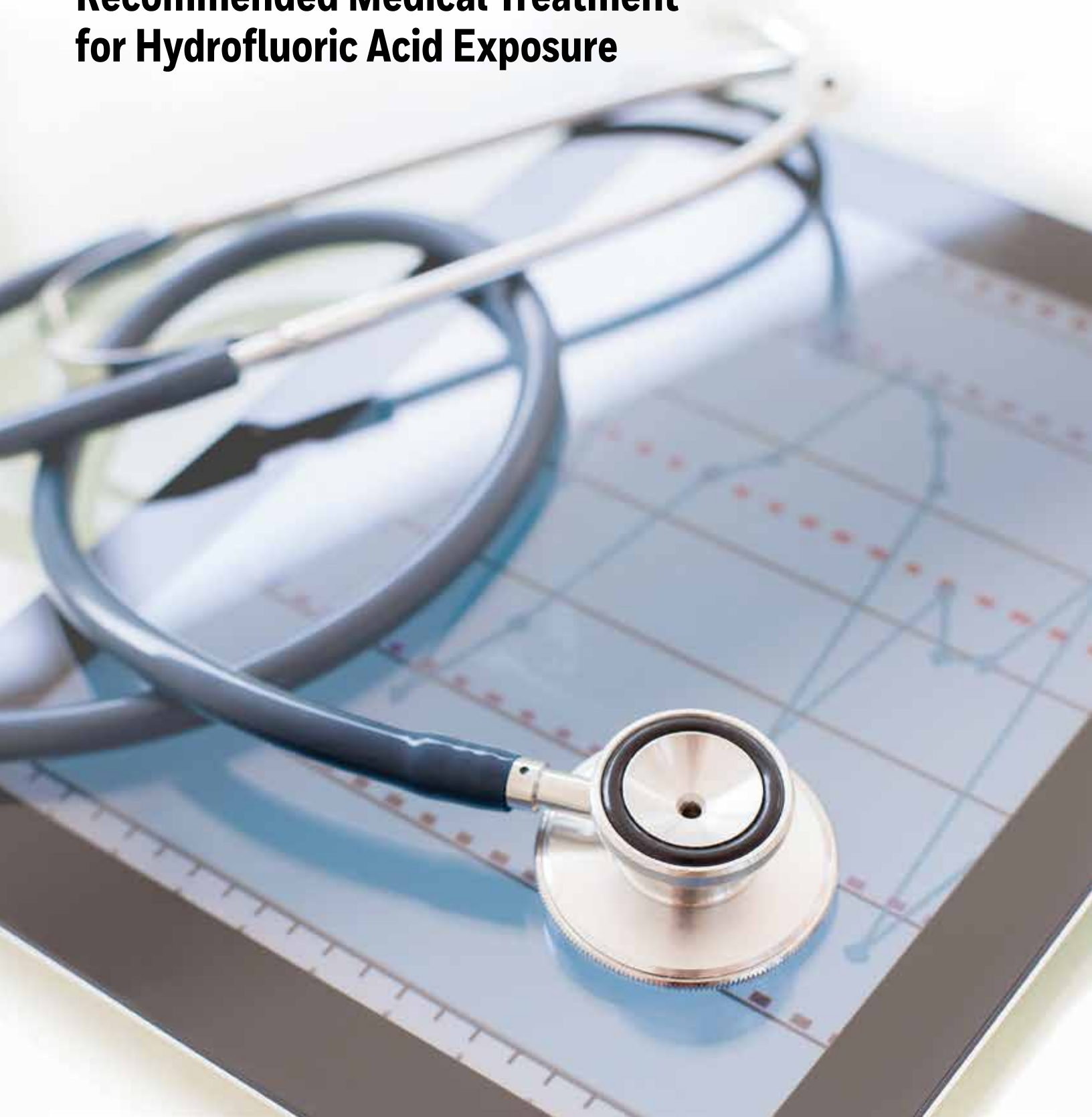


Recommended Medical Treatment for Hydrofluoric Acid Exposure



Introduction

Because the medical treatment of hydrofluoric acid (HF) is so specialized and differs from the treatment of other inorganic acid exposures, physicians may be unaware of appropriate treatment measures. It is recommended that HF users ensure that their local medical resources are familiar with the toxicity of HF and the treatment of HF exposure. This would include, at a minimum, thoroughly reviewing this booklet and making sure that treatment facilities and supplies are available.

Hydrofluoric Acid (CAS # 7664-39-3) is very aggressive physiologically because of the fluoride ion. Both anhydrous hydrofluoric acid (hydrogen fluoride) and its solutions are clear, colorless liquids. When exposed to air, concentrated solutions and anhydrous HF acid produce pungent vapors which are especially dangerous. Unless heated, dilute concentrations of HF acid in water (e.g., less than 40% HF) do not produce significant vapor concentrations.

NOTE: Persons unfamiliar with hydrofluoric acid often mistake it for, or confuse it with, hydrochloric acid. Although hydrofluoric acid (HF) and hydrochloric acid (HCl) have similar sounding names, the toxicity of these two acids is very different. To decrease or avoid confusion, we recommend that **hydrofluoric acid** and **hydrogen fluoride** be referred to as "HF".

HF is primarily an industrial raw material. It is used in fluorocarbon production, stainless steel manufacturing, metal finishing, aluminum manufacturing, inorganic and organic chemical manufacturing, petroleum refining, mineral processing, glassmaking, and electronic components manufacturing. It is also used in certain industrial and consumer cleaning compounds. The use of HF in consumer products is discouraged because of its potential toxicity.

Most non-industrial burns are caused by dilute concentrations of HF (e.g., less than 15% HF). Most of the HF used in the electronics industry is less than 50%. However, many industrial uses of HF involve concentrated (50-100%) HF.

