IMPROVED HEMODIALYSIS WATER THROUGH ULTRA-PURE WATER TREATMENT

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THE IMPORTANCE OF USING ULTRA-PURE WATER

Water is the number one “medicine” in the dialysis process. It has been shown that providing water as close as possible to USP water for injection improves the treatment for the patient.

Since hemodialysis patients have diminished renal function, they have less ability to excrete toxic substances in their urine. The combination of this diminished capacity and their extensive exposure, places the hemodialysis patient at much greater risk to water-borne contaminants than the normal population. Today, there is a consensus that purer water (ultra-pure) with a very low level of endotoxin and other bacterial byproducts, is best for patients.

ULTRA-PURE WATER FOR DIALYSIS

Water that meets or exceeds the AAMI/ISO chemical standards and the new microbiological standards is considered ultra-pure water for dialysis. The new microbiological standards of 100 CFU with an action level of 50 CFU for bacteria and 0.25 EU with an action level of 0.125 EU for endotoxin will be difficult to meet unless post filtration is used after reverse osmosis.

In addition, other bacterial byproducts such as DNA, RNA, and metabolites cause chronic micro-inflammation and challenge patients’ immune systems.

Water Contaminants and Adverse Patient Reactions

Acute symptoms associated with chemical and microbiological water contaminants:

- Usually sudden in onset and often affect more than one patient at a time.
- Sometimes confused with existing illness, chronic renal failure or medication reactions.

Chronic symptoms associated with chemical and microbiological water contaminants:

- Very frequent, insidious and develop slowly over time.
- Develop at different rates and degrees in each patient.
- Often mistaken for symptoms of chronic renal failure or other comorbid illnesses.

Health Related Problems Associated with Contaminants

Symptom	**Possible Water Contaminant**
Anemia	Aluminum, Chloramine, Copper, Zinc
Bone Disease	Aluminum, Fluoride
Hemolysis	Chloramines, Copper, Nitrates
Hypertension	Calcium, Sodium
Hypotension	Bacteria, Endotoxin, Nitrates
Metabolic Acidosis	Low pH, Sulfates
Muscle Weakness	Calcium, Magnesium
Nausea and Vomiting	Bacteria, Calcium, Copper, Endotoxin, Low pH, Magnesium Nitrates, Sulphate, Zinc
Neurological Deterioration	Aluminum

ULTRA-PURE WATER TREATMENT FOR DIALYSIS

An ultra-pure water treatment system designed for dialysis has to remove inorganic and organic contaminants to prevent patients from being exposed to them. Most water treatment systems can do a good job of removing these substances with reasonable amounts of maintenance and monitoring. Bacteria and its endotoxin byproducts are a universal problem in all dialysis water systems and require a concerted effort to maintain them at low levels. Both the 2006 AAMI Water Standards and 2010 AAMI/ISO Dialysate Standards make it very clear that maintaining these contaminants at very low levels in ultra-pure water is essential for dialysis.

Generally the ultra-pure water quality for hemodialysis should have a total chlorine level below 0.1 ppm, a conductivity below 10 µS/cm (100,000 ohms/cm), a bacterial level below 10 CFU, and an endotoxin level below 0.25 EU.

Based on the AAMI standards and our knowledge of water treatment for dialysis, it is recommended that the following be utilized to provide ultra-pure water for dialysis.

1. Disinfection of all water systems, including the reverse osmosis machine and components, should be performed <u>at least</u> monthly.
2. Disinfection of bicarb mixing and distribution should be performed <u>at least</u> weekly.
3. Aseptic sampling for bacteria and endotoxin should be prior to disinfection.
4. Utilization of disinfectant procedures with ozone, heat, peracidic acid or chlorine of sufficient concentrations to not only kill bacteria, but also burn out endotoxin and attack and destroy biofilms that develop in the system.
5. Loop endotoxin filters must be utilized on any indirect loop design (storage tank system), UV irradiator or deionizer. It's also suggested on direct feed design.
6. Recirculation flow in the loop must be maintained at 3-5 feet per second with all dialysis machines on line.(See chart). The flow rate in the loop should be verified.
7. Daily logs of the water treatment system with written protocols and parameters need to be maintained.
8. The dialysis staff must be properly trained on proper techniques of sampling water and dialysate for bacterial and endotoxin testing.

