Theraworx Protect: Clinical Value, Mechanism of Action, and Evidence

Supplier Submission

Avadim Health
600A Centerpark Drive • Asheville, NC 28805
Phone: (877) 677-2723 • Fax: (828) 274-7986
avadimhealth.com

Chris Tiemann
National Director of Clinical Health, Corporate Accounts & Business Development
(314) 482-0694
chris.tiemann@avadimhealth.com

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Introduction

Core Product - Avadim Health's flagship clinical product is Theraworx® Protect, a novel, advanced skin hygiene product that has been clinically proven, published and documented effective in several clinical areas of infection prevention, skin integrity and barrier maintenance. It is a combination of 18 different ingredients which are designed to enhance and preserve the natural protective elements of the stratum corneum, the outer layer of the epidermis, as described in detail under the Mechanism of Action Section.

Theraworx Protect formulation focuses in on the pathophysiology and skin science around epidermal pH. This gives Theraworx Protect an efficacy and safety profile unlike other products in the market. Theraworx is published in the American Journal of Infection Control as non-inferior to 4% CHG at the 10 minute and 6 hour markers while being safe for use in mucosa thus allowing for use in the meatus, perineum, and on the face.

The combination of Safety and Efficacy allows for Theraworx Protect to fill several current Gaps in Care that can lead to infections and skin breakdown. Most notable is managing pathogens when and where CHG can't be used filling Gaps in Care in Pediatric, and Adult Hospitals, and Post-Acute Settings as part of the following bundles:

- CAUTI Bundle: for Insertion and Maintenance of Indwelling Catheters and Pericare to Reduce HAIs. CHG Contraindicated for use in Mucous Membranes.
- CLABSI & SSI Bundle for Pediatric and Adult Hospitals
    - ICU Bathing Standardization 1 product that is safe and effective to be used head - toe.
    - CHG bathing alternative for ICU & surgical patients who cannot use CHG. Peds: Birth to 2 months & Hema/Onc and adults with Skin Conditions & Allergies
- Skin Integrity and Barrier Maintenance Bundle: Topical application to aid in the prevention and assist in healing of compromised skin due to Moisture Associated Skin Damage (MASD) and similar skin issues

Product Configurations - Theraworx Protect is available in multiple configurations to help support nursing practice: a 2 pack of pre-moistened disposable wipes, an 8 Pack of pre-moistened disposable wipes, an 8 oz and 4 oz foamer, a 2 oz spray, and our UPAK with 60ct wipes and 4 oz foam for at home use. Samples available.

Mechanism of Action

To fully understand the benefits of Theraworx Protect and the science behind it, it is important to know the most recent advances in the knowledge of the protective elements of the stratum corneum, the outer layer of the skin. The following summary provides a detailed recap of this science. The key protective elements of the outer layer of the epidermis, the stratum corneum, have been the subject of substantial research over the last 50 years.

It was not until the 1960's that research dermatologists were able to overcome faulty staining methods and initiate intensive study of this tissue, and to begin to gain understanding of its basic structure, and its relative importance to overall survival and protection against the many environmental challenges of life in a terrestrial environment. Understanding of the stratum corneum's basic "bricks and mortar" structure, with the enucleated terminal keratinocytes, called corneocytes, surrounded by a unique and biochemically active lipid matrix to a depth of approximately 28 microns, has increased steadily. So too has the study of the basic physiology of this tissue, and the many biochemical processes that occur within it, to the point where we now understand the criticality of maintaining the basal low pH condition of this tissue. Normal adult human stratum corneum is at a pH of about 4.9, more than 100 times more acidic than neutral pH of 7, and it is this acidic environment that is critical to several of the most significant protections to the body provided by this outer layer of the skin. Specifically:

1. The "acidic mantle" of the stratum corneum is naturally antimicrobial, for several reasons. The nominal low pH of this tissue is a perfect environment for the multitude of various bacteria, yeast, and fungi that inhabit the outer layer of the stratum corneum, and comprise the normal healthy microbiome of the skin. The importance of this normal microbiome to overall health, both on the skin, in the gut, brain, and throughout the human body, is now the subject of significant research. The healthy skin microbiome, thriving in its optimal low pH environment, competes successfully for nutrition and space on the skin surface, protecting against invasion by pathogens and resulting infections. This healthy microbiome creates acidic metabolites which reinforce its own healthy low pH environment, and also secrete substances which are naturally antimicrobial to pathogens. But when pH rises, the normal healthy microbiome suffers, and pathogenic organisms begin to thrive. It is therefore essential that health care facilities select topical skin care products for use which will protect and enhance the natural low pH condition of the skin, thus supporting the health of the normal skin microbiome and the protective biochemistry active in this environment.

2. The nominal low pH environment in the stratum corneum also supports normal structure and development of the stratum corneum lipids, the "mortar" that provides not only additional structural protection against invasion by pathogens, but also provides perhaps the most critical of all protections, the establishment and maintenance of the "permeability barrier" of the skin, without which normal osmotic action, between the very high moisture content of the interior body and the relatively dry environment in which we live, would result in increasing desiccation and eventual death, particularly in low humidity conditions. The three key lipids which form the basis of this protective lipid barrier--cholesterol, ceramides, and long chain free fatty acids--are all produced lower in the skin, in metabolic "factories" called lamellar bodies, and this lipid production requires the normal low pH environment to effectively produce and maintain the proper lipid ratio which is key to skin health and protection. In the face of insult or injury, signaling molecules "crank up" lipid production, as well as additional infection prevention through the production of antimicrobial peptides. And, as it also relates to infection prevention, one of the three types of lipids, free fatty acids, also has very effective antimicrobial action. So once more, the importance of maintaining low stratum corneum pH is critical to the production of lipids which form the key protective element of the stratum corneum, the body's permeability barrier, and which also support the natural antimicrobial protection of the skin.

Mechanism of Action cont.

3. A third key protective element of stratum corneum is its ability to control the proper rate

of skin sloughing ("desquamation"). Every layer of the epidermis is constantly moving upward, as keratinocytes are formed in the lower level to replace terminal corneocytes as they are constantly sloughing off at the skin surface, maintaining skin health and suppleness. The key to the correct rate of skin sloughing are small protein rivets that bind the corneocytes together, called corneodesmosomes, and the enzymes that control the "holding power" of these corneodesmosomes are pH dependent. Under nominal low pH conditions, the desquamation rate is perfect, and skin cohesion and integrity is maintained. However, when the skin pH increases, the strength of the corneodesmosomes is lessened, and skin sloughing proceeds at too fast of a pace. In addition, external biological factors and substances can impact skin integrity and cohesion. Hospital or long-term care patients who are either urine or fecal incontinent, or both, create substances which have dramatic pH elevating impact on the skin surface. Urine byproducts, urea and ammonia, are both high in pH, up to 9.5, and fecal material contain proteases which are extremely active in a high pH environment, becoming literally digestive to human skin. Both incontinent conditions, particularly in situations where active steps are not regularly taken to reverse the higher pH conditions they produce, can quickly lead to degradation in skin quality, incontinent-associated dermatitis, and eventually to aggressive skin breakdown, ulceration, and open wounds.

The primary reference for the science discussed above is a review paper written by Dr. Peter Elias, a dermatology research expert who has published more than 700 papers
on the stratum corneum. The title of the paper is **"The Skin Barrier As an Innate Immune Element"**,

4. Colloidal Nano Silver Particles (AgNPs)

The mechanism of action of silver nanoparticles (AgNPs) involves their unique physical and chemical properties, which enable them to interact with microbial cells and disrupt essential cellular processes. AgNPs exert their antimicrobial effects through several mechanisms, making them effective against bacteria, fungi, and viruses. Here are some key mechanisms of AgNPs' action:

1. Cell Membrane Interaction: AgNPs can interact with the microbial cell membrane due to their small size and high surface area. They can disrupt the lipid bilayer structure of the cell membrane, leading to increased permeability and leakage of cellular contents. This disruption can disturb essential cellular functions and ultimately result in cell death.

2. Reactive Oxygen Species (ROS) Generation: AgNPs can induce the generation of reactive oxygen species (ROS) within microbial cells. ROS, such as superoxide radicals (O2-) and hydroxyl radicals (OH-), are highly reactive molecules that can cause oxidative stress by damaging cellular components like DNA, proteins, and lipids. The accumulation of ROS can lead to cellular dysfunction and death.

3. DNA Binding and Damage: AgNPs can interact with microbial DNA, leading to DNA damage and inhibition of DNA replication and transcription. This interference with genetic material disrupts vital cellular processes, preventing the microorganisms from proliferating.

4. Protein Inhibition: AgNPs can bind to microbial proteins and enzymes, altering their structure and function. This disruption of protein function can hinder essential metabolic pathways and enzymatic processes necessary for microbial survival.

5. Intracellular Ion Disruption: AgNPs can enter microbial cells and disrupt ion homeostasis by interfering with ion channels and transporters. This disruption can disrupt cellular signaling and vital ion-dependent processes.

6 Biofilm Disruption: AgNPs have been shown to inhibit the formation of microbial biofilms and disperse existing biofilms. Biofilms are complex communities of microorganisms encased in a protective matrix, making them highly resistant to antibiotics and immune responses.

References:
1.Rai, M., Yadav, A., & Gade, A. (2009). Silver nanoparticles as a new generation of antimicrobials. Biotechnology Advances, 27(1), 76-83.
2.Li, P., Li, J., Wu, C., Wu, Q., Li, J., & Synergistic antibacterial effects of silver nanoparticles@ usnic acid composites. Colloids and Surfaces B: Biointerfaces, 184, 110521.
3.Sondi, I., & Salopek-Sondi, B. (2004). Silver nanoparticles as antimicrobial agent: a case study on E. coli as a model for Gram-negative bacteria. Journal of Colloid and Interface Science, 275(1), 177-182.
4.Chernousova, S., & Epple, M. (2013). Silver as antibacterial agent: ion, nanoparticle, and metal. Angewandte Chemie International Edition, 52(6), 1636-1653

Antibacterial Properties:
Numerous studies have demonstrated the potent antibacterial activity of nano silver in solution against both Gram-positive and Gram-negative bacteria. The mechanism of action involves the release of silver ions that interact with bacterial cell membranes, leading to disruption of membrane integrity, oxidative stress, and inhibition of bacterial growth. Nano silver has exhibited efficacy against antibiotic-resistant strains, such as methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant Pseudomonas aeruginosa. [Reference 1]

Antifungal Properties:
Nano silver in solution has also shown antifungal activity against various fungal pathogens, including Candida species, Aspergillus species, and dermatophytes. The mode of action against fungi involves the penetration of silver nanoparticles into fungal cells, leading to disruption of cell membranes and interference with vital cellular processes. Nano silver has demonstrated potential as an alternative or adjunct treatment for fungal infections, particularly in cases of drug-resistant fungal strains. [Reference 2]

Antiviral Properties:
Emerging research suggests that nano silver in solution possesses antiviral properties that can inhibit the replication of a range of viruses. The interaction between silver nanoparticles and viral particles can disrupt viral envelopes or protein coats, thereby preventing viral attachment and entry into host cells. Studies have shown promising results against enveloped viruses like influenza virus, human immunodeficiency virus (HIV), and herpes simplex virus (HSV). [Reference 3]

References:

1.Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. Biotechnology Advances. 2009;27(1):76-83.
2.Lara HH, Ayala-Nuñez NV, Ixtepan-Turrent L, Rodriguez-Padilla C. Mode of antiviral action of silver nanoparticles against HIV-1. Journal of Nanobiotechnology. 2010;8:1.
3.Elechiguerra JL, Burt JL, Morones JR, et al. Interaction of silver nanoparticles with HIV-1. Journal of Nanobiotechnology. 2005;3:6.

Theraworx Benefits and Competitive Comparison

According to the NHSN data in Pediatric Hospitals there are 15 pathogens that account for over 88% of healthcare aquired infections (HAIs). Of these 15 pathogens, 9 are considered gut-related. 53% of all Pediatric HAIs are caused by gut-related pathogens, including 85% of CAUTIs and 48% of CLABSIs.

In the Adult Hospital setting there are 15 pathogens that account for over 86% of HAIs. Of these 15 pathogens, 11 are considered gut related and cause over 57% of HAIs including 87.8% of CAUTIs, 50% of SSIs, and 46.9% of CLABSIs.

Managing gut-related organisms at the source requires a unique safety and efficacy profile that Theraworx using pH possesses being hostile to pathogens while being non-cytotoxic to mucous membranes. The issue for HCP is that antiseptics are toxic to mucous membranes and not recommended and non-antiseptic products like soap and water do not have the efficacy to manage these pathogens. Leaving no recommended safe and effective options to manage gut related pathogens at the source perineum, with the exception of Theraworx -which proven as both safe and effect.

Some topical substances, most notably the 50-year-old standard of topical skin infection prevention, chlorhexidine gluconate (CHG), while initially low in pH, can damage the lipid structure of the skin, particularly with repeated use, and lead to negative impact on the permeability barrier, as well as both skin drying and irritation. In addition, with the increasing awareness of the importance of maintaining the healthy microbiome of the skin, there is growing concern that CHG's antimicrobial activity is so dramatic that not only are pathogens killed by the use of this substance, but also healthy microbiome is negatively impacted.

The CDC guidelines for actions recommended to protect against surgical site infections were published, and the CDC officially removed CHG from the list of products recommended for use in pre-surgical bathing- JAMA Surg. doi:10.1001/jamasurg.2017.0904 Published online May 3, 2017.

Theraworx Protect technology is the first topical solution which has been proven to be non-toxic, mucous membrane-safe, and biocompatible, while demonstrating the ability to support the healthy low pH condition of the stratum corneum, thus preserving all four of the key protective elements described above—the antimicrobial acidic mantle of the skin, the body's permeability barrier, and skin cohesion and integrity, even in incontinent patient populations. The low pH Theraworx formulation not only penetrates the stratum corneum, but demonstrates a persistent characteristic for an extended period of time. This ability to penetrate and persist allows low stratum corneum pH to be supported with periodic applications, and its nontoxic and mucous membrane-safe nature allows the use of the product in every area of the body, even the face and the perineum, where the caustic nature of other topical solutions like CHG make them not suitable, and not recommended for use.

The non-toxic, biocompatible, "skin-friendly nature" of Theraworx allows our bathing system, foams and sprays to be used in and around mucous membranes unlike CHG/alcohol. It is this safety in and around mucous membranes, as well as the challenges of hygiene in the face, perineal/ perianal area, that has resulted in the increasing adoption of Theraworx as a preferred product in both the high acuity perineal cleansing and preparation for insertion of indwelling urinary catheters, and also in the maintenance hygiene associated with care of these patients. While good sterile technique can prevent "insertion CAUTI's," the risk of CAUTI increases exponentially with longer term indwelling catheterization, and Theraworx has proven to be a key tool in helping to maintain the catheter and lower CAUTI/CLABSI rates in hospitals using the product.

Helen Devos Children's hospital had a CAUTI rate above national benchmark in the PICU. As part of their intervention stratgey they implemented Theraworx bathing product becasue it is designed for CAUTI prevention and recognized 0 CAUTI for 498 days and a 77% reduction overall.

In a peer-reviewed, published multifacility retrospective analysis of outcomes achieved by hospitals using Theraworx Protect for this application in the high acuity setting, the most challenging environment and the units most likely to see long-term catheterizations, the mean reduction in CAUTI rates, comparing periods averaging 22 months prior to implementation to 14 months after implementation of Theraworx products and protocols, was 54%. This peer-reviewed, published study is included in the reference material.

Theraworx Benefits and Competitive Comparison Cont.

A second application where Theraworx offers an innovative alternative to other topical products, and particularly chlorhexidine gluconate (CHG), is the use of a Theraworx-impregnated 8-cloth bathing system to do daily bathing of patients in Pediatric and Adult hospitals ICU's. The practice of including antimicrobial bathing as part of the multifactorial clinical protocol in these patients daily, to reduce the presence of pathogens, has become standard in these units, in large part as a strategy to reduce the possibility of central line-associated blood stream infections (CLABSI).

CHG has been the product of choice over the last several years. Concerns about the drying and irritation of patients' skin, ICU patients with Skin and allegic conditions not able to use CHG, and limited usage in the Peditarice Populations from birth to 2 months and with Hemotology Oncology patients, have resulted in many hospitals moving to Theraworx.

A safe alternative to CHG that still has efficacy is critical in these patients as part of Infection Prevention Bundles.

Lucile Packard Children's Hospital - Stanford did a six month trial comparing Theraworx to CHG wipes in Hem/ONC and Stem Cell Transplant patients with tunneled central lines. They found an increase in bathing compliance of 23% with Theraworx (75% with CHG to 92% with Theraworx) and a CLABSI reduction of 75% with Theraworx (n=1 vs n=4).

In the Journal of Critical Care Nursing National Teaching Institute, Theraworx Protect when used in place of CHG 2% was associated with a significant reduction in rate of CLABSI per 1000 catheter days in a high acuity ICU and the ICU remained CLABSI free for more than two years.

An additional benefit of the use of Theraworx for this application is the fact that the Theraworx bathing system contains eight cloths, instead of six in CHG systems, since the nontoxic nature of Theraworx allows it to be used in both the facial area, and the perineum, in addition to the front, back and four extremities. Keep in mind that NHSN data shows that close to 50% of CLABSIs in Pediatric and Adult Hospitals are caused by gut-related organisms. Managing gut-related organisms in the Perinuem or at the source has a profound effect on reducing CLABSIs. For the first time, true "full body ICU bathing" is possible utilizing the Theraworx 8-cloth system. This important distinction is gaining support among physicians and ICU clinicians.

In a significant poster study which will be presented at ANCC National Magnet Hospital Association Meeting Fall Session by a large two-hospital system in northern California, John Muir Health, Theraworx was added to the CLABSI prevention protocols. The system reported a 46% and 35% reduction in CLABSI, in the Walnut Creek and Concord campuses respectively, after this addition. This poster is included in the reference material.

A third clinical application for the use of Theraworx, and perhaps the highest potential application in the 16,000 nursing homes, and approximately two million residents of these facilities in the U.S., is for the treatment of skin issues, most notably incontinence-associated dermatitis (IAD), in urine and/or fecal incontinent patients within these facilities (on average, up to 70% of all long term care residents have incontinence (fecal, urine or mixed) and 70% of those with incontinence are diagnosed with chronic Incontinence Associated Dermatitis (IAD). There are similar patients in the acute care setting as well, but the largest market for this application is certainly the long-term care facilities.

The presence of urine and high pH urine byproducts urea and ammonia, as well as fecal material in fecal incontinence, create a highly damaging environment in the perineal area, driven by the increase in pH, destruction of the healthy skin microbiome and normal antimicrobial protections, as well as degradation in standard skin integrity and cohesion also resulting from declining acidity. A poster study presented at the Symposia for Advanced Wound Care (SAWC) spring 2017 session, showed patients with severe grade 2 skin damage, who were refractory (not responsive) to traditional barrier treatment, Theraworx use resulted in a 93% resolution overall. This poster is included in the reference material.

Another significant potential application for Theraworx in the long-term care market is for prevention of non-catheter associated urinary tract infections (UTI) in this same urine and/or fecal incontinent population. While the use of indwelling catheters in the nursing home population is not as prevalent as in hospitals, the rise in pH in the perineum resulting from presence of high pH urine byproducts results in much higher UTI rates in this incontinent population. Regular perineal hygiene protocols using Theraworx as the hygiene agent have demonstrated significant impact on UTI rates in the long-term care patient population. In a poster study done over a two-year period by clinicians at 17 long term care homes in the Peterson Healthcare system, a large system in the Midwest U.S., the incidence of UTI in the urine/fecal incontinent population within the system was reduced from a rate of approximately 2.0 UTI/1000 resident days to 0.5 UTI/1000 resident days after implementation for perineal care and cleanup after incontinent events, a reduction of 75% during the nine-month period after implementation of Theraworx protocols. This study is included in the reference material.

It is important to note that Theraworx, is not a drug such as CHG, or an antiseptic such as alcohol or triclosan. Like many cosmetic products, it does contain some preservatives like EDTA, and colloidal silver, in a small quantity (less than 1%), which is used by many medical companies, but is not recognized currently by the FDA as an antimicrobial product. It is our strong belief that the data presented within this document which shows either the ability of Theraworx to be effective in reducing the population of pathogens, or in reducing infection rates in a clinical settings, is due primarily to the action of the product on the stratum corneum, and particularly its ability to help maintain a low pH condition on the stratum corneum, providing natural antimicrobial activity within the stratum corneum, thus also encouraging preservation of the normal healthy skin microbiome, producing additional naturally pathogenic action.

It is the fact that Theraworx does not contain any antiseptic FDA approved drugs but has demonstrated proven and published outcomes in high risk patient populations that substantiates the breakthrough Innovative technology of the Theraworx mechanisms of action.

Competitive Comparison

Head to Head Comparisons with Standard Practice Approaches Including Chlorhexidine Gluconate, Alcohol, Benzalkonium Chloride, Soap and Water Wipes

1. Chlorhexidine Gluconate:

(A.) In a randomized controlled study comparing Theraworx Protect Towels to 4% CHG in the inguinal crease, axilla, sub clavicular and mid-line abdomen and knee which are areas of the body traditionally considered high areas of bioburden. Theraworx Protect demonstrated greater log reduction or equivalent in all areas when used as a hygiene and barrier product.

(B.) In a second head to head comparison following FDA final tentative monograph standard testing method E1173-15 Theraworx Protect was shown to be non-inferior to CHG 4% (Hibiclens) and is published in the American Journal of Infection Control.

(C.) In a third study Theraworx Protect was shown to be superior to CHG when measuring TEWL (Transepidermal Water Loss) and skin breakdown in a repeated application design study.

(D.) In a fourth head to head study Theraworx Protect was shown to be superior to CHG when measuring cell death in mucosa including Epi-Airway Mucosa, Gingival, Vaginal and Instestinal.

(E.) In a fifth head to head study conducted at St Jude Children's Theraworx Protect was shown to be non-toxic in children with graft vs host disease receiving hematopoietic stem cell transplantation whereas CHG was shown to drive stage IV toxicities.

2. Alcohol:

(A.) Duration of action testing to evaluate the antimicrobial performance of Theraworx® Protect vs 67% alcohol against Methicillin Resistant Staphylococcus Aureus was performed using a collagen based repeat inoculation model. At 15 minutes, 30, 60, 120 and 180 minutes when challenged repeatedly Theraworx Protect was shown superior to alcohol at all time intervals.

(B.) Duration of Action testing at 15, 30, 60, 120, 180 minutes with Theraworx Protect vs alcohol 62% vs the Corona Virus OC43 to determine persistence related efficacy. Theraworx Protect was shown to be superior to alcohol 62% at all time intervals.

(C.) Duration of Action Testing in human subjects comparing Theraworx Protect to Alcohol 62% was performed using a repeat inoculation model and at 15, 30, 60, 120 ad 180 minutes Theraworx Protect was shown to demonstrate a 3-fold + greater efficacy on human skin than alcohol 62% vs the corona virus OC43.

3. Benzalkonium Chloride:

(A.) Theraworx Protect was compared to BZK bathing towels was superior when challenged with Vancomycin Resistant enterococcus, Candida Albicans and MRSA.

4. Soap and Water Equivalent Wipes:

(A.) These wipes have a similar safety profile to regarding cytotoxic response when used on skin with that of Theraworx Protect, however these products lack the evidence of being able to manage pathogens including resistant Pathogens that lead to Healthcare Acquired Infections. Typically used for general floor bathing and in ICU or critical care areas where and when CHG is not used in areas like the Perineum and for bathing of ICU Peds from birth to 2 months. However, lack of evidence against pathogens causing HAIs is a concern for these products.

Evidence Based Innovation

Much of our claim substantiation is based on the science of the stratum corneum, and the two published, peer-reviewed review papers on specific protections to the body by this critical tissue are critical to the understanding of the mechanism of action of Theraworx. These papers, previously referred to in the Important Features and Benefit Section, are key reference documents for our application.

1. "The Skin Barrier as an Innate Immune Element" Research review published in peer-reviewed Seminars in Immunopathology journal, 2007.
2. "pH Directly Regulates Epidermal Permeability Homeostasis, and Stratum Corneum Integrity/Cohesion" Research paper published in peer-reviewed Journal of Investigative Dermatology, 2003.

Full Value Concept - The individual elements of the Full Value Concept for Theraworx are discussed below.

CAUTI BUNDLE

Quite simply, Theraworx, as a skin-friendly, non-drying or irritating cosmetic product, has demonstrated strong patient care outcomes in both infection rate reduction and in improved skin cohesion and integrity, outcomes which are non-inferior or superior to other antiseptic and drug products, while also eliciting a strong staff acceptance and patient satisfaction profile.

The most widely-accepted application of Theraworx is for perineal prep prior to insertion of a Foley catheter, as well as subsequent perineal cleaning and care throughout insertion and maintenance. The following published studies and verifiable information on clinical outcomes are submitted within our reference document package, at the end of this application.

The clinical compendium around CAUTI and UTI reduction shows a 50% to 100% reduction when Theraworx is added to institutions bundles.

Additional benefit is the ability of Theraworx to manage the gut-related organisms in the perineum of these patients that have shown to cause additional HAIs like CLABSI and SSIs.

Theraworx Protect is safe for use in Mucous Membranes where CHG isn't, filling a crucial gap in care knowing that 57% and 53% of HAIs in Adult and Pediatric Hospitals come from gut-related organisms.

Theraworx Protect UPAK includes an option for patients to do Catheter Maintenance in the home setting to support reducing CAUTI and Readmissions.

1. "One Year Cauti Free A multi-disciplinary Team approach to Reducing CAUTI in Pediatric Intensive Care Unit. Helen Devos Children's Hospital Grand Rapids, Michigan Auth: Jessica McClusky, MSN, RN, CPN, CIC.
2. Zero CAUTI, Zero CLABSI: evaluating the evidence-based effectiveness of a silver, PH acidic, multi modal skin decolonizing wipe to reduce CAUTI and CLABSI in the ICU setting: a retrospective review. Doctors Medical Center of Modesto, 2020 Auth: Asif Saiyed, MBA, CIC, Director of Infection Prevention
3. Can't Attribute UTI To Insertion: Utilizing Data to Prevent CAUTI. University of Washington Medical Center, Seattle, WA Auth Smith, N.C, Granich, M. Lien, H. Schipper, A.
4. Evaluating the effectiveness of a multidimensional bundle to reduce urinary tract infection in long-term care spinal cord injury/disordered patients: a retroactive review. Journal of Wound Ostomy and Continence Nursing, May 2020
5. "Innovative Microbiome friendly skin care formulation reduces nosocomial associated CAUTI rates when used for insertion and maintenance of urinary catheters". Moderated presentation, American Urological Association meeting, May 2017. (reference document no. 16, pp) Also published peer-reviewed study in Journal of Medical and Surgical Investigations, Volume 2 (2) 1-3, April 2017. Grade 3 multi-facility non-randomized cohort study.
6. "Targeting Zero—One Hospital's Journey to Reduce CAUTI." Article in Journal of Nursing Management 18-20, December 2014. Grade 3 non-randomized historical cohort study.
7. "Equipping Clinicians with Advanced Care Options Leads to Reductions in Urinary Tract Infections". Poster presentation by Nexion Meadowview Health and Rehab Center at American Healthcare Association (AHCA) Spring Session 2017. Grade 3 non-randomized historical cohort study.
8. "Preventing Chronic Urinary Tract Infections from Urinary and Fecal Incontinence: The Impact of Theraworx" Poster presentation September 2016 by Peterson Healthcare, Grade 3 non-randomized cohort study.
9. "Impact of Theraworx for the Prevention of Catheter-Associated Urinary Tract Infections: Results from John Muir Health Concord." Poster from John Muir Health and the University of Louisville Department of Infectious Diseases, September 2017. Grade 3 non-randomized cohort study.
10. "Strategies to Prevent Urinary Tract Infection from Foley Catheter Insertion in the Emergency Department." Peer-reviewed published study from Augusta Medical Center, Augusta GA. November 2010, peer-reviewed Journal of Emergency Nursing. Grade 3 non-randomized cohort study.
11. "Effects of Education and Improved Foley Catheter Care on Nurse's Knowledge and Associated Urinary Tract Infections." Poster by First Health Carolinas, February 2013. Grade 3, non-randomized cohort study.

Evidence Based Innovation

ICU Bathing & SSI Bundle: Alternative to CHG

A second major application for Theraworx that is growing in acceptance is the use of the product for full body ICU & Pre Surgical bathing in Pediatric and Adult Hospitals. The skin-friendly, biocompatible, non-toxic cosmetic characteristic of the product, even in long term use, compares very favorably to CHG.

Theraworx was compared to CHG 2% in two randomized controlled in-vivo comparison studies implementing two FDA mandated testing methods (ASTM E1173) and (ASTM E 2783) to compare the efficacy for decolonization and time to kill across a broad array of microbes. A two factor analysis of variance (ANOVA) showed the two products were statistically equivalent for decolonization and time to kill.

In a second head to head comparison following the FDA final tentative monograph standard testing method E1173-15 Theraworx Protect was shown ot be non-inferior to CHG 4% (Hibiclens) and is published in the American Journal of Infection Control. Full Study Included

With the emergence of a resistant Candida (AURIS) which has been shown to be resistant to Azoles and Endochins we tested Theraworx efficacy to be considered for patients colonized with C-Auris. Theraworx was shown to have a 6- log reduction at 24 hours when challenged with 5b isolates.

In addition, staff acceptance of the product has been very positive, particularly when compared to CHG. The following studies, observations, and publications are also included in the reference document package, with full details, and address outcomes, specific decolonization results and comparisons, and two key safety and patient comfort areas, skin drying and safety around mucosal tissue.

Lucile Packard Children's Hospital (Stanford Medicine) in a 6 months trial comparing Theraworx to CHG wipes in the Hematology Oncology and Stem Cell Transplant patients found and increase of compliance of 25% with Theraworx (75% CHG to 92% Theraworx) and a decrease in CLABSIs of 75% to CHG (CHG 4 - Theraworx -1). This has lead to them implementing Theraworx bathing for all ICU units.

Theraworx has been used at OU Children's Hospital at 34 weeks gestational age for over 1 year with no major adverse events. It has been used at 38 weeks gestational age for several years at McLane's Children's Hospital with no Major Adverse Events. McLane's is starting a trial at 28 weeks gestational age + 7 days after birth in August of 2023, will share data as soon as it is available.

Theraworx ICU bathing to be used as a Standardized bathing protocol for ICUs and as an alternative to CHG bathing for patients in Pediatric and Adult Hospitals that cannot use CHG.

1. "Effectiveness of Bath Wipes After Hematopoietic Cell Transplantation: A Randomized Trial." St. Jude Children's Hospital. Journal of Pediatric Oncology Nursing 2020.
2. Beyond the Bundles: A Pilot to Evaluate a Silver Based Bathing Product to Reduce Central Line-Associared Bloodstream Infections. Lucile Packard Chidlren's Hospital (Stanford Health) Auth: Lisa Pinner, RN, MSN, CNS, CPON, BMTCN, Rachel Frisch, BSN, BMTCN, Jenna Kruger, MPH, CPHQ and Lianna Marks, MD. Published 2021
3. Zero CAUTI, Zero CLABSI: evaluating the evidence-based effectiveness of a silver, PH acidic, multi modal skin decolonizing wipe to reduce CAUTI and CLABSI in the ICU setting: a retrospective review. Doctors Medical Center of Modesto, 2020 Auth: Asif Saiyed, MBA, CIC, Director of Infection Prevention
4. "Theraworx vs. Chlorhexidine Gluconate Bathing and Peri-operative Skin Cleansing Study." St. John's Medical Research Institute, September 2009. Grade 2 compare contemporary simulated patient intervention, selection bias not controlled.
5. "CLABSI (Central Line Associated Blood Stream Infections) Reduction Seen with Multifactorial Nurse Initiative". Poster presentation ANCC National Magnet convention. non-randomized cohort study.
6. "Efficacy and Safety of a novel skin cleansing formulation versus Cholrhexidine Gluconate" Study published in the peer-reviewed American Journal of Infection Control
7. "Efficacy of novel skin antiseptic against carbapenem-resistant Enterobacteriaceae." Study published in peer-reviewed American Journal of Infection Control. simulated skin study of effectiveness of Theraworx against two different strains of CRE.
8. "Duration of Action of Theraworx Against Methicillin-Resistant Staphylococcus Aureus Utilizing an Inoculated Collagen Model." St. John's Medical Research Institute, September 2009 report. In-vitro comparison of duration of action against this organism vs. alcohol skin cleanser.
9. "Forearm Controlled Application Test for Evaluating Relative Mildness and Skin Moisturization Effectiveness of Two Products" BioScience Laboratories, June 2017. Unpublished independent study using non-invasive instrument testing of Theraworx versus CHG. non-randomized controlled study.
10. "Cytotoxicity Sensitivity Response in Epi-airway, Epi-gingival, Epi-vaginal, Epi-intestinal Mucosa: Theraworx Vs. Chlorhexidine Gluconate." BioScience Laboratory independent study using MTT assays. non-randomized controlled study.
11. "Non-inferiority Testing, Randomized Controlled- in-vitro and in-vivo decolonization in a pre-operative US FDA mandated ASTM E1173 test method Theraworx compared the 2% CHG- unpublished submitted for publication by Biosciences of America-
12. "Non-inferiority Testing, Randomized Controlled- in-vitro and in-vivo decolonization in a pre-operative US FDA mandated ASTM E1173 test method Theraworx compared the 2% CHG- unpublished submitted for publication by Biosciences of America- , non-randomized controlled study
13. "Non-inferiority Testing Randomized Controlled- in-vitro and in-vivo Time to Kill Efficacy Study following the FDA ASTM E2783 test method across a broad range of microbes vs 2% CHG- unpublished submitted for publication by Biosciences of America- , non-randomized controlled study
14. AN EVALUATION OF ONE TEST PRODUCT FOR ITS ANTIMICROBTAL PROPERTIES WHEN CHALLENGED WITH THREE MICROORGANISMS USING AN IN.VTTRO TIME-KILL- Candida Auris testing- A time to kill and duration study- unpublished- prepared for publication. non-randomized controlled study

Evidence Based Innovation

Skin Integrity and Barrier Maintenance Bundle:

A third and rapidly growing Theraworx application in both acute care high acuity settings and post-acute care is in the treatment of Incontinence Associated Dermatitis and other types of Moisture Associated Skin Damage including intertrigo, peristomal dermatitis and peri wound dermatitis. The following published articles, studies and observations deal with the skin cohesion/ integrity advantages of Theraworx and its unique, low pH promoting activity on the stratum corneum protections in this area. Full details available at www.hcp.theraworxprotect.com/learn-all.

1. "Non-toxic Skin Formulation Promotes Healing of Dermatitis and Skin Injuries That are Prone to Infection in Long-Term Care Facility Residents (Case Report). Published in peer reviewed Annals of Infectious Disease and Epidemiology, November 2016.

2. "Successful Healing of IAD when Traditional Barriers Fail, Using an Innovative Topical Formulation." Poster presentation at Symposia for Advanced Wound Care, Spring Session 2017.

3. "Novel Skin Care System Helps in Healing Skin Wounds and Other Problematic Skin Disorders in Patients in Long-Term Care Facilities." Poster presentation at W.O.W. (Wild on Wounds) National Conference, Fall Session 2016.

4. "Harnessing the microbiome to rapidly resolve peristomal complications." Poster presentation at Symposium on Advanced Wound Care, Spring Session 2019

5. Effect of an innovative pH lowering wound Therpeutic on MMP levels and bacterial bifofilm colonization of chronic non-healing wounds. Poster presentation at Symposium on Advanced Wound Care, Fall 2019

6. "Effect of an innovative pH lowering wound Therapeutic on MMP levels and bacterial biofilm colonization of chronic non-healing wounds." Poster presentation at Symposium on Advanced Wound Care, Fall 2018

Additional Benefits

Theraworx patent-pending protocols in the clinical applications described above have been developed. Compliance with these protocols has been shown to be a key element of the positive outcomes that have been achieved while using Theraworx product and protocols. An example, the graphic depiction of the protocol for regular re- establishment of the "zone of inhibition" for Foley catheterized patients, is included in our package. These protocols are what guide our field in-service efforts. Our goal here is to reinforce proper technique and provide the very best opportunity for improved outcomes among all customers of our product.

Additionally, we have a discharge product called Theraworx Protect U-PAK that is designed for patients discharging with Indwelling Urinary Catheters to be able to use at home. Considering population health and giving hospitals access to a product that can help continue therapy at home to help reduce the risk of hospital readmission

Managing Emerging Infection Concerns:

Most recently with the emergence of **SARS COV-2, RSV, and Candida Auris** Pediatric, Adult Hospitals, and Post Acute Care Facilities have employed Theraworx Protect technology as the biochemical barrier for the Transmission Zone (eyes, nose, mouth). Theraworx has been studied with excellent results in vivo against Covid, RSV, and Candida Auris providing an option to Clinicians that has both Efficacy and Safety data against these most challenging viruses. This gives clinicans the opportunity to safely use a product in and around the entry points for these pathogens -eyes, nose, mouth, and even ears. We are investing in further evidence with studies in patients in the hospital and post-acute care settings looking at decolonization and containment.

1. "Another tool in the toolbox: a novel, multimodal, surfactant-based skin cleanser vs 62% ethanol on the human corona-virus OC43 on human tissue." Journal of Clinical and Medial Investigations, October 2020

2. "Activity of a novel, multimodal, surfactant-based skin cleanser on coronaviruses, in-vitro." Journal of Clinical and Medical Investigations, September 2020

3. "An Evaluation of One Test Product for It's Antimicrobial Properties when Challenged with Three Microorganisms Using an In-Vitro Time-Kill Candida Auris Testing." Unpublished Bioscience Laboratories, Inc.

4. "Evaluation of One Test Article for Virucidal Properties upon the ASTM E1052-20 Method when Challenged with Respiratory Syncytial Virus (RSV). Unpublished Nelson Labs.

Clostridioides difficile (C. Diff): Has emerged as a difficult issue in the health care system. According to the CDC there are almost half a million infections in the US each year. About 1 in 6 patients who get C. Diff will get it again in the subsequent 2-8 weeks. One in 11 people over age 65 diagnosed with a Healthcare-associated C. diff infection die within one month. This is very concerning and drives home the importance of being able to control spread and minimize impact in clinical settings. Our low pH formulation and in-vivo data shows good results against C Diff spores.

We have 2 published posters both showing a significant reduction in CDI:

- 60% (Peconic Bay) when replacing Soap and water wipes with Theraworx and
- 68% (Levindale) when replacing CHG with Theraworx in their CDI bundles: (Published Studies in Reference Materials)

1. "Preventing Hosptial Acquired Clostridum Difficile Infection in ICU Patients: The Efficacy of Theraworx, a Novel Silver-Based Cleanser." Peconinc Bay Medical Center Northwell Health

2. Reducing the Incidence of Clostridium Difficile Infections, Antibiotics and Costs In A Long-Term Acute Care Setting - A surveillance Expereince. Levindale Hebrew Geriatric Center and Hospital

Financial Benefits

Product cost is the most direct and measurable savings in this area, and it is our experience that Theraworx is priced lower than many products which it would replace, particularly those containing CHG. Our bathing system is typically offered at a price that is less than the comparable CHG Preoperative Skin Cleansing Products used for bathing, even though the non-toxic, mucous membrane-safe properties of Theraworx allow us to package 8 cloths in our system, versus 6 for CHG. In terms of demonstrated deletion of certain processes of care, the use of our product for IAD prevention and treatment typically allows for the reduction in use of several other products used in peri-anal care, including moisturizers, barrier creams, and anti-fungal creams.

Success against IAD in both the long-term care and the acute care clinical setting would potentially prevent physician consultation and involvement in a condition that is typically a nursing responsibility, a direct savings as well. In addition, while Theraworx is only approved for use on intact skin, its ability to resolve IAD type skin issues quickly and successful may avoid skin breakdown and pressure skin injuries, and additional care required, some of which may be unreimbursed.

Considering the volume of evidence presented within the reference documents showing many instances of the improved outcomes demonstrated through the use of Theraworx for infections, we believe Theraworx can quantitatively impact several key elements of the CMS programs that are now in place as they push the industry away from the historical fee-for-service approach and move it to a new paradigm of overall cost, quality and outcomes. Value Based Payment and the Healthcare Acquired Conditions (HAC) Penalty include Infections Rates.

More significant is the Hospital Acquired Conditions (HAC) penalty, where approximately 800 of the largest hospitals in the country are subject to loss of 1% of total CMS reimbursement, if the individual hospital scores in the bottom 25% of this group in key measures, which again, are heavily weighted on CAUTI and CLABSI, and include other hospital acquired infections (HAI) that Theraworx has data on, MRSA, C. Diff, and SSIs.

The challenge of the HAC penalty is that “standing still” on controlling HAC’s may not be enough, since the scores are re-calculated every year, so a hospital can find itself scored the same as prior year, but see other improving hospitals move above them in scoring, pushing that hospital down into the bottom 25% level.

Finally, several studies have shown that of the patients readmitted to the hospital within 30 days of discharge, 20-35% experienced an HAI during their primary admission. The Readmission Penalty, which can be high, is based on an extremely complicated formula, but the bottom line is that avoidance of an HAI during primary admission gives the hospital a much better chance of avoiding at least some readmits that will impact their scoring on the Readmission Penalty. Put it all together, and a total of 6% of total CMS reimbursement is at risk, with infections playing a major role in the scoring of the penalties. For a hospital with high Medicare/Medicaid payment mix, these programs can be the difference between the bottom line being black or red.

Theraworx Protect UPAK discharge program is designed to help patients care for their catheter at home after discharge from the hospital.

Product Classification, Regulatory & Safety

Classification - Theraworx is Manufactured and distributed by Avadim Holdings, Inc. DBA Avadim Health. Avadim Manufactures Theraworx in compliance with "Good Manufacturing Practices" as required by the Food and Drug Administration's statuary requirements of CFR 211 for monographed drugs. In addition, Avadim's manufacturing processes are in substantial compliance with the ISO 13485:2003 Standard for Medical Devices.

Regulatory - Theraworx has met and exceeds the Biocompatibility Safety Testing requirements for acute systemic, skin irritation, skin sensitivity and cytotoxicity as required for Medical Devices. Theraworx is classified as a cosmetic skin cleanser with preservatives: therefore a 510(k) is not required. Cosmetic firms are responsible for substantiating the safety of their products and ingredients before marketing. Avadim has compiled numerous clinical abstracts and white papers substantiating the safety and effectiveness of Theraworx. A summary document on biocompatibility testing results with Theraworx is enclosed in the reference documents.

Safety Profile - The primary safety benefit of the Theraworx range of products is to the patient. The reference documents include results of cytotoxicity, irritant and biocompatibility testing. Avadim has tested the safety profile of Theraworx versus CHG in mucosal tissue, and those results are also included in the reference documents. The advantage of having a skin-friendly product which helps protect the natural microbiome through its low pH characteristics, and is also safe for use in all body areas, while still having significant effectiveness, is a key part of why we feel that the product represents a New and Innovative Technology. Having effective potency, and non-toxic biocompatibility, at the same time represents unique skin hygiene technology. Compared to CHG, Theraworx presents a safety profile that mitigates potential concerns of nurses regarding irritation or allergic reactions.

Clinical Evidence - Listing of all Studies (Full Studies available at ***www.hcp.theraworxprotect.com/learn-all****)*

Head to Head Studies

1. **Another tool in the toolbox: a novel, multimodal, surfactant-based skin cleanser vs. 62% ethanol on the human coronavirus OC43 on human tissue.**
   Paulson DS. Journal of Clinical and Medical Investigations, October 2020 .....

2. **Activity of a novel, multimodal, surfactant-based skin cleanser on coronaviruses, in-vitro.**
   Paulson DS. Journal of Clinical and Medical Investigations, September 2020 .....

3. **Efficacy and safety of a novel skin cleansing formulation versus chlorhexidine gluconate.**
   Paulson DS, Topp R, Boykin RE, Schultz G, Yang Q. American Journal of Infection Control, 2018 .....

4. **Antimicrobial effectiveness of rinse-free hospital bathing cleansers after 24 h of initial exposure to common pathogenic micro-organisms.**
   Olivi J, Austin CL, Thompson SJ. Journal of Patient Care, 2018. .....

5. **Forearm Controlled Application Test for Evaluating the Relative Mildness and Skin Moisturization Effectiveness of Two Products**
   Independent Testing by BioScience Laboratories, Phoenix, AZ .....

6. **Theraworx V. Chlorhexidine Gluconate Bathing and Peri-Operative Skin Cleansing Study**
   St. John's Research Center, Huckfeldt R, et al, controlled comparative study .....

7. **Duration of Action of Theraworx Against Methicillin-resistant Staphylococcus Aureus Utilizing an Innoculated Collagen Model**
   Huckfeldt R, St. John's Research Institute, controlled comparative study.....

Institutional Quality International Studies

8. **Effectiveness of bath wipes after hematopoietic sStem cell transplantation: a randomized trial- St Jude Children's.**
   Margie K, Qudeimat A, Browne E, Keerthi D, Sunkara A, Kang G, et al. Journal of Pediatric Oncology Nursing, 2020. .....

9. **Change has arrived: antimicrobial bathing and CLABSI. University of Southern California (Verdugo Hills) EB8**
   Sung P, Virgallito M, Murphy T, Boghossian R, Young R. Journal of Critical Care Nursing, April 2020 .....

10. **Closing the gap: targeting CAUTIs with a novel approach to perineal care. (University of Maryland Health)** EB9
    Hargett L, Anderson T. Journal of Critical Care Nursing, April 2020.....

11. **Evaluating the effectiveness of a multidimensional bundle to reduce urinary tract infection in long-term care spinal cord injury/disordered patients: a retroactive review.**
    Chaiken N, Pazzaglia J, Polakkattil B, Tower-Woods W, Schwartz R, Lombardo R. Journal of Wound Ostomy & Continence Nursing, May 2020. .....

12. **Zero CAUTI, zero CLABSI: evaluating the evidence-based effectiveness of a silver, pH acidic, multimodal skin decolonizing wipe to reduce catheter associated urinary tract infection and central line blood stream infections in the ICU setting: a retrospective review.** Saiyed A. Tenet Health - Medical Center of Modesto,2020. .....

13. **Preventing hospital acquired clostridium difficile infection in ICU patients: the efficacy of Theraworx, a novel silver-based cleanser.** Mupo P, Fischer H, Dhansew T, Masih M, Collins A, Orlov V. Journal of Critical Care Nursing, 2019.....

Clinical Evidence - Listing of all Studies (Full Studies available at www.hcp.theraworxprotect.com/learn-all)

14. **Innovative "Eco-Friendly" skin care formulation reduces nosocomial associated CAUTI rates when used for insertion and maintenance of urinary catheters.** George A Turini III M.D, MSc., Joseph F. Renzulli II M.D., Department of Urology - Section of Minimally Invasive Urologic Surgery.....

15. **Theraworx Skin Care Formulation Reduces Nosocomial Associated CAUTI Rates When Used For Urinary Catheter Insertion and Maintenance**
Renzulli J, Journ of Clin and Med Investg. Vol 2(2): 1-3 .....

17. **Strategies to Prevent Urinary Tract Infection from Urinary Catheter Insertion in the Emergency Department**
Journal of Emerg Nursing, 36(6) November 2010 .....

18. **CLABSI Reduction Seen with Multifactorial Nurse Initiative** John Muir Health, CA. Poster submittal, ANCC Magnet Association, Fall Session, 2017.....

19. **Impact of Theraworx for the Prevention of Catheter-Associated Urinary Tract Infections: Results from John Muir Health Concord**
JusterRet.al.,Posterpresentation.....

20. **Effects of Education and Improved Foley Catheter Care on Nurse's Knowledge and CAUTI**
First Health of the Carolinas, Walters G, Lee J, Riddle L, Poster presentation .....

21. **Preventing Chronic Urinary Tract Infections From Urine and Fecal Incontinence: The Impact of Theraworx**
PetersonHealthcare,PeoriaIL,Posterpresentation.....

22. **Assessing the Efficacy and Cost-Effectiveness of Theraworx Protect to Existing Regimens and Products- a 120- day Intervention: Emergency Department, ICU, SDU, Neuro** Sutter Health Infectious Disease: Jeffery Silvers, MD.....

23. **Equipping Clinicians with Advanced Care Options Leads to Reduction in UTI**
Theraworx Works Wonders Meadowview Health and Rehab Center, Poster presentation, AHCA Spring Session, 2017 .....

24. **Targeting Zero: One Hospital's Journey to Reduce CAUTI** Roser L, Piercy EC, Altpeter, T. Journ. Of Nurs Mgt 18-20 Dec 2014.....

25. **Can't Attribute Uti To Insertion: Utilizing Data to Prevent CAUTI**
University of Washington Medical Center, Smith, N.C., Granich, M., Lein, H., Schipper, A.Poster Presentation, 2018.....

26. **Reducing The Incidence of Clostridium Difficile Infections, Antibiotics and Costs in a Long-Term Cre Setting - A surveillance Experience**
Levindale Hebrew Geriatric Center and Hospital, Susan M Johnston, BSN, CIC Director of Infection Prevention & Control, Poster Presentation, 2018.....

27. **Beyond the Bundles: A Pilot to Evaluate a Silver Based Bathing Product to Reduce Central Line-Associated Bloodstream Infections.**
Lucile Packard Children's Hospital -Stanford Medicine, Lisa Pinner, RN, MSN, CNS, CPON, BMTCN, Rachel Frisch, BSN, BMTCN, Jenna Kruger, CPHQ, and Lianna Marks MD, Poster Presentation June 2021.....

28. **One Year CAUTI Free: A Mutli-Disciplinary Team Approach to Reducing CAUTI in a Pediatric Intensive Care Unit.**
Helen DeVos Children's Hospital Spectrum Health, Jessica McClusky, MSN, RN, CPN, CIC, Poster Presentation 2018.....

Clinical Evidence - Listing of all Studies (Full Studies available at www.hcp.theraworxprotect.com/learn-all)

Wound and Skin Integrity

29. **Effect of an innovative pH lowering wound therapeutic on MMP levels and bacterial biofilm colonization of chronic non-healing wounds.**
Marston W, Schultz G. Poster presentation, Symposium on Advanced Wound Care, Fall 2019. .....

30. **Harnessing the microbiome to rapidly resolve peristomal skin complications.**
Gallagher D, Juergens J. Poster presentation, Symposium on Advanced Wound Care, Spring 2019. .....

31. **Successful healing of IAD when traditional barriers fail using an innovative topical formulation.**
Gallagher D, Miller J. Poster presentation, Symposium on Advanced Wound Care, Fall 2018.....

32. **Non-toxic skin formulation promotes healing of dermatitis and skin injuries that are prone to infection in long-term care facility residents.**
Miller J, Renzulli JF. Annals of Infectious Disease and Epidemiology, November 2016. .....

33. **Novel Skin Care System Helps in Healing Skin Wounds and Other Problematic Skin Disorders in Patients at Long-term Care facilities**
W.O.W.Caseseries(WildonWounds)NationalConfFallsession2016.....

Safety

34. **Cytotoxicity Sensitivity Response in Epi-airway, Epi-gingival, Epi-vaginal, Epi-Intestinal Mucosa: Theraworx Versus Chlorhexidine Gluconate**
Independent Testing by BioScience Laboratories, Phoenix, AZ .....

Organism Studies

35 **Efficacy of a Novel Skin Antiseptic Against Carpapenum-resistant Enterobacteriaceae** American Journ of Infection Control, April 2015 1-3 .....

36.. **Summary of Theraworx Biocompatiblity and Microbial Testing Executive Summary test results**.....

37. **An Evaluation of One Test Product For It's Antimicrobial Properties When Challenged with Three Microorganisms Using An Tn.Vttro Time-Kill**
Candida Auris testing - A time to kill and duration study unpublished, prepared for publication .....

38. **Evaluation of One Test Article for Virucidal Properties Based Upon the ASTM E1052-20 Method. Respiratory Syncytial Virus (RSV)**
Nelson Labs January 2023 .....

Relevant Study Summaries

Full Text Studies Available at

www.hcp.theraworxprotect.com/learn-all

Oklahoma Children's Hospital OU Health

Guidelines for use of Theraworx for Prevention of CLABSI/CAUTI in the NICU

Theraworx is a colloidal silver impregnated wipe shown to safely decrease infectious organisms on the surface of the skin. The wipes also contain the moisturizing ingredients allantoin, aloe, and Vitamin E.

The wipes should be used on infants greater than or equal to 34 weeks gestation who have an indwelling central line (subclavian, UVC, UAC, or PICC) or an indwelling urinary catheter. Infants less than 34 weeks may not have the mature skin structure needed to prevent over absorption of the silver content in the wipes. Do not use on infants with congenital skin disorders such as icthyosis or epidermolysis bullosa.

Theraworx is safe to use on the face and perineum area. Avoid the mouth, eyes and inside of ears. The wipes may replace routine baths for infants with central lines or urinary catheters. If a bath with soap and water is given, apply Theraworx directly after the bath.

CHG bathing wipes should still be used prior to surgery.

Theraworx instructions:

1. Remove any stool prior to using wipes.
2. Move the wipe in circular or back and forth motion across the skin
   - Wipe 1: Use on face, neck, chest, then abdomen
   - Wipe 2: Use on arms, then legs
   - Wipe 3, Use on back
   - Wipe 4: Use on perineum, then buttocks
3. Allow to dry on the skin. Check skin fold to ensure the product dries completely.
4. Once dry, emollient can be applied.

References:

Oranges T, et al. Skin Physiology of the Neonate and Infant: Clinical Implications. Adv Wound Care 2015;4(10):587-595.

Khattak AZ, et al. A randomized controlled evaluation of absorption of silver with the use of silver alginate (Algidex) patches in very low birth weight (VLBW) infants with central lines. J Perinatol 2020;30(5):337-342.).

Kjellin M, Qudeimat A, Browne E, Keerthi D, Sunkara A, Kang G, Winfield A, Giannini MA, Maron G, Hayden R, Leung W, Triplett B, Srinivasan A. Effectiveness of Bath Wipes After Hematopoietic Cell Transplantation: A Randomized Trial. J Pediatr Oncol Nurs. 2020 Nov/Dec;37(6):390-397. doi: 10.1177/1043454220944061. Epub 2020 Jul 24. PMID: 32706285; PMCID: PMC7802025.

Executive Summary

Microbial Testing

1.0 Objective

1.1 The objective of this summary is to briefly delineate the scope of testing that has been conducted to assure the safety and effectiveness of the Theraworx platform.

2.0 Scope

2.1 The scope of this report shall cover the original testing completed as part of the patented process (2002), as well as all subsequent antimicrobial and biocompatibility testing recently conducted.

3.0 References

3.1 AATCC Method 100: Antibacterial Finishes on Textile Materials: Assessment of

3.2 ISO/DIS 10993: Biological evaluation of Medical Devices - Part 1: Evaluation and Testing

4.0 Attachments

4.1 Test reports available upon request.

5.0 Definitions

5.1 Theraworx - A Patented, pH and Hygiene Management System.

6.0 Testing Data

6.1 Original Testing

6.1.1 Antimicrobial Activity Testing

Testing was conducted by Microbiological Consultants, Inc. on behalf of Harod Enterprises, Inc. on January 15, 1998.

Test Organism	ATCC No.	Initial Inoculum	Percent Reduction
E. Coli	11229	2.32×10^3	>99.9%
S. aureus (MRSA)	33591	1.06×10^3	>99.9%
C. albicans	10231	1.06×10^4	>99.9%

6.1.2 Antimicrobial Efficacy Testing

Testing was conducted by Microbiological Consultants, Inc. on behalf of Harod Enterprises, Inc. on June 12, 2000

Test Organism	ATCC No.	Initial Inoculum	Percent Reduction
E. faecalis	29212	1.36×10^4	>99.9%
S. aureus (MRSA)	33591	6.6×10^4	>99.9%

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Executive Summary

Microbial Testing

6.1.3 Antiviral Efficacy Testing

Testing was conducted by Microbiological Consultants, Inc. on behalf of Harod Enterprises, Inc. on July 3, 2000.

Test Organism	Initial Inoculum	Percent Reduction
Influenza A	$1.0 \times 10^{4.5}$	>99.9%
Herpes Simplex	$1.0 \times 10^{4.5}$	>99.9%

6.2 Antimicrobial Testing

6.2.1 AATCC Method 100 Antimicrobial Testing

Testing was conducted by Apptec Laboratories on behalf of Avadim, LLC between September 5, 2007 through June 12, 2008

Test Organism	ATCC No.	Initial Inoculum	Percent Reduction
C. albicans	10231	1.1×10^5	>99.9%
M. luteus	49732	1.1×10^5	>99.9%
C. ammoniagenes	6872	1.7×10^5	>99.9%
S. epidermidis	12228	1.3×10^5	>99.9%
S. aureus (MRSA)	33591	1.3×10^5	>99.99%
Acinetobacter baumannii	15308	1.4×10^6	>99.99%
E. faecalis	51575	1.4×10^6	>99.99%
E. coli	8739	1.6×10^6	>99.99%
P. aeruginosa	9027	1.2×10^6	>99.99%
C. difficile	9689	2.4×10^7	>99.99%
Carbapenem resistant E. Coli	A15667	7.8×10^6	>99.9%
Klebsiella pneumoniae Carbapenem resistant	A15666	7.8×10^4	99.30%

6.2.2 Antimicrobial Efficacy Duration Study

Testing was conducted by St. John's Research Institute on behalf of Avadim, LLC on November 14, 2007. This study was based upon a one-time application of collegen and re-inoculated at various time periods.

Time	Test Organism	Initial Inoculum	Percent Reduction
15 minutes	S. aureus (MRSA)	3.0×10^5	>99%
30 minutes	S. aureus (MRSA)	3.0×10^5	>99%
60 minutes	S. aureus (MRSA)	3.0×10^5	>99%
120 minutes	S. aureus (MRSA)	3.0×10^5	>99%
180 minutes	S. aureus (MRSA)	3.0×10^5	>99%

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Executive Summary

Microbial Testing

6.3 Biocompatability Testing

6.3.1 Outline

Theraworx has been subject to *in vitro* and *in vivo* biocompatibility testing (ISO Intracutaneous Reactivity Test, ISO Acute Systemic Injection Test, ISO Guinea Pig Maximization Sensitization Test, and MEM-Elution using L-929 Mouse Fibroblast Cells(ISO) (Cytotoxicity)). These tests support the safe use of TheraworxTM in contact with breached or compromised skin.