The recommended medical procedures described in this brochure are based on a review of the available literature, shared experiences with others who have dealt with the health effects of HF, the personal knowledge and experiences of Honeywell physicians, nurses and other professionals in dealing with the unique hazards of this product, and experimental laboratory work sponsored by Honeywell.

Every effort must be made to prevent exposure to HF. If exposure does occur, the specialized procedures which follow are recommended to avoid the very serious consequences that might otherwise occur.

Exposure Limits

The Permissible Exposure Limit (PEL) set by the U.S. Occupational Safety and Health Administration (OSHA) is a time weighted average exposure for 8 hours of 3 ppm. (25) The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a ceiling level of 2 ppm (1.53 mg/m³) with a 0.5 ppm TLV-TWA. (26) The National Institute for Occupational Safety and Health (NIOSH) has established the level that is immediately dangerous to life and health (IDLH) at 30 ppm. (27, 28) The American Industrial Hygiene Association (AIHA) has published an Emergency Response Planning Guideline setting 50 ppm as the maximum level below which nearly all individuals could be exposed for one hour without experiencing or developing life-threatening health effects (ERPG-3), 20 ppm as the maximum level below which nearly all individuals could be exposed for one hour without

WARNING:
Burns with concentrated HF are usually very serious, with the potential for significant complications due to fluoride toxicity. Concentrated HF, liquid or vapor, may cause severe burns, metabolic imbalances, pulmonary edema, and life threatening cardiac arrhythmias. Even moderate exposures to concentrated HF may rapidly progress to fatality.

developing irreversible health effects or symptoms which would impair taking protective action (ERPG-2), and 2 ppm as the maximum level below which nearly all individuals could be exposed up to one hour without experiencing other than mild, transient adverse health effects (ERPG-1). (29) The California Occupational Safety and Health Standards Board has established a PEL of 0.4 ppm 8hr TWA [$.33\text{mg}/\text{m}^3$] with a STEL (Short term exposure level) of 1 ppm [$0.83\text{mg}/\text{m}^3$]. (32)

Acute Toxicity

Skin Contact

HF can cause serious, painful burns of the skin. Specialized first aid and medical treatment is required. Burns larger than 25 square inches (160 square cm) may result in serious systemic toxicity.

HF is a highly corrosive acid which can severely burn skin, eyes, and mucous membranes. The vapors from anhydrous HF acid or its concentrated solutions can also burn these tissues.

HF is similar to other acids in that the initial extent of a burn depends on the concentration, the temperature, the duration of contact with the acid and the size of the burn. **HF acid differs, however, from other acids because the fluoride ion readily penetrates the skin, causing destruction of deep tissue layers. Unlike other acids which are rapidly neutralized, this process may continue for days if left untreated.**

Strong acid concentrations (over 50%), and particularly anhydrous HF (AHF or 100% HF), cause immediate, severe, burning pain and a whitish discoloration of the skin often followed by blister formation. Skin exposure to HF vapors can result in similar burns.

HF skin burns are usually accompanied by severe, throbbing pain which is thought to be due to irritation of nerve endings by increased levels of potassium ions entering the extracellular space to compensate for the reduced levels of calcium ions.

The usual initial signs of an HF burn are redness, edema, and blistering. With more concentrated acids, a blanched white area appears. The fluoride ion penetrates the upper layers of the skin. A thick granular exudate may form under blisters due to liquefaction necrosis. In rare (and untreated) cases, there may be penetration to underlying bone with decalcification. **HF burns require immediate and specialized first aid and medical treatment** (2, 3, 4, 5, 6, 7) differing from the treatment of other chemical burns. If untreated or if improperly treated, permanent damage, disability or death may result. (8) If, however, the burns are promptly and properly recognized and managed, the results of treatment are generally favorable.

Treatment is directed toward binding the fluoride ions to prevent tissue destruction. High molecular weight quaternary ammonium compounds, such as benzalkonium chloride, are used as soaking agents. (9, 10, 11) Calcium gluconate gel can be applied locally, and calcium gluconate solution may be injected (subcutaneously, intravenously, or intra-arterially) or used as an irrigant. (3, 12, 13, 14, 15)

Speed is of the essence. Delays in first aid care or medical treatment or improper medical treatment will likely result in greater damage or may, in some cases, result in a fatal outcome. **During transportation to a medical facility or while waiting for care within a facility, the initial treatment (whether with benzalkonium chloride or topical calcium gluconate) should be continued.**

In contrast to the immediate effects of concentrated HF, the effects of contact with more dilute HF acid or its vapors may be delayed, and this is one of the problems with the recognition of some HF burns. Skin contact with acid concentrations in the 20% to 50% range may not produce clinical signs or symptoms for 1 to 8 hours. With concentrations less than 20%, the latent period may be up to 24 hours. HF concentrations as low as 2% may cause symptoms if the skin contact time is long enough. (1)

Eye Contact

HF acid can cause severe eye burns with destruction or opacification of the cornea. Blindness may result from severe or untreated exposures. Immediate first aid and specialized medical care is required. (3,13)

Inhalation

HF acid vapors may cause laryngospasm, laryngeal edema, bronchospasm, and/or acute or delayed pulmonary edema. Acute symptoms may include coughing, choking, chest tightness, chills, fever, and cyanosis. Many reported fatalities from HF exposures have been due to severe pulmonary edema (coupled with systemic toxicity) that did not respond to usual medical treatment.

Burns from vapors or liquid contact to the oropharyngeal mucosa or upper airway may cause severe swelling to the point of requiring a tracheostomy. It is recommended that all patients with such exposures be hospitalized for observation and/or treatment.

