Skin and Wound Care in Lymphedema Patients: A Taxonomy, Primer, and Literature Review

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ABSTRACT

BACKGROUND: Lymphedema is a condition of localized protein-rich swelling from damaged or malfunctioning lymphatics. Because the immune system is compromised, there is a high risk of infection. Infection in patients with lymphedema may present in a variety of ways.

OBJECTIVE: The goals of this review were to standardize the terminology of skin breakdown in the context of lymphedema, synthesize the available information to create best practice recommendations in support of the American Lymphedema Framework Project update to its Best Practices document, and create recommendations for further research.

DATA SOURCES: Publications on skin care and wounds were retrieved, summarized, and evaluated by a team of investigators and clinical experts.

STUDY SELECTION AND DATA EXTRACTION: Terms for lymphedema-associated skin breakdown were compiled and paired with photographs of commonly noted skin changes among patients with lymphedema. A list of standard dermatological terms was created. A more extensive literature search was then conducted by all authors.

DATA SYNTHESIS: Skin disorders associated with lymphedema have been classified into 5 categories. Descriptions, photographs, and recommendations for treatment are presented.

CONCLUSIONS: Skin care is an important defense against infection. Because of the lack of research, a consensus of thought and content leaders' opinion should guide the best practices for wound care in lymphedema.

KEYWORDS: best practices, literature review, lymphedema, skin care, wounds

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INTRODUCTION

As part of a systematic review to evaluate the level of evidence of contemporary peer-reviewed lymphedema literature in support of the second edition of a Best Practices document, publications on skin care and wounds were retrieved, summarized, and evaluated by teams of investigators and clinical experts. A joint project of the American Lymphedema Framework Project and the International Lymphoedema Framework, the objectives are to provide evidence of the best practices in lymphedema care and management and to increase lymphedema awareness in the United States and worldwide.

BACKGROUND

Lymphedema is a disfiguring condition that can result in significant impairment in quality of life and function.[1] The skin constitutes the first line of defense against external pathogens. Skin breakdown from lymphedema can result in catastrophic, and even life-threatening, health consequences.[2] Patients with lymphedema-related infection may present with cellulitis, lymphangitis, or lymphadenitis.[3] In a prospective study of 167 patients admitted to the hospital with cellulitis, lymphedema (not diabetes) was the most prominent risk factor.[4] Bacteria may colonize the interstitial spaces,[5] thriving in the protein-rich fluid of a lymphedematous region. When combined with lymphedema-associated immune compromise, persistent and recurrent infection is highly likely.[2] Among 568 patients hospitalized with cellulitis in the United Kingdom, lower limb edema (30.1%) and preexisting ulceration (24%) were the 2 characteristics that identified patients at high mortality risk.[2] Because virtually all cutaneous wounds are colonized with bacteria, most wound care regimens for patients with lymphedema should be designed to reduce bacterial bioburden.

Profound inflammation of skin and soft tissues can result in dramatic permanent cutaneous changes that lead to the physical

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distortion of the affected limb. Drainage from lymphatic tissue can be copious, making absorbency perhaps the most important functional aspect of wound dressings. Dressing an open wound complicates lymphedema management: it is difficult to pull compression garments over a bulky bandage, particularly if the limb is misshapen, and compression can be painful on open wounds. The chronic and intractable nature of open wounds in patients with lymphedema can also be expensive because of dressing costs, clinic visits, and lost time at work. One British case report estimated the long-term cost of nursing and home care products (excluding hospitalization) for a patient with chronically draining ulcers at £260,000 (approximately $325,000 in 2017 USD).[6]

The overarching principles of moist wound care are now widely accepted. Because epithelialization occurs from the wound periphery, maceration from a copiously draining wound can impair epithelial migration. Thus, moisture balance is crucial to effective healing, as is bacterial colonization control. Wound care products represent a multibillion dollar US industry with numerous dressing categories aimed at a variety of wound bed optimization aspects. Products may be classified by intended purpose (eg, absorption of drainage, debridement) or materials (eg, hydrocolloid, calcium alginate). Since the development of hydrocolloid dressings in 1980, many different dressing categories have come to market, and the list continues to grow. Small randomized controlled trials (RCTs) have been performed to determine the efficacy of particular dressing products in specific wound models. The most common wound models are diabetic foot ulcers, venous stasis ulcers, and pressure injuries. Although these chronic ulcers may differ in etiology, biochemical studies show that they differ little at the cellular level. All chronic nonhealing ulcerations share common features: senescent cells with low replicative capacity, low populations of healing-associated growth factors, imbalanced cytokine and chemokine levels, and high concentrations of extracellular matrix–degrading enzymes. Thus, it is likely that a diabetic foot ulcer–healing topical product will be similarly beneficial in healing lymphedema-associated ulcerations.

Wound care clinical trials consistently confirm that correction of the underlying factor(s) leading to the chronic ulcer formation (eg, pressure, edema) is more important than the choice of topical dressing and is the intervention most essential to effecting healing. Thus, studies have consistently failed to show substantial superiority of one dressing over another in any wound model, if indeed basic moist wound care principles were followed. Few RCTs have assessed the efficacy of specific dressing products in lymphedema.

The goals of this review were to standardize the terminology of skin breakdown in the lymphedema context, synthesize available information to form best practice recommendations, and create further research recommendations.

