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# Water Treatment in Hemodialysis

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# Introduction

- Survival of HD patients is steadily improving
- Increasing problems due to contaminants of dialysis water
- HD patients are exposed to 25-30 times of H<sub>2</sub>O compared to normal individuals
- Contaminants enter the blood compartment of dialysate and accumulate in the body

# Introduction

- Water treatment for preparation of dialysate is probably the most neglected area of RRT with dialysis
- Quality of water contributes very significantly in acute and long term morbidity and prognosis

# Exposure to Water and Contaminants

## Average Population

- Drinks approximately 14 L/week (2L/day)
- Able to excrete toxic substances in urine
- Contaminants selectively absorbed in GI tract, indirectly exposed to blood

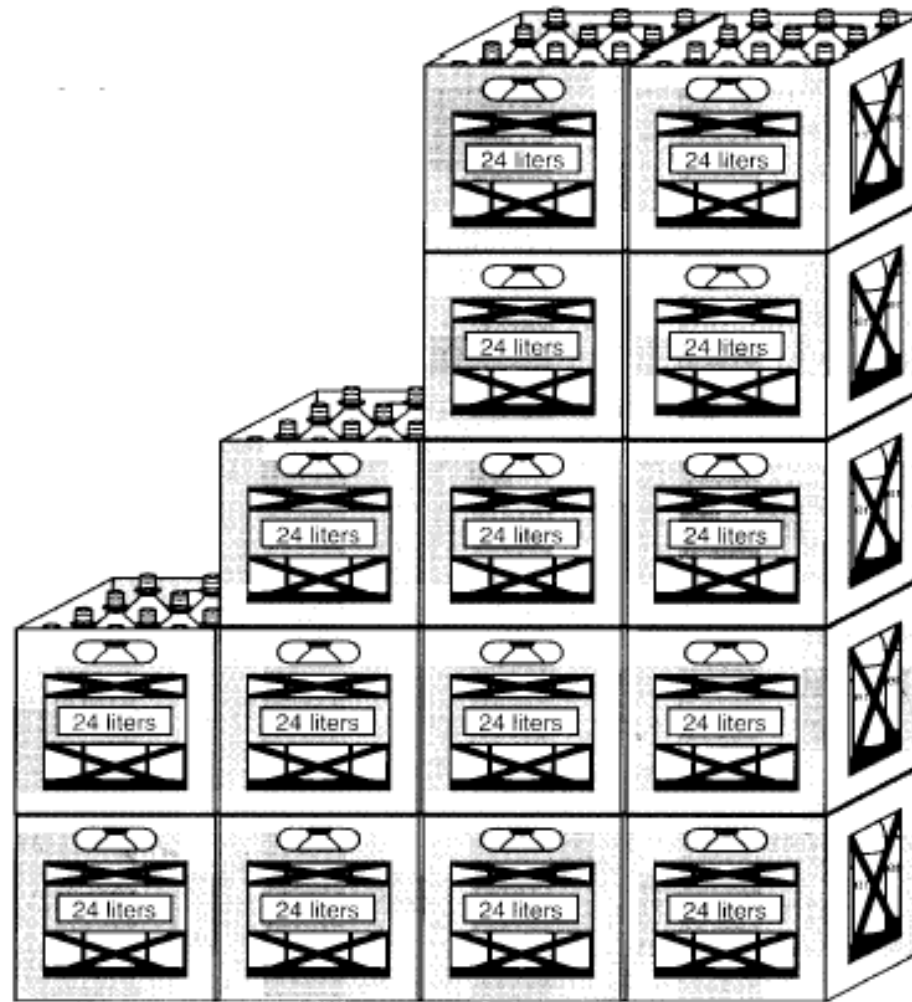
## Hemodialysis Patient

- Exposed to approximately 360 L/week (120 L/treatment)
- Kidneys unable to excrete toxic substances
- Contaminants directly exposed to blood via dialyzer membrane

