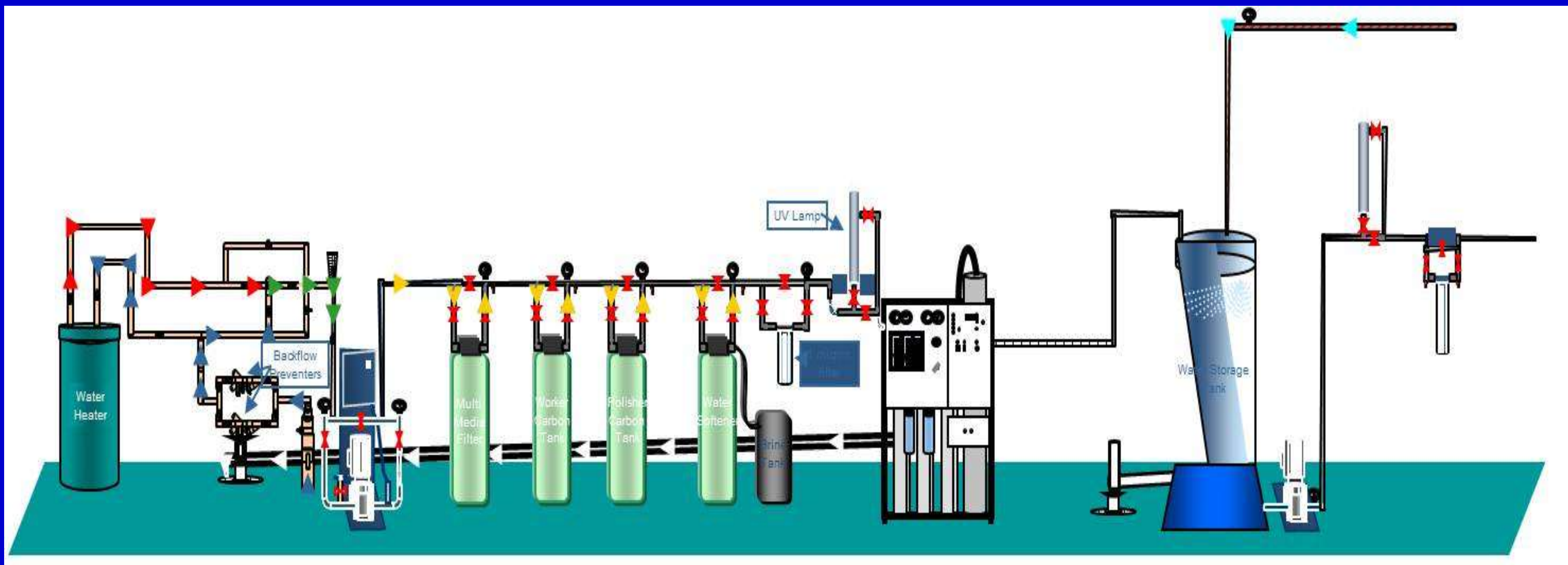
Water Treatment for Hemodialysis

"It is not exaggerated to state that inadequate water treatment is one of the gravest risks posed to the health of the patient on dialysis."

PR Keshaviah(dialysis pioneer)

Water Purification System



Overview

- Water
  - Water treatment- Why and How
  - Consequences of inadequate water treatment

Water contaminants

- Contaminants in ground or surface water
  - Chemical contaminants
    - Nitrates, sulphates, calcium, magnesium, trace metals, heavy metals, pesticides
  - Bacterial contaminants
    - Excreted bacterial pathogens
      - e.g faecal bacteria from animals
    - Pathogens growing in water supplies
      - e.g cyanobacteria
- Chemicals added during municipal treatment

Water delivered to the consumer complies with EPA requirements in respect of contaminant levels but is unsuitable for use in dialysate preparation unless subjected to further treatment

Why treat water further?

- Typically a dialysis patient is exposed to 360 liters of water per week, i.e 25 times more than the average person drinks in a week
- A dialysis patient is exposed to more water in three years than the average person in a lifetime
- Transfer of contaminants from drinking water is prevented in the gut, but for dialysis patients blood is separated from water used in the preparation of dialysis fluid by a semi permeable membrane.

Water for dialysis

- Standards for water used in the production of dialysis fluid define acceptable contaminant limits. These limits are more strict than for drinking water and are achieved by additional treatment.
- In the USA the manufacturer of the water treatment plant is responsible for the provision of water complying with the required standard. The physician is responsible in ensuring that the contaminant levels in dialysis fluid remain within acceptable limits. e.g as defined by AAMI standards(American Association for Medical Instrumentation)

AAMI WATER QUALITY STANDARDS - RD62:2001

SUBSTANCES IN DIALYSATE	
CALCIUM	2
MAGNESIUM	4
SODIUM	70
POTASSIUM	8
TOXIC SUBSTANCES (SDWA)	
ANTIMONY	0.006
ARSENIC	0.005
BERYLLIUM	0.0004
BARIUM	0.1
CADMIUM	0.001
CHROMIUM	0.014
LEAD	0.005
MERCURY	0.0002
SELENIUM	0.09
SILVER	0.005
THALIUM	0.002

SUBSTANCES TOXIC IN DIALYSIS	
ALUMINUM	0.01
CHLORAMINES	0.10
FREE CHLORINE	0.5
COPPER	0.10
FLUORIDE	0.20
NITRATE (as N)	2.0
SULFATE	100
ZINC	0.10
MICROBIOLOGICAL CONTAMINANTS	
BACTERIA	200
ACTION LEVEL	50
ENDOTOXIN	2
ACTION LEVEL	1

