# WATER TREATMENT FOR HEMODIALYSIS


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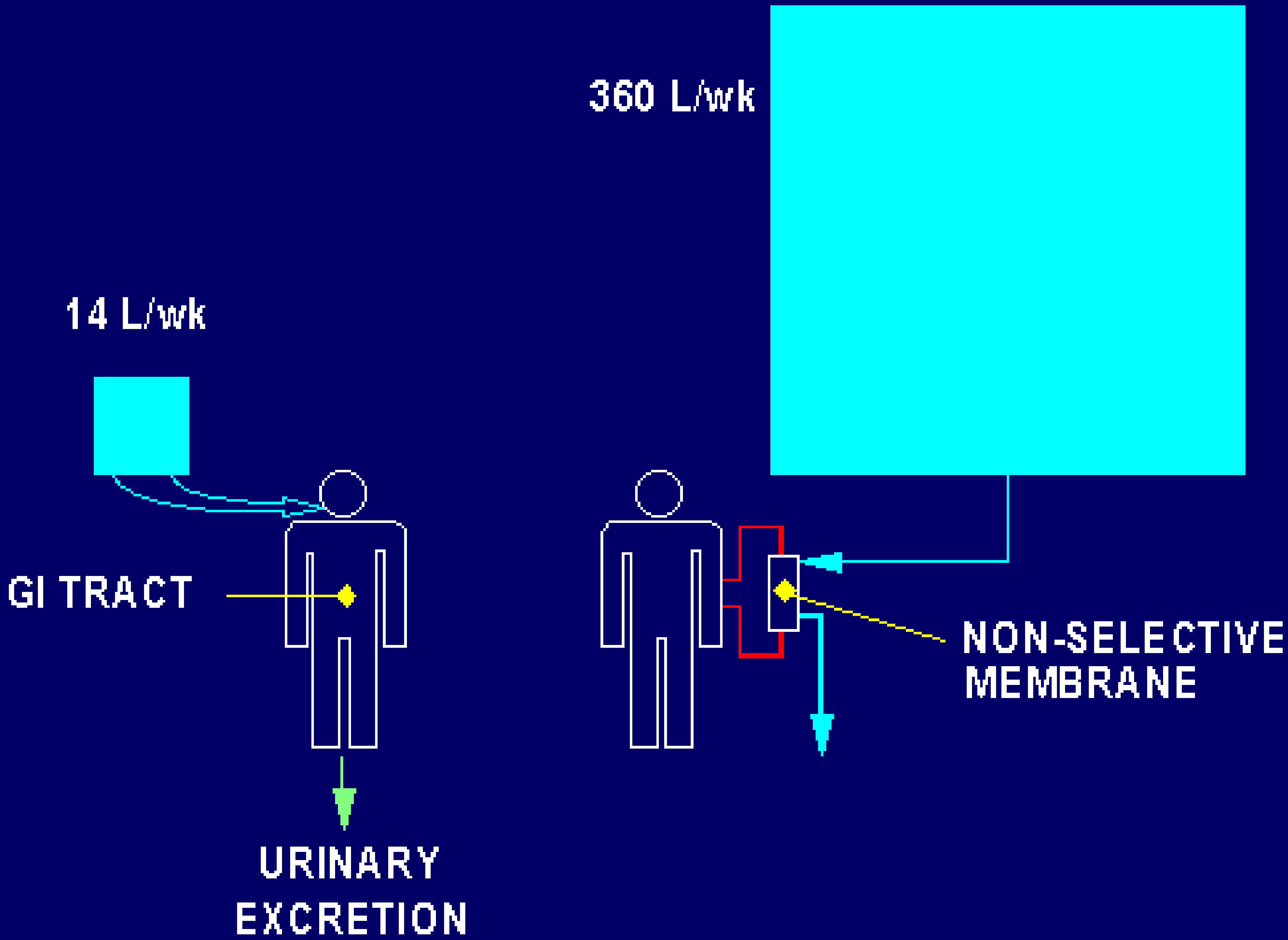
# WATER TREATMENT FOR HEMODIALYSIS

1. Water does not exist in  pure form in nature.
   Inspite of apparent clarity water may contain large amount of suspended particles, microorganisms and dissolved impurities.
2. Treating naturally available water to make it safe for it's use is essential
3. Nature of water treatment depends on the use  and quantity needed and on the contaminants in feed water.


360 L/wk
14 L/wk
GI TRACT
NON-SELECTIVE
MEMBRANE
URINARY
EXCRETION

# CONTAMINANTS IN WATER

CHEMICAL IMPURITIES

MICROBIOLOGICAL

ENDOTOXINS

# AAMI AND EPA MAXIMUM ALLOWABLE LEVELS OF CONTAMINANTS IN WATER

| Contaminant | EPA maximum for drinking water (mg/L) 2000 (condensed list) | AAMI maximum concentration for dialysis water (mg/L) | Lowest concentration associated with dialysis toxicity (mg/L) |
|---|---|---|---|
| Calcium | Not regulated | 2 (0.1 mEq/L) | 88 |
| Magnesium | Not regulated | 4 (0.3 mEq/L | |
| Potassium | Not regulated | 8 (0.2 mEq/L) | |
| Sodium | Not regulated | 70 (3.0 mEq/L) | 300 |
| Antimony | 0.006 | 0.006 | New to AAMI 2001 |
| Arsenic | 0.005 | 0.05 | |
| Barium | 2 | 0.10 | |
| Beryllium | 0.004 | 0.0004 | New to AAMI 2001 |
| Cadmium | 0.005 | 0.001 | |
| Chromium | 0.10 | 0.014 | |
| Lead | 0.015** | 0.005 | |
| Mercury | 0.002 | 0.0002 | |
| Selenium | 0.05 | 0.09 | |
| Silver | 0.10* | 0.005 | |
| Aluminum | 0.05-0.2* | 0.01 | 0.06 |
| Chloramines | 4.0* | 0.10 | 0.25 |
| Free Chlorine | 4.0* | 0.50 | |
| Copper | 1.3** | 0.10 | 0.49 |
| Fluoride | 4.0 | 0.20 | 1.0 |
| Nitrate (as Nitrogen) | 10 | 2.0 | 21 |
| Sulfate | 250* | 100 | 200 |
| Thallium | 0.002 | 0.002 | New to AAMI 2001 |
| Zinc | 5* | 0.10 | 0.2 |
| Bacteria | HPC Bacteria: 500 cfu/ml<br>Coliform bacteria: 0*** | 200 cfu/ml<br>(action level 50 cfu/ml) | 200 cfu/ml |
| Endotoxin | Not regulated | 2 EU/ml<br>(action level 1 EU/ml) | 5 EU/kg/body weight |

