Since its inception, osteopathic medicine has been concerned with the lymphatic system. Research has demonstrated the effectiveness of lymphatic osteopathic manipulative treatment (OMT) techniques in affecting fluid management and immune function. Many of the functions provided by the lymphatic system and augmented by OMT are necessary for proper wound healing. The authors highlight the unique contribution of the lymphatics to wound healing, as well as the unique contribution of OMT to lymphatic-directed treatment of patients with chronic wounds. The authors propose that this information be used as a basis for research into the effects of OMT on chronic wound healing in patients.

Since its tenets were first announced by Andrew Taylor Still, MD, DO, in 1874, osteopathic medicine has been concerned with the lymphatic system and its role in health and healing. Dr Still believed that “by and from [the lymphatics] ... any division of the body receives what we call reconstruction, or is built anew.”¹ Indeed, Dr Still viewed the lymphatics as a “fountain of life-giving water, provided by nature to wash away impurities as they accumulate in our bodies.”¹ Although Dr Still did not seek to produce a handbook of osteopathic manipulative treatment (OMT) techniques, several lymphatic OMT techniques have been presented and examined in the osteopathic medical literature since the late 19th century.²

Much like the concept of the lymphatics, the history of wound healing in medical literature far predates osteopathic medicine. However, only relatively recently have we begun to understand the various mechanisms of wound healing—and there are a great many components of the wound-healing process that remain a mystery. Among the particulars of the wound-healing process that we do understand, many are directly influenced by the lymphatic system.

In the present article, the state of research regarding lymphatic OMT techniques is reviewed. An overview of the wound-healing process is also presented, including research that demonstrates the influence of lymphatics on wound healing. Finally, we propose that additional research be conducted into the effects of OMT on chronic wound healing in patients—a potentially fertile field for osteopathic medical research.

Lymphatics in Osteopathic Medical Literature

History

Dr Still expressed his reverence for the lymphatic system when he stated “we strike at the source of life and death when we go to the lymphatics.”¹ Unfortunately, Dr Still left a paucity of instruction in specific lymphatic OMT techniques. Nevertheless, evidence indicates that Dr Still and his earliest students used manipulative techniques that were directed at the lymphatic system.²

Since that time, the osteopathic medical literature has included much research on the immune functions of the lymphatic system and secondary lymphoid tissues.²⁻⁵ In addition to osteopathic medical research on immune function, a body of literature has investigated the role of lymphatic OMT in fluid management. Some research suggests that lymphatic OMT techniques produce effects locally and globally that influence vascular and lymphatic flow, with important implications for both congestion and edema.⁶

As early as 1910, published research demonstrated that OMT enhanced immune function.⁴ The OMT techniques described in the early literature were directed toward acute infections.⁵⁻⁷⁻⁸ Perhaps the most celebrated application of lymphatic OMT techniques in regard to infection occurred during the 1918 influenza epidemic.⁹⁻¹⁰ In early osteopathic medical literature, lymphatic OMT is purported to have aided in the removal of waste products and toxins, lymph flow and healing, absorption and processing of toxins, and stimulation of an immune response.⁵ Various lymphatic techniques have
been presented in the literature, most notably the Miller thoracic pump, the hepatic pump, and the splenic pump.\textsuperscript{2,4,5}

**Modern Research**

The efficacy of various manual lymphatic techniques has been evaluated in regard to lymph flow. Dery et al\textsuperscript{4} evaluated a thoracic pump in a rat model. Fluorescein-labeled bovine albumin was injected into the potential space of the rats’ thighs, and the diffusion of this tracer was monitored by sampling blood from a nick in the rats’ tails. This indirect measure demonstrated enhanced lymphatic flow with application of the thoracic pump.\textsuperscript{11}

A more direct measure of lymphatic flow in response to thoracic and abdominal pumps in a canine model was undertaken by Knott et al.\textsuperscript{12} Lymphatic flow was measured by insertion of a flow transducer directly into the thoracic duct. Measurements were made at baseline, after application of thoracic and abdominal lymphatic pump techniques, and during and after exercise. The use of lymphatic pumps resulted in statistically significant, albeit transient, increases in lymph flow in the thoracic duct ($P<.05$).\textsuperscript{12}

Downey et al\textsuperscript{13} directly measured lymph flow in the thoracic duct of dogs in response to application of an abdominal pump, expansion of extracellular fluid volume, and exercise. Again, the efficacy of the lymphatic pump was demonstrated. Thus, we can see that lymphatic flow is directly enhanced by OMT.

