

**ULTRAPURE DIALYSATE:  
WHAT IS IT AND SHOULD EVERYBODY HAVE IT?**

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**OVERVIEW**

- WHAT IS ULTRAPURE DIALYSATE?
- WHY SHOULD WE USE ULTRAPURE DIALYSATE?
- CAN ULTRAPURE DIALYSATE BE PRODUCED ROUTINELY?

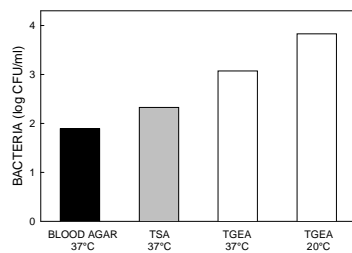
**QUESTION**

What is ultrapure dialysate?

**DEFINITIONS OF DIALYSATE QUALITY FOR HEMODIALYSIS**

	Allowable Level	
	Bacteria (cfu/ml)	Endotoxin (EU/ml)
Standard (AAMI RD52)	< 200	< 2
Standard (EDTA-ERA BPG)	< 100	< 0.25
Standard (Swedish Pharmacopoeia)	< 100	< 0.25
Ultrapure	< 0.1	< 0.03
Sterile	10 <sup>-6</sup>	< 0.03

**EFFECT OF CULTURE CONDITIONS ON COLONY COUNT IN DIALYSATE**



Ledebo I, Nystrand R. *Artif Organs* 23:37-43, 1999

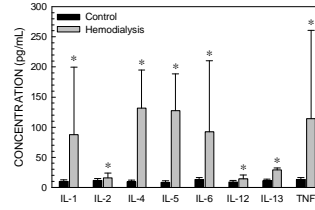
**LIMITATIONS OF CURRENT MICROBIOLOGICAL SURVEILLANCE METHODS**

- Recovery of bacteria dependent on the culture medium, incubation time and incubation temperature.
- Some bacteria, such as mycobacteria, require special culturing conditions not normally used in dialysis applications.
- Surveillance cultures detect planktonic bacteria; they do not detect the presence of biofilm.
- No surveillance for yeasts and fungi.
- *Limulus* amebocyte lysate (LAL) assay detects endotoxin, but may not detect endotoxin fragments and does not detect peptidoglycans, exotoxins, or bacterial DNA fragments.

### QUESTION

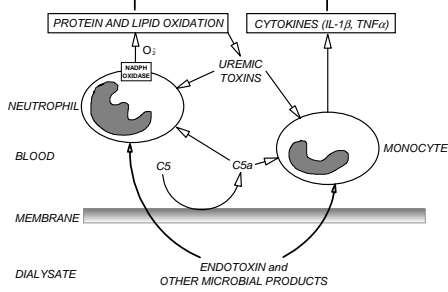
Why use ultrapure dialysate?

### INFLAMMATION IN HEMODIALYSIS PATIENTS



Kimmel P, et al. *Kidney Int* 1998;54:236-244

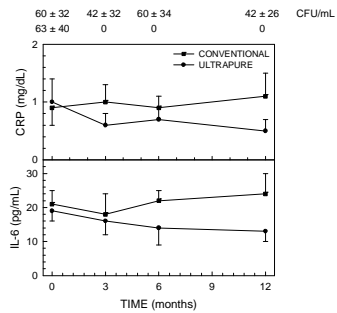
### INFLAMMATION



### POTENTIAL ADVANTAGES OF WATER AND DIALYSATE OF HIGH MICROBIOLOGICAL PURITY

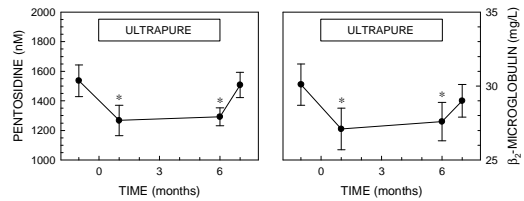
- LESS INFLAMMATORY STIMULUS
- LESS MORBIDITY ASSOCIATED WITH INFLAMMATION
  - Reduced incidence of  $\beta_2$ -microglobulin amyloid disease.
  - Improved responsiveness to erythropoietin.
  - Improved nutritional status.
  - Improved preservation of residual renal function.