CHEMICAL CONCENTRATIONS IN mg/L, BACTERIA CFU/ml, ENDOTOXIN EU/ml

TOXIC WATER CONTAMINANTS

CONTAMINANT	SOURCE	ADVERSE EVENT
ALUMINIUM	MUNICIPAL WATER	ENCEPHALOPATHY, BONE DISEASE, ANEMIA
CHLORAMINES	MUNICIPAL WATER	HEMOLYSIS
FLUORIDE	MUNICIPAL WATER	FATAL ARRHYTHMIA, BONE DISEASE (?)
CYANOTOXIN	SOURCE WATER	LIVER FAILURE
NITRATES	SOURCE WATER	ANEMIA
ENDOTOXIN	DIALYSIS UNIT	PYROGENIC REACTIONS, CHRONIC INFLAMMATION
COPPER	DIALYSIS UNIT	HEMOLYSIS, NAUSEA, VOMITING
ZINC	DIALYSIS UNIT	HEMOLYSIS, NAUSEA, VOMITING
CALCIUM, MAGNESIUM	SOURCE WATER, MUNICIPAL WATER	NAUSEA, VOMITING

Consequences of inappropriate water quality

- Nearly every water contaminant has the ability to cause problems in ESRD patients. Over a long period it may not be easily distinguishable from problems arising from ESRD
- Chemical contaminants
  - Aluminium
  - Chlorine and chloramine
- Bacterial contamination

Three Deaths Associated With Excess Aluminum in Dialysate

Three recent deaths among patients on dialysis have been tied to excessive serum aluminum levels leached in through a dialysis unit's dialysate delivery system, according to the Food and Drug Administration (FDA).

FDA SAFETY ALERT: ALUMINUM AND OTHER TRACE ELEMENT CONTAMINATION DISCOVERED IN DIALYSIS FACILITIES

This is to alert you to a pot... tially hazardous situat... which dialysis patients h... exposed to dialysate... sive aluminum le... levels were lea... component... ery syst... (e.g.

Cover-up alleged at dialysis clinic

Contamination danger hidden, suits say

Tests Show Water Quality At Unit Below Standards

R.O. System Bypassed, D.I. Tanks Exchanged on Same Day as Reactions Seen

Glycol Intoxication ... Water Systems

Overexposure to Fluoride Blamed in Chicago Deaths

by Mark E. Neumann

...Chicago Medical Center officials and investigators from the ...liminary findings show that acute ...University-

Deaths in Chicago

FDA Says Unit Staff May Have Misread Warning on Water Treatment System

Agency Issues Alert Recommending Audible Alarms for all Dialysis Units

by Mark E. Neumann

...f Public Health in ... ad some symptoms similar to the patients ... at the unit were hospitalized for observation and discharged the next ... While not all the patients ... ift, they all experienced ... rs said. Some of the eight

Controversies in Water Treatment

More Deaths Reported From Algae in Brazil; High Aluminum Concentrate Kills Patients in The Netherlands

Patient Injury in Hemodialysis

1992 – 3 Patients die in Chicago.

Fluoride poisoning

1996 - 60 patients die in Caruaru, Brazil.

Water system contaminated with high levels of blue green algae

Patient Injuries in Hemodialysis

1996 - 9 patients die in the Netherlands Antilles.

High levels of aluminum in water

1998 - 3 patients die in Hong Kong

Disinfectant contaminated water.

Patient Injuries in Hemodialysis

2000 - 2 patients die, 17 injured in Youngstown, Ohio.

High levels of bacteria found in the water distribution loop

Dialysate

1992 - 3 deaths associated with excess aluminum in dialysate

1995 - Patient dies hours after dialysate accident

2008 – 22 Patients hospitalized with anemia after undetected chloramine breakthrough

No matter how good the source water supply is, it cannot be considered suitable for dialysis without further purification.

