Polyhexamethylene Biguanide (PHMB): An Addendum to Current Topical Antimicrobials

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Abstract: Antimicrobials are routinely used in the treatment of chronic and problematic wounds. Despite the on-going increase in numbers and types of products, well-designed clinical trials that support their efficacy are limited. Antimicrobial products are applied with understanding of their mechanisms of action and role in wound repair. This manuscript reviews the major categories of products on the market, providing the clinician with information on the different types of products and their purported effect on wounds. A new product containing polyhexamethylene biguanide is described in greater detail with relevant case presentations and cost data. This new product does not appear to have any known cytotoxicity in the dressing configuration and may be applied to a wide range of wounds.

Chronic wounds are often complex, difficult to heal, and may persist for months or years due to underlying disease processes or complications within the healing process.

Treating chronic wounds requires a multifaceted approach in order to address the underlying pathophysiology while promoting healing of the wound. Before a wound can close, the wound bed status needs to be addressed to assist in creating an environment conducive to tissue repair. This may require 1) removal of nonviable tissue, 2) maintenance of a moisture balance, 3) resolution of any bacterial imbalance, and 4) removal of impediments to healing at the epidermal margins. While each of these require attention, concern with bacterial imbalance in the wound bed has lead to the development and commercialization of a variety of antimicrobial products and therapies.

Bacterial imbalance. When wounds fail to heal or are classified as recalcitrant, one of the factors delaying healing that merits consideration is bacterial load in the wound bed and its effect on the tissue repair process. All chronic wounds are believed to have some level of bacterial bioburden. Depending on the number of organisms, the level of bacteria in the wound bed may be classified as contaminated, colonized, critically colonized, or infected. Contamination (the presence of organisms in a wound) and colonization (the proliferation of those organisms) are not routinely treated with oral or systemic antibiotics. Once a wound becomes critically colonized...
(a level of colonization affecting skin cell proliferation and tissue repair), it may progress to a "classic" infection, which may include erythema, cellulitis, edema, and increases in odor, pain, exudate, white blood cell count, and increased body temperature."

Delayed closure may suggest the formation of an extracellular polysaccharide matrix film or layer (sometimes called a glycocalyx) that shields the bacteria from attack while maintaining the moist environment in which they thrive. These colonies of bacteria are called biofilms and are produced by *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *E coli*, among others. The biofilm makes it difficult to eliminate pathogens by requiring as much as 50-1000 times the minimal inhibitory concentration (MIC) of an antibiotic or antiseptic.

Clinicians may attempt to address the bacterial imbalance by combining treatment modalities. To address infection in the wound bed systemic or oral antibiotics should be considered the first line of therapy, especially in complicated skin infections with clinical signs of cellulitis, leukocytosis, or fever. In conjunction with systemic therapy, there are a number of antimicrobial dressings currently on the market indicated for use on infected wounds. Antimicrobial dressings are comprised of a variety of different base materials to which antimicrobial agents are added. The major purported benefits of these dressings are that they may reduce the presence of pathogens and decrease the risk of infection while creating a wound bed that will readily support the normal sequence of wound repair.

**Antimicrobial Agents in Wound Care**

The use of topical antimicrobial agents for wound care gained a wide acceptance in the 1960s once it was discovered that treating burns with silver nitrate decreased the number of deaths that were a result of sepsis from 60% to 28%. Antiseptic silver sulfadiazine (SSD) was associated with additional decreases in infection, eventually making a place for itself in general wound care. Silver sulfadiazine demonstrated improved outcomes and decreased infection rates. Antiseptics differ from antibiotics in that they have broad-spectrum activity and can be effective against many types of organisms including aerobic and anaerobic bacteria, yeasts, fungi, and molds. While there is concern that certain antiseptics may delay healing as a result of cytotoxicity to viable cells, current wound treatment products must demonstrate biocompatibility and effectiveness to reduce bioburden prior to approval for an antimicrobial indication. Antiseptics used in current wound dressings include silver, iodine, and polyhexamethylene biguanide (PHMB).