6.3.2 MEM Elution Using L-929 Mouse Fibroblast Cells (ISO) (Cytotoxicity)

6.3.1.1 Reference:	ISO 10993-1
6.3.1.2 Report No.	66958
6.3.1.3 Date Tested:	November 9,2007
6.3.1.4 Conducted By:	Apptec Laboratories
6.3.1.5 Results:	Test was considered valid as the control results were within acceptable parameter. The test article PASSED and is considered NON-TOXIC under the test conditions employed.

6.3.3 ISO Intracutaneous Reactivity Test

6.3.2.1 Reference:	ISO 10993-1
6.3.2.2 Report No.	66959
6.3.2.3 Date Tested:	December 10,2007
6.3.2.4 Conducted By:	Apptec Laboratories
6.3.2.5 Results:	The test article is considered a NON-IRRITANT.

6.3.4 ISO Acute Systemic Injection Test

6.3.3.1 Reference:	ISO 10993-1
6.3.3.2 Report No.	101611
6.3.3.3 Date Tested:	February 11,2008
6.3.3.4 Conducted By:	Apptec Laboratories
6.3.3.5 Results:	No potential toxic effects as a result of a single-dose systemic injection were observed; test article PASSED the test.

6.3.5 ISO Guinea Pig Maximization Sensitization Test

6.3.4.1 Reference:	ISO 10993-1
6.3.4.2 Report No.	101612
6.3.4.3 Date Tested:	March 13, 2008
6.3.4.4 Conducted By:	Apptec Laboratories
6.3.4.5 Results:	None of the test animals challenged with the test article extracts were observed with a sensitization response greater than "0". Test article did NOT elicit a sensitization response.

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American Journal of Infection Control- 0196-6553/ https://doi.org/10.1016/j.ajic.2018.04.232

Efficacy and safety of a novel skin cleansing formulation versus chlorhexidine gluconate

Daryl S. Paulson PhD a, Robert Topp RN, PhD b,*, Robert E. Boykin MD, RN, PhD c, Gregory Schultz PhD d, Qingping Yang MS

BACKGROUND

Health care–associated infections (HAIs) continue to plague patients in the United States. Annually, there are >1.7 million HAIs in the United States resulting in almost 100,000 deaths and costs to the medical care system of $6.5 billion. The Centers for Disease Control and Prevention estimate that 1 in 25 patients will contract an HAI during their inpatient hospitalization, underscoring the need for novel prevention strategies. The recent ompendium of strategies to prevent HAIs strongly recommends the use of topical antiseptics for HAI risk reduction in acute care settings. Chlorhexidine gluconate (CHG) has been widely used as an antiseptic for decolonizing the skin before surgery and for daily bathing while hospitalized because of its proven immediate and persistent antimicrobial activity after skin application. However, not all trials have been positive,8 and reports have implicated CHG in cases of site irritation, allergic and anaphylactic reactions, and patient discomfort. This is problematic, particularly for already compromised skin. Further, continued antimicrobial resistance has been documented, suggesting greater control may be necessary from an antimicrobial stewardship perspective. In particular, establishing antisepsis in the inguinal area before urinary catheter insertion is important in preventing urinary tract infections. Because of this, it is important to continue to explore skin antiseptics that provide broad-spectrum antimicrobial activity. The objective of this study was to evaluate if a novel, multi-ingredient surfactant colloidal silver technology was noninferior to a commonly used 4% CHG containing skin antiseptic in terms of immediate and persistent antimicrobial activity.

Test period

Clinical efficacy testing was performed based on procedures outlined in the Food and Drug Administration's (FDA) Tentative Final Monograph9 and the ASTM Method E1173-15 for a simulated preoperative skin preparation.

Statistical Analysis

Table 1
Results from 10-minute kill studies

Product	Sample size	Recovery	Average treatment effect	95% Confidence interval (upper limit)
Colloidal silver	40	3.83 (0.82)	0.21	0.58
4% CHG	41	3.64 (0.96)		

CHG, chlorhexidine gluconate.

Table 2
Results from 6-hour kill studies

Product	Sample size	Recovery	Average treatment effect	95% Confidence interval (upper limit)
Colloidal silver	40	3.49 (0.97)	0.18	0.61
4% CHG	41	3.34 (1.18)		

RESULTS

A total of 40 subjects were enrolled and tested in the colloidal silver arm and 41 were enrolled in the 4% CHG arm. For efficacy 10 minutes after application, the mean recovery for the colloidal silver product was 3.83, whereas the mean recovery for the 4% CHG was 3.64. The average treatment effect was 0.21, with the upper limit of the 95% CI at 0.58. Because the upper bound of the 95% CI for the noninferior statistic was 0.58 (Table 1), this was lower than 0.65, so the colloidal silver was noninferior to the 4% CHG. For efficacy of the 6-hour time point, the mean for the recovery of the colloidal silver was 3.49 and for the 4% CHG it was 3.34. The average treatment effect was 0.18. The upper bounds of the 95% CI was 0.61, which was within the limit of 0.65, so the colloidal silver was noninferior to the 4% CHG (Table 2).

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Major Article

Efficacy and safety of a novel skin cleansing formulation versus chlorhexidine gluconate

Daryl S. Paulson PhD [a], Robert Topp RN, PhD [b,*], Robert E. Boykin MD [c], Gregory Schultz PhD [d], Qingping Yang MS [e]

[a] BioScience Laboratories, Inc, Bozeman, MT
[b] Hahn School of Nursing and Health Sciences, University of San Diego, San Diego, CA
[c] Sports Medicine and Shoulder Surgery Blue Ridge Bone and Joint/EmergeOrtho, Asheville, NC
[d] Department of Obstetrics and Gynecology, University of Florida, Gainesville, FL
[e] Institute for Wound Research, University of Florida, Gainesville, FL

Key Words:
Health care–associated infections
colloidal silver
chlorhexidine gluconate
noninferiority study

Background: This study evaluated whether a multi-ingredient surfactant colloidal silver technology was noninferior to a 4% chlorhexidine gluconate (CHG) antiseptic on immediate and persistent antimicrobial activity.
Methods: The inguinal regions of 81 healthy adults were demarcated into 4 quadrants, and 3 were used for testing each product at baseline, 10 minutes, and 6 hours postapplication. The log of the number of colony forming units was obtained using a cylinder sampling technique. The 95% confidence interval of the test product to the control product with a margin of 0.65 was established as the upper limit of noninferiority.
Results: A total of 81 individuals were enrolled. The colloidal silver product was found to be noninferior to 4% CHG at both 10 minutes and 6 hours postapplication.
Conclusions: The colloidal silver-based product was noninferior to the 4% CHG product at 10 minutes and 6 hours postapplication.

BACKGROUND

Health care–associated infections (HAIs) continue to plague patients in the United States. Annually, there are >1.7 million HAIs in the United States resulting in almost 100,000 deaths and costs to the medical care system of $6.5 billion.[1] The Centers for Disease Control and Prevention estimate that 1 in 25 patients will contract an HAI during their inpatient hospitalization,[2] underscoring the need for novel prevention strategies.

The recent compendium of strategies to prevent HAIs strongly recommends the use of topical antiseptics for HAI risk reduction in acute care settings.[3] Chlorhexidine gluconate (CHG) has been widely used as an antiseptic for decolonizing the skin before surgery and for daily bathing while hospitalized[4-6] because of its proven immediate and persistent antimicrobial activity after skin application.[7] However, not all trials have been positive,[8] and reports have implicated CHG in cases of site irritation, allergic and anaphylactic reactions, and patient discomfort.[9-11] This is problematic, particularly for already compromised skin. Further, continued antimicrobial resistance has been documented,[12,13] suggesting greater control may be necessary from an antimicrobial stewardship perspective.[14,15] In particular, establishing antisepsis in the inguinal area before urinary catheter insertion is important in preventing urinary tract infections.[16] Because of this, it is important to continue to explore skin antiseptics that provide broad-spectrum antimicrobial activity.

The objective of this study was to evaluate if a novel, multi-ingredient surfactant colloidal silver technology was noninferior to a commonly used 4% CHG containing skin antiseptic in terms of immediate and persistent antimicrobial activity.

MATERIALS AND METHODS

This was a noninferiority study evaluating the antimicrobial activity of 2 products, a surfactant, multi-ingredient colloidal silver technology (Theraworx Specialty Care Pack; Avadim Technologies, Asheville, NC) and a 4% CHG antiseptic (Hibiclens; Molnlycke Health

* Address correspondence to Robert Topp, PhD, RN, BINR 325, Hahn School of Nursing and Health Sciences, University of San Diego, 5998 Alcala Park, San Diego, CA 92110.
E-mail address: rtopp@sandiego.edu (R. Topp).
Conflicts of interest: None to report.

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Care, Norcross, GA), with respect to immediate and persistent antimicrobial activity on the skin. This study was conducted to identify if the colloidal silver technology was an effective antiseptic and could be used prior to insertion of a urinary catheter to clean the inguinal area.

Pretest period

The 14 days prior to the test portion of the study was defined as the pretest period. During this time, subjects avoided using medicated soaps, lotions, deodorants, shampoos, and skin contact with solvents, detergents, acids and bases, or any other products known to affect the normal microbial populations of the skin.

Baseline screening sampling and inclusion and exclusion criteria

Adult subjects ≥18 years of age were invited to participate and were recruited using a convenience sample at Bioscience Laboratories, Bozeman, Montana, between January 10, 2017, and January 30, 2017. Inclusion criteria included the following: (1) ability to read and provide written informed consent; (2) in good health without a medical diagnosis of a current or recent severe illness, medicated or controlled diabetes, hepatitis B or C virus infection, prior organ transplant, mitral valve prolapse with heart murmur, fibromyalgia, ulcerative colitis, Crohn disease, or an immunocompromised condition, such as HIV infection, lupus, or medicated multiple sclerosis; (3) skin within 15.24 cm of the test sites free from tattoos, dermatoses, abrasions, cuts, lesions or other skin disorders; and (4) minimal hair density at test sites. Skin samples were taken on the day after the pretest period using the cylinder sampling technique in the center of the sampling areas at the inguinal evaluation sites. A minimum of 72 hours elapsed between the end of the screening period and the beginning of the experimental period. Baseline criteria for including the inguinal site consisted of ≥5.0 $\log_{10}$ and ≤7.5 $\log_{10}$ colony forming units (CFU)/cm^2. Failure to document these counts resulted in exclusion from the study.

Cylinder sampling techniques

A sterile cylinder (Fig 1, marker A) with an inside area of 3.46 cm^2 was held firmly onto the test site for sampling. Three milliliters of sterile stripping fluid with product neutralizers (SSF++) (1.167% w/v lecithin, consumer grade; 10.0% v/v Polysorbate 80 [bioWORLD]; 0.04% w/v KH_2PO_4 [Sigma Aldrich]; 1.01% w/v Na_2HPO_4 [Sigma Aldrich]; 0.01% v/v Triton X-100 [JT Baker]; 0.5% w/v sodium thiosulfate pentahydrate [Sigma Aldrich]; 0.1% v/v Tamol SN [Rohm Haas], 1.25 mL Butterfield's Phosphate Buffer Diluent Stock Solution [3.4% w/v KH_2PO_4; Sigma Aldrich], pH 7.8-7.9; Bioscience Laboratories, Bozeman, MT) was placed into the cylinder, and the skin area inside the cylinder was massaged in a circumferential manner for 1 minute with a sterile rubber policeman (Fig 1, marker B). The SSF++ was removed with a sterile pipette and transferred into a sterile test tube. A second 3.0-mL aliquot of SSF++ was placed into the cylinder and completed in the same manner, therefore pooling the aliquots for microbial enumeration.

Test period

Clinical efficacy testing was performed based on procedures outlined in the Food and Drug Administration's (FDA) Tentative Final Monograph[9] and the ASTM Method E1173-15 for a simulated preoperative skin preparation.[10]

Fig 1. Cylinder sampling technique. Marker A shows the cylinder, and marker B shows the rubber-tipped policeman.

On each subject's inguinal region, 4 areas were demarcated (2 × 5 in) using a sterile surgical marker, on each inguinal side. Only 3 of the 4 sites were sampled (one at baseline, one at 10 minutes, and one at 6 hours). All areas were chosen visually to be of similar physical condition. Bilaterally, 2 areas (one for each product) were used for testing. Products under evaluation were randomly allocated using a computer-generated randomization scheme for each of the inguinal test sites, such that both products were used on each subject. Sites were sampled for microbial loads 10 minutes ± 30 seconds postproduct application using the cylinder sampling technique. The 6-hour sites were covered with sterile gauze and semi-occlusive bandages and were sampled 6 hours ± 30 minutes after product application using the cylinder sampling technique.

Diluting and plating

Aliquots of the microorganism suspension (10^0 dilution) were serially diluted in Butterfield's Phosphate Buffer Solution with product neutralizers (1.167% w/v lecithin, consumer grade; 10.0% v/v Polysorbate 80 [BioWORLD, Irving, TX]; 0.0523% w/v KH_2PO_4 [Sigma Aldrich]; 1.673% w/v K_2HPO_4 [EMD Chemicals]; 0.01% v/v Triton X-100 [JT Baker, Pittsburgh, PA]; 0.5% w/v sodium thiosulfate pentahydrate [Sigma Aldrich, Milwaukee, WI]; 0.1% v/v Tamol SN [Rohm Haas, Philadelphia, PA]; 1.25 mL Butterfield's Phosphate Buffer Diluent Stock Solution [3.4% w/v KH_2PO_4; Sigma Aldrich]; pH 7.8-7.9; Bioscience Laboratories), as appropriate. Duplicate pour plates were prepared from each of these dilutions on tryptic soy agar with neutralizers for each product (Tryptic Soy Agar with Lecithin and Polysorbate 80; Hardy Diagnostics CRITERION Tryptic Soy Agar with 0.07% w/v Lecithin and 0.5% w/v Tween 80; Bioscience Laboratories) and incubated at 30°C ± 2°C for approximately 72 hours. Microbial colonies were manually counted, and data were recorded on data collection forms.

Statistical analyses

The estimated $\log_{10}$ number of viable microorganisms per square centimeter recovered from each sample site was designated as the *R* value. To convert the volumetric sample measurement into the number of CFU per square centimeter, the following formula was used:

$$R = Log_{10}\left[\frac{F\left(\frac{\sum_{i=1}^{n} c_i}{n}\right)10^{-D}}{A}\right]$$

where *R* is the average CFU count in the $\log_{10}$ scale per square centimeter of sampling surface; *F* is the total number of milliliters of stripping fluid added to the sampling cylinder (in this study, $F = 6$ mL); $\frac{\sum_{i=1}^{n} c_i}{n}$ is the average of the duplicate colony counts used for each sample collected; *D* is the dilution factor of the plate counts; and *A* is the inside area of the cylinder in square centimeters (in this study, $A = 3.46$ cm^2).

Counts of <1 CFU/cm^2 were treated as 1 CFU/cm^2, so that the $\log_{10}$ transformation was zero instead of a negative number. The *R* values were the values used in this study for baseline, 10 minutes, and 6 hours.

A noninferiority test required by the FDA[17] was conducted for both immediate (10 minutes) and persistent (6 hours) activity. If the upper limits of the 95% confidence interval (CI) of the average treatment effect (colloidal silver minus 4% CHG), estimated by a multiple linear regression, was equal to or below the noninferiority margin (0.65), noninferiority was established. The multiple regression equation used was the $\log_{10}$ recovery data as the dependent variable and the $\log_{10}$ baseline count as the continuous predictor variable and the two products as the categorical predictor variables. The 2 products as the qualitative independent variable were also in the model. The equation used is as follows:

$$\hat{y} = b_0 + b_1x_1 + b_2x_2 + e$$

where $\hat{y}$ is the $\log_{10}$ recoveries; b_0 is the standard *y* intercept; b_1 and b_2 are the computed values using the least squares method; x_1 is the $\log_{10}$ baseline value; $x_2 = 1$, if the test product (colloidal silver) was used, and $x_2 = 0$, if the control product (Hibiclens) was used; and *e* is the error term.

Minitab version 18 (Minitab, State College, PA) was used for analysis.

RESULTS

A total of 40 subjects were enrolled and tested in the colloidal silver arm and 41 were enrolled in the 4% CHG arm. For efficacy 10 minutes after application, the mean recovery for the colloidal silver product was 3.83, whereas the mean recovery for the 4% CHG was 3.64. The average treatment effect was 0.21, with the upper limit of the 95% CI at 0.58. Because the upper bound of the 95% CI for the noninferior statistic was 0.58 (Table 1), this was lower than 0.65, so the colloidal silver was noninferior to the 4% CHG. For efficacy of the 6-hour time point, the mean for the recovery of the colloidal silver was 3.49 and for the 4% CHG it was 3.34. The average treatment effect was 0.18. The upper bounds of the 95% CI was 0.61, which was within the limit of 0.65, so the colloidal silver was noninferior to the 4% CHG (Table 2).

Table 1
Results from 10-minute kill studies

Product	Sample size	Recovery	Average treatment effect	95% Confidence interval (upper limit)
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4% CHG	41	3.64 (0.96)		

CHG, chlorhexidine gluconate.

Table 2
Results from 6-hour kill studies

Product	Sample size	Recovery	Average treatment effect	95% Confidence interval (upper limit)
Colloidal silver	40	3.49 (0.97)	0.18	0.61
4% CHG	41	3.34 (1.18)		

CHG, chlorhexidine gluconate.

DISCUSSION

This study indicates that a novel, multi-ingredient colloidal silver-based skin cleanser and antiseptic was noninferior to a 4% CHG-based agent with respect to recovery in microbial flora in the inguinal region at 10 minutes and 6 hours. Therefore, it could be used as a replacement for common uses of 4% CHG-based skin antiseptics, particularly in the inguinal region.

For the 10-minute time point, upper limit of the 95% confidence interval was 0.58, well within the error margin of 0.65. For the 6-hour time point, the upper limit of the 95% confidence interval was 0.61, again well within the limit of 0.65. However, because only 40 and 41 subjects were used, the 95% CI was very wide. Had more subjects been used in this study, it would have narrowed the 95% CI to be within the 0.5 limit, which is customarily used.

One important implication of these results stems from the recent guidance from the FDA that CHG-containing products have greater safety concerns. This rule took effect December 20, 2017.[18] Given the many facilities using CHG for various practices from peri-care to daily bathing, this change in the protocol substantially impacts daily practice. Given the limited alternatives to CHG, the results of this study suggest that this colloidal silver-containing product may be a suitable replacement.

The results of this study regarding the efficacy of the test product are supported by other studies showing its efficacy against various microorganisms such as carbapenem-resistant *Enterobacteriaceae*.[19] Additional work conducted by Schultz et al[20] at the University of Florida Institute for Wound Research confirmed the test formulation has demonstrated activity against mature biofilms (methicillin-resistant *Staphylococcus aureus* and *Pseudomonas* sp). Furthermore, the product includes several active ingredients that result in an antiseptic effect by multiple purported mechanisms. The acidic pH enhances the skin's permeability barrier by activating a suite of enzymes that generate lipids that mediate this function.[21] Finally, the low pH also enhances the skin's cohesion, adhesion, and integrity by downregulating another group of enzymes that leads to the shedding of the stratum corneum that becomes activated in high pH environments, such as incontinence-associated dermatitis or moisture-associated skin damage. A more cohesive stratum corneum, replete with intercellular lipids, prevents the penetration of pathogens into the skin.[21]

The pH of the colloidal silver product is acidic (4.6-4.8), mimicking the pH of normal skin. This acidic characteristic can be attributed to its citrus-based ingredient. Undiluted grapefruit extract or Citricidal (GSE, Ripton, VT), which is enriched in citric acid, exhibits a pH of 2.0-3.0, which is designed to support the naturally acidic environment of the skin. In a prior review,[22] the authors concluded that Citricidal displays antimicrobial activity against a wide variety of gram-negative and gram-positive organisms, even at low concentrations (1:128), specifically by disrupting the integrity of the pathogen cell membranes. In a more recent comprehensive review of the literature, Nagoba et al[17] concluded that topical applications of various, mildly acidic compounds, such as citric acid, facilitate the health of the skin cells and accelerate wound healing by controlling wound infection, increasing antimicrobial activity, altering protease activity, releasing oxygen, reducing the toxicity of bacterial end products, and enhancing epithelialization and angiogenesis. Therefore, the grapefruit extract supports the acid mantle of the skin by inhibiting colonization of skin by pathogens, while simultaneously facilitating the growth of the skin's normal healthy microbiome.

CONCLUSIONS

The results of this study indicate that the colloidal silver-based product was noninferior to the 4% CHG product for the immediate sample time of 10 minutes and at the persistent sample time of 6 hours. This product may be an alternative to topical CHG, particularly for inguinal site care in hospitalized settings.

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Effectiveness of Bath Wipes After Hematopoietic Cell Transplantation: A Randomized Trial- St Jude Children's

Margie Kjellin, MSN1, Amr Qudeimat, MD1, Emily Browne, DNP1,
Dinesh Keerthi, MS1, Anusha Sunkara, MS1, Guolian Kang, PhD1,
Alicia Winfield, CRRP1, Mary Anne Giannini, MT1, Gabriela Maron, MD1,
Randall Hayden, MD1, Wing Leung, MD, PhD1,2, Brandon Triplett, MD1,2,
and Ashok Srinivasan, MD1,2

Abstract:

Objective: Bacteremia is a leading cause of morbidity and mortality in children undergoing hematopoietic cell transplantation (HCT). Infections of vancomycin-resistant enterococci (VRE) and multidrug resistant (MDR) gram negative rods (GNRs) are common in this population. Our objective was to assess whether experimental bath wipes containing silver were more effective than standard bath wipes containing soap at reducing skin colonization by VRE and MDR GNRs, and nonmucosal barrier injury bacteremia.

Study Design: Patients undergoing autologous or allogeneic HCT in a tertiary referral center were randomized to receive experimental or standard bath wipes for 60 days post-HCT. Skin swabs were collected at baseline, discharge, and day +60 post-HCT. The rate of VRE colonization was chosen as the marker for efficacy.

Results: Experimental bath wipes were well tolerated. Before the study, the rate of colonization with VRE in HCT recipients was 25%. In an interim analysis of 127 children, one (2%) patient in the experimental arm and two (3%) in the standard arm were colonized with VRE. Two (3%) patients had nonmucosal barrier injury bacteremia in the standard arm, with none in the experimental arm. MDR GNRs were not isolated. The trial was halted because the interim analyses indicated equivalent efficacy of the two methods.

Conclusions: VRE colonization was substantially lower than the 25% incidence noted in the pre-study period in patients using soap and water for bathing. CLABSI rates were also substantially lower compared with previously published St. Jude reports of an 8% risk of CLABSI in the first 28 days after allogeneic and autologous HCT, predominantly due to non-MBI bacteremia in patients using soap and water for bathing Srinivasan et al., 2013;
Srinivasan et al., 2014).

Satisfaction Data

Variable	Overall (n = 127)	Experimental (n = 61)	Standard (n = 66)	p value
Patients completing survey	78 (61)	42 (69)	36 (55)	.11
Did your child experience skin irritation as a result of using the wipes?				.85
Moderate	1 (1)	1 (1)	0 (0)	
Minimal	9 (7)	4 (7)	5 (8)	
None	68 (53)	37 (61)	31 (47)	
How easy were the bath wipes to use?				.15
Neither easy nor difficult	1 (1)	1 (1)	0 (0)	
Easy	19 (15)	13 (22)	6 (9)	
Very easy	58 (45)	28 (46)	30 (46)	
How often did you use the bath wipes?				.84
Some days	8 (6)	5 (8)	3 (5)	
Most days	25 (20)	14 (23)	11 (17)	
Every day	45 (35)	23 (38)	22 (33)	
How satisfied were you with the feel of the wipes on your child's skin?				.65
Very dissatisfied	1 (1)	0 (0)	1 (1)	
Neither satisfied nor dissatisfied	11 (8)	5 (8)	6 (9)	
Satisfied	31 (24)	16 (26)	15 (23)	
Very satisfied	35 (28)	21 (35)	14 (22)	
How well do you think the wipes cleaned your child's skin?				.21
Poorly	3 (2)	0 (0)	3 (5)	
Moderately well	8 (6)	6 (10)	2 (3)	
Well	28 (22)	15 (25)	13 (20)	
Very well	39 (31)	21 (34)	18 (27)	

Note. Data are number of patients (%), unless otherwise indicated.

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Effectiveness of Bath Wipes After Hematopoietic Cell Transplantation: A Randomized Trial

Margie Kjellin, MSN[1], Amr Qudeimat, MD[1], Emily Browne, DNP[1], Dinesh Keerthi, MS[1], Anusha Sunkara, MS[1], Guolian Kang, PhD[1], Alicia Winfield, CRRP[1], Mary Anne Giannini, MT[1], Gabriela Maron, MD[1], Randall Hayden, MD[1], Wing Leung, MD, PhD[1,2], Brandon Triplett, MD[1,2], and Ashok Srinivasan, MD[1,2]

Abstract

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Keywords

hematopoietic stem cell transplantation (HSCT), infection, pediatric, safety

Introduction

Health care–associated infections have substantial morbidity, mortality, and cost burden in children undergoing hematopoietic cell transplantation (HCT; Dandoy et al., 2016; Srinivasan et al., 2013; Wilson et al., 2014). The incidence of colonization with vancomycin-resistant enterococci (VRE), and multidrug resistant (MDR) gram-negative rods (GNRs) in HCT recipients is rapidly increasing (Ford et al., 2017; Girmenia et al., 2015). Colonization with VRE and MDR GNRs increases the risk of bacteremia and nonrelapse mortality and decreases overall survival (Bilinski et al., 2016; Ford et al., 2017; Girmenia et al., 2015; Poutsiaka et al., 2007).

Nonmucosal barrier injury (non-MBI) bacteremia is often caused by the patient's own skin flora. Hence, skin decontamination is expected to decrease the risk of infection. Daily bathing with chlorhexidine gluconate compared with standard bathing practices reduced bacteremia in critically ill children (Milstone et al., 2013). However, chlorhexidine is not tolerated by patients with skin graft-versus-host disease (GVHD), which is common after HCT. Increased bacterial resistance to chlorhexidine has been reported (Wand et al., 2017). Strategies to limit pathogen transmission have focused on improving the adherence of health care workers to

[1]St. Jude Children's Research Hospital, Memphis, TN, USA
[2]University of Tennessee Health Science Center, Memphis, TN, USA

Corresponding Author:
Margie Kjellin, Department of Nursing, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS 1540, Memphis, TN 38105-3678, USA.
Email: margie.kjellin@stjude.org

recommended infection control practices. However, these measures require scrupulous adherence by numerous personnel and can be difficult to sustain (Siegel et al., 2007). Levofloxacin prophylaxis has not been effective in reducing bacteremia in children undergoing HCT (Alexander et al., 2018).

The emergence and persistence of MDR GNRs have led to renewed interest in the antimicrobial properties of silver. Silver-coated dressings suppress microbial infection in burn wounds (Yabanoglu et al., 2013). Resistance to silver is uncommon, and these dressings are well tolerated (Klasen, 2000). Therefore, we hypothesized that experimental bath wipes containing silver would be safe and reduce colonization by VRE and MDR GNRs and non-MBI bacteremia in children undergoing HCT.

Method

Study Design

Patients ≤21 years of age on the date of enrollment who were scheduled to undergo an autologous or allogeneic HCT were eligible to participate in a randomized controlled trial (RCT) at St. Jude Children's Research Hospital (St. Jude), Memphis, Tennessee, from October 2014 to September 2017 (both inclusive), which compared experimental and standard bath wipes for skin cleansing. The study excluded females who were pregnant or lactating as well as participants (or parents) who did not provide written informed consent. The study was approved by the St. Jude Institutional Review Board.

The primary objectives were to assess the safety of experimental bath wipes in the first 12 patients enrolled, and skin colonization with VRE and MDR GNRs, and rates of non-MBI bacteremia in all patients. Other objectives included comparing the incidence of acute skin GVHD, and parent and patient satisfaction with experimental and standard bath wipes. Acute skin GVHD was assessed by using consensus criteria (Przepiorka et al., 1995).

The trial was registered under *ClinicalTrials.gov* NCT02241005. Patients were randomized to receive either experimental or standard bath wipes at a 1:1 ratio from the Division of Nursing Research. Investigators, physicians, nurse practitioners, and clinical research staff were blinded to the randomization. Both types of wipes were packaged in a similar manner but differed in texture. Bath wipes were started on the day of admission to the inpatient unit and were used once daily for 60 days post-HCT. They were used on all parts of the body, including areas with abrasions and skin rashes. A single bath wipe was used for a region of the body. Bath wipes were not used on days of thiotepa administration or during radiation therapy. Experimental bath wipes (Theraworx, Avadim Technologies, Inc., Asheville, North Carolina) contained allantoin, colloidal silver, preservatives, vitamin E, aloe, and lauryl glucoside. Standard bath wipes (Comfort bath PBS Wipe Solution, Sage Products, Inc., Cary, Illinois) contained rinse-free soap and lotion. No other method of bathing was used for participants. Wipes were placed in occlusive bags after warming, by a third party to protect blinding. Comfort bath wipes were called "standard" bath wipes to differentiate them from the experimental wipes. Standard of care for nonstudy patients remained bathing with soap and water.

Baseline skin swabs were collected from the axilla and groin before initiating the conditioning regimen. Skin swabs from these two sites were repeated when the patient was discharged from the inpatient unit, and day +60 post-HCT when the patient was taken off study. Patients for whom skin swabs were not collected by the 7-day window period at discharge were considered unevaluable. Skin swabs were collected using a single e-swab (Covance, Nashville, Tennessee). Rectal surveillance cultures were obtained from all patients before admission and weekly until discharge. Blood cultures were obtained for patients with fever with or without neutropenia according to our standard operating procedures. Positive blood cultures from admission until time of discharge were evaluated. Conventional bacteriologic culture media was used. Susceptibility testing was done by the E-test and the automated MIC method.

Satisfaction Survey

A satisfaction survey was administered to the patient and/or legal guardian at the end of the study. Patients and parents documented their compliance with the bath regimen daily by using a diary, which was reviewed daily while inpatient, and weekly while outpatient by nursing staff. Nursing staff received education about the study through a web-based learning module. Competency in the use of bath wipes was validated by a nurse educator. Patients and parent competency in the use of bath wipes was confirmed by direct nursing observation.

Statistical Analysis

The statistical design was an RCT stratified by the type of HCT (autologous vs. allogeneic), and conditioning with total body irradiation versus no total body irradiation. Block randomization with block sizes varying randomly between two and four was used in each stratum. Randomization was performed by the Division of Nursing Research, using the randomization software program developed by the Department of Biostatistics. All randomized and evaluable patients were included in the analyses, consistent with an intention-to-treat principle.

The null hypothesis for efficacy (H_0) was that rates of VRE colonization in HCT patients using the experimental (p_A) and standard bath wipes (p_C) are equal, and the alternative hypothesis (H_1) was that rates of VRE colonization with experimental bath wipes are less than those with standard bath wipes, represented by the formula H_0: $p_A = p_C \leftrightarrow H_1$: $p_A < p_C$. The rate of colonization with VRE in HCT recipients from the date of admission to initial discharge at St. Jude, over a 12-month period, from January 2013 to December 2013 (both months inclusive), was 25% (unpublished data). The standard for cleansing was with soap and water. Using design parameters at a significance level set at $\alpha = .05$ power of 90%, and $p_A = 10\%$, 250 evaluable patients (125 for each group) were required by the one-sided two-sample test for difference of proportions (Cytel, n.d.), assuming one interim analysis to assess efficacy and futility after enrolling 125 patients. The trial was designed to be halted in favor of H_1 if the p value was less than .006, and in favor of H_0 if the p value was greater than .47. If the p value for testing H_0 after study completion was less than .05, the rate of VRE colonization was expected to decrease by at least 15%.

The rate of VRE colonization was chosen as a marker of efficacy since its prevalence was high and colonization is a predictor of bacteremia. Besides monitoring the primary endpoint of VRE colonization, the trial was designed to be stopped if the central line–associated blood stream infection (CLABSI) rate between the two arms was significantly different by the Fischer's exact test.

Descriptive statistics for patients in the experimental and standard arms were reported and compared by the Fischer's exact test. The number and proportion of patients with VRE, MDR GNRs, and non-MBI CLABSI from admission until discharge from the inpatient unit were provided. Colonization was defined as a swab testing positive for VRE or MDR GNRs, with a negative baseline swab. Fischer's exact test was used to test for the null hypothesis. Although the wipes were used for a period of 60 days, VRE colonization and CLABSI rates from admission until discharge were used for statistical analysis. Patients came off study on day +60. If a patient was discharged beyond day +60, day +60 was used as cutoff.

Non-MBI bacteremia was classified according to the Centers for Disease Control and Prevention National Health Safety Network 2019 guidelines (Centers for Disease Control and Prevention, 2019). MBI bacteremia was noted but not analyzed, as it was unlikely to be affected by a skin-cleansing regimen. The use of prophylactic antibiotics and management of fever and neutropenia in both arms from admission until discharge was according to standard operating procedures. The number of patients with acute skin GVHD in the two arms was compared by the Fischer's exact test. For patient and parent satisfaction, measurements were scored on a nominal scale and compared by Fischer's exact or chi-square test, respectively, between the two groups. The p values were two-sided except as noted and were considered significant if $<.05$.

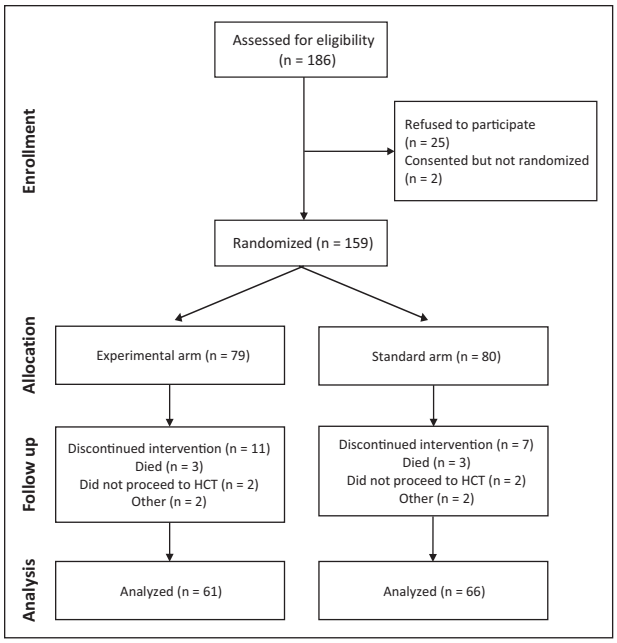

Figure 1. Participant flow diagram.

Results

Patient Characteristics

A total of 186 eligible patients were approached for consent. Of them, 25 declined to participate in the study. These patients used standard bath wipes and/or soap and water for bathing. Two patients gave consent but were not randomized. Of the 159 patients who were randomized, 32 dropped out of the study due to dissatisfaction with the wipes ($n = 18$), death ($n = 6$), not proceeding to HCT ($n = 4$), or other reasons ($n = 4$). The patients who dropped out due to dissatisfaction with the wipes were equally distributed between the two arms ($p = .33$; Figure 1). These patients preferred soap and water for bathing. No patients were lost to follow-up. Thus, a total of 127 patients were analyzed: 61 in the experimental arm and 66 in the standard arm.

Table 1 gives demographic, disease, and treatment characteristics of 127 patients in the experimental and standard arms. Age, ethnicity, gender, diagnosis, remission status, donor and product type, and receipt of multiple HCT were comparable between the two arms. Prophylactic antibiotics (Srinivasan et al., 2013; Srinivasan et al., 2014) and management of febrile episodes in the period between admission and initial discharge did not differ between the two arms. For eight quarters prior to the study, the daily bathing compliance

Table 1. Transplant Characteristics of Patients on Experimental and Standard Study Arm.

Variable	Experimental study arm ($n = 61$)	Standard study arm ($n = 66$)	p value
Age			.20
Mean age at HCT	9.68[a] (6.24)	8.29 (6.18)	
Median	10.01	6.08	
Range	.26-20.95	.43-21.12	
Race			.39
White	41 (67)	42 (64)	
African American	6 (10)	12 (18)	
Other	14 (23)	12 (18)	
Male	27 (44)	37 (56)	.22
Diagnosis			.92
Heme malignancy	38 (62)	45 (68)	
Solid tumor	15 (24)	13 (20)	
Hematologic	4 (7)	4 (6)	
Immunologic	4 (7)	4 (6)	
Remission before HCT	31 (51)	41 (62)	.21
Product			.85
HPC, A	37 (61)	43 (65)	
HPC, M	23 (38)	22 (34)	
HPC, C	1 (1)	1 (1)	
Donor			.57
Haploidentical	20 (33)	28 (43)	
Matched	23 (38)	18 (27)	
Mismatched unrelated	1 (1)	2 (3)	
Autologous	17 (28)	18 (27)	
Myeloablation	32 (52)	29 (44)	.38
Multiple HCT	7 (11)	9 (14)	.79

Note. Data are number of patients (%), unless otherwise indicated. HCT = hematopoietic cell transplantation; HPC = human progenitor cells; A = apheresis; M = marrow; C = cord.
[a]Mean with standard deviation.

was an average of 60%. All patients on study were compliant with use of the wipes in the inpatient unit. For all 127 patients, skin swabs were collected at discharge within the window period; for 103 (81%) patients, skin swabs were collected on day +60.

Safety

Safety was determined by Grade IV skin toxicity (National Cancer Institute Common Terminology Criteria version 3.0) as a result of using wipes that occurred until the time of discharge in the first 12 patients enrolled in the experimental arm. Experimental bath wipes were well tolerated. No patient in either study arm had a skin rash or Grade I skin toxicity attributable to wipes.

Clinical Outcomes

Table 2 summarizes the results of the interim analysis. One (2%) patient in the experimental arm was colonized with VRE. In the standard arm, two (3%) patients were colonized with VRE ($p = 1.0$). There were no patients with non-MBI bacteremia in the experimental arm, and two (3%) with non-MBI bacteremia in the standard arm ($p = .50$). MDR GNRs were not isolated from patients in either arm. The RCT was halted because the interim analyses indicated equivalent efficacy of the two methods. The p value of testing the differences in rates of VRE colonization between the two arms was 1.

Table 2. VRE, MDRO Colonization and Non-MBI Bacteremia in Patients on Experimental and Standard Arms.

	Study arm			
Variable	Experimental ($n = 61$)	Standard ($n = 66$)	p value*	Overall ($n = 127$)
VRE	1 (2)	2 (3)	1	3 (2)
MDRO	0 (0)	0 (0)	NA	0 (0)
Non-MBI CLABSI	0 (0)	2 (3)	.50	2 (2)

Note. VRE = vancomycin-resistant enterococcus; MDRO = multidrug resistant organisms; MBI = mucosal barrier injury; CLABSI = central-line associated blood stream infection.
*p value compares characteristics of patients on experimental and standard study arms.

The two patients with non-MBI bacteremia in the standard arm included a 14-year-old male patient with *Staphylococcus epidermidis* bacteremia on day +9 after a second haploidentical HCT for lymphoma, and an infant with *Pseudomonas aeuroginosa* bacteremia on Day 0 after a haploidentical HCT for relapsed acute lymphoblastic leukemia. Both patients recovered from the bacteremia.

There were eight patients with acute skin GVHD in the experimental arm and nine patients in the standard arm ($p = 1.00$), all Grades I to II in severity. GVHD was manifested as palmar and/or plantar erythema.

Patient and Parent Satisfaction

Patient and parent surveys showed no significant differences in the degree of skin irritation after using wipes, frequency of use of wipes as outpatients, and ease and satisfaction with use of wipes (Table 3). No patient withdrew because of skin irritation related to the use of bath wipes.

There were 24 protocol deviations: discharge swab was missed at the time of discharge but collected within the window period in 10 patients. Two patients consented to the study but were not randomized. The day +60 swab was not collected in another 12 patients who withdrew from the study due to dissatisfaction with the wipes. These patients preferred soap and water for bathing.

Table 3. Survey Data.

Variable	Overall ($n = 127$)	Experimental ($n = 61$)	Standard ($n = 66$)	p value
Patients completing survey	78 (61)	42 (69)	36 (55)	.11
Did your child experience skin irritation as a result of using the wipes?				.85
Moderate	1 (1)	1 (1)	0 (0)	
Minimal	9 (7)	4 (7)	5 (8)	
None	68 (53)	37 (61)	31 (47)	
How easy were the bath wipes to use?				.15
Neither easy nor difficult	1 (1)	1 (1)	0 (0)	
Easy	19 (15)	13 (22)	6 (9)	
Very easy	58 (45)	28 (46)	30 (46)	
How often did you use the bath wipes?				.84
Some days	8 (6)	5 (8)	3 (5)	
Most days	25 (20)	14 (23)	11 (17)	
Every day	45 (35)	23 (38)	22 (33)	
How satisfied were you with the feel of the wipes on your child's skin?				.65
Very dissatisfied	1 (1)	0 (0)	1 (1)	
Neither satisfied nor dissatisfied	11 (8)	5 (8)	6 (9)	
Satisfied	31 (24)	16 (26)	15 (23)	
Very satisfied	35 (28)	21 (35)	14 (22)	
How well do you think the wipes cleaned your child's skin?				.21
Poorly	3 (2)	0 (0)	3 (5)	
Moderately well	8 (6)	6 (10)	2 (3)	
Well	28 (22)	15 (25)	13 (20)	
Very well	39 (31)	21 (34)	18 (27)	

Note. Data are number of patients (%), unless otherwise indicated.

Discussion

Experimental bath wipes constitute a self-drying cleansing agent that combines specialized surfactant and skin-healthy ingredients such as aloe, allantoin, and vitamin E to moisturize and nourish the skin, as well as silver, which has broad-spectrum antimicrobial activity (Yabanoglu et al., 2013). The colloidal silver-based skin cleanser was not inferior to 4% chlorhexidine, as confirmed by log of the number of colony-forming units of viable organisms recovered in the inguinal region of healthy adults (Paulson et al., 2018). Clinical use of experimental bath wipes in children has not been previously reported.

Our RCT showed that the experimental bath wipes were well tolerated in children, and no patient experienced Grade I toxicity. There was no difference in skin colonization with VRE and MDR GNRs, rates of non-MBI bacteremia or the incidence of acute skin GVHD between patients in the two arms. More than half of the patients/parents surveyed expressed satisfaction with the use of the wipes.

The rate of VRE colonization was chosen as a marker of efficacy since its prevalence was high comparable with other studies (Bilinski et al., 2016; Ford et al., 2017). Colonization with vancomycin-resistant enterococci is a significant predictor of bacteremia after HCT (Kamboj et al., 2010; Vydra et al., 2012). Patients with VRE bacteremia have poor 1-year survival (Vydra et al., 2012).

VRE colonization was substantially lower than the 25% incidence noted in the prestudy period in patients using soap and water for bathing. CLABSI rates were also substantially lower compared with previously published St. Jude reports of an 8% risk of CLABSI in the first 28 days after allogeneic and autologous HCT, predominantly due to non-MBI bacteremia in patients using soap and water for bathing (Srinivasan et al., 2013; Srinivasan et al., 2014).

We investigated potential sources of bias. The CLABSI bundle (O'Grady et al., 2011) was implemented in January 2013, 20 months before initiating this study. There were no major changes in infection control practices and antimicrobial stewardship between the prestudy (2013) and the study period (2014-2017). Metronidazole was used for GVHD prophylaxis in all HCT patients and discontinued in April 2016, midway through the study. Rectal surveillance cultures were obtained on all HCT patients before admission and weekly until discharge, both in the prestudy and study period. Additional swabs were obtained on

study patients. Patients who declined to participate in the study used a combination of standard wipes and/or soap and water for bathing, and compliance was poor. Hence, a comparison was not made with patients on study.

It has been shown that VRE colonizes the patients' skin, contaminates environmental surfaces and the hands of health care workers, resulting in dissemination to other patients (Duckro et al., 2005; Sundermann et al., 2019). A prospective single-arm clinical trial reported that cleansing patients with chlorhexidine-saturated cloths was a simple and effective strategy to reduce VRE contamination of patients' skin, leading to a reduction in the incidence of acquiring VRE. There was also lower VRE contamination of environmental surfaces and health care workers' hands than when soap and water baths were used (Vernon et al., 2006). This was confirmed in a multicenter study, where daily bathing with chlorhexidine in intensive care units decreased the rate of acquiring VRE by 50%, with significant reduction in VRE bacteremia (Climo et al., 2009). However, chlorhexidine wipes cannot be used in patients with skin GVHD, which occurred in 13% of our patients. Vernon et al. (2006) demonstrated that chlorhexidine-medicated wipes resulted in significantly fewer patients developing skin breakdown compared with bathing with soap and water. It is possible that skin abrasions with soap and water baths may increase the risk for colonization.

Compliance with the use of bath wipes and parent/patient education in the period between admission and discharge most likely contributed to the effectiveness of the wipes (Page et al., 2016). For eight quarters prior to the study, the daily bathing compliance was an average of only 60%, which increased to 100% for patients on study in the inpatient unit. This nurse-led initiative highlights the impact of improvements to nursing practice (i.e., bath compliance) on nursing-sensitive indicators (i.e., prevention of hospital-acquired infections). The study had the support of nursing leadership, quality of delivery was assessed by conducting direct observations and performing audits, nursing staff underwent sessions in patient education, and feedback was provided.

The strengths of this study include an RCT design with complete follow-up of all patients. Patient-centered outcomes were assessed. The study was blinded to investigators and clinicians in a high-risk population that largely comprised patients with refractory hematologic malignancies and solid tumors, half of whom were not in remission before transplantation, and with 10% to 14% of patients undergoing a second allogeneic HCT. In a recent prospective multicenter study on a similar high-risk population, the overall cumulative incidence of gram-negative bacteremia was 17% at 30 days after allogeneic HCT, and 9% at 20 days after autologous HCT (Girmenia et al., 2017).

A major limitation of this study is the lack of a control arm with soap and water baths, which was the standard for cleansing prior to the trial. However, this would have been beyond the scope of a single institutional study and interfered with blinding. The wipes differed in texture; hence, the study was not completely blinded to the patients and parents. Only 60% of patients and/or parents completed the satisfaction survey.

Conclusion

Experimental bath wipes were well tolerated. No difference was noted in the extremely low rates of skin colonization with VRE and MDR GNRs and rates of non-MBI bacteremia in patients using experimental and standard wipes. Future studies in other high-risk populations are required to confirm these results. Mortality from MDR GNRs and VRE bacteremia is high and may be lowered by implementing the use of wipes instead of soap and water baths if confirmed by other studies, in combination with nursing and family education, pre- and post-HCT rectal and skin surveillance for MDR GNRs, isolation precautions for patients at risk, and use of the CLABSI bundle.

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ORCID iDs

Margie Kjellin https://orcid.org/0000-0002-6138-4920
Emily Browne https://orcid.org/0000-0003-2098-365X

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Author Biographies

Margie Kjellin, MSN, is director of inpatient nursing at St. Jude Children's Research Hospital in Memphis, Tennessee.

Amr Qudeimat, MD, is an assistant member of Bone Marrow Transplant & Cellular Therapy at St. Jude Children's Research Hospital in Memphis, Tennessee.

Emily Browne, DNP, is director of the Transition Oncology Program at St. Jude Children's Research Hospital in Memphis, Tennessee.

Dinesh Keerthi, MS, is a project manager in Bone Marrow Transplant & Cellular Therapy at St. Jude Children's Research Hospital in Memphis, Tennessee.

Anusha Sunkara, MS, worked in biostatistics at St. Jude Children's Research Hospital in Memphis, Tennessee.

Guolian Kang, PhD, is an associate member of biostatistics at St. Jude Children's Research Hospital in Memphis, Tennessee.

Alicia Winfield, CRRP, was a clinical research assistant at St. Jude Children's Research Hospital in Memphis, Tennessee.

Mary Anne Giannini, MT, is a supervisor in Infection Prevention & Control at St. Jude Children's Research Hospital in Memphis, Tennessee.

Gabriela Maron, MD, is an associate member of infectious diseases at St. Jude Children's Research Hospital in Memphis, Tennessee.

Randall Hayden, MD, is a member of pathology at St. Jude Children's Research Hospital in Memphis, Tennessee.

Wing Leung, MD, PhD, was the chair of Bone Marrow Transplant & Cellular Therapy at St. Jude Children's Research Hospital in Memphis, Tennessee.

Brandon Triplett, MD, is an associate member of Bone Marrow Transplant & Cellular Therapy at St. Jude Children's Research Hospital in Memphis, Tennessee.

Ashok Srinivasan, MD, is an associate member of Bone Marrow Transplant & Cellular Therapy at St. Jude Children's Research Hospital in Memphis, Tennessee.

Ensuring Internal Validity of a Bone Marrow Transplant Research Study Through Education and Process Evaluation

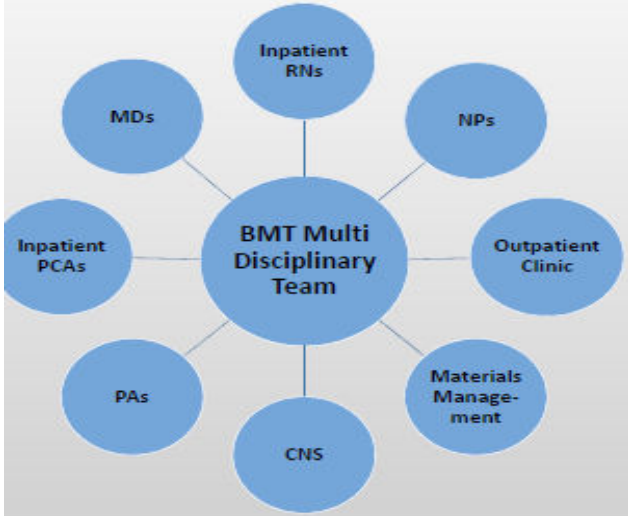
Marty Steed, BSN, RN, Margie Kjellin, MSN, RN, Sara Day, PhD, RN

Background

A nurse driven blinded research protocol was developed to determine if use of a new bath wipe compared to the standard bath wipe could reduce skin colonization with vancomycin-resistant enterococci (VRE) in Hematopoietic Stem Cell Transplant (HSCT) patients. Educating staff and confirming the correct process for using the bath wipes are fundamental to this study's internal validity.

Process

- Plan developed for implementation
- Key departments involved
- Education planned for a multidisciplinary team
- Random Post-enrollment monitoring



Education

Prior to the study implementation, the nursing education department taught pertinent staff that would be using the bath wipes. A variety of didactic and hands on instruction required planning with a multidisciplinary team approach including:

- Protocol responsibilities for the inpatient staff
- Protocol responsibilities for the outpatient staff
- How to maintain blinding for two disposable bath products
- New bath Standard of Care
- Process of daily bathing using wipes
- Documentation of bath with wipes
- Patient/family bath log
- Ordering of discharge bath supplies
- Outpatient
  - ✓ Protocol Consent
  - ✓ Skin swab collection
  - ✓ Review of daily bath diary
  - ✓ Patient satisfaction survey

Evaluation

- In 2015, 12 patients were monitored in the 4 categories, 7 meeting all criteria. Of the 5 who did not, education was provided on site.
- In 2016, 4 additional patients have been monitored, with an additional category. Caregiver teaching was completed during the bath.

Patient	Correct Wipe Chosen	Wipes Concealed	Bath Administered Correctly	Bath Documented Correctly	Bath given by
#1	X	X	X	X	NA
#2	X	X	X	X	NA
#3	X	X	X	X	NA
#4	X	X	NO	X	NA
#5	X	X	X	X	NA
#6	X	X	X	X	NA
#7	X	NO	X	X	NA
#8	X	X	X	X	NA
#9	X	NO	X	X	NA
#10	X	NO	X	X	NA
#11	X	X	X	X	NA
#12	X	NO	X	X	NA
#13	X	X	X	X	PCA
#14	X	X	X	X	PCA
#15	X	NO	NO	X	Parent
#16	X	X	X	X	Grandparent

Conclusion

- Process evaluation is key to ensuring internal validity of research.
- We are continuing to randomly monitor inpatient baths as additional and ongoing education is often required.

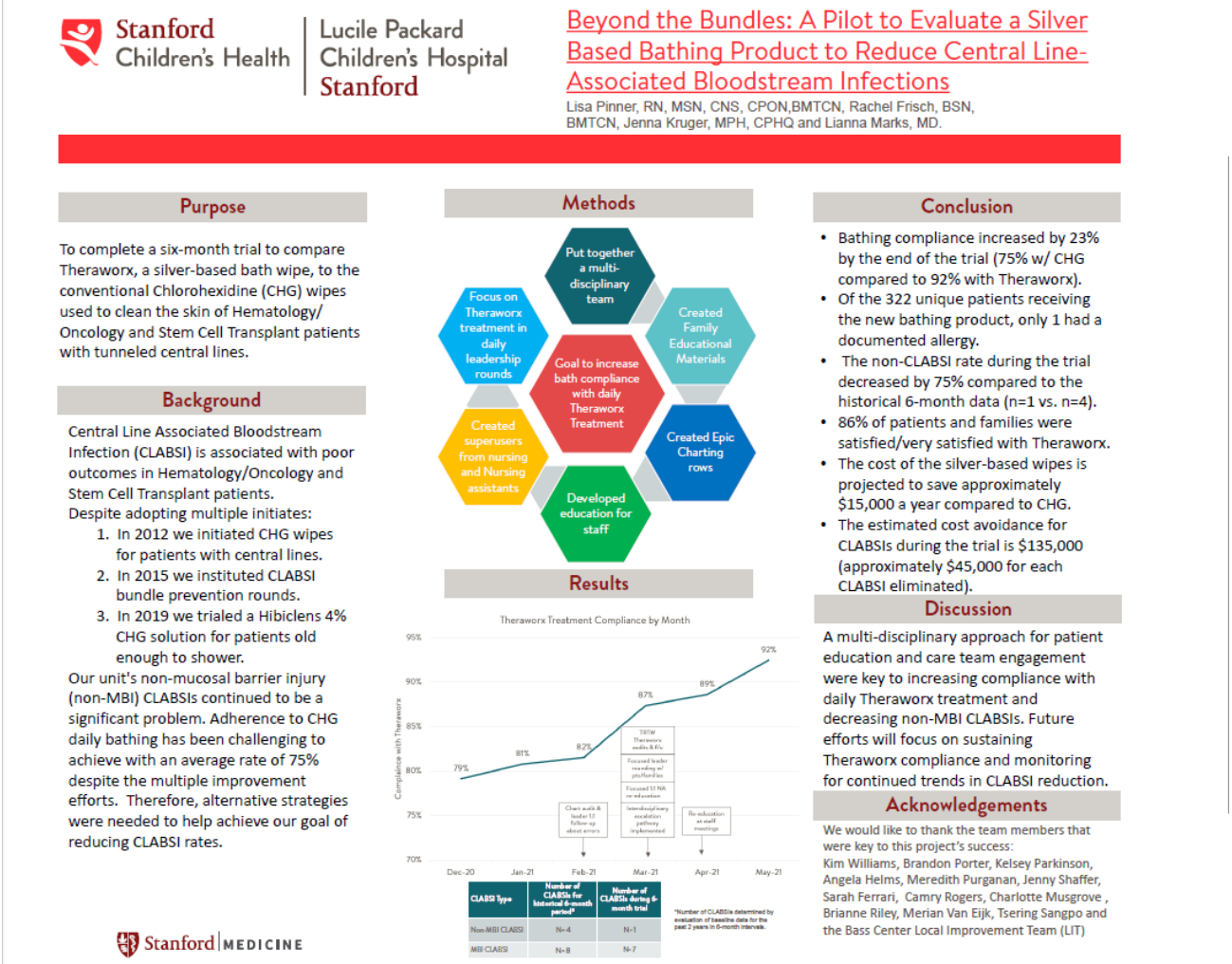
Beyond the Bundles: A pilot to Evaluate a Silver Based Bathing Product to Reduce Central Line-Associated Bloodstream Infections. Lucile Packard Chidren's Hospital Stanford, 2021

Background: Central Line Associated Bloodstream Infection (CLABSI) is associated with poor outcomes in Hematology/Oncology and Stem Cell Transplant patients.
Despite adopting multiple initiates:

1. In 2012 we initiated CHG wipes for patients with central lines.
2. In 2015 we instituted CLABSI bundle prevention rounds.
3. In 2019 we trialed a Hibiclens 4% CHG solution for patients old enough to shower.

Our unit's non-mucosal barrier injury (non-MBI) CLABSIs continued to be a significant problem. Adherence to CHG daily bathing has been challenging to achieve with an average rate of 75% despite the multiple improvement efforts. Therefore, alternative strategies were needed to help achieve our goal of reducing CLABSI rates.

Conclusion: Bathing compliance increased by 23% by the end of the trial (75% w/ CHG compared to 92% with Theraworx).
•Of the 322 unique patients receiving the new bathing product, only 1 had a documented allergy.
•The non-CLABSI rate during the trial decreased by 75% compared to the historical 6-month data (n=1 vs. n=4).
•86% of patients and families were satisfied/very satisfied with Theraworx.
•The cost of the silver-based wipes is projected to save approximately $15,000 a year compared to CHG.
•The estimated cost avoidance for CLABSIs during the trial is $135,000 (approximately $45,000 for each CLABSI eliminated)



Stanford Children's Health | Lucile Packard Children's Hospital Stanford

Beyond the Bundles: A Pilot to Evaluate a Silver Based Bathing Product to Reduce Central Line-Associated Bloodstream Infections

Lisa Pinner, RN, MSN, CNS, CPON,BMTCN, Rachel Frisch, BSN, BMTCN, Jenna Kruger, MPH, CPHQ and Lianna Marks, MD.

Purpose

To complete a six-month trial to compare Theraworx, a silver-based bath wipe, to the conventional Chlorohexidine (CHG) wipes used to clean the skin of Hematology/ Oncology and Stem Cell Transplant patients with tunneled central lines.

Background

Central Line Associated Bloodstream Infection (CLABSI) is associated with poor outcomes in Hematology/Oncology and Stem Cell Transplant patients.
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Methods

Results

CLABSI Type	Number of CLABSIs for historical 6-month period*	Number of CLABSIs during 6-month trial
Non-MBI CLABSI	N=4	N=1
MBI CLABSI	N=8	N=7

*Number of CLABSIs determined by evaluation of baseline data for the past 2 years in 6-month intervals.

Conclusion

- Bathing compliance increased by 23% by the end of the trial (75% w/ CHG compared to 92% with Theraworx).
- Of the 322 unique patients receiving the new bathing product, only 1 had a documented allergy.
- The non-CLABSI rate during the trial decreased by 75% compared to the historical 6-month data (n=1 vs. n=4).
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- The cost of the silver-based wipes is projected to save approximately $15,000 a year compared to CHG.
- The estimated cost avoidance for CLABSIs during the trial is $135,000 (approximately $45,000 for each CLABSI eliminated).