METHODS

After the initial literature search, it was determined that no consistent terminology existed for lymphedema-associated skin breakdown and pathologic changes. Inconsistent terminology made assessing relevant literature difficult. A list of all terms for lymphedema-associated skin breakdown was created from the first literature review (Table 1). This was paired with photographs (Figures 1–15) of commonly noted lymphedema skin changes seen within the authors' (C.E.F. and W.F.) practices and reviewed by a dermatologist experienced in treating lymphedema (A.A.H.). A second, more extensive, literature search was conducted using this list of dermatological terms. This second set of articles was reviewed by all authors and is described in Table 2.

FINDINGS

A variety of skin changes are associated with lymphedema. Some result directly from lymphedema-related inflammatory processes and can result in disfigurement of the associated limb or affected limb. Lymphatic fluid can drain directly through the skin (lymphorrhea), causing tissue maceration and breakdown. Several pathologic findings are indirectly due to lymphedema (eg, pressure ulceration from heavy limbs). The underlying lymphedema-inducing conditions may precipitate skin breakdown (eg, venous stasis causing venous ulceration). Lymphedema treatment may result in skin breakdown with ill-fitting garments or bandage misapplication. Therefore, the authors have classified lymphedema-associated skin disorders into 5 categories: (1) directly caused by lymphedema, (2) indirectly related to lymphedema, (3) of mixed venous/lymphatic origin, (4) associated with the diseases causing lymphedema, and (5) associated with lymphedema treatment. The RCTs identified have been performed only among patients with venous ulcers (outside the scope of this review) and for malignant ulcerations.

LYMPHEDEMA SKIN CARE

Over-the-Counter Topical Agents

Emollients containing lactic acid, urea, ceramides, glycerin, dimethicone, olive fruit oil, or salicylic acid have been recommended to assist in hyperkeratotic skin desquamation.[11] Salicylic acid is also a keratolytic agent that may or may not enhance the penetration of other topical agents. The compatibility of the concomitantly applied agent will determine if penetration is enhanced, diminished, or unchanged. Salicylic acid ointment (6%), along with skin and nail care regimens, has been reported to reduce filariasis-related adenolymphangitis (ADL) attacks.[23] Adenolymphangitis involves painful lymphadenopathy and retrograde lymphangitis, usually affecting the inguinal nodes, genitalia, and lower extremities, which leads to extreme swelling, elephantiasis, secondary infection, and sometimes skin breakdown.

Table 1.

A RUBRIC FOR LYMPHEDEMA SKIN DISORDERS

Skin disorders directly caused by lymphedema	Lymphedema rubra	The blanchable redness of affected skin due to vasodilation within lymphedematous tissue, often confused with cellulitis.[7] This clinical constellation of findings is not "hot" to the touch and usually resolves with elevation. Lymphedema rubra is felt to represent hyperemia due to proinflammatory changes from the altered protein content of the interstitium and may be similar to the pathology of acute lipodermatosclerosis (LDS). See Figures 1A and 1B. In addition, cellulitis has a distinct red margin in contrast to lymphedema rubra, where the margin is indistinct.
	Skin fissures	Breaks in the epithelium developing between adjacent skin lobules. These slit-like changes in the skin can be superficial or deep, prone to breakdown and wound formation from moisture accumulation. They are common sites for initial manifestations of fungal infections. See Figure 2.
	Dermal lichenification	Hyperkeratosis, parakeratosis, and irregular acanthosis due to overproduction of keratin layers in the skin.[8,9] The skin is thickened as a function of lymphedema, perhaps exacerbated by chronic scratching and rubbing due to the pruritus of stasis dermatitis.
	Papillomas and fibromas	Benign tumors of epithelial, fibrous, or connective tissue growing exophytically in finger-like fronds, resulting from the chronic inflammation associated with lymphedema. These tumors can range in size from only a few millimeters to tumors larger than the patient's digits.[9] Small sandpaper-type papillomas are called fine papillomatosis. See Figure 3.
	"Mossy" lesions (eg, "mossy foot")	Extensive fine papillomatosis,[8,10] often with associated lymphorrhea. See Figures 4A and 4B. Internationally, the term "mossy foot" may be reserved for "podoconiosis," a unique form of lymphedema caused by years of barefoot contact with silicate-rich soil. The term "mossy foot" has been used to describe the fine extensive papillomatosis and not necessarily the disease podoconiosis.
	"Frog's spawn"	Multiple larger papillomas[9–11] that develop due to chronic lymphedema. See Figures 5A and 5B.
	Dermal fibrosis	Woody changes of the skin.[12] When associated with venous stasis, the legs are often referred to as having an "inverted champagne bottle" shape or a "bowling pin" deformity. See Figure 6. The term LDS has also been used to name these clinical findings.
	Nodular fibrosis	Protruding isolated fibrotic lesions due to chronic inflammatory process of the skin.[13,14] See Figure 7.
	Lymphangiectasia/lymphangioma	Dilated lymphatic vessels[9,11]
	Lymphorrhea/lymphocutaneous fistula	Leakage or weeping of lymph fluid through the skin surface. Drainage can be copious. Lymphatic fluid may transude through a region of the skin[9,12] or may be caused by a lymphocutaneous fistula (passageway between a lymphatic vessel and the skin).
	Elephantiasis verrucosa nostra	Characterized clinically by malodorous hyperkeratosis with generalized lichenification, cobblestoned papules, and verrucous changes of the skin. This is often associated with chronic lymphedema that is associated with extreme enlargement of the involved body part. Without intervention, slowly progressive cutaneous changes will result in grotesque enlargement of the affected area.[15] Castellani coined the term "elephantiasis nostra" (meaning "from our region" and not due to filarial disease). Castellani theorized that regardless of subtype the cause was repetitive streptococcal bacterial invasion causing lymphangitis with subsequent obstruction of lymphatic outflow and the development of elephantiasis. Although striking clinically, histologic examination reveals only pseudoepitheliomatous hyperplasia with dilated lymphatic spaces in the dermis, accompanied by chronic inflammation and fibroblast proliferation.[8,10] See Figures 8A and 8B.
	Massive localized lymphedema (MLL)	Large solitary polyps, solid or papillomatous plaques, pendulous swellings, or tumors mimicking sarcoma. These findings are usually associated with obesity and are often mistaken for malignant tumors, hence the term "pseudosarcoma." A series of 24 patients with MLL reported that the tumors were significantly correlated with history of cellulitis and obesity ($P = .05$).[16] The mechanism is assumed to be stagnation of proteins and associated water in the interstitium, which leads to inflammation and an accumulation of fibroblasts, adipocytes, and keratinocytes that transform the initially soft edematous tissue into hard fibrotic tissue with stiff, thick skin. Activated cytokines stimulate the development of redundant tissue. Histologically, all cases exhibited dermal edema, fibroplasia, dilated lymphatic vessels, uniformly distributed stromal cells and varying degrees of papillated epidermal hyperplasia, inflammatory infiltrates, and hyperkeratosis.[9,11,16] See Figures 9 and 10.
	Lymphangiosarcoma	A rare malignant tumor that can occur in patients with long-standing lymphedema[17]