# PURIFIED WATER ACCORDING TO EUROPEAN & US PHARMACOPEIA. HIGHLY PURIFIED WATER [ULTRAPURE WATER] ACCORDING TO SEMICONDUCTIOR INDUSTRY NEEDS

| | Purified water [European &] US phamacopoeia] | Ultrapure water 5MΩ cm |
|---|---|---|
| pH | 5.0-7.0 | 5.0-7.0 |
| Chloride,mg/l | ≤ 0.10 | ≤ 0.06 |
| Sulfate,mg/l | ≤ 0.10 | ≤ 0.08 |
| Ammonia,mg/l | ≤ 0.10 | ≤ 0.03 |
| Calcium,mg/l | ≤ 1.00 | ≤ 0.04 |
| Carbon dioxide, mg/l | ≤ 5.00 | < 0.20 |
| Heavy metals, mg/l | ≤ 0.10 | ≤ 0.01 |
| Total solids, mg/l | ≤ 10.0 | ≤ 0.50 |
| Total bacteria count, CFU/ml | ≤ 100 | ≤10.0 |
| Pyrogen Endotoxin,UE/ml | ? | ≤ 0.25 |

# Contaminants of water and their toxic effects as documented in hemodialysis patient

| Contaminants | Toxic effect |
|---|---|
| Aluminium | Dialysis encephalopathy, bone disease, microcytic anemia |
| Calcium-Magnesium | Hard water syndrome:nausea, vomiting,muscular weakness, headache, hypertension, malaise |
| Chloramines | Hemolysis, anemia, methemoglobinemia |
| Copper | Nausea,chills, headache, severe hemolysis,hepatitis |
| Fluoride | Bone disease:osteomalacia |
| Nitrate | Methemoglobinemia,cyanosis, hypotension,nausea |
| Sodium | Hypertension,pulmonary oedema,confusion, headache,thirst, tachycardia, seizures,coma |
| Sulfate | Nausea, vomiting,metabolic acidosis |
| Zinc | Anemia, nausea, vomiting, fever |
| Microbial | Chills, fever, nausea, septicemia |
| Pyrogen | Pyrogenic reaction,hypotension,cyanosis, shock |

# Signs and Symptoms and possible water contaminant-related causes

| Symptom | Possible Water Contaminants |
| --- | --- |
| Anemia | Al,chloramines,Cu,Zn |
| Bone Disease | Al,Fl |
| Hemolysis | Cu,Nitrates,Chloramines |
| Hypertension | Ca, Na |
| Hypotension | Bacteria, Endotoxin,nitrates |
| Metabolic acidosis | Low pH,sulfates |
| Neurological deterioration | Al |
| Nausea and vomiting | Bacteria,Ca,Cu,endotoxin, low pH,Mg,nitrates,sulfates,Zn |
| Death | Al,Fl,endotoxin,bacteria, chloramine |

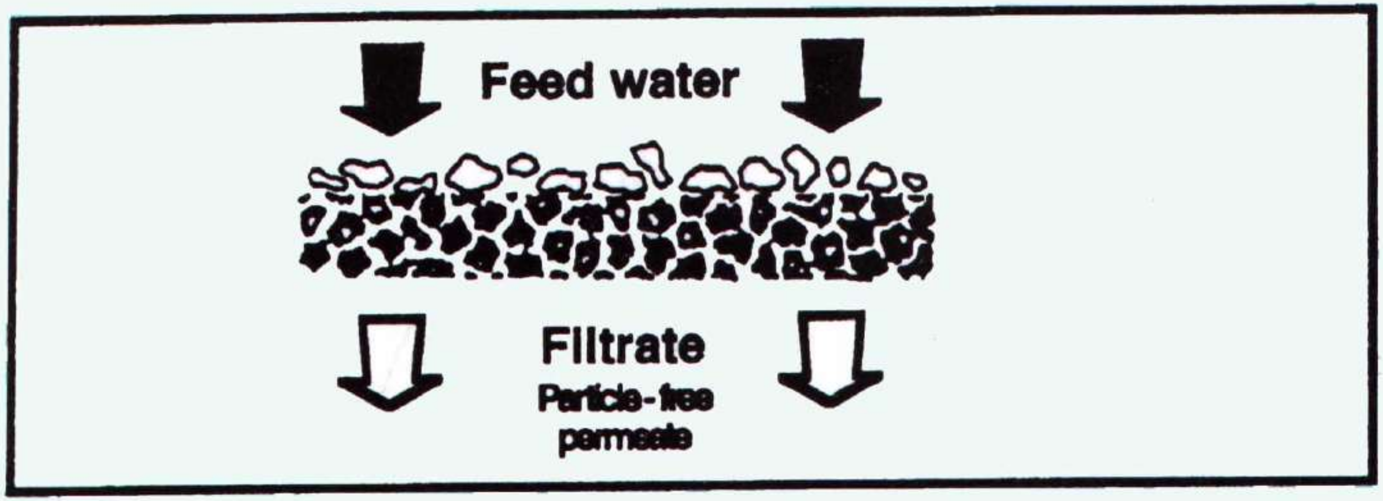
# WATER TREATMENT DEVICES

- **Filter**
  - Sediment Filter
  - Micro Filter
- **Carbon Adsorption**
- **Ion exchange systems**
  - Softeners
  - Deioniser
- **Reverse Osmosis**
- **Ultra violet Radiation**
- **Ultra Filter**

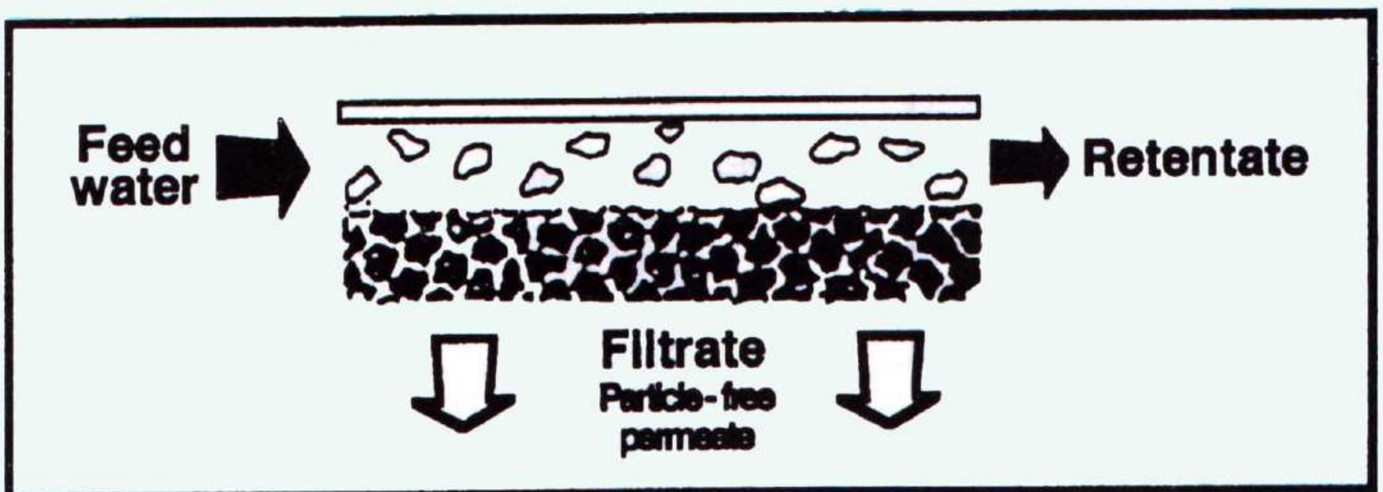
# MULTIMEDIA DEPTH FILTER

1. The first layer is usually composed of anthracite coal followed by layers of garnet, sand and then gravel.
2. Should produce water having “silt density index” [SDI] less than 5.
3. Should be back washed on regular basis [daily]
4. Monitor delta pressure daily, when the delta pressure exceeds 8 psi or more backwash is needed.