Because of the strong irritant nature of HF, an individual inhaling HF vapors will usually experience upper respiratory injury, with mucous membrane irritation and cough. All individuals suspected of having inhaled HF should be observed for pulmonary effects. This would include those individuals with significant upper respiratory irritation, bronchoconstriction by pulmonary auscultation or spirometry, and any individual with HF exposure to the head, chest, or neck areas. It has been reported that pulmonary edema may be delayed for several hours and even up to 2 days. If there is no initial upper respiratory irritation, significant inhalation exposure is unlikely.

Ingestion

Ingestion of HF may result in severe burns to the mouth, esophagus, and stomach. Severe systemic effects are common. Ingestion of even small amounts of dilute HF have resulted in death. (30)

Burns of the Skin – General Treatment Principles

Burns from dilute acid are difficult to distinguish from other chemical burns and usually appear as areas of erythema. However, they may progress, if not treated, to areas of blistering, necrosis, or ulceration. Burns from more concentrated acid have a characteristic appearance and present as severely reddened, swollen areas with blanched, whitish regions which rapidly progress to blistering and necrosis. A thick granular exudate usually appears under these blisters and requires debridement and removal.

Concentrated HF burns cause extreme pain. The pain is thought to result from nerve ending irritation due to increased levels of potassium ions in extracellular spaces to compensate for the reduced levels of calcium ions which have been bound by the fluoride. **Relief of pain is an excellent indication of the success of treatment and therefore, local anesthetics should be avoided if possible.**

Many different types of therapies have been suggested for HF burns. The aim of all treatment is to chemically sequester the fluoride ion and to prevent extensive, deep-tissue destruction. (37, 38)

After treatment of recognized burned areas is begun, the victim should be carefully examined to ensure there are no other burn sites which may have been overlooked.

Quaternary Ammonium Compounds

Most HF burns can be satisfactorily treated by immersion of the burned part in an iced, aqueous solution of a quaternary ammonium compound. The most experience is with a solution of 0.13% benzalkonium chloride. Benzalkonium chloride is currently (Spring, 2018) available as a nonprescription drug in the United States, however, this status may change, so readers are advised to check the current regulatory status. In December, 2017 the U.S. Food and Drug Administration (FDA) issued a final rule establishing that certain active ingredients used in nonprescription (also known as over-the-counter or OTC) antiseptic products intended for use by health care professionals in a hospital setting or other health care situations outside the hospital are not generally recognized as safe and effective (GRAS/GRAE). Although benzalkonium chloride was considered as part of this FDA ruling, the FDA deferred rule making on it (and 5 other OTC antiseptics) to allow for further study. (56)

The solutions should be cooled with ice cubes. **Shaved or crushed ice may cause excessive cooling, with the danger of frostbite.**

If immersion in the solution is not practical, soaked compresses of the same iced solution should be applied to the burned area. The immersion or compresses should be used for **at least 2 hours**. Compresses should be changed or soaked with additional solution approximately every 2 to 4 minutes.

If blisters are present, they should be opened and drained and necrotic tissue should be debrided by a physician or qualified health care practitioner as soon as possible. However, immersion in benzalkonium chloride or use of compresses should not be delayed if debridement cannot be accomplished immediately.

Immersion in the iced benzalkonium chloride bath may result in discomfort due to excess chilling. Relief may be obtained by removing the burned part from the bath every 10 to 15 minutes. If pain in the burned area recurs, resume soaking in the iced benzalkonium solution. After the initial 30 to 60 minutes of treatment, less ice can be used so the bath is cool rather than cold.

The success of this treatment is indicated by relief of the severe pain in the burned area. If there is no significant relief of pain within 30 to 40 minutes, the use of 2.5-5% calcium gluconate injections may be necessary. If pain recurs when the treatment is stopped at the end of the first 2 hours, immersion or compresses should be resumed until pain is relieved. A total of 4 to 6 hours of immersion or use of compresses of benzalkonium chloride may be required for the treatment of most burns. No further treatment will be required in many instances. Iced quaternary ammonium compound solutions offer several advantages over topical calcium gluconate gel:

- Ability to treat burns on multiple surfaces, such as the hand, more efficiently;
- Reduction of local pain due to the cooling effect of ice;
- Possible slowing of the passage of the fluoride ion into deeper tissues and into the bloodstream due to local vasoconstriction;
- Does not require continuous massaging

Quaternary ammonium compounds should not be used for burns on the face, ears or other sensitive areas due to their irritating nature. It is preferable to use calcium gluconate gel or calcium gluconate injection in these areas.

Calcium Gluconate Gel

Calcium gluconate gel, consisting of 2.5% USP calcium gluconate in a surgical water soluble lubricant, is widely used for first aid and/or primary treatment of HF burns of the skin. The gel is convenient to carry and can be used to initially treat small burns that might occur away from medical care. (The gel is not recommended for burns with concentrated HF except as a first aid measure). The gel is used by massaging it promptly and repeatedly into the burned area, until pain is relieved. Surgical gloves should be worn during initial application of the gel, so the person providing treatment will not receive a secondary HF burn. This treatment can be started without waiting for medical direction. Several commercially available calcium gluconate gel formulations have been evaluated and found to give comparable outcomes. (35)

If used as the only method of treatment, liberal quantities of calcium gluconate gel must be massaged into the burned area continuously for up to several hours. Relief of pain can be used to assess the efficacy of this treatment. If good relief of pain is not obtained after 30 to 40 minutes, alternate methods of treatment, such as calcium gluconate injections or benzalkonium chloride soaks, should be considered.

The gel is especially useful for burns on the face, particularly near the mouth, eyes, on the ears, or for small, dilute acid burns elsewhere. It may be convenient to use the gel for very small burns where the victim can easily apply and massage the gel into the burned area. Use of the gel may be more convenient for dilute acid burns such as those that can occur with commercial products like rust removers, aluminum cleaners, or etching solutions.