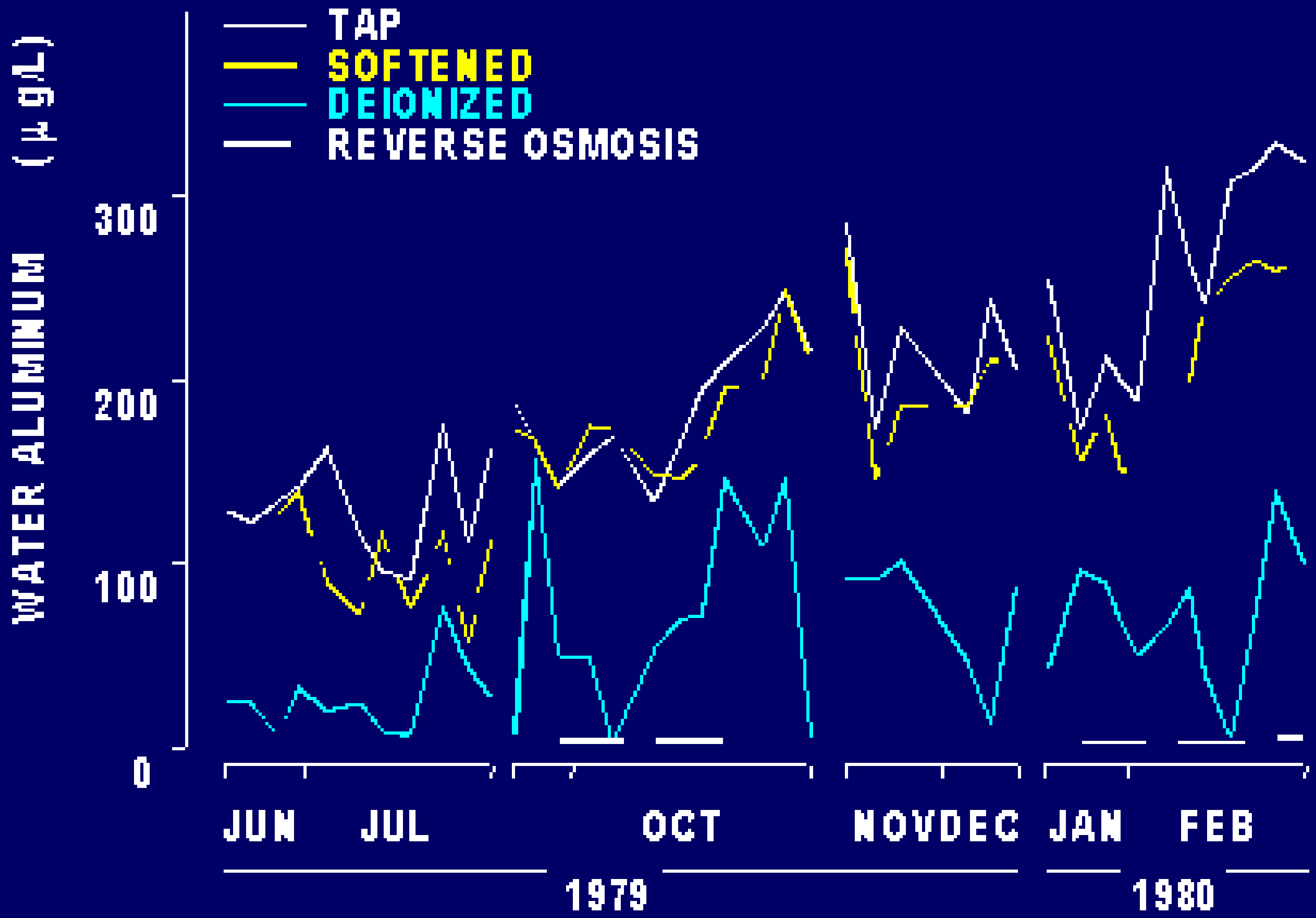
Aluminium

Aluminium

- Regulatory standard for drinking water
  - 0.2mg/l [0.2ppm]
- Desirable level in water used for the preparation of haemodialysis fluid
  - 0.01 mg/l [0.01 ppm]NOTICE THE DIFFERENCE
- Principal mode of removal
  - Reverse osmosis
  - Some may also be removed by deionizer

EFFECT OF TREATMENT ON WATER Al CONTENT

Parkinson IS et al. J Clin Pathol 34:1285-1294, 1981



Chlorine and Chloramine

CHLOROMINE-INDUCED HEMOLYSIS

YEAR	PLACE	PTS Tx	CAUSE
1970	MINNEAPOLIS	?	WATER TREATMENT SYSTEM
1974	MADRID	?	?
1981	SYDNEY	13	MUNICIPAL WATER
1984	LOS ANGELES	25	WATER TREATMENT SYSTEM
1984	SAN DIEGO	10	WATER TREATMENT SYSTEM
1987	PHILADELPHIA	41	WATER TREATMENT SYSTEM
1989	SEOUL	24	MUNICIPAL WATER
1996	RAMAT-GAN	?	WATER TREATMENT SYSTEM
1996	LONDON	0	MUNICIPAL WATER
1998	DURHAM	1	?

Chlorine and chloramine

- Chlorine (Cl)
- Chloramine ($C_7H_8ClNO_2S.Na$)
  - Condensation products of chlorine and ammonia
- By products
  - Trihalomethanes (THM) and Haloacetic Acids (HAA5) are formed when chlorine or other disinfectants react with naturally occurring organic and inorganic matter in water.
  - Their presence in water is regulated as both have demonstrated carcinogenic activity in laboratory animals and linked to an increased risk of miscarriage.


Carbon
Filter
Carbon
Filter

Chloramine and chlorine removal from water

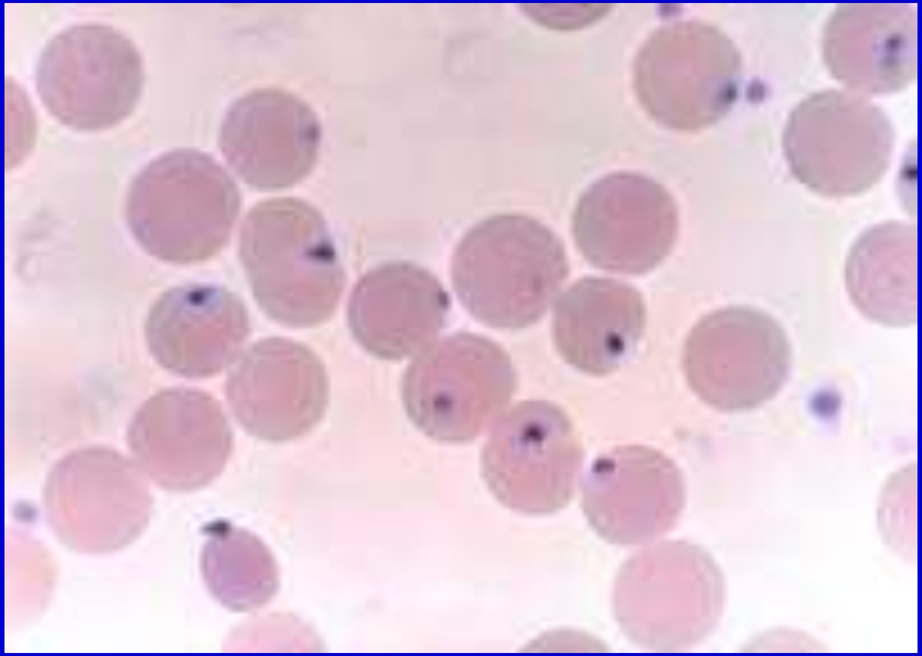
- Carbon filtration is the only effective method for the removal of chlorine and chloramines
- Desirable features of carbon used
  - Empty bed contact time [EBCT] with water 10 minutes minimum
  - Adsorptive capacity [Iodine number] 900-1000
- Requires polisher configuration for optimum effect
- Effectiveness of carbon is dependent on a range of factors, but it is estimated that 200kg of carbon is required for 1000 litres of water(8 patients for 4 hours of treatment)

What is the optimal chloramine concentration?