# Conventional Filtration




# Cross-Flow Filtration



# FILTERS

Various sizes: 5u, 1u, 0.45u, 0.22u

*Advantages*

- Eliminates particulates and micro-organisms
- Limited maintenance

Capital cost: medium
Maintenance cost : low

Monitoring: pressure drop

*Drawbacks*

- No regeneration
- Bacterial contamination
- Saturation and release risk

# ADVANTAGES AND DRAWBACKS OF THE DIFFERENT WATER TREATMENT MODULES

**Microfiltration**

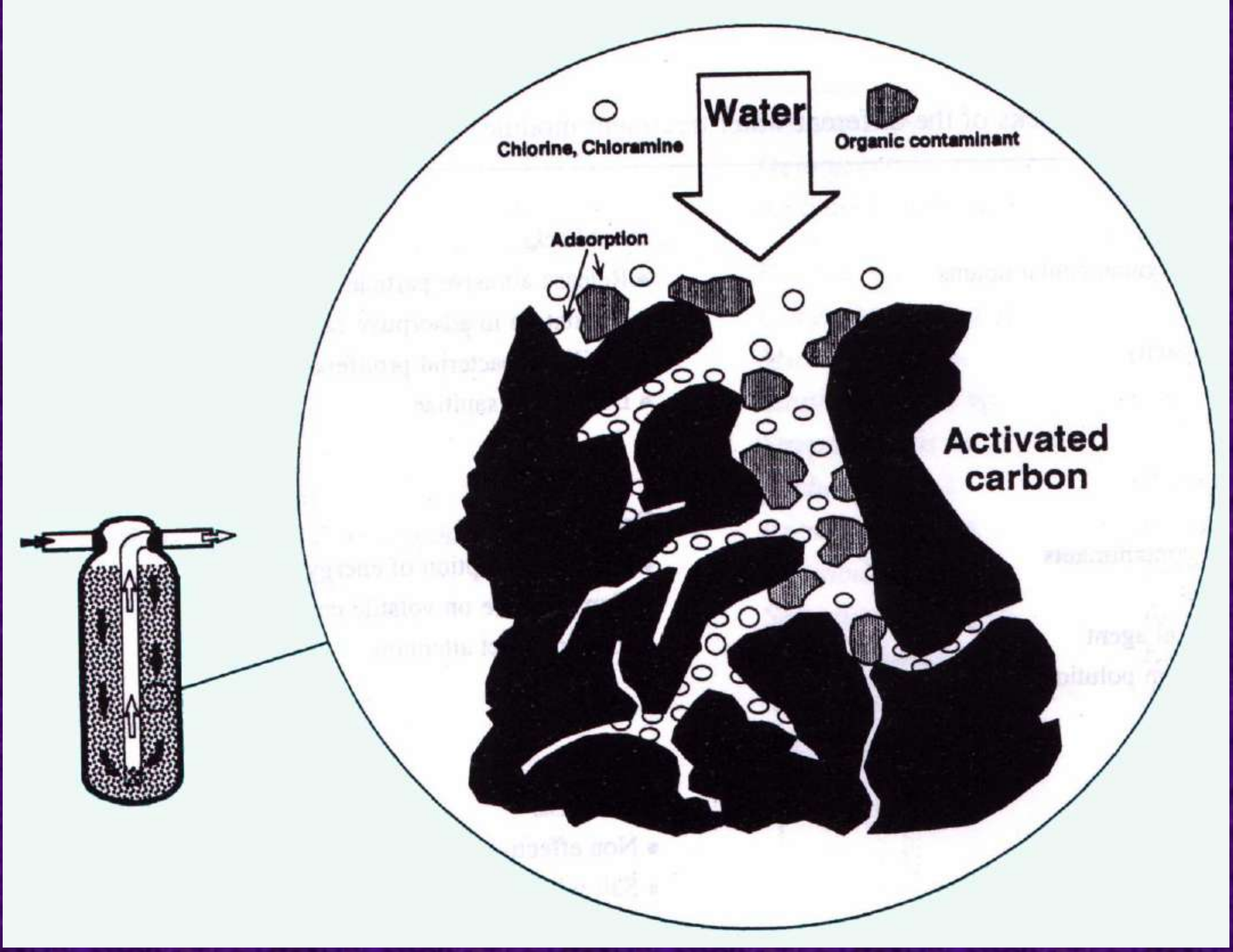
**Advantages**

- Eliminate all micro-organisms, particles according to permeability of the membrane
- Limited maintenance

**Drawbacks**

- No regeneration
- Non effective for dissolved ,mineral, pyrogens, nor colloids
- Saturation and release risks
- Bacterial growth and contamination risk

# ACTIVATED CARBON



# CARBON FILTERS

1. Needed because chlorine & chloramines are not removed by RO or DM
2. Removes many low molecular weight organic chemicals eg.herbicides, pesticides and industrial solvents as well as chlorines & chloramines.
3. Use acid washed carbon only otherwise it tends to leach metals like aluminium
4. Carbon is rated in terms of “Iodine number” For dialysis iodine number 900 or greater is recommended.
5. Carbon for dialysis should be “virgin” and not reburned
6. Most critical aspect is contact time [empty bed contact time]

   $$EBCT = \frac{V \times 7.48}{Q}$$

   V= carbon media
   Q= water in gallon/min

   Recommendation:10min    Replace at 5 mins
7. Can not be regenerated    Back wash is must

# ADVANTAGES AND DRAWBACKS OF THE DIFFERENT WATER TREATMENT MODULES

## Activated carbon

### Advantages

- Remove adequate organic contaminants chloride, chloramine
- Large adsorptive capacity
- Low cost

### Drawbacks

- Release abrasive particles [fines]
- Limitation in adsorptive capacity [spill-over]
- Facilitate bacterial proliferation
- Difficult to sanitize

# CHLORAMINE-INDUCED HEMODIALYSIS PRESENTING AS ERYTHROPOIETIN RESISTANCE

**Background:** In December,1996 we identified an outbreak of erythropoietin (rHuEpo) resistance requiring a substantial increase in rHuEpo dosage in one of our four hemodialysis (HD) units. The dialysate chloramine levels in this unit had risen from <0.1 p.p.m. in 1996 to 0.25-0.3 p.p.m. in 1997. In the other three HD units levels remained <0.1 p.p.m. Other parameters of water quality were within Accepted standards.

**Conclusions:** This is the first report linking chloramine exposure and rHuEpo resistance, with only subtle signs of hemodialysis. Unheralded changes in mains water constituents can directly after dialysate water quality and clinical outcomes.

