

Non-cytotoxic Wound Bed Preparation:

Vashe Hypochlorous Acid
Wound Cleansing Solution

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Brief history of early wound cleansers

Different agents for cleansing wounds have been reported since antiquity. Originally it was necessary to remove foreign bodies and debris from wounds. After the discovery of bacteria and the development of the germ theory of disease in the 1860s, the removal of pathogens also became desirable. The problem with early agents for wound cleansing, which still remains today, is that many agents are injurious to the wound tissue and actually impede wound healing.

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Once it was understood that wounds must be cleansed of bacteria as well as debris, wound cleansers often had additional antimicrobial properties. This was especially important in traumatic wounds during times of armed conflict. Overwhelming fatal wound sepsis was a major problem following combat wounds during World War I. To attempt to control the problem a research team was organized consisting of Henry Dakin, an English chemist and Alexis Carrel, a French Army surgeon. Dakin wanted a chemical that was as effective as carbolic acid at killing bacteria, but less cytotoxic to the wound tissue. Dakin found that sodium hypochlorite at a concentration of 0.5% fulfilled his requirement¹. He had Carrel continually flood the wound site with the solution through rubber catheters inserted into the wound dressings. This became known as Dakin's solution. The problem is that it has a high pH and when neutralized became ineffective. It was also extremely unstable which was the reason repeated irrigations were needed. Half strength and quarter strength Dakin's solution (0.25% and 0.125%) became more popular in an attempt to decrease the injurious effects to normal tissue.

In 1991, research done in Robson's laboratories at the University of Texas Medical Branch demonstrated that a much more dilute solution of sodium hypochlorite (0.025%) could satisfactorily kill bacteria in wound tissue and not injure normal cells². Most clinicians who say that they use and prefer Dakin's Solution today are actually using a more dilute solution of sodium hypochlorite than Dakin originally described as Dakin's Solution. The problem is that more recent work has demonstrated that any amount of sodium

hypochlorite is cytotoxic. Hildago, et al. reported that even dilutions as small as 0.0005% depleted cellular ATP levels when exposed to cultured fibroblasts³. Dilute Dakin's solution still has a pH of 10-11 and is very unstable, becoming salt and water within minutes after application.

Hypochlorous acid as a wound cleanser

Hypochlorous acid (HOCl) is a more stable compound than sodium hypochlorite and still has the antibacterial effects previously demonstrated for sodium hypochlorite. Hypochlorous acid is the final product of the oxidative burst pathway inside the human white blood cell that kills invading pathogens as part of the natural human immune inflammatory response (Fig.1).

The Human Inflammatory Response

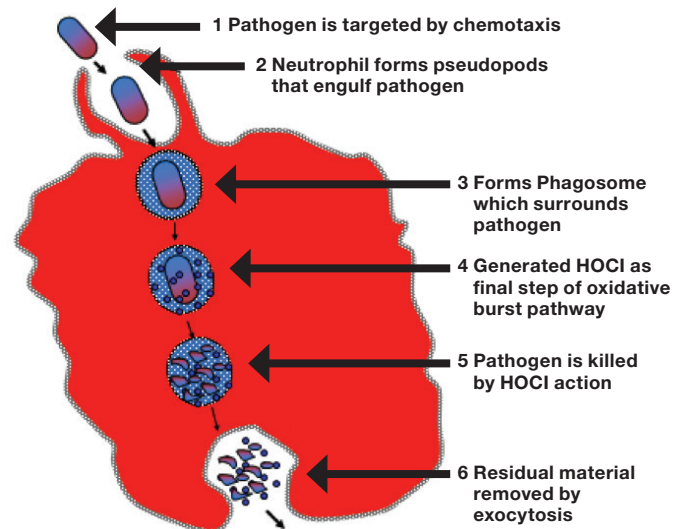


Figure 1: Demonstration of how the leukocyte generates HOCl to kill invading pathogens

The early question was did the known *in vitro* antibacterial effects of hypochlorous acid transfer to tissue levels of bacteria in the *in vivo* wound situation. Robson, et al. demonstrated that hypochlorous acid decreased the tissue level of bacteria in chronic granulating wounds while simultaneously allowing wound healing to proceed without any cytotoxicity⁴.