First Aid Treatments

Skin Contact

1. Move victim immediately under safety shower or other water source and flush affected area thoroughly with large amounts of running water. Speed and thoroughness in washing off the acid is of primary importance.
2. Begin flushing even before removing clothing. Remove all contaminated clothing while continuing to flush with water under a safety shower.
3. While the victim is being rinsed with water, someone should alert first aid or medical personnel and arrange for subsequent treatment.
4. If the exposure is limited to HF and other water soluble substances, 5 minutes of water decontamination after the removal of all PPE, clothing, and jewelry should be sufficient. Concomitant exposure with hydrocarbons or other substances with limited water solubility may require longer water decontamination or the use of other decontaminating agents. If a more definitive treatment (0.13% benzalkonium chloride solution or 2.5% calcium gluconate) is not available, water irrigation should continue until one of these agents is available or transportation to a medical facility is initiated.

5. Immediately after thorough washing, use one of the measures below:
 - a. Begin soaking the affected areas in iced 0.13% benzalkonium chloride solution.
Use ice cubes, *not* shaved ice, to prevent frostbite.
If immersion is not practical, towels should be soaked with iced 0.13% benzalkonium chloride solution and used as compresses for the burned area. Compresses should be changed every 2 to 4 minutes. Do not use benzalkonium chloride solution for irrigation of the eyes. Exercise caution when using benzalkonium chloride solution near the eyes as it is an eye irritant. Benzalkonium chloride soaks or compresses should be continued until pain is relieved or until more definitive medical treatment is provided.
 - b. Start massaging 2.5% calcium gluconate gel into the burn site.
Apply gel frequently and massage continuously until pain and/or redness disappear or until more definitive medical care is given. The individual applying the calcium gluconate gel should wear surgical gloves to prevent a secondary HF burn.
6. After treatment of burned areas is begun, the victim should be examined to ensure there are no other burn sites which have been overlooked.
7. Arrange to have the victim seen by a physician. If burns are small and/or caused by weak acid, and treatment has been provided by an experienced individual, evaluation by a physician may not be necessary. **During transportation to medical care and while waiting to see a medical provider, it is extremely important to continue the first aid care, whether with benzalkonium chloride or massaging calcium gluconate gel.** In many situations, particularly for minor burns covering a small skin area or for burns caused by dilute HF, continued treatment with soaks or gel may be effective as the sole type of medical care. All persons with extensive burns or burns with significant blister formation or with the appearance of whitish or dead skin need to be seen by a physician. All persons with HF burns which do not respond to either calcium gluconate gel or benzalkonium chloride soaks or compresses within 30 minutes should be evaluated by a physician.

NOTE:

Clinical experience has shown that both benzalkonium chloride and calcium gluconate gel are effective when used correctly in appropriate situations. In an animal model, benzalkonium chloride soaks were superior to calcium gluconate gel under the experimental conditions used. (37, 38)

Eye Contact

1. **Immediately** flush the eyes for at least 15 minutes with large amounts of gently flowing water. Hold the eyelids open and away from the eye during irrigation to allow thorough flushing of the eyes. **Do not use the benzalkonium chloride solutions described for skin treatment.** If the person is wearing contact lenses, the lenses should be removed, if possible. However, flushing with water should not be interrupted, and the lenses should be removed by a person who is qualified to do so. If sterile 1% calcium gluconate solution is available, **water washing may be limited to 5 minutes**, after which the 1% calcium gluconate solution should be used to irrigate the eye using a syringe or a continuous irrigation device.
2. Take the victim to a doctor, preferably an eye specialist, as soon as possible. Ice water compresses may be applied to the eyes while transporting the victim to the doctor.
3. If a physician is not immediately available, apply one or two drops of 0.5% tetracaine hydrochloride, 0.5% proparacaine, or other aqueous, topical ophthalmic anesthetic and continue irrigation. Use no other medications unless instructed to do so by a physician. Rubbing of the eyes is to be avoided.

Inhalation

1. Immediately move victim to fresh air and get medical attention.
2. Keep victim warm, quiet, and comfortable.
3. If breathing has stopped, start artificial respiration at once.
4. 100% oxygen should be administered as soon as possible by a trained individual. Continue oxygen while awaiting medical attention unless instructed otherwise by a physician.
5. A nebulized solution of 2.5% calcium gluconate may be administered with oxygen by inhalation.
6. Do not give stimulants unless instructed to do so by a physician.
7. The victim should be examined by a physician and held under observation for at least a 24-hour period.

Ingestion

1. Do not induce vomiting.
2. Get immediate medical attention. Ingestion of HF is a life-threatening emergency.

Medical Treatments

Initial medical treatment for HF exposures is a continuation of first aid treatments. For the skin, this would include continued use of iced benzalkonium chloride soaks/compresses, or use of topical calcium gluconate gel.

NOTE:

Because prolonged immersion in the ice bath may result in discomfort, relief may be obtained by removing the part from the bath every 10 minutes for a minute or so and then reimmersing it. After the initial 30 to 60 minutes of treatment, less ice can be used so the bath is cool, rather than cold.

If the physician advises continued treatment with benzalkonium chloride soaks or compresses, the soaks or compresses may be required for 2 to 4 hours. Significant relief of pain should be noted within the first 30 minutes. If this does not occur, more definitive care should be instituted. If the pain is substantially relieved within the first 30 minutes, continue the treatment for a total of 2 hours. After that time, discontinue treatment and observe for the recurrence of pain. If pain recurs, continue soaks or compresses until relief of pain occurs. Soaking for 6 hours is sometimes needed.

Calcium gluconate gel may be used for several hours or even repeated over a period of a few days. However, if significant relief of pain does not occur within 30 to 40 minutes, more definitive treatment such as calcium gluconate injections or iced benzalkonium chloride is required.