Discussion

A multi-disciplinary approach for patient education and care team engagement were key to increasing compliance with daily Theraworx treatment and decreasing non-MBI CLABSIs. Future efforts will focus on sustaining Theraworx compliance and monitoring for continued trends in CLABSI reduction.

Acknowledgements

We would like to thank the team members that were key to this project's success:
Kim Williams, Brandon Porter, Kelsey Parkinson, Angela Helms, Meredith Purganan, Jenny Shaffer, Sarah Ferrari, Camry Rogers, Charlotte Musgrove , Brianne Riley, Merian Van Eijk, Tsering Sangpo and the Bass Center Local Improvement Team (LIT)

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Methods

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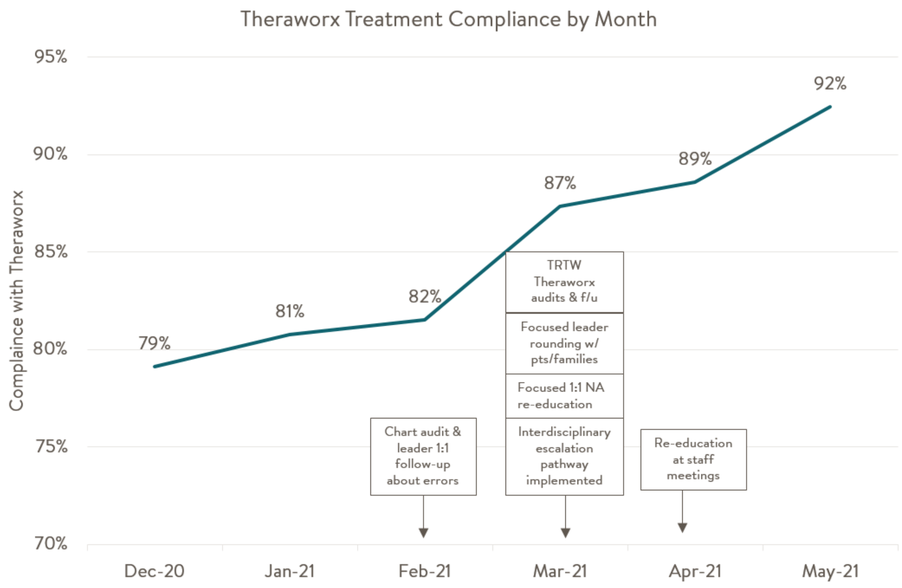

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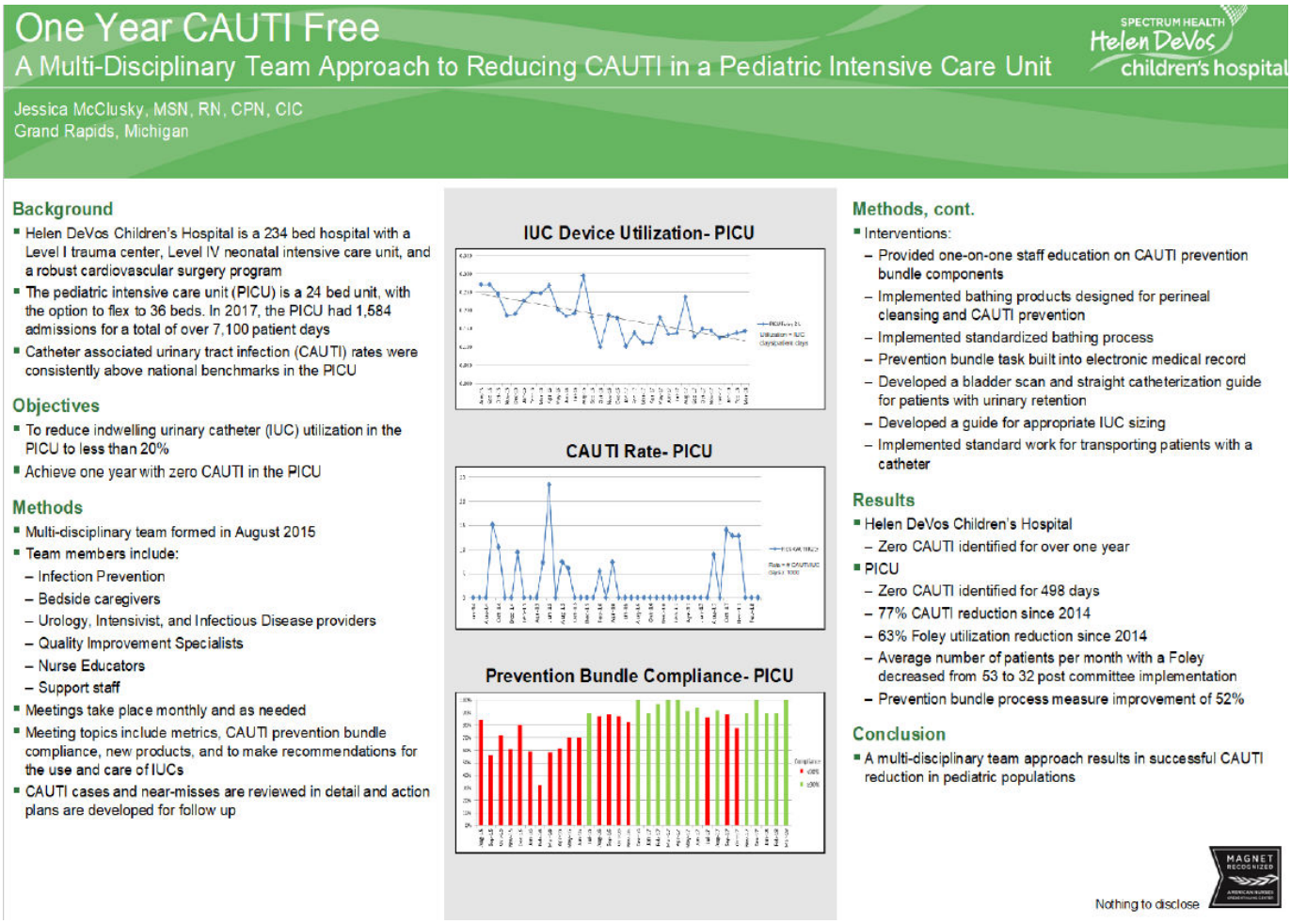
One Year CAUTI Free: A multi-discilinary Team Approach to Reducing CAUTI in a Pediatric ICU. Helen DeVos Children's Hospital Spectrum Health

Background: Helen DeVos Children's Hospital is a 234 bed hospital with a Level I trauma center, Level IV neonatal intensive care unit, and a robust cardiovascular surgery program.
The pediatric intensive care unit (PICU) is a 24 bed unit, with the option to flex to 36 beds. In 2017, the PICU had 1,584 admissions for a total of over 7,100 patient days.
Catheter associated urinary tract infection (CAUTI) rates were consistently above national benchmarks in the PICU.

Conclusion:
Helen DeVos Children's Hospital
Zero CAUTI identified for over one year
- PICU

-Zero CAUTI identified for 498 days
-77% CAUTI reduction since 2014
-3% Foley utilization reduction since 2014
-Average number of patients per month with a Foley decreased from 53 to 32 post committee implementation
Prevention bundle process measure improvement of 52%



One Year CAUTI Free

A Multi-Disciplinary Team Approach to Reducing CAUTI in a Pediatric Intensive Care Unit

Jessica McClusky, MSN, RN, CPN, CIC
Grand Rapids, Michigan

SPECTRUM HEALTH Helen DeVos children's hospital

Background

- Helen DeVos Children's Hospital is a 234 bed hospital with a Level I trauma center, Level IV neonatal intensive care unit, and a robust cardiovascular surgery program
- The pediatric intensive care unit (PICU) is a 24 bed unit, with the option to flex to 36 beds. In 2017, the PICU had 1,584 admissions for a total of over 7,100 patient days
- Catheter associated urinary tract infection (CAUTI) rates were consistently above national benchmarks in the PICU

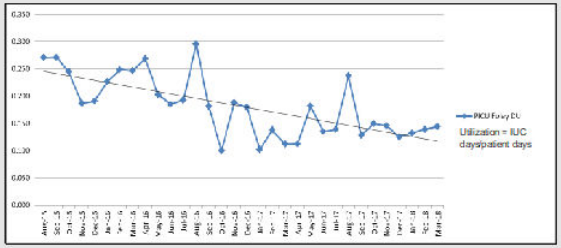
Objectives

- To reduce indwelling urinary catheter (IUC) utilization in the PICU to less than 20%
- Achieve one year with zero CAUTI in the PICU

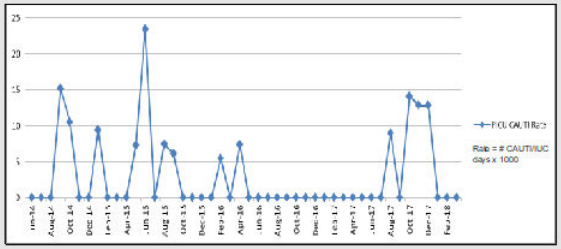
Methods

- Multi-disciplinary team formed in August 2015
- Team members include:
  - Infection Prevention
  - Bedside caregivers
  - Urology, Intensivist, and Infectious Disease providers
  - Quality Improvement Specialists
  - Nurse Educators
  - Support staff
- Meetings take place monthly and as needed
- Meeting topics include metrics, CAUTI prevention bundle compliance, new products, and to make recommendations for the use and care of IUCs
- CAUTI cases and near-misses are reviewed in detail and action plans are developed for follow up

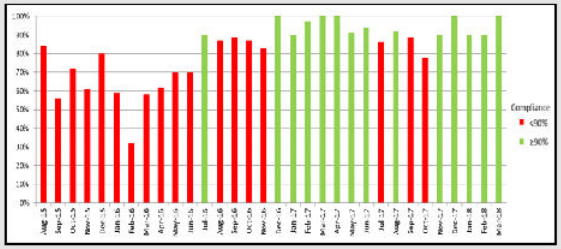
IUC Device Utilization- PICU



CAUTI Rate- PICU



Prevention Bundle Compliance- PICU



Methods, cont.

- Interventions:
  - Provided one-on-one staff education on CAUTI prevention bundle components
  - Implemented bathing products designed for perineal cleansing and CAUTI prevention
  - Implemented standardized bathing process
  - Prevention bundle task built into electronic medical record
  - Developed a bladder scan and straight catheterization guide for patients with urinary retention
  - Developed a guide for appropriate IUC sizing
  - Implemented standard work for transporting patients with a catheter

Results

- Helen DeVos Children's Hospital
  - Zero CAUTI identified for over one year
- PICU
  - Zero CAUTI identified for 498 days
  - 77% CAUTI reduction since 2014
  - 63% Foley utilization reduction since 2014
  - Average number of patients per month with a Foley decreased from 53 to 32 post committee implementation
  - Prevention bundle process measure improvement of 52%

Conclusion

- A multi-disciplinary team approach results in successful CAUTI reduction in pediatric populations

Nothing to disclose

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

Quality Intervention: Hine Veterans Hospital In Patients with Spinal Cord Injury and Brain Trauma

Evaluating the Effectiveness of a Multidimensional Bundle to Reduce Urinary Tract Infection in Longterm Spinal Cord Injury/Disordered Patients: A Retroactive Review

Nancy Chaiken, NP-C, MS, CWOCN, James Pazzaglia, RN,BSN, Binu Polakkattil, MSN,RN.CCRN Whitney Tower-Woods RN, CRRN, Robert Schwartz,MSN,CWOCN, Raphaelle Lombardo PharmD, BCPS

Published Journal of Wound Ostomy Nursing

Background:

Urinary Tract Infections remain the most frequently encountered secondary health condition in the Spinal Cord Injury/Disorder (SCI/D) population that adversely impacts overall health and quality of life. Efforts to reduce CAUTI/UTIs have historically been unsuccessful in this population.

Methods:

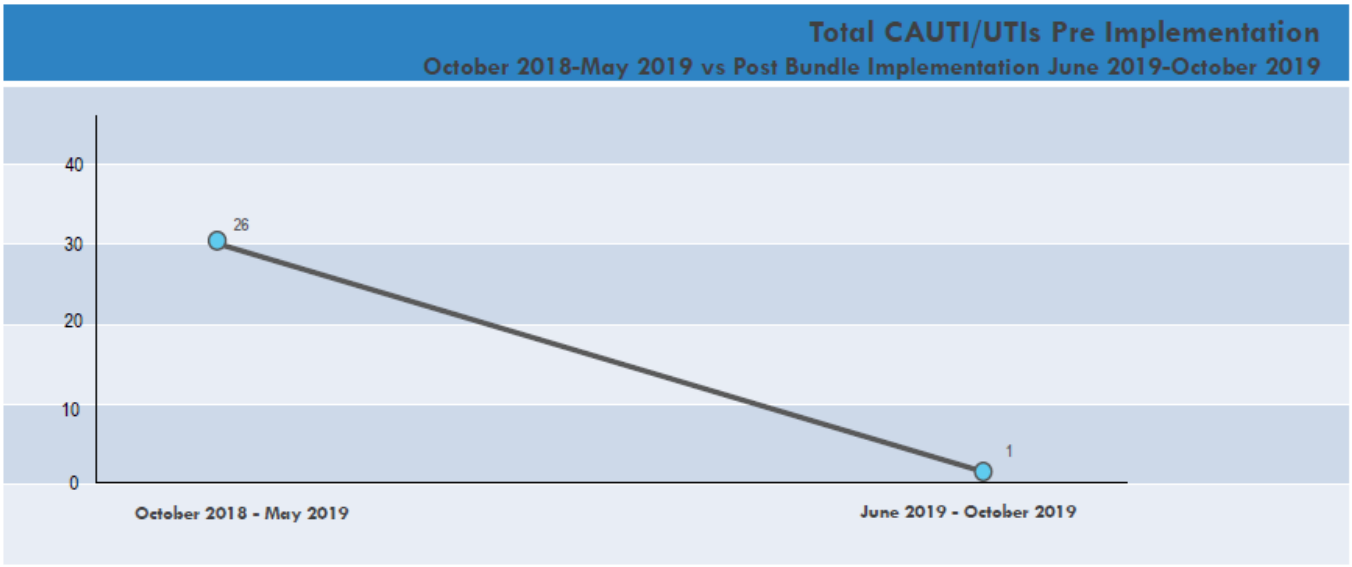
The methodology utilized was a retrospective, pre- and post -implementation analysis of a multi-factorial process approach to reduce CAUTIs and UTIs in the long-term care spinal cord unit. The relationship between the multi-factorial process approach and CAUTI/UTI rates were reviewed. The five interventions that made up the multi-factorial process approach included:

1. Implementation of a novel topical adjunctive therapy*
2. Reduction of bath basins in daily hygienic care
3. Implementation of 100% silicone catheters for those veterans that experienced catheter leakage
4. Standardized Education
5. Reduction of routine catheter flushing

*Theraworx Protect

Results:

CAUTI/UTI rates were substantially reduced from twenty-six (18 CAUTI & 8 UTI) to one (1 CAUTI and 0 UTI) after implementation of the quality improvement bundle. The multifactorial bundle achieved the projects aim in reducing CAUTI/UTI rates by 96%. Post intervention patients also demonstrated a 60% relative risk reduction in the need for IV antibiotics secondary to UTI.



Evaluating the Effectiveness of a Multidimensional Bundle to Reduce Urinary Tract Infection in Long-term Spinal Cord Injury/Disordered Patients: A Retroactive Review

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PROBLEM:

Urinary Tract Infections remain the most frequently encountered secondary health condition in the Spinal Cord Injury/Disorder population that adversely impacts overall health and quality of life. Efforts to reduce CAUTI/UTIs have historically been unsuccessful in this population.

CAUTI/UTI definition:

- Fever >100.4°F
- Nausea/vomiting
- Positive Urine culture: 100,000CFU/ml
- Increased spasms/hematuria/ change in urine output
- Increased WBC

METHODS:

A retrospective, pre- and post -implementation analysis of a multi-factorial bundle was piloted on twenty-eight (28) Spinal cord patients at a large midwestern veterans administration hospital. The impact of the nursing interventions was measured by calculating CAUT/UTI incidence rates during a baseline period of October 2018 through May 2019. Baseline rates were then compared to CAUTI/UTI rates calculated from the intervention period of June 2019 through November 2019.

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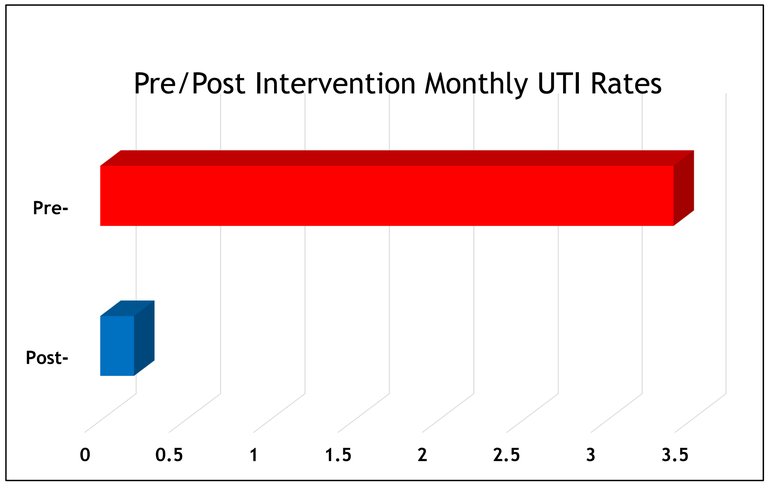
PURPOSE:

Reduce Catheter Associated Urinary Tract Infections (CAUTI) and Urinary Tract Infections (UTI) in the SCI/D population in a Long-Term Care facility, through the implementation of a multi-factorial bundle.

PROCESS:

Five Nursing Intervention Bundle:

- ✓ Clean 2 times per day with a novel topical adjunctive therapy cleanser *
- ✓ Removal of all bath basins for bathing
- ✓ Implementation of silicone catheters vs latex catheters to prevent leakage and prevent biofilm adherence
- ✓ Reduction of catheter flushing
- ✓ Standardized education



OUTCOME:

CAUTI/UTI rates were substantially reduced from twenty-six (18 CAUTI & 8 UTI) to one (1 CAUTI and 0 UTI) after implementation of the quality improvement bundle.

The multifactorial bundle achieved the projects aim in reducing CAUTI/UTI rates by 96%.

* Theraworx Protect foam and wipes

The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government. The authors declare that they do not have a conflict of interest.

References per request: Nancy.chaiken@va.gov

American Journal of Infection Control: http://dx.doi.org/10.1016/j.ajic.2014.12.007

Efficacy of a novel skin antiseptic against carbapenem-resistant Enterobacteriaceae

Timothy L. Wiemken PhD, MPH, CIC *, Robert R. Kelley PhD, Ruth M. Carrico PhD, RN, FSHEA, CIC, Laura E. Binford BA, Brian E. Guinn BSN, William A. Mattingly PhD, Paula Peyrani MD, Julio A. Ramirez MD, FACP
University of Louisville School of Medicine, Department of Medicine, Division of Infectious Diseases, Clinical and Translational Research Support Unit, Healthcare Epidemiology Program, Louisville, KY

Background

Infections caused by carbapenem-resistant Enterobacteriaceae (CRE) are increasing on a global scale and represent a significant public health concern.1,2 Prevention and control of the spread of CRE can be difficult because Enterobacteriaceae are enteric organisms and are consistently shed to the environment and to the hands of health care workers from colonized or infected hosts. Reduction in skin and environmental bioburden are important prevention interventions for organisms transmitted via this route. The highest quantities of CRE are likely to be on colonized or infected patients, making source control important. Although primarily present in the gastrointestinal tract, these organisms are identified on inguinal and axillary surfaces nearly as often as in the rectum.3 These data support the concept that daily bathing with antiseptic solutions may decrease the CRE skin bioburden4 and therefore reduce transmission. To provide a safe health care environment for patients, it is critical to continue to identify products that are nontoxic and effective for daily bathing while maintaining activity against epidemiologically important organisms, such as these multi -drug resistant Enterobacteriaceae. The current study describes the efficacy of a novel skin antiseptic against 2 different CRE.

Methods

This was a laboratory-based efficacy study evaluating a nontoxic, silver-based skin antiseptic (Theraworx, Avadim Technologies, Asheville, NC) against carbapenem-resistant Escherichia coli and carbapenem-resistant Klebsiella pneumoniae. To evaluate the potential efficacy of this product for antisepsis on human skin, the VITRO-SKIN model (IMS, Portland, ME) was used. This model consists of a substrate that simulates human skin, with similar topography, pH, surface tension, and ionic strength. Organisms E coli and K pneumoniae isolates were obtained from the American Type Culture Collection, numbers 81,371 and BAA-1705, respectively. The modified Hodge test was used to document carbapenem resistance in each isolate.

Table 1
Efficacy of a novel silver-based skin antiseptic against carbapenem-resistant *Escherichia coli* using a skin model in the presence of 5% bovine serum

	Survivors			
	Replicate 1	Replicate 2	Replicate 1	Replicate 2
Dilution volume	15-min exposure		60-min exposure	
10^{0} (1.00 mL)	60	40	185	41
10^{0} (1.00 mL)	8	6	20	6
10^{-1} (1.00 mL)	1	0	2	0
10^{-2} (1.00 mL)	0	0	0	0
10^{-3} (1.00 mL)	0	0	0	0
CFU/carrier	1.2×10^{3}	8.2×10^{2}	3.7×10^{3}	8.2×10^{2}
Log_{10} CFU/carrier	3.08	2.91	3.57	2.91
Average log_{10}	3.00		3.24	
Geometric mean (CFU/carrier)	1.00×10^{3}		1.74×10^{3}	
Log_{10} reduction	3.84		3.60	
Percent reduction	>99.9		>99.9	

NOTE. Data represent CFU unless otherwise noted.
CFU, colony forming units.

Table 2
Efficacy of a novel silver-based skin antiseptic against carbapenem-resistant *Klebsiella pneumoniae* using a skin model in the presence of 5% bovine serum

	Survivors			
	Replicate 1	Replicate 2	Replicate 1	Replicate 2
Dilution volume	15-min exposure		60-min exposure	
10^{0} (1.00 mL)	>300	>300	>300	>300
10^{0} (1.00 mL)	132	>300	109	107
10^{-1} (1.00 mL)	24	40	22	22
10^{-2} (1.00 mL)	3	2	2	3
10^{-3} (1.00 mL)	1	1	0	1
CFU/carrier	2.64×10^{4}	8.0×10^{4}	2.18×10^{4}	2.14×10^{4}
Log_{10} CFU/carrier	4.42	4.90	4.34	4.33
Average log_{10}	4.66		4.34	
Geometric mean (CFU/carrier)	4.57×10^{4}		2.19×10^{4}	
Log_{10} reduction	1.86		2.18	
Percent reduction	98.6		99.3	

NOTE. Data represent CFU unless otherwise noted.
CFU, colony forming units.

Our study documents that this particular silver-based antiseptic may be useful for skin antisepsis in patients colonized or infected with CRE because of its confirmed activity against 2 of these organisms on a human skin analog. Being silver based, it may have excellent activity against a broad range of organisms other than CRE.5 Furthermore, this antiseptic provides many benefits over soap and water, including (compared with data available for hand hygiene)6 antibacterial activity, skin nourishment, pH maintenance, and promotion of cell growth and skin barrier protection. Each ingredient is considered nontoxic and has been tested in whole for biocompatibility and toxicity (testing results and safety data sheet available from Avadim Technologies). These properties make it an attractive option for skin antisepsis in hospitalized patients, and the enhanced antibacterial activity should reduce transmission of pathogens similarly to other available skin antiseptics.

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Brief report

Efficacy of a novel skin antiseptic against carbapenem-resistant Enterobacteriaceae

Timothy L. Wiemken PhD, MPH, CIC *, Robert R. Kelley PhD, Ruth M. Carrico PhD, RN, FSHEA, CIC, Laura E. Binford BA, Brian E. Guinn BSN, William A. Mattingly PhD, Paula Peyrani MD, Julio A. Ramirez MD, FACP

University of Louisville School of Medicine, Department of Medicine, Division of Infectious Diseases, Clinical and Translational Research Support Unit, Healthcare Epidemiology Program, Louisville, KY

Key Words:
Daily bathing
Skin antisepsis
Colloidal silver
Carbapenemase

Infections caused by carbapenem-resistant Enterobacteriaceae (CRE) are increasing on a global scale. Because of the need for CRE transmission prevention and control, we sought to evaluate the efficacy of a silver-based skin antiseptic against these organisms. Using a human skin analog, a third party laboratory conducted efficacy testing. The results suggest that this product provides antimicrobial activity against CRE on human skin. Because of the unique properties, this antiseptic may be useful for daily bathing of hospitalized patients to assist in the control of CRE.

Infections caused by carbapenem-resistant Enterobacteriaceae (CRE) are increasing on a global scale and represent a significant public health concern.[1,2] Prevention and control of the spread of CRE can be difficult because Enterobacteriaceae are enteric organisms and are consistently shed to the environment and to the hands of health care workers from colonized or infected hosts. Reduction in skin and environmental bioburden are important prevention interventions for organisms transmitted via this route.

The highest quantities of CRE are likely to be on colonized or infected patients, making source control important. Although primarily present in the gastrointestinal tract, these organisms are identified on inguinal and axillary surfaces nearly as often as in the rectum.[3] These data support the concept that daily bathing with antiseptic solutions may decrease the CRE skin bioburden[4] and therefore reduce transmission.

To provide a safe health care environment for patients, it is critical to continue to identify products that are nontoxic and effective for daily bathing while maintaining activity against epidemiologically important organisms, such as these multidrug-resistant Enterobacteriaceae. The current study describes the efficacy of a novel skin antiseptic against 2 different CRE.

METHODS

Study design

This was a laboratory-based efficacy study evaluating a nontoxic, silver-based skin antiseptic (Theraworx, Avadim Technologies, Asheville, NC) against carbapenem-resistant *Escherichia coli* and carbapenem-resistant *Klebsiella pneumoniae*. To evaluate the potential efficacy of this product for antisepsis on human skin, the VITRO-SKIN model (IMS, Portland, ME) was used. This model consists of a substrate that simulates human skin, with similar topography, pH, surface tension, and ionic strength.

Organisms

E coli and *K pneumoniae* isolates were obtained from the American Type Culture Collection, numbers 81,371 and BAA-1705, respectively. The modified Hodge test was used to document carbapenem resistance in each isolate.

Laboratory methods

A third party, ATS Laboratories (Eagan, MN), conducted all tests and reported results back to the investigators. Controls for purity,

* Address correspondence to Timothy L. Wiemken, PhD, MPH, CIC, Clinical and Translational Research Support Unit, Division of Infectious Diseases, Department of Medicine, Louisville, University of Louisville School of Medicine, Louisville, KY 40205.

E-mail address: tim.wiemken@louisville.edu (T.L. Wiemken).

Conflicts of interest: Dr Wiemken is a consultant for Avadim Technologies and Clorox Healthcare.

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Table 1
Efficacy of a novel silver-based skin antiseptic against carbapenem-resistant *Escherichia coli* using a skin model in the presence of 5% bovine serum

	Survivors			
	Replicate 1	Replicate 2	Replicate 1	Replicate 2
Dilution volume	15-min exposure		60-min exposure	
10^{0} (1.00 mL)	60	40	185	41
10^{0} (1.00 mL)	8	6	20	6
10^{-1} (1.00 mL)	1	0	2	0
10^{-2} (1.00 mL)	0	0	0	0
10^{-3} (1.00 mL)	0	0	0	0
CFU/carrier	1.2×10^3	8.2×10^2	3.7×10^3	8.2×10^2
Log_{10} CFU/carrier	3.08	2.91	3.57	2.91
Average log_{10}	3.00		3.24	
Geometric mean (CFU/carrier)	1.00×10^3		1.74×10^3	
Log_{10} reduction	3.84		3.60	
Percent reduction	>99.9		>99.9	

NOTE. Data represent CFU unless otherwise noted.
CFU, colony forming units.

Table 2
Efficacy of a novel silver-based skin antiseptic against carbapenem-resistant *Klebsiella pneumoniae* using a skin model in the presence of 5% bovine serum

	Survivors			
	Replicate 1	Replicate 2	Replicate 1	Replicate 2
Dilution volume	15-min exposure		60-min exposure	
10^{0} (1.00 mL)	>300	>300	>300	>300
10^{0} (1.00 mL)	132	>300	109	107
10^{-1} (1.00 mL)	24	40	22	22
10^{-2} (1.00 mL)	3	2	2	3
10^{-3} (1.00 mL)	1	1	0	1
CFU/carrier	2.64×10^4	8.0×10^4	2.18×10^4	2.14×10^4
Log_{10} CFU/carrier	4.42	4.90	4.34	4.33
Average log_{10}	4.66		4.34	
Geometric mean (CFU/carrier)	4.57×10^4		2.19×10^4	
Log_{10} reduction	1.86		2.18	
Percent reduction	98.6		99.3	

NOTE. Data represent CFU unless otherwise noted.
CFU, colony forming units.

organic soil (5% fetal bovine serum) sterility, neutralizer sterility (Letheen Broth, VWR-America, Radnor, PA), and carrier (silver-based antiseptic) sterility were also performed for each test and are available on request.

Initially, a standard suspension of approximately 3 log_{10} of the organism under study was prepared. Then, 1 mL of the suspension was dried on a 2.54 cm^2 area of a 3.81 cm^2 rehydrated VITRO-SKIN carrier at ambient air temperature. The surface was then wiped with a silver-based antiseptic impregnated towelette over and back twice (4 passes total) for all tests. After the appropriate time under study (15 and 60 minutes elapsed time since antiseptic contact), the product was neutralized, and the organisms were plated at 35-37°C for 48 hours on Tryptic Soy Agar with 5% Sheep Blood (BAP, Remel, Lenexa, KS).

Both organisms were tested in the presence of organic material (5% fetal bovine serum). Each test was performed on the undiluted sample and on 4 serial dilutions.

RESULTS

All American Type Culture Collection organisms evaluated were documented to be carbapenem resistant via the modified Hodge test. Tables 1 and 2 outline the average efficacy of the silver-based antiseptic against carbapenem-resistant *E coli* and *K pneumoniae* at 15 and 60 minutes after antiseptic contact, in the presence of 5% fetal bovine serum. All control results for culture purity, organic soil load sterility, neutralizer sterility, and population and neutralization confirmation were considered acceptable by the third party laboratory.

CONCLUSIONS

Our study documents that this particular silver-based antiseptic may be useful for skin antisepsis in patients colonized or infected with CRE because of its confirmed activity against 2 of these organisms on a human skin analog. Being silver based, it may have excellent activity against a broad range of organisms other than CRE.[5] Furthermore, this antiseptic provides many benefits over soap and water, including (compared with data available for hand hygiene)[6] antibacterial activity, skin nourishment, pH maintenance, and promotion of cell growth and skin barrier protection. Each ingredient is considered nontoxic and has been tested in whole for biocompatibility and toxicity (testing results and safety data sheet available from Avadim Technologies). These properties make it an attractive option for skin antisepsis in hospitalized patients, and the enhanced antibacterial activity should reduce transmission of pathogens similarly to other available skin antiseptics.[7]

Development of resistance is always a concern with any antimicrobial agent. Although silver resistance is possible through *sil*-mediated binding and efflux pumps,[8] clinically documented resistance even in the presence of silver resistance genes remains limited and controversial.[9,10] It will be critical to maintain surveillance for clinically resistant isolates as silver becomes an important agent in the infection prevention arsenal.

This study has some limitations. First, we did not evaluate all Enterobacteriaceae, and other genus and species may have varied susceptibilities. Therefore, these results cannot be extrapolated directly to other organisms. We also used a human skin analog as opposed to actual skin. It is possible that activity on human skin may be different than on the analog because of the skin microbiome and other properties that may not have been accounted for in the skin analog. Finally, we did not have a direct comparison with an active and inactive control antiseptic, limiting the generalizability. The strengths of this study include the use of a third party certified laboratory with significant experience conducting efficacy testing and the multiple tests conducted.

In conclusion, this study documented antimicrobial activity of a novel, nontoxic, silver-based skin antiseptic against 2 CRE in a human skin model. It will be important to evaluate the effectiveness of this product in the clinical setting to ensure activity in practice. Nevertheless, this antiseptic may be useful for daily bathing of hospitalized patients to assist in the control of CRE transmission.

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FINAL REPORT #2211575-402

TITLE **EVALUATION OF ONE TEST ARTICLE FOR VIRUCIDAL PROPERTIES BASED UPON THE ASTM E1052-20 METHOD**

PURPOSE

This study evaluated virucidal properties of one test article when challenged with Respiratory Syncytial Virus. The testing was based upon ASTM E1052-20, *Standard Practice to Assess the Activity of Microbicides against Viruses in Suspension*. All testing was performed in accordance with Food and Drug Administration Good Laboratory Practices, as specified in 21 CFR Part 58, with the exception that the characterization of the identity, strength, purity, composition, stability, and solubility of the test article remained the responsibility of the sponsor and was not performed by the testing facility (GLP 58.105).

SCOPE

This study was designed to evaluate the virucidal properties of one test article versus Respiratory Syncytial Virus strain Long (ATCC #VR-26) using a Virucidal Suspension Test (*In-Vitro* Time-Kill method) based upon ASTM E1052-20, *Standard Practice to Assess the Activity of Microbicides against Viruses in Suspension*. The percent and $\log_{10}$ reductions from the initial population of the viral strain were determined following exposure to the test article for 30 minutes, 3 hours and 6 hours. Testing was performed in one replicate. Plating was performed in four replicates.

The protocol, included in the addendum to this final report, presents the study methodology, in detail. No deviations from the protocol or from applicable standard operating procedures occurred during the course of this evaluation.

TABLE 3

Test Article: Theraworx Protect Foam (Lot #520669)
Virus: Respiratory Syncytial Virus strain Long (ATCC #VR-26)
Host Cell Line: HEp-2 (ATCC #CCL-23)

Dilution (- $\log_{10}$)	Virus Control	Test	Neutralization Control	Neutralizer Toxicity Control	Cytotoxicity Control	Cell Control
		30 Minutes				0000
-2	NT	0000	NT	NT	0000	N/A
-3	++++	0000	++++	++++	0000	
-4	++++	0000	++++	++++	0000	
-5	++++	0000	00++	+0+0	NT	
-6	0000	0000	0000	0000	NT	
-7	0000	0000	0000	0000	NT	
$TCID_{50}$ ($\log_{10}$)	5.50	≤1.50	5.00	5.00	≤1.50	
$\log_{10}$ Reduction	N/A	≥4.00	N/A			
Percent Reduction		≥99.99%				

\+ Virus infected cells present
0 Virus infected cells not detected
NT Not tested
N/A Not applicable

Independent Laboratory Study: Bioscience Laboratories Final Report #1703130-201

AN EVALUATION OF ONE TEST PRODUCT FOR ITS ANTIMICROBTAL PROPERTIES WHEN CHALLENGED WITH THREE MICROORGANISMS USING AN INVTTRO TIME-KILL METHOD- CANDIDA AURIS

Background

Candida auris is an emerging fungus that presents a serious global health threat. CDC is concerned about C. auris for three main reasons: 1. It is often multidrug-resistant, meaning that it is resistant to multiple antifungal drugs commonly used to treat Candida infections. Some strains are resistant to all three available classes of antifungals.2. It is difficult to identify with standard laboratory methods, and it can be misidentified in labs without specific technology. Misidentification may lead to inappropriate management. 3. It has caused outbreaks in healthcare settings. For this reason, it is important to quickly identify C. auris in a hospitalized patient so that healthcare facilities can take special precautions to stop its spread.

Methods/Results

An ln-Vitro Time-Kill evaluation of one test product was performed versus three microorganisms - Candida auris (AR-Bank #0385), Candida auris (AR-Bank #0389), and Candida auris (AR-Bank #0390). All testing was performed based upon the method described in ASTM 82783-17, Standard Test Method for Assessment of Antimicrobial Activity of Waler Miscible Compounds Using a Time-Kill Procedure.

Results

The percent and $\log_{10}$ reductions from the numbers control population of the challenge microorganism was determined following exposure to the test product for 4 hours, 8 hours, and 24 hours. All agar-plating was performed in duplicate. Test Product, Broad Spectrum Hygiene Management, 4 oz Foam (Lot #16180-l), reduced the populations of the three challenge microorganisms -- Candida auris (AR-Bank #0385), Candida auris (AR-Bank #0389), and Candida arris (AR-Bank #0390) by greater than 0.5 $\log_{10}$ following a 4 hour exposure time, by greater than 1.0 $\log_{10}$ following a 8 hour exposure time, and by greater than 6.0 $\log_{10}$ following a 24 hour exposure time.

TABLE 2

Test Product: Broad Spectrum Hygiene Management (4 oz Foam)
Lot Number: 16180-1

Microorganism Species (ATCC #)	Initial Population (CFU/mL)	Exposure Time	Numbers Control Population (CFU/mL)	Post-Exposure Population (CFU/mL)	Log_{10} Reduction	Percent Reduction
Candida auris (AR-Bank #0385)	5.050×10^9	4 hours	5.00×10^7	1.320×10^7	0.5784	73.6000%
		8 hours	5.150×10^7	4.250×10^6	1.0834	91.7476%
		24 hours	4.00×10^7	$< 1.00 \times 10^1$	6.6021	99.9999%
Candida auris (AR-Bank #0389)	5.10×10^9	4 hours	5.950×10^7	9.350×10^6	0.8037	84.2857%
		8 hours	6.250×10^7	3.90×10^5	2.2048	99.3760%
		24 hours	5.750×10^7	$< 1.00 \times 10^1$	6.7597	99.9999%
Candida auris (AR-Bank #0390)	5.950×10^9	4 hours	4.00×10^7	1.4550×10^6	1.4392	96.3625%
		8 hours	5.10×10^7	1.4050×10^4	3.5599	99.9725%
		24 hours	4.80×10^7	$< 1.00 \times 10^1$	6.6812	99.9999%

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Theraworx skin care formulation reduces nosocomial associated CAUTI rates when used for urinary catheter insertion and maintenance

Multi-Center Study Conducted in High-Risk Neurological, Cardiovascular and Trauma Critical Care Settings, and Joseph F Renzulli*
Associate Professor of Surgery (Urology), Alpert Medical School of Brown University and CMO, Avadim Technologies, USA

Background

Catheter associated urinary tract infections (CAUTI) continue to be the most challenging of all hospital and institutional acquired conditions. According to the Centers for Disease Control and Infection Prevention urinary tract infections (UTIs) are the most common type of healthcare-associated infection reported to the National Healthcare Safety Network (NHSN) [1]. Urinary infections are the source for more than 50% of all infections in long term care facilities and more than 40% of all hospital acquired infections [2]. Despite extreme efforts, including the off-label use of topical drugs, the CAUTI rate world-wide continues to rise. This is only further complicated by the emergence of multi-drug resistant organisms (MDROs). Considerable personnel time, direct and indirect costs are expended by health care institutions to reduce the rate of hospital acquired infections, especially those that occur in patients with signs and symptoms referable to the urinary tract. UTIs are classified as either uncomplicated or complicated infections and treatment often differs based on this classification. However, all nosocomial and catheter associated urinary tract infections are considered complicated. Nosocomial infections are further complicated by advanced patient age and multiple comorbidities [3]. The likelihood of treatment failure and serious complications, particularly the development of antimicrobial resistance, is more common in CAUTI. Multiple drug resistant organisms including Carbapenem Resistant Enterobacteriaceae (CRE), in particular, an E coli isolate, adds to the complex challenge as many ICU patients with indwelling catheters experience fecal incontinence [4]. The removal of macroscopic debris during cleansing of incontinent patients is not sufficient to prevent infections. Therefore, topical antiseptic solutions and cleansers should have proven efficacy demonstrating the ability to decolonize these resistant organisms on human skin and mucosa without disrupting the normal host immunity, while preserving mucosal integrity and the microbiome [5,6].

Results

Ten of the hospitals from which data was requested provided both pre- and post-intervention data. Eight of the ten reporting hospitals complied with recommended clinical protocols. The average pre-intervention period for these eight hospitals was 22.9 months. The average post-intervention period was 14 months. All eight hospitals reported that Theraworx use markedly reduced their CAUTI rate. The reductions ranged from 22.47% (UHS-San Antonio in San Antonio, Tex.) to 100% at two hospitals (Centennial Hospital, in Frisco, Texas and Peace health St. Joseph Medical Center, in Bellingham, Washington). CAUTIs were completely eliminated at the latter two sites. The mean pre-intervention CAUTI rate for the eight compliant hospitals was 3.65/1,000 catheter days. The mean post-intervention CAUTI rate for those same hospitals was 1.72/1,000 catheter days, a difference of 1.93/1,000 catheter days. Therefore, the mean change in CAUTI rate was a reduction of 52.88% for compliant institutions. Evaluation of the two hospitals that acknowledged that proper protocols for Theraworx use were not consistently followed during the study period revealed troubling data. One of these hospitals reported no change in CAUTI rates; while the other reported a 30.31% increase.

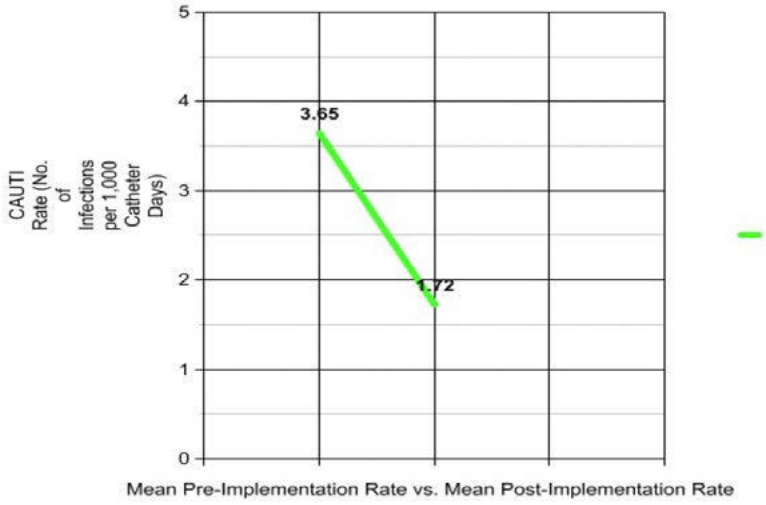

Figure 1. Mean CAUTI Rate Reduction with Theraworx Use.

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Clinical and Medical Investigations

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Multi-Center Study Conducted in High-Risk Neurological, Cardiovascular and Trauma Critical Care Settings, and Joseph F Renzulli*

Associate Professor of Surgery (Urology), Alpert Medical School of Brown University and CMO, Avadim Technologies, USA

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The diligence required to maintain an indwelling catheter is reported as a main contributor to whether infection develops. The demands on nursing and ancillary staff can prove to prohibit necessary catheter maintenance steps to prevent CAUTI. Effective perineal protocols require nursing management, quality and supply chain acceptance and commitment for each institution. To date, only two methodologies have consistently proven to be effective in reducing CAUTI rates; implementing closed catheter systems and early removal of the catheter [7]. Scheduled cleansing of the catheter and urethral meatus, referred to as catheter care and maintenance, deserves scrutiny when designing a program to prevent CAUTI. Multiple studies have evaluated the effectiveness of antiseptic cleansers, ointments, or creams. Dr. Mikel Gray sites work by Dr. Koskeroglu *et al.* evaluating the effectiveness of 4 separate protocols for urethral meatus care in ICU patients. The techniques employed were as follows: (1) cleansing plus once daily application of a 9% povidone- iodine solution, (2) cleansing plus twice daily application of a 9% povidone-iodine solution, (3) once-daily cleansing using a 4% chlorhexidine gluconate, (4) twice daily cleansing with a 4% chlorhexidine gluconate, and (5) a control group. None of the protocols that employed antiseptic solutions proved more effective for preventing CAUTI, bacteriuria, or bacterial colonization at the urethral meatus than routine cleansing alone [8].

In June 2016, The National Comprehensive Unit-Based Safety Program which is funded by the Agency for Healthcare Research and Quality reported on their 5 year outcomes of their national prevention program initiative which was implemented in 926 units across hospitals in 32 states. This included 60% non-ICU based units and 40% ICU based

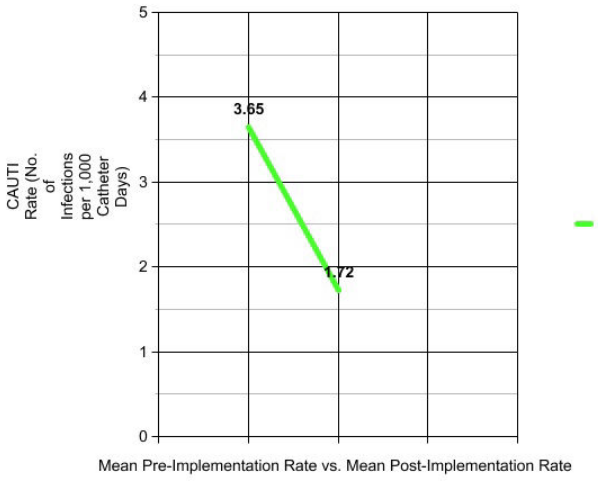

Figure 1. Mean CAUTI Rate Reduction with Theraworx Use.

Correspondence to: Joseph F Renzulli, Associate Professor of Surgery (Urology), Alpert Medical School of Brown University, USA, Tel: (401)272-1229; E-mail: Jrenzulli@lifespan.org

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Table 1. Results by Hospital.

Site	CAUTI Rate Pre-Intervention Period (per 1,000 catheter days)	Pre-Intervention Period Start Date	Pre-Intervention Period End Date	Pre-Intervention Period in Months	CAUTI Rates Post-Theraworx Intervention (per 1,000 catheter days)	Post-Theraworx Intervention Start Date	End Date of Theraworx Intervention Data	Post-Theraworx Intervention Period in Months	Percent Change
University Hospital (San Antonio, Tex.)	3.16	1/2015	3/2015	2	2.45	4/2015	6/2016	14	-22.47%
Baylor Scott & White Medical Center – Centennial (Frisco, Tex.)	1.84	11/2013	10/2015	23	0	11/2015	6/2016	7	-100.00%
South Miami Hospital/Baptist Health South Florida (South Miami, Fla.)	3.04	1/2013	12/2014	23	0.51	12/2014	6/2016	18	-83.22%
First Health [TK – need to know which of the four First Health hospitals this is]	1.25	1/2012	12/2013	23	0.65	1/2014	12/2015	23	-48.00%
Mercy Hospital Springfield (Springfield, Mo.)	2.34	8/2013	7/2015	23	1.4	8/2015	7/2016	11	-40.17%
St. Joseph Medical Center (Towson, Md.)	3.34	7/2013	10/2015	27	0	12/2015	6/2016	5	-100.00%
Little Company of Mary Hospital (Evergreen Park, Ill.)	2.93	1/2012	12/2014	35	1.17	1/2015	9/2016	20	-60.07%
Regional Medical Center at Memphis, Memphis, Tenn.	11.3	N/A	N/A	-	7.55	N/A	N/A	-	-33.19%
Large Florida university hospital (NON-COMPLIANT SITE)	2.87	1/2015	8/2015	7	3.74	10/2015	9/2016	11	30.31%
Large Kansas City hospital (NON-COMPLIANT SITE)	1.2	1/2013	5/2015	28	1.2	5/2015	1/2016	8	0.00%
Total for compliant sites	3.65			22.29	1.72			14	-52.88%

units. Their conclusions were that only non-ICU based units benefited from participation in their program with a 14% decrease in CAUTIs over a 4-year period. ICU based units saw an alarming 9% increase in CAUTI in the same 4-year period. Importantly, their protocol did not suggest the implementation of any products that have been suggested to reduce CAUTI rates [9].

Recently, the CDC conducted the CUSP study to determine the effectiveness of soap and water cleansing in reducing CAUTI in more than 600 hospitals and found that this contributed to only a 1% reduction in ICU setting and 14% reduction on general medical floors [10]. This demonstrates the soap and water care is beneficial as an initial step in a protocol to reduce macroscopic debris and prepare the perineum for application of other agents that may be additive in their effect on reducing CAUTI. Less than expected results from all products and methodology point to the need for quality improvement oversight and implementation for evidenced based practice guidelines including comprehensive education across all departments [11-14]

Methodology

Ten hospitals which have implemented the Theraworx skin care system protocol for an extended period of greater than 20 months and which demonstrated excellent quality in providing confirmed data for the 40+ month period were queried for their outcome data regarding CAUTIs. These institutions applied Theraworx in a variety of care settings including high-risk neurological, cardiovascular and trauma intensive care units. Many patients were incontinent of urine, feces or both in these settings. Theraworx was used in all of its available forms: foam, spray or moisture-impregnated cloths. The clinical protocol was to apply Theraworx to the meatus and surrounding tissue, prior to insertion of a catheter, to establish a zone of inhibition, then reapply the product TID and after each incident of fecal incontinence as a maintenance intervention. The hospitals were asked to provide insertion and maintenance details on utilization, pre-and post-implementation CAUTI rates as reported to the National Healthcare Safety Network. The hospitals reported their outcome data and were included in our retrospective analysis. Compliance to the protocol was assessed at each institution. Post implementation results were then compared to an extended pre-implementation period with analogous patient populations. CAUTI were reported per 1,000 catheter days consistent with the CDC reporting nomenclature and AHRQ [9].

Results

Ten of the hospitals from which data was requested provided both pre- and post-intervention data. Eight of the ten reporting hospitals complied with recommended clinical protocols.

The average pre-intervention period for these eight hospitals was 22.9 months. The average post-intervention period was 14 months. All eight hospitals reported that Theraworx use markedly reduced their CAUTI rate. The reductions ranged from 22.47% (UHS-San Antonio in San Antonio, Tex.) to 100% at two hospitals (Centennial Hospital, in Frisco, Texas and Peace health St. Joseph Medical Center, in Bellingham, Washington). CAUTIs were completely eliminated at the latter two sites. The mean pre-intervention CAUTI rate for the eight compliant hospitals was 3.65/1,000 catheter days. The mean post-intervention CAUTI rate for those same hospitals was 1.72/1,000 catheter days, a difference of 1.93/1,000 catheter days. Therefore, the mean change in CAUTI rate was a reduction of 52.88% for compliant institutions.

Evaluation of the two hospitals that acknowledged that proper protocols for Theraworx use were not consistently followed during the study period revealed troubling data. One of these hospitals reported no change in CAUTI rates; while the other reported a 30.31% increase.

Discussion

The Theraworx skin care system (Avadim Technologies, Asheville, NC), is a non-toxic topical skin and mucosal membrane application that was associated with a significant reduction in CAUTIs over a period of 20 months or more of implementation at hospitals, across the United States, in a myriad of high risk ICU patient care settings. Upon implementation of the Theraworx protocol, CAUTI rates decreased between 22.47% and 100% (complete elimination of CAUTIs) in 8 of the 10 institutions which remained compliant. This represented a mean overall decrease in CAUTIs of more than 53% among responding hospitals that followed the recommended clinical protocols. It is also notable that the 2 noncompliant sites were the only sites that did not achieve a substantial improvement in their CAUTI rates and in one instance CAUTI rates actually increased.

This study encompassed several different acute care settings including high risk hospital units such as neurological, cardiovascular and trauma ICUs. Further, many of the patients treated with the novel skin formulation were at an increased risk for urinary tract infection due to their concomitant medical comorbidities and urinary/fecal incontinence.

The proposed mechanism of action is reduction in the pH, and therefore optimization, of the stratum corneum layer of the skin, urethral meatus and vaginal mucosa. By reducing the pH to 5-5.5 the stratum corneum is able to function at its maximal immune and barrier capacity. Further, at the lower pH the normal dermal microbiome is preserved thus reducing the presence of more virulent bacteria, fungi or viruses. This paradigm shift is an exciting approach to the prevention of infections and additional attempts at the reduction of the further development of multi-drug resistant organisms by reducing antibiotic use.

Our study has limitations due to its non-randomized and retrospective nature. It is very difficult to get multiple institutions and staff individuals to adhere to a protocol for catheter insertion and maintenance, especially in the ICU setting given the complexity of the patient's disease state. The inclusion of the non-compliant sites is evidence to this and there lack of improvement or increase in CAUTI rate reflects the need for implementation and adherence to such protocols.

Conclusion

Results of this aggregated data set suggest that patients at hospitals with CAUTIs may benefit from use of Theraworx skin formulation at catheter insertion and for catheter maintenance. This approach may be especially appropriate for institutions that are failing to meet their own or national CAUTI benchmarks and suffering financial penalties for these critical HAIs. We encourage institutions to consider including the Theraworx protocol into their CAUTI clinical pathway to potentially achieve additional reduction in their CAUTI rates.

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Can't Attribute UTI TO Insertion: Utilizing Data to Prevent CAUTI. Univeristy of Washington Medical Center 2018

Background: • Per the CDC, urinary tract infections (UTI) are the 4th most common type ofhealthcare-associated infection and virtually all arecaused by instrumentation of the urinary tract

- On average, 12-16% of all adult inpatients will have anindwelling urinary catheter(IUC)
- Each day the IUC is in placethe patient has 3-7% increased risk of acquiring a CAUTI
- Estimated cost of CAUTI~ $11,000 per case
- Aside from medical complications such as cystitis, pyelonephritis, & bacteremia, CAUTI maycause patients discomfort, extend hospitalizations, &increased costs and mortality

Conclusion: Through multi-disciplinary engagement & review of epidemiologic data, high riskpopulations for CAUTI wereidentified

- The high risk populations related to maintenance ofIUC, not insertion
- With the implementation of a NDP & a trial of a novel peri-care product, CAUTI rates reduced 46%
- Colloidal silver wipes are now available for CAUTI prevention hospital-wide

UW Medicine
UNIVERSITY OF WASHINGTON MEDICAL CENTER

Can't Attribute UTI To Insertion: Utilizing Data to Prevent CAUTI

Smith, N.C., Granich, M., Lien, H., Schipper, A.
University of Washington Medical Center, Seattle, WA

MAGNET RECOGNIZED

PURPOSE

- To utilize data to identify populations at risk & develop focused initiatives to further decrease catheter associated urinary tract infections (CAUTI)

BACKGROUND

- Per the CDC, urinary tract infections (UTI) are the 4th most common type of healthcare-associated infection and virtually all are caused by instrumentation of the urinary tract
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INITIATIVES

Multidisciplinary Engagement

A multidisciplinary steering committee created to address rising CAUTI rates including:

- Nursing Leadership and Staff Nurses from ICU, Med-Surg, ED, OR
- Providers
- Infection Prevention Specialists
- Informatics

Identify High Risk Populations

Intensive case review of CAUTI identified these factors:

- Prolonged catheterization - 96% occurred 3 days after placement
- 82% Fecal incontinence
- 78% Enteric pathogens
- Patient risk factors: female gender, obesity, immobility, multiple organ failure
- Primary Services: Cardiology, Cardiothoracic Surgery, Abdominal Surgery, Medicine

Implement Nurse Driven Protocol (NDP)

NDP empowers nurses to insert, maintain, & remove urethral catheters based on specific criteria.

Indications for IUC:

- Intensive monitoring (q1-2 hrs)
- End of Life request
- Profound prolonged immobility (unstable spine)
- Urinary incontinence & perineum wound breakdown
- Urinary outlet obstruction
- Urological surgery
- Bladder dysfunction

Trial Novel Peri-Care Product & EMR Enhancements

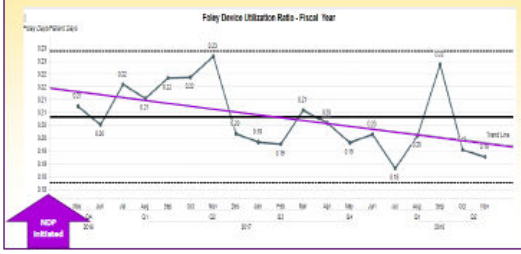
A trial of colloidal silver wipes (bactericidal & bacteriostatic) in all 4 intensive care units & 2 step down units.

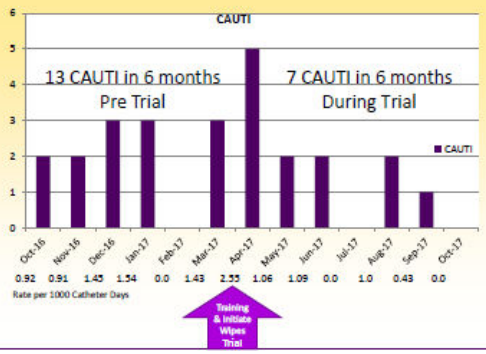
Colloidal silver wipes (Theraworx®) utilized with peri-care twice a day, & as needed after incontinence.

EMR documentation of peri-care revised to improve workflow & to facilitate data capture of CAUTI prevention bundle elements.

EVALUATION/OUTCOMES

- Urinary catheter device utilization decreased since NDP implemented
- CAUTI rate per 1,000 catheter days decreased
- 46% reduction in CAUTI events during trial





IMPLICATIONS FOR PRACTICE

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FUTURE WORK

Further implications for study include:

- The development of an automated report based on nursing documentation that identifies patients at high risk for CAUTI in real-time
- Identifying potential barriers to NDP adherence & develop strategies to enhance use
- Consider alternate uses of colloidal silver wipes – alternative for CLABSI, total body decolonization

ACKNOWLEGEMENTS

UWMC CAUTI Steering Committee & Staff

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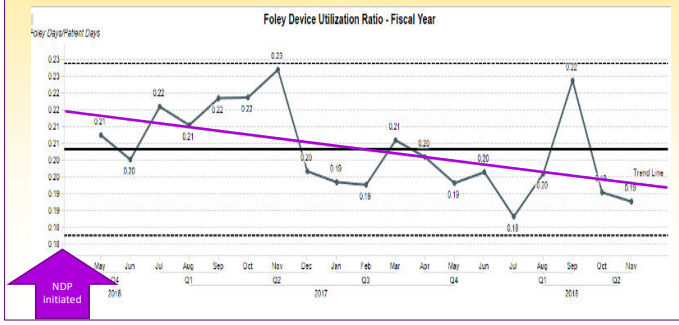

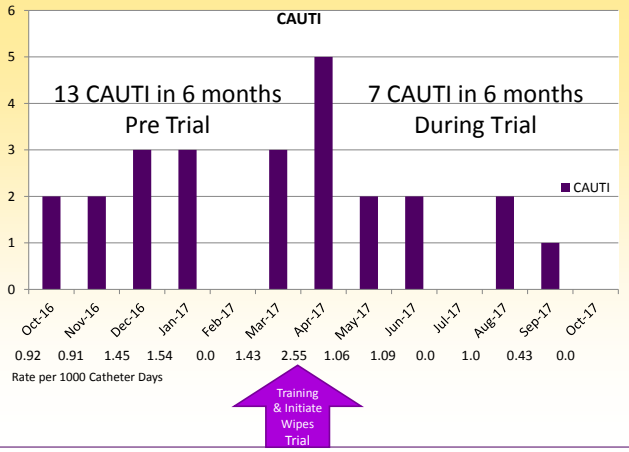

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Change Has Arrived: Antimicrobial Bathing and CLABSI

Patricia Sung, Mary Virgallito, Theresa Murphy, Raffi Boghossian, Rose Young;
University of Southern California, Verdugo Hills Hospital, Glendale, California

Purpose: Persistent central catheter–associate bloodstream infections (CLABSIs) occurred each quarter from 2014 to 2016 in our 12-bed intensive care unit (ICU), prompting an infection prevention (IP) assessment in November 2016. Low compliance with the bathing protocol was identified as a gap in practice. Staff surveys indicated confusion about chlorhexidine (CHG) application and dissatisfaction with effects on patients' skin. A topical immune health system was introduced to replace CHG bathing products in an effort to improve staff satisfaction, raise compliance, and reduce CLABSI rates.