Vashe wound cleansing solution is a commercially available product of hypochlorous acid that has long-term stability as opposed to sodium hypochlorite. It is a safe and effective non-antibiotic alternative wound treatment for acute and chronic wounds that is demonstrated to be extremely gentle and hypoallergenic. It has a pH that mimics the pH of 5.1-5.5

Table I: *In vitro* time kill assay test results measuring pathogenic colony log reductions in Vashe wound cleansing solution

Pathogenic Bacteria	Log ¹⁰ Control	Vashe Log Reduction	Time Kill 15 Second Contact (% Kill)
Methicillin Resistant Staphylococcus aureus (MRSA)	6.20	≥5.20	≥99.999%
Vancomycin Resistant Enterococcus faecalis (VRE)	6.20	≥5.20	≥99.999%
Escherichia coli	6.28	≥5.28	≥99.999%
Acinetobacter baumannii	6.15	≥5.15	≥99.999%
Bacteroides fragilis	6.66	≥5.66	≥99.999%
Candida albicans	6.63	≥5.63	≥99.999%
Enterobacter aerogenes	6.43	≥5.43	≥99.999%
Enterococcus faecium	6.08	≥5.08	≥99.999%
Haemophilus influenzae	6.59	≥5.59	≥99.999%
Klebsiella oxytoca	6.18	≥5.18	≥99.999%
Micrococcus luteus	6.04	≥5.04	≥99.999%
Proteus mirabilis	6.40	≥5.40	≥99.999%
Pseudomonas aeruginosa	6.11	≥5.11	≥99.999%
Serratia marcescens	6.08	≥5.08	≥99.999%
Staphylococcus epidermidis	6.69	≥5.69	≥99.999%
Staphylococcus haemolyticus	6.57	≥5.57	≥99.999%
Staphylococcus hominis	6.68	≥5.68	≥99.999%
Staphylococcus saprophyticus	6.68	≥5.68	≥99.999%
Staphylococcus pyogenes	6.53	≥5.53	≥99.999%
Klebsiella pneumoniae	6.70	≥5.70	≥99.999%
Micrococcus luteus	6.04	≥5.04	≥99.999%
Proteus mirabilis	6.40	≥5.4	≥99.999%

of human skin. Vashe has been rigorously safety tested and is non-cytotoxic, non-irritating, non-sensitizing, and has no oral toxicity or clinical contraindications for use. As opposed to agents with lower or higher pH or that contain sodium hypochlorite, it can be used around the eyes, ears, mouth, genitalia, and in children without concern. Vashe is intended for use in cleansing, irrigating, moistening, debridement and removal of foreign material including microorganisms from acute and chronic dermal lesions, such as stage I-IV pressure ulcers, venous insufficiency (stasis) ulcers, diabetic ulcers, post-surgical wounds, first- and second-degree burns, abrasions, and minor irritations of the skin.

The graph below demonstrates the hypochlorous acid curve showing the distribution of chlorine species as a function of pH (Fig. 2)⁵. One can see that the highest concentration of HOCl is at pH approximately 5.5. That is the pH of Vashe and is different from other products.

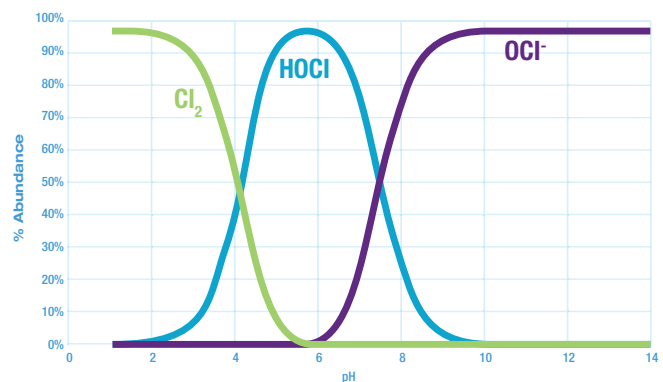


Figure 2: Distribution of chlorine species as a function of pH. The highest concentration of hypochlorous acid is approximately pH 5.5.

Vashe Wound Cleanser and wound bed preparation

According to Schultz, et al., “Wound bed preparation is the management of a wound in order to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures”⁶. Vashe serves several roles in wound bed preparation. Its action is derived from its *in vitro* antibacterial and antifungal properties and its use as a soak and gentle debrider when the soaked tissue is wiped away from the wound⁷. This effectively removes debris, slough, and bacteria from the wound. The antibacterial action is rapid as seen in Table I (left).