# Weekly Water Exposure



The average person drinks between  
10 and 14 liters of fluid per week



The average dialysis patient is exposed to about  
360 liters of fluid per week

# Toxic effects of water contaminants in HD

| Contaminant           | Possible effects                                                   |
|-----------------------|--------------------------------------------------------------------|
| Aluminum              | Dialysis encephalopathy, renal bone disease                        |
| Calcium, Magnesium    | Hard water syndrome, hypertension, hypotension                     |
| Chloramine            | Hemolysis, anemia, methemoglobinemia                               |
| Copper                | Nausea, headache, liver damage, fatal hemolysis                    |
| Fluoride              | Osteomalacia, osteoporosis                                         |
| Sodium                | Hypertension, pulmonary edema, confusion, headache, seizures, coma |
| Microbial             | Pyrexia reactions, chills, fever, shock                            |
| Nitrate               | Methemoglobinemia, hypotension, nausea                             |
| High iron             | Hemosiderosis                                                      |
| Sulfate               | Nausea, vomiting, metabolic acidosis                               |
| Zinc                  | Anemia, vomiting, fever                                            |
| Aromatic hydrocarbons | Potential chemical carcinogens                                     |

# Progressive Dialysis Encephalopathy from Dialysate Aluminium

Arch Intern Med V138, 1978

- 8 cases of fatal dialysis encephalopathy observed in 22 months (38% of all patients)
- Coincided with addition of Al SO<sub>4</sub> and Na aluminate to city water resulting in dialysis fluid Al concentration of 200-1000 ug/l
- The outbreak ended after installation of deionizer that reduced dialysis fluid Al to < 1 ug/l



# Human intoxication by microcystins during renal dialysis treatment in Caruaru—Brazil

Sandra M.F.O. Azevedo<sup>a,\*</sup>, Wayne W. Carmichael<sup>b</sup>, Elise M. Jochimsen<sup>c</sup>, Kenneth L. Rinehart<sup>d</sup>, Sharon Lau<sup>d</sup>, Glen R. Shaw<sup>e</sup>, Geoff K. Eaglesham<sup>f</sup>

Toxicology 181 182 (2002) 441 446

- In February 1996, Caruaru, Brazil, 116 (89%) of 131 patients experienced visual disturbances, nausea, vomiting, and muscle weakness, following routine HD treatment. Subsequently, 100 patients developed acute liver failure. As of December 1996, 52 deaths occurred.
- Two groups of hepatotoxic cyanotoxins were identified: microcystins, specifically microcystin-YR, -LR and -AR.
- The outbreak occurred in one of two HD units using same water source

Arnold PM et al. An outbreak of fatal fluoride intoxication in a long-term hemodialysis unit. *Ann Intern Med* 1994;121:339-344.

- On 16 July 1993, 12 patients treated at a long-term HD unit in Chicago became ill during or soon after HD.
- The patients experienced symptoms of severe pruritus, headache, nausea, and chest or back pain.
- Three patients arrested and died due to ventricular fibrillation after completion of dialysis that day.
- Subsequent investigations found that fluoride was released from the deionization system after the ion exchange resin inside was exhausted.
- The investigator concluded that the incident was caused by errors in maintenance of the deionization system

# Components of water treatment plant

1. Water supply
2. Back-flow preventer
3. Temperature blending valve
4. Booster pump
5. Acid injection metering device
6. Multimedia depth filter
7. Water softener
8. Brine tank
9. Carbon tanks
10. Reverse osmosis (RO) system
11. RO membrane
12. Dionizer (optional)
12. Distribution system

# Purification Processes

| Process           | Contaminant                             |
|-------------------|-----------------------------------------|
| Carbon Adsorption | Chloramine, organics                    |
| Softener          | Calcium, Mg                             |
| Reverse osmosis   | Ionic contaminants, bacteria, endotoxin |
| Deionization      | Ionic contaminants                      |
| Ultrafiltration   | Bacteria, endotoxin                     |

Data from: Association  
for the Advancement of  
Medical Instrumentation.  
Water for Hemodialysis  
and Related Therapies,  
ANSI/AAMI/ISO  
13959:2009, AAMI,  
Arlington, VA 2011.