**Sarah Fluck et al NDT 1999 14:1687-1691**

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# CHLORAMINE REACTIONS

Chloramine generation

$Cl_2 + H_2O \rightarrow ClH + HClO$

$NH_3 + HClO \rightarrow NH_2Cl + H_2O$

Reactions for removing chloramine

Activated carbon

$C + 2\,HClO \rightarrow CO_2 + 2ClH$

$C + 2\,NH_2Cl + 2\,H_2O \rightarrow CO_2 + 2NH_4 + 2Cl^-$

Bisulfite reaction

$Cl_2 + H_2O + Na_2SO_3 \rightarrow Na_2SO_4 + 2\,ClH$

$Cl_2 + H_2O + NaSO_3H \rightarrow NaSO_4H + 2ClH$

$NH_2Cl + SO_3H_2 + H_2O \rightarrow NH_4SO_4H + ClH$

**Rafael Perez et al NDT 1999 14:2579-2582**

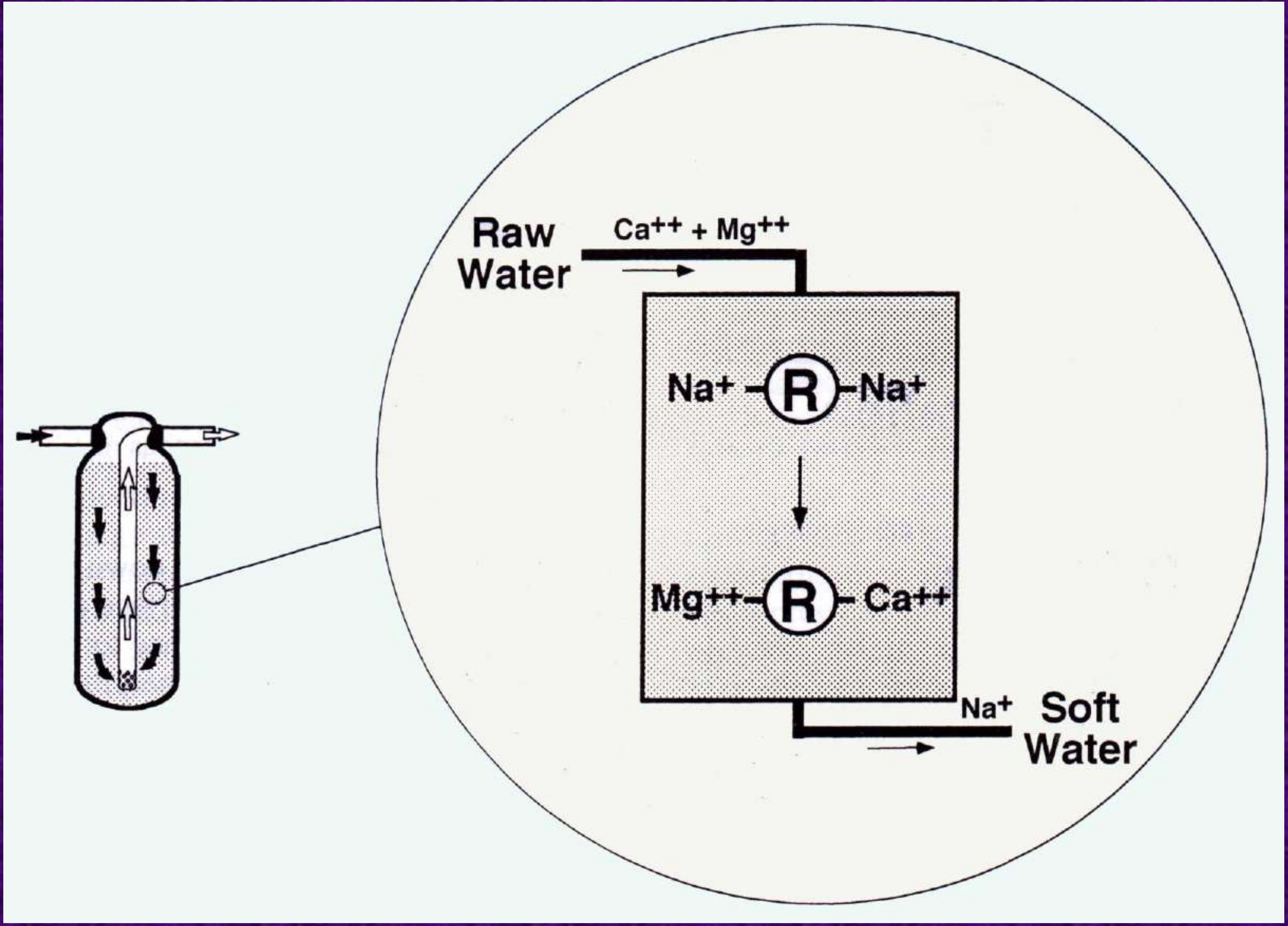
# WATER SOFTENER

CATION EXCHANGE RESINS

exchange $CA^{++}$ & $MG^{++}$ for $2Na^{+}$

1. Hardness of water is measured in grains/gallon[gpg] or mg/ml of $CaCO_3$
2. Needed to protect the RO membrane
3. Resin life decreases when exposed to excess chlorine & chloramine in feedwater.
4. Needs regular regeneration with Brine
5. Backwash before regeneration
6. Recommended hardness after softener is 2gpg or 35mg/L

# SOFTENERS



# SOFTENERS

*Advantages*

- Reduces effectively water hardness
- Regenerable at ease

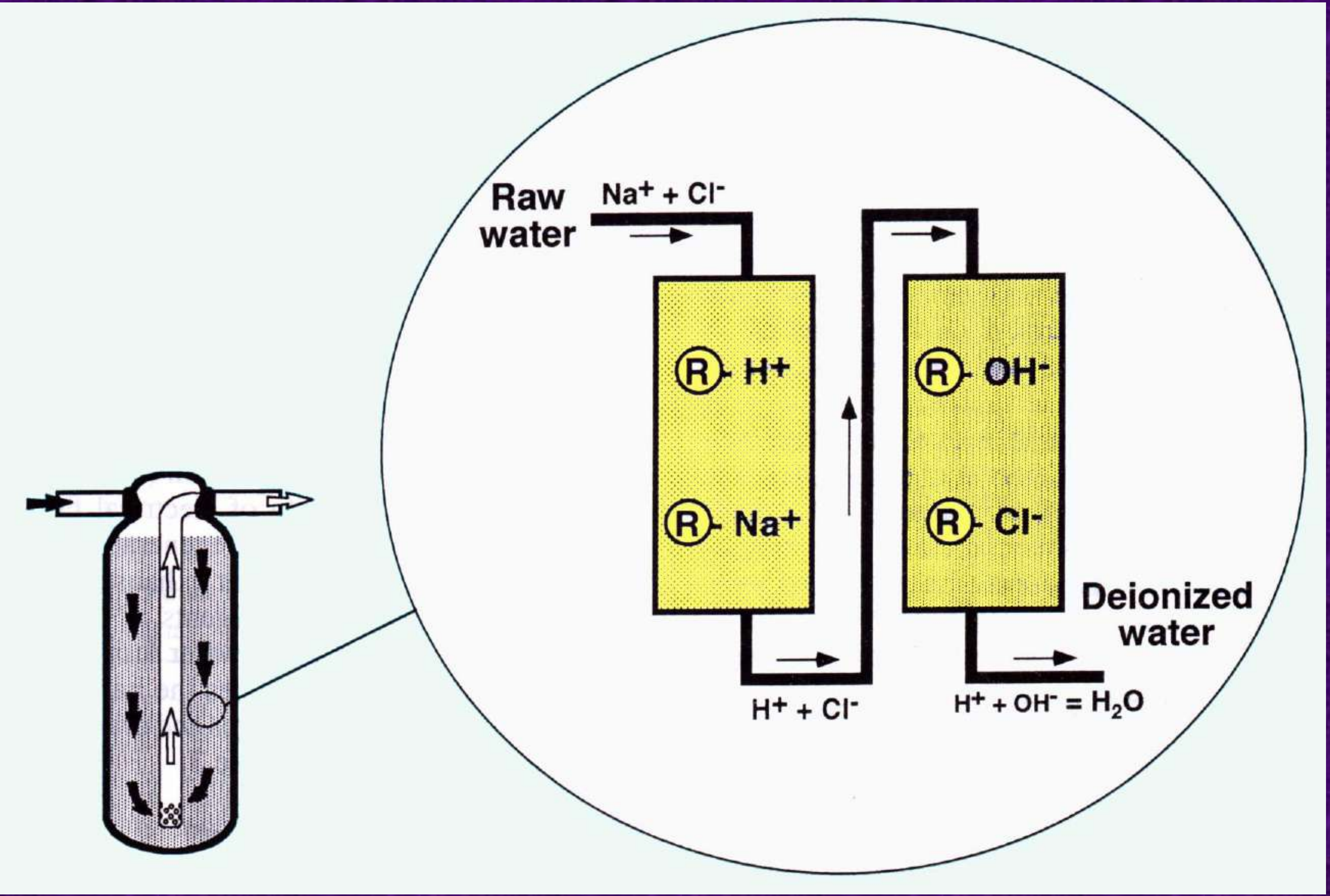
Capital cost: Medium
Operating cost: medium

