

Chloramine Removal From Water Used in Hemodialysis

David M. Ward

Several outbreaks of hemolysis in hemodialysis patients have occurred when chloramines in the public water supply have not been adequately removed by the dialysis unit's water purification system. Chloramines are not removed by reverse osmosis or deionization, and need to be either adsorbed by filtration through granular activated carbon (GAC) or neutralized by chemical reduction by ascorbic acid (vitamin C) added to the dialysate. Chloramine levels in the incoming water can fluctuate unpredictably, and failures of both systems have occurred when chloramines have exhausted their capacity. The medical and technical issues associated with both methods are explored in detail. Safety depends on critical care in the design of the system and rigorous testing more than once daily. Most dialysis units now depend on GAC filters, two of which should be placed in series so that chloramine breakthrough can be detected after the first one, before the second one fails. Comprehensive standards in force in California have not yet been applied universally.

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Index Words: Chloramine, hemodialysis, hemolytic anemia, water purification, ascorbic acid, trihalomethanes.

The presence of chloramines in the dialysate during hemodialysis can cause oxidant injury to red cells and potentially life-threatening hemolysis. This was first discovered and investigated in 1970 to 1973 in Minneapolis.^{1,2} Despite full recognition of the problem and of the means of preventing it, serious outbreaks of chloramine-induced hemolysis have continued to occur, injuring scores of patients. Well-documented occurrences include those in Sydney in 1981,³ Los Angeles in 1984,⁴ and Philadelphia in 1987.⁵ Many of the victims of these overt incidents became acutely and seriously ill. In addition, chloramines can have subclinical consequences including exacerbation of anemia⁶ and potentially other oxidative damage in dialysis patients.⁷ The prevention of chloramine-induced injury requires rigorous attention to both the design and the operation of water purification systems in dialysis units.⁸

Chloramines in Public Water Supplies

The use of chloramines instead of free chlorine to sanitize public drinking water arose from the need to reduce levels of trihalomethanes (THMs), which are carcinogenic^{9,10} and probably teratogenic.¹¹ Water from surface sources may contain natural organic residues (including humic acid, hydrocarbons, and bromine) that on chlorination lead to the formation of THMs, including chloroform (CHCl₃),

bromodichloromethane (CHCl₂Br), and chlorodibromomethane (CHClBr₂). In the United States, a ruling by the Environmental Protection Agency (EPA) in 1979 set a limit on THMs of 0.1 mg per liter (100 parts per billion) in drinking water, with a deadline for major water suppliers to meet that standard by November 1981, and for minor suppliers by November 1983.¹² These deadlines were subsequently extended because of the practical difficulties encountered. Among several alternative methods, the substitution of chloramine for chlorine was found by most water districts to be satisfactory in reducing THM formation while retaining adequate inhibition of bacterial growth. Chloramination is now widely used for municipal water supplies in North America and Europe.

Chloramination is achieved at the water treatment facility by introducing both chlorine (Cl₂) and ammonia (NH₃), which in aqueous solution rapidly combine to form monochloramine (NH₂Cl), dichloramine (NHCl₂), and even small quantities of trichloramine (nitrogen trichloride, NCl₃). The relative quantities of these different species depend on the ratio of

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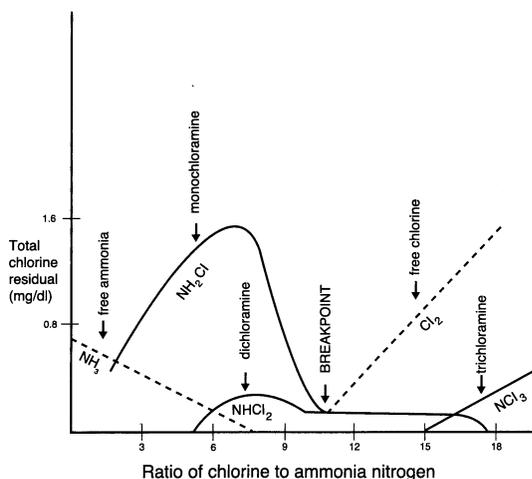