## Chemical quality standards for water used in hemodialysis applications in the United States

| Contaminant                                                | Maximum concentration (mg/L) |
|------------------------------------------------------------|------------------------------|
| <b>Substances normally included in dialysate</b>           |                              |
| Calcium                                                    | 2 (0.1 mEq/L)                |
| Magnesium                                                  | 4 (0.3 mEq/L)                |
| Potassium                                                  | 8 (0.2 mEq/L)                |
| Sodium                                                     | 70 (3.0 mEq/L)               |
| <b>Substances regulated by the Safe Water Drinking Act</b> |                              |
| Antimony                                                   | 0.006                        |
| Arsenic                                                    | 0.005                        |
| Barium                                                     | 0.10                         |
| Beryllium                                                  | 0.0004                       |
| Cadmium                                                    | 0.001                        |
| Chromium                                                   | 0.014                        |
| Mercury                                                    | 0.0002                       |
| Selenium                                                   | 0.09                         |
| Silver                                                     | 0.005                        |
| Thallium                                                   | 0.002                        |
| <b>Substances known to be toxic in hemodialysis</b>        |                              |
| Aluminum                                                   | 0.01                         |
| Total chlorine*                                            | 0.10                         |
| Copper                                                     | 0.10                         |
| Fluoride                                                   | 0.20                         |
| Lead                                                       | 0.005                        |
| Nitrate (as N)                                             | 2.0                          |
| Sulfate                                                    | 100                          |
| Zinc                                                       | 0.10                         |

**Table 2** Recommended maximum levels of microbiological contaminants in water used for hemodialysis

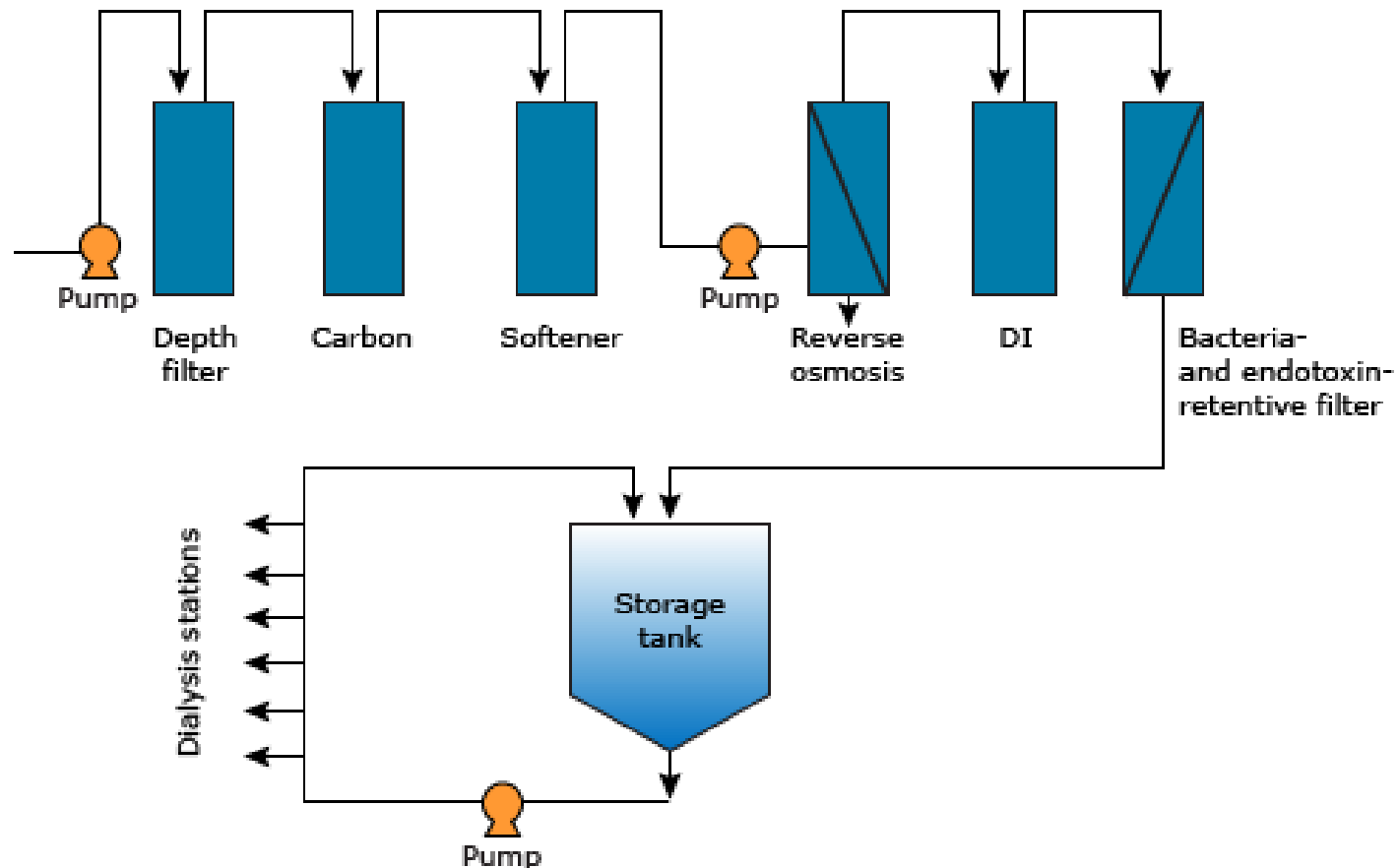
|                                                        | Bacteria<br>(CFU/mL) | Endotoxin<br>(EU/mL) |
|--------------------------------------------------------|----------------------|----------------------|
| AAMI <sup>8</sup>                                      | 200                  | 2                    |
| Canadian Standards Association <sup>7</sup>            | 100                  | 2                    |
| United States Pharmacopoeia <sup>11</sup>              | 100                  | 2                    |
| European Pharmacopoeia <sup>10</sup>                   | 100                  | 0.25                 |
| Swedish Pharmacopoeia <sup>16</sup>                    | 100                  | 0.25                 |
| ERA-EDTA <sup>12a</sup>                                | 100                  | 0.25                 |
| Japanese Society for<br>Dialysis Therapy <sup>13</sup> |                      | 0.25                 |
| Italian Society of Nephrology <sup>17a</sup>           | 100                  | 0.25                 |

