Lymphedema

**Strategies for Management**

Sara R. Cohen, OTR/L¹
David K. Payne, Ph.D.²
Richard S. Tunkel, M.D.³

¹ Rehabilitation Service, Evelyn H. Lauder Breast Center, Memorial Sloan-Kettering Cancer Center, New York, New York.
² Department of Psychiatry and Behavioral Sciences, Memorial Sloan-Kettering Cancer Center, New York, New York.
³ Rehabilitation Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, New York.

An important sequela of cancer treatment is lymphedema. Management of this condition must be based on the physiologic functioning of the lymphatic system and tailored to the individual patient's presentation of the disease. Early diagnosis and treatment are essential to prevent worsening of the condition and to help assuage the psychologic impact of the disease. A review of the normal and impaired lymphatic system is presented in this article. Current assessment and treatment options are described, including education of patients in precautions, positioning, exercise, compression garments and bandages, pneumatic pumps, and lymphatic massage. Also included is a discussion of the psychologic impact of the disease as well as management of psychologic symptoms. Various strategies for management of the physical aspects of lymphedema are available. Studies have shown that use of physical treatments such as exercise, compression, and lymphatic massage are effective in reducing the amount of swelling in affected limbs. The specific type, amount, and combination of these treatments continues to be debated. The development of lymphedema is commonly associated with significant psychologic distress that can impact on compliance with physical treatments. Because there is no consensus as to the optimal treatment approach for management of lymphedema, additional research must ensue to determine the efficacy of existing treatments and to develop new management techniques. Clinicians must be attuned to the signs and symptoms of lymphedema in order to make prompt referrals for treatment. *Cancer* 2001;92:980–7. © 2001 American Cancer Society.

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As newer and more effective modes of treatment have become available, cancer survivorship has continued to increase. The role of rehabilitation for this patient population has also increased. Not only can there be residual functional deficits from malignancies, but, more importantly, sequelae from therapeutic interventions can result in functional impairment and decreased quality of life. An important and sometimes overlooked sequela is lymphedema of a limb. In the patient with cancer, this may arise following removal of pelvic or axillary lymph nodes; after radiation therapy to one of these areas; or consequent to malignancy, which may obstruct lymphatic flow out of the limb. In many patients, swelling of the limb is not merely a cosmetic problem. Stretching of soft tissues can be painful, especially with the initial onset or acute exacerbation. More significant swelling may impact function and, if severe, may lead to skin changes and further functional restrictions. Regardless of the amount of edema, for some patients the swelling may cause significant psychologic distress.
The Normal Lymphatic System
The lymphatic system, which is composed of both superficial and deep vessels as well as lymph nodes, is responsible for helping prevent the buildup of interstitial fluid. This drainage system is separate from the general circulatory system and is the conduit for returning tissue fluids to it. The superficial lymphatic system begins with initial lymphatics, which are formed from endothelial cells one layer thick, overlapping each other but not forming a continuous connection. Each of the cells is fastened to the surrounding tissue by anchoring filaments. When there is a change in tissue pressure caused by arterial pulsation, muscle contraction, or respiration, or when the skin is lightly stretched, the anchoring filaments pull on the cells of the initial lymphatics. Because of this, the gap between the cells opens, and fluid drains into the vessels.

Initial lymphatics combine to form larger vessels called precollectors and collectors, which in turn lead to four major groups of lymph nodes in the axillary and inguinal regions. The collector vessels of the lymphatic system contain smooth muscle and valves to regulate flow. The regional lymph nodes drain fluid from the ipsilateral limb and torso quadrant. Deep lymph nodes are located along major arteries for visceral drainage. Major somatic drainage areas are connected via subcutaneous collateral channels, both anteriorly and posteriorly. Lymph returns to the blood circulation at the venous angles, which are formed by the junctures of the internal jugular and subclavian veins. Most of the lymph in the body drains via the thoracic duct, which enters the circulation at the left venous angle. Only the right upper torso, arm, face, and neck drain into circulation on the right side via the right lymphatic duct, which empties into the right subclavian vein.

An important function of the lymphatic system is the prevention of infection. The lymphatic system is responsible for picking up excess interstitial water and protein as well as other cells, including bacteria, which can enter the tissue through small cuts or breaks in the skin. Bacteria and other antigens are transported by the lymphatic system from the interstitium to lymphocytes in the lymph nodes, where an immune response may be initiated.