Calcium Gluconate Injections

After first aid measures have been taken, injection of a 2.5%-5% calcium gluconate solution is indicated as the primary medical treatment for larger burns. For smaller burns, if benzalkonium chloride soaks or calcium gluconate gel do not result in significant relief of pain within 30 to 40 minutes, injection of calcium gluconate solution is indicated. Injection of calcium gluconate solution may also be indicated for burns in which treatment has been delayed. The physician should inject

NOTE:

Calcium chloride solution should not be used for local injection. Injection of calcium chloride into muscle or into subcutaneous or perivascular tissue may cause severe necrosis and sloughing.

sterile 2.5–5% aqueous calcium gluconate beneath, around, and into the burned area. Calcium gluconate is packaged as a 10% solution, and must be diluted 50:50 or 25:75 with normal saline to make 5% or 2.5% solutions.

If subcutaneous calcium gluconate injections are used, the amount injected initially is small and should not exceed 0.5 cc per square centimeter of affected skin surface. The injections should not distort the appearance of the skin. A small-gauge needle (27–30 gauge) should be used, and the burned area should be injected through multiple sites. With successful treatment, pain relief following injection of 2.5%–5% calcium gluconate solution is very rapid. The patient can usually advise when the pain stops, and this is an indicator of adequate treatment. Multiple injections in skin that has compromised integrity may increase the risk of infection, and the use of a topical antibiotic cream or ointment should be considered following such treatment. Local anesthetics should not be used since they mask pain relief which is an important indication of adequacy of treatment.

Calcium Gluconate Solution

In some instances, a 5% or 10% calcium gluconate solution may be used in compresses or for irrigation. For example, irrigating with a calcium gluconate solution may be the best treatment should HF enter the external ear canal. In this instance, referral to an otolaryngologist is recommended.

Burns of the Fingers and Nails

Burns of the fingers often create special problems in treatment. Finger and toe nails permit penetration of fluoride ions but prevent soaks or gels from being effective. It may be necessary to drill, split, or even remove nails to allow the topical methods of treatment to be effective. One author has cautioned that removal of the nail should rarely be necessary in the case of dilute HF acid (less than 10%) burns. (40) The treating physician must consider the morbidity associated with removal of the nail versus the need to treat the HF exposure.

If immersion in benzalkonium chloride solution is started immediately, it may be possible to avoid removing the nail. Sometimes better penetration under the nail can be accomplished by splitting the nail or by drilling several burr holes in the nail using a large gauge needle or a nail drill. If calcium gluconate injection is used as treatment, the nail may still need to be split or removed. If nail removal is necessary, using a short acting regional or ring-block anesthetic may facilitate this procedure and not interfere with using pain relief as an indicator of effective treatment. When using calcium gluconate injections in the digits, the volume injected must be limited to avoid compromising the circulation in the digit.

If benzalkonium chloride soaks are not available, finger or hand burns can be treated by using a glove filled with calcium gluconate gel. Initially, calcium gluconate gel should be massaged into the burned area. Following this, the hand is inserted into an oversize surgical glove partially filled with calcium gluconate gel. The gloved hand may be immersed in ice water, if available, which may aid pain relief. This treatment works best for burns where there is no blistering, or after the burns have been debrided. As in other cases where calcium gluconate gel is used, alternate methods of treatment should be considered if good relief of pain is not achieved within 30 to 45 minutes. If pain is relieved, the glove should remain in place for 3 to 4 hours.

Calcium Infusion Intra-arterial and Intravenous

Reports in the literature have described the use of intra-arterial injection or infusion of dilute calcium gluconate solutions to treat HF burns of the hand and digits. This method, although rather involved, should be considered in selected cases, especially where inadequate or delayed treatment has occurred. The method is described as follows:

“A long catheter was inserted percutaneously into the radial artery using standard aseptic technique. Intra-arterial catheter placement was confirmed by pressure transducer and oscilloscope. If the burn involved only the thumb, index, or long fingers, the catheter was advanced only a few centimeters proximally in preparation for digital subtraction arteriography. If the burn involved the ring or small fingers, the catheter was advanced proximally into the brachial artery because access to the ulnar circulation was necessary.

Following satisfactory placement of the arterial catheter, digital subtraction arteriography was performed on all patients in our series to identify the origin of vascular supply to digits involved.

Once the tip of the arterial catheter was in the desired location, a dilute preparation of calcium gluconate (10 ml of a 10% solution mixed in 40 to 50 ml 5% dextrose) was infused with a pump apparatus into the catheter over 4 hours. Each patient was observed closely during the infusion period for progression of symptoms and potential complications of the procedure, such as alterations of distal vascular supply.

Following the 4-hour infusion, the arterial catheter was maintained in place in the usual manner while the patient underwent an observation period. If typical HF pain returned within 4 hours, a second calcium infusion was repeated until the patient was pain free 4 hours following completion of the calcium infusion.” (14)

A case series from China reports the use of intra-arterial infusion in 118 patients over the period 2008-2011, with use in both the upper and lower extremity. Of note, more than 50% of their cases were first treated more than 12 hours after the HF injury. HF concentrations were not reported. Burns ranged from 1-3% body surface area. (55)

Calcium gluconate infusion via the Bier Block method has been used to treat HF burns of the upper extremity. (41, 42, 43) Graudins, et al. describe their method:

“An intravenous catheter was placed on the dorsum of the affected hand. The superficial veins were exsanguinated by elevation. A double-cuffed pneumatic tourniquet was applied above the elbow, inflated to 100 mm Hg above systolic blood pressure, and 10 ml of 10% calcium gluconate diluted with 30 to 40 ml of 0.9% saline solution was then infused. Ischemia was maintained for 25 minutes; the cuff was sequentially released over 3 to 5 minutes.”