Evaluation/Outcome: Pre -implementation assessment identified gaps in practice. Staff indicated CHG was "too sticky," and "too complicated; patients don't like it." In July 2019, a questionnaire was
administered to ICU nurses after the change to the new antimicrobial bathing product. Of 20 responses received from nurses, all stated they like the product. In response to an open-ended question asking why staff and/or patients like the product, 4 nurses (20%) cited the ease of use, and 7 (35%) cited the protective effects on the patients' skin. A random sample audit of patient bathing compliance before (5 of 10) and after (10 of 10) implementation identified a statistically significant difference (P = .02).
The ICU achieved a rate of 0 CLABSI in February 2018 and has remained at zero through April 2020.

***Statistical Significance in ICU Bathing Compliance after implementing Theraworx Protect at (P= .02)**

***CLABSI Rate since converting to Theraworx Protect from CHG 2% has remained at zero since February 2018**

NTI Abstracts-2020 National Teaching-Institute Evidence-Based Solutions Abstracts
Journal of Critical Care Nursing: American Association of Critical-Care Nurses
doi:https://doi.org/10.4037/ccn2020670
CriticalCareNurse Vol 40, No. 2, APRIL 2020

Closing the Gap: Targeting CAUTIs With a Novel Approach to Perineal Care

Lisa Hargett, Theresa Anderson; University of Maryland
St. Joseph Medical Center, Towson, Maryland

Purpose: Persistent catheter-associated urinary tract infections (CAUTIs) occurred in University of Maryland St. Joseph Medical Center's 28-bed critical care unit despite a robust prevention bundle. Root-cause analyses identified poor compliance with perineal and urinary catheter care as a gap in evidence-based practice. A change from applying soap and water with a washcloth from a basin to a topical immune health system wipe–based product was implemented to standardize process, improve compliance, and eliminate CAUTIs.

Summary: Despite continuous efforts to reduce infections, patients in the medical-surgical intensive care unit (MSICU) continued to have CAUTIs. Although a 44% reduction from fiscal year (FY)14 to FY15 was achieved, 1 infection was still too many. Root-cause analyses were performed on each CAUTI to identify a potential reason for the infection. Compliance with perineal and urinary catheter care was identified as a potential root cause and an opportunity to improve. In November 2015, the MSICU implemented a new process for managing bowel incontinence and enhancing perineal and urinary catheter care. These interventions included baby wipes for incontinence care and a topical immune health system wipe for perineal and urinary catheter care. The topical immune health system is used during the following situations: before and after insertion of a urinary catheter; to clean every 6 hours, or every 4 hours for catheters indwelling longer than 5 days, patients with urinary catheters; as a final cleaning step for any incontinence events; as a final cleaning step during the daily CHG bath; and before straight catheterization. With this new practice, perineal and urinary catheter care increased from once per day to up to 6 times per day, based on the duration of the catheter. Frontline staff were involved in the solution and implementation processes.

Evaluation/Outcome: Staff satisfaction was very high with the new standard of care. Staff survey results were notable for ease of use (100%), preference over previous practice (97%), and catheter care being worth the extra step (100%). Compliance with perineal care also improved. After implementation, the MSICU celebrated 351 days without a CAUTI. The success has continued: the unit recently celebrated 365 days CAUTI free. Our standardized infection ratio also decreased by 49% from before to after implementation of the new interventions. It is important to acknowledge that this success is not the result of a single intervention but rather multiple interventions designed to reduce CAUTIs.

100% Staff Satisfaction

Improved Compliance

365 continuous Days Zero CAUTI

Reduction in Standardized Infection Ratio by 49%

Quality Intervention: Tenet Healthcare- CLABSI/CAUTI Intervention

Zero CAUTI, Zero CLABSI: Evaluating the evidence-based effectiveness of a Silver, pH Acidic, Multimodal Skin decolonizing wipe to Reduce Catheter Associated Urinary Tract Infection and Central Line Blood Stream Infections in the ICU setting: A Retrospective Review

Tenet Health - Doctors Medical Center Modesto, CA
Asif Saiyed, MBA, CIC, Director Infection Prevention

Background

CAUTI and CLABSI continue to be a significant problem for patients in the ICU setting. Despite successful implementation of recommended protocol bundles, Acute care hospitals, still struggle with these infections. Compliance with CHG bathing wipes can be challenging because of skin irritation and allergic reactions. Microbe resistance and antiseptic contamination recalls mean that Hospitals should investigate safe, effective alternatives to the status quo antiseptics. Non-antimicrobial urinary catheter bathing products do not effectively address the root cause of CAUTI. In order to improve CAUTI and CLABSI rates an evidence based, safe, effective, skin friendly, approach was implemented. The focus was to improve patient satisfaction, efficiency, bathing compliance, promote antimicrobial stewardship and significantly reduce both CAUTI and CLABSI rates.

Methods

A retrospective, 6- month, pre- and post -implementation infection rate analysis was used to measure changes in CAUTI rate per 1,000 catheter days and CLABSI rates per 1,000 central line days consistent with the CDC reporting nomenclature and AHRQ standards. Clinical evaluation was completed in CCU, NCCU, SICU, CVICU between November 2019 and April 2020. April 2019 and September 2019 were used for comparison. October 2019 was the product transition month.

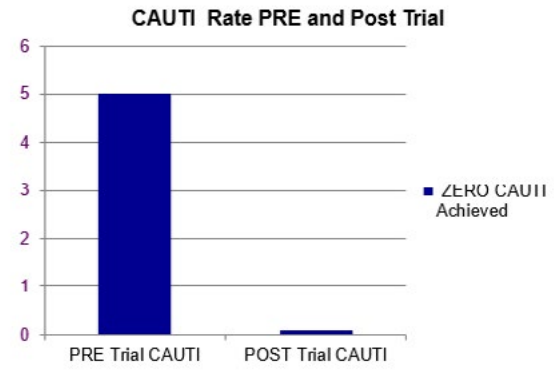
Pre-and post-implementation CAUTI and CLABSI surveillance was completed monthly using electronic medical record chart audits during the study intervention period and compared them with retrospective analysis of past infection rates within the same units. Historically CAUTI and CLABSI rates are analyzed and reported monthly by Infection Control Services.

Nurse satisfaction survey to measure ease of use, efficiency of use, patient satisfaction, patient refusal, and perception of improved over compliance.

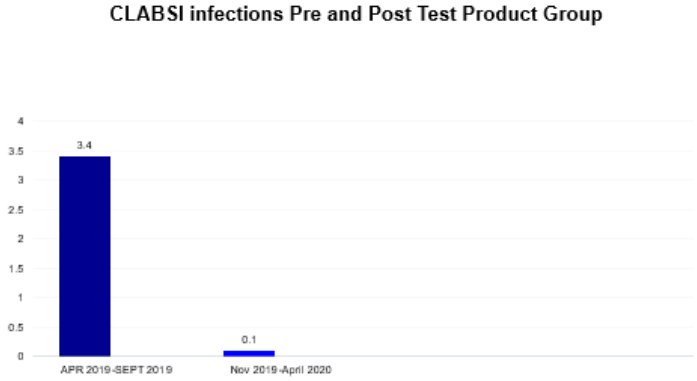
Results

This retrospective analysis involved CCU, NCCU, SICU, CVICU patients with central line catheters and / or indwelling urinary catheters. The new impregnated wipes test product trial started on SIR rate 2019 .442 Data collected from chart reviews and monitoring of electronic records were reviewed and infections were recorded when they met NHSN reporting guidelines for either CAUTI or CLABSI. SIR rate January 1 – June 30, 2020 0.00

CAUTI rates were substantially reduced from a SIR rate of .442 Pretrial group to a SIR rate of in the Post test group



CLABSI Rates were reduced from an SIR rate of .348 in 2019 in the pre-test group to a SIR of 0.0 Jan 1 – June 30 in the Post – test product and protocol group



Goal: Zero CAUTI, Zero CLABSI: Evaluating the evidence-based effectiveness of a Silver, pH Acidic, Multimodal Skin decolonizing wipe to Reduce Catheter Associated Urinary Tract Infection and Central Line Blood Stream Infections in the ICU setting: A Retrospective Review

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Asif Saiyed, MBA, CIC, Director Infection Prevention

Background

CAUTI and CLABSI continue to be a significant problem for patients in the ICU setting. Despite successful implementation of recommended protocol bundles, Acute care hospitals, still struggle with these infections. Compliance with CHG bathing wipes can be challenging because of skin irritation and allergic reactions. Microbe resistance and antiseptic contamination recalls mean that Hospitals should investigate safe, effective alternatives to the status quo antiseptics. Non-antimicrobial urinary catheter bathing products do not effectively address the root cause of CAUTI. In order to improve CAUTI and CLABSI rates an evidence based, safe, effective, skin friendly approach was implemented. The focus was to improve patient satisfaction, efficiency, bathing compliance, promote antimicrobial stewardship and significantly reduce both CAUTI and CLABSI rates.

Methods

A retrospective, 6 month, pre- and post -implementation infection rate analysis was used to measure changes in CAUTI rate per 1,000 catheter days and CLABSI rates per 1,000 central line days consistent with the CDC reporting nomenclature and AHRQ standards.

Clinical evaluation was completed in CCU, NCCU, SICU, CVICU between November 2019 and April 2020. April 2019 and September 2019 were used for comparison. October 2019 was the product transition month.

Pre-and post-implementation CAUTI and CLABSI surveillance was completed monthly using electronic medical record chart audits during the study intervention period and compared them with retrospective analysis of past infection rates within the same units. Historically CAUTI and CLABSI rates are analyzed and reported monthly by Infection Control Services.

Nurse satisfaction survey to measure ease of use, efficiency of use, patient satisfaction, patient refusal, and perception of improved compliance.

DOCTORS MEDICAL CENTER

Tenet Health

The Multimodal Skin Cleanser and Barrier Protection test product and protocol transition

Intervention 1- The Addition of a Novel Topical Multimodal Skin Cleansing Therapy

The first Intervention was to introduce and educate staff on the addition of the new topical multimodal skin cleansing / decolonization and skin barrier protection product that will be replacing CHG impregnated wipes, Non-antimicrobial perineum bathing wipes, and dimethicone skin barrier protection wipes. The novel topical adjunct (Theraworx Protect) is available in a foam bottle, spay bottle, or solution impregnated wipe package. We chose the wipes in the 8 cloth configuration for single use total body Q24 application (unlike CHG wipes, includes the face and perineum) and the two cloth configuration for additional Q12 hour perineum skin cleansing / decolonization for patients with urinary catheters. The test product has been published in the American Journal of Infection Control on two occasions proving the product was effective against highly resistant bacteria, Carbapenem Resistant Enterobacteriaceae and was also proven to be equipotent to Chlorhexidine Gluconate 4%. Test product was again presented at wound care symposiums (SAWC, 2016, 2018, 2019) showing it to be safe and effective for use on wounds and dermatitis.

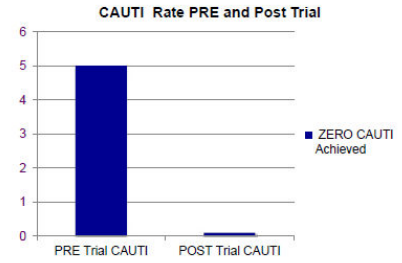
Intervention 2- Removal of CHG impregnated wipes, standard perineum bath wipes, aloe wipes, and dimethicone wipes replaced by new novel product and bathing protocol. 8 cloth package and 2 cloth package. Reducing the number of products from 3 to 1.

Intervention 3 – Protocol Education: The protocol we implemented is nearly identical to our previous protocol to include once daily total body bathing / decolonization and Q12 hour perineum bathing / catheter care. The difference being the new test product is safely applied on and around the mucous membranes allowing for a one product, one step, to include the perineum and the head, neck, and facial cleansing with a single 8 cloth packaged product.
We scheduled the additional perineum / catheter care cleansing with the 2 cloth test solution impregnated wipe approximately 12 hours after the first 8 cloth total body bathing application (per hospital policy) replacing our standard non-antimicrobial perineum wipe. Patients with fecal incontinence episodes would be cleaned and skin barrier protected with either the 8 cloth or 2 cloth test product as needed. Replacing aloe wipe, perineum / catheter wipe and the dimethicone barrier wipe.

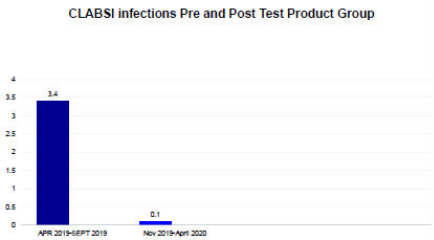
Results

This retrospective analysis involved CCU, NCCU, SICU, CVICU patients with central line catheters and / or indwelling urinary catheters. The new impregnated wipes test product trial started on **SIR rate 2019 .442** Data collected from chart reviews and monitoring of electronic records were reviewed and infections were recorded when they met NHSN reporting guidelines for either CAUTI or CLABSI. SIR rate January 1 – June 30, 2020 0.00

CAUTI rates were substantially reduced from a SIR rate of .442 Pretrial group to a SIR rate of in the Post test group



CLABSI Rates were reduced from an SIR rate of .348 in 2019 in the pre-test group to a SIR of 0.0 Jan 1 – June 30 in the Post – test product and protocol group



Discussion

The results of this evaluation suggest that higher rates of patient and nurse satisfaction can be achieved while simultaneously lowering infection rates and practicing antimicrobial stewardship. Antiseptics are now a part of antimicrobial stewardship initiatives. The most commonly used antiseptics in healthcare have been in use for 60 years. New, equipotent, hypo-allergenic, skin friendly alternatives are showing great promise. Due to the skin friendly nature of the test product (Theraworx protect) we found significant improvement in patient satisfaction and a dramatic decrease in patient refusal compared to our previous antiseptic bathing product. Due to the test products safety profile, we are able to apply this product to the mucous membranes in the perineum and critically important, the face, and neck. The mucous membranes of the face and neck are proven to be the main entry points of virus into the patients' blood stream. Adding these area's to our decolonization bathing should further reduce the chances of cross contamination when patients touch their faces. The nursing surveys also revealed many additional skin condition improvements in particular fungal dermatitis, moisture dermatitis, and incontinent dermatitis. Compromised skin odors also decreased. The low toxicity risk, SKU reduction, cost savings, efficiency, outcome improvement and high satisfaction and compliance rates should warrant continued investigation. A larger, randomized prospective project maybe warranted to confirm these results.

Our goal of ZERO CAUTI and CLABSI rates were achieved in the first 6 months and we are optimistic that we can maintain these rates by continuing the use of this new addition to our infection prevention bundle.

The contents do not represent the views of the TENET Health corporation.

The authors declare that they do not have a conflict of interest.

Correspondence: Asif Saiyed MBA, CIC, Director Infection Prevention, Doctors Medical Center 1441 Florida Ave Modesto, CA 95350
asif.saiyed@tenethealth.com

Quality Intervention: Northwell Health- Theraworx Protect Protocol Effect on C. diff Rates

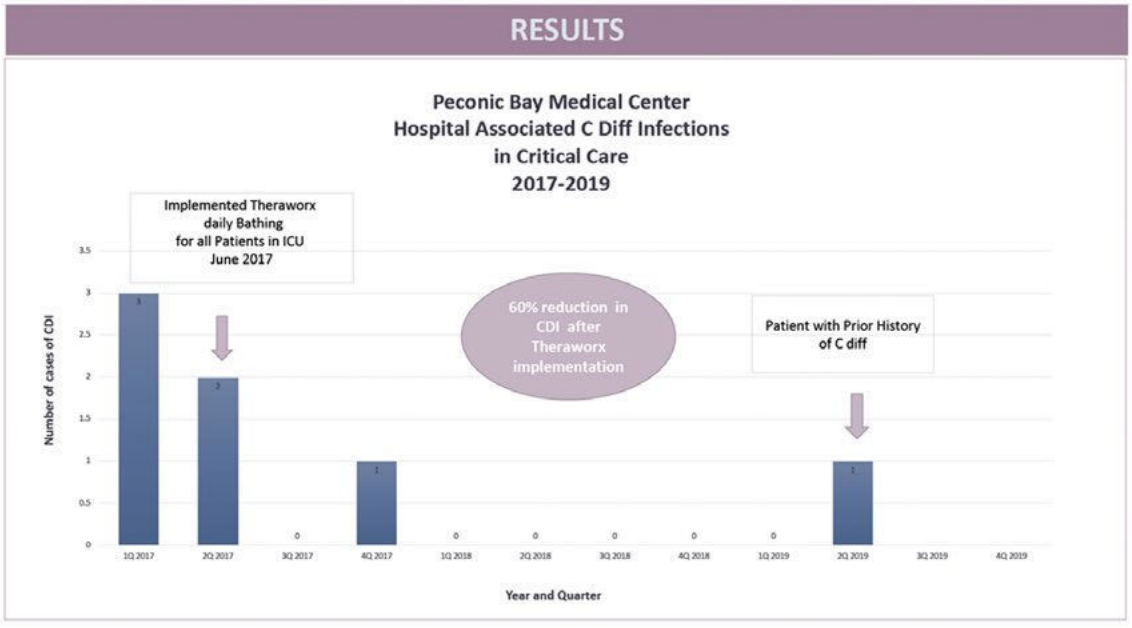
Preventing Hospital Acquired Clostridium Difficile Infection in ICU Patients: The Efficacy of Theraworx, a Novel Silver-Based Cleanser: Journal of Critical Care Nursing

Patty Mupo, RN, BSN; Holly Fischer, RN, BSN; Tarayn Dhansew, DO; Maria Masih, MD; Ashley Collins, DO; Vladimir Orlov DO; Faculty Advisor: Pooja Paunikar MD, MPH

Background

Prevention of hospital acquired clostridium difficile infection (CDI) continues to be an ongoing concern due to the prevalence, increase in patient morbidity and mortality, and impact on health care costs. It is estimated that 75% of CDI cases are hospital acquired with an estimated annual healthcare cost is $1.5- 3.2 billion [5]. Literature has shown a multimodal approach is required for effective transmission prevention. Patient bathing aims to reduce skin contamination and eliminate spores that can survive for up to five months. However, Studies have shown that spores are resistant to the commonly used disinfectants, including Chlorhexidine gluconate (CHG) [5]. A global review of infection prevention strategies revealed significant gaps in consistency and standardization of policies regarding patient bathing techniques [7]. Lack of standardization leaves room for non-compliance and variance, ultimately affecting patient outcomes and increasing the risk of CDI. Review of literature examining the efficacy of CHG bathing shows gaps in CDI prevention. A study evaluating CHG bathing on the rates of CDI in SICU patients was inconclusive [1]. A review of 17 trials examining CHG bathing against health-care associated infections in ICU patients did show evidence for reduction against CLABSI and CAUTI. However, effectiveness against other HAI, including CDI, were inconclusive [4]. A clinical trial has also showed a concern that CHG bathing may increase microbial resistance and CHG was not effective against multi-drug resistant bacteria [4, 3]. To address the gap in current practice, a study conducted to evaluate the safety and efficacy of Theraworx showed the colloidal silver-based product was non-inferior to the 4% CHG product [2]. Theraworx also has antimicrobial activity against gram positive and gram-negative organisms even at low concentrations and has components that supports the skin's innate immune system [2,8]

RESULTS



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Preventing Hospital Acquired Clostridium Difficile Infection in ICU Patients: The Efficacy of Theraworx, a Novel Silver-Based Cleanser

Patty Mupo, RN, BSN; Holly Fischer, RN, BSN; Tarayn Dhansew, DO; Maria Masih, MD; Ashley Collins, DO; Vladimir Orlov DO;
Faculty Advisor: Pooja Paunikar MD, MPH
Department of infection Prevention and the Department of Family Medicine, GME
Peconic Bay Medical Center, Northwell Health

Introduction

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Review of literature examining the efficacy of CHG bathing shows gaps in CDI prevention. A study evaluating CHG bathing on the rates of CDI in SICU patients was inconclusive [1]. A review of 17 trials examining CHG bathing against health-care associated infections in ICU patients did show evidence for reduction against CLABSI and CAUTI. However, effectiveness against other HAI, including CDI, were inconclusive [4]. A clinical trial has also showed a concern that CHG bathing may increase microbial resistance and CHG was not effective against multi-drug resistant bacteria [4, 3].

To address the gap in current practice, a study conducted to evaluate the safety and efficacy of Theraworx showed the colloidal silver-based product was non-inferior to the 4% CHG product [2]. Theraworx also has antimicrobial activity against gram positive and gram negative organisms even at low concentrations and has components that supports the skin's innate immune system [2, 6].

Purpose

We planned to explore a non-toxic silver-based skin antiseptic, Theraworx, to address skin contamination and spore eradication with a goal of preventing CDI in our ICU patients.

Methods

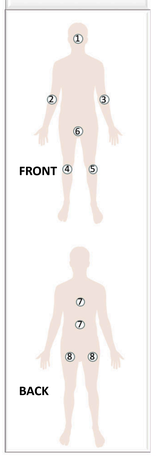
Creation and Implementation of Theraworx Protocol

- Theraworx patient bathing protocol was created by the Department of Infection Prevention at PBMC and was initiated in June 2017 for all ICU patients
- The protocol was communicated to nurses and patient care technicians, who were responsible for patient bathing
- Packet of wipes from warmer (warmer temperature auto regulated not to exceed 115 degrees F) or warm sealed packet under warm water

One packet (8 wipes total) per patient according to protocol

1. Use one cloth to wipe face, neck, chest and abdomen.
2. Use one cloth to wipe right arm and right hand.
3. Use one cloth to wipe left arm and left hand.
4. Use one cloth to wipe right leg and right foot.
5. Use one cloth to wipe left leg and left foot
6. Take one cloth and cleanse perineum. If patient has a foley catheter wipe catheter from meatus down the entire catheter.
7. Proceed to back area and with one wipe cleanse back.
8. Take one wipe, cleanse buttocks.

8 wipes total



Analysis of Results

- Results were analyzed by the Infection Prevention Department comparing data from rates of CDI prior to implementation of protocol (June 2017) and rates after implementation. Data included all patients in the ICU, including those with a prior history of CDI

Theraworx PROTECT

The Theraworx Advantage: A Topical Immunity Health System

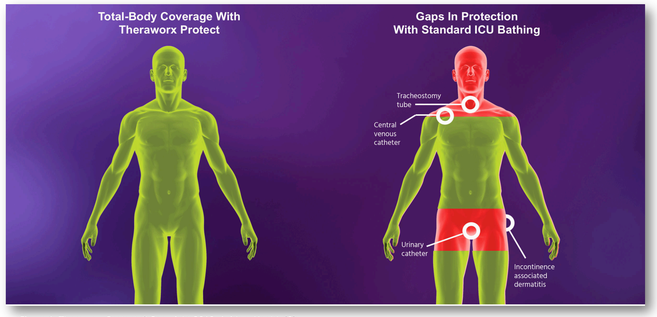
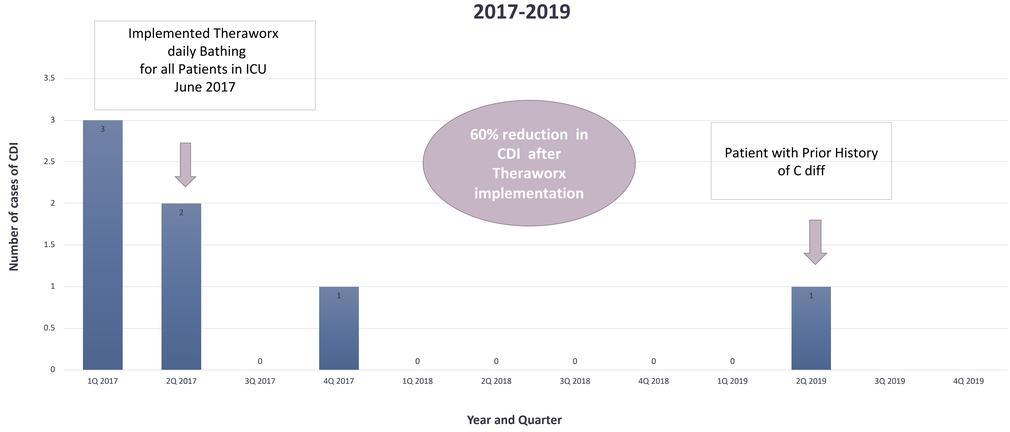
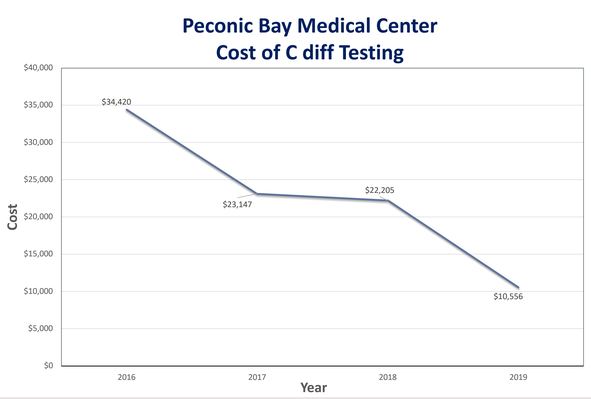


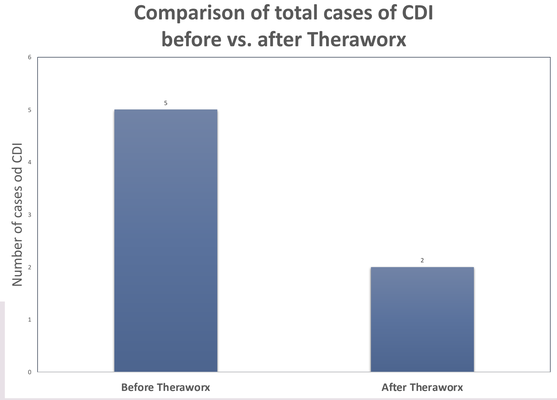
Figure 1: Theraworx Protect ® Copyright 2019, Avidam Health [9]

- Theraworx Protect is a novel silver-based, non-toxic cleanser line that offers numerous benefits that are lacking from the current standard of care:
  - This cleanser can be used on the face, mucosa, and perineum
  - Does not require rinsing after application
  - Acidic pH Supports the natural skin biome and optimizes the stratum corneum, an important barrier which prevents penetration of pathogens into the skin

RESULTS







Discussion

This study demonstrated that Theraworx is a superior cleanser in our ICU patients compared to the standard bathing protocol. In 2016-2017, there were 5 cases of CDI in our ICU. Our study showed that implementing Theraworx daily bathing lead to a 60% reduction in CDI rates. In the second quarter of 2019, there was one incidence of CDI in a patient with a known prior history of C.diff. Colonization by C.diff could have contributed to this occurrence. In addition, there has been an overall reduction in costs related to C.diff testing by more than $12,000.

Theraworx has several benefits in comparison to CHG. The perineum is an area that is commonly colonized by C. diff. Theraworx bath wipes can be applied to the perineum, while CHG bathing cannot. As a silver-based product, Theraworx maintains the normal acidic pH of the skin. It provides nourishment, supports cell growth and skin barrier protection. Overall, Theraworx enhances skin adhesion and integrity to prevent penetration of pathogens (2, 12).

As a no rinse formulation therefore eliminating extra steps which are required in daily bathing thus promoting better compliance.

Conclusion

Daily Theraworx bathing in the ICU has led to a reduction in hospital acquired C. difficile infection rates in these patients. Although our patient population was restricted to the ICU, we believe there is potential that implementing Theraworx in other units may lead to similar results. The benefits of Theraworx can have a great impact on reducing overall healthcare costs by reducing CDI rates.

Our findings of the effectiveness of Theraworx on reducing hospital acquired C. difficile may be helpful in the development of a hospital-wide and perhaps a system-wide standard patient bathing protocol.

Next Steps

Currently, Theraworx bathing is being implemented on inpatient medicine-surgery units who are at high-risk or have a history of C. difficile infection.

We have also seen a reduction in CLABSI and CAUTI rates in the ICU with daily Theraworx bathing used on patients with central indwelling catheters. We plan to further explore the effectiveness of Theraworx on other HAI.

We have also implemented Theraworx bathing for pre-operative and post-operative bathing to further prevent hospital acquired infections.

We hope to implement Theraworx bathing in other hospitals in our system to determine if similar results are attainable. If successful, this research may inform practice changing guidelines for patient bathing protocols.

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Reducing the Incidence o Clostridium Difficile Infections, Antibiotics and Costs In A Long-Term Acute Care Setting - A Surveillance Experience. Levindale Hebrew Geriatric Center and Hospital 2018.

Background: Clostridium difficile is the most common cause of acute infectious diarrhea in the hospital setting as well as in long-term care facilities (LTCFs), and disproportionately affects individuals who are >65 years old. Although the incidence of other healthcare-associatedinfections has declined, the incidence of C difficile infections (CDIs) has increasedand is the most common hospital infection from 3,000 reported in 2000 to 14,000 reported in 2007. More than 90% of the cases are reported in persons aged 65 years and older. Levindale Hebrew Geriatric Center and Hospital is a 330-licensed-bed facility. Levindale's geriatric center includes 126 comprehensive care (long-term care) beds, 35 subacutebeds, 28 dementia care beds and a 21-bed respiratory care unit. The Specialty Hospital at Levindale consists of a 40-bed high intensity care unit and an 80-bed behavioral health unit. The facility is directly adjacent to a large 500-bed acute care trauma hospital in Baltimore, Maryland. Burke 2 is a 21-bed licensed LTC respiratory care unit that has semi-private rooms and includes patients with ventilator support, wounds, tracheostomy's, hyperalimentation, G-tube feedings, indwelling urinary catheters, and vascular access. It is estimated that 2.5 million hospital-acquired infections (HAIs) occur annually in the United States. These infections are considered preventable but are associated with 90,000 patient deaths and financial costs exceeding $4.5 billion annually. [1] It is believedthe primary causes of these patient injuries are poor technique and non-compliance to hand hygiene protocols. [2] In 2008, as a response to the American epidemic of HAIs, the Centers for Medicare and Medicaid Services, as part of the affordable care act, created new rules penalizing hospital reimbursement for costs associated with conditions not present on admission and diagnosed during the hospital stay.[3]
[5,6,7].

Results: Due to recurring skin related adverse events associated with CHG the decision was made to replace CHG with a proven non-inferior CHG 4% alternative, with a low toxicity characteristic. In 2016 (baseline) 6,539 patients were admitted to the long- term care respiratory unit and the CDI rate was 9.18 per 10,000 resident days substantiated through confirmed and documented cultures. In 2017 (experiment), 6,959 patients were admitted to the unit and the infection rate was 2.87 per 10,000 resident days representing a 68% reduction. Antibiotic use and cultures decreased 41% and 30% respectively. There were no changes in culture policy 2016 to 2017. In 2017, two cases of hospital-onset C. Dfficile occurred (One in June and One in December). The rate was 2.87 per 10,000 resident days, a 68% reduction compared to CY16.

LEVINDALE
A LifeBridge Health Center

REDUCING THE INCIDENCE OF CLOSTRIDIUM DIFFICILE INFECTIONS, ANTIBIOTICS AND COSTS IN A LONG- TERM ACUTE CARE SETTING- A SURVEILLANCE EXPERIENCE.

SUSAN M. JOHNSTON, BSN CIC - Director of Infection Prevention & Control Levindale Hebrew Geriatric Center and Hospital

Levindale Hebrew Geriatric Center and Hospital
A long-term care center and specialty hospital

Background

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Burke 2 is a 21-bed licensed LTC respiratory care unit that has semi-private rooms and includes patients with ventilator support, wounds, tracheostomy's, hyperalimentation, G-tube feedings, indwelling urinary catheters, and vascular access.

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In a global review of guidelines, recommendations and strategies by Ballsells et. al. and printed in the Journal of Global Health, December 2016, [4] the importance and challenges associated with effective hand hygiene in the context of C. difficile were discussed. Special attention was drawn to limitations of disinfection hand with alcohol–based hand rubs (ABHR) as they are non–sporicidal and do not remove C. difficile spores from contaminated hands. The flash kill nature of alcohol has been shown to cause vegetative C-diff to sporulate. Guidance on best practices varied and included the preferential use of soap and water when caring for patients with CDI, especially during outbreaks, raising awareness and warning health care providers about the limitations of ABHRs [5,6,7].

Objective

C. difficile Baseline: In 2016 there were six cases of Hospital-onset C. difficile on the unit. Surveillance is conducted utilizing CDC's NHSN surveillance definitions. The rate of infection was 9.18 per 10,000 resident days.

Methods

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A silver colloidal skin cleansing agent was introduced to the unit to assist with resident bathing, peri care and wound healing in December 2016. This agent was selected as an alternative to chlorhexidine gluconate due prolonged lengths of stay and skin integrity issues in this patient population. Education on the product and bathing / peri care protocol was performed from December – July 2017. All patients received twice daily applications under the guidelines of the University of North Carolina human studies subcommitte.

Results

Due to recurring skin related adverse events associated with CHG the decision was made to replace CHG with a proven non-inferior CHG 4% alternative, with a low toxicity characteristic. In 2016 (baseline) 6,539 patients were admitted to the long- term care respiratory unit and the CDI rate was 9.18 per 10,000 resident days substantiated through confirmed and documented cultures. In 2017 (experiment), 6,959 patients were admitted to the unit and the infection rate was 2.87 per 10,000 resident days representing a 68% reduction. Antibiotic use and cultures decreased 41% and 30% respectively. There were no changes in culture policy 2016 to 2017.
In 2017, two cases of hospital-onset C. Dfficile occurred (One in June and One in December). The rate was 2.87 per 10,000 resident days, a 68% reduction compared to CY16.

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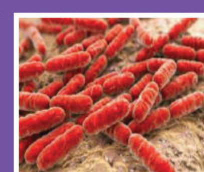
(The cost of gloves per box decrease by $1 in 2017 by supplier.) The increase glove order in 2017 indicates Standard Precautions were followed after lifting Transmission-based Precautions.

Considerations

Hand hygiene interventions and compliance rates did not change over the 2016- 2017 nor did the patient population being served. One change that may also influence C. difficile acquisition was an increase from once daily to a twice a day patient room bleach cleaning protocol for C. difficile positive patients implemented in April 2016. Limitations: Small unit / Unique population being served.

Clostridum Difficile



Clostridum Difficile

Discussion

Intervention of twice daily treatments with silver colloidal cleansing wipes may prevent fecal oral transmission of C. difficile in a long-term care unit. Intervention of twice daily treatments with silver colloidal cleanings wipes may have assisted in reducing the number of positive cultures in a long-term care unit thereby preventing unnecessary antibiotic exposure, contributing to C. difficile infection. Recent trials have also shown the topical intervention to be effective with reduction on MMP9 protease levels and Biofilm activity in vivo which could correlate to these results concerning C. difficile. [8] Implementing the non-inferior 4% CHG alternative was effective in reducing C difficile incidence, antibiotic use, number of cultures and overall costs. CHG intolerability is clearly documented, forcing the use of basins and other regimens not shown to manage micro-debris and proven alternatives warrant further investigation.

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Funded in part by a testing agreement from Avadim Health, Inc.

Reducing the incidence of clostridium difficile infections, antibiotics and costs in a long- term acute care setting- a surveillance experience.

SUSAN M. JOHNSTON, BSN CIC - Director of Infection Prevention & Control Levindale Hebrew Geriatric Center and Hospital

Levindale Hebrew Geriatric Center and Hospital

A long-term care center and specialty hospital

Background

Clostridium difficile is the most common cause of acute infectious diarrhea in the hospital setting as well as in long-term care facilities (LTCFs), and disproportionately affects individuals who are >65 years old. Although the incidence of other healthcare-associated infections has declined, the incidence of C difficile infections (CDIs) has increased and is the most common hospital infection from 3,000 reported in 2000 to 14,000 reported in 2007. More than 90% of the cases are reported in persons aged 65 years and older.

Levindale Hebrew Geriatric Center and Hospital is a 330-licensed-bed facility. Levindale's geriatric center includes 126 comprehensive care (long-term care) beds, 35 subacute beds, 28 dementia care beds and a 21-bed respiratory care unit. The Specialty Hospital at Levindale consists of a 40-bed high intensity care unit and an 80-bed behavioral health unit. The facility is directly adjacent to a large 500-bed acute care trauma hospital in Baltimore, Maryland.

Burke 2 is a 21-bed licensed LTC respiratory care unit that has semi-private rooms and includes patients with ventilator support, wounds, tracheostomy's, hyperalimentation, G-tube feedings, indwelling urinary catheters, and vascular access.

It is estimated that 2.5 million hospital-acquired infections (HAIs) occur annually in the United States. These infections are considered preventable but are associated with 90,000 patient deaths and financial costs exceeding $4.5 billion annually. [1] It is believed the primary causes of these patient injuries are poor technique and non-compliance to hand hygiene protocols. [2] In 2008, as a response to the American epidemic of HAIs, the Centers for Medicare and Medicaid Services, as part of the affordable care act, created new rules penalizing hospital reimbursement for costs associated with conditions not present on admission and diagnosed during the hospital stay.[3]

In a global review of guidelines, recommendations and strategies by Ballsells et. al. and printed in the Journal of Global Health, December 2016, [4] the importance and challenges associated with effective hand hygiene in the context of C. difficile were discussed. Special attention was drawn to limitations of disinfection hand with alcohol–based hand rubs (ABHR) as they are non–sporicidal and do not remove C. difficile spores from contaminated hands. The flash kill nature of alcohol has been shown to cause vegetative C-diff to sporulate. Guidance on best practices varied and included the preferential use of soap and water when caring for patients with CDI, especially during outbreaks, raising awareness and warning health care providers about the limitations of ABHRs [5,6,7].

Objective

C. difficile Baseline: In 2016 there were six cases of Hospital-onset C. difficile on the unit. Surveillance is conducted utilizing CDC's NHSN surveillance definitions. The rate of infection was 9.18 per 10,000 resident days.

Methods

A 12-month (2017), experimental, open label clinical trial of replacing chlorhexidine gluconate (CHG) with a novel skin formulation was conducted in a high acuity long term care unit. The primary measure was C difficile documented incidence through reported and confirmed cultures compared to baseline year (2016). Surveillance was conducted utilizing Center for Disease Control (CDC) National Healthcare Safety Network (NHSN) surveillance definitions.

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Results

Due to recurring skin related adverse events associated with CHG the decision was made to replace CHG with a proven non-inferior CHG 4% alternative, with a low toxicity characteristic. In 2016 (baseline) 6,539 patients were admitted to the long- term care respiratory unit and the CDI rate was 9.18 per 10,000 resident days substantiated through confirmed and documented cultures. In 2017 (experiment), 6,959 patients were admitted to the unit and the infection rate was 2.87 per 10,000 resident days representing a 68% reduction. Antibiotic use and cultures decreased 41% and 30% respectively. There were no changes in culture policy 2016 to 2017.
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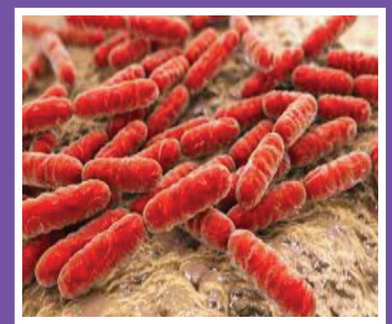

Clostridum Difficile

Discussion

Intervention of twice daily treatments with silver colloidal cleansing wipes may prevent fecal oral transmission of C. difficile in a long-term care unit. Intervention of twice daily treatments with silver colloidal cleanings wipes may have assisted in reducing the number of positive cultures in a long-term care unit thereby preventing unnecessary antibiotic exposure, contributing to C. difficile infection. Recent trials have also shown the topical intervention to be effective with reduction on MMP9 protease levels and Biofilm activity in vivo which could correlate to these results concerning C. difficile. [8] Implementing the non-inferior 4% CHG alternative was effective in reducing C difficile incidence, antibiotic use, number of cultures and overall costs. CHG intolerability is clearly documented, forcing the use of basins and other regimens not shown to manage micro-debris and proven alternatives warrant further investigation.

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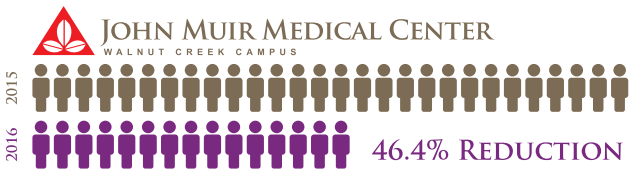
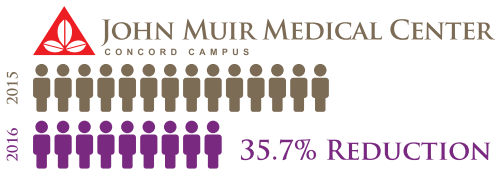
Funded in part by a testing agreement from **Avadim Health, Inc.**

CLABSI (Central Line Associated Blood Stream Infections) Reduction Seen with Multifactorial Nurse Initiative.

****To be presented at the Fall ANCC national convention****

John Muir Health includes two of the largest medical centers in Contra Costa County: John Muir Medi-cal Center, Walnut Creek, a 554-licensed bed medical center that serves as Contra Costa County's only designated trauma center; and John Muir Medical Center, Concord, a 245-licensed bed medical center in Concord. Together, they are recognized as preeminent centers for neurosciences, orthopedics, cancer care, cardiovascular care and high-risk obstetrics. John Muir a two-hospital health system observed an unacceptable increase in central line-associated bloodstream infections (CLABSIs) reported to National Healthcare Safety Network. Hospital acquired infections (HAIs) are a well-recognized cause of morbidity and mortality in the United States, and catheter-related bloodstream infections are 1 of the top 4 causes of HAI.1 It sought to reduce CLABSIs in a manner consistent with Magnet Hospital values. CLABSI's rep-resent a major source of HAIs and can significantly impact a patient's clinical course. Identification of an increased rate of CLABSI's prompted a multi-disciplinary approach to critically evaluating and then alter-ation and implementation of a protocol to reduce these infections thus optimizing patient outcomes. This nursing led initiative exemplified the Magnet criteria by involving clinical nurses, administrative nurses and infection prevention experts. Originally, an evidence-based central line insertion/maintenance bun-dle was adopted that included bathing central-catheterized patients with chlorhexidine gluconate (CHG). CHG proved harsh on patients' skin, compromising compliance and isn't indicated for mucous membranes where MDRO's colonize and was abandoned. It was replaced with a novel non-toxic skin formulation that has natural antimicrobial properties- Theraworx®. (A CHG scrub was still used at the local site prior to invasive procedure.) In January 2016, a performance improvement team was formed to support adherence to the bundle. In March 2016, the novel formulation (Theraworx®) was added to CHG use at the catheter insertion site. Upon, introduction of a novel non-toxic skin formulation (Theraworx®) to the central line insertion and maintenance protocol a marked reduction in CLABSIs was realized. At one hospital CLABSIs dropped from 28 in 2015 to 15 in 2016, (46.4% reduction). At the other hospital they dropped from 14 in 2015 to 9 in 2016 (35.7%). These data demonstrate a significant clinical reduction in CLABSIs, a major hospital acquired infection.





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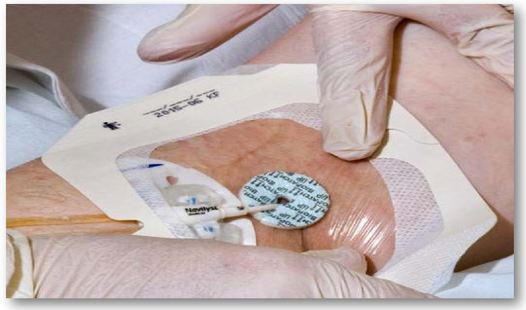
Nurse-led Practice Initiative Reduces CLABSI Standardized Infection Ratio (SIR)

Statement of the Problem

Nurse clinicians in two hospitals of a Northern California healthcare system with approximately 800 licensed beds, applied Centers for Disease Control (CDC) guidelines for Central Line-Associated bloodstream infection (CLABSI) prevention. Despite their best efforts, CLABSI incidents continued at an unacceptable rate.



Background & Significance

In hospitalized patients, use of central line venous catheters (CVC) is associated with a risk for CLABSI, increasing morbidity, mortality, length of hospital stay and cost. According to the U.S. Department of Health & Human Services, approximately *41,000* central line-associated deaths occur each year in the United States[1].

CLABSIs are largely preventable when evidence-based guidelines for insertion and maintenance of CVCs are followed. CDC Guidelines provide evidence-based recommendations, including:

1. Training for personnel who insert and maintain catheters.
2. Daily antimicrobial bathing.
3. Maximal sterile barrier precautions during central venous catheter insertion.
4. Using a > 0.5% chlorhexidine skin preparation with alcohol for antisepsis.
5. Minimizing routine catheter replacement..
6. Using antiseptic chlorhexidine impregnated sponge dressings.

CDC Guidelines also recommend adopting bundled care elements and documenting compliance with bundles.

Lowered CLABSI rates significantly improve patient outcomes and favorably impact financial stability.

1. U.S. Department of Health & Human Services, Partnership for Patients HealthCare.gov

Aim of this Project

The aim was to find a creative, evidence-based solution to ensure all practice standards were implemented to decrease CLABSI rates and create better patient outcomes.

Strategy

Infection Prevention practitioners teamed with front-line clinical nurses to review CLABSI prevention bundles already in place and to further standardize maintenance care.

A central line bundle had been adopted in 2014 that included bathing CVC patients with chlorhexidine gluconate (CHG). However, CHG was not appropriate for all patients and couldn't be used body-wide. CHG was replaced with a non-toxic skin formula, Theraworx[2], for use on the skin site prior to invasive procedures.

2. Theraworx™ (Antimicrobial Wipes) contains a self-drying, leave-on cleanser consisting of a specialized surfactant and skin-healthy antimicrobial agents: aloe, allantoin, vitamin E and silver, the primary antimicrobial ingredient.

Implementation

1. March 2015: Theraworx bathing was expanded to all patients (not just those with devices).
2. December 2016: Maintenance care previously performed by Critical Care nurses was transferred to the Parenteral Services Team to reduce variations in CVC dressing-change technique.
3. January 2016: A performance improvement team formed to support adherence with the initiative.
4. March 2016: Theraworx pre-cleaning at catheter insertion sites was added prior to CHG use. Hands-on education was given to the Parenteral Services Team.
5. June 2016: Bedside nurses received both online and hands-on education on management of central lines.

Implications for Practice

Frontline staff designed a protocol to deploy evidence-based, standardized care bundles to improve patient outcomes.

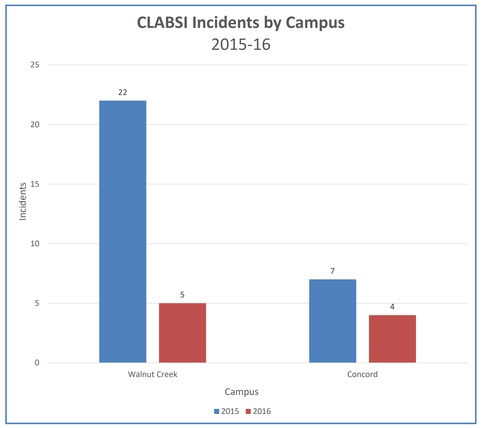
Outcomes

CLABSI SIRs[3] dropped sharply with Theraworx bathing and the addition of performance team improvements to existing JMH practice standards.

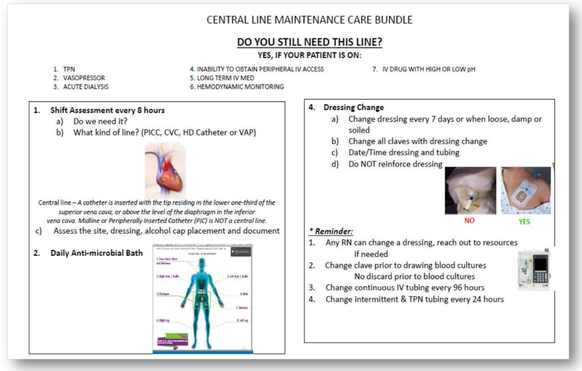
- At JMH Walnut Creek, SIR dropped by 75%, from 1.0 to 0.25.
- At JMH Concord, SIR dropped by almost 50%, 1.5 to 0.77.

3. Standard infection ratio (SIR) compares infections in an organization to infections "predicted" for a hospital of that size based on nationally reported data. A ratio below 1.0 indicates an organization has fewer infections than expected, based on national data.

CLABSI Incidents and Ratios



CLABSI Care Bundles



CENTRAL LINE MAINTENANCE CARE BUNDLE

DO YOU STILL NEED THIS LINE?

YES, IF YOUR PATIENT IS ON:

1. TPN
2. VASOPRESSOR
3. ACUTE DIALYSIS
4. INABILITY TO OBTAIN PERIPHERAL IV ACCESS
5. LONG TERM IV MED
6. HEMODYNAMIC MONITORING
7. IV DRUG WITH HIGH OR LOW pH

1. Shift Assessment every 8 hours
- a) Do we need it?
- b) What kind of line? (PICC, CVC, HD Catheter or VAP)

Central line – A catheter is inserted with the tip residing in the lower one-third of the superior vena cava, or above the level of the diaphragm in the inferior vena cava. Midline or Peripherally Inserted Catheter (PIC) is NOT a central line.

- c) Assess the site, dressing, alcohol cap placement and document

2. Daily Anti-microbial Bath

4. Dressing Change
- a) Change dressing every 7 days or when loose, damp or soiled
- b) Change all claves with dressing change
- c) Date/Time dressing and tubing
- d) Do NOT reinforce dressing

NO YES

Reminder:
1. Any RN can change a dressing, reach out to resources if needed
2. Change clave prior to drawing blood cultures
   No discard prior to blood cultures
3. Change continuous IV tubing every 96 hours
4. Change intermittent & TPN tubing every 24 hours

CENTRAL LINE REMOVAL CARE BUNDLE

TAKE IT OUT!

REMOVAL PROCESS

1. Call trained RN staff
2. Position patient so the level of the catheter site is at or below the heart
3. Apply gauze to site and maintain for 30 seconds or until hemostasis
   CAUTION: for patients on anticoagulant therapy, hemostasis may take an extended period of time to achieve.
4. Apply petroleum-based jelly ointment to the site
5. Apply occlusive dressing
6. Maintain in sitting or recumbent position for 30 minutes past removal
7. Change dressing every 24 hours until healed

Acknowledgements

John Muir Health Parenteral Services

John Muir Health Infection Prevention

John Muir Health CLABSI Team

John Muir Health clinical nurses

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U.S. Department of Health & Human Services Partnership for Patients HealthCare.gov

Nancy Gibbs MSN, RN, Clinical Nurse Educator nancy.gibbs@johnmuirhealth.com

Joanna Mills, MSN, RN, CNS, CIC, Manager Infection Prevention joanna.mills@johnmuirhealth.com

JOHN MUIR HEALTH

Clinical Poster: Symposia For Advanced Wound Care Fall 2019

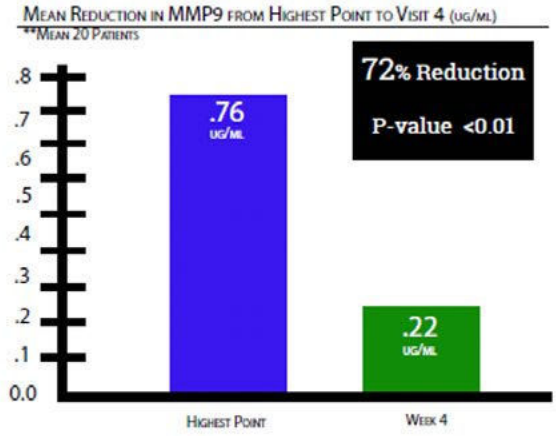
Effect of an Innovative pH Lowering Wound Therapeutic on MMP Levels and Bacterial Biofilm Colonization of Chronic Non-Healing Wounds.

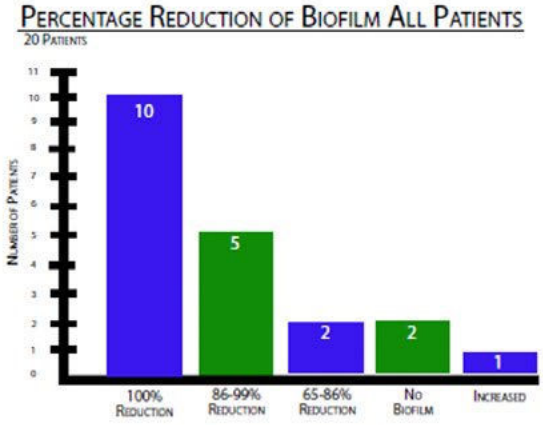
William Marston, MD.
Greg Schultz, PhD

Background:
Patients with chronic non-healing lower extremity wounds often are found to have chronic inflammation associated with biofilm bacterial colonization of the wound bed. Eradication of this biofilm and control of upregulated inflammation can be difficult to achieve without the use of long courses of systemic antibiotic administration. A novel wound therapy, Theraworx Protect (TWX), has been developed that reduces the pH of skin and wound tissue, increasing their resistance to bacterial colonization. This product has been shown to be effective at reducing the incidence of catheter-associated UTIs and central line associated infections. In this study we have applied TWX to chronic non-healing leg ulcers and measured matrix metalloproteinase (MMP) levels in wound fluid and bacterial biofilm involvement of the wound bed before and after 4 weeks of TWX therapy.

Methods:
Twenty patients with chronic non-healing lower extremity ulcers of >4 weeks duration were identified and agreed to participate. Patients were included with diabetic foot ulcers, venous leg ulcers and ulcers associated with chronic arterial insufficiency. Baseline patient demographics and wound characteristics were recorded. Prior to treatment with TWX, samples of wound fluid and tissue samples were obtained for MMP and bacterial biofilm analysis. MMP activities were measured using a synthetic seven amino acid peptide with a fluorochrome-quencher pair that generates a fluorescent signal when the peptide is cut by MMPs. 1 Colony forming units (CFU) of viable bacteria in biofilm phenotype were measured by standard dilution plating technique following brief (10 minute) exposure of ultrasonically dispersed biofilm communities to dilute bleach (0.1%) followed by neutralization with 0.15% sodium metabisulfite.2 The patients were treated for 4 weeks with standard treatment for the wound etiology plus application of TWX to the wound and peri-wound areas at all dressing changes. At weekly visits, wound characteristics were obtained and repeat wound fluid and tissue samples were obtained for MMP and bacterial analysis. At the completion of 4 weeks of treatment, wound size was re-measured to determine the percentage of wound healing over the 4 weeks of treatment. The study was approved and conducted under the guidelines of the University of North Carolina human studies subcommittee.

Results:
Sixty-seven percent of patients healed >30% over the 4-week treatment phase. The mean wound size decreased significantly from 29.8 ± 27.2 cm2 at baseline to 20.1 ± 20.5 cm2 after 4 weeks (P = .01). At peak level as opposed to baseline, the mean MMP-9 level was 0.76 ug/ml. After 4 weeks of TWX treatment, this level decreased to 0.22 ± 0.1 ug/ml (P < 0.01). At baseline, 15 of 20 patients had detectable levels of biofilm activity with a mean of 207,144 CFU/ml of homogenate. Among the 18 patients with detectable biofilm during the study, 10 had elimination of all detectable biofilm activity after 4 weeks of TWX treatment. Five patients experienced reduction of biofilm activity by > 86%. The total mean activity after 4 weeks of TWX treatment was 3109 CF U/ml of homo genate (P= 0.10).





Effect of an Innovative pH Lowering Wound Therapeutic on MMP Levels and Bacterial Biofilm Colonization of Chronic Non-Healing Wounds.

UNC Medical Center
UNC Health Care
Department Of Vascular Surgery & Podiatry

William A. Marston, M.D. - Professor and Chief, University of North Carolina Division of Vascular Surgery, Medical Director, Wound Management Center
Greg Schultz, PhD. - University of Florida Shands, Professor, Department of Obstetrics and Gynecology; Director, Institute for Wound Research

UFHealth
University of Florida Health
Institute For Wounds Research

Background

Patients with chronic non-healing lower extremity wounds often are found to have chronic inflammation associated with biofilm bacterial colonization of the wound bed. Eradication of this biofilm and control of upregulated inflammation can be difficult to achieve without the use of long courses of systemic antibiotic administration. A novel wound therapy, Theraworx Protect (TWX), has been developed that reduces the pH of skin and wound tissue, increasing their resistance to bacterial colonization. This product has been shown to be effective at reducing the incidence of catheter-associated UTIs and central line associated infections. In this study we have applied TWX to 10 chronic non-healing leg ulcers and measured matrix metalloproteinase (MMP) levels in wound fluid and bacterial biofilm involvement of the wound bed before and after 4 weeks of TWX therapy.

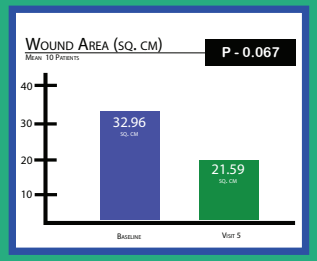
Objective

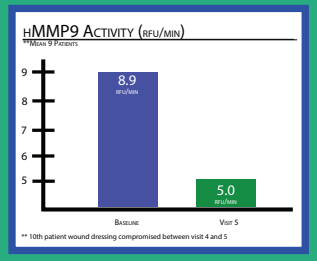
The primary study objective is to determine changes in MMP levels and biofilm involvement of chronic wounds treated with TWX over one month time and the correlation of these levels with wound healing.