AAMI (2011)

100

0.25

# Schematic diagram example of a water treatment system for hemodialysis

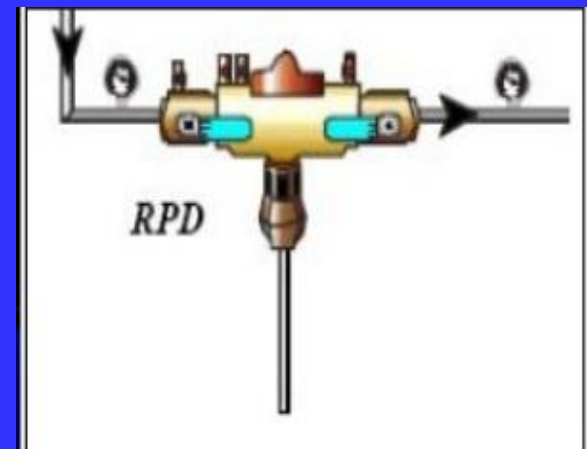


# Water supply

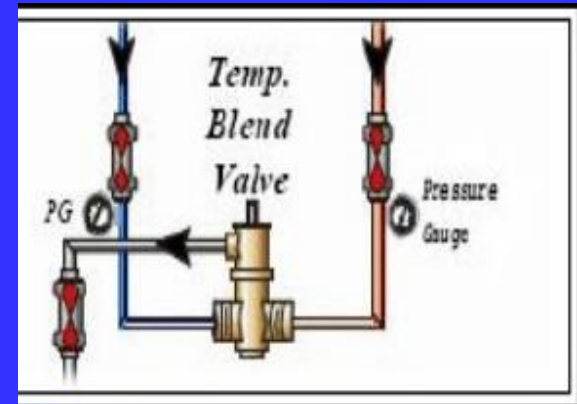
- There are 2 sources of municipal water: surface water and ground water
- Surface water is generally more contaminated with organisms and microbes, industrial wastes, fertilizers, and sewage.
- Ground water is generally lower in organic materials but contains higher inorganic ions such as iron, ca, mg and sulfate



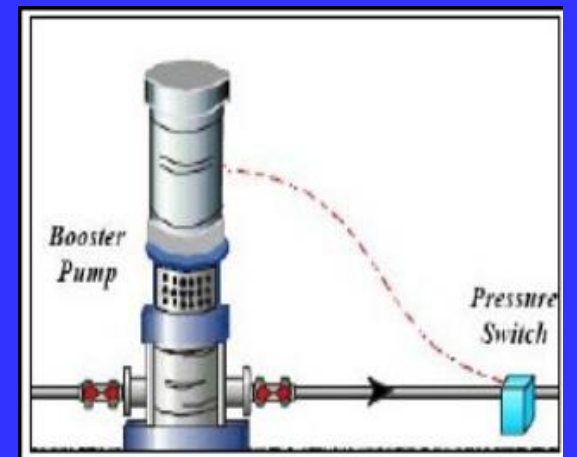
**Back flow preventer:** inhibits flow back of treated water into municipal water