This Bier Block method was most successful for burns due to dilute acid. If the use of intravenous calcium gluconate was not successful in relieving pain (which occurred with burns due to 49% HF, the highest concentration seen in the series of patients), Graudins et al. turned to intra-arterial calcium gluconate infusion without repeating the Bier Block infusion. More recent articles have described repeat use of the Bier Block infusion technique, as well as use in the lower extremity. (57) Articles describing intra-arterial calcium gluconate infusions have described repeated infusions for initial treatment failures. (14, 55)

Eye Injuries

As with skin exposures, medical treatment of HF eye burns is a continuation of the first aid treatment. After water irrigation, the eyes are irrigated with a 1% calcium gluconate solution. Use of local anesthetic eye drops is recommended. Irrigation devices, such as a Morgan Lens[®], or an inverted two-pronged nasal oxygen cannula, may be utilized to instill the solution over a period of 1 to 2 hours. Consult an ophthalmologist regarding additional treatment.

Inhalation Injuries

Patients with inhalation exposures are at high risk for systemic toxicity in addition to local effects on the respiratory tract.

Exposure to HF acid vapors can cause acute respiratory irritation, bronchospasm, and/or pulmonary edema. Medical personnel should also be alert to the possibility of inhalation injury when extensive burns of the face, neck, or chest have occurred.

The victim should be removed from exposure and administered 100% oxygen immediately. The use of 2.5% aqueous calcium gluconate given by nebulizer with 100% oxygen, or with intermittent positive pressure, is recommended. In addition to its local effect on the respiratory tract, nebulized calcium gluconate provides a significant source of calcium and can reduce the risk of systemic toxicity from inhalation exposure. Repeated use of nebulized calcium gluconate, every 4 hours for 48 hours after a significant inhalation exposure, has been described. (51) As advanced treatments for inhalation injuries become more widely available, such as extracorporeal membrane oxygenation (ECMO), their use for HF inhalation injuries will be more common. (58)

Due to the high risk of systemic toxicity from inhalation exposures to HF, starting an IV and providing supplemental calcium and magnesium should be considered.

Ingestion

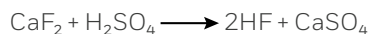
HF ingestion is not anticipated in industrial settings. The presence of HF in consumer products increases the likelihood of ingestions, either intentional or accidental. The concentration of HF in consumer products is generally less than 10%. In addition to local effects in the mouth and esophagus, HF ingestion poses a serious risk for systemic toxicity. Numerous fatalities have been reported from HF ingestions, both intentional and accidental.

Previous recommendations were to give patients who had ingested HF milk or water to drink, followed by oral administration of a calcium or magnesium containing compound. Most patients who have ingested HF vomit spontaneously. Giving anything by mouth raises the risk of vomiting, with concurrent risk of aspiration of acidic vomitus. In addition, limited experimental studies have not supported the efficacy of oral calcium or magnesium agents in improving survival from HF ingestions. (39) This is likely due to providing insufficient calcium and magnesium to affect the systemic electrolyte disturbances.

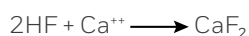
Therefore, current recommendations are to give oral treatments only to conscious patients and under the direct advice of a physician. Patients with HF ingestion need immediate transport to a hospital for further treatment and evaluation. If supplies and trained personnel are available, starting an intravenous line and administering IV calcium gluconate is recommended as preemptive treatment for impending systemic toxicity.

Systemic Absorption and Toxicity

To produce HF, calcium fluoride is reacted with sulfuric acid:



This production process requires a great deal of energy to accomplish. On the other hand, in the body:



This process releases energy, and therefore occurs very readily. The toxic effect of HF on body calcium is certainly more complicated than this. There is some evidence that fluoride may combine with calcium and phosphate, so that 5 calcium ions are tied up for each fluoride ion (e.g., $\text{Ca}_5\text{F}(\text{PO}_4)_3$), rather than two. There is also some evidence that there may be high intracellular levels of calcium in some tissues, rather than low levels, as would intuitively be expected. (16) However, the reaction of fluoride with body calcium is one of the major toxic effects and forms the basis for many treatment recommendations.

One of the most serious consequences of severe exposure to HF by any route is the marked lowering of serum calcium (hypocalcemia) and other metabolic changes, which may result in a fatal outcome if not recognized and treated. Hypocalcemia should be considered a potential risk in all instances of inhalation or ingestion, and **whenever skin burns exceed 25 square inches** (160 square centimeters). Serum magnesium may also be lowered, and elevations in serum potassium have been reported to further complicate the metabolic imbalances which need to be monitored and corrected. (16, 17, 18) High levels of fluorides have been noted both in the blood and body organs. Hemodialysis has been reported to be effective therapy for cases of severe systemic fluoride intoxication. (19, 20, 21) Treatment for shock may also be required as for other severe injuries.

Other effects reported from fluoride exposure include coagulation defects and inhibition of a number of enzymes, including preglycolytic enzymes, phosphatases, and cholinesterase. The results of this enzyme inhibition include inhibition of cellular glucose phosphorylation and subsequent glycolysis, inhibition of respiration, and increased sensitivity of cholinergic mechanisms to acetyl cholinesterase. (22)

While hypocalcemia has been traditionally considered the major systemic effect of severe poisoning with HF, it is apparent that hypomagnesemia, hyperkalemia, the cardiodepressing and vasodilating effects of fluoride, and effects on pulmonary hemodynamics and systemic capacitance vessels, including an increase in pulmonary vascular resistance, all play a role in systemic toxicity. Although some of these effects have been described, the implications for therapeutic measures have not been well defined. (23, 24)

Significant amounts of fluoride ion may be absorbed by skin contact, inhalation, or by ingestion. If systemic absorption of fluoride occurs, hypocalcemia, hypomagnesemia, and hyperkalemia may also occur. These parameters need to be monitored and appropriate therapeutic measures instituted. The patient should be observed for clinical signs of hypocalcemia following any ingestion or inhalation exposure.