The Onset and Progression of Lymphedema
Normally, patients may have some degree of postsurgical swelling. This does not portend the onset of chronic lymphedema. However, when the lymphatic system has been damaged during surgery or radiation treatment, its capacity to absorb excess water and cells from the interstitial space is reduced. If the transport capacity of the lymphatic system is reduced enough so that it cannot handle this increase in lymphatic load, an insufficiency of the lymphatic system may occur. This process can develop weeks, months, or years after treatment for cancer.

A common precursor to the development of lymphedema is infection, such as cellulitis or lymphangitis, potentially resulting from any small break in the skin. The decreased capacity of the lymphatic system to carry bacteria away from the tissue, as well as the presence of protein- and oxygen-rich interstitial fluid (which provides a breeding ground for bacteria), may result in the development of an infection. Signs of infection include macular or maculopapular erythematous rash or line, increased warmth, swelling, pain, and fever. With the development of an infection, there may not be an obvious break in the skin. Patients are treated with either oral or intravenous antibiotics. In general, an antibiotic needs to cover the normal skin flora (i.e., gram-positive cocci) and have good skin penetration. Therapy with an intravenous antibiotic is considered when there is more significant local or systemic infection. Some patients develop chronic infections that may necessitate ongoing antibiotic therapy.

In addition to infection, any situation that causes an increase in lymphatic load can predispose patients to development or worsening of lymphedema. The onset of lymphedema may be provoked in a variety of common situations that occur on a daily basis: muscle fatigue resulting from overuse of the limb; vasodilatation following exposure to local or systemic heat; local trauma; vigorous massage; constriction or a “tourniquet effect,” which causes swelling distal to that point; or sustained dependency of the limb. Other situations that may increase lymphatic load include airplane flights and higher elevations; these situations involve decreased atmospheric pressure and may result in increased filtration into the tissue from the blood capillaries.

In the initial stage of lymphedema, the edema may be soft, pitting, and temporarily reduced by elevating the limb. The swelling may appear in only one portion of the limb or throughout the entire limb. One commonly overlooked symptom of lymphedema is pain. Pain may occur from stretching of soft tissues, but it may also be related to conditions such as infection, thrombosis, nerve injury, entrapment syndromes, or tumor recurrence. In one study, 35% of patients being treated for lymphedema reported pain. Many patients also complain of heaviness, fullness, achingness, or fatigue of the limb.

Over time, if left untreated, the edema can be-
come more fibrotic, although the exact mechanism of this process is not clearly understood. A chronic inflammatory state may develop with increased tissue congestion resulting from deposition of collagen and fat in the tissue, which further compromises dilated, incompetent lymphatic vessels and leads to a reduced capacity to evacuate proteinaceous debris. At this stage, the tissue becomes less pitting, more firm or brawny, and elevation of the limb may no longer result in reduction of the edema. The transition to this stage of lymphedema is highly variable. Fibrosis may develop quickly in some patients and take months or years to develop in others. Without treatment, the swelling may continue to increase. Extreme depressions of the natural skinfolds may develop, as well as hyperkeratosis, skin papillomas, ulcerations, lymphatic fistulae, and lymphoceles. Patients with advanced lymphedema, also referred to as elephantiasis, are at great risk for bacterial and fungal infections. Lymphorrhea, a condition that involves external drainage of lymphatic fluid, is an uncommon complication of chronic lymphedema. In rare cases, lymphedema may progress to Stewart-Treves syndrome or lymphangiosarcoma, a highly malignant form of cancer.

**Assessment**

A comprehensive initial evaluation by clinicians with knowledge of the lymphatic system is crucial in determining appropriate treatment for each patient. Deep vein thrombosis may need to be ruled out by venous Doppler studies. Suspicion of recurrent malignancy causing obstruction of lymphatic outflow may require imaging studies, such as magnetic resonance imaging or computed tomography scans. A complete evaluation should include the following: full medical history, including all anticancer therapies; history of edema in the affected limb(s), including other associated symptoms, such as pain or fatigue; history of infection in the affected limb(s); past medical history; a neurologic evaluation; range-of-motion testing; social history, including a discussion of current daily activities and hobbies; and a discussion about the psychologic impact of lymphedema on the patient.

Although various methods exist for assessing the quantity and quality of the edema, the most commonly used assessment technique involves measuring the circumference at several points along the limb. Some have calculated an approximate volume of the limb using these circumferences. Another accurate but clinically impractical method entails volumetric measurements taken via water displacement. Tools that have been utilized include the Harpenden skinfold caliper used to assess trunk swelling, the tissue thickness of lymphedema on the patient.