### EFFECT OF DIALYSATE PURITY ON INFLAMMATION



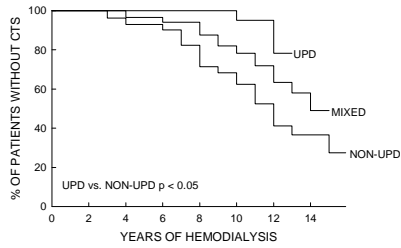
Schiff H et al. *Nephrol Dial Transplant* 16:1863-1869, 2001

### EFFECT OF WATER QUALITY ON OXIDANT STRESS AND $\beta_2$ -MICROGLOBULIN



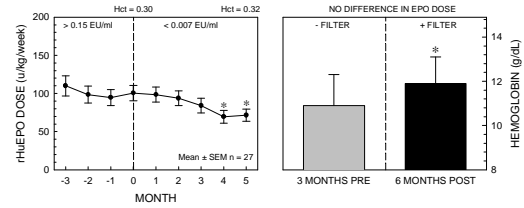
Furuya R, et al. *Blood Purif* 23:311-316, 2005

### CARPAL TUNNEL SYNDROME IN PATIENTS TREATED WITH ULTRAPURE WATER



Baz M et al. *Int J Artif Organs* 14:681-685, 1991

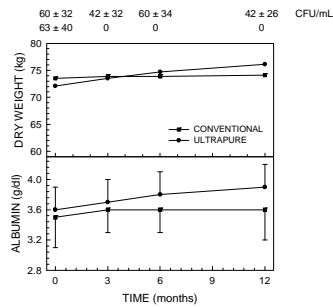
### EFFECT OF IMPROVED WATER QUALITY ON ANEMIA CORRECTION



Matsuhashi N and Yoshioka T. *Nephron* 92:601-604, 2002

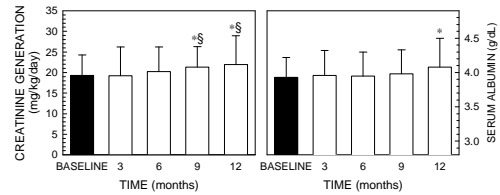
Rahmati MA et al. *Int J Artif Organs* 27:723-727, 2004

### EFFECT OF DIALYSATE PURITY ON NUTRITION



Schiffi H et al. *Nephrol Dial Transplant* 16:1863-1869, 2001

### EFFECT OF FILTERED DIALYSATE ON MUSCLE MASS AND SERUM ALBUMIN



Ouseph R, et al. *Nephrol Dial Transplant* 22: 2269-2275, 2007

	# Patients	Inflammation	Anemia Correction	Nutritional Status	$\beta_2$ -microglobulin
Arizona (2004)	23	+↑+	+↑+	+↑+	+↑+
Baz (1991)	226				+↑+
Furuya (2005)	16	+↑+		↔↔↔	+↑+
Go (2007)	61	+↑+	+↑+		
Hsu (2004)	34	+↑+	+↑+	↔↔↔	
Izuhara (2004)	84	↔↔↔		↔↔↔	↔↔↔
Kleophas (1998)	399			+↑+	+↑+
Lamas (2006)	78	↔↔↔	↔↔↔	↔↔↔	
Matsuhashi (2002)	27	+↑+	+↑+	↔↔↔	
Molina (2007)	107	+↑+	+↑+	↔↔↔	
Ouseph (2007)	105	↔↔↔	↔↔↔	+↑+	+↑+
Rahmati (2004)	342	+↑+	+↑+	+↑+	
Schiffi (2000)	89				+↑+
Schiffi (2001)	48	+↑+		+↑+	
Sitter (2000)	30	+↑+	+↑+		