The following has been proposed as framework for risk of systemic toxicity (53):

- HF burns with a high risk to develop lethal electrolyte imbalances
- 1% BSA burn with anhydrous HF
- 5% BSA burn with >70% concentrated HF
- 7% BSA burn with 50–70% concentrated HF
- 10% BSA burn with 20–50% concentrated HF
- 20% BSA burn with <20% concentrated HF
- Prolonged exposure or long delay for treatment in minor HF burns
- Ingestion of HF at concentrations >5%
- Inhalation of HF at concentrations >5%

Note: BSA (body surface area).

Serum calcium determinations must be performed immediately and periodically to monitor and treat hypocalcemia. Severe lowering of serum calcium levels can occur within 1 to 2 hours, even with HF burns covering less than 2.5% of body surface area. (8) Electrolyte disturbances of calcium, magnesium, and potassium leading to asystole were reported in a worker who had a 3% body surface area exposure to 20% HF, despite prompt irrigation and use of topical calcium gluconate gel. (54) Continuous EKG monitoring to observe prolongation of the QT interval may be useful to detect early changes in serum calcium, although profound hypocalcemia following HF exposure has been reported in the absence of EKG changes or in the absence of other signs of tetany. In addition, EKG tracings may continue to be abnormal even after serum calcium, magnesium, and potassium have normalized. It is suggested that electrocardiographic monitoring should be continued beyond electrolytes normalization. (16)

The fall in serum calcium may occur precipitously following HF exposure. In 2 reported cases of exposure to anhydrous HF, the serum calcium fell to levels around 3 milliequivalents per liter (mEq/L) [normal = 8.8-10.3 mEq/L] within 1 to 3 hours of exposure. (8)

If necessary, aqueous calcium gluconate may be given intravenously. Calcium gluconate as a 10% solution must be given slowly since excess calcium can produce vagal bradycardia, ventricular arrhythmias, and ventricular fibrillation. The IV calcium gluconate should be repeated until serum calcium levels return to, and remain at, normal levels. In one fatal case, 280 mEq of calcium over 4 hours was not sufficient to correct the profound hypocalcemia. (8) Without additional measures such as hemodialysis, it may not be possible to correct extreme hypocalcemia.

Serum magnesium levels should also be monitored and magnesium loss should be replaced intravenously. Yamaura, et al. have reported a case of HF exposure in which prolonged QT interval was observed while ionized calcium levels were relatively high, but the magnesium level was low. (49) Serum potassium must also be carefully monitored. Significant elevations of serum potassium have been noted in cases of fluoride toxicity and in laboratory studies. Hyperkalemia has also been implicated as a causative factor in cardiovascular collapse, and should be treated appropriately. Several authors have reported clinically significant hypokalemia resulting from significant

HF exposures. This may be a result of hypomagnesemia, as magnesium plays a pivotal role in maintenance of intracellular potassium concentration by regulating potassium movement through myocardial cell membranes. The correction of hypomagnesemia will reduce potassium excretion to the urine and help correct hypokalemia.

Even with normalization of serum calcium and potassium, life threatening ventricle arrhythmia may occur, possibly due to a direct toxic effect of the fluoride ion on the myocardium. (36)

Additional Treatment Options

Hemodialysis with fluoride free water (and normal to low potassium and slightly higher calcium concentrations), in conjunction with other treatments mentioned, should be considered in all cases of serious burns and may need to be repeated if indicated. (19, 20, 21) Serum fluoride levels should be monitored. Normal plasma fluoride levels may differ because of various methodologies and analytical techniques. The decision to use dialysis should be based on the HF exposure (concentration, body surface area) and the clinical condition of the patient, including the serum levels of fluoride, calcium, and potassium. Continuous Renal Replacement Therapy (CRRT) has been utilized in a patient with systemic toxicity due to a significant (60%) total body surface area burn from HF and concomitant inhalation injury. CRRT is a mode of renal replacement therapy for hemodynamically unstable, fluid overloaded patients and patients with sepsis and septic shock in management of acute renal failure, especially in the intensive care unit setting. (58)

Primary excision or surgical removal of tissue has been recommended by some practitioners as a method of reducing systemic absorption of fluoride. (50) While this is potentially life-saving, it is a drastic measure. It is likely that renal dialysis could be used to effectively treat systemic toxicity and would not result in the disfigurement, disability, or morbidity which would result from primary excision.

Chronic Toxicity

Chronic toxicity from long term, high exposure to fluoride salts (e.g., SnF₂, NaF, Na₂FPO₃) has been reported to result in tooth mottling in children, bone fluorosis, and sometimes osteosclerosis in adults and children. Because of its irritant properties, repeated exposures to HF sufficient to pose a risk of chronic toxicity are unlikely.

Skeletal fluorosis is known to be associated with excessive exposure to fluoride compounds. Cases of skeletal fluorosis have been reported in populations exposed to naturally occurring drinking water containing greater than 10 ppm of fluoride ion and in individuals exposed to high levels of fluoride containing dusts. However, skeletal fluorosis has not been reported as a consequence of HF exposure.

Because of the use of fluoride to prevent dental caries, there is ongoing evaluation of fluorides for the potential to cause cancer. There is no evidence that fluoride is genotoxic except in some in vitro assays at cytotoxic concentrations. Epidemiological studies have not demonstrated an association between fluoride in drinking water and an increase in cancer. The International Agency for Research on Cancer (IARC) has not classified hydrogen fluoride as to its human carcinogenicity, and neither fluorides nor HF are listed by IARC, NTP, OSHA, ACGIH, NIOSH, the State of California, or other governmental agencies as causing cancer. (31, 32) In animal studies, fluoride salts have caused effects in off-spring only at high, maternally toxic levels. Some animal studies have shown effects on

male fertility, e.g. decreased sperm counts. Fluoride exposures should be kept below recommended levels to assure no adverse effects to the developing fetal skeletal system or teeth.