**Temperature blending valve:** brings water to a standard temperature of 25 oC for proper function of RO system



**Booster pump:** maintains adequate flow and pressure of water so the system operates successfully.





# Acid injection metering device

- By increasing the pH of the city water supply using lime softening agents or  $\text{CaCO}_3$  prevent leaching of lead, copper from the piping system
- For proper function of RO and carbon tanks, incoming water pH should be between 5-8.5

# Multimedia depth filter

- Large particulates of  $>10$  microns such as dirt, are removed by a multimedia depth filter.
- Floculants can clog the carbon and softener tanks, destroy the RO pump, and foul the RO membrane
- Contain multiple layers of various sized rocks that trap the large particles as the water filtered downward

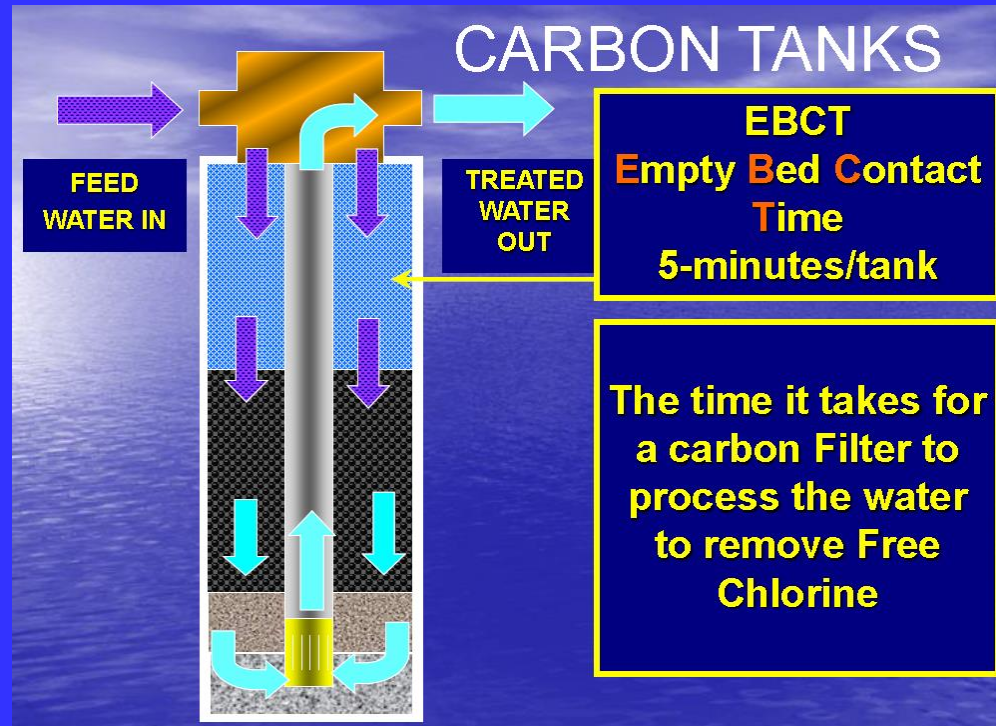






# Carbon Tank

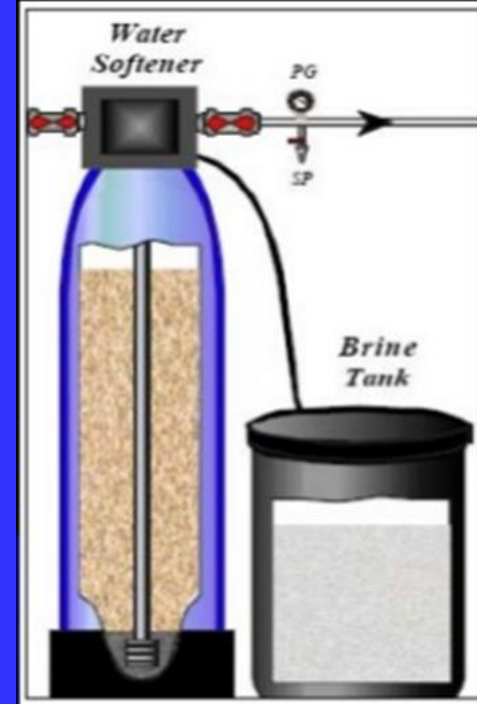
- Removes chlorine and chloramine
- These are high level oxidative chemicals. They are added to municipal water systems to kill bacteria, but they also cause hemolysis