*Drawbacks*

- Not effective for organics other ions
- Bacterial proliferation
- Difficult to sanitize

monitoring: water hardness; Ca <10mg\L

# DEIONIZERS



# DEIONIZATION

1. Cation and anions from water are exchanged with hydroxyl [$OH^-$] and hydrogen [$H^+$] in resin beads.
2. When exhausted the resins will dump captured ions in mass quantity: weakly attached ions like aluminium & fluoride are first to be released.
3. Conducive to bacterial growth. Bacteria and endotoxins do not have a charge  hence are not removed by DI
4. Resistively which is the opposite of conductivity should read above 1 meg-ohm/cm

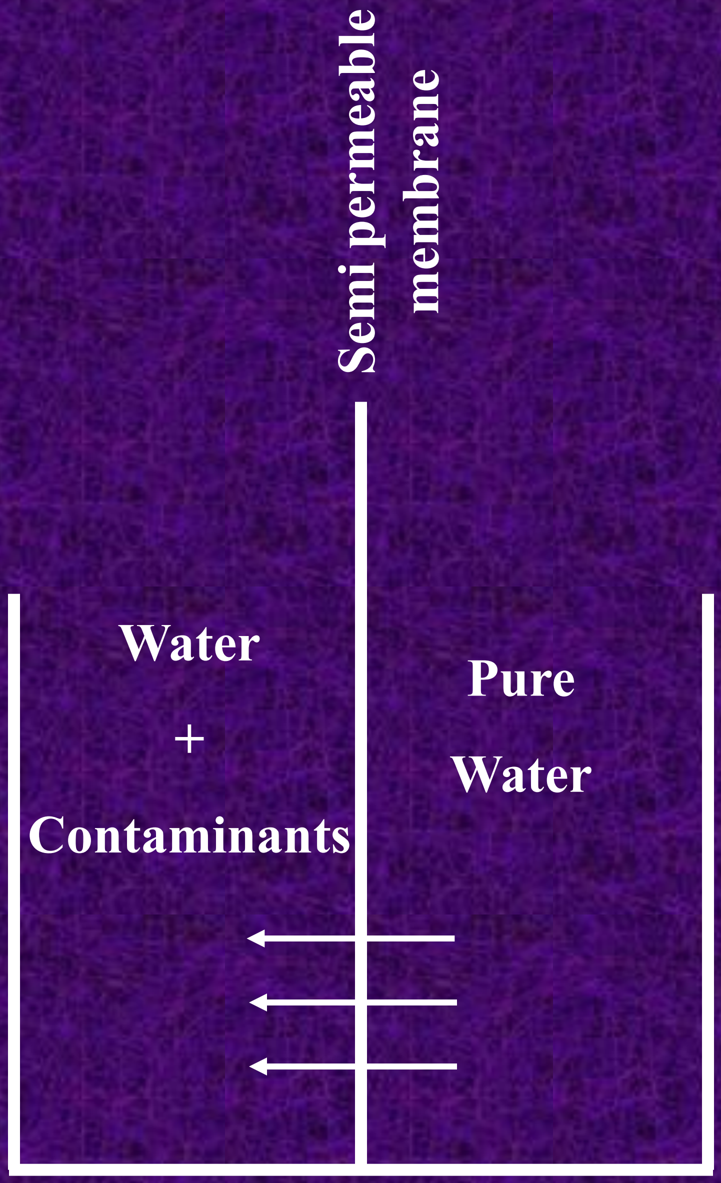
# ADVANTAGES AND DRAWBACKS OF THE DIFFERENT WATER TREATMENT MODULES

**Mixed bed of deionization**

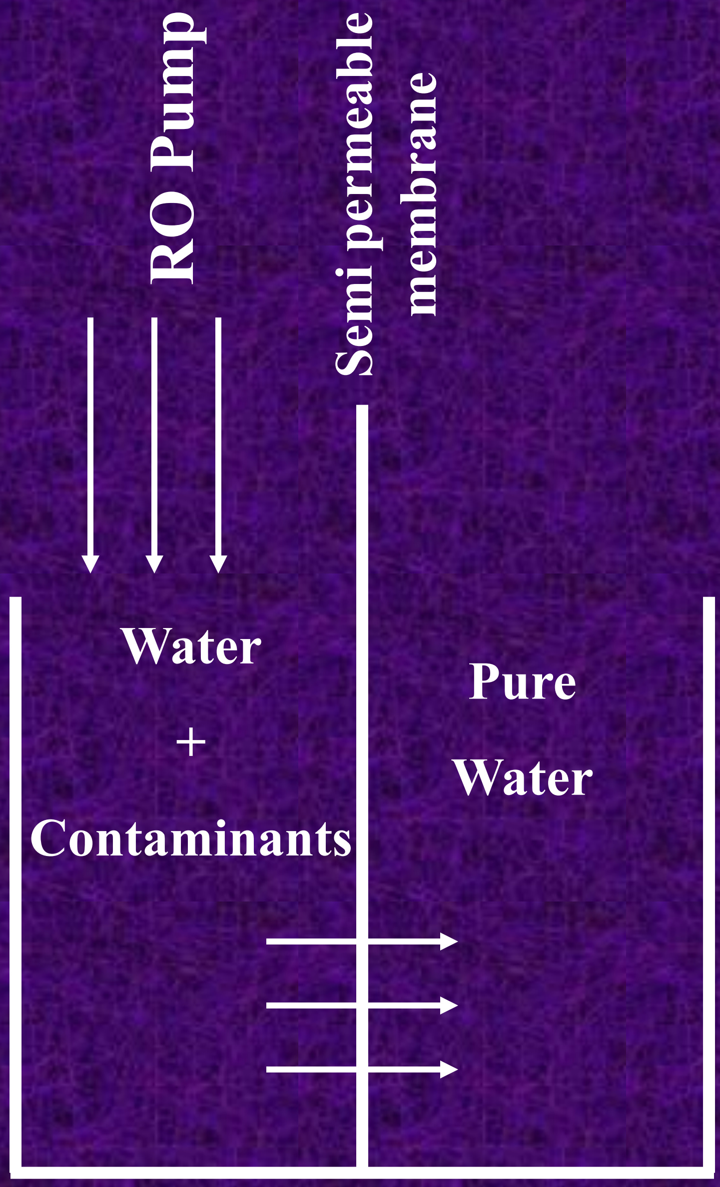
| Advantages | Drawbacks |
| --- | --- |
| * Eliminate ions | * Non effective in organic components, nor micro-organisms |
| * Regenerable without limitations | * Potentiate bacterial growth |
| * Low cost in use | * Release of particles |
| | * Exhaustion of resins |