Figure 1. Chloramine breakpoint curve (approximate).

chlorine to ammonia, as shown in Figure 1. The acidity of the reaction is another factor, because trichloramine and dichloramine are preferentially produced at a pH of 4 or 5, but monochloramine when the pH is 8.¹³ Thus it is easy and desirable to produce water in which monochloramine predominates. Also, dichloramine and trichloramine are to be avoided because they contribute to a less acceptable taste and odor.¹⁴

Chloramines are more stable than free chlorine, so that adequate residual antibacterial activity can be maintained with lower total chlorine exposure, reducing the production of chlorinated residues, including THMs. For the same reason, however, in situations in which free chlorine would be rapidly reduced, chloramines can persist and cause problems for biological systems that are sensitive to oxidant damage. For instance, changing from free chlorine to a chloraminated water supply kills aquarium fish unless the water is treated with reducing agents.¹ The changeover to chloramines by the Metropolitan Water District in the Los Angeles area in 1984 was preceded by an extensive public awareness and education campaign targeting aquarium owners. It is ironic that dialysis facilities, although also notified, did not in every case make adequate modifications. It is not known how many fish died when the change to chloramines took place, but it was extensively reported that numerous patients in at least 12 hemodialysis units suffered significant hemolysis. Some 25

patients required blood transfusions, and several required hospitalization. The State Department of Health Services responded by placing a temporary ban on the use of chloramines in all public water supplies in California until mandatory standards for water treatment in dialysis facilities could be developed and complied with.⁴ The procedures adopted in these standards have proved themselves to be effective and have withstood the test of time. If applied nationally they probably would have prevented the Philadelphia occurrence.⁸

Hemolysis Caused by Chloramines

Red blood cell (RBC) survival is shorter in hemodialysis (HD) patients than normal subjects.¹⁵ The most prominent contributing factors pertain to oxidative stress.¹⁶ Peroxidation of lipids in the red cell membrane, which is reflected in elevated malondialdehyde levels, is increased in hemodialyzed subjects.^{7,17} Interestingly, peroxidation of lipids has been implicated also as a cause of accelerated atherosclerosis in HD patients.^{7,18} Lipid peroxidation in RBCs, together with a resulting reduction in cation permeability¹⁹ and membrane fluidity,²⁰ leads to reduced RBC deformability. In addition to this increased fragility of the RBCs, resistance to oxidants is impaired in HD patients, as evidenced by impaired hexose monophosphate shunt activity,²¹ reduced levels of glutathione,^{22,23} diminished activities of the enzymes catalase, glutathione peroxidase, and superoxide dismutase,^{24,25} and impairment of other antioxidant systems.⁷

Thus acute oxidative stress is poorly tolerated, and direct exposure of the blood to chloramines in the dialysate can readily lead to RBC injury. The mildest form is methemoglobin formation, which may correct spontaneously by chemical reduction by the time of the next dialysis. However, the effects of repeated chloramine exposure can be cumulative, and more severe oxidative denaturation of hemoglobin leads to its precipitation as Heinz bodies within the RBCs, which are then destroyed in the spleen.²⁶ The most severe cases have presented with immediately obvious clinical features of acute hemolysis, such as dark blood in the dialyzer venous line or acute dyspnea and distress.^{2,27}

Table 1. Reported Chloramine-Induced Hemolysis

Date	Place (References)	No. of Pts Transfused*	Apparent Cause
1970	Minneapolis ^{1,2}	?	First identification; solved by carbon, later vitamin C neutralization
1974	Madrid ⁶	?	No system for chloramine removal in place; solved by using vitamin C
1977	Minneapolis ²⁶	?	Heavy bloom of lake algae, extra chloramine added, exceeding vitamin C neutralizing power
1981	Sydney ³	13	Inadequate carbon filter
1984	Los Angeles ^{4,28}	25	Inadequate carbon installed in preparation for chloramine introduction (12 facilities)
1984	San Diego ^{4,28,29}	10	Vitamin C neutralization system using only 8.4 mg/L of dialysate
1987	Philadelphia ^{5,8,27}	41+	Carbon filter system became inadequate when water demand was increased
1989	Seoul ³⁰	34	Sewage contamination of water supply

*The number of patients transfused as a result of chloramine exposure may be imprecise because of a background of ongoing transfusion needs.