(continues)

Table 1.

A RUBRIC FOR LYMPHEDEMA SKIN DISORDERS, CONTINUED

Skin disorders indirectly related to lymphedema/obesity	Folliculitis, lymphangitis, cellulitis	Abidha et al[18]
	Dermatitis and eczema	Fife et al[9]
	Lichen simplex chronicus	Thickened, leathery, hyperpigmented skin usually caused by recurrent irritation such as the "itch-scratch" cycle. See Figure 11.
	Fungal infections	Fife et al.[9] See Figure 12.
	Pressure injuries	Often from heavy limbs.[9] See Figure 10.
	Limb enlargement and distortion	Often due to fatty deposition. See Figure 2.
Skin disorders associated with diseases causing lymphedema	Nonhealing surgical wounds	
	Irradiated wounds	
	Malignant wounds	
	Traumatic wounds	
	Venous stasis ulcers and phlebolymphedema	
	LDS and stocking erythroderma	
Skin disorders in mixed venous and lymphatic disease	Due to the common association of venous insufficiency and ulceration with lymphedema, some additional discussion of skin disorders in mixed venous and lymphatic disease (phlebolymphedema) is warranted. Phlebolymphedema occurs due to mixed venous/lymphatic disease. In the presence of venous hypertension, the increase in lymphatic load becomes greater than the lymphatic transport capacity. Initially, the edema is low-protein edema, which is commonly associated with venous disease. However, the long-standing increase in lymph pressure results in the accumulation of proinflammatory and other proteins in the surrounding soft tissue. Thus, phlebolymphedema is distinct from the edema resulting from pure venous insufficiency. The majority of patients with venous insufficiency will have normal lymphatic systems, which are overwhelmed by the venous load due to 1 or more systemic contributing factors.[19,20] See Figures 6, 7, 8, 13, and 14. Phlebolymphedema can be further differentiated into 2 subtypes[21]:	
	Dynamic insufficiency phlebolymphedema	In the most common type of phlebolymphedema, there is normal lymphatic function, but the lymphatics are overwhelmed by the load of the venous and interstitial system. Many systemic contributing factors potentially contribute to the etiology of this condition including primary and secondary lymphedema (a more detailed discussion is beyond the scope of this article).
	Lymphatic insufficiency phlebolymphedema	Also called mechanical insufficiency phlebolymphedema. This occurs when there is damage to the lymphatics resulting in an inability to transport the venous and interstitial fluid loads, eventually leading to an accumulation of proteins and proinflammatory mediators.
	Regardless of etiology of phlebolymphedema, the skin findings are similar and are thought to be due to proinflammatory lymph fluid in the interstitium resulting in chronic panniculitis–type inflammation and fibrosis of the dermal and epifascial tissues. Acute and chronic LDS are both forms of panniculitis (inflammation of subcutaneous fat) in which patients present with skin induration (due to dermal fibrosis) and increased pigmentation.[22] The pathology is variable and can show fibrosis of dermal layers and lobular and septal panniculitis. Both acute and chronic LDS are reversible if the swelling is reduced and compression is maintained. See Figures 7 and 13.	

Recurrent attacks can last 4 to 7 days and occur up to 4 times per year, depending on the severity of the lymphedema.

Pharmacologic Topical Agents

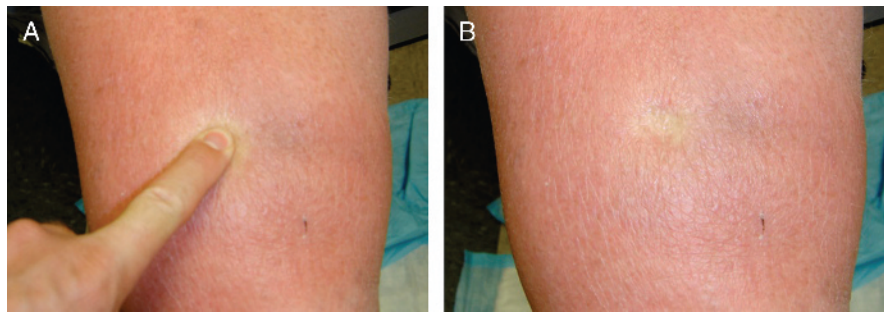
Topical steroids are available in cream, lotion, foam, or ointment form and divided into 7 classes by potency. These pharmacologic agents may be fluorinated or nonfluorinated, and they are the mainstay of treatment for inflammatory dermatoses, such as dermatitis. Excellent references are available to guide the clinician in the proper use of topical steroids.[24,25] The FDA-approved medications for atopic dermatitis include the topical calcineurin inhibitors tacrolimus and pimecrolimus,[26] which may have beneficial off-label use in treating stasis dermatitis.