**Continuous Electric Deionizer**

| Advantages | Drawbacks |
| --- | --- |
| * Eliminate adequately ions | * Non effective for organic components, particles and micro-organisms |
| * Permanent regeneration | * Sensitivity of membranes |
| * Low cost of maintenance | * Aging and loss of efficacy with time |
| * Not source for bacterial growth | |



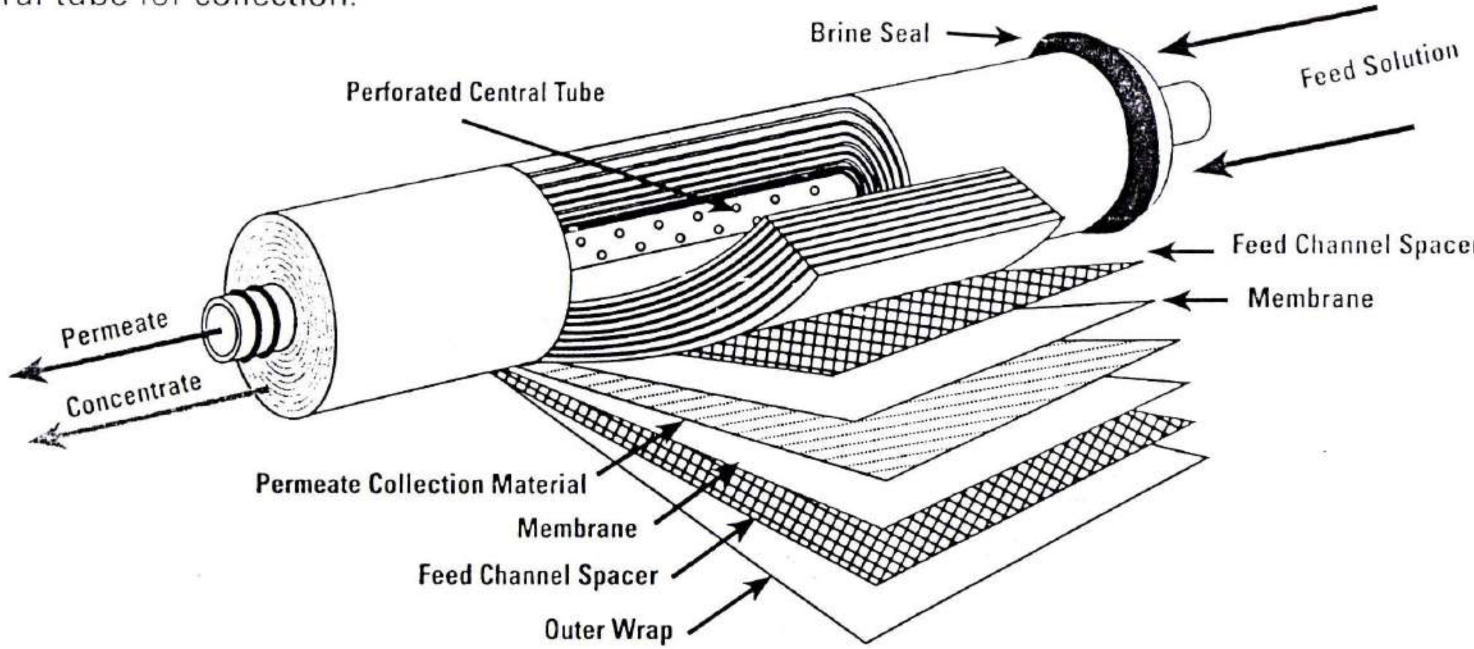

**Osmotic Pressure**
**A**




**Reverse Osmotic Pressure**
**B**

# How the Membrane System Works

The spiral membrane is constructed of one or more membrane envelopes wound around a perforated central tube. The permeate passes through the membrane into the envelope and spirals inward to the central tube for collection.




***The illustration above represents a simplified spiral-wound membrane element. Recovery can be as high as 90% and systems may be capable of chemical cleaning in place (CIP).***

# REVERSE OSMOSIS

1. Colder the source water, less purified the product water 1°F temperature drop the RO membrane produces 1.5% less purified water.
2. RO membranes are heat intolerant and can be destroyed with temperatures above manufacturer's recommendation.
3. Ideal incoming water pH should be between 5 and 8.5

# OUTBREAK OF LEAD POISONING IN A HEMODIALYSIS UNIT

Lead poisoning usually occurs as a consequence of occupational and environmental exposure. Contaminated dialysate as a source of lead poisoning has not been previously reported. We report an outbreak of lead poisoning in a dialysis unit consequent to a contamination in the central dialysate delivery system.

**Pranay Kathuria et al. J Am Soc Nephrol 2004; 15: 617A**

# EPIDEMIC ALUMINUM INTOXICATION IN HEMODIALYSIS PATIENTS TRACED TO USE OF AN ALUMINUM PUMP

We found that epidemic aluminum intoxication was caused by the use of an electric pump with aluminum housing to deliver acid concentrate used in bicarbonate dialysis. This outbreak demonstrates why it is essential to insure that all Fluid pathways, storage tanks, central delivery systems, and pumps are compatible with low pH fluids before converting from  acetate to bicarbonate dialysis.