Reported outbreaks of chloramine-induced hemolytic disease are listed in Table 1.^{1-6,8,26-30} Most have not been recognized until unusual decreases in hematocrit or hemoglobin levels have been noticed in several patients, with sudden increased transfusion require-

ments.^{3,5,28} However, in some outbreaks, many patients had symptoms whose significance soon became apparent, including malaise, headaches, shortness of breath, palpitations, vomiting, and other complaints.²⁷ Diagnosis can be confirmed by finding evidence of hemolysis, methemoglobin, and Heinz bodies in the blood, and showing chloramine in the dialysate in the absence of copper, nitrates, or other oxidants.^{2,3} Although an increased mortality rate was questioned after one incident, there apparently have been no deaths directly attributable to chloramines or occurring within 2 weeks of exposure.⁵

Chloramine Concentrations and Testing

Dialysate water quality standards recommended by the Association for the Advancement of Medical Instrumentation (AAMI) include a maximum concentration for chloramines of 0.1 mg/L.³¹ The same limit has been adopted in Canada.³² This standard leaves little margin for error, because hemolysis has been shown with concentrations of chloramine in the dialysate as low as 0.25 mg/L.^{6,33} Dialysis units have to produce water of dialysis quality from public water supplies that typically contain chloramines in the range of 1.0 to 2.5 mg/L (Table 2). However, considerable fluctuations are common, and unexpectedly high levels in the public water supply have been implicated as contributing factors in several of the major hemolysis outbreaks.^{3,5,26,29} Some fluctuations reflect intentional increases in chloramine input at the water treatment plant in response to seasonal variations in the source water^{3,14,26}; it has also

Table 2. Chloramine Levels and Standards

	Chloraminated Tap Water (Typical)	Hemodialysis Maximum (AAMI Standard*)
Chlorine (free)	0.3-0.8 mg/L	0.5 mg/L
Chloramines	1.0-2.5 mg/L	0.1 mg/L

Note: Chloramine levels are calculated as the difference between measured total chlorine and measured free chlorine.

*AAMI standard is the maximum recommended for hemodialysis water as determined by the American National Standards Institute (ANSI) and the Association for Advancement of Medical Instrumentation (AAMI).³¹

been suggested that excess sterilant may occasionally be introduced when repairs are made to water mains.²⁹ However, day-to-day and hour-to-hour variations in the chloramine content of the mains water as delivered to the consumer may reflect other influences, including differing transit times attributable to variations in water demand. As chlorine is lost through chemical reactions or evaporation, changes occur also in the relative amounts of free chlorine, monochloramine, dichloramine, and free ammonia, as illustrated in Figure 1.

Chloramine levels are usually measured as the difference between "free chlorine" and "total chlorine" (total chlorine is chlorine in both free and combined forms, including chloramines). The common method of testing in dialysis units is a colorimetric assay using DPD (N,N-diethyl-o-phenylenediamine), which forms a pink color in proportion to the concentration of chlorine. Commercially available test kits provide formats for measuring both free chlorine and total chlorine. Suitable systems include the Hach DPD chlorine test kit (Hach Company, Loveland, CO) and the LaMotte-Palin DPD chlorine test equipment (LaMotte Chemical Products Company, Chestertown, MD). The unpredictability of chloramine levels in water supplies makes it necessary to test dialysate water more than once daily; California regulations require testing for each shift of patients. Because chloramines are unstable, the test must be performed immediately once the water sample is obtained, otherwise an incorrect low value will be measured.