Bacterial resistance to antibiotics is extensively documented in medical literature. Resistance to antiseptics, however, has only been studied more recently. Tambe and associates compared the ability of *Staphylococcus epidermidis* to develop resistance to various antibiotics and antiseptics after 20 *S epidermidis* cell culture passages. Results suggested that the bacteria developed resistance to the antibiotics minocycline and rifampicin, however no evidence of resistance was observed with chlorhexidine, silver sulfadiazine, and PHMB. Minor resistance was seen with Triclosan.

**Silver.** Silver has been used as an antimicrobial agent for thousands of years. Silver ions exert varying antimicrobial effects depending on their binding site. When binding occurs at the bacterial cell wall, ruptures can occur. When bound to proteins involved in respiration and nutrition of the organism, silver blocks these processes and the bacterium dies. When binding to DNA, silver can affect the replication and division of the organism.

The activity of silver lies in its ionic form. Elemental silver and silver salts demonstrate substantially less effectiveness against microbes. Previously, silver salt solutions, such as silver nitrate, were used to bathe the wound. These required large amounts of silver to achieve the desired effect. Silver sulfadiazine (SSD) creams enable much lower amounts of silver to be effective and act by discharging silver ions when in contact with wound exudate. Fox and Modak describe the mechanism by which sulfadiazine binds the silver and releases it into the wound over time at concentrations that are bactericidal. The silver ions, however, may be rapidly neutralized and require daily or more frequent application of SSD. The amount of silver released into the wound is not always clearly defined and can be a concern for toxicity in healthy tissue. More recent technological advancements have lead to methods of delivering silver to wounds over longer periods of time and at more predictable levels.

There are a variety of silver containing wound dressings available. Delivery systems vary and include polyethylene mesh (Acticoat, Smith and Nephew, Largo, Fla), polyurethane foam (Contreet Ag, Coloplast, Holtedahm, Denmark), activated carbon (Actisorb 220, Johnson and Johnson, Somerville, NJ), hydrocolloid (Contreet-H,
Coloplast), alginate with polymers (Arglaes®, Medline, Mundelein, IL), alginate with carboxymethylcellulose (CMC) (SilverCel®, Johnson and Johnson), sodium carboxymethylcellulose (Aquacel Ag®, Convatec, Skillman, NJ), nylon (Silverlon®, Argentum Medical, Asheville, NC), and polyacrylate (Silvasorb®, Medline).

Thomas and McCubbin 20, 21 compared the in-vitro effectiveness of various silver containing products using 3 methods—zone of inhibition, challenge testing, and microbial transmission testing to demonstrate differences in the various dressings. Results against Staphylococcus aureus, Escherichia coli, and Candida albicans suggested that polyethylene mesh had the most rapid antimicrobial effect due to its rapid release of silver. Hydrocolloid was similar but had a slower onset. Activated carbon had little activity on the surface, but organisms that were absorbed into the dressing were inactivated by the silver. 20

Jones et al 22 found that some of the differences observed between polyethylene mesh and sodium CMC may be related to the conformability of the dressing. A greater wound bed conformability and contact correlated with an increased antimicrobial effect.

As described in the literature, 6, 20, 21 there are a wide variety of silver dressings available and various in-vitro responses from these dressings. Well-designed and adequately powered randomized trials to support the clinical benefits of silver are lacking, are warranted, and requested by the medical community.

Iodine. Iodine is used as a disinfectant for cleaning surfaces and storage containers, in skin soaps, medicines, and for purifying water. It has been purported to have negative effects on wound healing, however some hypothesize that it may be due to the carrier. 23 Carriers for iodine have demonstrated less toxicity by releasing iodine at a slower rate, yet show the same lethality as iodine in other forms. Cadexomer iodine (Iodoflex® and Iodosorb®, marketed in the United States by Smith & Nephew, Largo, Fla) is a 3-dimensional starch lattice formed into spherical microspheres that trap iodine in the lattice. As fluid is absorbed, the pore size of the lattice increases, releasing iodine. Mertz et al 24 tested cadexomer iodine against MRSA in an in-vitro porcine model. They demonstrated significant reduction of the bacteria over a period of 72 hours.