**Dale Burwen et al 1995 KI 48;469-474**

## Limits on Disinfectant Residues and Bacterial Contamination

| | AAMI recommended limit | Manufacturer's suggested level |
|---|---|---|
| **Disinfectant** | | |
| Formaldehyde | <5mg/L | -- |
| Glutaraldehyde | -- | <3mg/L |
| Peracetic acid | -- | <3mg/L |
| Sodium hypochlorite [bleach] | -- | <0.5mg/L |
| **Bacteria** | | |
| Concentrate | <200 cfu/mL | -- |
| Dialysate | <2.000 cfu/mL | -- |
| Water | <200 cfu/mL | |
| **Endotoxin** | | |
| Water of reuse | <1ng 5 EU | -- |

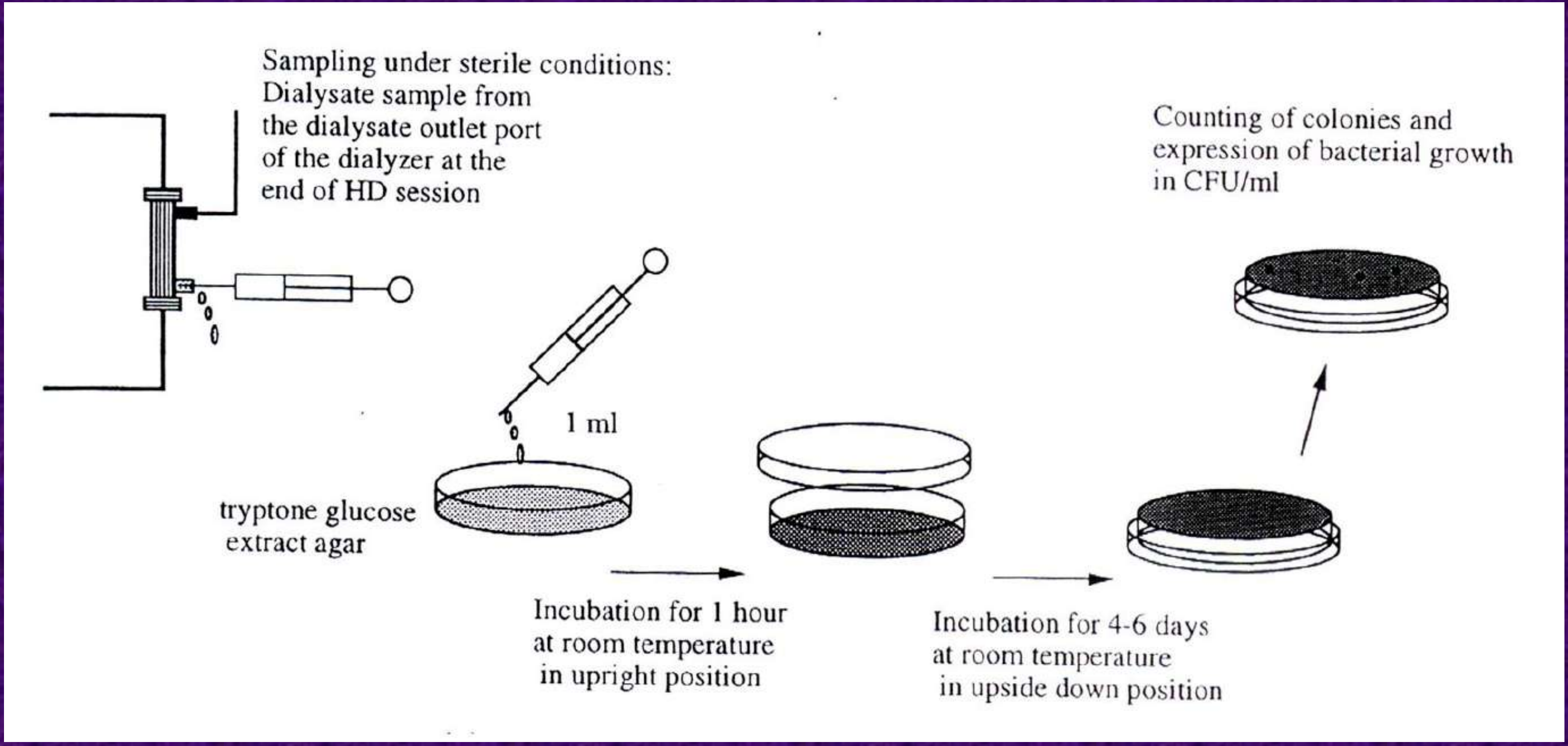
# WATERBORNE BACTERIA USUSALLY IDENTIFIED IN WATER TREATMENT SYSTEM

| Bacteria | Tap water | Softeners<br>Deionizers<br>Activated charcoal | Dialysate |
|---|---|---|---|
| Gram negative | Pseudomonas sp.<br>[P.aeruginosa,P.<br>Maltophilia,P.<br>Flavobacterium sp. | Eschericia coli<br>Pseudomonas sp.<br>Flavobacter sp.<br>Serratia sp.<br>Achromobacter sp.<br>Aerobacter sp.<br>Alcaligenes sp. | Pseudomonas sp.<br>Flavobacer sp.<br>Acinetobacter sp.<br>Alcaligenes sp.<br>Erwinia sp.<br>Achromobacter sp.<br>Aeromononas sp.<br>Xanthomononas sp.<br>Serratia sp.<br>Moraxella sp.<br>Klebsiella sp.<br>Enterobacter cloacae |
| Anaerobic | Mycobacteria<br>M.Chelonei<br>M.xenopi<br>M.gordonae<br>M.scrofulaceum | Clostridium sp.<br>Mycobacter sp. | M.Chelonei<br>M.chelonei-like |

# BACTERIA-DERIVED PYROGENS

| | Molecular weight [daltons] |
|---|---|
| **Cell Wall Components** | |
| Lipopolysaccharide [LPS] | >100,000 |
| Lipid A-related LPS fragments | 2-4000 |
| Other LPS fragments | <8000 |
| Peptidoglycans | 1000-20,000 |
| Muramylpeptides | 400-1000 |
| **Actively Secreted Toxins** | |
| Exotoxin A | 71,000 |
| Exotoxin A fragments | <5000 |
| **Unkown Pyrogens** | <20,000 |

# BACTERIOLOGICAL MONITORING



# IMPROVED BACTERIOLOGICAL SURVEILLANCE OF HEMODIALYSIS FLUIDS: A COMPARISON BETWEEN TRYPTIC SOY AGAR AND REASONER'S 2A MEDIA

**Conclusion:**

Microbiological surveillance of hemodialysis fluids, including pre-treated dialysis water samples collected from RO treatment systems, can be performed more precisely with R2A media than TSA, when incubated at 25$\pm$2 C for 10 days.