# Water Softener

- Water containing Ca and Mg form deposits on RO membrane
- Softeners work on ion exchange basis. The resin beads within the tank have a high affinity for the cations Ca and Mg (divalents) present in the source water and release 2 sodium ions (monovalent) for one Ca or Mg captured





# Water Softener

- The softener needs regenerating on a routine basis with concentrated NaCl solution (brine) before the resin capacity is used up
- The resin is backwashed to loosen the media and clean any particulates from the tank. After the backwashing step, the brine solution is drawn into the tank



# Reverse osmosis pre-filter

- Prefilters are particulate filters positioned immediately before the RO pump and membrane
- Carbon fines, resin beads, and other debris exiting the pretreatment could destroy the pump and RO membrane
- Prefilters range in pore size from 3-5 microns

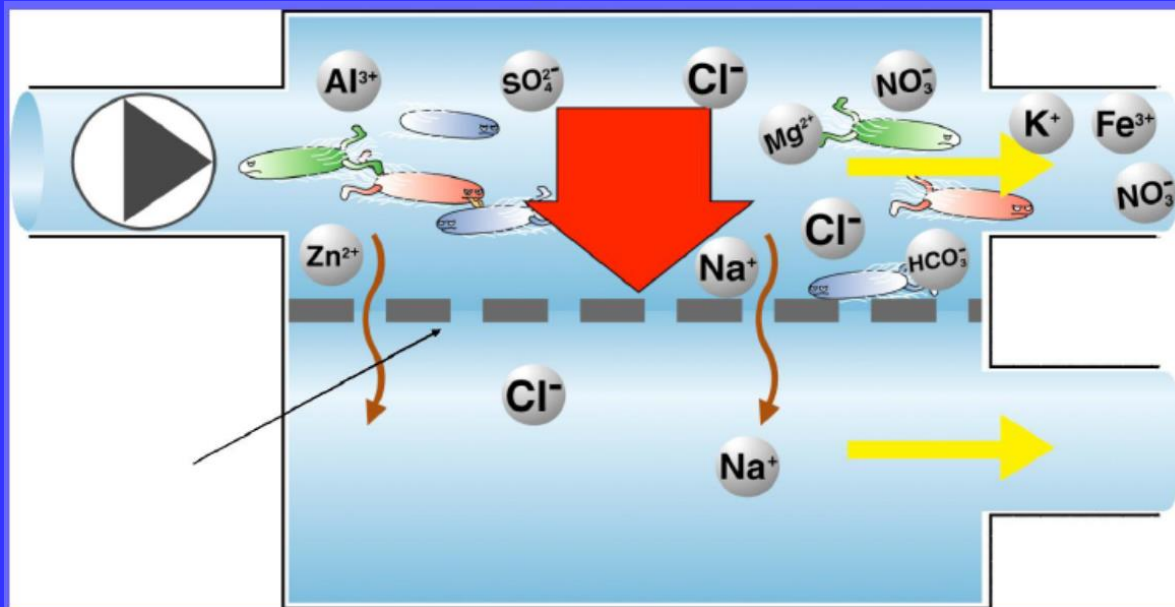






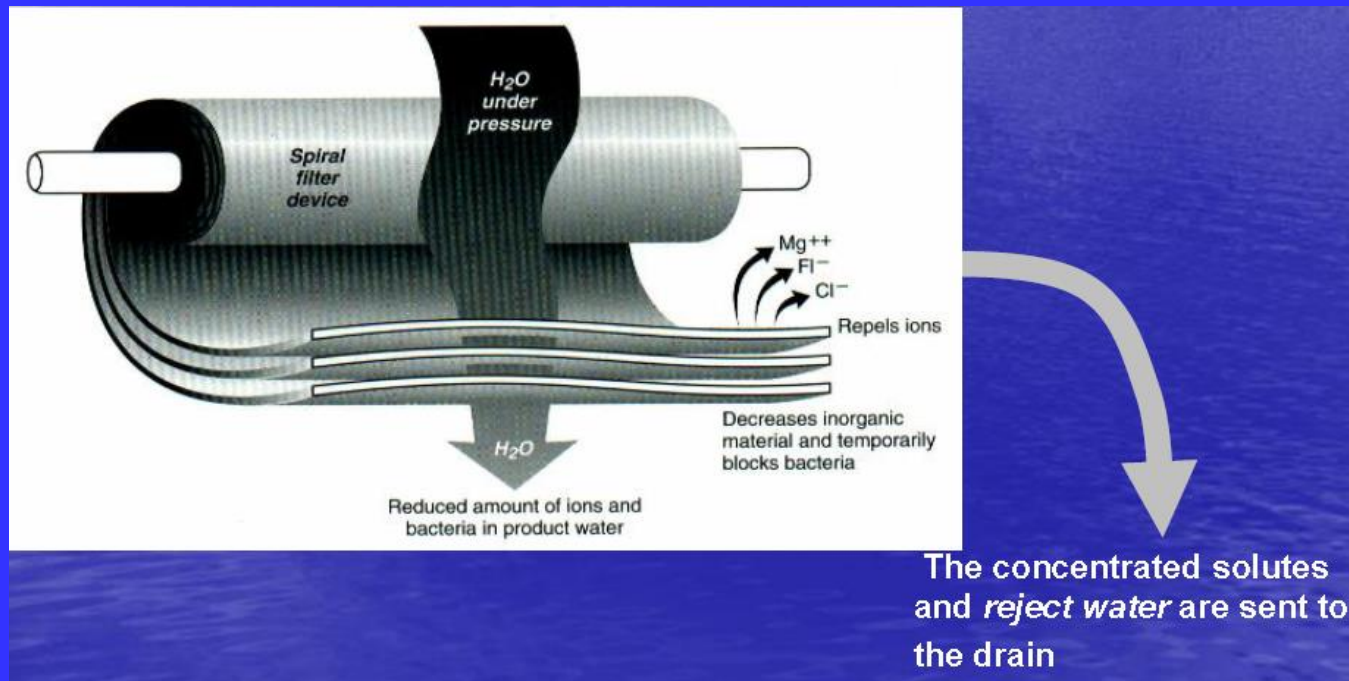
# Reverse Osmosis

- RO overcomes natural osmosis by forcing feed water under pressure thru a semi-permeable membrane leaving contaminants behind (ions, organics)



# Reverse Osmosis system

- The RO membrane most important component of the system
- Produces purified water thru RO.
- Polyamide thin membranes most common in HD