Monitoring of urine for fluorides is an accepted method of determining exposure. (34) Urine fluoride levels above 2 mg/liter at the beginning of a work shift, or above 3 mg/liter at the end of a work shift, may indicate excessive absorption of fluoride. As fluorides are present in drinking water and foods, there may be significant background levels in persons without occupational exposure. Thus, urine fluoride determination is not specific for HF. (26)

A case of toxic myocarditis has been reported, occurring about 4 months after an intentional HF ingestion. While it was impossible to prove beyond doubt that the HF systemic toxicity was the cause, the timeline and absence of other evident causes of myocarditis led the authors to conclude that the HF exposure was the most plausible and probable explanation. (52)

Additional and Unproven Therapies

Both Williams, et al. (44) and Cox, et al. (45) have investigated the use of intravenous magnesium sulfate to treat localized HF skin burns in animal models. Cox showed that intravenous magnesium sulfate resulted in shallower wound depth and faster wound healing than HF skin burns treated only with 5 minutes of water washing. The rabbits in this study were exposed to 49% HF for 5 minutes before the water washing, and magnesium sulfate administration was not initiated until 30 minutes after acid application. In the Williams study, using rats, the exposure duration was 1 minute (52% HF) followed by 5 minutes of water irrigation. A significant number of control rats (37%) died within 24 hours, presumably due to adverse effects from HF, although no electrolyte values are presented to support this. Rats treated with high dose intravenous magnesium sulfate had fewer high grade (penetration of lower dermis, subcutaneous tissue, or skeletal muscle) burns than controls or those treated with subcutaneous injected 10% calcium gluconate.

Seyb, et al. (47) performed an experiment in rats using a topically applied solution of 50% aqueous dimethyl sulfoxide (DMSO) containing calcium gluconate (20% wt./vol.). This treatment gave results comparable to injecting 10% calcium gluconate or 10% magnesium sulfate, and was superior to calcium gluconate gel in treating experimental HF burns. DMSO is not approved for human use in the United States, so this treatment has not been pursued.

A product developed in France, "Hexafluorine" (46), has been marketed in Europe and the United States for use as a decontamination solution for HF skin and eye exposure. Honeywell has conducted animal studies on this product with equivocal test results for skin exposures. Given the equivocal results and the cost of the product (versus decontamination with water), we feel that there is insufficient evidence to recommend its use. (48)

Researchers in Turkey investigated the use of Epidermal Growth Factors (EGF) to promote healing of HF burns, noting that EGF has shown efficacy in wound healing and treatment of thermal burns. While their study did show improved healing of HF burns with EGF, it does not seem generalizable to industrial settings. Of note, this study did not involve any efforts at skin decontamination (water washing) prior to proceeding to the experimental treatments. The authors also noted the expense and limited availability of EGF, at least at the time of their study in 2014. (33)

Recommended Medical Treatment for Hydrofluoric Acid (HF) Exposure

Quick Reference

NOTE: In addition to the usual medical history, the physician should obtain the following information:

- Concentration of HF
- Date and time of exposure
- Duration of exposure
- How exposure occurred
- Body parts exposed/affected
- First aid measures instituted (what, when, how long)

Injuries due to dilute HF solutions or low concentrations of vapors may result in delays in clinical presentation up to 24–hours following exposure.

SKIN BURNS		EYE EXPOSURE		INHALATION		INGESTION
FIRST AID						
<p>CONCENTRATED HF</p> <p>Water Wash THEN... Iced Benzalkonium Chloride 0.13% Soaks OR... Calcium Gluconate 2.5% Gel</p>	<p>DILUTE HF</p> <p>Water Wash THEN... Iced Benzalkonium Chloride 0.13% Soaks OR... Calcium Gluconate 2.5% Gel</p>	<p>ALL HF</p> <p>Water Wash OR... Saline Wash</p>	<p>CONCENTRATED HF</p> <p>Oxygen AND... 2.5% Calcium Gluconate by Nebulizer Consider Starting an IV with 10% Calcium Gluconate</p>	<p>(Mild Exposures) DILUTE HF</p> <p>Oxygen THEN... Consider 2.5% Calcium Gluconate by Nebulizer</p>	<p>ALL HF</p> <p>DO NOT INDUCE VOMITING Consider Starting an IV with 10% Calcium Gluconate</p>	
MEDICAL TREATMENT						
<p>CONCENTRATED HF</p> <p>Debride (if necessary) THEN... Continue Soaks OR... Calcium Gluconate 2.5% - 5% Injection AND... Observe for/Treat Systemic Effects (especially if > 25 sq. in.)</p>	<p>DILUTE HF</p> <p>Debride (if necessary) THEN... Continue Soaks OR... Calcium Gluconate 2.5% Gel OR... Calcium Gluconate 2.5% - 5% Injection Systemic Effects Unlikely</p>	<p>ALL HF</p> <p>Topical Tetracaine Hydrochloride THEN... 1% Calcium Gluconate Irrigation AND... Consult Ophthalmologist</p>	<p>CONCENTRATED HF</p> <p>Continue Calcium Gluconate by Nebulizer Observe and Treat for Respiratory Distress, Bronchoconstriction, Pulmonary Edema, Systemic Effects (Inhaled Steroids and/or Bronchodilators as Needed)</p>	<p>DILUTE HF</p> <p>Continue Calcium Gluconate by Nebulizer Observe Serious Effects Unlikely Inhalation of HF Vapors from Diluted Acid is Uncommon</p>	<p>ALL HF</p> <p>Lavage with Calcium Chloride or Calcium Gluconate AND... Treat Systemic Effects</p>	

This Quick Reference Chart is also available as a laminated wall poster
To order call 800-622-5002

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