- Concentration of 0.1 mg/l set in the standards
  - At low levels effects are countered by patients natural antioxidants, however in patients with renal failure these are diminished
- Concentrations 0.1-0.2 mg/l
  - Red cell half life is diminished and this translates to a higher rEPO requirement
- Concentrations 0.2-0.25 mg/l
  - Clinical manifestations present-hemolysis

Clinical effects of chlorine and chloramines

- Acute haemolytic anaemia
  - Heinz-body hemolysis consisting of a cellular inclusion in a red blood cell seen in hemodialysed patients caused by chloramines in tap water



Bacterial contamination

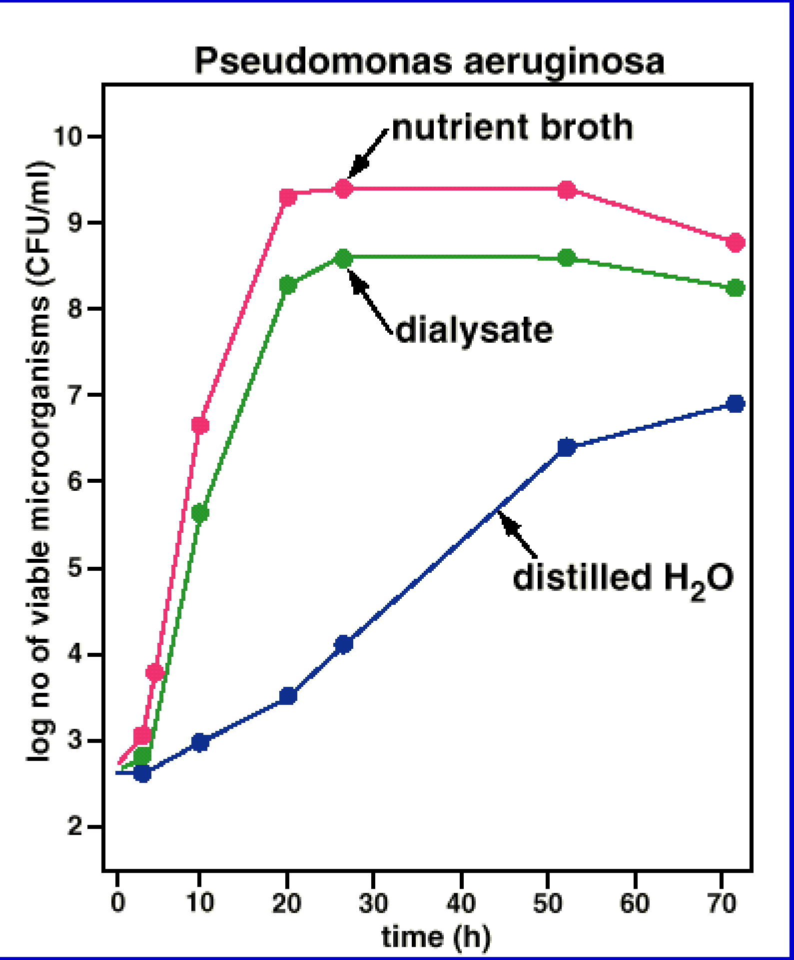
Bacterial contamination of drinking water

- Water supplied to the consumer has mandatory standards for microbiological quality
- Water routinely monitored for faecal bacteria, but may also contain cryptosporidium, a parasite which causes cryptosporidiosis an illness that can be serious or fatal for patients with compromised immune systems.