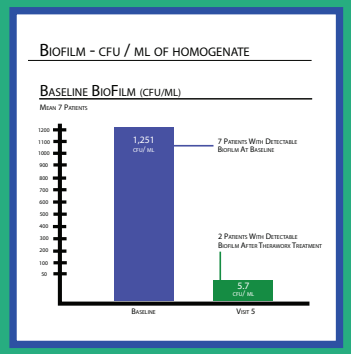
Methods

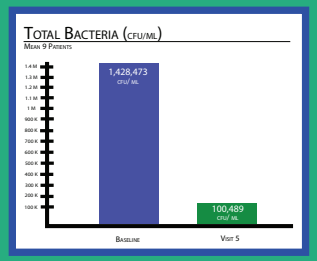
Ten patients with chronic non-healing lower extremity ulcers of >4 weeks duration were identified and agreed to participate. Patients were included with diabetic foot ulcers, venous leg ulcers and ulcers associated with chronic arterial insufficiency. Baseline patient demographics and wound characteristics were recorded. Prior to treatment with TWX, samples of wound fluid and tissue samples were obtained for MMP and bacterial biofilm analysis. MMP activities were measured using a synthetic seven amino acid peptide with a fluorochrome-quencher pair that generates a fluorescent signal when the peptide is cut by MMPs. [1] Colony forming units (CFU) of vial bacteria in biofilm phenotype were measured by standard dilution plating technique following brief (10 minute) exposure of ultrasonically dispersed biofilm communities to dilute bleach (0.1%) followed by neutralization with 0.15% sodium metabisulfite.[2] The patients were treated for 4 weeks with standard treatment for the wound etiology plus application of TWX to the wound and peri-wound areas at all dressing changes. At weekly visits, wound characteristics were obtained and repeat wound fluid and tissue samples were obtained for MMP and bacterial analysis. At the completion of 4 weeks of treatment, wound size was re-measured to determine the percentage of wound healing over the 4 weeks of treatment. The study was approved and conducted under the guidelines of the University of North Carolina human studies subcommitte

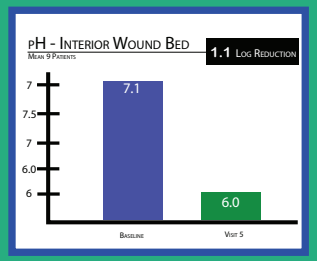
Results





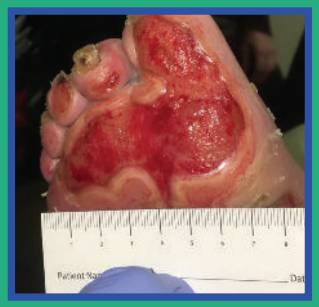




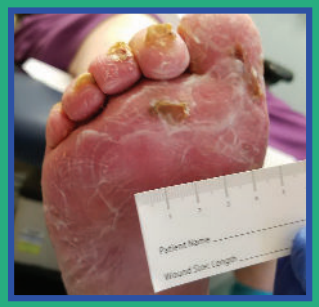


Results

Nine of the 10 patients completed the 4-week treatment protocol. Of these patients, 6 healed >30% over the 4-week treatment phase. Mean area of wounds at baseline was 33.0 sq. cm. and was reduced to 21.6 sq. cm. after TWX treatment. The mean pH level as measured in the wound bed before cleaning and debridement was 7.1 at baseline and 6.0 after 4 weeks, a 1.1 log reduction. At baseline, 7 of 10 patients had significant detectable levels of biofilm activity with a mean of 1,217 CFU/ml of homogenate. After TWX treatment, only 2 of the seven had detectable biofilm activity in wound samples with a mean activity of 5.7 CFU/ml of homogenate. At baseline, the mean MMP-9 level was 8.9 ± 8.1 RFU/min. After 4 weeks of TWX treatment, this level decreased to 5.0 ± 4.5 RFU/min.



Patient 004 Visit Baseline



Patients 004 Visit 5

Discussion

While these data are suggestive of a trend towards a reduction in MMP activity, biofilms and total bacteria levels, they are not statistically significant due to the sample size. Additional patients are being entered into the study.

Conclusion

Treatment of chronic non-healing wounds with standard treatment protocol plus TWX therapy resulted in reduction in the incidence of significant biofilm wound involvement and reduction in MMP-9 levels. Most wounds, despite lack of response to standard therapy prior to study enrollment, achieved >30% closure during the 4-week treatment phase. Study in additional patients will continue to further define the beneficial effects of TWX on chronic non-healing wounds.

References

1 US Patent 8,058,024B2
2 P.L. Phillips, Q. Yang, G.S. Schultz. The Effect of Negative Pressure Wound Therapy with Periodic Instillation Using Antimicrobial Solutions on Pseudomonas Aeruginosa Biofilm on Porcine Skin Explants. International Wound J, 10 (suppl. 1) 48-55, 2013.

SAWC FALL
NOVEMBER 2 - 4, 2015 LAS VEGAS

Funded in part by a testing agreement from Avadim Health, Inc.

Effect of an Innovative pH lowering wound therapeutic on MMP levels and bacterial biofilm colonization of chronic non-healing wounds.

UNC Medical Center – UNC Health Care
Department Of Vascular Surgery & Podiatry

William A. Marston, M.D. - Professor of Surgery, University of North Carolina Division of Vascular Surgery, Medical Director, Wound Management Center
Greg Schultz, PhD. - University of Florida Shands, Professor, Department of Obstetrics and Gynecology; Director, Institute for Wound Research

UF Health – University of Florida Health
Institute For Wounds Research

Background

Patients with chronic non-healing lower extremity wounds often are found to have chronic inflammation associated with biofilm bacterial colonization of the wound bed. Eradication of this biofilm and control of upregulated inflammation can be difficult to achieve without the use of long courses of systemic antibiotic administration. A novel wound therapy, Theraworx Protect (TWX), has been developed that reduces the pH of skin and wound tissue, increasing their resistance to bacterial colonization. This product has been shown to be effective at reducing the incidence of catheter-associated UTIs and central line associated infections. In this study we have applied TWX to chronic non-healing leg ulcers and measured matrix metalloproteinase (MMP) levels in wound fluid and bacterial biofilm involvement of the wound bed before and after 4 weeks of TWX therapy.

Objective

The primary study objective is to determine changes in MMP levels and biofilm involvement of chronic wounds treated with TWX over one month time and the correlation of these levels with wound healing.

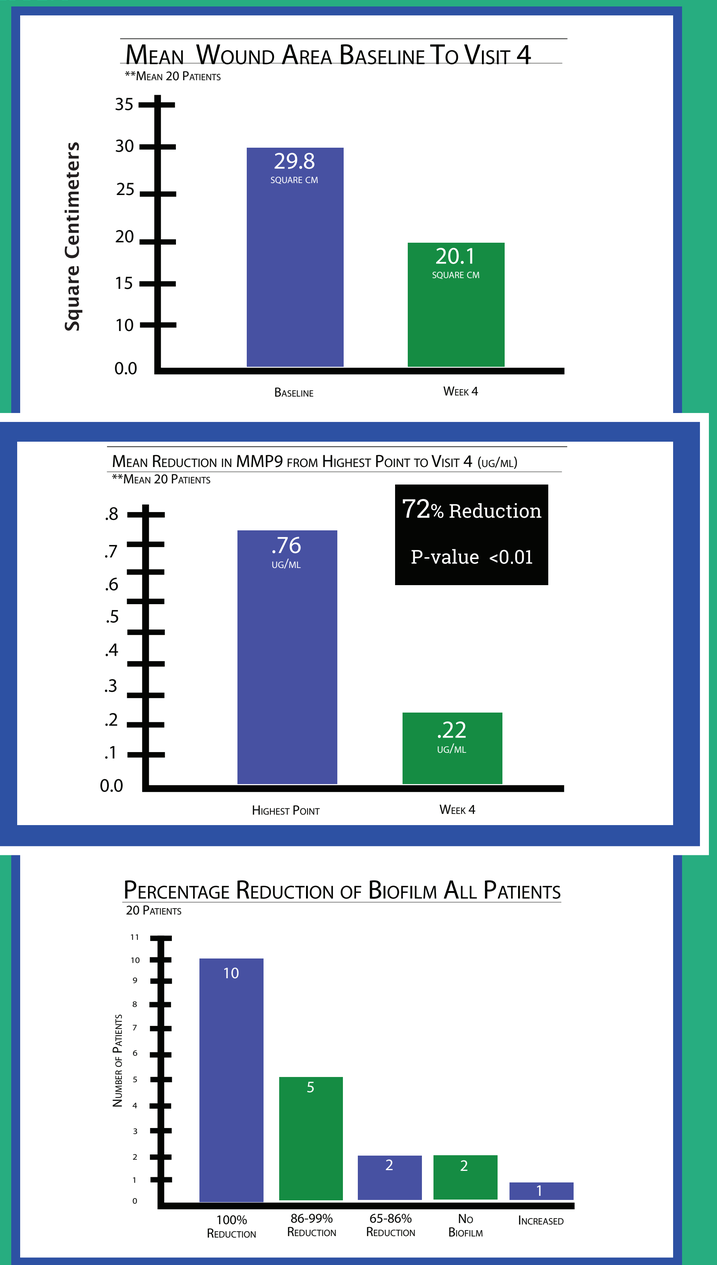
Methods

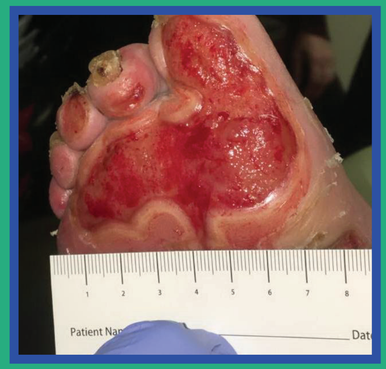
Twenty patients with chronic non-healing lower extremity ulcers of >4 weeks duration were identified and agreed to participate. Patients were included with diabetic foot ulcers, venous leg ulcers and ulcers associated with chronic arterial insufficiency. Baseline patient demographics and wound characteristics were recorded. Prior to treatment with TWX, samples of wound fluid and tissue samples were obtained for MMP and bacterial biofilm analysis. MMP activities were measured using a synthetic seven amino acid peptide with a fluorochrome-quencher pair that generates a fluorescent signal when the peptide is cut by MMPs. [1] Colony forming units (CFU) of viable bacteria in biofilm phenotype were measured by standard dilution plating technique following brief (10 minute) exposure of ultrasonically dispersed biofilm communities to dilute bleach (0.1%) followed by neutralization with 0.15% sodium metabisulfite.[2] The patients were treated for 4 weeks with standard treatment for the wound etiology plus application of TWX to the wound and peri-wound areas at all dressing changes. At weekly visits, wound characteristics were obtained and repeat wound fluid and tissue samples were obtained for MMP and bacterial analysis. At the completion of 4 weeks of treatment, wound size was re-measured to determine the percentage of wound healing over the 4 weeks of treatment. The study was approved and conducted under the guidelines of the University of North Carolina human studies subcommittee.

Results

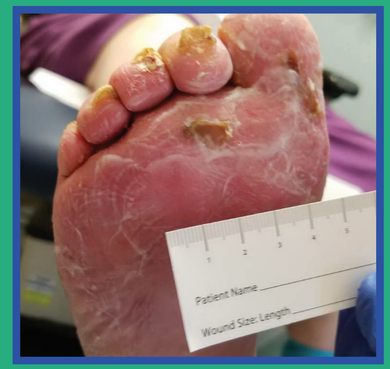
Sixty-seven percent of patients healed >30% over the 4-week treatment phase. The mean wound size decreased significantly from 29.8 ± 27.2 cm2 at baseline to 20.1 ± 20.5 cm2 after 4 weeks (P = .01). The mean MMP-9 at peak level was 0.76 ug/ml. After 4 weeks of TWX treatment, this level decreased to 0.22 ± 0.1 ug/ml (P < 0.01). At baseline, 15 of 20 patients had detectable levels of biofilm activity with a mean of 207,144 CFU/ml of homogenate. Among the 18 patients with detectable biofilm during the study, 10 had elimination of all detectable biofilm activity after 4 weeks of TWX treatment. Five patients experienced reduction of biofilm activity by > 86%. The total mean activity after 4 weeks of TWX treatment was 3109 CFU/ml of homogenate (P = 0.10).

Results

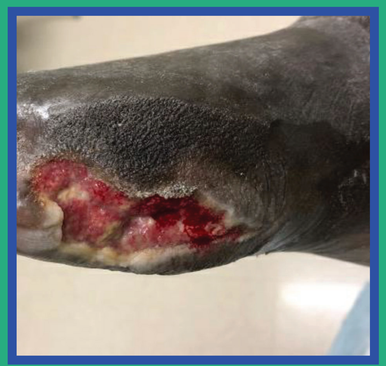




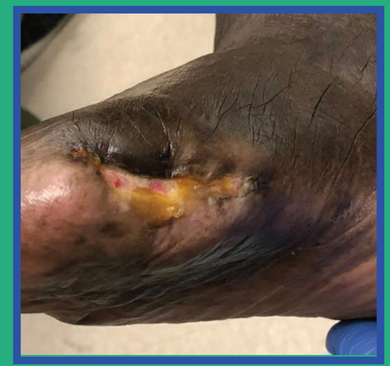
Patient 004 Visit Baseline



Patient 004 Week 4



Patient 018 Visit Baseline



Patient 018 Week 4

Discussion

These data are strongly suggestive of a trend towards a reduction in MMP activity and are statistically significant, but biofilms and total bacteria levels are not statistically significant due to the sample size. Additional patients are being entered into the study.

Conclusion

Treatment of chronic non-healing wounds with standard treatment protocol plus TWX therapy resulted in reduction in the incidence of biofilm and total bacteria wound involvement and statistically significant reduction in MMP-9 levels. Most wounds, despite lack of response to standard therapy prior to study enrollment, achieved >30% closure during the 4-week treatment phase. Study in additional patients will further define the beneficial effects of TWX on chronic non-healing wounds.

References

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2 P.L. Phillips, Q. Yang, G.S. Schultz. The Effect of Negative Pressure Wound Therapy with Periodic Instillation Using Antimicrobial Solutions on Pseudomonas Aeruginosa Biofilm on Porcine Skin Explants. International Wound J, 10 (suppl. 1) 48-55, 2013.

SAWC FALL
October 11-13 2019 Las Vegas

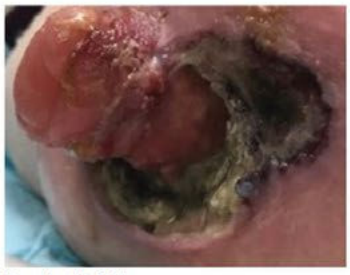
Funded in part by a testing agreement from Avadim Health, Inc.

Clinical Poster: Symposia For Advanced Wound Care Spring 2019

Harnessing the Microbiome to Rapidly Resolve Peristomal Skin Complications

Authors: Diana L. Gallagher, MS, RN, CWOCN, CFCN
Jennifer Juergens, BSN, RN, CWOCN, CFCN

Almost all ostomates experience peristomal complications at some time. In one study, the incidence ranged from 18-55% but is thought be grossly under-reported. Factors that predispose patients to complications include poorly sited and poorly constructed stomas, obesity, wound complications, and disease. Common peristomal complications include irritant dermatitis, candidiasis, folliculitis, trauma, contact dermatitis and pseudoverrucous lesions. These alterations in skin integrity result in inflammation, pain, pruritus, and changes in trans-epidermal water loss. All of these changes interfere with successful pouching. Pouch failures result in embarrassing leaks and worsening of these skin conditions with additional exposure to stool, urine, and trauma with frequent pouch changes. In the specific cases of Irritant Dermatitis and Pseudoverrocous papules and nodules (PPN), it is commonly believed that the underlying cause is prolonged exposure to liquid stool and/or urine. Along with the added moisture, the effluent increases the alkalinity of the skin. This damages the important acid mantle integral to skin's ability to withstand skin damage. This study expands the research on managing refractory Incontinence Associated Dermatitis (IAD) and the importance of pH with chronic wounds employing a technology which has shown the ability to down modulate tissue and wound pH. Prior research with IAD, showed this intervention lowered inflammation, enhanced skin's adhesion, cohesion, and integrity by down regulating a group of enzymes that leads to shedding of the stratum corneum. This study with over 20 patients resulted in rapid resolution or significant improvement of peristomal complications in 24-72 hours with a simple application before pouching. This was a marked improvement over standard of care.

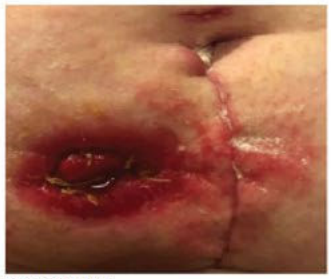


November 28, 2018

Peristomal Skin Necrosis

Good Pasture Syndrome is a rare autoimmune disease affecting collagen deposition in the lungs and kidneys. Although there is not much research on its effect on skin, this case shows the necrosis and skin erosion secondary to Good Pasture Syndrome following an emergency ostomy surgery secondary to a ruptured diverticulum. The immediate peristomal skin became necrotic but unlike mucocutaneous separation, the necrotic tissue advanced into a full thickness wound with slough and eschar. The surrounding skin and wound base were cleaned with the trial product applie to dry gauze. The wound cavity was then filled with a soft conformable wound filler rehydrated with the trial product. Routine pouching was done with the addition of a thin hydrocolloid base.

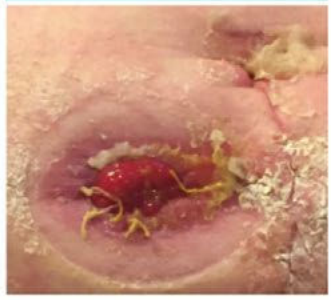
January 3, 2019



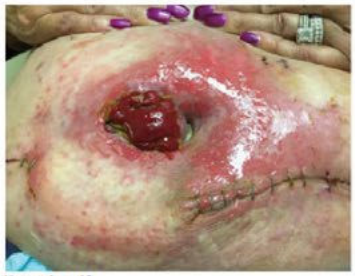
February 11, 2019

Irritant Dermatitis

Classic irritant dermatitis after multiple pouch failures in the immediate rehabilitation period. Patient taught to use tap water or approved cleanser to clean and then to apply a small amount of the trial product around the stoma. This was dried well before the ileostomy was pouched with appropriate caulking.



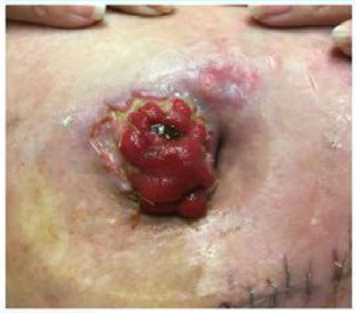
February 13, 2019



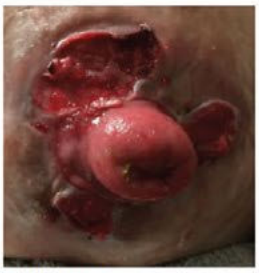
November, 16

Irritant dermatitis threatening incision line

Patient came in immediately after discharge from acute care after repeated pouch failures. Irritant dermatitis had caused inflammation and edema so severe that the incision line was threatened. Peristomal skin cleaned with tap water before being treated with trial product and routine pouching. No powder or skin sealant used. Dramatic improvement 2 days later.



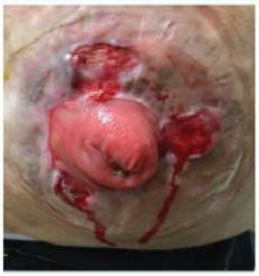
November, 18



August 20, 2019

Pyoderma Gangrenosum

Painful lesions greatly improved in both appearance and pain levels when the trial product was applied to the periwound skin and wound bases after cleansing. All wounds were then treated with a gentle, conformable wound filler to minimize pathergy



August 23, 2019

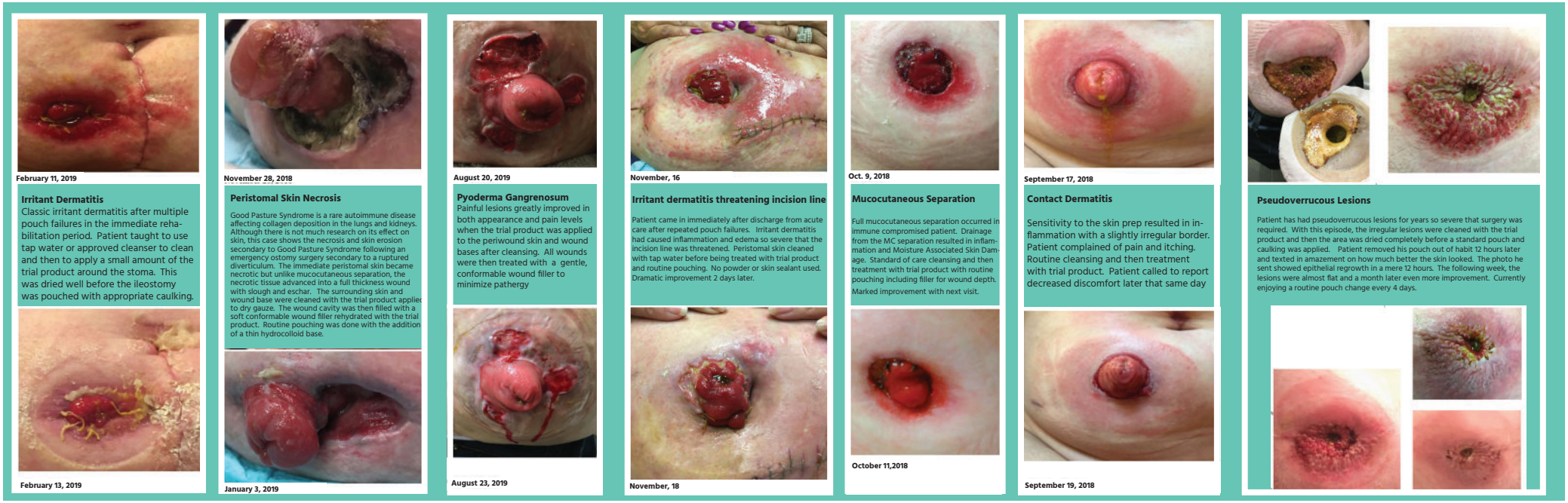
Harnessing the Microbiome to Rapidly Resolve Peristomal Skin Complications

Authors: Diana L. Gallagher, MS, RN, CWOCN, CFCN Jennifer Juergens, BSN, RN, CWOCN, CFCN

Almost all ostomates experience peristomal complications at some time. In one study, the incidence ranged from 18-55% but is thought be grossly under-reported. Factors that predispose patients to complications include poorly sited and poorly constructed stomas, obesity, wound complications, and disease. Common peristomal complications include irritant dermatitis, candidiasis, folliculitis, trauma, contact dermatitis and pseudoverrucous lesions. These alterations in skin integrity result in inflammation, pain, pruritus, and changes in trans-epidermal water loss. All of these changes interfere with successful pouching. Pouch failures result in embarrassing leaks and worsening of these skin conditions with additional exposure to stool, urine, and trauma with frequent pouch changes.

liquid stool and/or urine. Along with the added moisture, the effluent increases the alkalinity of the skin. This damages the important acid mantle integral to skin's ability to withstand skin damage.

This study expands the research on managing refractory Incontinence Associated Dermatitis (IAD) and the importance of pH with chronic wounds. Understanding the importance of achieving an acid mantle, a novel, low pH, microbiome optimizing treatment was used to treat peristomal skin after cleansing and before applying an appropriate pouching system. Prior research with IAD, showed this intervention lowered inflammation, enhanced skin's adhesion, cohesion, and integrity by down regulating a



Traditional management involves a variety of treatments including powders and sealants, improved pouching technique, correct use of pouches and accessories, as well as advanced treatments. All of these treatments are aimed at correcting the underlying problem but there is little attention to improving and strengthening the epithelium's outermost layer, the stratum corneum. Skin plays an important role in successful ostomy care as the foundation that the pouching system adheres to. A strong, intact, healthy epidermis and a well-fitting pouching system help assure reliable, sustained, and predictable wear time. Since skin is critical to pouching success, ensuring strong, healthy skin should be a primary goal.

In the specific cases of Irritant Dermatitis and Pseudoverrocous papules and nodules (PPN), it is commonly believed that the underlying cause is prolonged exposure to

group of enzymes that leads to shedding of the stratum corneum. This study with over 20 patients resulted in rapid resolution or significant improvement of peristomal complications in 24-72 hours with a simple application before pouching. This was a marked improvement over standard of care. Additional research is needed to further explore how optimizing the stratum corneum can impact practice in all areas of wound, ostomy, and continence.

REFERENCES

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Clinical Poster: Symposia For Advanced Wound Care Fall 2018

Successful Healing of IAD when Traditional Barriers Fail Using an Innovative Topical Formulation

Diana Lynn Gallagher MS, RN, CWOCN, CFCN
Janalynn Miller FNP-C, GNP, CWCN-AP

Problem

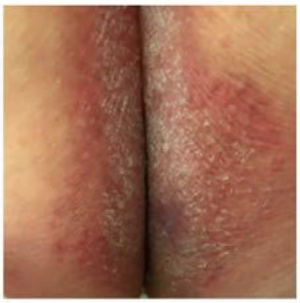
Incontinence Associated Dermatitis (IAD) is the result of urine and/ or feces damaging skin. IAD results in over-hydration, edema, and breakdown of the Stratum Corneum. This damage increases skin's susceptibility to friction, elevates pH, and escalates erythema and erosion. In spite of traditional management programs including gentle cleansing and protection with various barriers, IAD remains a major problem that can persist indefinitely. Affected individuals
experience discomfort and increased risk for complications (secondary infections and pressure injuries). With effective management, visible improvement is expected in 1–2 days with complete resolution in 1–2 weeks. Patients with IAD deserve a better approach than traditional management.

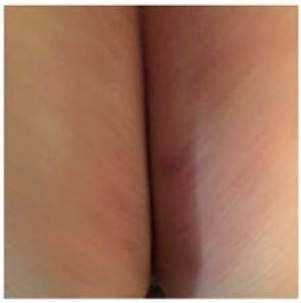
Research

Twenty residents with IAD unresolved with traditional barriers were recruited from 7 post-acute care facilities across two states. Two had fecal incontinence, four had urinary incontinence and the remainder had mixed incontinence. Education and data collection tools were provided to guide the process. Staff assessed affected skin daily using a 3- point IAD differentiation scale (0 for normal skin, 1 for erythema, and 2 for open lesions). The two- week treatment plan included discontinuation of other barrier products, gentle cleansing after incontinence followed by the application of a continuous topical barrier spray at least 4 times/24 hours. The spray optimizes skin quality and an acidic pH. Results In spite of education aimed at both nursing and nursing assistants and simple data collection tools, strict adherence to the plan was a significant challenge. In spite of compliance issues, results showed a significant improvement over traditional barrier products.

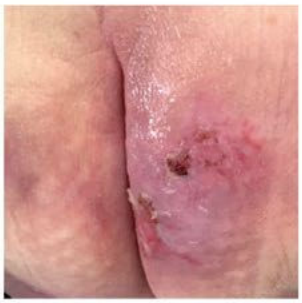
Results

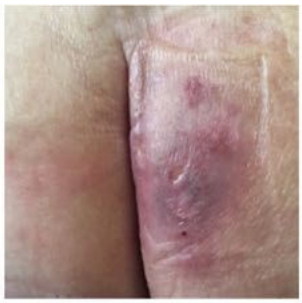
In spite of education aimed at both nursing and nursing assistants and simple data collection tools, strict adherence to the plan was a significant challenge. In spite of compliance issues, results showed a significant improvement over traditional barrier products. Further research is needed, but this preliminary study holds promise for a paradigm shift and improved, cost-effective health outcomes.





Before — After





Before — After

Fecal Incontinence	Mixed Incontinence	Urinary Incontinence
100% Resolution	93% Resolution	50% Resolution*

*A family switched back to traditional barriers, in spite of open lesions healing completely.

Successful Healing of IAD when Traditional Barriers Fail Using an Innovative Topical Formulation

Diana Lynn Gallagher MS, RN, CWOCN, CFCN
Janalynn Miller FNP-C, GNP, CWCN-AP

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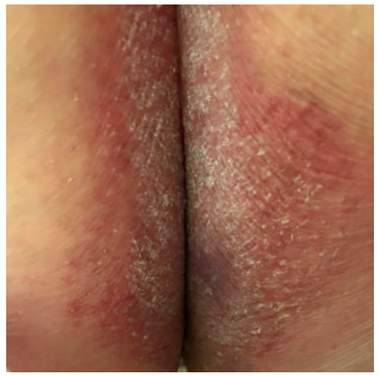
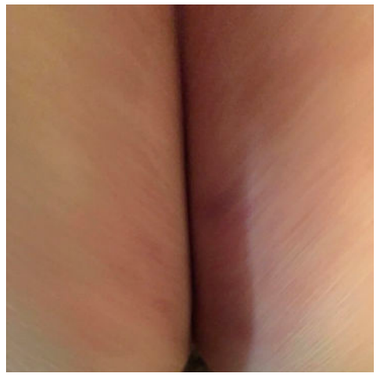


Before



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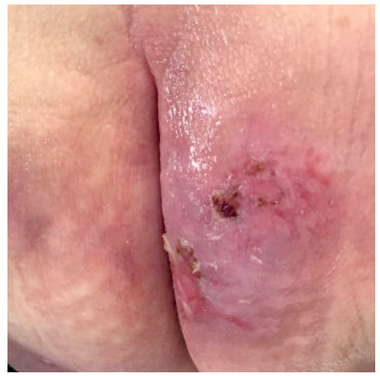

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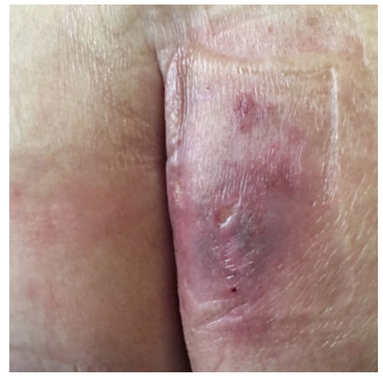

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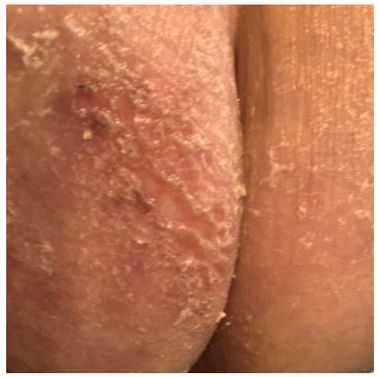

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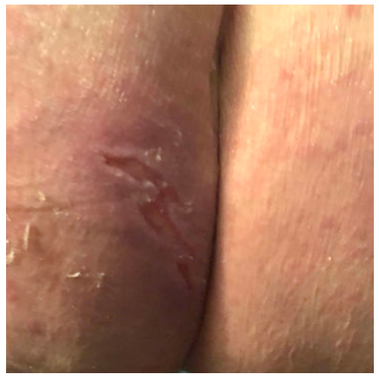

After

Fecal Incontinence	Mixed Incontinence	Urinary Incontinence
100% Resolution	93% Resolution	50% Resolution*

*A family switched back to traditional barriers, in spite of open lesions healing completely.

30th Anniversary SAWC SPRING | WHS

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BioScience Laboratories
May 2017

Cytotoxicity Sensitivity Response in Epi-airway, Epi-gingival, Epi-vaginal, Epi-Intestinal Mucosa: Theraworx® Versus Chlorhexidine Gluconate.

The purpose of this testing is to compare the Cytoxicity of Theraworx® versus Dyna-Hex® a chlorhexidine gluconate formulation. MTT assays were used. The MTT assay is a colorimetric assay for assessing cell metabolic activity. NAD(P)H-dependent cellular oxidoreductase enzymes may, under defined conditions, reflect the number of viable cells present. These enzymes are capable of reducing the tetrazolium dye MTT 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide to its insoluble formazan, which has a purple color. Other closely related tetrazolium dyes including XTT, MTS and the WSTs, are used in con-junction with the intermediate electron acceptor, 1-methoxy phenazine methosulfate (PMS). With WST-1, which is cell-impermeable, reduction occurs outside the cell via plasma membrane electron transport. Tetrazolium dye assays can also be used to measure cytotoxicity (loss of viable cells) or cytostatic activity (shift from proliferation to quiescence) of potential medicinal agents and toxic materials. MTT assays are usually done in the dark since the MTT reagent is sensitive to light. The MTT assay is a colorimetric assay for assessing cell metabolic activity.

The clinical purpose for this study was to determine if Theraworx®, in comparision to CHG would be vi-able for mucosal therapy if proven to be non-cytoxic. The researchers selected airway mucosa (the most sensitive), vaginal, intestinal and gingival mucosas. Theraworx® in comparision to CHG was significantly less toxic to epi-airway, gingival, intestinal and vaginal mucosa. When considering managing macro and micro debris topical formulations have to have the best balance of potency and biocompatibility. Thera-worx® is conluded to be a non-cytoxic formulation in mucous membrane tissues.

Tissue	Hours of Contact Before Seeing a Cytotoxic Response	
Epi-Airway	Theraworx® Dyna-Hex® (GHG)	5.07 0.05
Epi-Gingival	Theraworx® Dyna-Hex® (CHG)	399.36 8.86
Epi-Intestinal	Theraworx® Dyna-Hex®	56.13 1.42
Epi-Vaginal	Theraworx® Dyna-Hex®	34.19 6.16

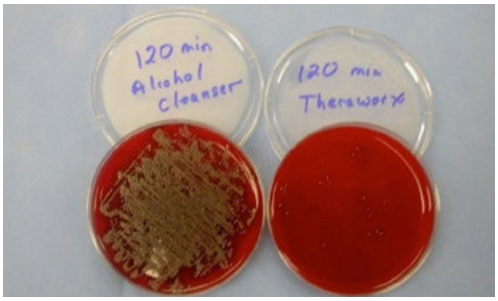
St. John's Medical Research Institute
September 2009

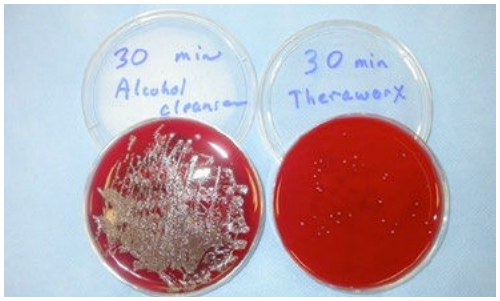
Duration of Action of Theraworx® Against Methicillin Resistant Staphylococcus Aureus Utilizing an Inoculated Collagen Model

Roger Huckfeldt, MD, FACS / St John's Medical Research Institute / Springfield, Missouri

In an in-vitro duration of action study the duration of action against methicillin resistant staphylococcus aureus (MRSA) of Theraworx®, an alcohol-based skin cleanser, and a control (normal saline), Theraworx® demonstrated significant duration of action, up to 180 minutes, against this potentially harmful pathogen. Even at the first interval tested, 15 minutes, the alcohol skin cleanser demonstrated no measurable duration of action, showing that alcohol-based cleansers have only short term disinfection capability.

Time	Normal Saline Control	Alcohol based skin cleanser	Theraworx®
15 minutes	Too numerous to count (TNTC)	Too numerous to count (TNTC)	>99% effective
30 minutes	TNTC	TNTC	>99% effective
60 minutes	TNTC	TNTC	>99% effective
2 hours	TNTC	TNTC	>99% effective
3 hours	TNTC	TNTC	>99% effective





Journal of Patient Care: Olivi et al., J Pat Care 2018, 3:3 DOI: 10.4172/2573-4598.1000134

Antimicrobial Effectiveness of Rinse-Free Hospital Bathing Cleansers after 24 h of Initial Exposure to Common Pathogenic Micro-Organisms

Joe Olivi1, Cindy L Austin1* and Simon J Thompson2
1Mercy Hospital, Springfield, Trauma and General Surgery, USA
2Mercy Hospital, Springfield, Trauma and Burn Research, USA

Abstract

Rinse-free disposable bathing clothes are increasingly more popular in the patient and home healthcare setting due to the antimicrobial properties, skin protection and convenience. Several rinse-free hospital bathing products are available for patient hygiene, but limited data exist regarding the comparative reduction in bioburden for epidemiologically important microorganisms causing hospital acquired infections. This study compared the antimicrobial effects of three common rinse-free hospital bathing cleansers. The antimicrobial effects of each cleanser (colloidal silver, benzalkonium chloride and methylpropanediol) were examined against ATCC bacterial strains (E. coli, VRE, MRSA) and one fungus (C. albicans). In addition, a patient derived sample of C. albicans and VRE was tested. With the exception of E. coli, across all test organisms and all cleansers, the Colloidal Silver solution sustained a substantially higher reduction in microbial growth proving after 24 h as an effective antimicrobial against multiple organisms including: MRSA, VRE, and C. albicans. Each pathogen presents unique risks to patients and challenges for the healthcare provider; therefore, the use of rinse-free bathing cleansers containing Colloidal Silver is warranted.

Methods

This was an in-vitro hospital laboratory-based study evaluating the effectiveness in reducing the bioburden of three FDA approved rinse free pre-packaged bathing cleansers: (i) A surfactant based formulation developed to sustain a skin pH based environment, containing colloidal silver (Colloidal Silver), (ii) A pH balanced formulation containing Benzalkonium chloride (Benzalkonium Chloride 0.12%), and (iii) A skin pH focused formulation containing methylpropanediol (Methylpropanediol) (Supplementary Data). Test organisms include three bacterial and one fungal pathogen; Escherichia coli, (E. coli ATCC 25922), Vancomycin-resistant Enterococci (VRE ATCC 51299), Methicillin-resistant Staphylococcus aureus (MRSA ATCC 43300) and Candida albicans (C. albicans 10231), respectively. ATCC biological standard specimens were used to ensure reliability and quality control applications [13]. Two clinical isolates were also derived from hospital patients to demonstrate effectiveness using higher resistance organisms. In order to reduce variables of the bathing wipes material and viscosity, cleansing liquid was aseptically extracted from each bathing wipe and placed in sterile tube to ensure equal volume.

Results

Overall, the Colloidal Silver solution demonstrated a substantially higher percentage reduction in every microorganism tested with the exception of E. coli (Figure 1). Methylpropanediol demonstrated kill power in C. albicans and MRSA. Benzalkonium Chloride demonstrated kill power C. albicans, MRSA, E. coli and VRE. The results are summarized in (Figure 1 and Table 1) as follows: C. albicans patient derived: The Colloidal Silver solution demonstrated a significantly higher reduction (56.2%) in fungal growth at 24 h with Methylpropanediol and Benzalkonium Chloride at 8.6% and 7.3%, respectively. C. albicans ATCC 10231: The Colloidal Silver solution demonstrated the highest percentage reduction (54.8%) in fungal growth in at 24 h with Methylpropanediol (9.7%) and Benzalkonium Chloride (12.8%). E. coli ATCC 25922: The Benzalkonium Chloride solution demonstrated the highest percentage reduction (6.3%) in growth followed by Colloidal Silver solution (3.0%). Methylpropanediol solution showed no reduction. MRSA ATCC 43300: The Colloidal Silver solution demonstrated the highest percentage reduction (29.8%) in microbial growth at 24 h with Benzalkonium Chloride (18.9%) Methylpropanediol (4.8%). VRE patient derived: The Colloidal Silver solution demonstrated the only microbial reduction (66.4%) at 24 h. No reduction in Benzalkonium Chloride or Methylpropanediol solution. VRE ATCC 51299: The Colloidal Silver solution demonstrated the highest percentage reduction (28.1%) and Benzalkonium Chloride (5.6%). Methylpropanediol solution showed no reduction.

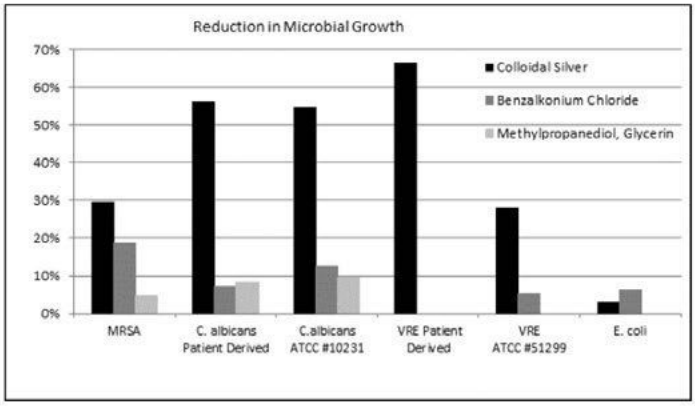


Figure 1: Depicts percentage reduction in microbial growth for each organism and each cleansing solution.

Journal of Patient Care

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Research Article Open Access

Antimicrobial Effectiveness of Rinse-Free Hospital Bathing Cleansers after 24 h of Initial Exposure to Common Pathogenic Micro-Organisms

Joe Olivi[1], **Cindy L Austin**[1*] **and Simon J Thompson**[2]

[1]*Mercy Hospital, Springfield, Trauma and General Surgery, USA*

[2]*Mercy Hospital, Springfield, Trauma and Burn Research, USA*

[*]**Corresponding author:** Cindy L Austin, Mercy Hospital, Springfield, Trauma and Burn Research, USA, Tel: (417) 820-7464; Fax: (417) 841-0252; E-mail: cindy.austin@mercy.net

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Abstract

Rinse-free disposable bathing clothes are increasingly more popular in the patient and home healthcare setting due to the antimicrobial properties, skin protection and convenience. Several rinse-free hospital bathing products are available for patient hygiene, but limited data exist regarding the comparative reduction in bioburden for epidemiologically important microorganisms causing hospital acquired infections. This study compared the antimicrobial effects of three common rinse-free hospital bathing cleansers. The antimicrobial effects of each cleanser (colloidal silver, benzalkonium chloride and methylpropanediol) were examined against ATCC bacterial strains (*E. coli*, VRE, MRSA) and one fungus (*C. albicans*). In addition, a patient derived sample of *C. albicans* and VRE was tested. With the exception of *E. coli*, across all test organisms and all cleansers, the Colloidal Silver solution sustained a substantially higher reduction in microbial growth proving after 24 h as an effective antimicrobial against multiple organisms including: MRSA, VRE, and *C. albicans*. Each pathogen presents unique risks to patients and challenges for the healthcare provider; therefore, the use of rinse-free bathing cleansers containing Colloidal Silver is warranted.

Keywords: Rinse-free bathing; Colloidal silver; Antimicrobial; Rinse-free bathing cleanser; Hospital acquired infection

Introduction

Antimicrobial stewardship is the organized effort to educate and influence antimicrobial providers to follow evidence-based prescribing, to stem antibiotic overuse, and thus antimicrobial resistance [1]. At hospitals, this may take the form of an antimicrobial stewardship program (ASP). Until recently, ASPs existed almost exclusively in the hospital setting, but due to antibiotic use in non-hospital settings greatly exceeding that in hospitals, led to implementation of ASPs across the health care field [2]. This is particularly seen within nursing facilities in the US, which provide medical and residential care for approximately 1.4 million persons on a daily basis and where infections are a common problem [3]. In light of this, recent revisions to regulations governing nursing facilities will require establishment of an ASP by November 2017 for participation in the Medicare and Medicaid programs [4].

Furthermore, traditionally chlorhexidine (CHG) has been a common, effective antiseptic used in healthcare facilities for disinfecting skin since the 1950's [5]. However, in 2015 the Association of perioperative Registered Nurses removed CHG from the standard practice protocol for pre-operative bathing for the prevention of surgical site infections [6]. As such, Kampf proposed establishing an 'Antiseptic Stewardship Initiative' citing research showing multiple microbial isolates are often CHG resistant [7]. In addition, the CDC recommendations for the prevention of surgical site infections moved CHG from a 1b recommendation to a "No Recommendation" [8]. Therefore, the need to find alternatives to CHG for patients in higher acuity settings is imperative.

As a result, to protect against healthcare associated infections (HAI's), rinse-free bathing cleansers are employed more frequently to fill this void in caring for intensive care, non-ambulatory and long-term care patients. Indeed, the skin is the largest organ of the body, therefore protecting skin integrity is an important factor in preventing microbial infections [9]. According to CDC National and State Healthcare-Associated Infections Progress Report, 2014, approximately one in 25 hospital patients have at least one HAI [10]. Healthcare associated infections confer excess cost to *healthcare* institutions and lead to substantial morbidity and mortality in hospitalized patients. Ensuring proper patient hygiene is one aspect of a cohesive approach to reduction in HAIs including central line, catheter-associated urinary and blood stream infections [11].

Several rinse-free hospital bathing products are available for patient hygiene, but limited data exists regarding the comparative reduction in bioburden for epidemiologically important microorganisms causing HAI's. Rinse-free disposable bathing clothes are increasingly more popular in the patient and home healthcare setting due to the antimicrobial properties, skin protection and convenience. Clinicians use rinse-free bathing cleansers on both intact and damaged skin caused by exposure to adhesives, incontinence, wound drainage, friction and pressure. This study takes a practical approach by evaluating the antimicrobial effectiveness of the cleanser coupled with the physical "Z" wiping motion similar to a method previously reported by Rutala [12]. The objective of this study was to evaluate the difference in bioburden reduction at 24 h among epidemiologically important organisms among three common rinse-free bathing cleansers.

Methods

This was an in-vitro hospital laboratory-based study evaluating the effectiveness in reducing the bioburden of three FDA approved rinse-free pre-packaged bathing cleansers: (i) A surfactant based formulation developed to sustain a skin pH based environment, containing colloidal silver (Colloidal Silver), (ii) A pH balanced formulation containing Benzalkonium chloride (Benzalkonium Chloride 0.12%), and (iii) A skin pH focused formulation containing methylpropanediol (Methylpropanediol) (Supplementary Data) . Test organisms include three bacterial and one fungal pathogen; *Escherichia coli*, (*E. coli* ATCC 25922), Vancomycin-resistant Enterococci (VRE ATCC 51299), Methicillin-resistant Staphylococcus aureus (MRSA ATCC 43300) and *Candida albicans* (*C. albicans* 10231), respectively. ATCC biological standard specimens were used to ensure reliability and quality control applications [13]. Two clinical isolates were also derived from hospital patients to demonstrate effectiveness using higher resistance organisms. In order to reduce variables of the bathing wipes material and viscosity, cleansing liquid was aseptically extracted from each bathing wipe and placed in sterile tube to ensure equal volume.

Laboratory methods

A confluent lawn of organisms was prepared using a 0.5 McFarland Standard for bacteria and a 2.0 McFarland Standard for yeast, on separate agar plates. Using aseptic technique, four 8 × 6 mm cellulose filters were soaked in 15 mL of one of each of the solutions (Colloidal Silver; Benzalkonium Chloride 0.12%; and Methylpropanediol) for 5 min.

Next, similar to a method previously reported by Rutala [12], a physical wiping "Z" pattern of approximately 6 cm total was streaked two times separately to ensure reliability in each quadrant of the agar plate. The "Z" streaking motion of approximately 6 cm total (following a template) was made twice in each quadrant of the agar plate (Supplementary Figure 1). This represents the wiping pattern used when cleansing a patient swiping one time over the skin rather than repeating over the same area. This was repeated for each of the test microorganisms with each of the bathing cleansers. Plates were incubated at 37°C for 24 h to assess for zones of inhibition and analyzed for reduction in microbial growth.

Results

Overall, the Colloidal Silver solution demonstrated a substantially higher percentage reduction in every microorganism tested with the exception of *E. coli* (Figure 1). Methylpropanediol demonstrated kill power in *C. albicans* and MRSA. Benzalkonium Chloride demonstrated kill power *C. albicans*, MRSA, *E. coli* and VRE. The results are summarized in (Figure 1 and Table 1) as follows:

C. albicans patient derived: The Colloidal Silver solution demonstrated a significantly higher reduction (56.2%) in fungal growth at 24 h with Methylpropanediol and Benzalkonium Chloride at 8.6% and 7.3%, respectively.

C. albicans ATCC 10231: The Colloidal Silver solution demonstrated the highest percentage reduction (54.8%) in fungal growth in at 24 h with Methylpropanediol (9.7%) and Benzalkonium Chloride (12.8%).

E. coli ATCC 25922: The Benzalkonium Chloride solution demonstrated the highest percentage reduction (6.3%) in growth followed by Colloidal Silver solution (3.0%). Methylpropanediol solution showed no reduction.

MRSA ATCC 43300: The Colloidal Silver solution demonstrated the highest percentage reduction (29.8%) in microbial growth at 24 h with Benzalkonium Chloride (18.9%) Methylpropanediol (4.8%).

VRE patient derived: The Colloidal Silver solution demonstrated the only microbial reduction (66.4%) at 24 h. No reduction in Benzalkonium Chloride or Methylpropanediol solution.

VRE ATCC 51299: The Colloidal Silver solution demonstrated the highest percentage reduction (28.1%) and Benzalkonium Chloride (5.6%). Methylpropanediol solution showed no reduction.

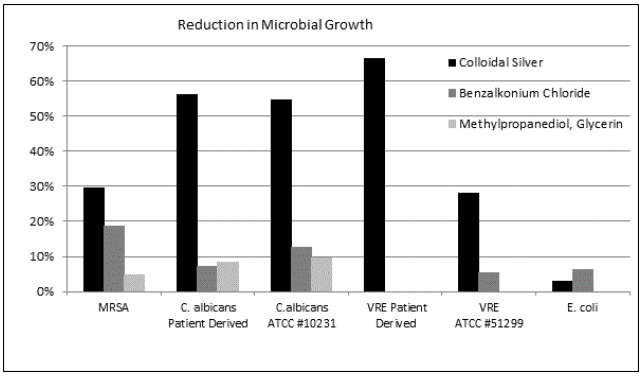

Figure 1: Depicts percentage reduction in microbial growth for each organism and each cleansing solution.

Discussion

Without a doubt, ensuring appropriate and routine patient cleansing is an important factor in preventing high risk HAI's [14]. Thus, the aim of this study was to investigate rinse-free bathing cleansers which sustain antimicrobial effectiveness of multiple clinically isolated pathogens for an extended time.

We utilized a novel in-vitro methodology and the overall results indicate the Colloidal Silver solution reduced growth in all the bacterial and fungal organisms tested at 24 h. Furthermore, in five out of the six organisms, Colloidal Silver demonstrated a substantially higher rate of antimicrobial effectiveness after 24 h when compared to the Benzalkonium Chloride and Methylpropanediol solution. Although Benzalkonium Chloride and Methylpropanediol demonstrated antimicrobial effectiveness, the percentage reduction was substantially lower compared to the Colloidal Silver solution.

These results are corroborated within the literature; in the case of *C. albicans*, Gajbhiye show nano particle silver enhances the inhibitory effect of fluconazole [15]. The efficacy against MRSA is substantiated in the literature by Ansari, where they used confocal laser scanning techniques to examine anti-biofilm activity of a silver nano particle coating for medical devices [16]. However, not all products enhanced with silver result in the same benefit; for example with VRE we see a growth reduction, which is substantiated by Tran [17], however, Boonkaew saw an apparent promotion of VRE [18] with the silver enhanced formulation they examined. Thus, formulation differences have a big impact on anti-microbial efficacy between the silver-enhanced products. Additionally, although the literature lacks evidence

supporting widespread silver resistance, it remains of interest warranted by the existence of clinically isolated silver resistance genetic determinants [19].

Treatment	Test Microorganism					
Rinse-free bathing solution	*C. albicans* Patient Derived	*C. albicans* ATCC 10231	*E. coli* ATCC 25922	MRSA ATCC 43300	VRE Patient Derived	VRE ATCC 51299
	% Reduction in Growth Area at 24 h					
Colloidal Silver Cleanser	56.2	54.8	3	29.8	66.4	28.1
Benzalkonium Chloride 0.12%	7.3	12.8	6.3	18.9	0	5.6
Methylpropanediol	8.6	9.7	0	4.8	0	0

Table 1: Reduction in bacterial and fungal growth at 24 h.

Another aspect of these cleansers is the application site, the skin. The key mechanism of epidermal protection is now generally accepted to localize to the stratum corneum [20]. The stratum corneum serves multiple protective functions including: permeability, anti-oxidation, hydration, limiting pathogen colonization, and more [21]. Therefore, improving the integrity of the skin is equally as important as the antimicrobial solution applied to the skin. And this is where other factors within the formulations of each of these products may provide additional benefits to those observed within this *in vitro* study. Based on the data outcomes of this study, the next phase will involve patient evaluation.

Conclusion

With antimicrobial and antiseptic stewardship becoming the norm within the healthcare landscape, the requirement for alternative approaches for preventing high risk hospital acquired infections comes to the fore. Based on the findings of this study, rinse-free bathing cleansers are not all the same when evaluating duration of antimicrobial effectiveness across multiple pathogens. With the exception of *E. coli* ATCC 25922, across all organisms and all rinse-free bathing cleansers tested, Colloidal Silver solution demonstrates to be a more effective antimicrobial after 24 h against multiple common hospital infections including: MRSA, VRE and *C. albicans* than other rinse-free bathing cleansers.

Overall, the Colloidal Silver solution demonstrated a substantially higher reduction in every microorganism tested with the exception of *E. coli*.

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Measuring the duration of antimicrobial effectiveness of hospital bathing cleansers after 24 hours using a novel "Z" methodology

J. Renzulli, M.D. [1], J. Olivi, M.D.[2], C. L. Austin, M.S.[3] & S. J Thompson, PhD[3].

; [2] General &Trauma Surgery, Mercy Springfield; & [3] Trauma & Burn Research, Mercy Springfield.

INTRODUCTION

The skin is the largest organ of the body, therefore protecting skin integrity is an important factor in preventing microbial infections.[1] According to *CDC National and State Healthcare-Associated Infections (HAI) Progress Report*, 2014, approximately one in 25 hospital patients has at least one healthcare-associated infection.[2] HAI's confer excess cost to healthcare institutions and lead to substantial morbidity and mortality in hospitalized patients. Ensuring proper patient hygiene is one aspect of a bundled approach to reduction in several HAIs including catheter-associated urinary tract infections (CAUTI), catheter-blood stream infections (CRBSI) [3] and central line associated-bloodstream infections (CLABSI).

The CDC surveillance system for health care–associated infections, the National Healthcare Safety Network (NHSN), provides information on incidence rates of common infections.

Several rinse-free hospital bathing products are available for patient hygiene but limited data exist regarding the comparative reduction in bioburden for epidemiologically important microorganisms causing HAI's. Rinse-free disposable bathing clothes are increasingly more popular in the patient care setting due to the antimicrobial properties, skin protection and convenience. Clinicians use rinse-free bathing cleansers on both intact and damaged skin caused by exposure to adhesives, incontinence, wound drainage, friction and pressure.

The objective of this pilot study was two-fold (**1**) Develop an in vtro methodology analogous the clinical use of these bathing products. (**2**) Evaluate the difference in bioburden reduction at 24 hours among epidemiologically important organisms with three common rinse-free bathing cleansers using a novel in vitro "Z" method.

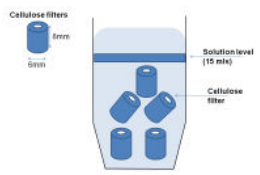
METHODS

Study Design: This was a laboratory based study evaluating the effectiveness of four different skin cleansers on reduction in bioburden of *Escherichia coli*, Vancomycin-resistant Enterococci (VRE), Methicillin-resistant *Staphylococcus aureus* (MRSA), and *Candida albicans*.

Laboratory Methods: Organisms were plated using 0.5 McFarland Standard for bacteria and 2.0 McFarland Standard for yeast on separate agar plates. Next, four 8x6mm cellulose filters were soaked in 15 mL of one of each of the following solutions for 5 minutes (**Figure 1**): Theraworx; Medline Ready Bath; M-Care; and Sage Bath.

Figure 1: Depiction of cellulose fiber solution preparation. The cellulose filters were placed into solution for 5 mins.

Then removed from the treatment solution.



METHODS - Continued

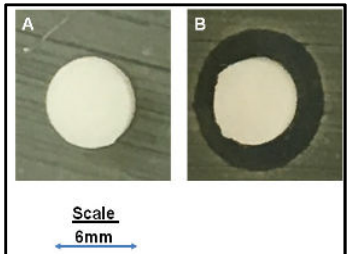


Figure 2: Cellulose tube soaked in solution for 5 mins and placed on a previously prepared agar plate with MRSA and grown overnight. (**A**) Sterile Saline. (**B**) Theraworx solution.

Next, aseptically the filters were blotted to remove excess liquid. Preliminary observations at this step can be seen in **Figure 2**.

A "z" streak of approximately 6cm total (following a template) was made twice in each quadrant of the agar plate (**Figure 3**).

This was repeated for each of the microorganisms. Plates were incubated at 37C for 24 hours and analyzed for reduction in growth.

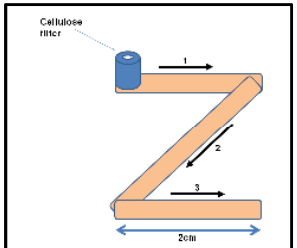


Figure 3: Depiction of cellulose filter with solution "z" streaks

RESULTS

Overall, the Colloidal Silver solution demonstrated a substantially higher percentage reduction in every pathogen/organism tested with the exception of *E.coli*. The Benzalkonium Chloride solution slightly surpassed reduction rate 6.4% compared to Colloidal Silver at 3.0%. The results are summarized as follows:

***C. albicans* Patient Derived (Figure 4).** The Colloidal Silver solution demonstrated a significantly higher reduction (56.2%) in fungal growth at 24 hours with, and Benzalkonium Chloride at 8.6% & 5.4%, respectively.

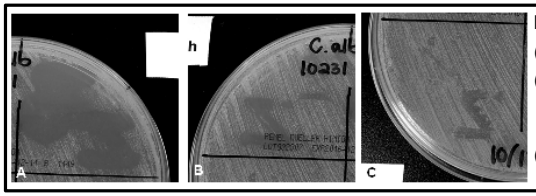


Figure 4:
(**A**) Theraworx
(**B**) Medline Ready Bath
(**C**) M Care.

***C. albicans* ATCC 10231.** The Colloidal Silver solution demonstrated the highest percentage reduction (54.8%) in fungal growth in at 24 hours with Methylpropanediol (14.6%), and Benzalkonium Chloride (12.8%).

RESULTS - Continued

***E. coli* ATCC 25922.** The Benzalkonium Chloride solution demonstrated the highest percentage reduction (6.3%) in growth followed by Colloidal Silver solution (3.0%). Methylpropanediol solution showed no reduction.

***MRSA* ATCC 43300.** The Colloidal Silver solution demonstrated the highest percentage reduction (29.8%) in microbial growth at 24 hours with Benzalkonium Chloride (18.9%)Methylpropanediol (4.8%).