The following chart shows the recirculation requirements for dialysis water systems.

FLOW IN GPM

	Direct Feed	Pumped Recirculation	
Pipe Size	**Velocity 1½ feet/second***	**Velocity 3 feet/second****	**Velocity 5 feet/second*****
⅜" Tubing	0.28 GPM	0.55 GPM	1.0 GPM
½" Tubing	0.55 GPM	1.1 GPM	1.75 GPM
½" Pipe	1.0 GPM	2.0 GPM	3.0 GPM
¾" Pipe	2.5 GPM	4.0 GPM	6.0 GPM
1" Pipe	3.5 GPM	6.0 GPM	11.5 GPM
1¼" Pipe	6.0 GPM	11.5 GPM	18.0 GPM

It has been shown that keeping a system flowing at an adequate velocity will substantially reduce bacteria growth.

* Direct feed loop (AAMI) during conditions of peak demand.
** Minimum for continuous loop (AAMI) during conditions of peak demand.
*** Preferred for continuous loop during conditions of peak demand.

Formula for determining the flow with all stations operating:

Number of Stations x 0.21 GPM + Pipe Size Flow Rate = Total Minimum Loop Flow.

Example:

1" loop and 24 stations with storage tank.

24 stations x 0.21 GPM + 6.0 GPM = 11 GPM

The Medical Director Has the Ultimate Responsibility

Water treatment manufacturer's must have FDA 510K marketing clearance for all components from the blending valve through the endotoxin retentive filter, which is now specified in AAMI and CMS standards. According to the standards, the medical director has the ultimate responsibility:

FDA 21 CFR801.109(b)(1)

> *"Caution: When used as a medical device, Federal law restricts this device to sale by or on the order of a physician."*

ANSI/AAMI RD62:2006

> *"The physician in charge of dialysis has the ultimate responsibility for selecting a water treatment system. The physician in charge of dialysis is also responsible for maintaining the performance of that system after control of the system has been transferred formally from the installer to the physician."*

The FDA's Code of Federal Regulations:

The dialysis water treatment devices are regulated by the FDA as a medical device. Sometimes a dialysis center asks for equipment or services that are in conflict with the regulations with which the vendor must comply. It is recommended that the dialysis provider and the water treatment vendor discuss the differences they might have so both can meet the needs, comply with applicable regulations, and provide safe and effective treatment for the patient.

On the following page is a chart showing the different types of water treatment components, the necessary features and monitoring for maintaining continuous high quality water.

Summary of AAMI/FDA/CMS Standards for Water Treatment for Dialysis

This summary chart was compiled to give the current components, the required features and monitoring to provide safe and effective water quality for the hemodialysis patient.

Component/System	Features	Monitor
Reverse Osmosis	On-line temperature-compensated continuous monitor of conductivity or TDS that allow determination of rejection rate (percent rejection). Conductivity activates audible and visual alarm at preset alarm limit, 3-minute reset on silence. Alarm in patient care area. Divert product water to drain on conductivity alarm (portable acute and home exempt). Verify meets AAMI water quality requirements at start-up, at membrane replacement, and yearly. Disinfect at least monthly (means to disinfect RO). Clean-in-place quarterly (means to clean RO). Best operation between 6 and 8 pH.	Daily Log: Product Flow Reject Flow Pump PSI Reject PSI Conductivity or TDS AAMI chemical test on start-up, membrane replacement and at least annually. Calibrate monitor annually. Monthly bacteria and endotoxin tests prior to disinfect.
Deionization (if used)	Minimum of one (1) megohm water quality on a continuous temperature-compensated resistivity meter. Audible and visual alarm in patient care area, 3-minute reset. Divert to drain on alarm (portable acute and home exempt) with a minimum sensitivity of 1 megohm-cm. Pre-treat with carbon. Replace DI worker at exhaustion within 72 hours provide polisher producing < 1 megohm-cm. Post-treat with endotoxin filter.	Daily Log: Resistivity (log twice each treatment day). AAMI chemical test on start-up and at least annually. Calibrate monitor annually.
Water Softener	Sized to handle hardness. RO lockout during regeneration. Visible up front timer to verify proper time of day.	Daily log: Time of day. Salt in brine tank at least ½ full. Hardness test at end of day <1 gpg.