Factors that Promote Bacterial Growth in Dialysis Fluid Systems

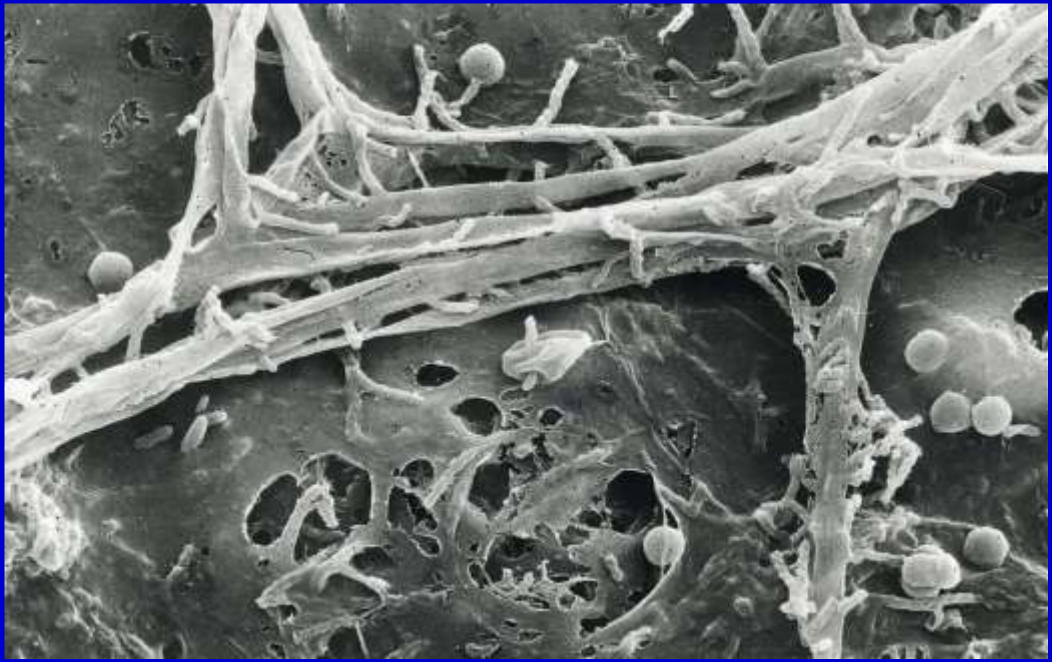
Favorable environment

- **Nutrients**
- **Water**
- **Room temperature**
- **No flow**
- **No disinfection**
- **Uneven surfaces/joints (biofilm formation)**

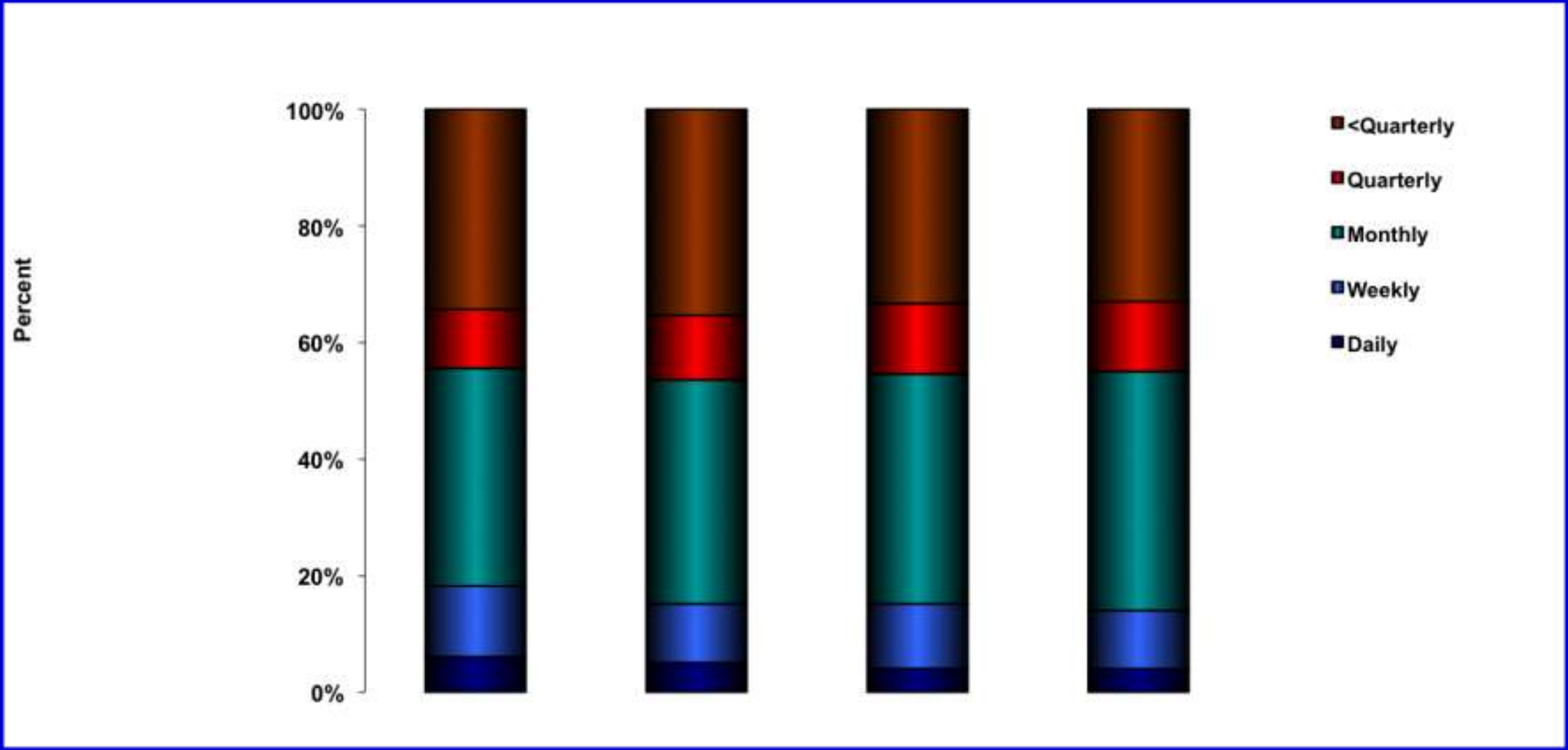


Development and consequences of biofilm within the water pipes

- Bacteria enters system
- Attaches to surface
- Multiplies and spreads
- Protective surface layer develops
- Fragments released
- Inflammatory response in patients



Sub-Optimal Frequency of Disinfection of Water Systems



Tokars, ASAIO J 1998, 44:98-107
Centers for Disease Control and Prevention (CDC), USA

Dialysate Bacterial Contaminants

Bacterial Toxins	Mol. Wt.
<u>Endotoxins - cell wall components</u> Lipopolysaccharide (LPS) LPS fragments with Lipid A	> 100kDa
<u>Other cell wall components</u> Peptidoglycans Muramyl peptides	 > 20 kDa < 5 kDa
<u>Exotoxins – secreted</u> Exotoxin A	 71 kDa