Antibiotics and Skin Hygiene

Patients with recurrent lymphangitis and systemic signs of infection may require long-term, prophylactic, systemic antibiotics to reduce infectious episodes.[27] There is ample evidence that repeated attacks of ADL contribute to lymphedema progression and elephantiasis development in filarial disease. A double-blind, placebo-controlled, prospective trial was performed in India among 150 patients with filarial disease who suffered at least 2 ADL attacks within a year.[23] Subjects were randomly allocated to a year-long regimen of intensive self-care or intensive self-care with 1 of 5 interventions composed of different combinations of penicillin, oral diethylcarbamazine (DEC), framycetin ointment (topical aminoglycoside similar to neomycin), placebo tablets, and zinc oxide ointment. Overall, mean incidence of ADL attacks decreased from 2.7 annual episodes per participant to 0.38 during the treatment year ($P < .01$). The greatest reduction in incidence was seen in 58 subjects who received penicillin (with or without DEC). Interestingly, in the subsequent year, incidence of ADL attacks increased from the treatment year, indicating that chemoprophylaxis should be continued for more than a year. Even in

Figure 1.

A. LYMPHEDEMA RUBRA IN PATIENT WITH PHLEBOLYMPHEDEMA. B. THIS PHOTOGRAPH WAS TAKEN DIRECTLY AFTER FINGER RELEASE



the placebo group, incidence of ADL in the treatment year significantly declined, indicating that intensive self-care alone may help prevent infection.[23] Whether diluted bleach baths can reduce bacteria colonization and prevent recurrent infections has yet to be studied in lymphedema-affected populations.

Another RCT in filarial-endemic India compared oral penicillin, DEC, and topical antiseptic (Betadine ointment).[28] Foot care was an integral component of all regimens. Approximately half of all patients had a 75% to 100% edema reduction after a 90-day treatment. All 3 drug regimens significantly reduced ADL frequency after 1 year, possibly because of the positive effect of foot care.[28]

Figure 2.

SEVERE ELEPHANTIASIS OF CHRONIC LYMPHEDEMA OF THE FOOT WITH PAPILLOMATOSIS, LIPODERMATOSCLEROSIS, NODULAR SCLEROSIS, AND FIBROSIS OF DERMAL SKIN (NOTE PROMINENT SKIN FISSURES)

Although neither study specifically included patients with open wounds, nearly a third of patients with filarial lymphedema have "entry lesions" (areas of broken skin) acting as potential infection sources.[29] All studies examining the effectiveness of antibiotic regimens demonstrated that basic hygiene, including good foot care, decreases infection incidence among patients with filarial-related lymphedema.

LYMPHEDEMA WOUND CARE

Pharmacologic Agents in Venous Ulcer Healing

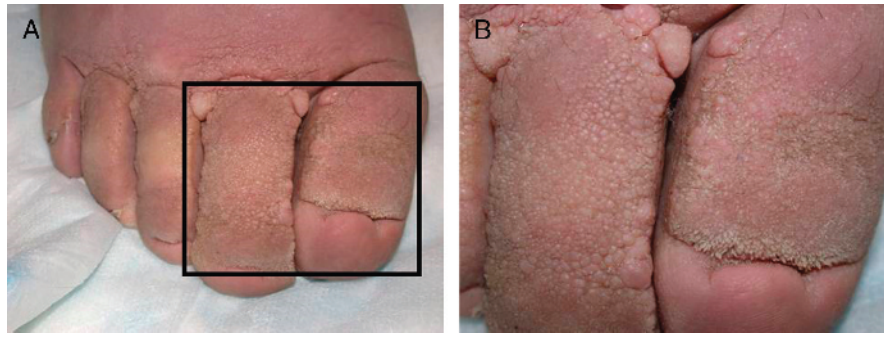
Many pharmacologic agents have been evaluated in venous ulcer healing. Horse chestnut seed extracts, flavonoids, red vine leaves extracts, alcoholic extracts from *Centella asiatica*, procyanidolic

Figure 3.

FIBROMA IN THE SETTING OF A LYMPHEDEMATOUS LOWER EXTREMITY

Figure 4.

A. MOSSY FOOT (SEE AREA INSIDE BOX ENLARGED, FIGURE 4B). B. NOTE FINE PAPILLOMATOSIS



oligomers, Pycnogenol, O-(β-hydroxyethyl)-rutosides, and pentoxifylline are suggested as effective prevention or treatment for venous ulcers by influencing microcirculation.[30,31] Some have supporting RCT data.[32,33] Effectiveness beyond venous disease requires further investigation.

Malignant Wound Management

Malignancy can arise from a chronic inflammatory state such as a "Marjolin's ulcer," an aggressive squamous cell carcinoma presenting in an area of chronically inflamed or scarred skin, such as a burn scar, post-radiotherapy scar, or a diabetic foot ulcer. Malignant tumors, either local or metastatic, may become rapidly progressive and exuberant, resulting in open wounds that are commonly referred to as "fungating,"[34] although the term is more colloquial than pathologic. Wounds with malignant cells cannot heal. Occasionally, patients may achieve healing of the area following surgery, radiation, or chemotherapy if malignancies are eradicated, but such wound care is usually palliative. The goals are to slow disease progression and optimize quality of life by alleviating physical symptoms (eg, exudate, odor, pain, bleeding) through appropriate dressing selection.[35] Compared with the normal wound bed, leukocytes in malignant wounds are reduced and exudate is increased because of secretion of vascular permeability factors. As the tumor extends into neighboring tissue, capillaries become disordered and tumor clotting mechanisms are altered. The tissue is friable and may bleed, requiring hemostatic agent application.[36,37] Odor from fungating malignant wounds can be difficult to control and may be the most distressing feature of these lesions (Figure 15).