Removal of Chloramine From Water

Because chloramines are small and nonionic, they are not removed by water softeners or reverse osmosis (RO) systems. Some reduction of chloramine levels may be seen in deionization (DI) systems because of direct adsorption on to the structural part of the ion-exchange resin molecules, but this effect is neither sufficient nor reliable.²⁸ Thus, although it is essential to have either an RO or a DI unit in a dialysis water purification system, and although either can remove virtually all other important contaminants, the removal of chloramines requires additional equipment.

Only two effective methods are known: charcoal filtration (perfusion through granular activated carbon), and chemical reduction by vitamin C (ascorbic acid).

Granular Activated Carbon

Charcoal filtration means treatment with granular activated carbon (GAC). The great majority of GAC is now manufactured from bituminous coal, although a variety of other raw materials may also be used, including pecan shells, coconut shells, hardwoods, lignite, pulp mill residues, carbonized resin, and petroleum.^{13,14} The charcoal from these sources is first crushed and then activated, which refers to treatment with superheated steam to increase the porosity and the internal surface area of the carbon. GACs have enormous surface areas. Those with the highest surface areas (up to 1400 m²/g or higher) tend to have the smallest pore sizes.¹⁴ These are the most efficient at adsorbing small organic molecules and halogen species (eg, molecular weight 60 to 300 D), but they will also bind larger organic molecules. However, the efficiency of the binding of monochloramine to GAC is less than that of dichloramine or free chlorine.

Different types of GAC vary in their adsorptive capacity and kinetics.^{13,34} The avidity of binding to the solid surface is conceptualized in terms of surface energy per unit area. The total adsorptive capacity is the product of the avidity and the available surface area. Adsorptive capacity can be quantitated by the measurement of the uptake of iodine at a specified equilibrium concentration, and the result is expressed as the iodine number.¹⁴ Recommended minimum iodine numbers for GACs used in dialysis water purification are 900³⁵ or 1000.³⁶ The size of the carbon granules is expressed as mesh size; a maximum mesh size of 40 (GAC-40) is suitable for dialysis unit use,³⁵ and corresponds to a mean particle diameter of 0.9 mm.¹⁴

GAC can be contained in anything from small disposable cartridges to large steel or fiberglass tanks. The size of the carbon bed has to match the water flow rate. The flow must be sufficient to allow percolation of water throughout the bed, but not so great as to create channeling, where water streams

through without effective contact with the GAC surface. The ratio of GAC volume to water flow rate is expressed as the empty bed contact time (EBCT), where:

$$\text{EBCT (min)} = \frac{\text{Volume of GAC (ft}^3\text{)} \times 7.48 \text{ (gal/ft}^3\text{)}}{\text{Maximum water flow rate (gal/min)}}$$

It is strongly recommended (and it is required by regulation in California) that there be two GAC tanks, each with an EBCT of at least 5 minutes, arranged in series.³⁵ This permits testing for chloramines between the two, to warn when the first is exhausted while the second is still functional. When this occurs, the second can be moved up to the first position and a fresh tank inserted in the second position. GAC tanks usually last several weeks, but when exhausted they must be replaced with tanks containing "virgin" GAC.³¹ GAC used in dialysis units cannot be regenerated, despite the popular misconception about backwashing. Backwashing at best serves only to expose residual usable surface area, and should not be used in this setting.

In dialysis water purification systems, the GAC tanks are usually placed upstream from the RO unit. Thin film composite (TFC) and polyamide types of RO membranes are damaged by chlorine or chloramine, and are thus best used in this configuration. In contrast, cellulose acetate RO membranes can withstand usual concentrations of chlorine and chloramine, and thus can be used in systems in which the GAC is placed downstream, but in this configuration the risk of microbial contamination of the final product water is increased. California regulations require the GAC to be placed upstream from the RO unit.³⁵