Standards for Water and Dialysis Fluid Quality

Max Limits	Water CFU/ml	Water EU/ml	Dialysate CFU/ml	Dialysate EU/ml
AAMI	200	2	2000	2
Europe	100	0.25	-	-
RRI	0.1	0.03	0.1	0.03

Definitions of Dialysis Fluid Quality

Max Limits	Bacteria CFU/ml	Endotoxin EU/ml
Standard	100	0.25
Ultra-pure	0.10	0.03
Sterile	10^{-6}	0.03

Minimization of bacterial products in the dialysis fluid

- Prevention of the formation of biofilm
- Monitoring
- Introduction of bacterial filters

Monitoring and control

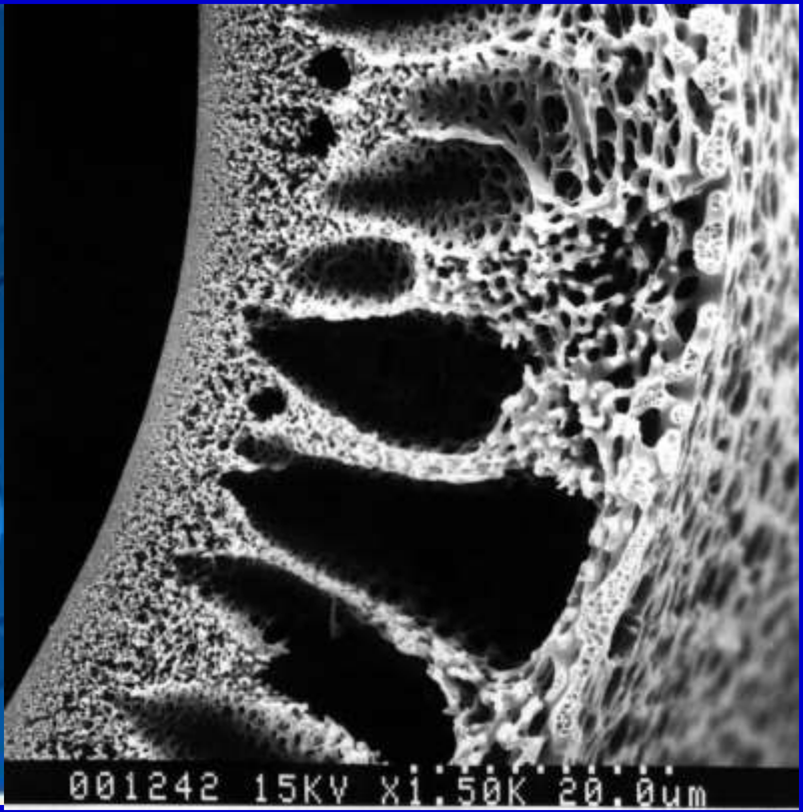
- Disinfect regularly
  - Prevents the development of bacterial growth
- Monitor regularly
  - Use appropriate methods
- Maintain records and QA charts

Monitoring Frequency

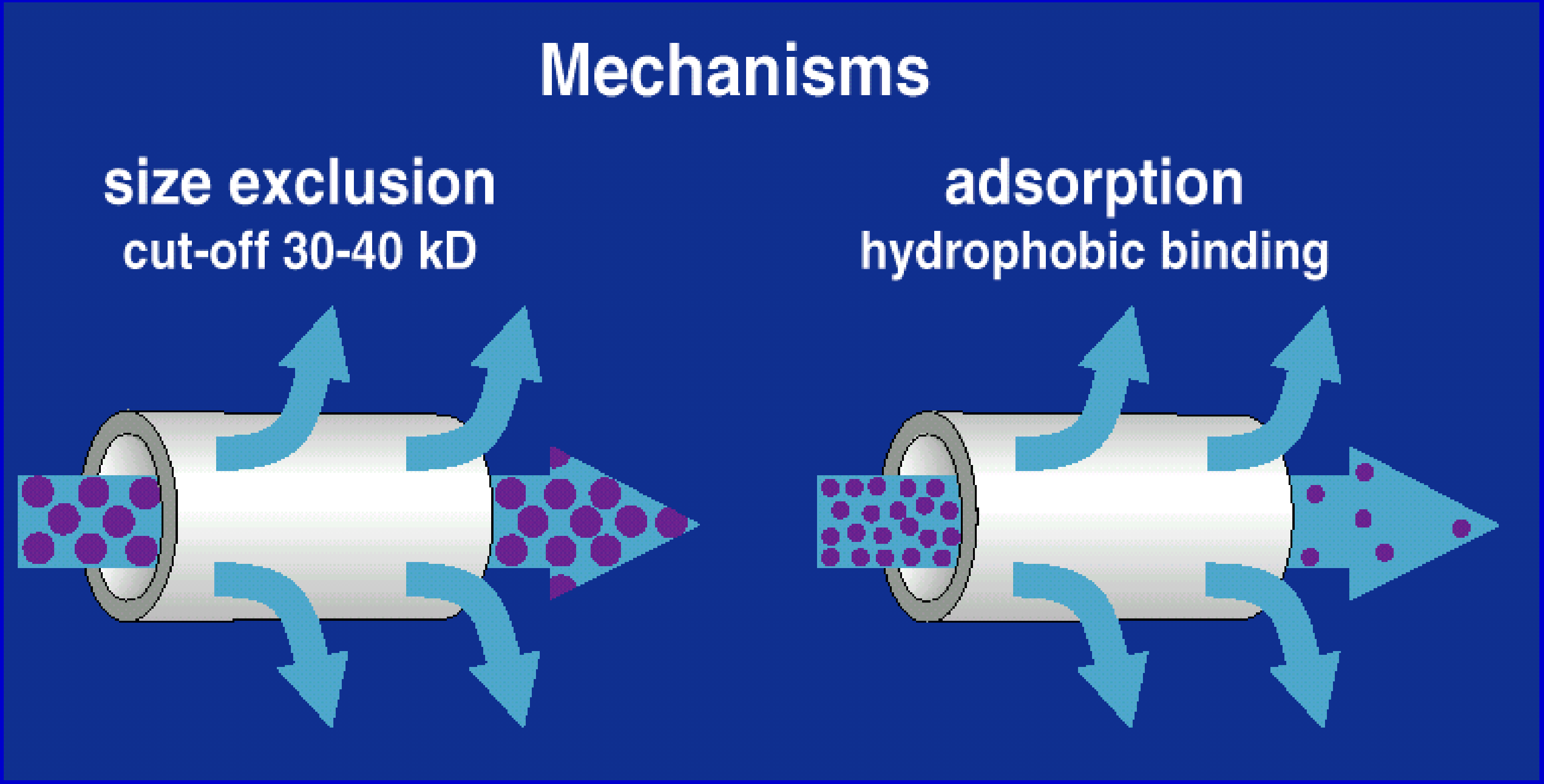
- Daily
  - Chlorine and chloramine (every shift)
  - Water softener
  - RO
- Weekly
  - Cultures for bacteria
  - LAL for endotoxin
- Monthly
  - All dialysis machines
- 6 monthly
  - Feed water quality