A Cochrane review of treatments for fungating wounds identified 2 trials that included 63 patients.[34] One RCT in women with superficial breast lesions reported that treatment with a 6%

Figure 5.

A. "FROG's EGGS" CHANGES IN A PATIENT WITH LYMPHOCUTANEOUS FISTULA OF THE GROIN. B. "FROG's EGGS" CHANGES ON THE LEG

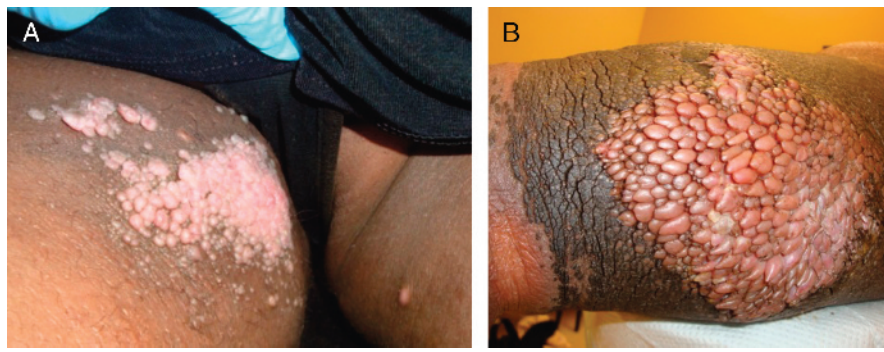


Figure 6.

CLASSIC "CHAMPAGNE BOTTLE" CHANGE OF PHLEBOLYMPHEDEMA. PATIENT HAS CHRONIC VENOUS INSUFFICIENCY WITH SECONDARY LYMPHEDEMA DEVELOPMENT AND WOODY CHANGE DERMAL FIBROSIS

miltefosine solution delayed tumor progression when compared with placebo. The study reported that time to treatment failure (defined as progression of lesions or subject withdrawal) was significantly longer in the miltefosine group (median, 56 days) than in the placebo group (median, 21 days). A second trial comparing topical metronidazole with placebo reported that metronidazole was effective in odor reduction.[34] Odor may also be controlled with use of charcoal dressings. Cadexomer iodine has been successfully used as a topical antimicrobial. Seaman's[35] review article discusses dressing options for malignant wounds based on exudate amount, location, pain, and other important factors. These recommendations are extensively referenced from case reports and series.

Antimicrobial Dressings

Silver is a broad-spectrum antimicrobial that is effective against problematic bacteria such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecalis*. The mechanism of action includes effects on bacterial respiration, nucleic acid structure, and cell membrane permeability. In addition, silver has low toxicity to mammalian cells and anti-inflammatory properties, perhaps in part by inhibiting matrix metalloprotease production.

A prospective trial was performed using a nanocrystalline silver hydrocellular dressing under a multilayer bandage system among 8 patients with chronic lower limb lymphedema and ulceration.[38] In this cohort, ulcers (associated with primary lymphedema, obesity, active tumor, and venous disease) of mean size 10.5 cm^2 were completely healed in an average of 26 days with daily dressing changes and no adverse events.[38] A case report from Ghana describes the use of a silver-containing polymer dressing to heal a large axillary lymphatic abscess later determined to be the result of active tuberculosis (untreated during wound care).[39] The dressing application also resulted in marked pain reduction, emphasizing one of the important roles of proper dressing selection.

The effect of a dressing regimen based on wound characteristics is demonstrated by a study of 12 women with malignant, fungating wounds due to progressive breast cancer.[40] The wounds were evaluated by size, stage, and exudate, and a protocol based on appropriate cleansing, moist wound care, periwound area protection, and contaminant avoidance was prescribed using several dressings: alginate (Algisite; Smith & Nephew, Fort Worth, Texas), hydrocellular (Allevyn Adhesive; Smith & Nephew), hydrogel (Intrasite Gel; Smith & Nephew), and carbon (Actisorb Plus; Systagenix, an Acelity Company, San Antonio, Texas). All women reported that these wound care products were more comfortable and provided increased quality of life because of odor and exudate management. Results suggest that dressings selected according to basic wound care principles can improve palliation.[40]

APPLICATIONS TO CLINICAL (BEST) PRACTICE FOR LYMPHEDEMA SKIN AND WOUND CARE

Skin Care

Skin and nail care is a vital component of lymphedema management, as proper care may prevent ulceration, as well as facilitate ulcer healing with RCT-reported evidence to reduce

Figure 7.

PATIENT WITH EXTENSIVE NODULAR FIBROSIS CHANGES OF ADVANCED PHLEBOLYMPHEDEMA WITH LIPODERMATOSCLEROSIS

Figure 8.

A. ELEPHANTIASIS VERRUCOSA NOSTRA. B. ELEPHANTIASIS VERRUCOSA NOSTRA (SAME PATIENT) AFTER MONTHS OF TREATMENT WITH LACTIC ACID AND HYDROCOLLOID DRESSINGS

Figure 9.