Component/System	Features	Monitor
Carbon and Chloramine/Chlorine Removal	Note: pH above 8.5 may interfere with carbon function. Supplemental treatment may be required. Worker-Polisher arrangement (single worker-single polisher or parallel group worker-parallel group polisher). Sample ports after worker(s) and polisher(s). Test for total chlorine before each patient shift or at least every 4 hours. Replace old media with new in all tanks at least every 2 years. Carbon minimum iodine number of 900 or greater. EBCT = 10 minutes = RO feed flow x 10 ÷ 7.48 = cubic feet total carbon. Replace carbon at breakthrough of worker within 72 hours. Monitor polisher every hour until replacement of all carbon. Visible up front timer to verify proper time of day. Home and portable acute are exempt from 10-Minute EBCT and worker/polisher arrangement.	Daily Log: Total chlorine < 0.1 ppm between the beds prior to each shift or at least every 4 hours; at least every 1 hour if only polisher is working. ΔP through filters (ΔP < 15 psi). Time of Day on backwashing filters. Log must include actual time testing is done if only polisher is working.
Supplementing Carbon: UV-185 Irradiator (TOC reduction) Dealkalizer Redox or KDF Media Acid Injection	185nm wavelength UV bulbs reduce chlorine and chloramines to chloride which the RO or DI removes. Usually sized three times larger than disinfection UV for the same flow rate. Anion exchange of alkalinity for chlorides. Water softener pre-treat. Decreases pH. Follow with water softener. Means of regulating the metering pump. Continuous monitoring of pH of water with alarm in patient care area Low pH alarm with shutdown of metering pump. Chemical added only when water is flowing.	Daily Log: Continuously monitor the milliwatt-sec/cm² of at least 16 with alarm. Test alkalinity daily at end of day. Test pH. Total chlorine <0.1ppm at least every 4 hours. (Log) Daily pH. Level of chemical in reservoir Injector function

Component/System	Features	Monitor
Supplementing Carbon Cont. Sodium Bisulphite Injection	Means to determine chemical being used (level in reservoir).	Total chlorine <0.1ppm at least every 4 hours.
Media Sediment Filter	The removed particulate clogs the filter and the pressure drop across the filter increases. Backwash periodically. Visible up front timer to verify proper time of day. Gauges to monitor differential pressure.	Daily Log: Pressure drop (ΔP) less than 15 psi. Time of Day.
Cartridge Filters	Designed for the flow rate needed. Micron size for particle removal needed. Opaque housing. Gauges to monitor differential pressure.	Daily Log: Pressure drop (ΔP) less than 10 psi.
Blend Valve	Sized for all flow rates. Check valves on hot and cold sides. Means to monitor outlet temperature.	Daily Log: Outlet temperature (normal between 70ºF and 85ºF).
Water Storage Tanks	Conical bottom with drain from lowest point of bottom. Tight fitting lid. Vented through a 0.2 micron hydrophobic vent filter. Internal spray down to facilitate effective disinfection.	Monthly bacteria and endotoxin. Inspect for leaks daily. Document on Log.
Endotoxin Retentive Filters	Required after storage tank, deionizer or ultra-violet. Must be validated for endotoxin removal. Opaque housing. Gauges to monitor differential pressure.	Daily Log: Pressure drop (ΔP) usually less than 20 psi (some ΔP is necessary to verify operation). Monthly testing after filter for bacteria and endotoxin. Pre- and post-endotoxin retentive filter bacteria and endotoxin testing following installation and when specific type of filter is changed.