Hansson and colleagues 25 compared cadexomer iodine to hydrocolloid and paraffin gauze dressings in a randomized, open, controlled, multicenter clinical trial. In the 153-patient study they demonstrated 62% reduction in ulcer size with the cadexomer iodine as compared to 41% and 24% for the hydrocolloid and paraffin gauze, respectively. Patients were treated until the wound was dry or until 12 weeks, whichever came first. The investigators also compared the cost of the dressing over the 12-week period and demonstrated cost savings with the cadexomer iodine. 24

Studies suggest that iodine’s mechanism of action is through destabilization of the bacterial cell wall and disruption of the membrane that results in leakage of the intracellular components. 25

Polyhexamethylene biguanide (PHMB). Polyhexamethylene biguanide (PHMB), also known as polyhexanide and polyaminopropyl biguanide, is a commonly used antiseptic. It is used in a variety of products including wound care dressings, contact lens cleaning solutions, perioperative cleansing products, and swimming pool cleaners.

Wound care products containing PHMB include Kerlix AMD™, Excilon AMD™, and Telfa AMD™ (all from Tyco HealthCare Group, Mansfield, Mass) and XCell® Cellulose Wound Dressing Antimicrobial (Xylos Corp, Langhorne, Pa).

A review of the literature demonstrates in-vitro and in-vitro safety and effectiveness of PHMB for a number of applications. For wound dressings, Wright and colleagues 26 compared the effectiveness of a silver dressing to a dry gauze dressing containing PHMB (Kerlix AMD). Results demonstrated reduction in bioburden with both dressings when tested in an in-vitro bactericidal assay. Using a Kirby-Bauer zone of inhibition study, the gauze was not as effective. This was believed to be due to a tight bond between the dressing and PHMB, which was not released and therefore did not result in killing beyond the edge of the dressing. 26 Alternatively, Motta and associates 25 demonstrated a good response using Kerlix AMD compared to gauze without PHMB in wounds where packing the dressing into the wound was required. Results suggested that the PHMB in the gauze resulted in a decrease in the number of organisms present in the wound.

The majority of literature describes effectiveness of PHMB on various microorganisms associated with contact lens disinfecting solutions. Antimicrobial effectiveness has been demonstrated on Acanthamoeba polyphaga, A. castellanii, and A. baetelli. 25, 27, 28 Additional effectiveness was demonstrated for PHMB use in water treatment. Barker and colleagues 29 tested the effect of PHMB on Legionella pneumophila. This bacterium caus-
es Legionnaire’s disease and can be found in water systems, air conditioning machinery, and cooling towers.

Gilbert and colleagues\(^{30,31}\) have performed numerous studies on bacteria, especially those that form biofilms, such as Klebsiella pneumoniae. In studying biofilms produced from E. coli and S. epidermidis, they noted that those compounds with higher activity against planktonic bacteria, including PHMB, were also the most effective agents against sessile bacteria found within biofilms. They suggested that the differences in effects of concentration of PHMB on planktonic versus sessile bacteria was due to either the mechanism of action or the number or disposition of cationic binding sites.\(^{30-32}\) Kramer et al\(^{33}\) have studied the effects of various antiseptics including PHMB on fibroblast proliferation and cytotoxicity. They noted that while octenidine-based products retarded wound healing, PHMB promoted contraction and aided wound closure significantly more than octenidine and placebo.

The mechanism of action of PHMB has been described in a number of articles. Broxton et al\(^{34,35}\) demonstrated that maximal activity of the PHMB occurs at between pH 5-6 and that initially the biocide interacts with the surface of the bacteria and then is transferred to the cytoplasm and cytoplasmic membrane. Ikeda and colleagues\(^{36}\) showed that the cationic PHMB had little effect on neutral phospholipids in the bacterial membrane—its effect was mainly on the acidic negatively charged species where it induced aggregation leading to increased fluidity and permeability. This results in the release of lipopolysaccharides from the outer membrane, potassium ion efflux, and eventual organism death.\(^{37}\)

Clinically, PHMB has been used as a perioperative cleansing agent,\(^{38}\) in mouth wash,\(^{39}\) in ophthalmology,\(^{38,40}\) and as a topical wash.\(^{16}\) Hohaus et al\(^{19}\) reported on the oral use of PHMB (Lavasept 1%, Fresenius-Kabi, Bad Homburg, Germany). A combination of oral terbinafine and topical ciclopirox and PHMB were used to successfully treat a deep fungal infection (Trichophyton mentagrophytes) of the throat. Petrou-Binder\(^{14}\) describes the germicidal effects of PHMB (Lavasept 0.02%) as eye drops prior to cataract surgery. It was well tolerated with low tissue response and minimal patient discomfort.