**Klaas van der Linde et al 1999 NDT 14:2433-2437**

# LIVER FAILURE AND DEATH AFTER EXPOSURE TO MICROCYSTINS AT A HEMODIALYSIS CENTRE IN BRAZIL

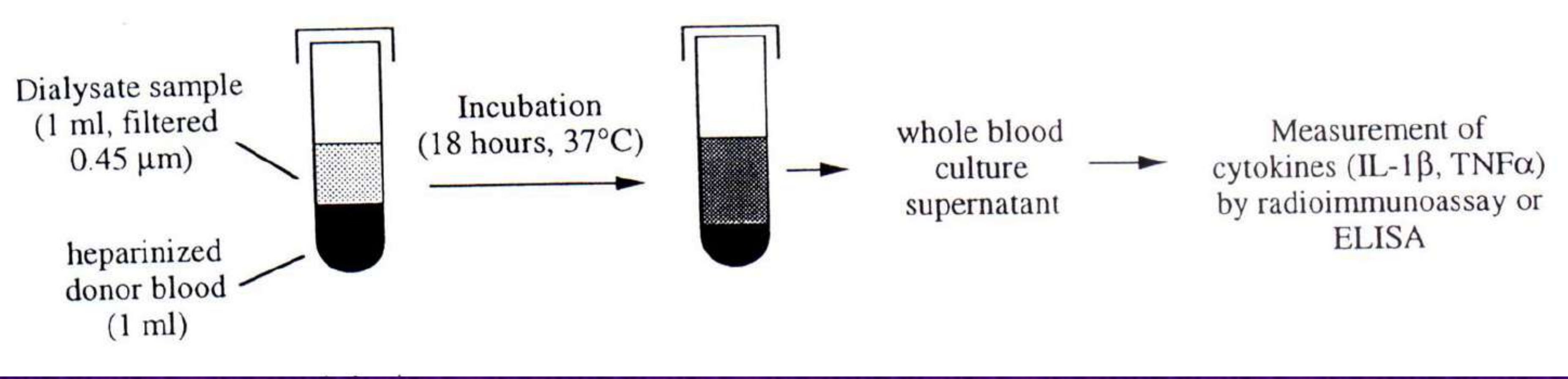
*Hemodialysis is a common but potentially hazardous procedure. From February 17 to 20,1996, 116 of 130 patients (89%) in Caruaru,Brazil had visual disturbances, nausea and vomiting associated with hemodialysis. By March 24,26 of the patients had died of acute liver failure.

*Both centres received water from a nearby reservoir. However, the water supplied to dialysis centre B was treated, filtered, and chlorinated, whereas the water supplied to dialysis centre A was not. Microcystins produced by cyanobacteria were detected in water from the reservoir and from dialysis centre A and in serum and liver tissue of case patients.

*Conclusion:Water used for hemodialysis can contain toxic materials and its quality should therefore be carefully monitored.

Elise Jochimsen et al NEJM 1998 Vol.338 No.13; 873-875

# ENDOTOXIN MONITORING



# LAL TEST : once every month

**METHODOLOGY**

Add 0.1 ml. of reconstituted pyrotell (0.03/0.125 EU/ml.) .

Added 0.1ml. test specimen or control

Mix Vigorously (vortex) for 20-30 secs.

Place the reaction tubes at $37 \pm 1\ ^{0}C$ water bath for 60 minutes.

Remove reaction tubes & invert the tubes in one smooth motion.

A positive test is indicated by the formation of a gel which does not collapse when the tube is inverted by 180 Degree.

# INFLUENCE OF WATER TREATMENT UPGRADE ON PATIENT BIOCHEMICAL AND HEMATOLOGICAL PARAMETERS

| Parameter | Before upgrade | After upgrade | p |
|---|---|---|---|
| EPO dose [U] | 85,800[70,000] | 82,500[731,500] | NS |
| Iron dose [mg] | 100 [350] | 125[400] | NS |
| Hb [g/dl] | 10.9±1.4 | 11.3±1.2 | <0/0001* |
| EPO/hematocrit ratio | 8134[6929] | 7095[7407] | 0.07 |
| Albumin [g/dl] | 3.9±0.37 | 3.94±0.36 | 0.0002* |
| Ferritin [ng/ml] | 251 [389] | 355[429] | <0/0001* |
| Transferrin saturation% | 26.0[14.5] | 30.5 [17.3] | <0.0001* |
| Creatinine [mg/dl] | 10.6±3.3 | 10.1±3.1 | <0.0001 |
| WBC [x10 /µl] | 6.5±2.1 | 6.5±1.9 | NS |
| CRP | 14.3 [21.0] | 12.2[19.6] | <0.0001* |

**Seminar in dialysis: Hoerich & Levi,2003 16[6]: 492-97**

# ULTRAPURE DIALYSIS FLUID SLOWS LOSS OF RESIDUAL RENAL FUNCTION IN NEW DIALYSIS PATIENTS

**Helmut Schiffl et al NDT 2002; 17:1814-1818**

Munich, 34 randomised to ultrapure or conventional water

Duration 24 months. $C_{cr,}$ hydration status,hypotensive episodes, CRP & il-6 and blood pressure.

**Conclusions:**

Ultrapure dialysis fluid combined with high-flux synthetic membrane are effective components of renal replacement Therapy to slow the loss of residual renal function in hemodialysis patients. These improvements of hemodialysis are desirable, but add to treatment costs.

# DIALYSIS FLUID PURITY

**Guideline IV.1**

A. Contemporary hemodialysis requires the use of pure water complying at a minimum with the recommendations of the European Pharmacopocia. The use of ultapure water is however strongly recommended for conventional and high-flux dialysis modalities.

**Guideline IV.2**

A. The water treatment system should consist of pre-treatment and RO modules feeding directly the dialysis machines. Storage tanks should be avoided. Pipe tubing material and plumbing should be designed to Prevent bacterial contamination and to be easily disinfected.

European Renal Association-European Dialysis & Transplantation Association
NDT 2002 17 (7);45-62

# DIALYSIS FLUID PURITY

**Guideline IV.3.1**

A. The chemical and bacteriological purity of the dialysis water must be monitored routinely and regularly and the results should be documented. There should be documented procedures, which come into effect once these limits are exceeded. These procedures will include temporary closure of the dialysis unit when the safe limits for contaminants are exceeded.

**Guideline IV.3.2**

A. Monitoring the microbiology of the water feeding dilaysis machine should be performed weekly during the validation phase and at least Monthly during the surveillance period.

European Renal Association-European Dialysis & Transplantation Association
NDT 2002 17 (7);45-62

# DIALYSIS FLUID PURITY

**Guideline IV.3.3**

**A. Regular and effective disinfection procedures are an integral part of the hygienic maintenance of the water Treatment system. Periodicity, type of disinfection (chemical,heat,mixed), periodic changes of components (filters,resins,filters) should be performed in accordance with manufacturer recommendations and adapted to microbiology monitoring results. Complete disinfection of the water treatment chain should be performed at least monthly.**

**Guideline IV.4.2**

**A.In order to reduce the risk of pyrogenic reactions and water-borne bacteraemia, the dialysis fluid must routinely meet as a minimum the European Pharmacopoeia microbiological standards.**
**(Evidence level:B)**

European Renal Association-European Dialysis & Transplantation Association
NDT 2002 17 (7);45-62

# ULTRAPURE DIALYSIS FLUID-HOW PURE IS IT AND DO WE NEED IT?

**Conclusion:**

It is unlikely that there will ever be a randomized, controlled study giving survival data for patients treated with ultrapure Vs standard quality dialysis fluid, so we must decide Whether it is important without such evidence. The European Best Practice Guidelines for Hemodialysis have Made this decision and recommend the use of ultrapure dialysis fluid as a goal for all patients and all modalities.

**European Best Practice Gidelines for Hemodialysis Part I, SECTION IV. Dialysis fluid purity. NDT 2002; 17 (Suppl.7):46-62**

# ASSEMBLING A WATER TREATMENT SYSTEM

STEPS:

1. Quality of feed water

2. Amount of water need

3. Space consideration

4. Concept of desired reduction of contaminant and process required

# WATER FOR HD MPUH NADIAD