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ORIGINAL ARTICLE

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Wound culture isolated antibiograms and caregiver-reported skin care practices in children with epidermolysis bullosa

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Abstract

Background/Objectives: Many patients with epidermolysis bullosa (EB) require intensive daily wound care and individualized treatment plans. Understanding patient's home skin care routines and emerging antibiotic resistance patterns in EB wounds is necessary to optimize treatment recommendations. The objective was to identify patterns of antimicrobial resistance in EB wounds and characterize patient's home practices of skin care and bathing.

Methods: This was an observational study of 23 children with EB at an outpatient pediatric dermatology practice in New York City from 2012 to 2014. Information on individual bathing and skin care practices and wound cultures was collected as part of routine examinations and an institutional review board–approved antibiogram protocol.

Results: Sixty wound cultures were collected from 23 patients. Eleven organisms were isolated, most commonly methicillin-susceptible *Staphylococcus aureus*, methicillin-resistant *S. aureus*, *Streptococcus* species, and *Pseudomonas aeruginosa*. Six patients (26%) were colonized with methicillin-resistant *S. aureus*. Over the course of the study, 13 patients (56%) were found to have mupirocin-resistant *S. aureus*. More than half of participants reported mupirocin or bacitracin use. Fewer than half indicated that they regularly used dilute bleach or dilute vinegar as part of their bathing routine.

Conclusion: Numerous organisms, including resistant bacteria, are known to colonize the wounds of individuals with EB. Mupirocin resistance was prevalent and more than half of the participants reported its use. Testing for mupirocin resistance may be considered for certain patients. These observations may help guide questions for future longitudinal multicenter studies with the goal of optimizing EB wound care recommendations.

KEYWORDS
epidermolysis bullosa, infection, bacterial, therapy, topical

1 | INTRODUCTION

Epidermolysis bullosa (EB) is a family of rare, inherited diseases with a broad range of phenotypic and molecular variability.[1] In daily clinical practice, an interdisciplinary approach and partnership with patients and their families is essential for appropriate management. Chronic wounds can predispose patients to systemic infection and are associated with future development of squamous cell carcinoma.[2] Even with proper daily skin care, appropriate cleansing routines, and fastidious antibiotic use, individuals with EB are at risk of chronic wounds, antibiotic resistance, and related sequelae. Understanding how patients care for their EB at home and characterizing their wound culture susceptibilities can help identify areas in need of improvement and may help optimize antimicrobial treatment recommendations.

The primary objective of this study was to assess wound culture results of individuals with EB, including antibiotic resistance patterns. A secondary objective was to gather patient-reported information regarding their use of topical antibiotics and home bathing routines.

2 | METHODS

The Columbia University Medical Center Institutional Review Board approved the study protocol and data collection. Patients with a diagnosis of EB were enrolled at the time of their appointment at an ambulatory pediatric dermatology practice in New York City from March 2012 to November 2014. As part of routine care, patient wounds were cultured and information regarding bacterial growth and antibiotic susceptibilities was documented. Information was collected from patients and their caregivers on the use of systemic and topical antibiotics and of dilute bleach or dilute vinegar baths at the time of the visit.

3 | RESULTS

Demographic data are outlined in Table 1. Twenty-three patients 2 months to 18 years of age (average 5.9 years) were enrolled (12 male, 11 female, one pair of siblings, one pair of double first cousins).

TABLE 1 Characteristics of enrolled patients (n = 23)

Characteristic	n
Sex	
Female	11
Male	12
Age	
<18 mo	4
18 mo - 3 y	5
3-8 y	5
>8 y	9
Patient relationship at time of enrollment	
New patient	9
Established patient	14
EB type	
Recessive DEB	15
Dominant DEB	1
DEB unknown subtype	2
EB simplex	3
Junctional EB	1
Unclassified	1

EB, epidermolysis bullosa; DEB, dystrophic EB.