***VRE* Patient Derived.** The Colloidal Silver solution demonstrated the only microbial reduction (66.4%) at 24 hours. No reduction in Benzalkonium Chloride or Methylpropanediol solution.

***VRE* ATCC 51299.** The Colloidal Silver solution demonstrated the highest percentage reduction (28.1%) and Benzalkonium Chloride (5.6%). Methylpropanediol solution showed no reduction.

Methylpropanediol demonstrated kill power in *C. albican* and *MRSA*. Benzalkonium Chloride demonstrated kill power *C. albicans*, *MRSA, E. coli,* and *VRE*.

Treatment	% Reduction In Growth Area at 24hrs					
Organism:	*C. albicans* Patient Derived	*C. albicans* ATCC 10231	*E. coli* ATCC 25922	*MRSA* ATCC 43300	*VRE* Patient Derived	*VRE* ATCC 51299
Theraworx	56.2	54.8	3.0	29.8	66.4	28.1
Medline	7.3	12.8	6.3	18.9	0.0	5.6
Sage	5.4	14.6	0.0	6.1	0.0	0.0
M Care	11.8	4.9	0.0	3.5	0.0	0.0

Table 1 Percentage reductions in growth for each organism and each cleanser.

CONCLUSIONS

With the exception of E.coli ATCC 25922, across all organisms and all solutions Theraworx had a substantially higher reduction in microbial growth at 24 hours. Ensuring appropriate patient cleansing is one important factor in a bundled approach to HAI reduction. When selecting products for patient cleansing, factors such as safety, ease of use, cost, and effectiveness for microbial reduction are all critical factors.

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Another Tool in the Toolbox: A Novel, Multimodal, Surfactant-Based Skin Cleanser vs. 62% Ethanol on the Human Coronavirus OC43 on Human Tissue

Author: Daryl S. Paulson, PhD

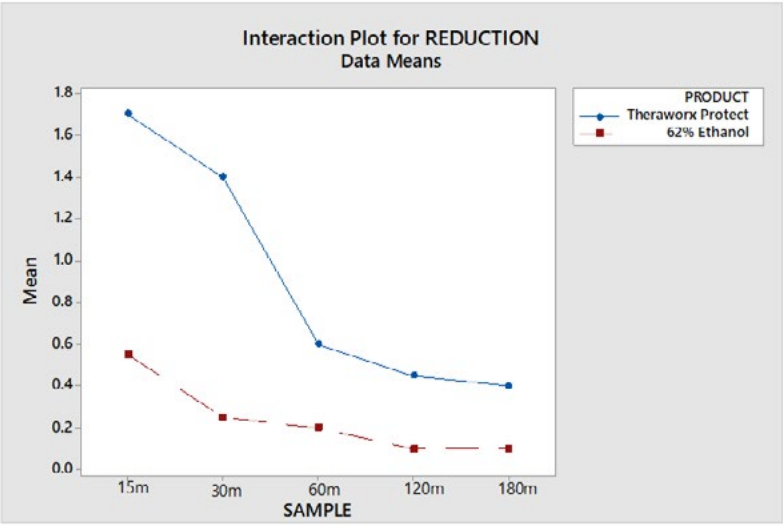
Background: This study evaluated the persistent efficacy of a novel, multi-ingredient colloidal silver skin cleanser vs. 62% ethanol against the coronavirus as a proxy for SARS-CoV-2 to determine the ability of each to reduce the coronavirus viral load after timed reinoculation on intact forearm skin of human volunteers.

Methods: Five volunteer test subjects had the test and comparator products applied to their skin. After allowing the products to dry, the subjects had a known titer of the human coronavirus strain OC43 (ZeptoMetrix Corporation #0810024CF) inoculated on treated skin sites located at randomized portions of the subjects' forearms and reinoculated with the virus again at 15 minutes, 30 minutes, 60 minutes, 120 minutes and 180 minutes post-treatment. Following each specified exposure time, samples were taken from the test sites and log10 reductions in the virus titer were compared to the baseline recovery.

Results: The Theraworx Protect product demonstrated post application improved virucidal activity, both immediate and residual over time.

Theraworx Protect demonstrated statistically greater log reduction at all time intervals compared to Alcohol during a repeat inoculation model.

Figure 2. Interaction Plot (Mean Log_{10} Reduction vs. Sample Time)



Clinical and Medical Investigations

Research Article

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Another tool in the toolbox: A novel, multimodal, silver and surfactant- based skin cleanser vs. 62% ethanol on the human coronavirus OC43 on human tissue

Daryl S Paulson*

BioScience Laboratories, Inc., 1765 South 19th Avenue; Bozeman, MT 59718, USA

Abstract

Background: This study evaluated the persistent efficacy of a novel, multi- ingredient colloidal silver skin cleanser vs. 62% ethanol against the coronavirus as a proxy for SARS-CoV-2 to determine the ability of each to reduce the coronavirus viral load after timed reinoculation on intact forearm skin of human volunteers.

Methods: Five volunteer test subjects had the test and comparator products applied to their skin. After allowing the products to dry, the subjects had a known titer of the human coronavirus strain OC43 (ZeptoMetrix Corporation #0810024CF) inoculated on treated skin sites located at randomized portions of the subjects' forearms and reinoculated with the virus again at 15 minutes, 30 minutes, 60 minutes, 120 minutes and 180 minutes post-treatment. Following each specified exposure time, samples were taken from the test sites and $\log_{10}$ reductions in the virus titer were compared to the baseline recovery.

Results: The Theraworx Protect product demonstrated post application improved virucidal activity to alcohol for both immediate and residual effects over time.

Conclusions: Both early and residual activity of the Theraworx Protect product against the coronavirus in reducing viral concentration was superior to the 62% ethanol solution.

Introduction

This study consists of the coronavirus.

The coronavirus has been on this planet for centuries and changes or mutates from time to time in order to survive. The COVID-19 is the strain of coronavirus that is causing the current pandemic. The virus's original host was animals, but in Wuhan, China, it switched hosts to humans. The virus mutated slightly in its replication process to become the COVID-19 strain, which is formally 2019-nCoV. It is an RNA (ribonucleic acid) virus, meaning that it needs the RNA in a human cell to reproduce. Through an electron microscope, it appears as an imperfect circle with portions that are erect or looks like a crown and, therefore, is termed the "corona" for "crown" virus (Figure 1).

The virus is composed of three simple structures:[1]

1. the inner core of ribonucleic acid,

2. a capsid or a shell around the inner core, and

3. glycoprotein spikes.

This year, the COVID-19 virus infected and maimed many individuals, and the pandemic is going strong.

Because this virus caught most countries, including the United States, unprepared with little scientific data regarding how to prevent its spread, immobilize it, and treat it.

The use of alcohol disinfectants as a tool for the hand sanitization of humans, including healthcare workers, has become a standard recommendation among public health officials to aid in preventing microorganism transmission during social interaction, as well as a means of reducing the transfer of it to the mucous membranes of the eyes, mouth, and nostrils on the face, which may lead to a subsequent infection. The use of hand sanitizers, wearing a mask, and social distancing are currently the most recommended public health tactics to prevent the spread of the COVID-19 virus.

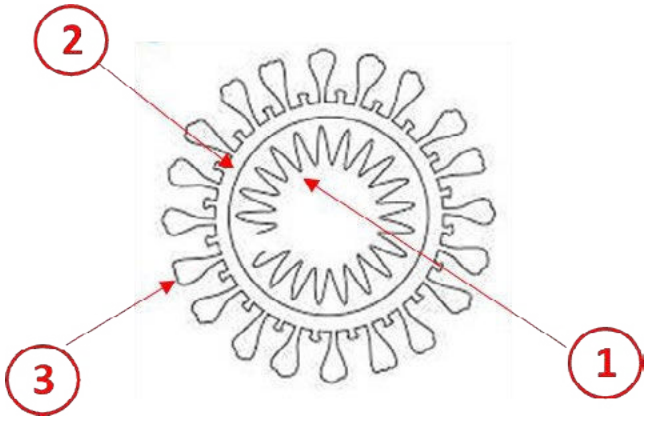

Figure 1. COVID-19 virus

Correspondence to: Daryl S Paulson, BioScience Laboratories, Inc., 1765 South 19th Avenue; Bozeman, MT 59718, USA, E-mail: DPaulson@biosciencelabs.com

Key words: *hand sanitizer, coronavirus, alcohol, colloidal silver*

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The most common alcohols used for skin disinfection are ethanol, isopropyl, and n-propanol, the latter being more popular in Europe than in the United States. Of the three, ethanol has been shown to be the most effective against viruses, but all three types of alcohol have shown reduced activity against this virus [2]. In general, higher concentrations of each type of alcohol have shown greater effectiveness, but elevated concentrations also can create serious issues with skin drying and damage to the stratum corneum. The most common public healthcare recommendation relating to the COVID-19 pandemic is the use of ethanol solutions of 60%-70% for hand sanitization.

With the importance of skin disinfection of the hands currently elevated because of the COVID-19 pandemic, the identification of effective alternatives to alcohol sanitizers can be an answer to the problems associated with alcohol-containing products. In addition to the skin drying and cracking caused by repeated application of ethanol because it removes the skin's oils, its frequent use can result in changes to normal skin flora and open the door to more frequent colonization by *staphylococci* and Gram-negative bacteria, alcohol has limited residual effects, as soon as it dries, there are no more antimicrobial actions, meaning frequent re- applications of alcohol-based hand sanitizers, which, in turn, causes more damage to the skin [3,4].

Additionally, alcohol-based hand sanitizers may work well only in clinical settings, where hands are not heavily soiled or greasy. In fact, alcohol hand sanitizers can be ineffective in removing bacteria if too little is applied or if it is wiped off before it completely dries on the skin [5]. Once alcohol dries, there are no more antimicrobial effects.

Another safety issue with alcohol-based hand sanitizers is ingestion. Ethanol-based hand sanitizers can cause alcohol poisoning if a person swallows more than two mouthfuls. In a new report from CDC, researchers analyzed data reported to the National Poison Data System (NPDS) from 2011–2014 on exposures to alcohol and non-alcohol-based hand sanitizers in children who were 12 years old or younger, and 65,293 (92% of reports) were alcohol-based exposures [6]. Emergency rooms nationwide have seen instances of both intoxication and hypoglycemia in children, and older children have been known to swallow hand sanitizers to become intoxicated purposely [7].

Another challenge with the use of alcohol-based hand sanitizers is that they present a significant flammability hazard, both in liquid form and as a vapor that can bleed off at higher temperatures. Alcohol-based hand sanitizers are classified as Class I Flammable Liquid substances, which means they have a flash point of less than100 degrees Fahrenheit. If hand sanitizer combusts, carbon monoxide and carbon dioxide can form.

As has been said, we need another tool in the toolbox, which alcohol cannot be used. A safer, non-inferior alternative to alcohol-based sanitizers could help combat the transmission of COVID-19 with fewer side effects.

This product has been on the market for years, used in hospital intensive care units for skin and wound cleansing. The objective of this test evaluation was to compare the efficacy of a silver-based skin cleanser to 62% ethanol against a seasonal coronavirus as a proxy for SARS-CoV-2 to determine the ability of each to reduce the number of coronavirus particles on the intact forearm skin of volunteers.

Materials and methods

For this test, a surrogate coronavirus, human coronavirus strain OC43 (ZeptoMetrix Corporation #0810024CF) was selected for ethical and safety considerations. The very similar morphological structure of these two coronavirus (both ~30kb genome size, both enveloped, positive-sense RNA viruses with protein spike, membrane and envelope imbedded in host-membrane derived lipid bilayer encapsulating the helical nucleoside comprising viral RNA) made the Cov- OC-43 virus a credible substitute for the COVID 19 virus in this test.

The comparator product was 62% ethanol (v/v) prepared by the 3rd party testing laboratory (BioScience Laboratories, Inc.; Bozeman, MT) by adding 36.3 mL (95% ethanol (Everclear) as aseptically added to 68.2 mL of sterile deionized water in a sterile glass bottle. The contents were swirled to mix to result in 104.5 mL of 62% ethanol solution, stored at ambient temperature.

After undergoing a 7-day pre-conditioning period, during which subjects had not used any substance to affect the skin, five subjects had the test and comparator products applied to their skin. Only five subjects were employed, because, at this time, there was no credible information on how COVID-19 would be at this time of total shutdown.

After allowing to the product to dry on the skin, the subjects then had a known titer of the human coronavirus strain OC43 (ZeptoMetrix Corporation #0810024CF) inoculated on treated skin sites located on the subjects' forearms. Randomized portions of the treated skin were repeatedly challenged with the virus at 15 minutes, 30 minutes, 60 minutes, 120 minutes, and 180 minutes post-treatment. Following each specified exposure time, samples were taken from the test sites and $\log_{10}$ of the 50% titration end point for infectivity. To calculate the viral titer, a 50% tissue culture infectious dose ($TCID_{50}$) calculation – the Quantal Test (Spearman-Kärber Method) – was applied.

$$LogTCID_{50} = L - d\,(s - 0.5)$$

where:

L = -Log_{10} of the lowest dilution;

d = Difference between dilution steps;

S = Sum of proportions of positive wells.

The $\log_{10}$ reductions were calculated as follows:

Log10 Reduction = (log10 TCID50 of the Baseline) – (log10 TCID50 of the Test Recovery)

The test protocols and consent forms were supplied to the Gallatin Institutional Review Board (GIRB) for review and approval, and the test was conducted in compliance with current Good Clinical Practice regulations, Good Laboratory Practice regulations (reference CFR 21, Parts 58), the standard operating procedures of BioScience Laboratories, Inc., the test protocol and any protocol amendments.

Results

For the analysis of this study, a blocked, two-factor Analysis of Variance (ANOVA) was used for the analysis. The model was:

$$\hat{y} = Blocks + A + B + (A \times B) + e$$

where:

$\hat{y}$= Log_{10} Reduction

Blocks = Subjects (each subject received the two products, one on each arm, randomly)

A = Products

1, if Test Product (multimodal colloidal silver skin cleanser) 2, if Comparator Product (62% ethanol alcohol)

B = Sample Times

1, if 15 minutes

2, if 30 minutes

3, if 60 minutes

4, if 120 minutes

5, if 180 minutes (A×B) = Interaction Term e = Error Term

The subjects were selected at random, but the product and sample times were "pre- determined," or chosen before the study began; hence, they were fixed effects Table 1. $\sqrt{s^2}$ The mean square error (MS_E) adjusted, or the variance (s^2) was 0.075, which provided a standard deviation of = s = 0.271. All *F*-values evaluated were significant ($p < 0.05$).

Interactions

The interaction between products and sample times was statistically significant ($p < 0.001$). Figure 2 demonstrates that at 15 and 30 minutes, there was a large difference between the Theraworx product (Test Product) and the 62% ethanol product (Comparator Product), with Theraworx having higher persistence. From 60 minutes to 180 minutes, the difference became less pronounced. The Test Product achieved greater persistence than the Comparator Product throughout the study.

Comparisons for reduction – products

In this portion of the evaluation, the two products were evaluated; the sample times were not measured, but they were kept in the model when the products were compared (Tables 2 and 3).

There was a statistically significant difference between the two products. The Theraworx product and 62% ethanol product were significantly different in persistence effects ($p = 0.00$) over all the sample times but leaving them in the model. The Theraworx product kept the virus counts down better than alcohol.

Comparisons for reduction – sample times

The sample times were compared, leaving the products in the model (Tables 4 and 5).

Grouping Information Using the Tukey Method and 95% Confidence

Means that do not share a letter are significantly different.

At 15 and 30 minutes, the persistent effects of the Theraworx product over the ethanol were statistically significant ($p < 0.05$). After the 30-minute sample time through the 180-minute sample time, the times were not statistically different. If a greater number of subjects were used, this would be statistically significant.

Table 1. General linear model

Factor	Type	Levels	Values					
SUBJECT	Random	5	3, 4, 6, 8, 12					
PRODUCT	Fixed	2	1, 2					
SAMPLE	Fixed	5	1, 2, 3, 4, 5					
Factor	Type	Levels	Values					
Analysis of Variance for Reduction, using Adjusted Sum of Squares for Tests								
Source	DF	Seq SS	Contribution	Adj SS	Adj MS	F-Value	P-Value	Significance
Subject	4	1.737	9.70%	1.737	0.43437	5.76	0.001	Significant
Product	1	5.611	31.34%	5.611	5.61125	74.47	0.000	Significant
Sample	4	5.912	33.02%	5.912	1.47812	19.62	0.000	Significant
Product*Sample	4	1.932	10.79%	1.932	0.48312	6.41	0.001	Significant
Error	36	2.713	15.15%	2.713	0.07535			
Total	49	17.906	100.00%					

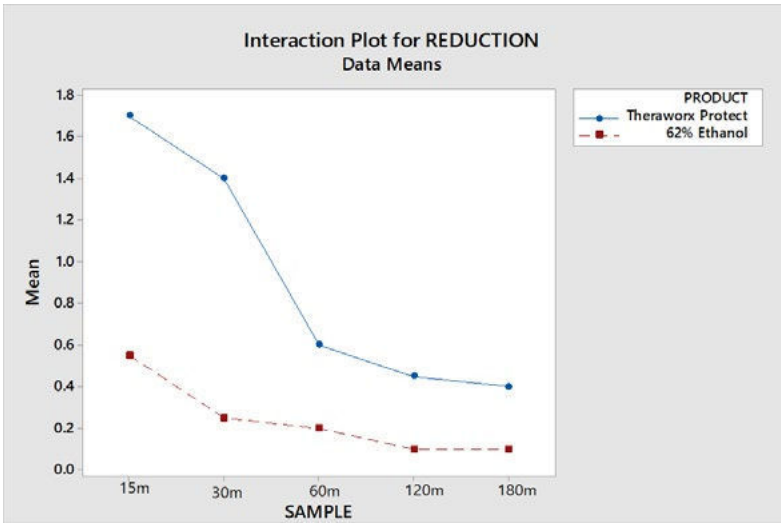

Figure 2. Interaction plot (Mean Log10 Reduction vs. Sample Time)

However, the Theraworx product had greater persistence effects over the 60- minute through 180-minute sample times than the Comparator Product (62% ethanol). There were not enough samples to justify this statistically.

Descriptive statistics are provided in Table 6, including sample size, means, standard deviations, and ranges.

Discussion

There was more residual activity of the Theraworx Protect product against the coronavirus in reducing viral concentration than the 62% ethanol solution. The viral load reductions shown by the Theraworx Protect product in this test can be contrasted to other viral reduction studies in two significant ways. First, many studies on viral load

Table 2. Tukey pairwise comparisons: Product

Product	*N*	Mean	Grouping
Test (Theraworx Protect)	25	0.91	A
Comparator (62% Ethanol)	25	0.24	B

Table 3. Tukey simultaneous tests for differences of means

Difference of Product Levels	Difference of Means	SE of Difference	Simultaneous 95% CI	T-Value	Adjusted P-Value	Significance (S/NS)
Comparator Product (62% Ethanol) Test Product (Theraworx Protect)	-0.6700	0.0776	(-0.8275, -0.5125)	-8.63	0.000	S

Table 4. Tukey pairwise comparisons: sample times

Sample	*N*	Mean	Grouping
15 minutes	10	1.125	A
30 minutes	10	0.825	A
60 minutes	10	0.400	B
120 minutes	10	0.275	B
180 minutes	10	0.250	B

Table 5. Tukey simultaneous tests for differences of means

Difference of Sample Levels	Difference of Means	SE of Difference	Simultaneous 95% CI	T-Value	Adjusted P-Value*	Significance
30 minutes – 15 minutes	-0.300	0.123	(-0.652, 0.052)	-2.44	0.127	Not Significant
60 minutes – 15 minutes	-0.725	0.123	(-1.077, -0.373)	-5.91	0.000	Significant
120 minutes – 15 minutes	-0.850	0.123	(-1.202, -0.498)	-6.92	0.000	Significant
180 minutes – 15 minutes	-0.875	0.123	(-1.227, -0.523)	-7.13	0.000	Significant
60 minutes – 30 minutes	-0.425	0.123	(-0.777, -0.073)	-3.46	0.011	Significant
120 minutes – 30 minutes	-0.550	0.123	(-0.902, -0.198)	-4.48	0.001	Significant
180 minutes – 30 minutes	-0.575	0.123	(-0.927, -0.223)	-4.68	0.000	Significant
120 minutes - 60 minutes	-0.125	0.123	(-0.477, 0.227)	-1.02	0.845	Not Significant
180 minutes - 60 minutes	-0.150	0.123	(-0.502, 0.202)	-1.22	0.739	Not Significant
180 minutes – 120 minutes	-0.025	0.123	(-0.377, 0.327)	-0.20	1.000	Not Significant

* Significant = $p \leq 0.05$; Not Significant = $p > 0.05$

Table 6. Descriptive statistics – reductions

Results for Product 1 (Test Product – Theraworx Protect)									
Variable	Sample	*N*	*N**	Mean	SE Mean	StDev	Minimum	Maximum	Range
Log10 Reduction	15 minutes	5	0	1.700	0.215	0.481	1.000	2.250	1.250
	30minutes	5	0	1.400	0.203	0.454	1.000	2.000	1.000
	60 minutes	5	0	0.600	0.203	0.454	0.000	1.250	1.250
	120 minutes	5	0	0.450	0.146	0.326	0.000	0.750	0.750
	180 minutes	5	0	0.400	0.127	0.285	0.000	0.750	0.750
Results for Product 2 (Comparator Product – 62% Ethanol)									
Variable	Sample	*N*	*N**	Mean	SE Mean	StDev	Minimum	Maximum	Range
Log10 Reduction	15 minutes	5	0	0.5500	0.0935	0.2092	0.2500	0.7500	0.5000
	30minutes	5	0	0.250	0.158	0.354	0.000	0.750	0.750
	60 minutes	5	0	0.2000	0.0935	0.2092	0.0000	0.5000	0.5000
	120 minutes	5	0	0.1000	0.0612	0.1369	0.0000	0.2500	0.2500
	180 minutes	5	0	0.100	0.100	0.224	0.000	0.500	0.500

reduction are done in in-vitro models, looking at log reduction in virus-containing solutions. Historically, testing done on the same agent in such in-vitro models vs. skin models shows significantly greater log reduction in the in- vitro models. In fact, any greater than 1 log reduction of viral load on a skin model is deemed very significant. Second, studies showing 3 log reductions in viral load typically utilize a 10-to-1 dilution in the initial viral inoculation, vs. this test in which there was no dilution in viral load in the initial inoculation.

Demonstrating an effective reduction in viral load, the Theraworx Protect product appears to be safer than alcohol-containing products for repeated use. In addition to being nonflammable, it can be used safely on mucous membranes. COVID-19 has made the public more aware of the importance of avoiding touching the face with one's hands, because of the possibility of transferring viral particles into the mouth, nose, or eyes, the entry points for respiratory viral infections [8].Theraworx Protect can be used not just as a hand disinfectant but also as a sanitizer around the "T- zone" (the eyes, nose, and mouth entryways for illnesses like COVID-19). The formula is non-toxic, safe, and gentle for use on the mucous membranes of the eyes, nose, and mouth. Plus, because Theraworx Protect is a low-pH formula containing surfactants and skin protectants, it also helps maintain the low-pH condition of healthy skin and can be used frequently without the potential for skin damage or drying over time.

Conclusions

This test attempted to compare the Theraworx product and alcohol to each other using the COVID-19 virus. While (depending on the disease) as few as 10 individual virus particles can cause infection, typical transmission events involve from 1,000 to 5,000 isolates. This test involved five instances of reinoculation of viral loads at a much higher level than the typical transmission event, and with lower transmission loads, demonstrating even more effectiveness in load reduction to safer levels.

The potential advantage of using Theraworx Protect in public health preventative practices associated with the current COVID-19 pandemic would seem to be significant, based on the results of this test. With some recent studies showing the COVID-19 virus persists longer with higher viral load and peaks later in the respiratory tissue of patients with severe disease [9], the ability to reduce viral load on the skin may have a positive impact on disease severity and therefore mortality.

More importantly, since COVID-19 can enter the body through the mucous membranes of the eyes, nose, and mouth, a safe and effective "face sanitizer" that is also a more effective hand sanitizer could be a welcomed new agent in the fight against not only COVID-19, but also influenza and other respiratory viruses and bacteria.

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Clin Med Invest, 2020 doi: 10.15761/CMI.1000215

Title: Activity of a Novel, Multimodal, Surfactant-Based Skin Cleanser on Coronaviruses, In-Vitro

Author: Daryl S. Paulson PhD.

Background: The primary objective of these tests was to evaluate the efficacy of a novel, multi-ingredient colloidal silver skin cleanser (Theraworx Protect, Avadim Technologies, Asheville, NC) on a seasonal coronavirus as a proxy for SARS-CoV-2 and 7 additional challenge microorganisms in vitro.

Methods: The coronavirus test measured percent and log10 reductions from the initial population of the viral strain(s) following exposure to the test product(s) at 1 minute, 30 minutes, and 1 hour. Plating was performed in four replicates.

The challenge microorganisms test used an In-Vitro Time-Kill Method to assess the antimicrobial properties of the test product and measured percent and log10 reduction in the microbial population of each challenge strain following exposure to each test material for 60 seconds, 10 minutes, and 30 minutes. Testing was performed in triplicate. All agar-plating was performed in duplicate.

Results: At 1 and 30 minutes, there was a 1.75 log reduction (98.22%) in SARS-CoV-2 virus. At 60 minutes, there was a 2.25 log reduction (99.44%) in virus.

The test product, Theraworx Protect (Lot #16180-1), reduced the populations of 7 challenge microorganisms – multidrug-resistant (MDR) Acinetobacter baumannii (ATCC#BAA-1605), Hemophilus influenzae (ATCC#19418), Pseudomonas aeruginosa (ATCC #15442), Staphylococcus epidermidis (ATCC #12228), Staphylococcus hominis (ATCC #700236), Streptococcus pneumoniae (ATCC #49619), Streptococcus pyogenes (ATCC #19615) - by an average of greater than 3.4 log10 following 1 minute and maintained or increased these reductions through all the remaining appropriate time points.

Conclusion: The results confirm the test product's efficacy as a waterless, leave-on, skin-compatible, topical solution to augment the use of flashing ethanol-based hand sanitizers.

TABLE 1

Test Formulation #1: Theraworx Protect
Virus: Coronavirus strain OC43 (ZeptoMetrix #0810024CF)
Host Cell Line: HCT-8 (ATCC #CCL-244)
Volume Plated per Well: 1.0 mL

Dilution (- Log_{10})	Virus Control			Test			NTC	NC	CTC	CC
	1 minute	30 minutes	60 minutes	1 minute	30 minutes	60 minutes				
										0000
-2	NT	NT	NT	CT	CT	CT	CT	NT	++++	
-3	++++	++++	++++	++++	++++	+++0	++++	++++	0000	
-4	++++	++++	++++	+++0	++00	0000	++++	++++	0000	
-5	++++	++++	++++	0000	0000	0000	+00+	+++0	NT	N/A
-6	00++	+000	0000	0000	0000	0000	++00	000+	NT	
-7	0000	0000	0000	0000	0000	0000	0000	0000	NT	
$TCID_{50}$ (log_{10})	6.00	5.75	5.50	4.25	4.00	3.25	5.50	5.50	2.50	
Log_{10} Reduction	N/A			**1.75**	**1.75**	**2.25**	N/A			
Percent Reduction				**98.22**	**98.22**	**99.44**				

Clinical and Medical Investigations

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Activity of a novel, multimodal, silver-based skin cleanser on coronaviruses, *in-vitro*

Daryl S Paulson*

BioScience Laboratories, Inc., 1765 South 19th Avenue; Bozeman, MT 59718, USA

Abstract

Background: The primary objective of these tests was to evaluate the efficacy of a novel, multi-ingredient colloidal silver skin cleanser (Theraworx Protect, Avadim Technologies, Asheville, NC) on a seasonal coronavirus as a proxy for SARS-CoV-2 and 7 additional challenge microorganisms in vitro.

Methods: The coronavirus test measured percent and log10 reductions from the initial population of the viral strain(s) following exposure to the test product(s) at 1 minute, 30 minutes, and 1 hour. Plating was performed in four replicates.

The challenge microorganisms test used an In-Vitro Time-Kill Method to assess the antimicrobial properties of the test product and measured percent and log10 reduction in the microbial population of each challenge strain following exposure to each test material for 60 seconds, 10 minutes, and 30 minutes. Testing was performed in triplicate. All agar-plating was performed in duplicate.

Results: At 1 and 30 minutes, there was a 1.75 log reduction (98.22%) in SARS-CoV-2 virus. At 60 minutes, there was a 2.25 log reduction (99.44%) in virus.

The test product, Theraworx Protect (Lot #16180-1), reduced the populations of 7 challenge microorganisms – multidrug-resistant (MDR) *Acinetobacter baumannii* (ATCC#BAA-1605), *Hemophilus influenzae* (ATCC#19418), *Pseudomonas aeruginosa* (ATCC #15442), *Staphylococcus epidermidis* (ATCC #12228), *Staphylococcus hominis* (ATCC #700236), *Streptococcus pneumoniae* (ATCC #49619), *Streptococcus pyogenes* (ATCC #19615) - by an average of greater than 3.4 log10 following 1 minute and maintained or increased these reductions through all the remaining appropriate time points.

Conclusion: The results confirm the test product's efficacy as a waterless, leave-on, skin-compatible, topical solution to augment the use of flashing ethanol-based hand sanitizers.

Background

Interventions to prevent and control infection are critical to reduce morbidity and mortality. Such interventions are often multimodal, with many different interventions in place for attacking transmission from various angles. This is because although each intervention (hand hygiene, social distancing, enhanced testing, quarantine, data sharing, media attention, etc.) is considered critical, none of them are foolproof. This model of safety incidents dates back 20 years in healthcare quality and improvement with James Reason naming it the "Swiss Cheese" model [1] In this paradigm, each intervention is like multiple pieces of swiss cheese, each slice having holes and unable to prevent something undesirable from one side reaching the other. No single slice (intervention) is perfect, so some undesirable consequences may pass through the holes of the cheese. However, if enough interventions are stacked, soon the holes are covered because not all interventions have the same faults or holes.

Autoinoculation of pathogens is a major mode of transmission for organisms capable of contact-type transmission. This pathway has historically considered only microbial contamination of the hands from environmental sources and instillation of those organisms into mucus membranes of the eyes, nose, or mouth. Currently, the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), is likely being transmitted via this autoinoculative pathway [2]. Because of this, hand hygiene is thought to be a critical prevention intervention for reducing the risk of transmission of this virus, and it is important to assess the activity of novel products on coronaviruses to identify potential adjunct or comparable modalities for intervention—similar to studies with SARS-CoV-1 [3].

The objective of this test was to evaluate the efficacy of a novel skin cleanser on a seasonal coronavirus as a proxy for SARS-CoV-2 and 7 additional challenge microorganisms: multidrug-resistant (MDR) *Acinetobacter baumannii*, *Pseudomonas aeruginosa, Staphylococcus epidermidis, Staphylococcus hominis, Streptococcus pneumonia*, *Streptococcus pyogenes* and *Hemophilus influenzae.*

Material and methods

The coronavirus study was designed to evaluate the virucidal properties of one test product [Theraworx Protect liquid, a novel, silver and surfactant-based, multimodal skin cleanser (Avadim Health; Asheville, NC)] against human coronavirus strain OC43 (ZeptoMetrix Corporation #0810024CF) and 7 challenge microorganisms using a virucidal suspension test (in vitro time-kill method). The host cells were

Correspondence to: Daryl S Paulson, BioScience Laboratories, Inc., 1765 South 19th Avenue; Bozeman, MT 59718, USA, E-mail: DPaulson@biosciencelabs.com

Key words: *coronavirus, hand sanitizer, colloidal silver, antimicrobial*

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HCT-8 (ATCC #CCL-244; epithelial human colon adenocarcinoma). A third-party laboratory provided all laboratory testing (BioScience Laboratories, Inc.; Bozeman, MT), and testing was based on the standard ASTM E1052-11, Standard Test Method to Assess the Activity of Microbicides against Viruses in Suspension. All testing was performed in accordance with Good Laboratory Practice regulations, as specified in 21 CFR Part 58. The percent and log10 reductions from the initial population of the viral strain(s) were determined following exposure to the test product(s) at 1 minute, 30 minutes, and 1 hour. Plating was performed in four replicates.

The challenge microorganisms test used an In-Vitro Time-Kill Method to assess the antimicrobial properties of the test product and one reference product when challenged with suspensions of 16 microorganisms. This procedure was based upon methodology described in ASTM E2783-11, Standard Test Method for Assessment of Antimicrobial Activity for Water Miscible Compounds Using a Time-Kill Procedure. The percent and log10 reduction in the microbial population of each challenge strain was determined following exposure to each test material for 60 seconds, 10 minutes, and 30 minutes. Testing was performed in triplicate. All agar-plating was performed in duplicate.

Results

At 1 and 30 minutes, there was a 1.75 log reduction (98.22%) in SARS-CoV-2 virus. At 60 minutes, there was a 2.25 log reduction (99.44%) in virus.

The test product, Theraworx Protect (Lot #16180-1), reduced the populations of 7 challenge microorganisms - multidrug-resistant (MDR) *Acinetobacter baumannii*, (ATCC#BAA-1605), *Hemophilus influenzae* (ATCC#19418), *Pseudomonas aeruginosa* (ATCC #15442), *Staphylococcus epidermidis* (ATCC #12228), *Staphylococcus hominis* (ATCC #700236), *Streptococcus pneumoniae* (ATCC #49619), *Streptococcus pyogenes* (ATCC #19615) - by an average of greater than 3.4 log10 following 1 minute and maintained or increased these reductions through all the remaining appropriate time points.

Discussion

The CDC guidelines for healthcare-related hand hygiene recommend alcohol-based hand sanitizers with at least 62% alcohol [4]. For the non-healthcare setting, the CDC recommends soap and water for hand hygiene [5]. The test product employs specialized surfactant technology, making the innovation compliant with the CDC soap and water recommendation. The product also improves skin quality and has demonstrated six-hour duration of action equivalent to 4% chlorhexidine gluconate, ASTM Method E1173-15 simulated pre-operative skin preparation [6]. What's more, the test product has been evaluated against a broad array of microorganisms, including multidrug-resistant (MDR) *Acinetobacter baumannii*, *Pseudomonas aeruginosa, Staphylococcus epidermidis, Staphylococcus hominis, Streptococcus pneumonia, Streptococcus pyogenes* and *Hemophilus influenzae*, demonstrating a greater than 3.4 log reduction after 1 minute.

Given the autoinoculative likelihood of various pathogens, including SARS-CoV-2, interventions such as this could be beneficial. Furthermore, this product has been shown to normalize the skin pH/acid mantle [7]. A critical aspect of maintaining skin barrier functions such as transient and resident flora regulation [8,9].

Conclusions

We have tested a novel skin cleanser against a seasonal coronavirus (OC43)-which represents the same virus as COVID-19 and equivalent susceptibility patterns to antiseptics as would SARS-CoV-2, the causative agent of COVID-19—and found reasonable reduction in virus, particularly after an hour post-application. At 60 seconds, the product demonstrated a 1.75 log reduction and greater than 2.0 log reduction (or 99%) at 60 minutes, demonstrating increasing efficacy with time. This novel product has greater persistence than alcohol, and it can be used as a persistent adjunct that is also safe to be used on mucus membranes including the eyes, nose and mouth (the main zone of transmission).

The results confirm the product's efficacy as a waterless, leave-on, skin-compatible, topical solution to augment the use of flashing ethanol-based hand sanitizers. Additionally, the results have shown this product's ability to hydrate and restore dermal tissue to a healthy state during the frequent use of traditional antiseptic actives, restoring the natural microflora as well as providing a persistent activity between ethanol product applications. Because of this, it may be possible that it could provide an extra layer of protection during the COVID-19 pandemic.

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Forearm Controlled Application Test For Evaluating the Relative Mildness and Skin Moisturization Effectiveness of Two Products

The purpose of this Forearm Controlled Application Technique (FCAT) evaluation was to determine the relative mildness and skin moisturizing effect of two cleansing test products. Visual evaluations and skin measurements were performed with non-invasive instrument evaluations during the test period.

In this Study, 27 subjects between the ages of 18 and 65 years completed testing. Visual evaluation were performed prior to enrollment in the study, to assure that subjects complied with the inclusion criteria that included appropriate inner are dryness and erythema levels. Upon completion of the 5-day conditioning period, the subjects underwent a 5-day treatment period with production application taking place twice daily. The product applications were performed on the lower inner forearms on each subject, randomly applying one test material per arm. Visual evaluations and measurements using Corneometer, Skicon, and Trans-epidermal Water Loss (TEWL) instrumentation were performed daily prior to the 1st and 2nd product applications on each of the 5 test days and again 2 to 3 hours after the 2nd product application on the fifth day.

Non-Inferiority Evaluation - The test product (Theraworx®) achieved a non-inferiority status compared to the comparator product (Hibiclens®) in all of the evaluations: Corneometer, SkiCon, TEWameter, Visual Erythema and Visual Dryness.

Non-Superiority Evaluation - For the Corneometer, SkiCon and TEWameter readings the test product (Theraworx®) was superior to the comparator product (Hibiclens®).

Equivalence Evaluation - For the Corneometer, SkiCon and TEWameter readings the test product (Theraworx®) to the control product (Hibiclens®)

Table 34. Descriptive Statistics Non-Superiority Test – Tewameter Readings

Variable	*N*	Mean	StDev	SE Mean
Test Product	277	3.0848	3.2925	0.19783
CHG Comparator	277	2.8314	2.7395	0.16461

Table 35. Difference: Mean (Test Product) – Mean (CHG Comparator)

Difference	SE	95% Upper Bound	Upper Limit
0.2534	0.25735	0.67747	0.2

The upper bound is not less than0.2. Cannot claim Mean (Test Product) – Mean (CHG Comparator) <0.2.

Table 36. Non-Superiority Test Non-Superiority Test – Tewameter Readings

Null hypothesis:	Mean (Test Product) – Mean (CHG Comparator) ≥ 0.2	Superior
Alternative hypothesis:	Mean (Test Product) – Mean (CHG Comparator) < 0.2	Non-Superior
α level:	0.05	

Degrees of Freedom	*T*-Value	*P*-Value
534	0.20761	0.582

The ***P*-Value** is >0.05. Cannot claim Mean (Test Product) – Mean (CHG Comparator) <0.2.
The test product is superior to the comparator product (Hibiclens®).

Theraworx® v. Chlorhexidine Gluconate Bathing and Peri-operative Skin Cleansing Study

Principal Investigator: Roger Huckfeldt, MD
Co-Investigators: Phillip Finley MS, Cindy Lowe MS, Keela Davis MS, Kara Childers MS

In a simulated patient decolonization comparative study, 30 healthy volunteers avoided bathing for 24 hours and were then randomized into two groups. The two groups were then observed as they utilized two bathing protocols. The first group performed a ten minute shower using CHG, following my a focused CHG scrub of four specific body areas, the sub-clavicular space, midline abdomen, groin and patellar area. The second group underwent a one minute scrub of the same four areas using a single Theraworx® impregnated cloth per area. After the chlorhexidine shower or Theraworx® scrub the subjects were clothed in freshly laundered surgical clothing and placed in a monitored room. Skin cultures using a standardized tube/scrub method were obtained prior to randomization as a baseline and again at two and six hours post intervention. Serial dilutions and agar plating were performed immediately and incubated for 48 hours. Colony counting was then performed and log reduction from pre-intervention counts performed. The Theraworx® product demonstrated a statistically better log reduction vs. CHG in three of four body areas, at the two hour cultures, and a statistically better log reduction vs. CHG in two of four body areas, at the four hour cultures.

Two Hour Cultures

1. Subclavicular space: Theraworx® showed a statistical difference at p=0.083 in greater log reduction of bacteria as compared to chlorhexidine gluconate.
2. Midline: No statistical difference observed (p=0.103).
3. Groin: Theraworx® showed a statistical difference at p=0.078 in greater log reduction of bacteria as compared to chlorhexidine gluconate.
4. Knee: Theraworx® showed a statistical difference at p<0.001in greater log reduction of bacteria as compared to chlorhexidine gluconate.

Six Hour Cultures

1. Subclavicular space: No statistical difference observed (p=0.172)
2. Midline: Theraworx® showed a statistical difference at p=0.062 in greater log reduction of bacteria as compared to chorhexidine gluconate
3. Groin: No statistical significance observed (p=0.371)
4. Knee: Theraworx® showed a statistical difference at p<0.003 in greater log reduction of bacteria as compared to chlorhexidine gluconate.

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Theraworx v. Chlorhexidine Gluconate
Bathing and Peri-operative Skin Cleansing Study

Principal Investigator: Roger Huckfeldt, MD
Co-Investigators: Phillip Finley MS, Cindy Lowe MS, Keela Davis MS,
Kara Childers MS

Purpose of study:
A comparison of the efficacy of Theraworx skin cleansing formulation and chlorhexidine gluconate in reducing bio-burden.

Background:
Chlorhexidine gluconate is commonly used to bath high risk patients in ICU settings as a means to help prevent hospital acquired infections. It is also widely used as a pre-operative shower/scrub to limit surgical site infections which may occur secondary to bacterial colonization or contamination at the surgical site. Success with the peri-operative shower/scrub relies on patient compliance, proper technique and preventing recontamination of the surgical site post shower/scrub. The use of chlorhexidine gluconate for bathing is complicated by increasing reports of skin irritation/reaction, limitations of use in areas such as the groin and around the eyes, cost and concerns of progressive bacterial resistance.

Theraworx is a self drying, leave on, skin cleansing agent that combines a specialized surfactant and skin healthy ingredients. Subjective reports from users of the Theraworx Bathing System indicate its success in controlling bio-burden without the use of additional antimicrobial agents.

Procedure:
Thirty healthy volunteers were recruited. These volunteers avoided bathing for 24 hours prior to the protocol. One half of the subjects were randomized to a chlorhexidine shower/scrub. These participants were given instructions and the shower was timed for ten minutes by study personnel. In addition to a total body shower, participants were asked to perform a focused scrub over the sub-clavicular space, midline abdomen, groin and patellar area. The second half of the subjects was randomized to the Theraworx group and underwent a one minute scrub of the same four areas using a single Theraworx impregnated cloth per area. After the chlorhexidine shower or Theraworx scrub the subjects were clothed in freshly laundered surgical clothing and placed in a monitored room. Skin cultures using a standardized tube/scrub method were obtained prior to

randomization as a baseline and again at two and six hours post intervention. Serial dilutions and agar plating were performed immediately and incubated for 48 hours. Colony counting was then performed and log reduction from pre-intervention counts performed.

Results:
Results were reported by site of preparation comparing the chlorhexidine gluconate group to the Theraworx group. Statistical difference was considered to be $p \leq 0.10$.

Two Hour Cultures:

1. Subclavicular space: Theraworx showed a statistical difference at p=.083 in greater log reduction of bacteria as compared to chlorhexidine gluconate.
2. Midline: No statistical difference observed (p=.103).
3. Groin: Theraworx showed a statistical difference at p=0.078 in greater log reduction of bacteria as compared to chlorhexidine gluconate.
4. Knee: Theraworx showed a statistical difference at p<0.001in greater log reduction of bacteria as compared to chlorhexidine gluconate.

Six Hour Cultures:

1. Subclavicular space: No statistical difference observed (p=0.172).
2. Midline: Theraworx showed a statistical difference at p=0.062 in greater log reduction of bacteria as compared to chorhexidine gluconate.
3. Groin: No statistical significance observed (p=0.371).
4. Knee: Theraworx showed a statistical difference at p<0.003 in greater log reduction of bacteria as compared to chlorhexidine gluconate.

Summary:
In all cases, Theraworx was equally effective or better at log reduction of bacteria as compared to a Chlorhexidine gluconate shower/scrub. At two hours, Theraworx was superior at the subclavicular space, groin and knee. At six hours, Theraworx was superior at the midline and knee.

Using Theraworx self drying cleanser in a one minute scrub should allow the practitioner to proceed without relying on the patient to perform an important aspect of surgical site prophylaxis correctly. The Theraworx Bathing System is an effective skin healthy alternative to chlorhexidine gluconate for bathing at risk bed bound patients without the risks associated with chlorhexidine gluconate.

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Change Has Arrived: Antimicrobial Bathing and CLABSI

Patricia Sung, Mary Virgallito, Theresa Murphy, Raffi Boghossian, Rose Young;
University of Southern California, Verdugo Hills Hospital, Glendale, California

Purpose: Persistent central catheter–associate bloodstream infections (CLABSIs) occurred each quarter from 2014 to 2016 in our 12-bed intensive care unit (ICU), prompting an infection prevention (IP) assessment in November 2016. Low compliance with the bathing protocol was identified as a gap in practice. Staff surveys indicated confusion about chlorhexidine (CHG) application and dissatisfaction with effects on patients' skin. A topical immune health system was introduced to replace CHG bathing products in an effort to improve staff satisfaction, raise compliance, and reduce CLABSI rates.

Evaluation/Outcome: Pre -implementation assessment identified gaps in practice. Staff indicated CHG was "too sticky," and "too complicated; patients don't like it." In July 2019, a questionnaire was
administered to ICU nurses after the change to the new antimicrobial bathing product. Of 20 responses received from nurses, all stated they like the product. In response to an open-ended question asking why staff and/or patients like the product, 4 nurses (20%) cited the ease of use, and 7 (35%) cited the protective effects on the patients' skin. A random sample audit of patient bathing compliance before (5 of 10) and after (10 of 10) implementation identified a statistically significant difference (P = .02).
The ICU achieved a rate of 0 CLABSI in February 2018 and has remained at zero through April 2020.

***Statistical Significance in ICU Bathing Compliance after implementing Theraworx Protect at (P= .02)**

***CLABSI Rate since converting to Theraworx Protect from CHG 2% has remained at zero since February 2018**

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Closing the Gap: Targeting CAUTIs With a Novel Approach to Perineal Care

Lisa Hargett, Theresa Anderson; University of Maryland
St. Joseph Medical Center, Towson, Maryland

Purpose: Persistent catheter-associated urinary tract infections (CAUTIs) occurred in University of Maryland St. Joseph Medical Center's 28-bed critical care unit despite a robust prevention bundle. Root-cause analyses identified poor compliance with perineal and urinary catheter care as a gap in evidence-based practice. A change from applying soap and water with a washcloth from a basin to a topical immune health system wipe–based product was implemented to standardize process, improve compliance, and eliminate CAUTIs.

Summary: Despite continuous efforts to reduce infections, patients in the medical-surgical intensive care unit (MSICU) continued to have CAUTIs. Although a 44% reduction from fiscal year (FY)14 to FY15 was achieved, 1 infection was still too many. Root-cause analyses were performed on each CAUTI to identify a potential reason for the infection. Compliance with perineal and urinary catheter care was identified as a potential root cause and an opportunity to improve. In November 2015, the MSICU implemented a new process for managing bowel incontinence and enhancing perineal and urinary catheter care. These interventions included baby wipes for incontinence care and a topical immune health system wipe for perineal and urinary catheter care. The topical immune health system is used during the following situations: before and after insertion of a urinary catheter; to clean every 6 hours, or every 4 hours for catheters indwelling longer than 5 days, patients with urinary catheters; as a final cleaning step for any incontinence events; as a final cleaning step during the daily CHG bath; and before straight catheterization. With this new practice, perineal and urinary catheter care increased from once per day to up to 6 times per day, based on the duration of the catheter. Frontline staff were involved in the solution and implementation processes.

Evaluation/Outcome: Staff satisfaction was very high with the new standard of care. Staff survey results were notable for ease of use (100%), preference over previous practice (97%), and catheter care being worth the extra step (100%). Compliance with perineal care also improved. After implementation, the MSICU celebrated 351 days without a CAUTI. The success has continued: the unit recently celebrated 365 days CAUTI free. Our standardized infection ratio also decreased by 49% from before to after implementation of the new interventions. It is important to acknowledge that this success is not the result of a single intervention but rather multiple interventions designed to reduce CAUTIs.

100% Staff Satisfaction

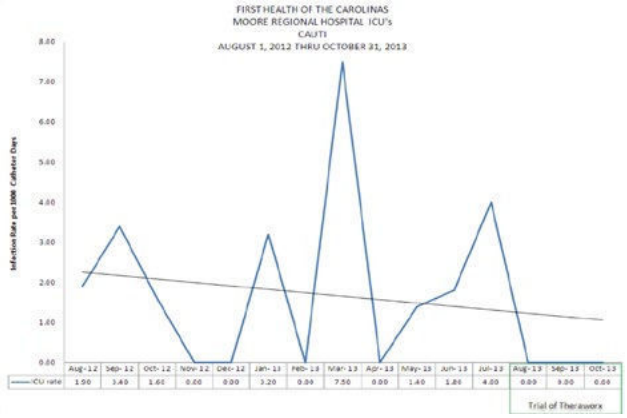
Improved Compliance

365 continuous Days Zero CAUTI

Reduction in Standardized Infection Ratio by 49%

Effects of Education and Improved Foley Catheter Care on Nurses' Knowledge and Catheter Associated Urinary Tract Infections

Urinary tract infection are the most common Hospital acquired infection, accounting for 40% of nosocomial infections annually. Approximately 70- 80% of UTIs are caused by indwelling foley catheters, and 56-89% of adults in critical care areas have foley catheters. The risk for catheter associated urinary tract infection (CAUTI) increases every day that the catheter is present; therefore, reducing the duration of catheterization and improving foley catheter care will result in lower infection rates. Additionally, the use of (Theraworx®) wipes and Theraworx® foam cleanser during foley insertion and for routine care have demonstrated reduced CAUTI rates in clinical studies. Furthermore, in the 3 months after staff education and implementation of Theraworx® there were 1667 catheter days, and the CAUTI rate was 0/1000 catheter days in the critical care areas. The previous year in the corresponding months there were 1728 catheter days, with a CAUTI rate of 2.3/1000 catheter days.



Effects of Education and Improved Foley Catheter Care on Nurses' Knowledge and Catheter Associated Urinary Tract Infections

FirstHealth OF THE CAROLINAS

ANCC MAGNET RECOGNITION

Gloria Walters MSN, RN-BC, CCRN
Jayne Lee BSN, MPH, RN, CIC
Leona Riddle BSN, RN

Background

Urinary tract infections are the most common hospital-acquired infection, accounting for 40% of nosocomial infections annually. Approximately 70- 80% of UTIs are caused by indwelling foley catheters, and 56-89% of adults in critical care areas have foley catheters. The risk for catheter associated urinary tract infection (CAUTI) increases every day that the catheter is present; therefore, reducing the duration of catheterization and improving foley catheter care will result in lower infection rates.

Additionally, the use of silver impregnated (TheraworxTM) wipes and TheraworxTM foam cleanser during foley insertion and for routine care have demonstrated reduced CAUTI rates in clinical studies.

The purpose of this study was to determine whether nurses' knowledge about foley catheter management increased after additional education and whether CAUTI rates were reduced after implementation of catheter care with TheraworxTM products.

Research Questions

1. Did nurses' test scores measuring their knowledge of catheter care improve after additional education?
2. Did CAUTI rates decrease after implementation of focused nursing education and the use of a new product for catheter insertion and care (TheraworxTM)?

Methods

A convenience sample of nursing staff was recruited from the critical care areas. A pre-test was administered and was comprised of questions pertaining to knowledge of foley catheter management and care. Following the pre-test, educational sessions were provided to reemphasize correct catheter insertion and maintenance both at Skills Fairs and at other times on the critical care units. Additionally, the use of TheraworxTM wipes and foam cleanser was implemented as a best practice with both foley insertion and routine catheter care. After staff education and implementation of the use of the wipes and foam cleanser for three months, a post-test was administered to the staff in the critical care areas.

Results

93 participants completed the pre-test, with a mean score of 68.60 (*SD*=12.73). 38 participants completed the post-test, with a mean score of 73.18 (*SD*=8.73). However, only 19 individuals completed both the pre-test and the post-test. Mann-Whitney U Test for the difference between the mean scores of the pre- and post-test for all participants was statistically significant (*Z*=-2.15, *p*=0.031). Wilcoxon Signed Rank Test for those that completed both the pre-and post-tests was also statistically significant (*Z*=-2.797, *p*=0.005).

Furthermore, in the 3 months after staff education and implementation of TheraworxTM there were 1667 catheter days, and the CAUTI rate was 0/1000 catheter days in the critical care areas. The previous year in the corresponding months there were 1728 catheter days, with a CAUTI rate of 2.3/1000 catheter days.

Conclusion

Education about best practices for foley catheter insertion and care increased nurses' knowledge. Increased knowledge and the implementation of the TheraworxTM products reduced CAUTIs in the critical care areas. Future research should evaluate whether these findings can be replicated in other settings.

Effects of Education and Improved Foley Catheter Care on Nurses' Knowledge and Catheter Associated Urinary Tract Infections

Gloria Walters MSN, RN-BC, CCRN
Jayne Lee BSN, MPH, RN, CIC
Leona Riddle BSN, RN

Background

Urinary tract infections are the most common hospital-acquired infection, accounting for 40% of nosocomial infections annually. Approximately 70- 80% of UTIs are caused by indwelling foley catheters, and 56-89% of adults in critical care areas have foley catheters. The risk for catheter associated urinary tract infection (CAUTI) increases every day that the catheter is present; therefore, reducing the duration of catheterization and improving foley catheter care will result in lower infection rates.

Additionally, the use of silver impregnated (TheraworxTM) wipes and TheraworxTM foam cleanser during foley insertion and for routine care have demonstrated reduced CAUTI rates in clinical studies.

The purpose of this study was to determine whether nurses' knowledge about foley catheter management increased after additional education and whether CAUTI rates were reduced after implementation of catheter care with TheraworxTM products.

Research Questions

1. Did nurses' test scores measuring their knowledge of catheter care improve after additional education?
2. Did CAUTI rates decrease after implementation of focused nursing education and the use of a new product for catheter insertion and care (TheraworxTM)?

Foley Catheter Knowledge Questionnaire
Results of this survey will be kept confidential.

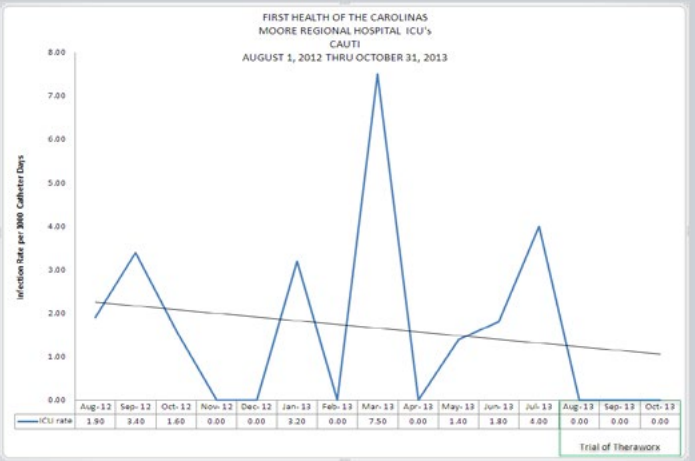
Employee Number_____;

Please circle true (T) or False (F) for the following items.

True or False…

T	F	1. The policy at FHC is to perform Foley catheter care twice a day and prn for stool incontinence.
T	F	2. To collect a urine specimen from the Foley catheter, the nurse should scrub the collection port with alcohol for 15 seconds prior to accessing the collection port.
T	F	3. When performing perineal care or Foley catheter care, nurses should use sterile gloves.
T	F	4. The securement device should be placed on the anterior aspect of the thigh.
T	F	5. A full drainage bag increases the risk of a catheter associated urinary tract infection.
T	F	6. The graduate used to empty urine from the Foley catheter drainage bag should be changed every 48 hours.
T	F	7. When collecting a urine specimen it is acceptable to raise the catheter tubing slightly to allow urine to flow backward to the collection port.
T	F	8. The Foley catheter bag should be kept below the level of the bladder except in special circumstances such as ambulation of the patient where it may be difficult to do so.
T	F	9. Catheter-associated urinary tract infections (CAUTIs) are responsible for up to 40% of all hospital acquired infections.
T	F	10. The tamper resistant seal on the Foley catheter tubing should not be broken to irrigate the tubing.

_____ Total Knowledge Score (0 – 10)



Methods

A convenience sample of nursing staff was recruited from the critical care areas. A pre-test was administered and was comprised of questions pertaining to knowledge of foley catheter management and care. Following the pre-test, educational sessions were provided to reemphasize correct catheter insertion and maintenance both at Skills Fairs and at other times on the critical care units. Additionally, the use of TheraworxTM wipes and foam cleanser was implemented as a best practice with both foley insertion and routine catheter care. After staff education and implementation of the use of the wipes and foam cleanser for three months, a post-test was administered to the staff in the critical care areas.

Results

93 participants completed the pre-test, with a mean score of 68.60 (*SD*=12.73). 38 participants completed the post-test, with a mean score of 73.18 (*SD*=8.73). However, only 19 individuals completed both the pre-test and the post-test. Mann-Whitney U Test for the difference between the mean scores of the pre- and post-test for all participants was statistically significant (Z=-2.15, p=0.031). Wilcoxon Signed Rank Test for those that completed both the pre-and post-tests was also statistically significant (Z=-2.797, p=0.005).

Furthermore, in the 3 months after staff education and implementation of TheraworxTM there were 1667 catheter days, and the CAUTI rate was 0/1000 catheter days in the critical care areas. The previous year in the corresponding months there were 1728 catheter days, with a CAUTI rate of 2.3/1000 catheter days.

Conclusion

Education about best practices for foley catheter insertion and care increased nurses' knowledge. Increased knowledge and the implementation of the TheraworxTM products reduced CAUTIs in the critical care areas. Future research should evaluate whether these findings can be replicated in other settings.

Preventing Chronic Urinary Tract Infections from Urinary and Fecal Incontinence: The Impact of Theraworx®

Urinary and fecal incontinence are common syndromes which can lead to significant morbidity, such as urinary tract infection.[1] It has been reported that over half of patients residing in long-term care facilities have urinary incontinence and nearly half have fecal incontinence.[2] Proper management of urinary and fecal incontinence can be costly due to nursing time,[3] but is critical to prevent urinary tract infection. Current management typically includes rapid cleansing with soap and water, however these interventions may be limited in effectiveness due to poor bactericidal activity of soap and water.

Peterson Healthcare initiated Theraworx® and its patented protocol in the recurrent UTI population who were also fecal and urine incontinent. The 16 site year long evaluation showed a significant reduction in monthly UTI rates. Previous to Theraworx® intervention these 16 sites averaged (27) infections per month for a full 12 months. After implementation of Theraworx® these same sites averaged 6.3 infections per month.