In addition to effects on lymphatic flow, influences of lymphatic OMT techniques on the immune system have been evaluated. Measel\textsuperscript{4} injected male medical students with pneumococcal polysaccharide and applied a thoracic lymphatic pump before testing their blood for evidence of immunity and comparing results to those of control students. The test group showed increases in antibody titers to many of the pneumococcal strains, as measured by hemagglutination. The Measel study\textsuperscript{4} suggests that the use of the lymphatic pump enhanced the B-cell component of the immune response.

Mesina et al\textsuperscript{14} demonstrated a transient increase in basophil levels in male medical students after application of a lymphatic OMT technique. Blood was analyzed for complete blood cell count before application, and at intervals after application, of pectoral traction and the splenic pump. A transient basophilia was observed in the test group compared to controls.\textsuperscript{14}

In another vaccine study, Jackson et al\textsuperscript{10} evaluated antibody response to hepatitis B vaccine in healthy individuals. Test group participants received active and passive thoracic pump and splenic pump OMT techniques. Compared with controls, test group participants demonstrated consistently higher titers, with more of the test group achieving protective immunity.\textsuperscript{10}

Additional studies of the effects of lymphatic pumps on the immune system have been conducted with canine models. Hodge et al\textsuperscript{15} subjected dogs to an abdominal lymphatic pump and tested leukocyte counts from thoracic duct samples by means of flow cytometry. Large increases in levels of macrophages, neutrophils, B lymphocytes, and T lymphocytes were observed.\textsuperscript{15} Hodge et al\textsuperscript{16} also demonstrated increases in lymph flow and leukocyte count in the thoracic and mesenteric ducts of dogs after application of an abdominal lymphatic pump technique. Populations of neutrophils, monocytes, CD4+ T cells, CB8+ T cells, and IgA+ B cells were all mobilized from gut-associated lymphoid tissue in response to the lymphatic pump technique.\textsuperscript{16}

From this body of research, it is clear that lymphatic OMT techniques influence the immune system by mobilizing immune cells and enhancing immunity.

There is a paucity of research evaluating the effectiveness of manual lymphatic techniques in regard to wound healing (Figure 1). Weiss\textsuperscript{17} described a case study in which a patient was left with leg edema and chronic wounds after sustaining severe musculoskeletal injuries and undergoing many reparative surgeries. Manual lymphatic drainage treatments—mainly massage-based interventions—were initiated a year after the initial injury. These treatments were augmented with compression dressings beginning in week 3. At the conclusion of 6 weeks of treatment, the patient was discharged with a compression stocking. At 10-week follow-up, a 93% reduction in wound area was observed, illustrating the connection between edema and wound healing.\textsuperscript{17}

Vairo et al\textsuperscript{18} reviewed the literature for the efficacy of manual lymphatic drainage techniques in sports medicine and rehabilitation applications. Their literature search revealed

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Figure 1. The limited research results available on the use of manual lymphatic techniques in wound healing.
3 randomized, controlled trials (with human participants) that met inclusion criteria. Only 1 of these studies was described as osteopathic. In that study, lymphatic drainage reduced pain and swelling and increased range of motion in patients with acute ankle sprains. However, Vairo et al18 also reported multiple case and pilot studies that demonstrated statistically significant improvements in wound healing, in addition to other beneficial results, with manual lymphatic drainage techniques.

Wound Healing
Cellular Responses
A wound—whether the result of 1 or more of a host of internal or external processes—is simply a disruption of normal anatomic architecture and function.19 Wound healing thus is the process of restoring integrity to tissue after the creation of a wound.17

The earliest accounts of wound healing date to about 2000 BC in ancient Sumeria.20 The ancient Egyptians were the first to differentiate between infected and noninfected wounds, and they introduced treatments that addressed asepsis, absorbance, and barriers. Much later, the Greeks categorized wounds as acute or chronic.20 Modern concepts of wound healing continue to build on these basic principles.

Wound healing is a complex process involving a variety of chemical compounds, cells, and tissues. The typical process involves phases of inflammation, cellular migration, proliferation, matrix deposition, and remodeling.20 The proper chemical, fluid, and cellular environment must be maintained to promote healing.