Component/System	Features	Monitor
Final Ultra-Filters	Installed after other water treatment to polish the water going to the patient. Absolute micron filtration at 0.025 micron or lower.	Monthly bacteria and endotoxin levels.
Labeling	Component device marking labels with manufacturer information and warnings. Piping labeled to identify contents and flow direction (color-coded arrow tape) Tags on action points (gauges, sample ports, valves). Schematic drawing or diagram with markings and tags. Major components labeled to identify device, describe its function, how performance is verified, and actions to take if out of parameters. Physician warning. Operation manual with specifications, detailed instructions, safety features, monitoring, construction materials, disinfection procedures and warnings.	
Safety (Alarms)	Include remote alarm in patient care area if water equipment is not in patient area. Monitors cannot be disabled without notice. Temperature compensated resistivity or conductivity meter. Audible alarm at 65 decibels at 3 meters distance. Silence function resets at 180 seconds (3 minutes) and sounds alarm.	Log alarms as operable daily. Monthly alarm test.
Ultra-Violet (UV) for Water Loop Bacteria Control	254nm wavelength at 30 milliwatt dose. Sized for maximum flow rate. On-line monitor of radiant energy with alarm at 16-milliwatt dose. Followed by endotoxin retentive filter.	Daily Log: Continuously monitor the milliwatt-sec/cm^2 of at least 16 with alarm.

Component/System	Features	Monitor
Ozone Disinfection	On-line monitor of dissolved ozone (O_3) or by analysis of samples using indigo trisulfate chemistry. Ambient air monitor (OSHA PEL).	Monitor ozone dose during disinfection process. >0.5 ppm or >800 ORP for 30-minutes.
Hot Water Disinfection	Hot water of at least 80ºC for a minimum manufacturer specified time with temperature monitored at the end of loop. System must be constructed of heat-resistant materials.	Log temperature and length of time.
Water Distribution Piping System	Continuous recirculation loop at 3-5 feet/second (home and portables are exempt). Loop materials and construction shall not contribute to chemical or microbiological contamination.	Monthly monitor bacteria and endotoxin. Daily log loop flow rate and pressure.
Note: All monitoring should have clearly established parameters on the daily log. Work with the equipment manufacturer to set the limits not established by AAMI.		

PROPOSED AAMI MICROBIOLOGICAL STANDARDS FOR CFU / BACTERIA LAL / ENDOTOXIN MONITORING OF WATER AND DIALYSATE

Contamination level for total viable microbial count for water used to prepare dialysate and dialysate (cultures).	100 CFU/mL
Action level for total viable microbial count.	50 CFU/mL
Contamination level for endotoxin concentration in water and dialysate (LAL's).	0.25 EU/mL
Action level for endotoxin concentration.	0.125 EU/mL

Monthly monitoring is required for:

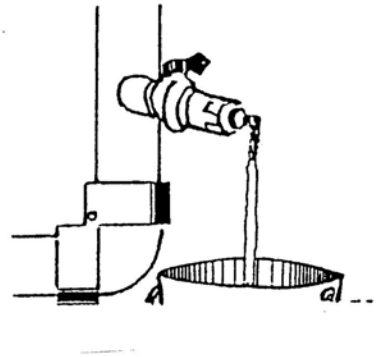
1. The product water from the RO water system and in the distribution system.

2. Conventional dialysate with sample collected from dialysate port of the dialyzer or from a sampling port in the inlet dialysate line that can be accessed using a syringe.

Note: Weekly monitoring is required at start-up or if levels exceed maximum levels until a pattern of consistent compliance with limits can be demonstrated.

The proper sampling procedure for bacteria cultures and endotoxin is very important to prevent false results. Sample ports should not be disinfected.

ANSI/AAMI RD52:2004 (7.2.2); 42 CFR 494.40 (a)(7.2.2) - Tag # V252



FLUSH SAMPLE PORT
Flush the sample port at full flow for 1-2 minutes.

CLEAN CATCH SAMPLE
Using aseptic procedure, clean catch the water in container and carefully cap.

Conclusion:

Water treatment manufacturers for dialysis must have FDA 510K marketing clearance to demonstrate safety and effectiveness prior to distribution.

Hemodialysis treatment has grown over the past thirty years. As the technology has improved, the patient survival rate has increased. The consensus is that ultra-pure water, with a very low level on endotoxin is best for patients.

Microbiological control is essential for ultra-pure water, especially endotoxin control.

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