Vashe can be used with other debriding techniques such as enzymatic debriding agents. In a study by Miller and Mouhlas, significant cost savings were achieved by using Vashe on a wound prior to application of Santyl enzymatic debriding agent⁸. In addition to removing foreign bodies, and bacteria, Vashe has been shown to disrupt biofilm in the wound, an impediment to optimal wound bed preparation^{9,10}. Using Vashe in combination with a hydroconductive dressing that draws off exudate, debris, bacteria, and deleterious cytokines has been demonstrated by Couch and Crossen to be extremely effective for optimal wound bed preparation in the most difficult of wounds¹¹.

Vashe uses in the treatment of thermal injuries

A non-cytotoxic agent to help control bacterial proliferation in burn wounds, skin-grafted wounds, and on the skin of patients in a burn center has been a goal for many years. Agents such as silver nitrate, Betadine, and 5% Sulfamylon solution have had periods of popularity. All have a degree of cytotoxicity. Foster, et al. recently compared Vashe directly to Sulfamylon solution and found it to be equally effective at protecting recent skin graft sites, preventing the necessity of re-grafting, and at significantly less cost¹². The same group has reported that daily bed baths with Vashe hypochlorous acid combined with Bactroban ointment intra-nasal application worked as a universal decontamination protocol to significantly decrease infection rates in a burn center¹³.

Cleansing and moistening micro-autograft fragments

Based on the experience of Vashe on STSGs in the burn arena, it has been used successfully to cleanse and moisten the fragments of micro-autografts that occur after mincing of skin grafts. The Xpansion micro-autograft device produces fragments of skin (dermis and epidermis) 0.8mm x 0.8mm in size¹⁴. When these small fragments are grafted onto a wound surface they are friable and must be kept from dessicat-

ing and be protected from infection. Soaking the graft fragments with Vashe at each dressing change provides protection to them as they coalesce into a solid sheet of skin to complete closure of the wound (Fig.3)

Figure 3: Small fragments of minced skin are demonstrated on the left and coalescing of the fragments is demonstrated on day 8 on the right.



Safety for pediatric use

Because of the non-cytotoxicity of Vashe and its pH equal to normal skin, it has been proven to be safe and useful in the pediatric age distribution. Many wound cleansers are contraindicated around the eyes, ears, nose, mouth, or genitalia. This makes them not useful in small children. Vashe does not have those limitations. Also since Vashe's pH is neither basic (as those cleansers with high percentages of sodium hypochlorite) nor acidic (as those cleansers with a pH of 4 or less), Vashe does not sting or burn upon application to a wound. This is extremely important in the pediatric population. It has been reported that there is a cool soothing feeling as Vashe is applied. Another advantage to Vashe is its clean, fresh, sanitary smell that is important in the younger child whose wound may be contaminated with urine or bowel contents. The use of a hydroconductive dressing slightly moistened with Vashe around tubes such as G-buttons, tracheostomy, gastro-jejunostomy, and chest tubes greatly decreases the instances of skin breakdown caused by moisture.

Comparison of Vashe with other hypochlorous acid products

There are other products that contain hypochlorous acid. However, none are in the pH range that Vashe wound cleansing solution occupies. As seen in Figure 2, the pH range of Vashe dictates that it has the purest percentage of hypochlorous acid. Other products are more in the acidic range and will have chlorine species or in the basic range and have a percentage of sodium hypochlorite in their formulation. Also stability has been a problem with some hypochlorous acid products.

Vashe Wound Cleanser comes in various sizes and dispensers. Its spiked dispenser which comes in up to 1 liter size is convenient for use with negative pressure wound therapy (NPWT). It can also be conveniently used with pressurized debridement systems such as the Versajet Hydrosurgery System (Smith & Nephew, Ft. Worth, TX).

Conclusion

As discussed, many wound cleansers historically have had characteristics that limit their desirability for use in wound care. Cytotoxicity to the cells necessary for optimal healing must be minimized. Stability of compounds affect the time a cleanser can be effective on a wound. Extremes of pH can make the cleanser range from uncomfortable to painful. Vashe has addressed each of these drawbacks and serves as an ideal wound cleanser. It is intended for cleaning, irrigating, moistening, debriding and removal of foreign material including microorganisms from acute and chronic dermal lesions, such as stage I-IV pressure ulcers, stasis ulcers, diabetic ulcers, post-surgical wounds, first and second degree burns, abrasions and minor irritations of the skin in addition to moistening and lubricating absorbent wound dressings. It is safe, non-cytotoxic, and contains the highest concentration of pure hypochlorous acid. It is the most natural of wound cleansers since hypochlorous acid is nature's way of dealing with pathogens in the human inflammatory system.

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