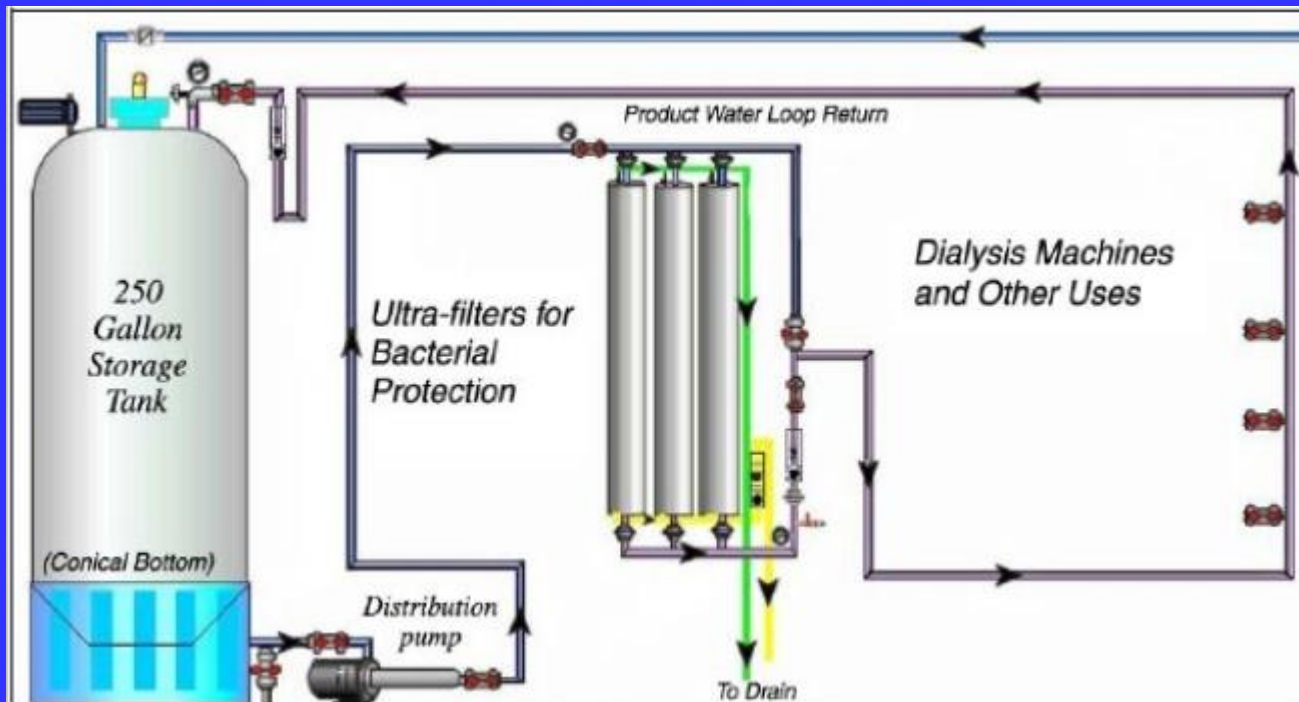


# Deionisation

- Do not remove nonionic contaminants, bacteria or endotoxins
- Cationic resins contain sulfuric radicals and exchange hydrogen radicals for other cations such as Na, Ca and Al
- Anionic resins contain ammonium radicals which exchange hydroxyl ions for chloride, PO<sub>4</sub> and flouride



# Bacterial filters



# Distribution system

- RO distribution systems: direct feed and indirect feed
- Direct feed: directly delivers the product water from the RO unit to the loop for distribution
- Indirect feed: involves a storage tank that accumulates the product water and delivers to the distribution loop
- Unused portions are recirculated back into the storage tank

# Distribution piping systems

- A continuous loop design is recommended by AAMI.
- No dead-ends or multiple branches should exist in the distribution system, as these are places for bacteria biofilm to grow

# Maintenance of Water Quality

- The key to maintaining water quality is the establishment of a facility-specific quality management program for the water treatment and distribution system
- It should detail maintenance practices, describe a structured monitoring program designed to verify satisfactory operation of the system
- The quality management system should be fully documented with clearly delineated lines of responsibility

# Bacteriological Monitoring: Hemodialyzers

- The maximum level of bacteria in water used to prepare dialysis fluid must not exceed the AAMI standard of 100 CFU. The AAMI action level is 50 CFU
- An action level is defined as a point when measures must be taken to correct the potential source to remain in compliance with AAMI standards

# Endotoxin standard

- The maximum level of endotoxin in water used to prepare dialysis fluid must not exceed the AAMI standard of 0.25 Endotoxin Units/ ml (EU/ml)
- The action level of endotoxin is 0.125 EU/ml

# Frequency of testing for bacteria and endotoxin levels

- Testing should be performed monthly
- If standards are exceeded, testing should be performed weekly until the problem is resolved



# Ultrapure dialysis solution

- Decreases CRP and IL-6
- Improves response to EPO
- Promotes better nutrition
- Reduces plasma levels of  $\beta$ -2-microglobulin
- Slows loss of residual renal function
- Lowers cardiovascular morbidity
- **Bacteria level below 0.1 cfu/ml and endotoxin level below 0.03 EU/ml**

*Susantitaphong P et al. Effect of ultrapure dialysate on markers of inflammation, oxidative stress, nutrition and anemia parameters: a meta-analysis. NDT (2013) 28: 438-446*

# Conclusion

- Water treatment is a generally neglected area of dialysis therapy
- Due to increased survival of dialysis patients, increased use of bicarbonate dialysate and high flux membranes, water treatment has become essential
- It is worthwhile achieving the goal of sterile, pyrogen free and chemically pure water for dialysis
- The above goal is achievable with a combination of various technologies available
- After designing and launching the appropriate system for HDU needs, it is essential to monitor the effluent water regularly



Thank you