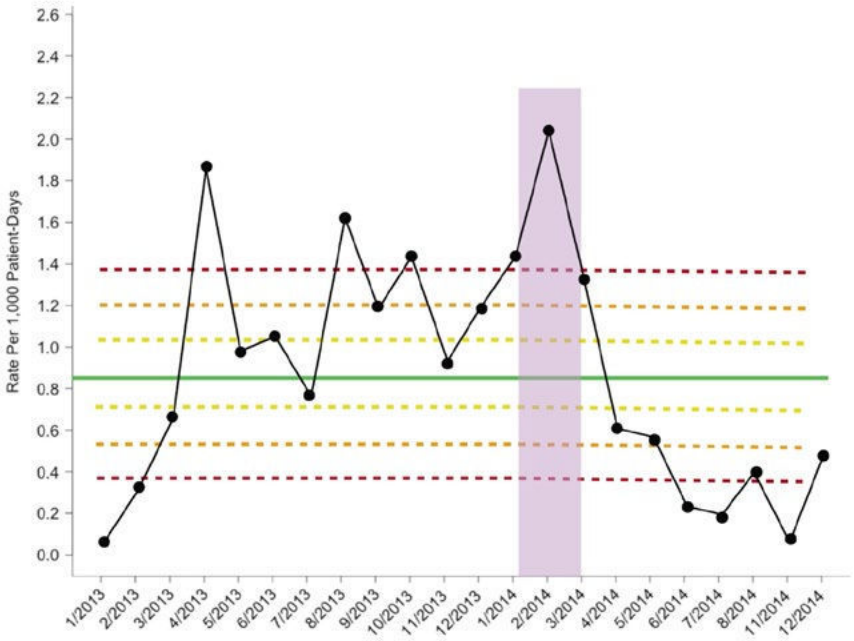


Figure 1. Chrnoic Urinary Tract Infection Rate Jan 2013–Dec 2014

1. THaab F. Chapter 1: The conditions of neurogenic detrusor overactivity and overactive bladder. Neurourol Urodyn. 2014 Jul;33 Suppl 3:S2-5. doi: 10.1002/nau.22636.
2. Kowal-Vern A, Poulakidas S, Barnett B, Conway D, Culver D, Cullum M, et al. Fecal containment in bedridden patients: economic impact of 2 commercial bowel catheter systems [corrected] [published erratum appears in AM J CRIT CARE 2010 Nov;19(6):488]. American Journal Of Critical Care. (2009, May 2); 18(3): S2-15.
3. Borrie MJ, Davidson HA. Incontinence in institutions: costs and contributing factors. CMAJ. 1992;147(3):322-328.

Preventing Chronic Urinary Tract Infections from Urinary and Fecal Incontinence: The Impact of Theraworx

Jacque Whitley RN; Jill West RN; Mariah Minor RN; Kate Loudon RN
Petersen Healthcare, Peoria, IL

INTRODUCTION

Urinary and fecal incontinence are common syndromes which can lead to significant morbidity, such as urinary tract infection (1). It has been reported that over half of patients residing in long-term care facilities have urinary incontinence and nearly half have fecal incontinence (2). Proper management of urinary and fecal incontinence can be costly due to nursing time (3), but is critical to prevent urinary tract infection. Current management typically includes rapid cleansing with soap and water, however these interventions may be limited in effectiveness due to poor bactericidal activity of soap and water.

The effectiveness of managing incontinence with a one-step antibacterial cleanser for the prevention of chronic urinary tract infection is not well studied.

The objective of this project was to evaluate the impact of post incontinence cleansing of the pelvic area with a novel skin antiseptic for the prevention of chronic urinary tract infection in long-term care residents.

METHODS

Study Design and Population

This was a quality improvement project undertaken from January 2014 through December 2014 in sixteen long-term care facilities throughout Illinois. After each episode of urinary or fecal incontinence, the nursing staff cleansed the pelvic area with Theraworx foam per the protocol outlined in Table 1. In-service training on the protocol was conducted in each facility during the first quarter of 2014.

Study Definitions

A urinary tract infection was defined as the following:

1. 100,000 colony forming units (CFU's) of organism/ml obtained aseptically from a) distal end of a catheter; b) sampling port; or c) clean-catch.

   in a resident without previous infection or with negative culture and clearing of symptoms following a previous UTI with other signs and symptoms supportive of infection;
2. 100,000 CFU's of a different organism in a subsequent culture, with clinical continuation or deterioration of condition, in a resident with previous UTI; or
3. New onset of signs and symptoms of UTI in a resident with or without positive culture.

Statistical Analysis

To evaluate the impact of Theraworx on chronic urinary tract infection prevention, a statistical process control u-chart (rates over time from a Poisson distribution) was used. Montgomery rules were used to determine special-cause variation on the charts (4).

RESULTS

Theraworx™

Incontinence Protocol

After each incidence of urinary or fecal incontinence, cleanse the umbilical area to mid thigh using a Theraworx wipe or a wash cloth containing 2-3 applications of Theraworx foam. Wipe front to back for women and in concentric circles around the glans penis for men. Allow to dry and do not rinse off (30 second dry time).

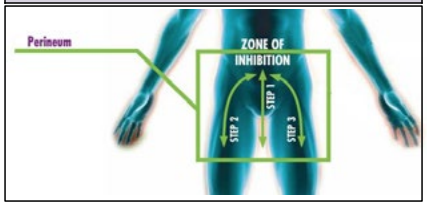


Table 1: Theraworx Protocol

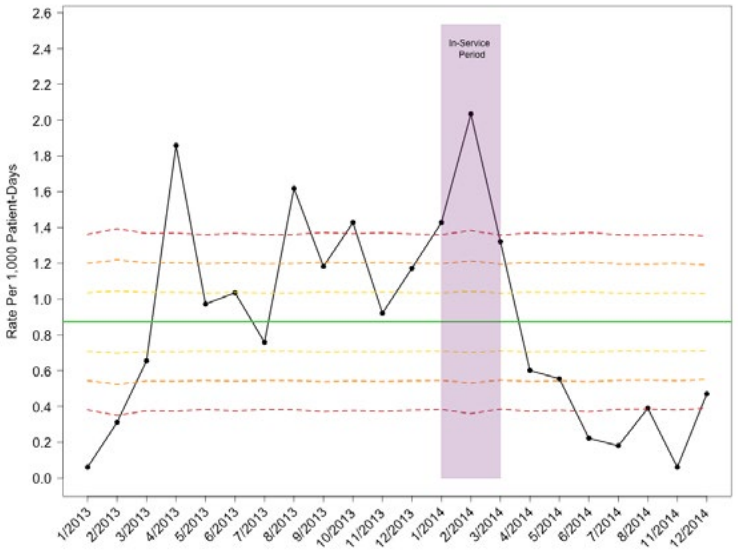


Figure 1: Chronic Urinary Tract Infection Rate Jan 2013 – Dec 2014

CONCLUSIONS

- After all facilities completed in-servicing on how to use the Theraworx protocol, the chronic urinary tract infection rate decreased significantly and was sustained throughout the remainder of the project, as indicated by special-cause variation from April 2014 through December 2014 (Figure 1).
- Theraworx provides many benefits over many other antiseptics including a broad spectrum of activity, pH maintenance, and it is safe to use in the peri-rectal area/mucus membranes.
- Theraworx appears to be an effective intervention for the prevention of chronic urinary tract infections due to urinary or fecal incontinence.

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Poster fully funded by "Eblen Charities"

1. Haab F. Chapter 1: The conditions of neurogenic detrusor overactivity and overactive bladder. Neurourol Urodyn. 2014 Jul;33 Suppl 3:S2-5. doi: 10.1002/nau.22636.
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3. Borrie MJ, Davidson HA. Incontinence in institutions: costs and contributing factors. CMAJ. 1992;147(3):322-328.
4. Montgomery DC. Introduction to statistical quality control. 6th ed. Hoboken, N.J.: Wiley; 2009. xiv, 734

Quality Intervention: Sutter Healthcare- CAUTI Intervention- Cost and Efficacy Comparison

Assessing the Efficacy and Cost-Effectiveness of Theraworx Protect to Existing Regimens and Products- a 120- day Intervention: Emergency Department, ICU, SDU, Neuro

Sutter Health Infectious Disease: Jeffery Silvers, MD

Sutter Health Infection Prevention:

Background

Sutter Health, one of the leading health IDN's in the country sought to compare the effectiveness, acceptability and cost-effective of Theraworx Protect to standard practices for the sole purpose to ease nursing demands, improve supply chain redundancies without compromising efficacy. These quality driven interventional studies are driven primarily for either cost or efficiency related challenges combined with the need to ever improve infection prevention outcomes.

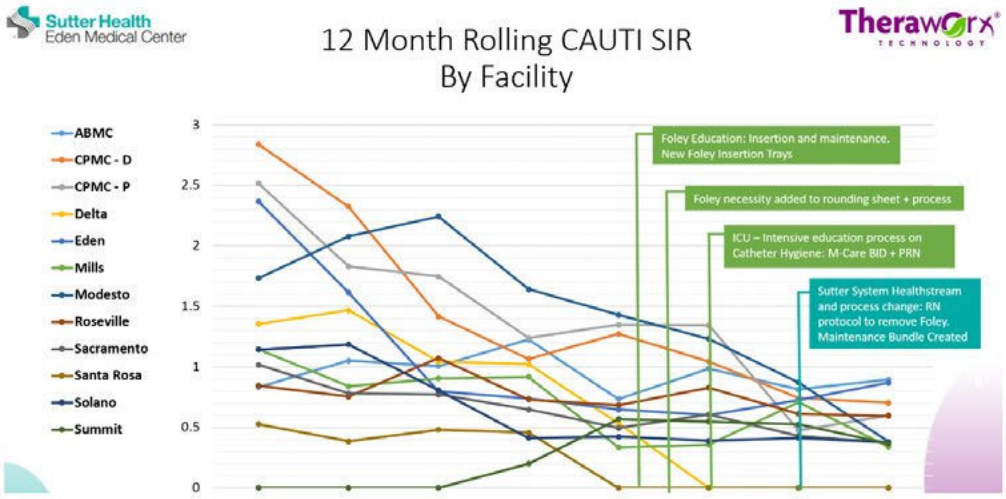
Method

The system Tracked Efficacy: 1. Photo record of moisture associated skin damage (MASD) pre and post intervention 2. Track usage of antifungal medications 3. Track rate of catheter associated urinary tract infections (CAUTI's)Assess Sutter System CAUTI trends With attention to the potential effects of other policy interventions Relative to products used.

The system tracked Cost: 1. Track unit census, and acuity/dependency of patient population for relevant time frames Track usage of linen: washcloths and towels 2. Track usage and costs of Theraworx during trial period 3. Track usage and costs of replaced products, antifungals and linens

The System Tracked Patient and Clinic Satisfaction: 1. Survey of clinicians who use Theraworx 2. Monitor product appropriation to o ther units 3. Survey of capable patients who have used Theraworx

Sutter Health
Eden Medical Center



Theraworx TECHNOLOGY

Non-ICU - Total Body Bathing + Decolonization				
Product	Application - Detail	Price	Sub-Total	Difference
Sage/ Comfort Bath Care Application - 8 cloths	Total body application	$ 2.30		
Dimethicone Skin Protectant Barrier cream	*Routine perineum care - 3 apps/ day @ $0.23 ea*	$ 0.69		
Bard/ other glycol based wipe	*Routine perineum care - 3 addt'l apps/ day @ $1.25 ea*	$ 3.75		
Sage/Bard System – cost per routine day			$ 6.74	
Theraworx Bathing/ Barrier System - 8 cloths	Total body application	$ 4.07		
Theraworx Spray Application	*Routine perineum care - 3 addt'l apps/ day @ $0.09 ea*	$ 0.27		
Theraworx System – cost per routine day			*$ 4.34*	
Difference per routine day				***$ (2.40)***
ICU - Total Body Bathing + Decolonization				
Product	Application - Detail	Price	Sub-Total	Difference
Sage/ other CHG Cloth Application - 6 cloths	Body application - **NOT** face and perineum	$ 5.52		
Glycol based wipe	Face and perineum care	$ 1.25		
Dimethicone Skin Protectant Barrier cream	*Routine perineum care - 3 apps/ day @ $0.23 ea*	$ 0.69		
Bard/ other glycol based wipe	*Routine perineum care - 3 addt'l apps/ day @ $1.25 ea*	$ 3.75		
Sage/CHG System – cost per routine day			*$ 11.21*	
Theraworx ICU Bathing/ Barrier System - 8 cloth	Total body application – including face and perineum	$ 4.07		
Theraworx Spray Application	*Routine perineum care - 3 addt'l apps/ day @ $0.09 ea*	$ 0.27		
Theraworx System – cost per routine day			*$ 4.34*	
Difference per routine day				**$ (6.87)**

American Healthcare Association (AHCA)
Spring Session 2017

Equipping Clinicians With Advanced Care Options Leads To Reductions In Urinary Tract Infections

Nexion Health and Rehab implemented a QAPI[1] and RCA (Quality Assurance and Performance Improvement) and (Root Cause Analysis) program to reduce the incidence of UTI's (Urinary Tract Infections) in the "recurrent UTI population" who were fecally and urine incontinent and ventilator dependent, all of which are of the highest acuity populations in long term care. The QAPI initiatied Theraworx® as a daily intervention. Nexion reduced their average # of new UTI cultures 53% over the 6 month implementation plan.

Improvement Steps We utilized:
• QAPI: Root Cause Analysis (RCA), Performance Improvement Plans and Validation;
• The expanded AHCA QIs;
• and the Baldrige Performance Excellence Framework
to meet measurable targets in line with the three key priorities: (initially) improvements in organizational success and (long term goal of) short-stay/post-acute care impact for readmissions.

Additionally, we employed a trainer for Theraworx® application and implementation. We continued to track the # of new Cultured UTIs per month from May (month of implementation) though October.

"In the critical battle against hospital acquired conditions, you now have an innovative new alternative—a simple, inexpensive, total body safe alternative— Theraworx® Technology, from Avadim Technologies, Inc. Theraworx, a new paradigm for skin hygiene, working to optimize the natural antimicrobial action of the skin's acidic mantle, preserving the low pH of the stratum corneum, the outer layer of the epidermis. Theraworx, working to preserve rather than degrade the skin's permeability barrier, allowing the skin to do its job in preventing water loss and avoiding dryness. Theraworx, a non-toxic product, safe for use around mucous membranes, including the perineum.

Now, for the first time, you have a product that is safe for use in Foley catheter insertion and care, safe for use in establishing a zone of inhibition for urine and fecal incontinence, safe for use in full-body bathing for a wide age and range of patient populations. Broad spectrum, non-drying, and available in a wide range of delivery systems, including an eight cloth full body bathing system that includes cloths for face and perineum..."
Source: theraworx.com

Theraworx® TECHNOLOGY nexion

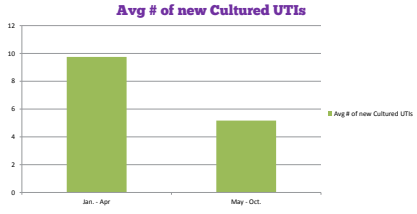
Meadowview Health & Rehab Center

Equipping Clinicians with Advanced Care Options Leads to Reduction in UTIs: Theraworx® Works Wonders

Goal: Meadowview Health and Rehab Center, a Nexion Affiliate and Ventilator Dependent Skilled Nursing Facility recognized a negative trend in # of new Cultured UTIs in the early part of 2016.

Upon the completion of a RCA, it was determined that there was not a significant concern with care or proper pericare. After consulting with the facility support team including its Certified Wound Care Specialist it was determined that Meadowview would trial a new an upcoming product-Theraworx®.

Avg # of new Cultured UTIs



Staff Involved Corporate Clinical Nurse, Physicians, Direct Care Staff, Director of Nursing and Operations.

Resources Theraworx® product and consultants were the necessary additional resources. We also allocated additional time of our Corporate Clinical Nurse and Certified Wound Care Specialist to aide in the process of being responsive to the Theraworx® team.

Challenges Meadowview's operator, Nexion Health, is very committed to a strict process in regards to best practices and care in order to ensure consistency among its affiliates. Reassuring Meadowview that is was "approved" to venture from its formulary was challenging at first but a rewarding and well needed reminder to be flexible when it makes sense.

SUCCESS We met and exceeded our goal to reduce the average # of new cultured UTIs by 50%. We reduced the average # of new cultured UTIs by 53%.

Plan to Sustain Improvement We will not vary from our commitment to the QAPI process. We will ensure that our staff have continued training, adequate supplies and understand the bigger picture of what the ultimate goals are-customer satisfaction through improved quality of care and quality of life with a long term goal of reducing hospital readmissions.

Business Outcomes We care for a very delicate and many times very sick population at our Meadowview facility. Our stakeholders are very pleased with our ability to consistently evaluate ourselves, look for opportunities for improvement especially in clinical outcomes and quality of care. Reducing UTIs impacts our operations through staff efficiencies, stakeholder satisfaction and quality measures. Our willingness to try new and innovative products and taking the steps to validate their impact also makes us a leader in our community.

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Source: theraworx.com

Theraworx® TECHNOLOGY

nexion

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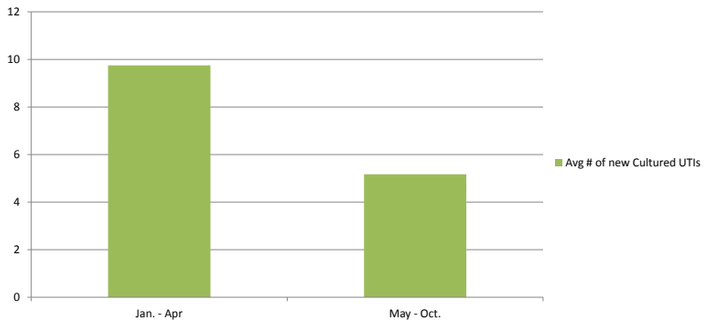

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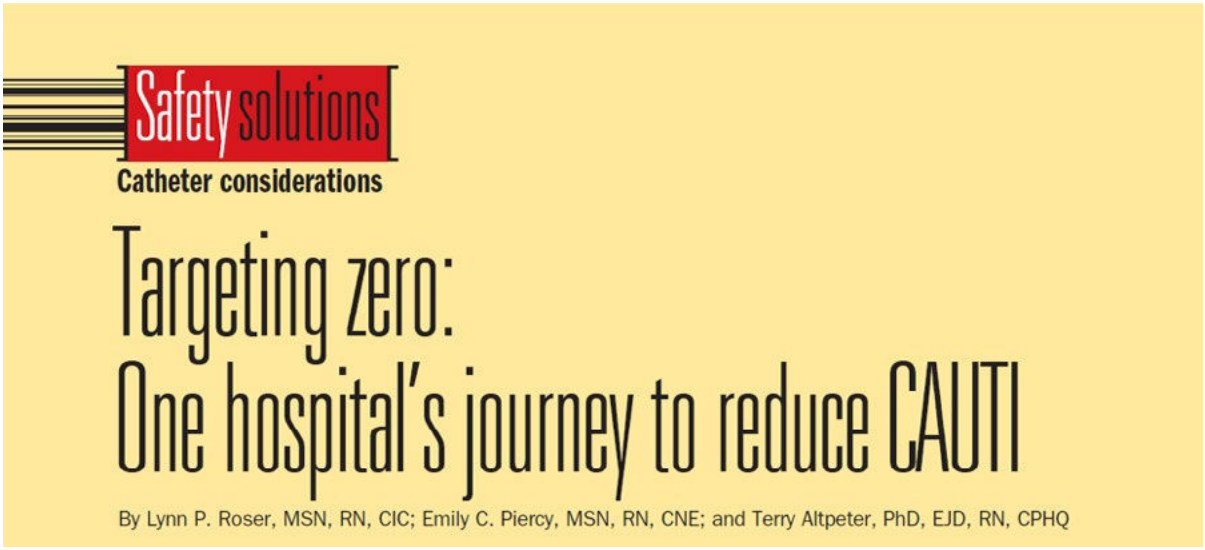
Journal of Nursing Management
18–20
December 2014

Targeting ZERO: One hospital's journey to reduce CAUTI

Baptist Health Lexington, a 383-bed Magnet® recognized community hospital, reduced catheter associated urinary tract infection (CAUTI) rates in all critical care environments by a minimum of 60% during 2013. Given the acuity level of patients in CCUs, the incidence of CAUTIs was higher in that population than those in other areas of the hospital. For this reason, ICU patients were targeted for the implementation of a performance improvement (PI) project targeted to reduce the rate of CAUTIs. The ICU nurses identified an antimicrobial bundle (composed of three cleansing products- Theraworx® Foam, Theraworx® Spray and Theraworx® Impregnated Towels) that works as an effective barrier against a broad array of Gram-positive and negative organisms potentially leading to CAUTI. Data collected from the ICU's revealed further decline in CAUTI over all previous interventions.



Annals of Infectious Disease and Epidemiology-Published: 25 Nov, 2016

Non-Toxic Skin Formulation Promotes Healing of Dermatitis and Skin Injuries That Are Prone To Infection in Long-Term Care Facility Residents

Janalynn Miller, FNP-C, GNP, CWCN-AP1,2* and Joseph F Renzulli1*
1Department of Urology, University Urological Associates, USA
2Extended Care Specialists, Inc

Elderly patients in long-term care facilities (LTCFs) often exhibit skin disorders caused by multiple factors, including aging skin and co-morbidities such as obesity, diabetes, dementia, and urinary and fecal incontinence. Conditions common at LTCFs can also exacerbate skin disorders. Finally, skin conditions such as fungal dermatitis, incontinence-associated dermatitis, moisture-associated skin damage, pressure injuries, and venous ulcers often occur in bodily creases, making it difficult for clinicians to assess the areas, particularly in obese patients. Standard remedies can be ineffective if they congeal in body folds, or aggravate moisture-relateddermatitis and skin injury if they contain a moisture or zinc additive. Cleansing agents used to clean patients with fecal incontinence can dry out the skin, making the patient more infection-prone. If the patient has fungal dermatitis, dryness can impede or prevent resolution. The two cases discussed herein demonstrate these issues and show how a novel skin care formulation used in place of standard approaches addressed the problems. The formulation is intended to restore the skin's normal pH level to support the natural antimicrobial action of the skin's outer layer, maintain the skin's permeability barrier to prevent moisture loss, reduce the bio-burden of potentially infectious skin flora, and moisturize dry skin. In the first case, a Stage 2 pressure injury closed and fungal dermatitis resolved after treatment with the formulation and Diflucan. In the second case, a venous ulcer improved markedly after treatment with the formulation following a year in which standard treatments produced no results.

Sacral Pressure Injury Case #1

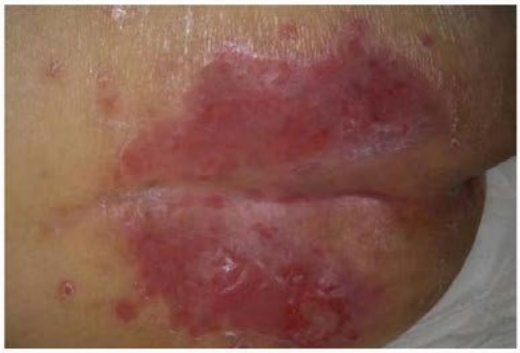


Figure 1: Stage 2 Pressure injury on left buttock and fungal dermatitis on bilateral buttock prior to treatment with skin care formulation and Diflucan. Length=1.8 cm, width=1.8 cm, depth=<0.1 cm.

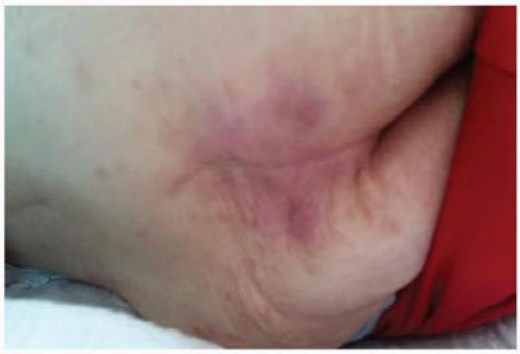


Figure 2: Less than two weeks after treatment with skin formulation began, pressure injury had closed and fungal dermatitis had resolved.

Refractory Venous Ulcer Case #2

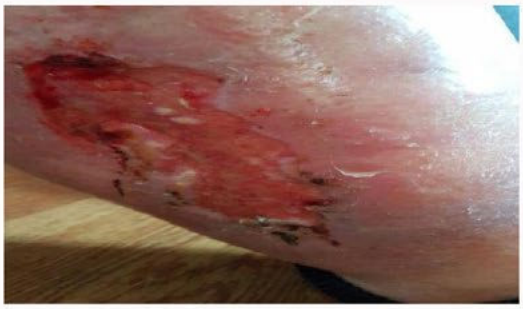


Figure 3: Venous ulcer prior to treatment with skin care formulation. Length = 12 cm, width = 3.5 cm, depth = 0.1 cm, wound bed tissue type = 90 % pink granular with islands of epithelialization and 10 % yellow slough. Wound edges exhibited dried serous drainage.

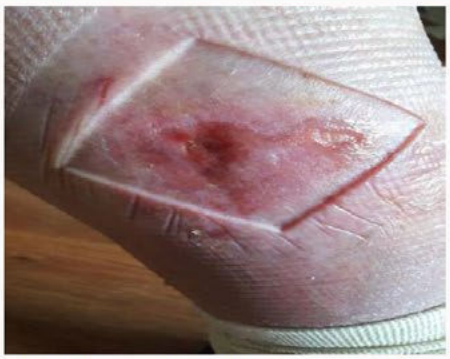


Figure 5: After six months of treatment with the skin care formulation, the wound had improved markedly. It measured approximately 0.1 cm by 0.2 cm with 100% red granular wound bed tissue type.

Annals of Infectious Disease and Epidemiology

Case Report
Published: 25 Nov, 2016

Non-Toxic Skin Formulation Promotes Healing of Dermatitis and Skin Injuries That Are Prone To Infection in Long-Term Care Facility Residents

Janalynn Miller, FNP-C, GNP, CWCN-AP[1,2] and Joseph F Renzulli[1]**

[1]Department of Urology, University Urological Associates, USA

[2]Extended Care Specialists, Inc

Abstract

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Standard remedies can be ineffective if they congeal in body folds, or aggravate moisture-related dermatitis and skin injury if they contain a moisture or zinc additive. Cleansing agents used to clean patients with fecal incontinence can dry out the skin, making the patient more infection-prone. If the patient has fungal dermatitis, dryness can impede or prevent resolution.

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OPEN ACCESS

***Correspondence:**
Joseph F Renzulli, Department of Urology, University Urological Associates,195 Collyer St, Suite 201, Providence, RI 02904, USA, Tel: (401)272-1229;
E-mail: Jrenzulli@lifespan.org

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Miller J, FNP-C, GNP, CWCN-AP, Renzulli JF. Non-Toxic Skin Formulation Promotes Healing of Dermatitis and Skin Injuries That Are Prone To Infection in Long-Term Care Facility Residents. Ann Infect Dis Epidemiol. 2016; 1(2): 1007.

Introduction

Elderly patients who reside in long-term care facilities (LTCFs) often present with a variety of skin disorders as a result of both their aging skin and co-morbidities common in their stage of life. LTCFs serve a population with high proportions of residentswith medical diagnosis such as obesity, diabetes, and dementia [1,2]. In addition, more than half of LTCF residents suffer urinary and fecal incontinence [3]. This becomes problematic when combined with the Co-morbidities and pre-existing dry skin of the elderly resident.

These issues can be amplified by external factors present that some LTCFs. When a facility is understaffed, incontinent residents may lie in their urine or feces for long periods. Patients who are not incontinent but are limited to their bed may not be repositioned per standard of care. Also, patients may be non-adherent to peri-care or repositioning, since it is their right to decline care.

These factors contribute to skin conditions such as fungal dermatitis, incontinence-associated dermatitis, moisture-associated skin damage, pressure injuries and venous ulcers. Those conditions create environments that can lead to infections, making treatment a challenge. They often occur in bodily creases such as skin folds or the patient's perineal area, buttocks, or underarms. Clinicians find it hard to assess these areas, especially if the patient is obese.

Standard remedies can aggravate moisture-related dermatitis and skin injuries. Common topical treatments either have a moisture or a zinc additive that worsens the problem. Fungal powders congeal in the body's folds, making them ineffective.

These factors are illustrated in two cases discussed herein. The lead author is a nurse practitioner

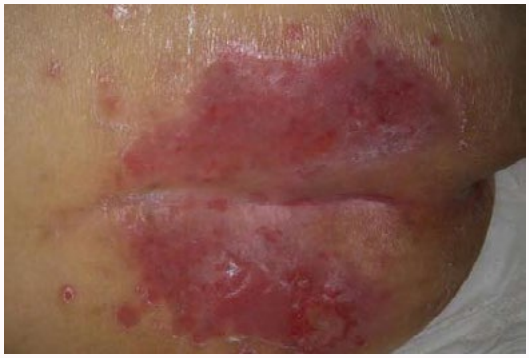

Figure 1: Stage 2 Pressure injury on left buttock and fungal dermatitis on bilateral buttock prior to treatment with skin care formulation and Diflucan. Length=1.8 cm, width=1.8 cm, depth=<0.1 cm.

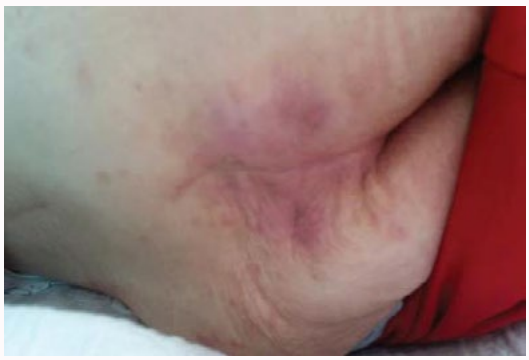

Figure 2: Less than two weeks after treatment with skin formulation began, pressure injury had closed and fungal dermatitis had resolved.

with Wound, Ostomy, and Continence Certification (CWCN-AP) who serves several LTCFs in her area. Residents in these cases had been treated according to customary standards of care, but they did not respond favorably to those approaches. Typical products for cleansing incontinent residents includevarious chemicals and soaps that can dry out patients' skin, leading to a raised skin pH, damage to the stratum corneum, and therefore an increased chance of infection.

The author decided to substitute a novel skin care formulation (Theraworx, Avadim Technologies). The formulation is a non-toxic topical application available as a foam, spray and moisture-impregnated cloth. It is intended to restore the skin's normal low, acidic pH and maintain the skin's permeability barrier, which prevents moisture loss. Normal skin pH supports the natural antimicrobial action of the skin's outer layer (stratum corneum). It reduces the bio-burden of potentially infectious skin flora. The formulation also has moisturizing properties that appear to alleviate incontinence-related skin conditions.

Case Presentation

Case 1

The patient in this case - an 89-year old, 147-pound woman with dementia and diabetes - developed fungal dermatitis and a Stage 2 pressure injury on her buttocks. The skin issues occurred as a downstream effect of prior treatment for an infection on her right heel. A previous caregiver had ordered the antibiotic Keflex (cephalexin) to address the heel infection. The patient had been hospitalized for the infection. At the hospital, she was diagnosed with *Clostridium difficile* (*C. diff*) from the impact of the antibiotic on her intestinal bacteria. The *C. diff* caused frequent, watery diarrhea and weakness, eventually leading to the fungal dermatitis and pressure injury.

After the patient was transferred to an LTCF, she came under the lead author's care. Use of Keflex was discontinued. Also discontinued was use of ineffective barrier creams. To treat the dermatitis and pressure injury, the novel skin formulation as a foam (three pumps of the dispenser) was applied to both buttocks, every four hours due to the severity of both skin issues. Compared to the creams, which create a thick white paste on the skin and interfere with visualization, the novel formulation is clear and allows for easy assessment

Because the patient still had *C. diff*, the author ordered use of the skin care formulation, as foam, for cleansing as well as to promote healing. To assist with the healing of the fungal dermatitis, the author also ordered use of the antifungal agent Diflucan (fluconazole). The dermatitis cleared quickly, less than two weeks after the start of treatment. It is the lead author's previous experience that Diflucan in combination with barrier creams has normally taken much longer to resolve similar cases, compared to the relatively quick improvement this patient experienced.

Pressure injury measurement when treatment began was: Length = 1.8 cm, width = 1.8 cm, depth = <0.1 cm. Less than two weeks after start of treatment, the pressure injury had closed and the fungal dermatitis had resolved.

Case 2

The patient, a 62-year-old, 281-pound male, had a chronic venous ulcer on his right lateral lower leg. He had a variety of co-morbid conditions contributing to or complicating the venous ulcer. He was a Type 2 diabetic with peripheral neuropathy, anoxic encephalopathy, lymphedema, and urinary incontinence. The patient was also bipolar and his behavioral issues played a role in aggravating his wound. Due to his mental state and the neuropathy, he did not always notice when he urinated so urine often ran down his leg and onto the ulcer, placing him at risk of infection for *E. coli* and other bacteria. The patient would also remove his dressings and refused treatments such as compression stockings that could control swelling.

The patient had been seen by a hospital-based wound clinic, which treated the ulcer with silver foam and compression wraps. The patient had also been placed on oral antibiotics periodically over the past year. In the author's opinion, this was a mistaken response by his medical provider to the redness of his affected leg. The condition was interpreted as evidence of cellulitis in a unilateral extremity when in fact it was venous dermatitis, which also causes redness.

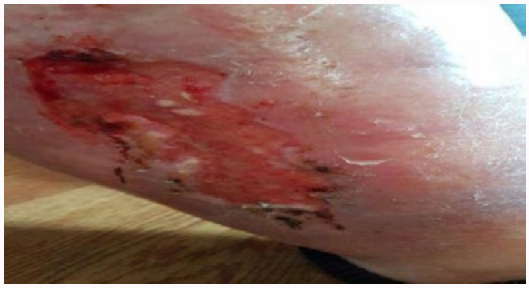

Figure 3: Venous ulcer prior to treatment with skin care formulation. Length = 12 cm, width = 3.5 cm, depth = 0.1 cm, wound bed tissue type = 90 % pink granular with islands of epithelialization and 10 % yellow slough. Wound edges exhibited dried serous drainage.

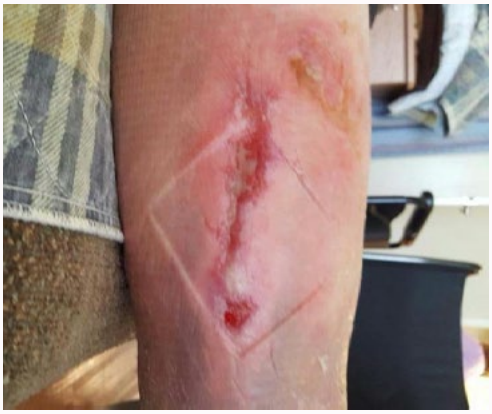

Figure 4: After 14 ½ weeks of treatment with the skin care formulation, the size of the venous ulcer had decreased substantially. Length = 4.5 cm, width = 1.0 cm, depth = <0.1 cm, wound bed tissue type 100% red granular. Treatment regimen continued.

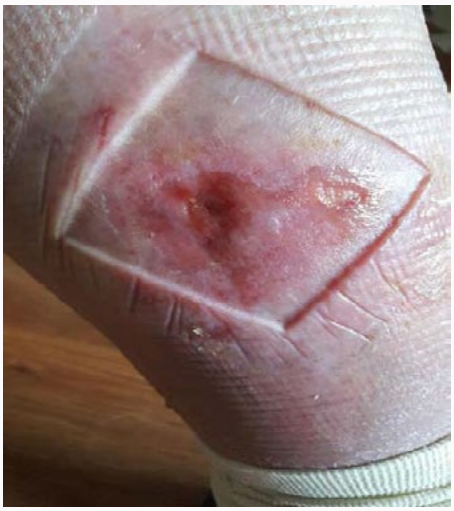

Figure 5: After six months of treatment with the skin care formulation, the wound had improved markedly. It measured approximately 0.1 cm by 0.2 cm with 100% red granular wound bed tissue type.

The lead author took over the case in October 2015. The ulcer had heavy serous drainage. The chronic drainage in combination with the venous dermatitis put the patient at high risk for chronic fungal growth on his leg. The author attempted standard venous ulcer wound treatments such as antimicrobial foam, collagen, and compression but they failed to produce results.

In late April 2016, treatment was switched to the skin formulation in spray form, applying the spray to the ulcer three times a week. The spray was applied to the wound. Then a collagen dressing was placed on the wound bed and covered with bordered foam and a compression bandage.

As of this writing in October 2016, the venous ulcer has improved markedly. It measures approximately 0.1 cm by 0.2 cm with 100% red granular wound bed tissue type. Before treatment with the skin formulation, it was 12.0 cm by 3.5 cm. The wound bed tissue type was 90% pale pink granular tissue and 10 % yellow slough. Prior to use of the new skin formulation, the wound size had remained the same for over a year.

Discussion

Diabetes and obesity along with the circumstantial factors at LTCFs can combine to cause and complicate skin disorders and injuries such as the fungal dermatitis, pressure injury, and chronic venous ulcer described here. If a cleansing agent used to clean a patient with fecal incontinence dries out the skin, the patient will be more prone to infection via bacteria entering any skin cracks that result. If the patient has fungal dermatitis, the dermatitis will be slower to resolve or may not improve at all because of the dryness.

In both of these case reports, we see an example of a non-toxic formulation apparently contributing to treatment success in part because it does not present these intrinsic concerns. It moisturizes instead of drying skin out when used to clean. It can be applied more efficaciously than creams or powders on chronically wet skin.

In addition, the novel formulation offers some positive properties that the products it replaces do not share. In Case 1 involving a very difficult case of fungal dermatitis, it provided a natural antimicrobial effect and a clear view of the wound. In Case 2, the formulation's silver antibacterial ability to reduce the biofilm that had caused the wound to stall (stop healing) - and to also offset the *E.coli* from his urine - showed efficacy above all other standard treatments already tested.

The cases discussed herein suggest that a more natural treatment approach – one that has positive healing properties and avoids counterproductive side effects-- may be appropriate in these clinical settings.

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Novel Skin Care System Helps in Healing Skin Wounds and Other Problematic Skin Disorders in Patients at Long-Term Care Facilities

Patients at long-term care facilities (LTCFs) commonly suffer from skin wounds and other skin disorders such as fungal dermatitis, incontinence-associated dermatitis and other forms of moisture-associated skin damage, pressure ulcers (bedsores), and venous ulcers. These conditions are difficult to heal and can precipitate infections. Causes include urinary/fecal incontinence, obesity, hypothyroidism, and diabetes that, combined with patients' bedridden circumstances, can lead to continual skin maceration and exposure to infectious bacteria. The bodily creases and recesses where these conditions occur—skin folds, perineal area, buttocks, underarms, etc.—are difficult to access and/or treat effectively. Finally, LTCFs are sometimes understaffed, so that patients may lie in their urine for excessive periods—adding to the problem. Traditional treatment options are not always effective. Powders can cake in the presence of moisture. The intrinsic moisture in creams can contribute to the excess wetness in affected areas. The author, a nurse practitioner with a Wound, Ostomy, and Continence Certification (CWCN-AP), sought a more efficacious treatment approach. The nurse practitioner implemented the use of Theraworx® for daily application for patients with moisture associated skin damage with comorbid fungal and bacterial infections and saw significant resolution except for in two patients who died secondary to other disease related morbidities which demonstrates the acuity of the patient population.

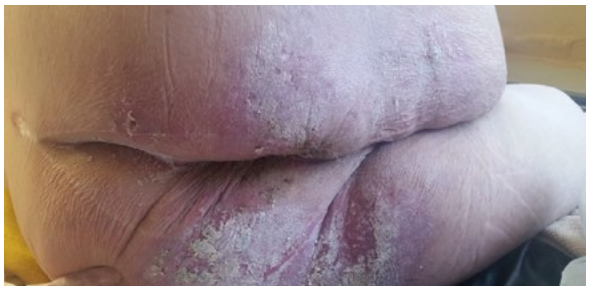
Case 1

Patient: Male, age 72, at LTCF in Fort Wayne, Ind. Bilateral amputee, non-ambulatory, diabetic (insulin dependent), atrial fibrillation (treated with blood thinner), peripheral vascular disease, chronic kidney disease (on dialysis).

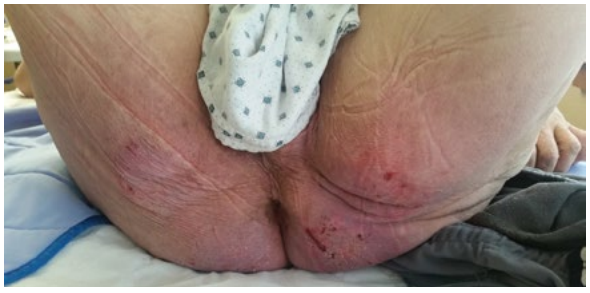
Skin Condition: Chronic dermatitis on posterior of thighs. Patient was complaining of pain and itching. Dermatitis displayed linear excoriation marks from patient scratching himself. Skin exhibited chronic deep purple discoloration.

Treatment: Dermatitis was treated for 2½ years–without success–with multiple barrier creams, wound gels, steroid creams, and compounded creams. All previous treatment approaches were discontinued and author began treating dermatitis with skin care systems in foam form every shift and at every incontinent episode.

Results: By three weeks into treatment regimen with skin care system (foam), purple discoloration had decreased and excoriated areas were resolving. After five weeks of treatment, discoloration had disappeared, excoriation was minimal, and patient had stopped complaining of pain and itching. Regimen continues, with progress maintained. Writing in 2016.



Chronic dermatitis before treatment with skin care system. Chronic deep purple discoloration, patient complaining of pain and itching, linear excoriation marks from patient scratching himself.



Progress has been maintained through three months of treatment with skin care system so regimen continues.

Novel Skin Care System Helps in Healing Skin Wounds and Other Problematic Skin Disorders in Patients at Long-Term Care Facilities

Janalynn Miller, FNP-C, GNP, CWCN-AP
Extended Care Specialists, Inc.
Fort Wayne, Indiana

As presented at:
WOW 2016 "Wild on Wounds" Conference
August 31–September 3, 2016
Las Vegas, Nevada

Statement of Clinical Problem

Patients at long-term care facilities (LTCFs) commonly suffer from skin wounds and other skin disorders such as fungal dermatitis, incontinence-associated dermatitis and other forms of moisture-associated skin damage, pressure ulcers (bedsores), and venous ulcers. These conditions are difficult to heal and can precipitate infections. Causes include urinary/fecal incontinence, obesity, hypothyroidism, and diabetes that, combined with patients' bedridden circumstances, can lead to continual skin maceration and exposure to infectious bacteria.

The bodily creases and recesses where these conditions occur—skin folds, perineal area, buttocks, underarms, etc.—are difficult to access and/or treat effectively. Finally, LTCFs are sometimes understaffed, so that patients may lie in their urine for excessive periods—adding to the problem.

Traditional treatment options are not always effective. Powders can cake in the presence of moisture. The intrinsic moisture in creams can contribute to the excess wetness in affected areas. The author, a nurse practitioner with a Wound, Ostomy, and Continence Certification (CWCN-AP), sought a more efficacious treatment approach.

Description of Clinical Treatment Approach

From March 2016 to the present, the author has treated these skin issues with a novel skin care system (Theraworx). The system, which includes colloidal silver (a natural antibiotic), is designed to help maintain low skin pH, thereby supporting skin cohesion and the natural antimicrobial action of the skin's outer layer (the stratum corneum). These effects help protect the skin from breakdown, disease and infection. The system is available as spray, foam and impregnated cloth wipe and does not cake like powders. Unlike creams, it adds just enough moisture to prevent dryness.

Patient Outcomes

The poster author has to date treated 10 patients with the novel formulation. All the patients had especially challenging conditions or circumstances and were not responding to traditional treatment methods. The skin condition of eight of the patients has markedly improved. Two patients died due to their debilitated state before the treatment's efficacy could be assessed.

Case Summaries

Here are three case summaries involving successful treatment with the skin care system:

Case 1

Patient: Male, age 72, at LTCF in Fort Wayne, Ind. Bilateral amputee, non-ambulatory, diabetic (insulin dependent), atrial fibrillation (treated with blood thinner), peripheral vascular disease, chronic kidney disease (on dialysis).

Skin Condition: Chronic dermatitis on posterior of thighs. Patient was complaining of pain and itching. Dermatitis displayed linear excoriation marks from patient scratching himself. Skin exhibited chronic deep purple discoloration.

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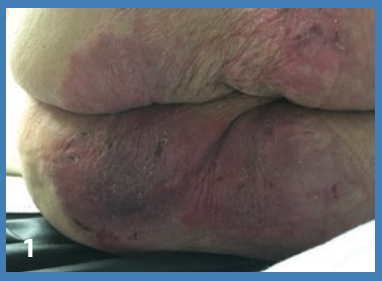
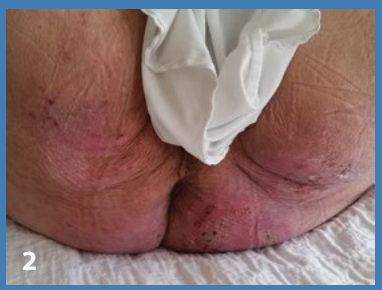


Chronic dermatitis before treatment with skin care system. Chronic deep purple discoloration, patient complaining of pain and itching, linear excoriation marks from patient scratching himself.



Progress has been maintained through three months of treatment with skin care system so regimen continues.

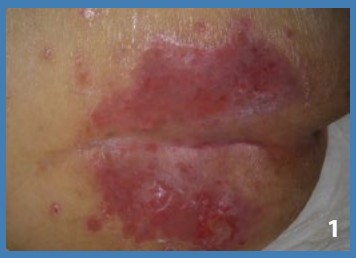
Case 2

Patient: Female, age 89, 138 lbs. at LCTF in Fort Wayne, Ind. with diabetes (130-200 labile due to inconsistent meal intake) and dementia (in locked memory unit)

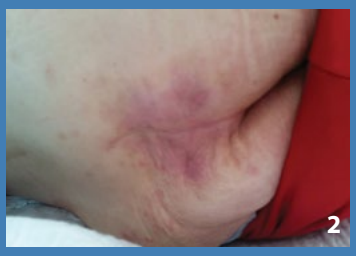
Wound: Stage 2 pressure ulcer on left buttock. Also fungal dermatitis on bilateral buttock including diffuse erythemic macular rash with satellite lesions (not measurable).

Treatment: Prior treatment with a variety of creams had been unsuccessful and was discontinued. An oral antifungal agent was ordered to help treat the dermatitis. To treat both the dermatitis and pressure ulcer, the skin care system (Theraworx foam) was applied to both buttocks every four hours due to severity of the dermatitis.

Results: Pressure ulcer measurement when treatment began was: Length = 1.8 cm, width = 1.8 cm, depth = <0.1 cm. Less than two weeks after start of treatment, the pressure ulcer had closed and the fungal dermatitis had resolved.



Stage 2 pressure ulcer on left buttock and fungal dermatitis on bilateral buttock before treatment. Length = 1.8 cm, width = 1.8 cm, depth = <0.1 cm.



Less than two weeks after start of treatment, pressure ulcer had closed and fungal dermatitis had resolved.

Case 3

Patient: Male, 62, 281 lbs. at LCTF in Fort Wayne, Ind. with Type 2 diabetes (treated with metformin), peripheral neuropathy, anoxic encephalopathy, lymphedema, bipolar. Patient is incontinent of urine; urine runs down his leg onto his wound. Does not inform staff when he has urinated on himself, removes his dressings, and refuses treatments such as compression stockings.

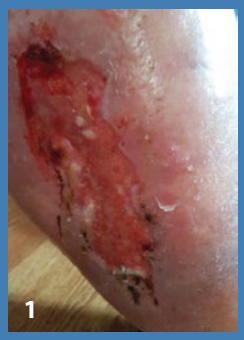
Wound: Chronic venous ulcer on right lateral lower leg.

Treatment: Wound was treated by wound clinic's personnel with silver foam and compression wraps for > 1 year without success. Beginning October 2015, author then treated the patient for approximately 6 ½ months with an antimicrobial foam dressing wrapped with gauze and elastic bandages. A collagen dressing was also attempted. Neither treatment was successful.

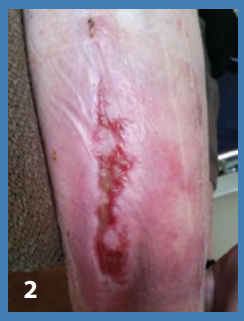
In late April 2016, author began treating the ulcer with the skin care system in spray form three times a week. Spray was allowed to dry, after which the wound was covered with a collagen dressing with bordered foam and a compression bandage.

Results: Wound measurement when Theraworx treatment began was: Length = 12 cm, width = 3.5 cm, depth = 0.1 cm. Wound bed's tissue type was 90 % pink granular with islands of epithelialization and 10 % yellow slough. Edges exhibited dried serous drainage. Periwound displayed venous stasis dermatitis.

After approximately 14 ½ weeks of the Theraworx treatment regimen, the wound size had decreased substantially: Length = 4.5 cm, width = 1.0 cm, depth = <0.1 cm. Wound bed tissue type was 100% red granular and the venous stasis dermatitis was resolved. Treatment with Theraworx continues as of this writing in August 2016.



Venous ulcer before treatment with Theraworx.



Wound size decreased substantially after approximately 14 ½ weeks of treatment with skin care system. Venous stasis dermatitis resolved. Treatment with skin care system continued.

Conclusions

While the initial sample size is very small, the system may be useful for a large proportion of patients in LTCFs, including patients for whom there are no other effective treatment solutions. Its properties enable wounds to begin healing, both mitigating and preventing infection. In addition to decreasing the size of skin wounds/disorders, it increases patient comfort due to the system's ability to increase blood flow to the area. The system may also have utility to prevent moisture-associated skin damage, a common problem for patients in LTCFs.

This approach also has potential cost advantages. It replaces multiple products, doesn't require prescription, and can be applied by a certified nursing assistant. This system should be further investigated with large patient populations at multiple facilities. If proven effective, it could have wide application for the aging patient population.

Email: jmiller@ecshealthcare.com

Acknowledgments: The maker of the skin care system provided assistance in poster preparation and meeting attendance. As the poster author, I am responsible for and prepared the data and text.

Independent Laboratory Study: ATS Labs Protocol # SJC01051614.EXVO

Ex-Vivo Antibacterial Evaluation of Topical Products Using a Vitro-Skin® Model- Vancomycin Resistant Enterococcus faeca/is - VRE (ATCC 51575) Matthew Sathe, B.S. Senior Microbiologist

Background

Enterococci are an emerging pathogen in hospitalized patients [1]. These pathogens ubiquitously occur in the hospital environment and show a high tenacity on inanimate surfaces [2,3,4]. As a result, enterococcal infections emerge with a rising frequency. Additionally, enterococci have the ability of acquiring resistances to multiple antimicrobial agents and the capacity to transfer resistances to other pathogens via mobile genetic elements [5,6,7]. For this reason the prevalence of vancomycin resistant enterococci (VRE) has increased intensively [1]. Vancomycin resistance is associated with enhanced mortality, e.g. among patients with enterococcal blood stream infections [8]. Within hospital settings prevention of VRE transmission is therefore a major objective.

Method

A film of the test organism dried onto a 1" x 1" demarcated area of 1.5" x 1.5" rehydrated Vitro-Skin® carriers was treated by wiping each carrier over and back twice with a saturated towelette for a total of 4 passes. Following treatment and exposure, each carrier was neutralized and assayed for survivors. Appropriate culture purity, neutralizer sterility, carrier sterility, population and neutralization confirmation controls were performed. Percent and Log10 reductions were determined for the test based on the test population control results.

Results

Theraworx Technology Lot 141291, ready to use, demonstrated a >99.99% (>4.80 log10) reduction of Vancomycin Resistant Enterococcus faecalis - VRE (ATCC 51575) following a 15-minute exposure time when tested at ambient temperature (20.90°C).

TABLE 3: POPULATION CONTROL RESULTS

Test Organism	Carrier #	CFU/Carrier	Log_{10} of CFU/Carrier	Average Log_{10}	Geometric Mean (CFU/Carrier)
Vancomycin Resistant *Enterococcus faecalis* - VRE (ATCC 51575)	1	1.3×10^6	6.11	6.10	1.26×10^6
	2	1.2×10^6	6.08		

CFU = Colony Forming Unit

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Executive Summary

Ebola Virus disease has been rapidly spreading through Western Africa since 2013. Several cases have been exported to industrialized nations, but person-to-person spread outside of Western Africa has been limited. The extreme contagiousness of the virus, coupled with the high mortality related to infection increases the need for novel interventions for preventing the spread of this virus.

Transmitted through blood and body fluids, Ebola Virus transmission can be limited through prevention of contact with these fluids. The difference between the transmission of Ebola Virus and other bloodborne pathogens such as HIV and Hepatitis B or C, lies in the very low infectious dose of this virus. The infectious dose is the number of viral particles it takes to cause an infection in a host. For Ebola Virus, the infectious dose is one virus. Where millions of virus are present in even small amounts of body fluids, it is clear that transmission prevention can be very difficult.

Due to the transmission route of this virus, one possible intervention for prevention of transmission may be skin antisepsis - killing of the virus on the skin in order to limit contact. Due to this possibility, Avadim Technologies collaborated with the Texas Biomedical Research Institute to study the efficacy of Theraworx, a novel silver-based skin antiseptic, against Ebola Virus on simulated human skin.

The research study was conducted as follows: First, two human skin analogs were placed in a high containment (Biosafety Level 4) laboratory at Texas Biomedical Research Institute. A standardized amount of Ebola Virus was placed on each skin surface. After 5 minutes of drying time, one of the areas was sprayed with a salt water solution, while the other area was sprayed with Theraworx. The salt water solution served as a control, as the salt water has no killing activity against the Ebola Virus. After 5 minutes, the skin surfaces were swabbed and the amount of Ebola Virus left on each skin surface was defined in terms of plaque forming units (PFU).

The skin surface sprayed with the saline solution had 200,000 PFUs left, while the Theraworx treated surface had 18,000 PFUs left. This is a 91% reduction in Ebola Virus on the human skin analog using Theraworx compared to no active treatment.

These results suggest that Theraworx has the ability to kill the Ebola Virus rapidly on human skin. It is possible that using this product on an infected person, or even on a caregiver may help to prevent the transmission of this deadly virus.

Appendix

Avadim HEALTH

Discovering
New Ways to Care

I am delighted to enthusiastically endorse the unique technology of Theraworx, from Avadim Technologies, Inc. . Our laboratory at the University of California San Francisco and the San Francisco Veterans Administration Hospital is actively studying the origins, functions and clinical implications of the skin's 'acid mantle'. Long thought to originate from exogenous sebaceous gland-derived free fatty acids, we showed that four endogenous mechanisms contribute to the strikingly low, pH of normal stratum corneum (the degradation of phospholipids to free fatty acids; the deimination of filaggrin-derived amino acids into polycarboxylic acids; the sodium-proton antiporter type 1; and melanin granule extrusion). Because of differences in their subcellular location, each of these mechanisms regulate different critical functions of the skin. The key functions of the cutaneous acid mantle include: 1) epidermal permeability barrier homeostasis; 2) stratum corneum integrity and cohesion; 3) antimicrobial defense; and 4) antiflammatory activity. Please find attached a recent review article which briefly summarizes our research findings and its clinical implications. Note: this review article follow in the reference documents, no. , pp)

This spectrum of activities in normal skin suggests broad applications for pH-related technology in clinical arenas ranging from infection control to prevention and treatment of inflamed skin. These benefits form the basis for Avadim's unique, pH-dependent technology. We have evaluated the impact of Avadim's Theraworx technology in normal human and hairless mouse skin, and found that topical applications indeed reduces the surface pH of the skin significantly; i.e., from an average of 5.5 to 4.5-5 (note that pH is an exponential function, and this decline translates into a 5-10-fold increase in the proton concentration within the stratum corneum. We have also compared the Theraworx product to Hibiclens in normal hairless mouse skin, and found that the latter does not achieve a comparable reduction in pH, and that it was more drying than the former.

These findings imply that the pH-dependent technology embodied in Theraworx products should provide superior benefits for antimicrobial defense (note that pathogenic flora, like *S. aureus* and *S. pyogenes* grow avidly at a high pH, while the cutaneous normal flora prefer a low pH); enhanced permeability bsarrier function; optimal cutaneous integrity and cohesion; and decreased propensity to develop inflammation. Based upon these studies, I believe that Avadim's novel pH-dependent technology, as embodied in Theraworx formulations, is very worthy of recognition in the form of a Breakthrough Technology Award. Please let me know, if you would like further information about our work in the pH arena, or our pre-clinical studies with the Theraworx formulations.

Sincerely,

Peter M. Elias, MD
VA Medical Center/UCSF
4150 Clement Street
Dermatology MS 190
San Francisco, CA 94121
ph: 415-750-2092

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REVIEW

The skin barrier as an innate immune element

Peter M. Elias

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Abstract Since life in a terrestrial environment threatens mammals continuously with desiccation, the structural, cellular, biochemical, and regulatory mechanisms that sustain permeability barrier homeostasis have justifiably comprised a major thrust of prior and recent research on epidermal barrier function. Yet, the epidermis mediates a broad set of protective 'barrier' functions that includes defense against pathogen challenges. Permeability and antimicrobial function are both co-regulated and interdependent, overlapping through the dual activities of their lipid/protein constituents. Most of the defensive (barrier) functions of the epidermis localize to the stratum corneum (SC), which limits pathogen colonization through its low water content, acidic pH, resident (normal) microflora, and surface-deposited antimicrobial lipids (1° free fatty acid). These various barrier functions are largely mediated by either the corneocyte or the extracellular matrix, and it is both the localization and the organization of secreted hydrophobic lipids into characteristic lamellar bilayers that is critical not only for permeability barrier function, but also for antimicrobial function through its contribution to the maintenance of SC integrity. Low constitutive levels of antimicrobial peptides under basal conditions emphasize the key role of epithelial structure in antimicrobial defense. But antimicrobial peptide synthesis and delivery to the SC interstices accelerates after external insults to the barrier.

P. M. Elias
Department of Dermatology,
University of California San Francisco Medical Center,
San Francisco, CA, USA

P. M. Elias (✉)
Dermatology Service (190), VA Medical Center,
4510 Clement Street,
San Francisco, CA 94121, USA
e-mail: eliasp@derm.ucsf.edu

Epidermis mediates multiple protective functions

Because life in a terrestrial environment threatens mammals continuously with desiccation, the structural, cellular, biochemical, and regulatory mechanisms that sustain permeability barrier homeostasis have justifiably comprised a major thrust of prior and recent research on epidermal barrier function [28, 32]. Yet, the epidermis mediates a broad set of protective (barrier) functions against; for example, microbial pathogen challenges, oxidant stress, including ultraviolet light, foreign chemical exclusion, mechanical insults, frictional resistance, and it serves as a distal outpost of the cutaneous inflammatory interface (Table 1).