In healing of acute wounds, platelets and wound-active substances initially achieve hemostasis and initiate inflammation. Next, cellular infiltration begins. Neutrophils are the first cells to arrive at the wound site, where they clear debris, control infection, and secrete cytokines. These cells are followed by macrophages, which also clear debris as well as contribute to angiogenesis, matrix deposition, and remodeling. The next cells to arrive are T lymphocytes. Fibroblasts and endothelial cells are the last cells to infiltrate the wound area, continuing the wound-healing process.20

Lymphatics in Wound Healing
In 1995, Mortimer21 suggested that chronic venous insufficiency and lymphatic insufficiency are associated in individuals who have or who are at risk of having chronic ulcers. He further postulated that a breakdown in the lymphatic system predisposes an individual to infection and compromises wound healing.21 In 2003, Macdonald and Mayrovitz22 reaffirmed that postulate. They asserted that managing lymphedema at a wound site enhances the wound-healing process in individuals with and individuals without venous insufficiency. They presented anecdotal evidence of improved wound healing by managing lymphedema in the absence of venous insufficiency, and they called for more research in this area.22

Mouta and Heroult23 asserted that inflammation and fluid overload are central factors in wound healing, with the inflammation triggering the lymphangiogenesis. Thus, in normal wound healing, the fluid overload and influx of leukocytes should be managed by the new lymph vessels.23

This point was further illustrated by Tabibiazar et al24 in 2006. In a murine model of acquired lymphatic insufficiency, the researchers demonstrated intense inflammatory changes and impaired mobilization of immunocompetent cells. Furthermore, they noted a marked upregulation of gene expression related to acute inflammation, immune response, and wound healing.24 These findings indicated that the lymphatic system is uniquely suited to managing inflammation and fluid overload in wounded tissue.

Labanaris et al19 studied the effects of topical negative pressure therapy (ie, vacuum-assisted closure) on lymph vessels in chronic wounds. In their study, patients with mostly intact wound-healing mechanisms demonstrated proliferation of lymph vessels throughout the vacuum-assisted closure procedure. Patients with less-then-robust wound-healing mechanisms caused by a variety of risk factors demonstrated various levels of lymph proliferation and regression. However, the researchers also found that an increase in the density of lymph vessels correlated with improved rates of healing and decreased length of hospital stays.19

Shah et al25 demonstrated yet another facet of the lymphatics’ influence on wound healing. In a contused rat lung, diversion of postinjury mesenteric lymph decreased early mobilization of hematopoietic progenitor cells from bone marrow. However, the decreased mobilization led to an increase in pulmonary infection and a decrease in wound healing. The authors concluded that mobilized bone marrow cells are necessary for wound healing, and that this mobilization is contingent on a properly functioning lymphatic system.25

A review of these studies (Figure 2) makes it clear that the lymphatics play an integral role in the management of many—if not all—types of wounds.

Chronic Wounds
Although there is no universally accepted timeline for classifying wound healing, chronic wounds are those that fail to proceed in an orderly manner through the healing process and thus last for extended durations or occur repetitively.26,27 There is no reliable estimate of the percentage of wounds that become chronic and subsequently require treatment. However, chronic wounds most often occur in the setting of other chronic disease and only rarely develop in healthy individuals.26 The most common comorbid conditions with chronic wounds include atherosclerosis, diabetes mellitus, hypertension, and venous insufficiency.26,27 The incidence of chronic wounds increases with age and obesity.26

There are many conditions that may contribute to the development of chronic wounds, and these conditions result in individuals with and individuals without venous insufficiency, and they called for more research in this area.
Several studies have shown that inflammation and fluid overload are central factors in wound healing, and inflammation triggers lymphangiogenesis. In a murine model of acquired lymphatic insufficiency, intense inflammatory changes and impaired mobilization of immunocompetent cells were demonstrated. Uprogulation of gene expression was related to acute inflammation, immune response, and wound healing. Patients with intact wound-healing mechanisms demonstrated proliferation of lymph vessels with vacuum-assisted closure. Patients with less-than-robust wound healing mechanisms demonstrated various levels of lymph proliferation and regression with vacuum-assisted closure. In contused rat lung, diversion of post-injury mesenteric lymph decreased early mobilization of hematopoietic progenitor cells from bone marrow, leading to an increase in pulmonary infection and a decrease in wound healing.