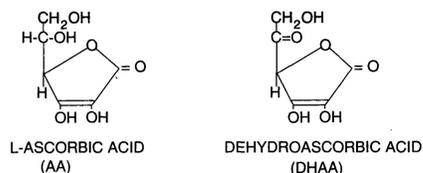
If used correctly, GAC tanks are effective and have several advantages, including adequately adsorbing occasional abnormally high peaks of chloramines in incoming water and removing other possible organic contaminants such as herbicides, pesticides, and solvents. Potential problems with GAC systems include bacterial overgrowth because the product water contains no chlorine or chloramine, and the GAC can trap organic residues that then encourage bacterial growth. An ultraviolet

light installation may be needed to help prevent bacterial contamination. In addition, spillage of carbon "fines" can be troublesome even though filters are routinely placed in the line between the GAC and the RO unit. It may help to thoroughly rinse a new GAC bed before its output is connected to the RO input. Another potential hazard is that new GAC may contain ash formed during heating of bituminous coal, and this ash may include aluminum residues. However, leaching of the aluminum is unlikely unless the incoming water is highly purified (eg, DI water), or the pH is greater than 9.0.¹⁴ In response to a recent EPA ruling regarding copper and lead levels, some municipalities now produce water with a pH > 9.0. In these circumstances, the effectiveness of downstream aluminum removal must be carefully monitored. High pH (>9.0) may also interfere with monochloramine adsorption to GAC, or promote the catalytic dissociation of chloramine on the GAC surface.³⁷ Adsorption in GAC tanks is also temperature dependent, and in cold locations hot water admixture may be necessary for optimal performance.

Practical experience with GAC for hemodialysis water purification has been very satisfactory in most instances, and it is the preferred method in the great majority of dialysis units. Although failures can prove disastrous, they happen only when system flaws coincide with inadequate monitoring.³⁻⁵

Ascorbic Acid Neutralization

Ascorbic acid (vitamin C) is a natural reducing agent (antioxidant) capable of neutralizing many oxidant species. The oxidation/reduction reaction between ascorbic acid and chloramines converts chloramines to ammonium chloride, whereas ascorbic acid (AA) is converted to dehydroascorbic acid (DHAA) (Fig 2). In 1972 the addition of ascorbic acid to dialysate was shown to be an effective way to abolish chloramine-induced red cell damage.¹ Methemoglobin production in dialysis patients was dramatically diminished, and RBC survival (measured by chromium labelling) was normalized.^{1,2,26} Ascorbic acid was used successfully for hemodialysis in Minneapolis for 5 years and was found to be cheap,



CHEMICAL REDUCTION OF CHLORAMINES

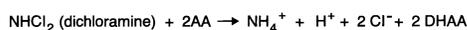


Figure 2. Chemical structure of ascorbic acid (vitamin C) and dehydroascorbic acid; reduction reactions with chloramines.

practical, and effective. However, in the summer of 1977, cases of hemolysis began to reappear.²⁶ It was discovered that the amount of chloramine added to the municipal water supply had been doubled to deal with an unusually heavy bloom of algae in the reservoirs providing the city's source water (Table 1). Doubling the amount of ascorbic acid in the dialysate proved effective (Table 3). The possibility that even higher fluctuations in chloramine levels might cause another breakthrough never happened in Minneapolis.²⁶ The 1984 incident in a free-standing dialysis unit in San Diego occurred when the concentration of ascorbic acid used was reportedly only 8.4 mg/L.^{28,29}

Ascorbic acid neutralization was developed using recirculating single-pass dialysis machines, in which the ascorbic acid was mixed into the individual patient's whole batch of dialysate before the start of each run. With the advent of dialysate proportioning systems,

sufficient ascorbic acid had to be added to the dialysate concentrate to achieve the same level in the final dialysate. However, in proportioning systems the contact time between the water (containing chloramines) and the dialysate concentrate (containing ascorbic acid) is much shorter, being of the order of 10 minutes with a central proportioning system, and no more than 2 to 3 minutes in single-patient machines of the types now in widespread use.²⁸ Thus the reaction time for complete neutralization of chloramines became an issue. Initial experiments suggested a half-time ($T_{1/2}$) of about 4 minutes for this reaction; however, despite using a dialysis system with a contact time of only 5 minutes, the same investigators could detect no chloramines, methemoglobin production, hemolysis, or shortened RBC survival.³³ The explanation for this apparent discrepancy came later when reassessment by other methods showed a $T_{1/2}$ closer to 1 minute.³⁸