3.1 | Patient-reported skin care routines

Patients were queried regarding their use of topical antibiotics on intact skin, "clean" wounds, and "dirty" wounds. The most commonly used medications were mupirocin and bacitracin ointment, with more than half of participants indicating their use. Polysporin ointment and medical-grade honey were less commonly reported. No patients indicated the use of retapamulin. Fewer than one-third of patients reported alternating between two or more different topical antibiotics on "dirty" wounds. Three patients reported the use of antibiotics on intact skin. Other products and antimicrobials reported included silver 55 ppm (Elta SilverGel, Swiss-American Products, Carrollton, TX), chlorhexidine gluconate (Hibiclens, Molnlycke, Norcross, GA), and silver sulfadiazine (Silvadene cream, Pfizer, New York, NY).

Fewer than half of patients indicated that they regularly used dilute bleach or dilute vinegar baths, rinses, or compresses as part of their skin cleansing routine. Participants who indicated using dilute bleach or dilute vinegar reported wide ranges in the concentration of antiseptic and in the frequency of bathing. Patient-reported quantities varied in units and were converted to cups per half-tub for comparison purposes, with one half-tub assumed to be 20 gallons. The amount of bleach reportedly added per half-tub ranged from 0.15 to 2.5 cups, with frequencies of one to seven dilute bleach baths per week. The amount of vinegar patients reported adding ranged from 0.15 to 5.0 cups per half-tub, with the use of dilute vinegar one to four times per week. Several patients also indicated that they added salt to baths, varying from 0.5 to 1.0 cup per tub. Many patients who were new to our practice had never used dilute bleach or dilute vinegar baths.

3.2 | Wound culture results

All enrolled patients had between one and five cultures performed on their acute or chronic wounds. A total of 60 wound cultures from 23 patients were analyzed. Eleven unique organisms grew, most commonly methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA), *Streptococcus* species, and *Pseudomonas aeruginosa*, with a complete list in Table 2. The resistance patterns of *S. aureus* species isolates from the 19 patients in which it was cultured are outlined in Table 3.

TABLE 2 Culture results from wounds of patients with epidermolysis bullosa

Organism	Children with positive cultures, (n = 23), n (%)	Positive cultures, (n = 60), n (%)
Staphylococcus spp.	22 (96)	51 (85)
Methicillin-susceptible *Staphylococcus aureus*	14 (61)	33 (55)
Methicillin-resistant *S. aureus*	6 (26)	11 (18)
Coagulase-negative staphylococci	5 (22)	7 (12)
Streptococcus spp.	7 (30)	11 (18)
Streptococcus Group A	5 (22)	8 (13)
Streptococcus Group B or G	2 (9)	3 (5)
Pseudomonas aeruginosa	5 (22)	8 (13)
Diphtheroids	3 (13)	5 (8)
Enterococcus spp.	2 (9)	3 (5)
Vancomycin-resistant *Enterococcus*	1 (4)	1 (2)
Candida spp.	2 (9)	3 (5)
Proteus mirabilis	1 (4)	2 (3)
Klebsiella pneumoniae	1 (4)	1 (2)
No growth	1 (4)	2 (3)

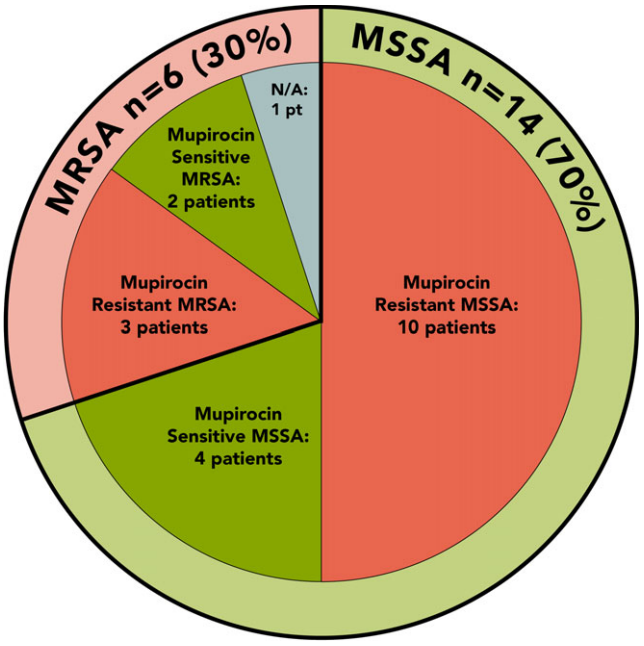

FIGURE 1 Patients with mupirocin resistance at any time from 2012 to 2014 (n = 20). Information on mupirocin susceptibility was not available for one patient with methicillin-resistant *Staphylococcus aureus*