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Figure 2. Various research results on the role of the lymphatics in wound healing.

In many types of chronic wounds, each type presents a considerable financial impact. Venous ulcers account for as many as 90% of lower leg ulcers, which is equivalent to about 600,000 wounds per year in the United States. Approximately one-third of treated patients may expect 4 or more recurrences of their chronic wounds. A single wound may persist for 5 or more years. The annual cost of treating patients with venous ulcers in the United States is estimated at $2.5 billion to $3.5 billion.26

Diabetic ulcers are another common type of chronic wound. Nearly 8% of the US population has diabetes mellitus. About 25% of people with diabetes mellitus will have a foot ulcer in their lifetime. Each year, a new foot ulcer will develop in 5% of people with diabetes mellitus. Two-thirds of individuals who have had an ulcer will have a recurrence.26 Treatment costs for each ulcer have been estimated at as much as $20,000 per year.26

Pressure ulcers also account for a substantial number of chronic wounds. Individuals at risk for pressure ulcers include elderly patients, debilitated patients, and patients with altered mobility. The estimated annual cost of managing pressure ulcers in the United States is $11 billion.26

There are many other types of chronic wounds, including arterial and mixed arterial-venous ulcers. It is estimated that 1% to 2% of the population in developed countries have chronic wounds. In the United States alone, more than 6.5 million patients have chronic wounds, resulting in an overall annual treatment cost of $25 billion.26

Current Wound Management

Various methods have been used over the centuries to augment, assist, or restore the natural processes of wound healing. Current treatments for patients with wounds may be administered in inpatient acute-care facilities, long-term care facilities, nursing homes, clinician offices, or more than 1000 outpatient wound centers in the United States. Wound care must include a multidisciplinary team-based holistic approach. Social conditions (eg, patient access to care, caregivers, and adequate nutrition; patient ability to care for self) must be evaluated and optimized. Underlying medical conditions, such as hypertension or diabetes mellitus, that cause or contribute to wounds or inhibit the healing process must be addressed and optimized. A patient’s use of medications must be reviewed and adjusted as needed, and nutrition status must be evaluated and optimized.

The characteristics of each wound must be evaluated to determine the underlying pathologic mechanisms that must be addressed. Some pathologic factors, such as vascular insufficiency, may need to be addressed surgically. Standard treatment options are generally directed at managing normal bacterial colonization vs infectious colonization. According to Fonder et al,27 local wound care should include the following:

- occlusive dressings to maintain moisture but avoid frank wetness
- debridement—removing slough, eschar, exudate, bacterial biofilms, and callus from the wound bed by enzymatic, sharp (ie, cutting with scalpel), or mechanical (eg, wet-to-dry dressings) means
- various barriers (eg, moisture-resistant barrier cream)
- various dressing materials, such as alginates and hydrofibers, films, foams, gauzes, hydrocolloids, and hydrogels
- adjuncts, such as compression for venous ulcers, growth factors, hyperbaric oxygen, negative pressure (ie, vacuum-assisted closure) dressings, skin substitutes

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Implications for Future Research

On the basis of the research reviewed in the present article, we see that OMT directed at the lymphatic system is effective in mobilizing fluid, increasing flow through lymphatic drainage, and mobilizing leukocytes. Furthermore, we see that the lymphatics can uniquely respond to and manage inflammation. We also see that in the cascade of wound healing, the lymphatic mechanisms of fluid and leukocyte mobilization and inflammation management are essential to efficient wound healing. Finally, we see that interventions directed at the lymphatic system have resulted in beneficial effects on wound healing.

With these facts as a foundation, it is clear that the time has arrived for research focused on the effects of OMT on wound healing in patients. This research could be conducted on a variety of wounds from multiple sources in many stages of healing, including chronic wounds. New referrals to a chronic wound clinic could be randomly assigned to receive either standard care alone or standard care plus OMT. Patients in the OMT group would be subjected to a standardized protocol of lymphatic-directed OMT administered by experienced osteopathic physicians. Outcomes measured would include wound size, granulation, infection rate, and patient disability.

Conclusion

The time is ripe to strengthen the osteopathic medical profession by expanding the body of evidence-based applications for OMT to include the healing of chronic wounds.

References