MASSIVE LOCALIZED LYMPHEDEMA OF THE POSTERIOR THIGH WITH ULCERATION

Figure 10.

MASSIVE LOCALIZED LYMPHEDEMA OF THE UPPER ARM WITH PRESSURE ULCERATION

Figure 11.
LICHEN SIMPLEX CHRONICUS

Figure 12.
FUNGAL INFECTION (TINEA PEDIS) OF THE SOLES OF THE FEET

Figure 13.
LIPODERMATOSCLEROSIS IN PATIENT WITH PHLEBOLYMPHEDEMA

Figure 14.
MILD PHLEBOLYMPHEDEMA PATIENT WITH SLIGHT SAUSAGE-TOE CHANGES AND LIPODERMATOSCLEROSIS AND VENOUS ULCERATION

Figure 15.

A,B. PATIENTS WITH BREAST CANCER LYMPHEDEMA WITH AUTOAMPUTATION-TYPE ULCERATIONS

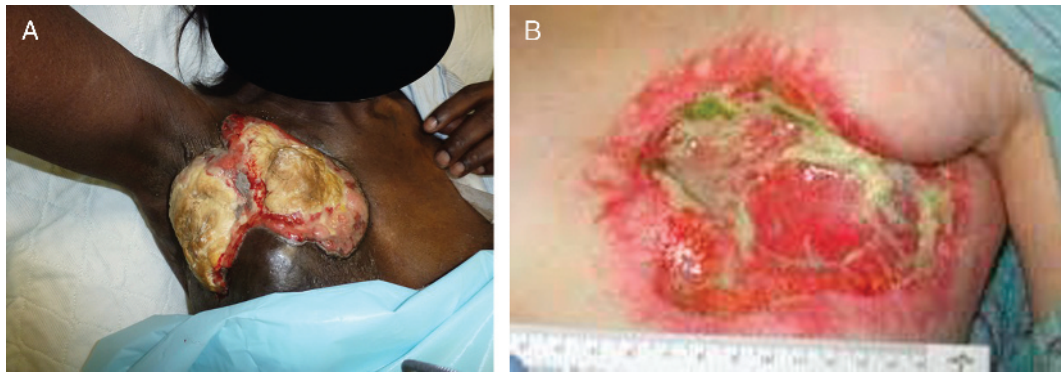


Table 2.

SUMMARY OF REVIEWED LITERATURE

Citation	Study Design	Reported Findings
Morgan et al[1]	Literature review: 6 qualitative studies 1 disease-specific tool 4 cross-sectional studies 8 longitudinal studies	Lymphedema has major physical, psychological, and social implications for health-related quality of life A coordinated approach to treatment and management including patient support Requires comprehensive, patient-centered education program for health professionals Health-related quality of life must be a key element when evaluating success of treatment and management
Tan et al[2]	Retrospective cohort 568 patients Diagnosis of cellulitis Recorded factors associated with acute hospital admissions and survival Used primary end point of deaths within 1 y of admission for cellulitis	Characteristics of patients at high risk of mortality: Lower limb edema Ulceration Previous myocardial infarction Blunt injury Additional significant predictors of mortality: Patient's age Penetrating injury Liver disease Long-term use of drugs causing sodium and water retention Treatment with intravenous flucloxacillin a significant predictor of survival
Cooper and White[3]	Literature review Expert commentary	Illustrates difficulties associated with management of cutaneous infections in lymphedema Knowledge of complex risk factors is increasing Contribution of repeated infections and acute inflammation to lymphatic deterioration are beginning to be understood Need to prevent and manage effectively is evident but not universally realized
Dupuy et al[4]	Case-control 167 patients admitted to hospital for erysipelas of the leg 294 controls in 7 hospitals	Independently associated with erysipelas of the leg: Disruption of the cutaneous barrier (leg ulcer, wound, fissurated toe-web intertrigo, pressure injury, or leg dermatosis) Lymphedema Venous insufficiency Leg edema Being overweight No association observed with diabetes, alcohol, or smoking
Olszewski et al[5]	30 patients in 4 stages of lower limb lymphedema Punch skin biopsy, tissue fluid, lymph fluid collected	Bacteria may colonize interstitial spaces of lymphedema patients Protein-rich fluid characteristic of lymphedema enhances bacterial growth Immune compromise often associated with lymphedema High likelihood of persistent and recurrent infection
McCann et al[6]	Case study	Open wounds are expensive because of dressing costs, doctor visits, and time lost from work Estimated cost of nursing and home care products is approximately $325,000
Zuther[7]	Text book	Text book

(continues)

Table 2.