High-level mupirocin resistance, with a minimal inhibitory concentration (MIC) of 1024 μg/mL or greater, was prevalent in *S. aureus* isolates from the wounds of our subjects with EB. On the day of study enrollment, seven (30%) had mupirocin-resistant (MupR) *S. aureus*: three MupR MRSA and four MupR MSSA. As our institution transitioned to routine testing for mupirocin susceptibility in *S. aureus*, we were able to prospectively observe the mupirocin susceptibilities of 20 patients who returned for follow-up care. Over the course of the study period, 13 (65%) patients had a documented MupR *S. aureus* isolate. Figure 1 illustrates the proportion of MupR MRSA and MupR MSSA in these patients. A chart review revealed that all patients except one reported previous or current use of mupirocin. Some patients became mupirocin susceptible several months after documented resistance.

4 | DISCUSSION

Our survey data provide a descriptive snapshot of home skin care and bathing practices of individuals with EB from which we can conclude several clinically relevant points. Overall, patients reported a wide variety of home skin care and bathing practices. This may be related to patient and family preferences but underscores the importance of understanding patient home care practices so that individualized recommendations can be optimized.

4.1 | Topical antibiotic use

The use of topical antimicrobials is often necessary for individuals with EB with infected wounds. Recommendations are that antibiotics be applied to critically colonized or infected lesions[3] and that topical

TABLE 3 *Staphylococcus aureus* susceptibilities from wounds of 19 EB patients

Antibiotic	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	Total I or R, n (%)
Oxacillin (Methicillin)	S	S	R	S	S	S	S	S	S	S	R	R	R	S	S	R	R	S	S	6 (32)
Clindamycin	R	S	S	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	2 (11)
Erythromycin	R	R	S	R	R	S	S	S	R	S	R	R	I	S	S	R	R	S	S	10 (53)
Levofloxacin	S	S	I	S	S	R	S	S	S	S	S	S	S	S	S	I	R	S	S	4 (21)
Tetracycline	S	S	S	S	S	S	I	S	S	S	S	S	S	S	S	S	S	S	S	1 (5)
Trimethoprim sulfamethoxazole	R	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	1 (5)

S, susceptible to antibiotic; I, intermediate level susceptibility; R, resistant to antibiotic; N, not reported.

medications used be rotated frequently to reduce widespread resistance.[4,5] Despite these guidelines, which form the basis of our practice regarding skin and wound care recommendations, several patients reported the use of antibiotics on intact skin, and many indicated the use of antibiotics on "clean" wounds. Mupirocin and bacitracin ointment were the most commonly used agents. Fewer than one-third of patients reported that they used more than one type of topical antimicrobial, suggesting that many of our patients with EB tend to rely on monotherapy when they apply a topical antibiotic. This discrepancy between guidelines and actual patient use highlights the importance of patient education with regard to reinforcing best practices for topical antibiotic use, especially in light of increasing antibiotic resistance.

4.2 | Bathing practices

Although many patients new to our practice were unfamiliar with the use of dilute bleach or dilute vinegar for skin cleansing, established patients had all received the same printed instructions for dilute bleach rinses or baths and dilute vinegar compresses. The printed directions for patients stated that 0.25 cup of bleach should be added per half-tub of water, resulting in a bleach concentration of approximately 0.005%. Assuming the starting concentration of 6.0% sodium hypochlorite in household bleach and that a half-tub is 20 gallons, the amount of bleach patients reported adding, from 0.15 to 2.5 cups, corresponds to a concentration range of 0.002%-0.047%. Improperly diluted bleach can be ineffective at killing bacteria if the concentration is too low or can cause skin irritation and impede wound healing if it is too high.

The instructions for diluting 5% acetic acid or white vinegar called for combining 1 part vinegar with 20 parts water, resulting in a final concentration of approximately 0.25% acetic acid. The amount of vinegar patients reported using in vinegar dilutions corresponded to concentrations of 0.0019%-0.08%, which are well below the target concentration. The wide ranges reported in the quantity of antiseptic added indicate that routinely reviewing the details of patient's bathing and other skin cleansing habits may provide opportunities for clarification and constructive dialogue between patients and providers, with the potential for better outcomes.