While there is no peer-reviewed clinical literature of PHMB used on wounds, industry literature describes the effectiveness of AMD Gauze (Kerlix) as a bacterial barrier against Staphylococcus epidermidis (penicillin resistant) on volunteers. Results suggest that clinically, this dressing was an effective barrier against bacterial colonization.\(^{42}\) The studies suggested that AMD gauze did not elicit any skin reactions.\(^{42}\)

**Biosynthesized Cellulose Wound Dressing—Antimicrobial (BWD-PHMB)**

Biosynthesized cellulose wound dressings (XCell Cellulose Wound Dressing and XCell Cellulose Wound Dressing Antimicrobial) were developed to maintain a moist wound environment without causing maceration, reduce pain, and enable autolytic debridement. This is possible because the dressings effectively absorb exudate and hydrate dry areas of a wound different from other dressings that have only a single function.\(^{43}\)

A 49-patient, multicenter, controlled, randomized clinical study was conducted to demonstrate effectiveness of BWD compared to standard of care on venous leg ulcers. Significantly more autolytic debridement, significantly reduced pain, and cleaner wound margins were demonstrated after the 12-week study period.\(^{44,45}\) Improved rate of wound closure, as demonstrated by increased epithelialization and granulation tissue, was also noted.\(^{43}\)

The antimicrobial version of BWD (BWD-PHMB) contains cellulose, water, and 0.3% polyhexamethylene biguanide (PHMB). BWD-PHMB is indicated for use on partial- and full-thickness wounds. It is designed to cover a wound or burn, absorb areas of wound exudate, and provide a moist wound environment that supports autolytic debridement of nonviable tissue. The dressing may be used on moderately exuding, nonexuding, and dry wounds. It also protects against abrasion, desiccation, and external contamination. The moist environment has a cooling effect that has demonstrated a significant reduction of pain.\(^{44}\)

**Preclinical efficacy testing.** BWD-PHMB demonstrates it effectiveness against a variety of organisms. Following a modified American Association of Textile Chemists and Colorists (AATCC) Method 100, samples were incubated with approximately 106 CFU/mL of the various challenge organisms. After 24 hours, a second count was made to determine the reduction in the number of organisms present. Results indicated 99.9% reduction of MRSA, Escherichia coli, Enterococcus faecalis, Bacillus subtilis, and Candida albicans within the 24-hour period.

**Release of PHMB from BWD-PHMB.** A study was performed to demonstrate the release of PHMB from BWD-PHMB. Five sterile 3.5-in x 3.5-in samples were used. One quarter of the dressing was used to determine the initial PHMB concentration in each dressing.
using UV-Vis (Ultraviolet-Visible) Spectroscopy (Genesys™ 10 UV, Thermo Spectronic, Rochester, NY) at a wavelength of 254 nm. The remainder of the sample was weighed and placed into 20 times its weight in filtered water. At various times, including 0.5, 1, 2, 3, 4, 5, 6, and 24 hr, the solution was assayed for PHMB concentration. At the 24-h time the dressing was removed from the tray, weighed, and an extract was taken and assayed for PHMB concentration.

Figure 1 illustrates the concentration of PHMB over time. Equilibrium was reached after about 3 hours with the concentration (in ppm) in the dressing equaling the concentration in the solution. This demonstrates that the PHMB is not bound to the cellulose and therefore can be released into surrounding fluid along a concentration gradient.

**Clinical case series.** BWD-PHMB was evaluated in an open enrollment, noncontrolled clinical trial. Standard procedures for wound care were followed and samples of wound fluid were tested for type and level of microbial colonization at initial administration and 1–7 days after BWD-PHMB placement.

**Materials and Methods**

BWD-PHMB pads (XCell Cellulose Wound Dressing-Antimicrobial) measuring 3.5-in x 3.5-in were provided to 2 clinical sites and used as the primary dressing. Secondary dressings, including compression wraps (where indicated), were the standard of care for the facilities. Patients were chosen on an “as needed” basis and neither randomized nor controlled.