Filtration

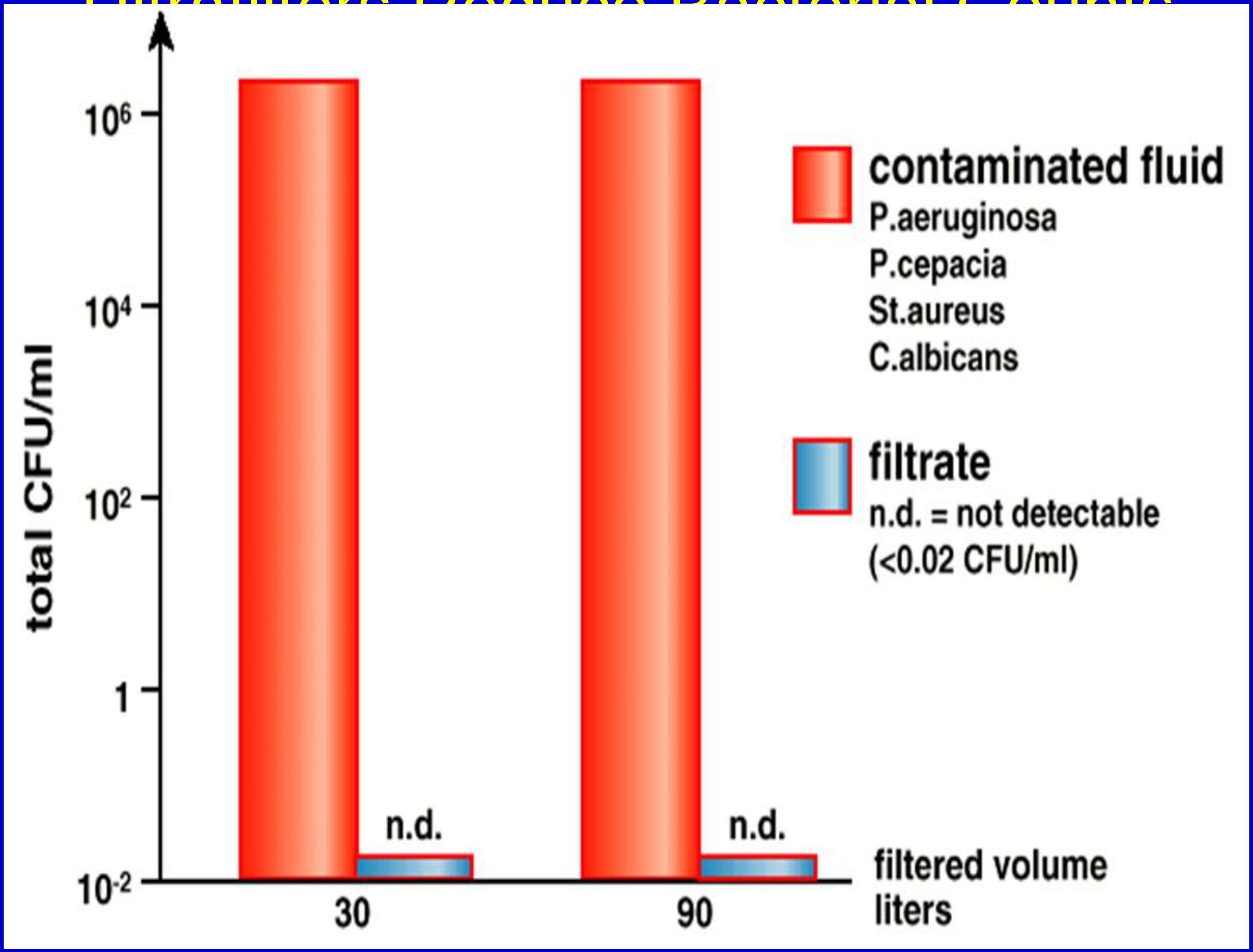
Filters incorporated into new generation of proportionating systems to minimize endotoxin exposure