EB consensus guidelines support that bathing frequency should be adjusted according to dressing type and wound severity and that dilute bleach, dilute vinegar, or chlorhexidine can be used to reduce bacterial carriage and augment the healing of lesions that may be colonized or infected.[4,5] Although fewer than half of our patients reported using dilute bleach or dilute vinegar baths, only one patient had wound cultures with no reported growth. No randomized trials have been performed to determine which cleansing and wound dressing protocols are superior for individuals with EB. Studies of dilute bleach baths in children with atopic dermatitis have not found a significant reduction in clinical rates of colonization and infection, although these results may not be applicable in individuals with EB with chronic wounds.[6,7] For individuals with EB who tolerate bathing, there is minimal risk associated with incorporating antiseptic cleansers at appropriate concentrations in home hygiene routines, and further study is needed to ascertain which bathing protocols affect colonization, clinical infection, and future outcomes.

Reports and studies on bathing recommendations in individuals with EB are often focused on pain management. A 2010 report on bathing in individuals with EB noted that the addition of salt to baths may reduce pain associated with bathing.[8] A retrospective observational study published in 2015 demonstrated decreases in reported pain in 16 individuals with EB who began adding salt to their baths in amounts varying from 0.25 cup to 2 pounds.[9] Several of our patients reported that they added salt to their baths: some in combination with bleach and others as salt alone.

4.3 | Culture results

All enrolled patients had one to five wounds cultured and all but one patient grew organisms in culture. Consistent with previous studies,[10,11] we found that numerous organisms, including resistant bacteria, colonize the acute (<3 weeks open) and chronic wounds of individuals with EB. A limitation of this study is that the clinical appearance of the wound was not formally recorded as part of the data collection. Susceptibility data provide necessary information about the bacteria present, but wound history and characteristics (chronicity, location, appearance, treatments used, associated symptoms) are necessary to assess whether cultured organisms are simply bystanders or impede healing.[5,11]

We found mupirocin resistance to be highly prevalent in our cohort. Over the course of the study, 13 patients of 20 had, at one point, *S. aureus* isolates that were positive for high-level mupirocin resistance. Of those patients, mupirocin resistance was seen in those with MSSA and MRSA. Once found to have MupR *S. aureus*, several patient cultures demonstrated that, over time, they could revert to mupirocin susceptible. More than half of the participants reported current mupirocin use, and from chart review, all but one patient had documented prior mupirocin use.

High rates of mupirocin resistance in children are consistent with rates reported in a retrospective study from this institution that also identified prior mupirocin use as a risk factor for resistance.[12] Mupirocin resistance is classified as low level (MIC 8-64 μg/mL) and high level (MIC ≥ 512 μg/mL). Low-level mupirocin resistance in *S. aureus* is most often due to base mutations in the native isoleucyl tRNA synthetase gene, whereas the *mupA* gene on an acquired plasmid mediates most high-level resistance. Conjugative plasmids can spread rapidly among bacteria, and it is thought that widespread dissemination of plasmids containing the *mupA* gene is driving the increase in mupirocin resistance in MRSA and MSSA.[13] Given the widespread resistance to many systemic and topical antibiotic agents in individuals with EB, surveillance cultures with routine testing for mupirocin resistance may help guide antibiotic stewardship and counseling.

5 | CONCLUSION

We found a wide range of patient-reported home practices for bathing and wound care. Areas of concern are the use of antibiotics on intact skin or "clean" wounds and reliance on one type of topical antibiotic rather than alternating medications. In addition, wound cultures revealed a variety of antibiotic-resistant organisms, with a high prevalence of mupirocin resistance in *S. aureus* isolates. Although limited by the small number of patients, our observations highlight the importance of understanding antibiotic resistance trends and optimizing EB wound care recommendations. Proper techniques for dilution of bleach and vinegar should be routinely reviewed with patients and barriers to best practices in skin care and bathing in individuals with EB should be addressed. Given the rarity of this condition, until there is a cure, longitudinal multicenter studies will be essential for determining the relationship between home bathing routines, antibiotic resistance, and which recommendations result in the best outcomes for the wide range of individuals with EB.

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