The 2 sites evaluated a total of 12 patients with 26 wounds of various etiologies including venous stasis ulcers (12), diabetic (4), traumatic (8), vasculitic (1), and necrobiotic diabetic lipoidica (1). Eleven of the 12 patients were unresponsive to a silver impregnated or an iodine containing dressing in the 3–4 weeks prior to use of the BWD-PHMB dressing. In these cases the wound had either increased in size or failed to progress. One patient was treated directly with BWD-PHMB.

Swabs of the wound were taken to determine if bacterial colonization was the reason for the lack of response to previous dressings. Organisms were identified in the wounds of 8 patients prior to and after BWD-PHMB application. Systemic antibiotics were not given in
conjunction with the use of BWD-PHMB to ensure bacterial reductions were solely due to the PHMB.

The organisms identified included methicillin-resistant Staphylococcus aureus (MRSA), Staphylococcus aureus, Pseudomonas aeruginosa, Proteus mirabilis, Diphtheroid gram-positive rods, beta hemolytic Streptococcus B, Enterobacter aerogenes, mixed skin flora, and Enterococcus sp. The most common was Staphylococcus (including MRSA) and Pseudomonas. The semi-quantitative scores ranged from 0 to 4+ (0 represents no bacterial growth and 4+ represents the largest amount of bacterial growth on the culture). The various bacteria found in the wounds of all 8 patients and the relative abundance prior to and after application of the BWD-PHMB dressing are shown in Table 1.

### Table 1. Bacteria found on wounds of patients that had wound swabs.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Organism</th>
<th>Pre-PHMB</th>
<th>Post-PHMB</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P. mirabilis</td>
<td>3+</td>
<td>2+</td>
</tr>
<tr>
<td></td>
<td>S. aureus</td>
<td>2+</td>
<td>2+</td>
</tr>
<tr>
<td></td>
<td>Diphtheroid gram+ rods</td>
<td>2+</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>S. aureus</td>
<td>3+</td>
<td>1+</td>
</tr>
<tr>
<td></td>
<td>P. aeruginosa</td>
<td>4+</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Streptococcus</td>
<td>3+</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>None</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>None</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>S. aureus</td>
<td>1+</td>
<td>LTF*</td>
</tr>
<tr>
<td></td>
<td>P. aeruginosa</td>
<td>4+</td>
<td>Not done</td>
</tr>
<tr>
<td></td>
<td>Diphtheroid gram+ rods</td>
<td>2+</td>
<td>Not done</td>
</tr>
<tr>
<td>7</td>
<td>P. aeruginosa</td>
<td>2+</td>
<td>1+</td>
</tr>
<tr>
<td></td>
<td>E. aerogenes</td>
<td>2+</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Mixed skin flora</td>
<td>1+</td>
<td>1+</td>
</tr>
<tr>
<td>8</td>
<td>MRSA</td>
<td>1+</td>
<td>1+</td>
</tr>
<tr>
<td></td>
<td>Enterococcus sp</td>
<td>0</td>
<td>1+</td>
</tr>
</tbody>
</table>

*LT = patient lost to follow-up

### Results

Four patients (5 wounds) from 1 site were used strictly for the economic analysis below. Of the remaining 8, 1 patient (3 wounds) was lost to follow-up after 1 week of BWD-PHMB treatment. The remaining patients had BWD-PHMB applied over periods of 1 to 7 weeks. Results of the 8 patients demonstrated a decrease in wound size on average from 6.79 cm² to 4.57 cm² (42% reduction) in an average of 25 days (Table 2). Two of the wounds completely healed during the study, 13 improved, and 2 showed a slight increase in size.

### Case Reports

**Case 1.** A 58-year-old woman presented with a full-thickness draining wound over the dorsal foot secondary to an incision (Figure 2). The patient's wound extended to the level of tendon and was recalcitrant to topical gels, ointments, foam dressings, silver dressings, and moist saline gauze. Past medical history was significant for Hodgkin's disease, heart valve replacement, pacemaker, hemolytic anemia, and chemo and radiation therapy for breast cancer, which was on-
going at the time of presentation. After 3 weeks of treatment with a papain-urea ointment (Panafil®, Healthpoint, Fort Worth, Tex), the majority of fibrotic tissue was removed although the wound did not decrease in size. The patient was then placed exclusively on BWD-PHMB for approximately 4 weeks with the dressing being changed once a week. The wound rapidly improved and progressed to complete closure during this time period.