It is now generally accepted that most of the defensive (barrier) functions of the epidermis localize to the stratum corneum (SC) [28]. These various barrier functions are largely mediated by either the corneocyte or the extracellular matrix, and they further localize to specific subcompartments in each (e.g., corneocyte envelope vs cytosol; Table 1). It is both the localization and the organization of the secreted hydrophobic lipids into characteristic lamellar bilayers that is critical not only for permeability barrier function but also for several other defensive functions through its contribution to the maintenance of SC integrity [30].

A key concept to emerge in recent years emphasizes the SC not as a dead tissue, but rather as possessing multiple types of catalytic (primarily catabolic) activity in both the cytosolic and membrane/extracellular compartments [25].

Table 1 Multiple protective functions of mammalian stratum corneum

Function	Principal compartment	Structural basis	Chemical basis	Regulatory signals (receptors)
Permeability[a,b]	Extracellular matrix	Lamellar bilayers	Ceramides, cholesterol, nonessential FA in proper ratio	IL-1α, Ca^{++}, nuclear hormone receptors, SP activation (PAR2)
Antimicrobial[a,b]	Extracellular matrix	Lamellar bilayers	Antimicrobial peptides, FFA, Sph	1,25 (OH)2D3; IL-1α
Antioxidant[b]	Extracellular matrix	Lamellar bilayers	Chol., FFA; secreted vit. E, redox gradient	?
Cohesion (integrity) →desquamation[a,b]	Extracellular matrix	Corneodesmosomes (CD)	Intercellular DSG1/DSC1 homodimers	pH, Ca^{++} (TPRV)
Mechanical/rheological[b]	Corneocyte	Cornified envelope; keratin filaments	γ-Glutamyl isopeptide bonds	Ca^{++}, CholSO4, nuclear hormone receptors
Chemical (antigen exclusion)[a,b]	Extracellular matrix	Extracellular lacunae	Hydrophilic products of CD	?
Psychosensory interface[b]	Extracellular matrix	Lamellar bilayers	Barrier lipids	Glucocorticoids, pH, heat osmotic Δs (TPRV1-3)
Hydration[b]	Corneocyte	Cytosol	Filaggrin proteolytic products; glycerol	Δs in relative humidity (TPRV4)
Electromagnetic radiation	Corneocyte	Cytosol	Cis-urocanic acid (histidase activity)	Δs in relative humidity
Initiation of inflammation (1° cytokine activation)[a,b]	Corneocyte	Cytosol	Proteolytic activation of pro-IL-1α/β	pH (TPRV1), SP activation

[a] Regulated by stratum corneum pH
[b] Abnormal in atopic dermatitis

Much of this activity either (1) generates the various 'barriers' described above, (2) regulates desquamation, (3) results in the generation of endogenous UV filters and osmotically active ingredients, and (4) results in the activation of primary cytokines.

Integrative aspects of various epidermal barriers

While each protective function of the skin can be considered as a discrete activity, these activities are often linked and even co-regulated [29]. For example, one type of external stressor, an increase in SC pH, can impact several defensive functions of the SC (Table 2). While an acidic pH is hostile to bacterial, yeast, and dermatophytic pathogens, elevations in pH instead support the growth of *Staphylococcus aureus*, *S. pyogenes*, and other pathogenic species [52]. In contrast, the negative impact of an increased pH on permeability barrier homeostasis, SC integrity/cohesion, and initiation of inflammation results from the activation of serine proteases, followed by signalling of diverse downstream mechanisms [39, 40].

A second type of stressor, which displays negative consequences for several epidermal functions, is psychological stress (PS; Table 2). PS, through an increase in endogenous glucocorticoids (GC), compromises permeability barrier homeostasis, SC integrity/cohesion [20, 50], and antimicrobial defense [2]. A mechanism that can largely account for these alterations comprises GC-mediated inhibition of epidermal lipid synthesis, resulting in a decline in lamellar body (LB) production [16, 50]. Ultimately, less LB contents get delivered to the SC interstices, protein into LB requires prior or concurrent lipid sequestration [71], antimicrobial peptide (AMP) cargo are not delivered to nascent LB [2]. For example, human β-defensin 2 (hBD2) and its murine homologue, mBD3, as well as the carboxyterminal product of human cathelicidin, LL-37, and its murine homologue, cathelicidin-related antimicrobial peptide (CRAMP), are first packaged within, and then secreted from LB [2, 10, 68]. Further, the negative effects of PS on the SC integrity/cohesion are also linked to the GC-induced lipid synthesis/secretory abnormality, although the responsible pathophysiologic mechanisms have not yet been elucidated. The proof of the link between decreased lipid generation and these three functional abnormalities could be demonstrated by the ability of topical physiologic lipid replenishment to largely or completely normalize these functions in the face of ongoing PS/GC [2, 14, 50].

Another type of functional interaction occurs when perturbations in one key function of the SC alter other defensive functions (Table 2), demonstrating that they are clearly-intertwined. For example, changes in SC hydration, resulting from either prolonged exposure to extremes of

Table 2 Linkage between multiple barrier functions

A. SINGLE STRESSOR CAN ALTER MULTIPLE FUNCTIONS

1) ↑ Psychological stress → ↑ Endogenous steroids →	↓ Permeability barrier ↓ SC Integrity/Cohesion ↓ Antimicrobial barrier
2) ↑ pH → ↑ Serine protease activity →	↓ Permeability barrier ↓ SC Integrity/Cohesion ↑ Cytokine activation ↓ Antimicrobial barrier by allowing pathogen colonization and ↑ Degradation of antimicrobial peptides
3) ↑ or ↓ SC hydration →	↑ or ↓ Permeability and antimicrobial barriers in parallel

B. ALTERATIONS IN 1 FUNCTION CAN ALTER ANOTHER FUNCTION

1) ↓ Mechanical strength → ↓ permeability barrier

2) Permeability barrier insults → ↑ antimicrobial and permeability barriers;
↓ resistance to percutaneous chemical/antigen/pathogen ingress
↑ inflammation

external humidity, or due to sudden shifts in extremes of humidity, produce significant alterations in permeability barrier function (Fig. 1). A further example pertinent to this review would be that barrier perturbations sufficient to accelerate transcutaneous water loss simultaneously allow ingress of xenobiotes [80], and likely antigens and pathogenic microorganisms, as well (Table 2). Moreover, while external insults to the permeability barrier can provoke inflammation by initiating the 'cytokine cascade,' some of these signalling molecules also signal certain physiologic production by epidermal keratinocytes (see below). The initiation of IL-1α and IL-1β activation at the level of the SC appears to occur through a pH-induced increase in the activity of at least one serine protease that is resident primarily within the SC (kallikrein 7 or SC chymotryptic enzyme) [67]. A further example of one function impacting another that is also relevant for antimicrobial defense, comprises the permeability barrier abnormalities that result from structural defects of the corneocyte [27, 74]. As a result of an inadequate scaffold, the organization of extracellular lipids into lamellar bilayers is disturbed. Indeed, an intact lamellar membrane system that completely engorges the SC extracellular domains is critical not only for permeability barrier homeostasis but also for antimicrobial defense (see below).

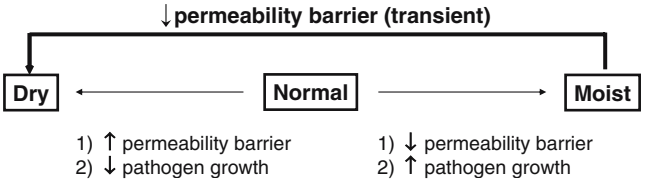

Fig. 1 Changes in external humidity alter permeability and antimicrobial barriers

Co-regulation of permeability and antimicrobial barriers

Of the several important protective functions of the epidermis that are linked and co-regulated, perhaps most integrated are antimicrobial defense and the permeability barrier through the multiple mechanisms listed in Table 3. With the notable exception of dermatophytes and *Candida albicans* that elaborate proteases that allow these pathogens to enter corneocytes [65, 72, 82], ultrastructural studies suggest that the extracellular matrix is the pathway through which bacterial pathogens, such as *S. aureus*, breach the SC [64] (Fig. 2). Therefore, the lamellar bilayers serve as an important physical as well as a chemical barrier. As noted above, epidermal LB deliver a family of lipids that form the permeability barrier and certain of these lipids, most notably free fatty acids (FFA) and sphingosine, that themselves exhibit potent activity against a variety of bacterial, yeast, and viral pathogens [9, 64, 85].

In addition, LBs deliver several non-lipid proteins that display AMP activity (Tables 3 and 4), including LL-37

Table 3 How permeability and antimicrobial barriers are linked

1) Co-localization in extracellular (mortar) domains
2) Pathogens attempt to invade through SC extracellular domains
3) Some permeability barrier lipids (e.g., free fatty acids and sphingosine) exhibit potent antimicrobial activity
4) Antimicrobial peptides (AMP) localize to lamellar bodies (along with lipids) and are co-delivered to SC extracellular domains
5) AMP expression and secretion of AMP both accelerate after permeability barrier disruption, paralleling increased lipid synthesis
6) At least one AMP (LL-37) is required for permeability barrier homeostasis

[10] and hBD2 [68] to the SC interstices (see below for further details).

The close relationship between permeability and antimicrobial function is most convincingly demonstrated by the recent demonstration that AMP expression increases after disruption of the permeability barrier [1]. Although this relationship is readily explained by the fact that barrier disruption removes extracellular AMP along with the lipids required for permeability barrier maintenance [29], the relationship between these two functions is more complex than simply a response to the co-removal of extracellular lipids and peptides. In fact, AMP appear to be important for permeability barrier homeostasis because transgenic mice that fail to express CRAMP, the murine homologue of LL-37, exhibit not only increased cutaneous streptococcal infections [66], but also a significant permeability barrier abnormality [1]. Ultrastructural studies suggest further that LL-37 (and perhaps other AMP) contribute to the supramolecular organization of the extracellular matrix into lamellar domains (op cit), perhaps through the requirement of relatively hydrophilic molecules for lamellar membrane organization. Thus, the AMP have a third set of functions in the epidermis that extends beyond their well-established dual roles as antimicrobial and signaling molecules; i.e., they are structural constituents of the epidermal permeability barrier.

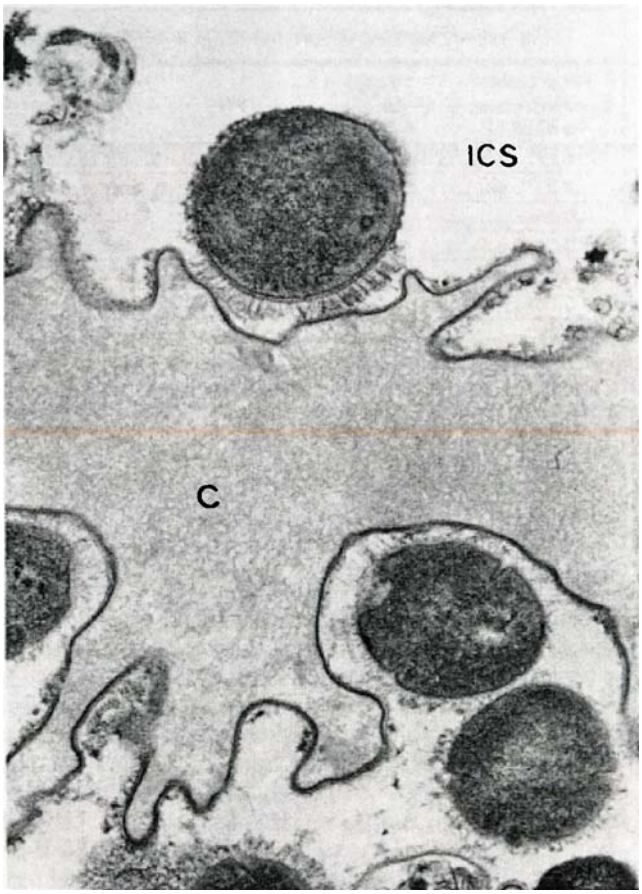

Fig. 2 Transmission electron microscopic study of biopsy specimen from culture-positive *Staphylococcus aureus* skin infection. Gram-positive cocci may be seen intercalating between corneocytes (C) within the stratum corneum, i.e., via intercellular spaces (ICS) occupied by the stratum corneum lipids (see text and [15, 16, 23]). Note that corneocytes do not appear damaged and are not traversed by bacteria (42,000×) (reprinted from [64], with permission)

The epidermal surface as an antimicrobial shield

Since AMP are expressed at only low levels under basal conditions, the importance of epithelial integrity in the protection against pathogen assault cannot be overemphasized. Intact SC deploys not only lipids with substantial antimicrobial activity, but also corneocyte 'bricks' with their chemically resistant cornified envelopes, as well as complex interdigitations with neighboring corneocytes, forming a formidable physical barrier to pathogen ingress (Table 5). In addition, the low water content and highly acidic surface pH (≈5.0) of non-occluded (non-intertriginous) SC presents a hostile milieu for common pathogens, such as *S. aureus* [3]. Yet, the acidic surface pH of normal SC provides ideal growth conditions for the normal cutaneous microflora, including both corynebacteriae and micrococceae, such as *S. epidermidis* [51, 52]. Recent studies have elucidated the origin of the SC's acidic pH, demonstrating critical roles for three endogenous mechanisms, including the sodium–proton antiporter, NHE1, phospholipase A_2-catalyzed generation of bulk FFA from LB-derived phospholipids, and a further likely contribution from filaggrin-derived amino acids, which after deimination, generate a variety of acidic metabolites, such as urocanic acid and pyrrolidone carboxylic acid (see below).

Table 4 Spectrum of stratum corneum antimicrobial peptides

Chemicals	Killing mechanism	Organism class			
		Gram+ Bacteria	Gram− Bacteria	Yeast	Viruses
Lipids					
(FFA, Sph)	? Detergent activity	+	+	+	(+ FFA)
Proteins					
LL-37	Pore formation	+	+	+	+
hBD2	Pore formation	−	+	−	?
Psoriasin	Trace element (Zn^{++}, Cu^{++}) sequestration	Minimal	+ (*E. coli*)		?
RNase7	Unknown	+	+ (*S. fecalis*)	+	?
Dermcidin	Unknown	+	+	+	?

1) Defensive characteristics of SC structural organization: Mammalian epidermal differentiation culminates in the formation of the anucleate layer, the SC, comprised of interlocking, vertical columns of 10–20 polyhedral corneocytes that interdigitate with several comparable neighboring stacks [18, 55, 63]. In frozen sections stained with fluorescent or non-fluorescent lipophilic reagents, individual corneocytes appear to be embedded within a highly hydrophobic lipid-enriched matrix, which on freeze–fractive replication, or after post-fixation with the highly reactive electron-dense reagent, ruthenium tetroxide, appears organized into a series of broad lamellar membranes of unique subcellular organization [22, 46]. In the lower SC, these extracellular membranes are bridged at regular intervals by specialized junctions, corneodesmosomes (CD) [42], containing the e-cadherins, desmoglein 1, and desmocollin 1, and an external coating of a novel, secreted protein, corneodesmosin [42, 77]. CD progressively disintegrate into lenticular lacunae as corneocytes migrate apically toward the cell surface [62]. While under low ambient humidities, these lacunae remain as isolated foci; with hydration, the lacunae expand until they interconnect, forming a potential 'pore pathway' across the SC [62] (Fig. 3). Although ultrastructural studies have shown that pathogens, such as *S. aureus*, bypass corneocytes as they attempt to penetrate the SC [64] (Fig. 2), whether they selectively traverse the interconnected pore pathway that is created in hydrated SC is not yet known. But the expansile nature of the lacunar network under hydrated/superhydrated conditions could provide a structural mechanism that bypasses the lamellar bilayers, thereby, facilitating pathogen invasion.

The two-compartment organization of the SC, i.e., of corneocytes embedded in a lipid-enriched extracellular matrix, has been analogized to a brick wall [23]. While corneocytes result from a specialized form of terminal differentiation 'physiologic apoptosis,' the matrix lipids and several extracellular structural, antimicrobial (see below) and enzymatic proteins are delivered to the SC interstices through epidermal LB secretion (Fig. 3). LB are relatively small (1/3–1/2 μm) ovoid organelles that are produced in abundance in the outer nucleated layers of the epidermis and secreted by compound exocytosis (i.e., end-to-end and side-to-side fusion) at the stratum granulosum (SG)–SC interface [26]. Within minutes of perturbation of the SC, much of the preformed pool of LB is deposited into the SG–SC interface [26], followed by amplified production and further secretion of nascent LB [61]. The net result is rapid on-going delivery of the full complement of LB contents to the SC interface as part of a rapid multi-pronged metabolic response to barrier insults (reviewed in Feingold [32]).

Table 5 Multiple levels of cutaneous antimicrobial defense

Levels	Activity
1) Epidermal (SC) surface	Microflora and products; ↓ pH; desiccation; sweat/sebum products (e.g., LL-37, dermcidin, RNase 7); SC and sebaceous lipids (e.g., free fatty acids); protease inhibitors
2) Epidermis →SC	Secreted and inducible antimicrobial proteins (LL-37, hBD2; psoriasin, RNase 7)
3) Epidermis+dendritic cells	Keratinocyte phagocytic activity; toll-like receptors (TLRs 2, 4, 7); cytokines (e.g., IL-18, IFNγ); chemokines
4) Mast cells	LL-37
5) Neutrophils	Lysozyme, α-defensins (hNP1-3)
6) Circulating T-cells (adaptive immunity)	TH1 induction

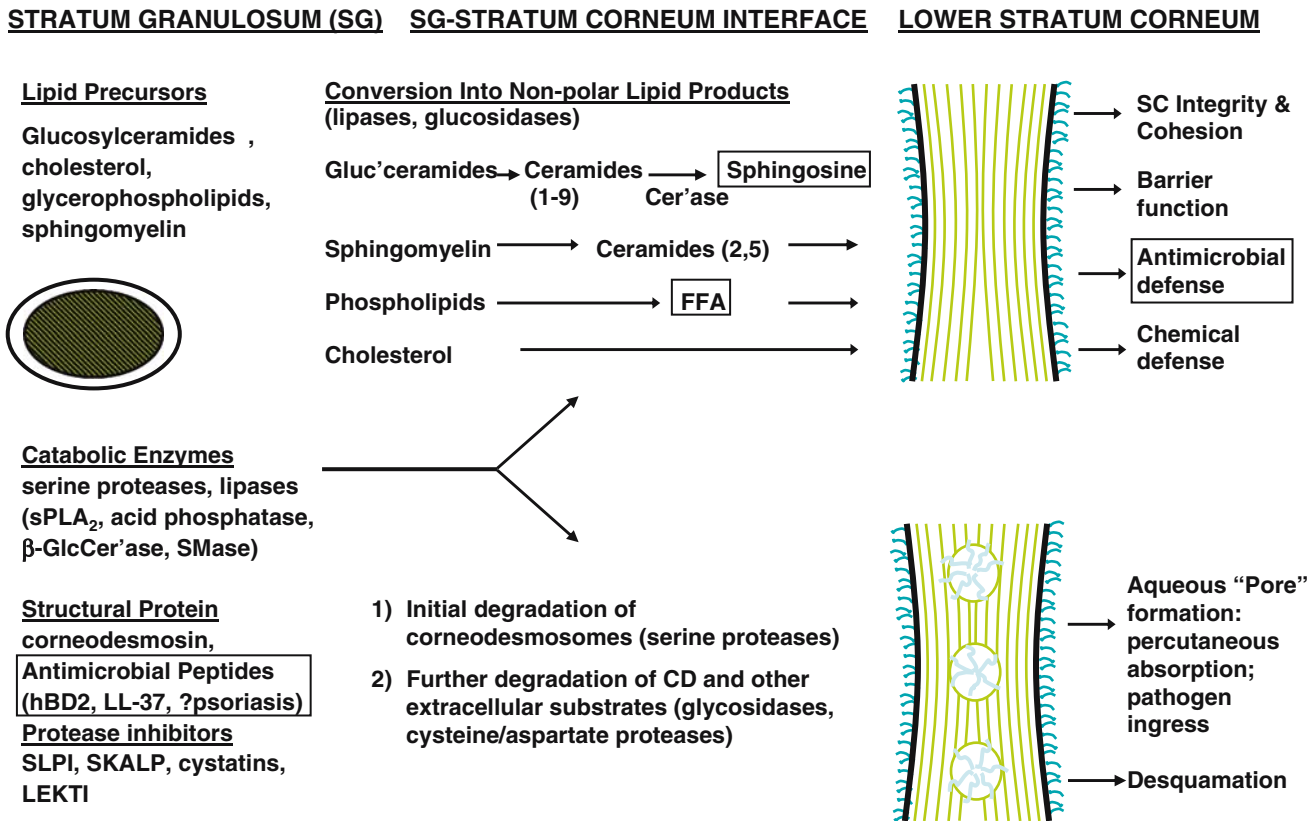

Fig. 3 Processes involved in generating the microbial barrier of stratum corneum

2) Normal cutaneous microflora: Because the SC lies at the interface with the external environment, it is continually threatened with xenobiotic assault. Yet, through a variety of mechanisms characteristic of epithelia in general and epidermis in particular (Table 5), it staunchly (and successfully) defends itself against the overwhelming majority of attempts by exogenous pathogens to colonize and invade. Epidermis has evolved multiple, largely tissue-specific strategies that deal with pathogen challenges (Table 5). Despite their overwhelming quantitative importance for cutaneous antimicrobial defense, these inherently "less-sexy" strategies have elicited very little systematic inquiry in comparison with epidermal AMP, toll-like receptors, and regulatory signalling mechanisms (Table 6), but undoubtedly, as each of these mechanisms is scrutinized further, their origins, biochemical basis, and regulation will become increasingly intriguing.

Perhaps, most important, yet least understood on a mechanistic level, is the substantial carriage of normal cutaneous flora in the outer SC and on the skin surface (about 10^2–10^3/cm^2 of micrococceae and propiononobacteriae [corynebacteriae]), first acquired during the birthing process, which rapidly spread to coat the skin surface (reviewed in Schröder and Harder [75]). It is widely assumed that the density of the normal flora is restricted by the process of epidermal cell renewal, which terminates in the desquamation of superficial corneocytes (with their resident organisms) from the skin surface. Yet, the presence of the cutaneous flora predicts a key role in antimicrobial defense through (a) competition with potential pathogens for niche occupancy, and (b) the limited availability of nutrients on the skin surface. Moreover, some strains of the normal flora can also secrete molecules, such as azelaic

Table 6 Basis for antimicrobial defense at the skin surface under basal conditions

Conditions
Intrinsic to stratum corneum
Geometry of intact SC layer
Replete lamellar bilayers
SC lipids; e.g., FFA, sphingosine
Acidic pH, low water content
Low, constitutive levels of hBD2 and LL-37 within extracellular matrix
From normal microbial flora
Niche occupancy; competition for nutrients
Secrete inhibitory metabolic products; e.g., acetic and propionic acids
Produce specific antimicrobial compounds; e.g., penicillin, azelaic acid
Surface-deposited antimicrobials
Sweat; e.g., dermcidin, ll-37
Sebum (lysozyme, FFA, RNase 7)

acid, propionic acid, and penicillin, which themselves inhibit pathogen colonization (Table 6). In vitro studies have shown that normal flora proliferate at a pH that duplicates the acidic milieu of the SC (≈5) [52], and through elaboration of acidic metabolites (azelaic and propionic acids), they could, in part, create the acidic conditions that favor their own persistence (see also below). Conversely, growth of the normal microflora is inhibited as skin surface pH rises [3], as is the case in chronic inflammatory dermatoses, such as atopic dermatitis (reviewed in [34]), although the neutral pH of inflamed skin instead favors the proliferation of microbial pathogens, most notably *S. aureus* and *S. pyogenes* [3, 52]. Finally, despite the presence of a spectrum of AMP with broad activities against multiple pathogens, there is evidence that the normal flora are resistant to AMP molecules [75].

3) The 'acid mantle' of the stratum corneum: The acidic character of skin surface pH has been long appreciated [59], and both in vitro [51, 52] and in vivo studies [3, 8, 64] suggest a teleological role for the 'acid mantle' in antimicrobial defense [34]. Yet, the origin of SC acidity and the functions that it impacts have only recently been methodically assessed. Previously assumed to be attributable to the surface deposition of (a) microbial metabolites (see above), (b) FFA from sebum, and/or (c) acidic eccrine gland products, such as lactic acid (reviewed in [34, 75]), recent studies have shown instead that these metabolites are not necessary for formation of an acidic surface pH [36]. Instead, SC acidity results largely from two or more endogenous mechanisms. Complete hydrolysis of epidermal phospholipids into FFA by one or more secretory PLA_2 ($sPLA_2$) occurs as the outer nucleated cell layers of the epidermis transition into the SC [57, 58]. The resultant largely non-essential FFA are not only critical structural components of the extracellular lamellar bilayers of the SC [57, 58], which physically exclude pathogens, but inhibitor studies have also shown that they contribute about 1 pH unit to the bulk acidic pH of SC [33]. Thus, by contributing to the bulk acidity and integrity of SC, the hydrolysis of PL into FFA helps form the compact acidic milieu that is so hostile to invading pathogens [57, 58]. Yet in addition, FFA are themselves potent antimicrobial species (see also below).

A second, endogenous source of the acidic pH of SC is the non-energy-dependent, sodium–proton exchange mechanism, NHE1. In the epidermis, this ubiquitous transporter localizes to the outer nucleated layers, where it acidifies extracellular domains at the granular layer (SG)–SC interface and in the lower SC [6]. Although it is a minor contributor to the bulk pH of SC, by selectively acidifying membrane microdomains in the lower SC, it impacts at least one key epidermal function that becomes established at this level, i.e., permeability barrier homeostasis [6, 7]. The age-associated decline in NHE1 activity, with a resultant net increase in SC pH, accounts, in part, for the decline in both permeability barrier function and SC integrity/cohesion in aging skin [17], and it could also account in part for the increased risk of pathogen invasion in aged skin.

Yet another, still-unproven source of SC acidification could be the filaggrin proteolytic pathway that culminates in the downstream generation of multiple, deiminated carboxylic acids, such as trans-transurocanic acid (UCA) [53]. Because the surface pH of hisidase-deficient (Peruvian) mice is normal [36] and humans with the common inherited disorder, histidinemia, who lack histidase activity exhibit no known cutaneous abnormalities, the importance of this mechanism for skin function remains uncertain. Moreover, the proteolytic step that initiates filaggrin proteolysis is humidity sensitive; i.e., it is inhibited at external relative humidities above 80% [76]. Because UCA would not be generated in a humid environment, it would be an inconstant contributor to SC pH. Yet, the increased propensity for *S. aureus* and gram-negative cutaneous infections to occur in superhydrated skin could, in theory, be linked to the down-regulation of this mechanism.

Recent studies have explored the functions of SC acidification in both humans and animals. Using topical applications of either 'superbases' (more basic than 1 N NaOH) or 'superacids' (more acidic than 1 N H_20 SO_4), such as the polyhydroxylacids (PHA), lactobionic acid, and gluconolactone, it is possible to modulate pH selectively at all levels of SC without evidence of toxicity to the underlying nucleated layers of the epidermis [39, 40]. This approach allows the manipulation of pH without the coexistence of other experimental variables, such as hydration or occlusion, which confounded earlier in vivo studies [3]. Accordingly, 'superbase'-induced elevations in SC pH in hairless mice modify both permeability barrier homeostasis and SC integrity/cohesion, largely through increased activity of SPs [3] which exhibit neutral pH optima [12]. Conversely, hyperacidification of SC with PHA generates a 'super' barrier and an even more cohesive SC than present in normal human and murine skin [41]. Yet, whether the pH-dependent changes in permeability barrier function and SC integrity/cohesion directly impact antimicrobial function, i.e., resistance to pathogen adhesion/invasion, has not yet been addressed. Because of the positive correlations between the permeability and antimicrobial barriers (Table 3), one would expect, however, that the antimicrobial barrier would change in parallel to alterations in permeability barrier function.

4) Hydration status: The water content of SC drops precipitously towards the surface of SC [83], creating

desiccating conditions that normally inhibit pathogen colonization [3]. Yet, the normal cutaneous microflora seem to thrive under similar conditions for reasons that are largely unknown. Conversely, pathogen colonization, particularly by *S. aureus* and *S. pyogenes*, is favored by the superhydration of SC [8], explaining the increased propensity for clinical infections in intertrigenous or occluded skin sites, such as the axillae, inframammary folds, groin, and plantar surfaces (reviewed in [34]). Likewise, the common occurrence of staphylococcal and streptococcal infections in tropical climates can be explained, in part, by the increased hydration of SC at these ambient humidities. Finally, as noted above, filaggrin proteolysis is inhibited under these conditions, resulting not only in an increased surface pH, but also in altered SC hydration. Filaggrin proteolysis generates not only the histidine metabolite, trans-UCA, but also a broad range of deiminated metabolites, often termed together as 'natural moisturizing factor' (NMF). Abundant glycerol, a potent endogenous humectant, is generated and surface-deposited through both the high rates of triglyceride turnover that occur in sebaceous glands [15, 35] and the importation from the circulation via the activities of one or more aquaporin channels (e.g., AQP3) that are expressed on keratinocyte cell membranes [43]. Finally, eccrine glands surface deposit other osmotically active ingredients, such as lactic acid. It is intriguing to consider the possibility that not only humidity-sensitive downregulation of filaggrin proteolysis but also, perhaps, AQP3 activity could be downregulated at high humidities in response to the broad requirements for a desiccated SC for antimicrobial defense.

5) Biochemical basis for SC antimicrobial defense—lipids: Even in hydrated SC, invading pathogens encounter and must overwhelm an impressive array of antimicrobial lipids and proteins that reside in the extracellular matrix (chemical defensive shield; Tables 4, 5, 6 and 7). SC lamellar lipids primarily comprise three major species: a family of nine ceramides (Cer), cholesterol, and essential/non-essential FFA present in an approximately equimolar ratio. Cer derive from the hydrolysis of glucosylCer and sphingomyelin [81], while FFA result from epidermal phospholipid hydrolysis [57, 58], as well as in sebaceous gland-enriched regions, and from the surface deposition of FFA derived from triglyceride catabolism [35]. The three major lipids are secreted from epidermal LB, largely as their precursors, but hydrolysis is completed in the lower SC, eventually resulting in the extracellular lamellar membranes unique to the epidermis (Fig. 3) [24]. Further, the partial hydrolysis of Cer into sphingosine (Sph) and FFA, catalyzed by two isoforms of ceramidase (Cer'ase), the acidic and alkaline forms, occurs more distally in SC [47]. This pathway doubtlessly impacts antimicrobial defense, as Sph and FFA are the two most potent antimicrobial lipid species in SC [9, 64, 85], and again, there could be a further contribution of Cer'ase-generated FFA to the acidic bulk pH of SC. In vitro studies have demonstrated a wide array of antimicrobial activity for both Sph and FFA against *S. aureus*, *pyogenes*, *C. albicans*, and dermatophytes, with lesser potency against gram negative organisms, such as pseudomonas [4, 9, 64, 85]. Other work has demonstrated additional antiviral activity of FFA, as well [79]. In the case of FFA, anti-staphylococcal activity is also chain-length dependent, with species less than or equal to 16 exhibiting greater potency more than or equal to C18 [64]. Further, the antimicrobial activities of FFA persist at low micromolar concentrations that are relevant for the absolute quantities of these FFA that are present within the SC interstices (whether levels of Sph are sufficient to mediate antimicrobial defense in vivo is not known). Finally, GlucCer also exhibit considerable in vitro activity against the same pathogens [64], but in intact cells, these lipids largely reside in focal lipid-raft domains of cell membranes, where they instead facilitate pathogen adherence to cells and could instead facilitate colonization and invasion [70].

These observations appear to be clinically relevant for atopic dermatitis (AD), where activity of a still-incompletely characterized sphingolipid deacylase degrades the two Cer precursors, glucosyl Cer and sphingomelin, resulting not only in Cer and FFA deficiency but also in a paucity of its downstream product, Sph [4], the most potent endogenous antimicrobial lipid [9]. The net result of a decrease in Cer and FFA content is a paucity of extracellular lamellar bilayers in AD [13, 31], with further abnormalities in lamellar membrane organization due to disturbed lipid

Table 7 Principal antimicrobial peptides of the skin surface

	β-Defensin2	hCAP product (LL-37)	Psoriasin	Dermcidin	RNase 7
Epidermis	Inducible (low → high abundance)	Inducible	Constitutive; focal high abundance	–	Constitutive and inducible (low → high)
Eccrine glands	–	Constitutive (low abundance)	–	Constitutive, abundant	–
Sebaceous glands	–	–	Constitutive and inducible (abundant)	–	–

distribution (i.e., not only is there a reduction in total extracellular lipids but also abnormalities in the molar ratio of the three key lipids critical for bilayer formation) [56]. While together these indirect observations strongly suggest that SC lipids are critical for antimicrobial defense, further in vivo studies using either inhibitors or genetic deletions of lipid-generating enzymes, e.g., one or more isoforms of secretory phospholipase A_2 or ceramidase, followed by microbial pathogen challenges, are still needed.

6) Biochemical basis for antimicrobial defense—proteins: Human epidermis and its appendages elaborate several proteins that exhibit antimicrobial activity [11, 37, 48, 54, 75]. In light of the skin's continuous risk of exposure to pathogenic microbes from the environment, it is not surprising that, where known, these proteins largely localize to the outer epidermis [75]. These include at least two members of the RNaseA100 superfamily, RNase 7 and psoriasin, as well as members of the supergene family that encodes β-defensins (hBD1–4) and one product of the epidermal cathelicidin, hCAP18, i.e., its carboxyterminal fragment, LL-37 (and its murine homologue, CRAMP). The carboxy- and amino-terminal products of hCAP display distinctive (non-overlapping) spectra of antimicrobial activity (Table 4). Both LL-37 and hBD2 are small, evolutionarily conserved, cationic, highly hydrophobic, cysteine-enriched that, because of their dual role as signalling molecules, are distal members of the innate immune system (reviewed in [11, 37, 54], and elsewhere in this volume). Both of these peptides appear to kill pathogens by disrupting the hydrophobic core of the organisms' lipid bilayers (e.g., [69]).

Recent studies suggest that these two molecules also have a third, previously unrecognized structural role, i.e., in maintaining epidermal integrity [72], as do related AMP in the gastrointestinal and alveolar epithelium [78]. hBD2 and 3, as well as hCAP, are expressed only at low levels in human epidermis under basal conditions [19], emphasizing the highly effective and sufficient role of the SC barrier under most circumstances (see above). Surface-deposited sebaceous and eccrine products, including not only LL-37, but also the eccrine products, dermcidin (DCD), a tissue-specific constitutively expressed eccrine gland protein, and its 31, 30, and 20 kDa catabolic products (reviewed in [75]) also contribute to basal antimicrobial defense (Tables 5 and 6). Sebaceous glands deposit not only FFA, but also the RNaseA100 protein, psoriasin, as well as lysozyme, a non-specific protease whose role in antimicrobial defense in vivo remains uncertain (Tables 6 and 7). Yet, the expression of both hBD2 and hCAP increases markedly after external injury, UV exposure, and pathogen challenge in certain inflammatory dermatoses and/or during wound healing [11, 37, 48, 75]. While hBD2 expression in keratinocytes is upregulated by several cytokines [37, 54], hCAP expression is regulated conversely by the class II nuclear hormone receptor ligands, retinoic acid, and 1,25 $(OH)_2$ vitamin D3 [45, 84].

The RNase superfamily of S100 proteins includes several proteins with inherent antimicrobial activity, such as eosinophil-derived cationic protein, calgranulin-β, eosinophil-derived neurotoxin, angiogenin, and psoriasin (S100A7). Only calgranulin-β and psoriasin are known to be upregulated in psoriasis [38, 60]. An additional, novel AMP, RNase7 is constitutively expressed in normal SC [44] and is further inducible by bacterial challenge and cytokines, such as IFNγ, TNFα, and IL-1β. RNase7 is a highly basic 14.5 kDa cysteine-enriched protein with multiple disulfide bridges, but with broad activity against yeast, as well as against both gram+ and gram− bacteria. Because its greatest activity is against *S. faecalis* (including vancomycin-resistent organisms), its major role may be to protect against infections originating in the gut [75]. Yet, not only is RNase7's killing mechanism unknown, both its mode of delivery to and sub-cellular localization within SC remain unknown [44].

Five members of the RNase S100A family fall under the rubric psoriasin, but only the S100C variant is present in normal SC, while S100A1S is the predominant variant in psoriatic scales [38]. Psoriasin is an 11-kDa protein with a terminal acyl group rendering this protein the most hydrophobic of all epidermal AMP. Although it is a multifunctional protein [21], it is readily extracted from normal SC by acetone washing, and therefore, it could be similarly secreted and co-sequestered with barrier lipids within the SC interstices, like hBD2 (mBD3) and LL-37 (CRAMP). Yet, psoriasin is not uniformly distributed over the skin surface—its preferential expression in hydrated and peri-orificial skin sites (e.g., nose and around openings of pilosebaceous ducts), coupled with its unusual antibacterial spectrum (primarily *Escherichia coli*, with lesser activity against other gram− organisms and *S. aureus*), suggest a specialized role in antimicrobial defense, specifically against gut-derived *E. coli* (Tables 4 and 7). In contrast to RNase 7, more is known about the molecular mechanism of psoriasin's microcidal activity, which includes not only perforating activity, like cathelicidins and β-defensins, but also Zn^{++} and/or Ca^{++} sequestration [75].

Finally, the SC must contend with an array of hydrolytic enzymes, elaborated by pathogens as they attempt to attach, colonize, and invade. In response, the outer epidermis elaborates and secretes via the LB secretory mechanism, an array of serine and cysteine protease inhibitors (SPI), which exhibit net antimicrobial activity by interdicting exogenous proteases [72] that not only can facilitate invasion but also can degrade AMP, such as LL-37 [73]. Yet, certain of these hydrolases could also be required to process AMP

precursor pro-peptides into their active fragments, while their inhibitors could regulate the kinetics of such activation. To date, little is as yet known about the regulation or localization of these processes in mammalian SC.

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2 CLOTH APPLICATION SYSTEM:

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1 **Urinary Tract Care Prior To Catheter Insertion**

- Use 1st cloth BEFORE opening the urinary catheter tray.
- Unfold 1st cloth completely, apply to urethral opening and perineal area. Apply front to back for women and in concentric circles around the glans penis for men. Fold and use for 2nd application as needed.

DO NOT FLUSH • DO NOT RINSE • DRY TIME 30 SECONDS

2 **Insert Foley in Accordance With Facility Protocol**

3 **Urinary Catheter Care Post Insertion**

- Apply 2nd cloth of Theraworx Protect AFTER insertion is completed. Apply around the meatus and catheter.
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- Apply the 2nd cloth to all areas from the umbilicus to the mid-thigh, creating a **Zone of Protection** (Include all skin folds and rectal area).

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Theraworx® PROTECT

Patient Pre-Surgical Bathing

Using Theraworx Protect 8-Pack Towels

You will be sent home with a purple and white package that has eight (8) cloths of **Theraworx Protect.** The night before your surgery, please take a shower and wash your hair as you normally do. Towel dry completely and apply Theraworx Protect as indicated:

☐ **Total body cleansing:**
Cleanse with **Theraworx Protect** using either side of cloth, scrub for a duration of **ONE MINUTE.** Follow these instructions for each area indicated on diagram utilizing all eight (8) cloths. Do not rinse. Allow to air dry.

☐ **Targeted skin cleansing:**
Apply (2 to 4) cloths and scrub for **ONE MINUTE** on and around area being operated on (see diagram below for body area). Do not rinse. Allow to air dry.

Cloth 1
Scrub on face, neck, chest and upper abdomen to the umbilical (belly button) area. ***It is safe to use around the eyes and mouth.***

Cloth 2
Scrub right arm and armpit, hand and fingers

Cloth 3
Scrub left arm and armpit, hand and fingers

Cloth 4
Scrub right leg, including behind the knee, feet and toes

Cloth 5
Scrub left leg, including behind the knee, feet and toes

Cloth 6
Scrub back area. You may need a helper!

Cloth 7
Scrub both buttocks, ending with the rectal area

Cloth 8
Start at the area where you urinate, scrub around that area and covering the entire genital area. Turn the cloth over and scrub from the lower abdomen from the umbilical area (belly button) to the mid thighs.

DO NOT MICROWAVE. DO NOT FLUSH.
Dispose cloths in household trash.

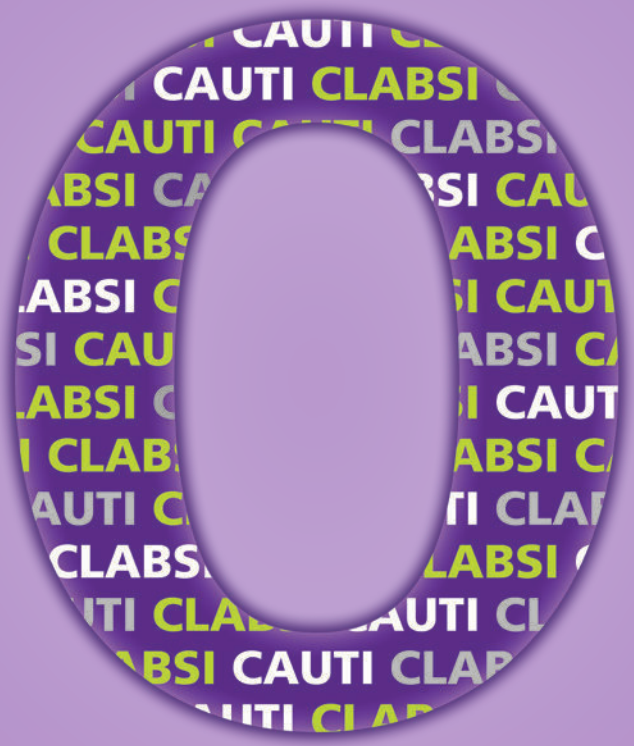
MICROBIOME COMPLIANT

When clean is not enough.

Avadim Technologies Inc. • 81 Thompson Street • Asheville, NC 28803 • 877.677.2723 • **theraworxprotect.com**

Does not contain antiseptic drugs

ATI18-003



Mission: Zero

P E D I A T R I C S

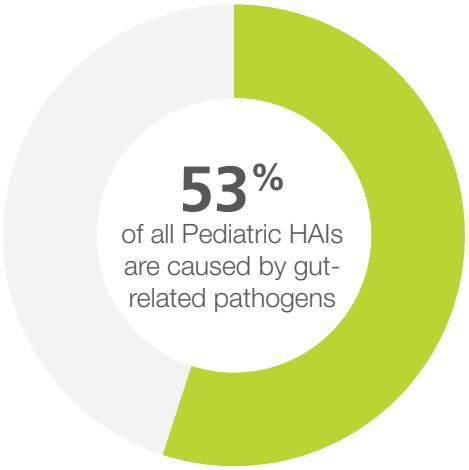
To Help Reduce And Eliminate HAIs, Including Catheter-Associated Urinary Tract Infections (**CAUTI)** And Central Line-Associated Blood Stream Infections (**CLABSI**) As A Part Of Your Infection Control Bundle

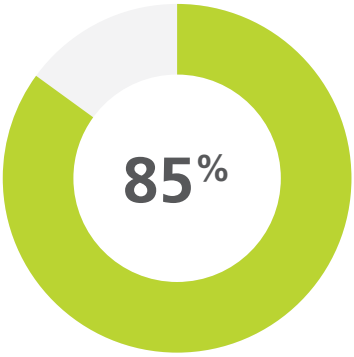
Theraworx®
PROTECT

Here Is What We Know: Pediatric HAIs

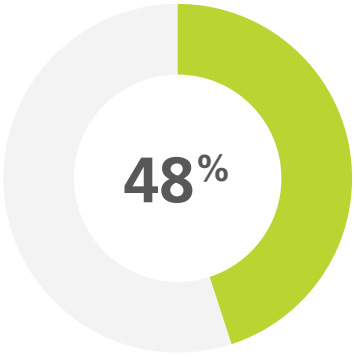
The CDC implicates **15 pathogens that account for over 88%** of healthcare-associated infections (**HAIs**)[1]. Of these opportunistic pathogens, **9 are considered gut-related.**

Gut Related Pathogens Are A Significant Cause of HAIs

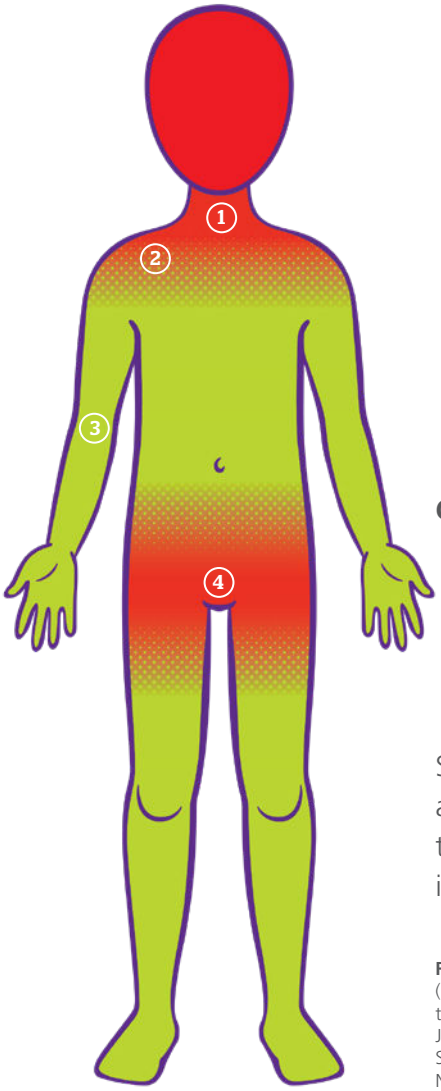




CAUTI



CLABSI



Gaps In Protection

CHG Bathing is not Recommended for Pediatrics under 2 months and Hematology / Oncology patients.

Most Hospitals decolonize Pediatric Patients over 2 months with Chlorhexidine Gluconate (CHG) but do not address perineum decolonization (red area) to address gut-related pathogens because of efficacy and safety concerns with CHG.

Pediatric ICU Patients that cannot use CHG: Around 10% of ICU patients cannot use CHG due to anaphylactic history, allergies and sensitivities, contraindications such as psoriasis, eczema, Stevens-Johnson syndrome, Graft vs Host disease, non-intact skin, patient refusals, and other reasons.

Current Practice leaves gaps in care which can lead to infection in:

1. Tracheotomy tube
2. Central venous catheter
3. PICC line
4. Urinary catheter
5. Surgical sites

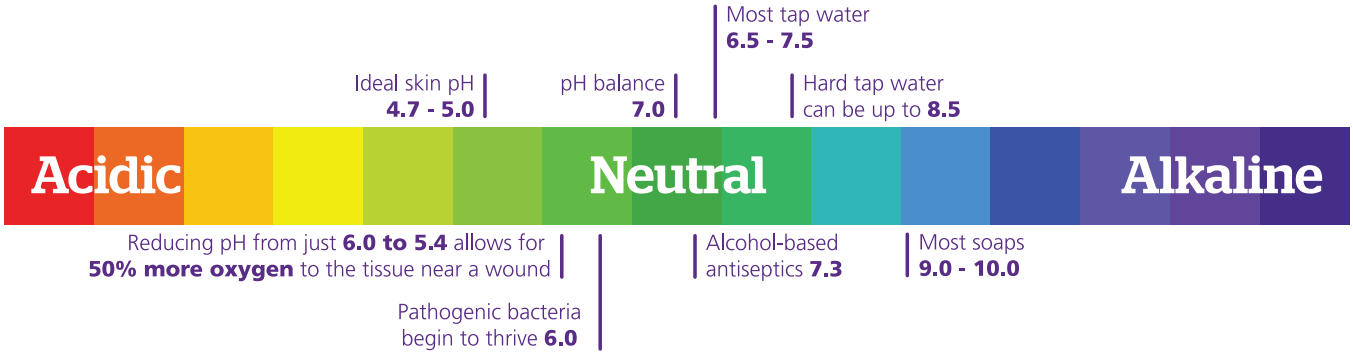
Soap and water or equivalent wipes do not decolonize the perineum and can strip away the skin's natural antimicrobial barrier and defensive functions. Most products that can decolonize the skin are either contraindicated for use in the perineum and in mucosa or lack safety and efficacy data.

References:
(1) Antimicrobial-resistant pathogens associated with pediatric healthcare-associated infections: Summary of data reported to the National Healthcare Safety Network, 2015–2017. Lindsey M. Weiner-Lastinger MPH , Sheila Abner PhD, Andrea L. Benin MD, Jonathan R. Edwards MStat, Alexander J. Kallen MD, MPH, Maria Karlsson PhD, Shelley S. Magill MD, PhD, Daniel Pollock MD, Isaac See MD, Minn M. Soe MBBS, MPH, Maroya S. Walters PhD and Margaret A. Dudeck MPH. Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

A Clear Solution: pH Matters

Healthy skin (mucosa) thrives in an optimal low pH environment. It competes successfully for nutrition and space on the skin surface, protecting against invasion by pathogens and resulting infections.

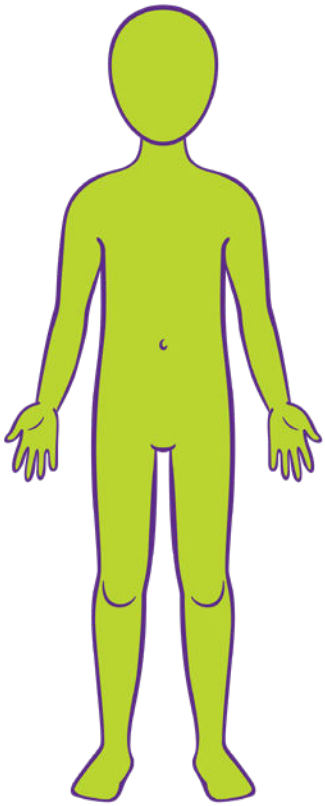
When pH rises, the normal healthy microbiome suffers, and pathogenic bacteria capitalizes on the change in pH.



Four Systems Supported By Theraworx Protect

An ideal acidic skin pH creates a hostile environment to pathogens, while supporting skin integrity and proper skin function. Theraworx Protect's unique low pH formulation **supports 4 systems** that are critical to driving quality and safety **while helping to reduce hurt and harm.**

pH Acidic Systems	Surfactant Systems	Barrier Systems	Preservative Systems
Key ingredient: Citrus Paradisi (Grapefruit Seed Extract)	**Key ingredient:** Cocamidopropyl Betaine	**Key ingredients:** Dimethicone, Allantoin	**Key ingredient:** Colloidal Silver



Theraworx Protect provides advanced total body and perineum care, trusted by hospitals and health care settings as a part of their infection control bundles.

Theraworx Protect Addresses the Gaps

- Advanced perineum care
- One step to total body and perineum protection–reducing time and human error
- Safe for use on compromised skin
- Low-pH formulation supports the skin's natural antimicrobial barrier and defensive functions
- Improve quality and safety while helping to reduce hurt and harm
- Contains NO CHG or antiseptic drugs
- Skin Friendly including ingredients that hydrate, nourish, and protect the skin
- Used by leading pediatric hospitals since 2015

01-101
Theraworx U-Pak

HXC-08Z
7.1 fl oz Foam

HXC-04Z
3.4 fl oz Foam

HXS-02Z
1.7 fl oz Pump Spray

Choose from several products to meet your care setting needs.

SCP-8802FF
2-Pack Fragrance Free Towels

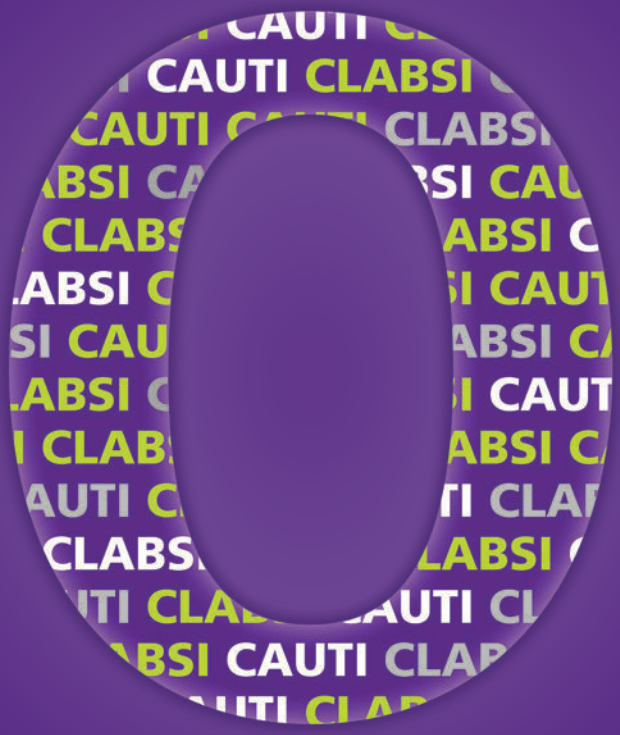
SCP-8802
2-Pack Towels

HX-8808FF
8-Pack Fragrance Free Towels

HX-8808
8-Pack Towels

Learn about Theraworx Protect's clinical data, visit
hcp.theraworxprotect.com/learn

SCAN ME



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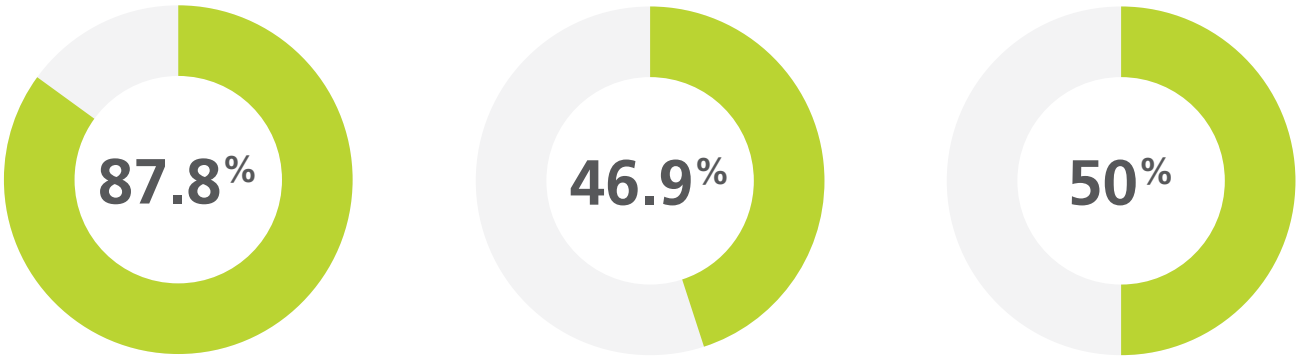

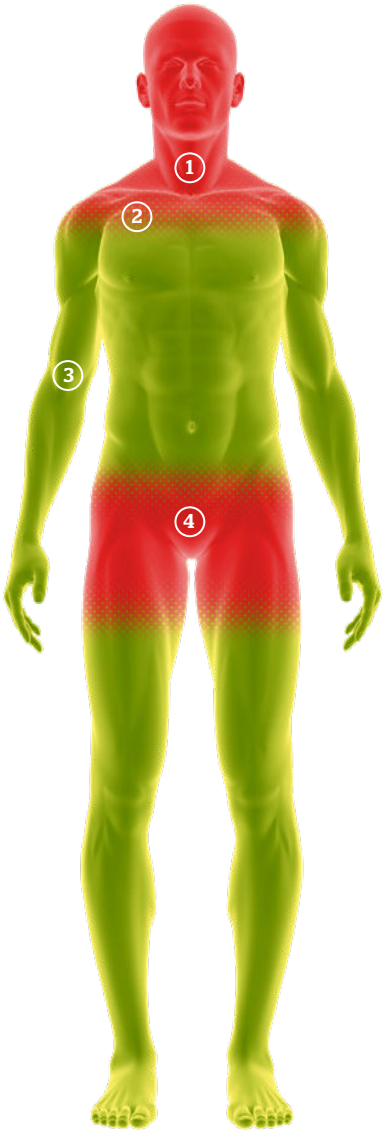

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ICU Patients that cannot use CHG: Around 10% of ICU patients cannot use it due to anaphylactic history with CHG, allergies and sensitivities, contraindications such as psoriasis, eczema, Stevens-Johnson syndrome, Graft-vs-host disease, non-intact skin and others.

CHG bathing is not recommended for pediatrics under 2 months and Hemotology / Oncology patients.[2]

Current Practice Does Not Address Gut Related Pathogens In The Perineum, Which Can Lead To Infections In:

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(2) https://www.jointcommission.org/-/media/tjc/documents/resources/hai/clabsi_monographpdf.pdf

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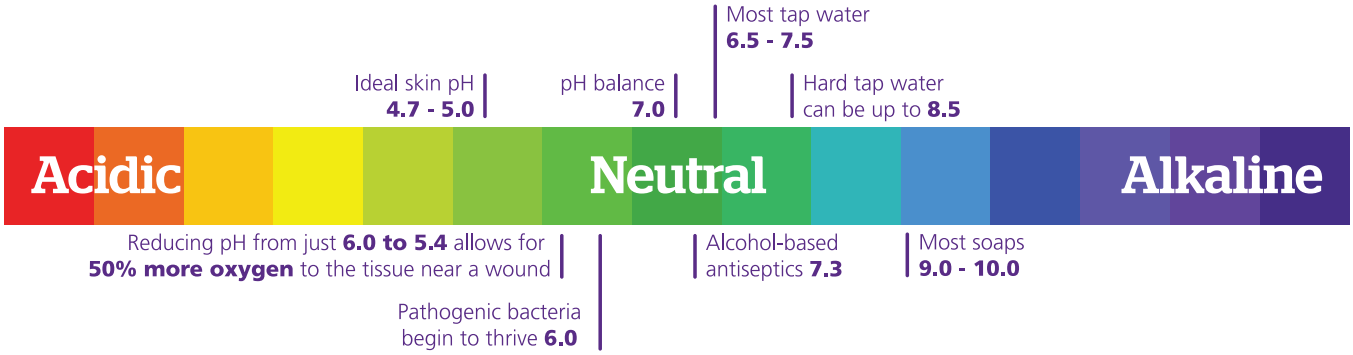

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- Low-pH formulation supports the skin's natural antimicrobial barrier and defensive functions
- Improve quality and safety while helping to reduce hurt and harm
- Cost effective
- No contraindications

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