A major concern about ascorbic acid (vitamin C) use is its toxicity in dialysis patients. Multiple studies have shown that any excess intake of vitamin C in renal failure patients is metabolized to oxalate, and causes a marked increase in blood oxalate levels.³⁹⁻⁴³ Oxalate is very insoluble in the presence of calcium, and can deposit extensively as crystals in various tissues. In patients with established renal impairment, excessive vitamin C intake can cause tubular oxalate precipitation presenting as accelerated renal failure⁴⁴ or even sudden permanent anuria.⁴⁵ In dialysis patients, serious oxalate-induced disease or damage has been documented in blood vessels, heart, kidneys, joints, and bones.⁴⁶⁻⁵⁰ However, the need for some routine vitamin C intake in hemodialysis patients is also well established, based on longstanding evidence of very low serum ascorbate levels in unsupplemented patients,^{51,52} and occasional cases of overt scurvy.⁵³ Because of the risk of secondary oxalosis on the one hand and serious vitamin C deficiency on the other, the optimum daily dose of vitamin C for hemodialysis patients is difficult to determine. Desirable blood levels are in the range of 6 to 10 mg/L ($\mu\text{g/mL}$). Careful studies to optimize blood vitamin C levels show other variables, such as significantly lower predialysis blood vitamin C lev-

Table 3. Ascorbic Acid Added to Dialysate

User	Ascorbic Acid Added	Dialysate Concentration
Univ. Minnesota (1972-1977)	2 g per 120 L dialysate	16.7 mg/L
Univ. Minnesota (1977-?)	4 g per 120 L dialysate	33.3 mg/L
UC San Diego (1981-1984)	4 g per gal concentrate	33.3 mg/L
UC San Diego (1984-1992)	2 g per gal concentrate	16.7 mg/L
UC San Diego (1992-present) (hybrid system including GAC adsorption)	2 g per gal concentrate	16.7 mg/L

els in patients using polyacrylonitrile dialyzers than those with cellulose acetate membranes.⁵⁴ Patients taking oral vitamin C have blood levels that are usually acceptable but sometimes excessive (5 to 153 mg/L).^{23,39,51,54} When vitamin C is used in the dialysate to neutralize chloramines, the amount used causes most patients to have predialysis blood levels of vitamin C that are close to the desirable range, provided the patients do not also take oral supplements.^{28,39} Blood oxalate levels measured in a small subset of patients were much lower in those receiving vitamin C in the dialysate than in those also receiving oral supplements.³⁹ Thus the method of ascorbic acid neutralization of chloramines appears not to increase the risk of secondary oxalosis, and alleviates the need for patients to take oral vitamin C supplements.

One disadvantage of using ascorbic acid is that in solution it can oxidize spontaneously if left open to the air, and so lose its effectiveness over time.³⁵ In addition, to keep track of whether ascorbic acid has or has not been added to a particular supply of concentrate requires meticulous labeling and record keeping. Because the GAC method is now standardized and reliable in most instances, ascorbic acid neutralization is no longer in widespread use in large dialysis units in the United States. However, for in-patient dialysis in wards or nursing facilities where portable water purification is necessary, and where individual testing for chloramines must be done anyway, ascorbic acid is still preferred by some to double GAC tanks.