**Case 2.** A 78-year-old woman presented with a large wound secondary to a hematoma occurring after trauma (Figure 3). The patient was not on anticoagulants and had a medical history significant for hypertension. The wound had been present for 1 week prior to presentation. Following extensive debridement, the patient was started exclusively on BWD-PHMB dressing changes every 4 days. The wound closed completely in approximately 2 months. The patient had a history of similar lesions that required up to 6 months of treatment.

Upon presentation, the LLE wound was 1.0 cm x 0.9 cm x 0.3 cm. It was treated for 156 days using various products including Acticoat® (46 applications, [Smith & Nephew, Largo, Fla]), Santyl® (7 applications, [Healthpoint, Fort Worth, Tex]), Apligraf® (6 applications, [Organogenesis, Canton, Mass]), and Xeroform™ (7 applications, [Tyco-Kendall HealthCare Group, Mansfield, Mass]). After these treatments the wound measured 9.0 cm x 4.4 cm x 0.1 cm. Following an initial decrease in size, the wound became unresponsive to these treatments. At that time, BWD-PHMB was substituted as the exclusive primary dressing. Over the next 42 days, a total of 10 BWD-PHMB dressings were applied. The patient subsequently went on to heal 1 week after her final treatment (49 days total) using this protocol.

**Figure 3.** Prior to BWD-PHMB (left) and after 2 months of BWD-PHMB (right).

**Figure 4.** Prior to BWD-PHMB (left) and after initial use of BWD-PHMB (right).

**Case 3.** An 89-year-old woman with diabetes presented with venous disease and psoriasis (Figure 4). She had 2 wounds, one each on her right and left lower extremities (RLE and LLE) that were treated separately over a period of 209 days.

Upon presentation, the RLE wound was 17.5 cm x 7.0 cm x 0.3 cm. It was treated for 167 days using various products including Acticoat (2 applications), XCell (2 applications), Santyl/Proafil (70 applications), Apligraf (4 applications), Sulfamylon (26 applications), Aquacel® (3 applications, [Convatec, Skillman, NJ]), OpSite™ (8 applications, [Smith & Nephew, Largo, Fla]), and Xeroform (7 applications). The wound remained unhealed after these treatments. The wound was recalcitrant to care; therefore, BWD-PHMB was substituted as the exclusive primary dressing. Over the next 53 days, a total of 12 BWD-PHMB dressings were applied as the exclusive treatment. The wound healed at approximately 60 days.

**Case 4.** A 79-year-old woman presented with venous leg ulcer on her lower extremity (Figure 5). She was treated over a period of 104 days. The wound was 15.0 cm x 9.0 cm x 0.1 cm. The wound was initially treated for
34 days using Panafil (13 applications) and Iodosorb (22 applications). After these treatments the wound measured 10.0 cm x 9.0 cm x 0.3 cm. The wound was determined to be recalcitrant after an initial decrease in size (15.0 cm x 9.0 cm to 10.0 cm x 9.0 cm, [≈ 35%]) and BWD-PHMB was substituted as the exclusive primary dressing. Over the next 70 days, a total of 10 BWD-PHMB dressings were applied.

Effect on wound bioburden and pain. By evaluating the bacterial load pre- and post-BWD-PHMB, it was demonstrated that the dressing resulted in elimination of Pseudomonas aeruginosa, Diptheroid gram-positive rods, beta hemolytic streptococcus, and Enterobacter aero-
gen in some patients. In other patients, decreased levels of Staphylococcus aureus, Pseudomonas aerugi-
nosa, and Proteus mirabilis were observed.

A reduction in pain has been noted with BWD\(^4\) as was observed in the present study.

Economics of BWD-PHMB. The estimated cost for the treatment of chronic wounds including services and associated products is close to $40,000 or in some cases even more.\(^5\) Any delay to heal a wound can increase that cost. Mulder\(^6\) described an economic model for determining the cost of 2 different treatments for removing necrotic tissue. The analysis demonstrated that a hydrogel/polyurethane combination was slightly more expensive than wet-to-dry gauze but was more cost effective when time to reach ≥ 50% debridement was included.