SUMMARY OF REVIEWED LITERATURE, CONTINUED

Citation	Study Design	Reported Findings
Duckworth et al[8]	Case study	Although striking in clinical appearance, biopsy revealed only moderately abnormal findings: Pseudoepitheliomatous hyperplasia with dilated lymphatic spaces in the dermis Chronic inflammation and fibroblast proliferation
Fife et al[9]	Case studies	Health-related quality of life often determined by number and type of comorbidities present with morbid obesity Complications of lymphedema and morbid obesity are magnified by their association → For example, cellulitis from lymphedema made more dangerous by diabetes
Richard et al[10]	Convenience sample 188 lymphedema patients Symptoms Treatment preferences Quality of life	Higher-stage lymphedema more likely to have an acute attack 80.3% had used treatments (68.1% traditional products, 38.8% scarification) Medication was preferred treatment for acute attacks Difficulties performing activities as a result of lymphedema (walking to field, carrying heavy load) Felt avoided by community and family 70% at high risk of depression, increased with lymphedema stage
Fife and Carter[11]	5-y retrospective review of data and case studies 575 men, 889 women Patient records (2000–2005)	Treatment of lymphedema made more complicated by comorbidities from morbid obesity Massive localized lymphedema will recur unless obesity is addressed Obesity must be treated with lymphedema if long-term success is to be achieved
Stigant[12]	Case study	Cohesive short-stretch bandages: Stayed in place, required fewer applications, and were well tolerated Cost-effective with nursing time—2/wk treatment, familiar protocols from ulcer management Allowed treatment in community, reducing need for specialist visits
Sadeghian et al[13]	Case Study	With progression of lymphedema, hyperplastic changes with warty epidermis and elephantiasis evident Disability due to limb swelling can be severe, but overall prognosis is good Nodular fibrosis is an uncommon complication of elephantiasis
Price[14]		Legacy literature
Schissel et al[15]	Case report	Without appropriate intervention, cutaneous changes culminate in massive, grotesque enlargement of the affected region Natural history and management of elephantiasis nostras are discussed
Lu et al[16]	Case studies, literature review 24 cases of localized lymphedema 18 females, 6 males	Localized lymphedema should be considered in etiology of skin tumors Trauma, obesity, infection, and/or inflammatory disorders contribute to localized elephantiasis
DeVita et al[17]	Text Book	Text book
Abidha et al[18]	Survey 56 lymphedema patients Determined care seeking	Majority of patients sought medical management only No difference in care between government/private facilities
Farrow[19]	Expert opinion	Systemic and contributing factors can exacerbate phlebolymphedema and should be corrected Accumulation of proinflammatory lymph in interstitium increases risk of infection and chronic lipodermatosclerosis → Standard of care for lymphedema should be complete decongestive therapy with goal to control swelling
Bunke et al[20]	Expert opinion	Phlebolymphedema is treatable, although larger trials are needed to validate these observations Venous insufficiency of phlebolymphedema is responsive to therapeutic measures that do not damage functioning lymphatics Sclerofoam and effective compression ablates venous abnormalities without damaging lymphatics Foam sclerotherapy yields a significant improvement in symptoms, physical functioning, and cosmetic appearance, with a marked decrease in longstanding lymphedema
Piller[21]	Expert opinion	Suggestions and guidance on differential diagnosis, diagnostic procedures and classification, early detection, staging, treatment, and management
Falanga[22]	29 patients 15 venous ulceration 14 other ulcers	Legacy study Pericapillary fibrin is easily demonstrable in dermis adjacent to venous ulcers Presence of dermal pericapillary fibrin may provide diagnostic help in unknown ulcers
Joseph et al[23]	Double-blind, placebo-controlled, clinical study 150 subjects ≥2 adenolymphangitis (ADL) attacks in 1 y Randomly allocated to self-care program 1/5 treatments for 12 mo	Mean incidence of ADL attacks decreased from 2.7 to 0.38 episode/person-year Greatest reduction was from penicillin (with or without oral diethylcarbamazine) Incidence of ADL significantly lower in control group → affected-limb care on its own helps to prevent some attacks ADL attacks posttreatment increased → chemoprophylaxis should be continued ≥1 y Streptococci have a role in the etiology of ADL → combination of penicillin prophylaxis and affected-limb care in filariasis-control programs to decrease morbidity
Williams and Venables[24]	Expert opinion	Legacy literature
Rich[25]	Expert opinion	Many skin changes in lymphedema can be minimized by good skin care in early stages Skin changes are a response to edema, chronic inflammation, and modified immune response Skin care aims to maintain skin integrity and reduce infection Good hygiene and regular application of emollients are important for good skin care

(continues)

Table 2.

SUMMARY OF REVIEWED LITERATURE, CONTINUED

Citation	Study Design	Reported Findings
Flugman and Clark[26]	Expert opinion	General reference
Olszewski[27]	Randomly-selected open clinical trial 45 patients	Long-term penicillin administration decreases the frequency of adenolymphangitis attacks A future double-blind, random, placebo-controlled clinical trial is needed
Kerketta et al[28]	RCT 300 patients Randomly allocated to 1 of 3 treatment regimens	Limb circumferences showed 50% of patients in all regimens had reduced edema after 90 days In all regimens, 20% of those whose edema improved experienced a reduction of 75%-100% Most others achieved a reduction of <25%
Yahathugoda et al[29]	Case studies In-depth interviews from 101 cases of lymphatic filariasis with lymphedema	Treatments were seen as ineffective and not often sought Modern lymphedema management had not reached this area
Belcaro et al[30]	Clinical trial 5-y follow-up (N = 388) 4 nonrandomized groups Various comorbidities and treatments	Decrease in cholesterol levels linked to copper-related lipoprotein oxidation Long-term efficacy of hydroxyethyl rutinosides (HR) in chronic venous insufficiency patients with mixed venous and diabetic microangiopathy HR treatment (even without compression) will prevent severe complications of chronic venous insufficiency (CVI)
Wollina et al[31]	Review CVI Excludes ulceration	Treatment of microcirculatory dysfunction → pharmacologic intervention, compression therapy, or a combination of both
Jull et al[32]	Systematic review Randomized controlled trials (RCTs) Venous leg ulcers Compared pentoxifylline, compression, placebo, and other treatments	Pentoxifylline gives added benefit to compression for venous ulcers and is effective without compression
Pittler and Ernst[33]	Intervention review	Horse chestnut seed extract is an efficacious, safe, short-term treatment for chronic venous insufficiency Larger, definitive RCTs are required to confirm the efficacy of Horse chestnut seed extract
Adderley and Smith[34]	Cochrane review 2 trials 63 patients Limitations and low power	Miltefosine delayed tumor progression when compared with placebo Topical metronidazole reduced malodor No statistically significant tumor delay when metronidazole was compared with placebo
Seaman[35]	Expert opinion and review	Cutaneous wound management in advanced cancer Assessment of malignant wounds Selection of appropriate dressings Related symptom management Patient and family support Implications: Thorough understanding of care of malignant wounds will assist palliative goals of care including optimal symptom management, odor and drainage control, and emotional support
Haynes[36]	Expert opinion	General reference
Moore[37]	Expert opinion, case study	Treatment of cutaneous metastases delays progressive disease, manages current symptoms, and maintains quality of life with chemotherapy, radiation therapy, and surgery Implications: skin assessment, treatment of skin lesions, and provision of psychosocial support
Forner-Corder et al[38]	Case studies 8 patients with ulcers were cleansed and dressed	All ulcers completely healed in 1-9 wk
Benskin and Bombande[39]	Industry-sponsored case study	Nonadhesive dressings and wound filler provided effective wound management for multiple ulcers on edematous lower legs from initiation of treatment to complete wound closure, even without the benefit of compression
Lund-Nielsen et al[40]	Case studies 12 women 4-wk wound care intervention Used evidence-based wound care principles and psychosocial support Pre-post interviews	Malodorous and oozing wounds: Trigger anxiety about seepage Clothing options limited Cause suppression of need for physical closeness and sexual activity With modern wound care products: Patients secured against seepage and odor Sense of comfort—able to dress as they wished Were given a sense of freedom they had not felt for a long time
Boyd et al[41]	Case study	History, clinical, pathology, newer treatments of elephantiasis nostras verrucosa are discussed
Lymphoedema Framework[42]		International consensus report
Franks and Morgan[43]		General reference