Hybrid System (GAC and Ascorbic Acid)

In modern hemodialysis units with single-patient proportioning machines and piped dialysate concentrates, one advantage of the ascorbic acid neutralization system is that the water is not depleted of chlorine or chloramine until it reaches the patient's machine. This ensures inhibition of bacterial growth within the water purification and distribution system. In contrast, GAC tanks are usually placed early in the water flowpath, and bacterial contamination of the RO unit and holding tank can occur. Because endotoxin formation

is of particular concern when using modern high-flux dialyzers, methods to prevent bacterial overgrowth are a high priority. One innovative solution (eg, at the University of California Los Angeles) has been to use GAC to remove chloramine, and then to reintroduce free chlorine in very low dose (0.05 to 0.2 mg/L) using a chlorinator just upstream from the RO system (cellulose acetate type). Because free chlorine in this concentration is harmless (the AAMI standard is 0.5 mg/L), subsequent removal is not necessary. When a similar system was placed in a new dialysis facility at the University of California San Diego in 1992, however, it was decided to temporarily retain ascorbic acid in the dialysate concentrates until the operating characteristics of the new water purification system were fully established. This was fortuitous because soon thereafter chloramines were intermittently detected in the purified water. The cause of this was elusive until testing for ammonia was done. This revealed 0.24 mg/L of ammonia in the city water supply, and 0.17 mg/L of ammonia after the carbon filters. The conclusion was that chloramines were being produced *de novo* at the rechlorinator injection site because of the presence there of free ammonia. Removal of free ammonia proved to be difficult, and was eventually overcome by adding an additional carbon filter and rechlorinator upstream, as shown in Figure 3. The additional chlorine combines with free ammonia to form chloramine, and pushes the equilibrium on the "breakpoint curve" to the right (Figure 1), toward the point where total dissolved residual chlorine is minimized.⁵⁵ This revised system proved effective in eliminating chloramines, while the low level (trace to 0.2 mg/L) of residual free chlorine in the product water allowed persistently negative tests for bacteria and pyrogens. Ammonia breakthrough is still possible, so chloramine testing downstream from the second rechlorinator is still mandatory, and ascorbic acid is maintained in the dialysate concentrates. The system appears complex, but the additional features are relatively inexpensive and easy to operate. The use of ascorbic acid relieves all oxidant stress and avoids the occasionally excessive blood levels of vitamin C seen in patients taking oral

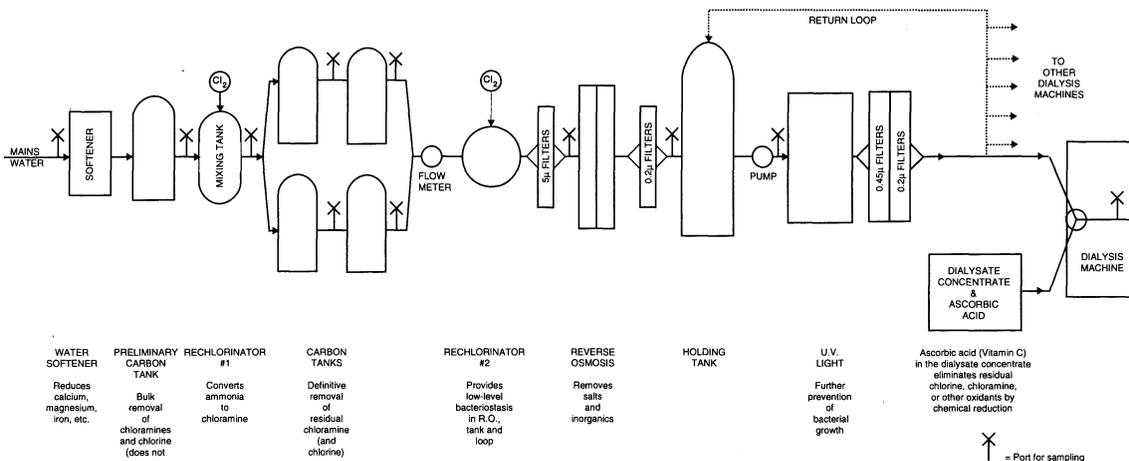


Figure 3. Example of a hybrid system for hemodialysis water purification, using both GAC for chloramine removal, and ascorbic acid neutralization to eliminate oxidants in the final dialysate. Rechlorinators are used (1) to remove ammonia and (2) to provide low-level bacteriostasis throughout the water treatment and distribution system. The final dialysate is free of endotoxin, organics, ammonia, chlorine, chloramine, and any other oxidant.

vitamin C supplements. The final dialysate contains no endotoxin, organics, ammonia, chloramine, or chlorine.