The cost of BWD-PHMB is similar to other advanced wound dressings. An economic analysis was performed in this study to determine the cost of BWD-PHMB use over time. An economic analysis of the use of BWD-
PHMB dressings demonstrates the low cost of using BWD-PHMB on recalcitrant wounds. The average cost of material was calculated to be $5.99 to $9.01 per day with the wounds demonstrating improvement or healing. No attempt was made to quantify the remaining cost of treat-
ment (clinic visit, staff time, etc.).

Data were gathered retrospectively for 2 patients that presented at the UCSD Healthcare System in San Diego, Calif. These patients had a total of 3 wounds that were initially treated with an array of advanced wound care products prior to exclusive use of a BWD-PHMB dress-
ing. The costs associated with the products used in Cases 3 and 4 appear in Tables 3 and 4, respectively. Table 5 illustrates the cost of the use of BWD-PHMB including the use of saline and gauze to clean the wound.

### Conclusion

A greater understanding of the role bacteria plays in the wound matrix repair process is resulting in an increasingly important role for antimicrobial dressings and products used in chronic wound care. The differences between various antimicrobial components and dressings require that clinicians have a basic understanding of different antimicrobial agents and their role in tis-

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**Table 3. Cost of dressings used in Case 3 (RLE wound).**

<table>
<thead>
<tr>
<th>Number of applications</th>
<th>Product</th>
<th>Cost per application</th>
<th>Total cost</th>
<th>Decrease in wound size</th>
<th>Time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>46</td>
<td>Acticoat</td>
<td>$44.00</td>
<td>$8774 w/Apligraf</td>
<td>68%</td>
<td>167</td>
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<tr>
<td>6</td>
<td>Apligraf</td>
<td>$1.100</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>7</td>
<td>Xeroform</td>
<td>$1.99</td>
<td>$2174 w/o Apligraf</td>
<td>64%</td>
<td>42</td>
</tr>
<tr>
<td>7</td>
<td>Santyl</td>
<td>$19.46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>XCell AM</td>
<td>$15.00</td>
<td>$150</td>
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**Table 4. Cost of dressings used in Case 4.**

<table>
<thead>
<tr>
<th>Number of applications</th>
<th>Product</th>
<th>Cost per application</th>
<th>Total cost</th>
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<th>Time (days)</th>
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<tr>
<td>13</td>
<td>Panafil</td>
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<td>$848</td>
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<td>22</td>
<td>Iodosorb</td>
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<tr>
<td>10</td>
<td>XCell</td>
<td>$15.00</td>
<td>$150</td>
<td>100%</td>
<td>70</td>
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**Table 5. Calculated BWD-PHMB total cost and cost/day.**

<table>
<thead>
<tr>
<th>Wound</th>
<th>Days</th>
<th>BWD-PHMB cost</th>
<th>Cost/day</th>
</tr>
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<tbody>
<tr>
<td>1 (Case 2)</td>
<td>70</td>
<td>$150</td>
<td>$2.14</td>
</tr>
<tr>
<td>2 (Case 3, Wound 1)</td>
<td>42</td>
<td>$150</td>
<td>$3.57</td>
</tr>
<tr>
<td>3 (Case 3, Wound 2)</td>
<td>53</td>
<td>$180</td>
<td>$3.40</td>
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</tbody>
</table>
sue repair before selecting the most appropriate dressing for a wound. The introduction of noncytotoxic levels of antimicrobial agents, including silver and PHMB, provides a means to potentially decrease levels of bacterial colonization that may impede closure while providing dressings that may assist with the development of a wound environment conducive to tissue repair, and ultimately, successful wound closure. Currently, PHMB does not have a history of resistance or cytotoxicity, has demonstrated promotion of healing, and may play a new and important role as an antimicrobial agent in dressings. The need for decreased frequency of dressing changes, dressing tolerance, and ease-of-use are factors, which are equally important when selecting an appropriate antimicrobial dressing.

The limited amount of information on the ability of antimicrobial dressings to significantly affect the healing process and wound closure supports the need for well designed and adequately powered clinical trials to determine the true role of these devices in the treatment of chronic wounds. Current information and publications indicate a potential benefit regarding the use of these products in wounds where bacterial burden may be delaying or impeding wound closure.

Acknowledgement
The authors thank Christine Dore, RN, and Ester Hernandez at the University of California San Diego, Wound Treatment and Research Center for generously giving their time and assistance in finalizing this manuscript.

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