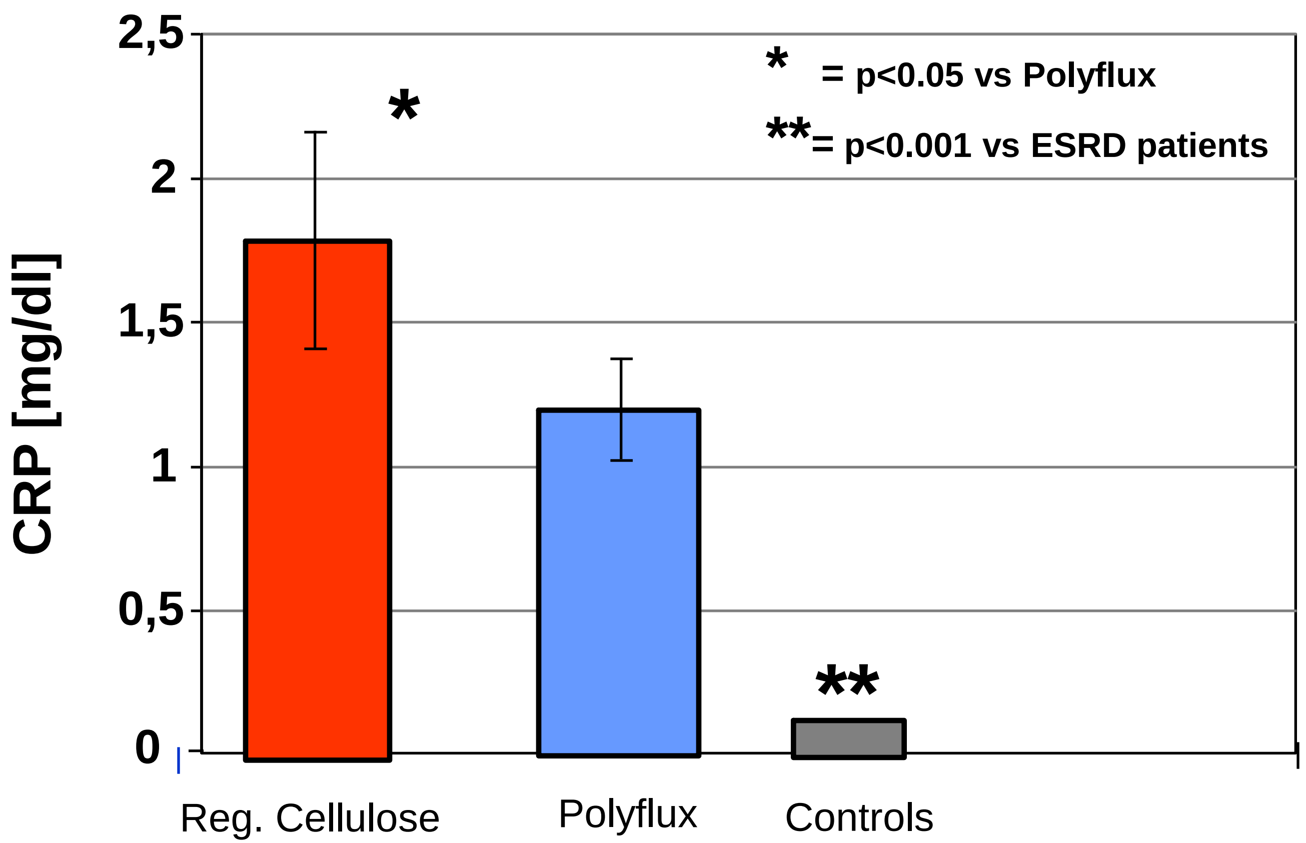
Ultrafilters Remove Bacterial Products by Size Exclusion and Adsorption



Ultrafilters Reduce Bacterial Counts



Reduced Microinflammation prospectively assessed in vivo by analysis of CRP



Schindler et. al, Clin Nephrol 2000

Filtered Fluid Reduces Inflammation in the patient

	standard fluid	filtered fluid	p<0.05
fluid quality (CFU/ml)	85 ⇨ 93	90 ⇨ 0	#
IL-6 (pg/ml)	34 ⇨ 40	38 ⇨ 18	#
CRP (mg/dl)	1.2 ⇨ 1.0	1.3 ⇨ 0.6	#
Hb (g/dl)	10.0 ⇨ 10.1	10.1 ⇨ 10.2	
rHuEPO (U/kg/week)	96 ⇨ 92	92 ⇨ 64	#

Sitter, NDT 2000
30 Patients randomized to standard or filtered fluid for 12 months

Filtered Fluid Reduces Inflammation and Improves Nutritional Markers

	standard fluid	ultrapure fluid	p<0.05
fluid quality (CFU/ml)	60 ⇨ 42	63 ⇨ 0	* #
IL-6 (pg/ml)	21 ⇨ 24	19 ⇨ 13	* #
CRP (mg/dl)	0.9 ⇨ 1.1	1.0 ⇨ 0.5	* #
dry weight (kg)	73.5 ⇨ 74.1	72.1 ⇨ 76.3	*
circumference (cm)	26.9 ⇨ 26.5	26.3 ⇨ 27.5	*
albumin (g/dl)	3.5 ⇨ 3.6	3.6 ⇨ 3.9	*

Schiffl, NDT 2001
48 patients in parallel groups studied for 12 months

Summary

- Water quality is an important contributor to morbidity and outcomes in ESRD patients
- Detailed attention to these aspects needs to be paid to ensure optimal outcomes associated with treatments
- Not doing it properly means mild to severe illness in most patients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