Selection and Operation of a Chloramine Removal System

The choice of system for water purification for hemodialysis is driven by cost considerations as well as safety issues. The cost of ascorbic acid neutralization is about 20 cents per dialysis (10 cents for the vitamin C itself and a further 10 cents for labor). The average cost of GAC treatment is of the order of 25 cents to 30 cents per dialysis, but there is a wide range depending on several factors. These estimates do not include the cost of routine chloramine testing, or other components of the water treatment system.

A GAC system that reliably avoids chloramine-induced hemolysis is likely to be regarded as sufficient in most facilities. Although the theoretical benefits of even better water quality may not be disputed, the additional complexity of a hybrid system is unlikely to gain favor unless it can be justified in terms of demonstrable improvements in patient outcomes. However, even the most sophisticated system does not guarantee safety. Several chloramine-induced hemolysis epi-

sodes have occurred in facilities where the water treatment system had just been modified or upgraded,^{4,5} emphasizing that the subtleties of design of such systems for hemodialysis may not be fully appreciated by those who install and operate them. When the State of California appointed a task force in 1984 to draft regulatory standards, it was realized that no single individual had all the specialized medical, technical, and engineering expertise needed to comprehensively evaluate every aspect of the issue.⁸ Nevertheless, although reliance must be placed on engineers and technical experts, the final responsibility for safety resides with the medical director of the dialysis unit.

The California standards remain the most rigorous anywhere.³⁵ As summarized in Table 4, they are quite comprehensive, and prohibit certain effective methods in preference for alternatives that were judged safer. For instance, GAC filters must be placed before the RO, not after. And for Redy machines, ascorbic acid is required; this was chosen in preference to an alternative method whereby the entire dialysate is passed through the device cartridge (which contains GAC) before initiating dialysis.²⁸ The most important features of the California standards are that two GAC filters must be used in series, and that careful

Table 4. Summary of California Regulations for Chloramine Removal From Renal Dialysis Water Supplies

1. Applies to all facilities that receive or have a potential to receive chloramines in the tap water. Product water to meet AAMI standard of 0.1 mg/L.
2. All installations subject to State review.
3. Granular activated carbon (GAC) requirements:
 - (A) Two filters in series, each with EBCT minimum 3 minutes (5 minutes preferred).
 - (B) GAC upstream from RO or DI; 0.45 μ m filter required before the patient.
 - (C) GAC maximum mesh size 12 \times 40; minimum iodine number 900.
4. Operating procedures for GAC:
 - (A) Chloramine testing where the water exits the first GAC filter and in the product water at least once per shift.
 - (B) Replacement of the first filter within 72 hours of chloramine breakthrough (second filter to first position, new one in second position).
5. Ascorbic acid requirements:
 - (A) Concentration in dialysate of 1.67 mg% (16.7 mg/L).
 - (B) Chloramine testing of the dialysate before each dialysis.
 - (C) Ascorbic acid to be added daily unless a variance is granted.
6. For Redy machines:
 - (A) Ascorbic acid in a concentration of 1.67 mg%.
 - (B) Chloramine testing of the dialysate before each dialysis.
7. Dialysis facility policies and procedures must specify:
 - (A) Chloramine testing methodology:
 - (1) DPD test kit (not OTA type)
 - (2) at least two testing locations, specify frequency
 - (3) log book and signatures
 - (4) adhere to recommendations for shelf life of chemical reagents
 - (B) What to do when chloramine limit exceeded.
 - (C) Testers' qualifications and competency certified by the medical director.
 - (D) Reporting of unusual incidents to licensing agency within 24 hours.
8. Applies to all entities responsible for hemodialysis treatments in California.
9. Effective April 1, 1985.

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testing for chloramines must be done after the first filter at each patient shift, not just daily. It would appear that none of the outbreaks listed in Table 1 could have occurred had these two standards been in force.

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