+↑+ IMPROVED

↔↔↔ NO CHANGE

-↓- WORSENER

### POOLED ESTIMATES OF CHANGE FOLLOWING INTRODUCTION OF ULTRAPURE DIALYSATE

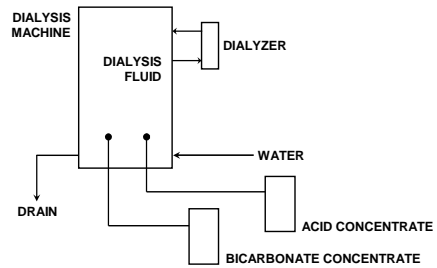
	BEFORE*	AFTER*	DIFFERENCE
CRP (mg/L)	9.9 (5.7, 14.2)	7.0 (4.8, 9.1)	-2.9
IL-8 (ng/L)	15.4 (6.4, 24.5)	10.7 (5.9, 15.5)	-4.7
Albumin (g/dL)	3.80 (3.70, 3.89)	3.89 (3.78, 3.99)	0.09
EPO (U/week)	8336 (3526, 13145)	9218 (4323, 14114)	882
$\beta_2$ -Microglobulin (mg/L)	32.1 (30.8, 33.4)	28.5 (26.0, 31.0)	-3.6

\* Pooled mean (95% confidence interval)

## QUESTION

Can ultrapure dialysate be produced routinely in a typical out-patient dialysis facility?

## PREPARATION OF DIALYSIS FLUID



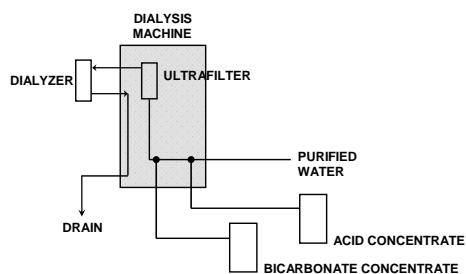
## ULTRAPURE DIALYSATE NEEDS AN INTEGRATED STRATEGY FOR CONTROL OF MICROBIOLOGICAL CONTAMINANTS

- PREVENTION OF BIOFILM FORMATION
  - SYSTEM DESIGN
  - SYSTEM OPERATION
  - DISINFECTION
- ELIMINATION OF CYTOKINE-INDUCING SUBSTANCES
  - POINT-OF-USE ULTRAFILTRATION

## DISINFECTION

- DISINFECTION SCHEDULES SHOULD BE DESIGNED TO **PREVENT**, NOT ELIMINATE, CONTAMINATION WITH BACTERIA AND BIOFILM.
- DISINFECTION SHOULD INCLUDE THE WATER STORAGE AND DISTRIBUTION SYSTEM, CONCENTRATE PREPARATION AND DISTRIBUTION SYSTEM, AND THE DIALYSIS MACHINE.
- MONITORING WITH SENSITIVE CULTURING METHODS (MEMBRANE FILTRATION) AND ENDOTOXIN LEVELS IS INTENDED TO **VERIFY** THE ADEQUACY OF DISINFECTION, **NOT** INDICATE WHEN DISINFECTION IS NEEDED.

## POINT-OF-USE ULTRAFILTRATION FOR PREPARATION OF ULTRAPURE DIALYSATE



## ULTRAPURE WATER AND DIALYSIS FLUID

- NOT REQUIRED BY AAMI, CSA, OR EP. NOT REQUIRED IN THE PROPOSED CMS REGULATIONS. ALTHOUGH COMMENTS ON THEIR USE WERE SOUGHT, RECOMMENDED IN ERA-EDTA BEST PRACTICE GUIDELINES
- ARE THE CLINICAL OUTCOMES DATA SUFFICIENTLY COMPELLING TO REQUIRE THEIR USE?
- CAN THE BENEFITS OF ULTRAPURE FLUIDS BE REALIZED IN THE PRESENCE OF DIALYZER REUSE?
- DO WE NEED A MULTICENTER, PROSPECTIVE, RANDOMIZED CLINICAL TRIAL?
- CAN WE ACHIEVE ROUTINE USE OF ULTRAPURE FLUIDS?