Table 3.

BASIC SKIN CARE REGIMEN

Daily hygiene with careful washing
Because soaps are drying, moisturizing soap substitutes are recommended.

Avoidance of skin damage or trauma
Protection from sunburn, cuts, insect bites, injections, and hot water includes the use of appropriate shoes for patients with lower extremity lymphedema and gloves for certain activities involving the affected upper extremities (eg, gardening). Use of an electric razor for shaving has been suggested to reduce risk of skin trauma.[44,45]

Daily application of emollients without perfume
Emollients are moisturizers that help the epidermis to retain water and diminish water loss (eg, bath oils): Regular use of ceramide-containing emollients reestablishes the skin's protective lipid layer, thus preventing water loss. These products are available as either lotions (oil and water preparations that usually have more water than oil and thus have a short-lived effect) or creams (oil-in-water or water-in-oil emulsions). Creams are often the best option for dry skin. As emollients may damage the elastic component of compression garments, current recommendations include avoiding application immediately before putting on hosiery.[25]

Dermatologic preparations for specific skin problems
Topical steroids, antifungals, and antimicrobials have been successfully used off-label for the conditions associated with lymphedema, such as tazarotene gel 0.1% for which there is a case report in the treatment of elephantiasis verrucous nostra.[41] Tacrolimus in topical formulation has been suggested for off-label use with severe stasis dermatitis as a possible alternative to topical steroids.

Good nail hygiene
This can reduce bacterial and fungal entry points into the body.

likelihood of recurrent infection.[23] Skin care regimens should aim to improve the condition of the epidermis so that it remains hydrated and supple and thus is more likely to remain intact. A basic skin care regimen is described in Table 3.

Lymphedema Wound Care Dressing Selection

Limited available data confirm that a standardized approach to dressing selection can reduce pain, improve quality of life, reduce system infection, and promote healing.[42] Even patients on palliative wound care protocols benefit from this approach. Modern dressing principles are based on appropriate cleansing routine, moist wound care, periwound area protection, and contaminant avoidance. Antimicrobial dressings may reduce bacterial bioburden. Control of exudate usually represents the primary challenge, requiring absorptive products.

FUTURE WORK RECOMMENDATIONS

There are no large RCTs that pertain specifically to management of lymphedema-related wounds. Studies of this type are very challenging owing to the heterogeneity of patients and multiple confounding factors affecting healing, complicating trial design. Furthermore, lymphedema-associated wounds represent a relatively small proportion of the wound care population (compared with diabetic foot ulcers, for instance).

When the International Lymphoedema Framework began to develop a best practice document for the management of patients with lymphedema, Moffat et al[42] questioned how clinicians should develop guidelines when traditional evidence of RCTs and quality observational studies was not available. In cases where clinical trial literature is scant, conflicting, or unclear, a consensus approach is recommended based on expert opinion regarding clinical vignettes. A group of experts should be asked to describe how to manage a particular patient in a primary care setting and address a set of questions about key areas of practice. Each vignette and set of questions is supported by the best available literature, systematic reviews, and existing (inter)national guidelines.[42] The use of consensus to develop best practice documents may be necessary in other healthcare areas because of lack of evidence to support many aspects of clinical practice.[43]

A similar consensus approach may be the best way to develop future lymphedema wound care guidelines. The "registry" concept[30] promises to be an excellent way to gather data regarding effectiveness of pharmacologic or topical agents among patients with lymphedema with venous insufficiency as a component of their disease process. The US Wound Registry, a Qualified Clinical Data Registry recognized by the Centers for Medicare & Medicaid Services, is currently collecting such data (www.uswoundregistry.com). Analysis of clinical and research data in the American Lymphedema Framework Project–initiated Minimum Data Set will enable more sophisticated analyses in the search for answers to these complex clinical questions. ●

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