**Treatment**

As in the area of assessment of lymphedema, no consensus regarding standards for the treatment of lymphedema exist. To address this issue, the International Society of Lymphology Executive Committee in 1995 developed a consensus document that offered an integrated view of the various approaches currently utilized for the treatment of lymphedema. The limited amount of controlled research in this field contributes to the controversy about the efficacy of individual treatment approaches and how treatments should be combined in specific situations.

Treatment options are selected for each patient based on a number of factors, including the patient’s medical history and status of the cancer, the amount and presentation of edema, the patient’s life-style and preferences, and insurance coverage/financial issues. Some schools of lymphedema therapy may recommend intensive daily treatments for all patients followed by patient participation in a home program, while other schools offer the option of a home program as an initial approach, particularly for milder cases. Relative contraindications to treatment include significant congestive heart failure, acute deep vein thrombosis, acute or untreated infection or inflammation of the affected limb, local massage over irradiated soft tissues, and active malignancy. Some have postulated that in the presence of active malignancy, physical treatments for lymphedema may promote spread of that malignancy. The patient’s primary oncologist or surgeon should be consulted to discuss possible contraindications to treatment in the unique context of each patient’s disease. Treatment may proceed with palliative intent, possibly with some limitations, but remains controversial. The hypothetic risk of the spread of cancer may be discussed with the patient.

The goals of treatment are as follows:

1. To educate patients about lymphedema and encourage participation in a home program
2. To stimulate the lymphatic system in order to promote a reduction of edema
3. To prevent further accumulation of edema
4. To reduce or prevent the recurrence of infection
5. To help patients cope with the psychologic sequelae of lymphedema
6. When possible, to involve friends and family in the patient’s care

Precautions
One of the most important aspects of treatment is educating patients about the structure and function of the lymphatic system, as well as helping them cultivate an awareness regarding what factors and activities exacerbate their condition and what strategies best control it. A particular situation or activity may be problematic for one patient and not for another. One focus of therapy is to help patients make informed decisions about their participation in daily activities, given the limits of clinical knowledge.

Precautions are discussed with each patient. Skin care is an important aspect of the treatment program related to the increased risk of local infection. Patients are instructed to avoid cuts or breaks in the skin (e.g., a paper cut, burn, insect bite, cat scratch, cutting the cuticle during a manicure or pedicure, or cracks in dry skin) and to protect the skin during daily activities (e.g., using gloves for washing dishes, cleaning, or gardening; pot holders when reaching into the oven; or a thimble when sewing). Any cuts that do occur should be cleaned, treated with a topical antibiotic, and covered. In addition, it is recommended that patients protect their skin by applying a moisturizer on a regular basis. Patients with lower-extremity lymphedema are cautioned to avoid wearing open-toed shoes and to check their feet for fungal infections and ingrown toenails. If signs of an infection are present, patients should contact their physician.

Medical procedures on the affected extremity, including blood pressure readings, blood draws, and injections, should be avoided. This is particularly problematic for patients with bilateral axillary lymph node dissections, because many health care providers are unaware of these precautions and lower-extremity venipuncture may be contraindicated. Extra caution should be taken when performing any medical procedure on a limb at risk for lymphedema.

As described previously, situations that result in increased lymphatic load can precipitate or worsen lymphedema. Patients are instructed to avoid muscle fatigue during resistive activity as well as light repetitive activity; exposure to heat (including use of hot packs applied locally; saunas; steam rooms; hot, humid weather; and sun exposure); bumps; bruises; vigorous massage; and tight clothing or jewelry that may restrict lymphatic flow. Because the onset of lymphedema is a highly unpredictable event, patients must use discretion in choosing their daily activities while also remaining attuned to the development of lymphedema.

Positioning
In a newly edematous or pitting extremity, many patients report reduced edema and discomfort after the limb has been at or above relative heart level overnight. Over time, or when the edema becomes more brawny and less pitting, patients report less benefit from elevation. Because continuous elevation is impractical and interferes with normal daily activities, other treatment options are utilized to help reduce the accumulation of fluid in the affected limb.

Exercise
The rationale behind the use of exercise in the lymphedema patient is predicated on the observation that muscle contraction promotes lymph flow and increases protein absorption. This “muscle pump” effect results from changes in tissue pressure that stimulate the initial lymphatic vessels to open and close and thus encourage movement of interstitial fluid into the lymphatic system. The use of nonfatiguing exercises and activity represents the ideal because these will not trigger additional interstitial fluid production. Some proponents of exercise promote carefully monitored, progressive, resistive exercises. Another school suggests sequential exercises that activate muscles proximally and in normal lymphatic quadrants prior to activating muscles in the affected quadrant. Given that no data are available that compare exercise regimens, controversy surrounds the amount and type of exercise to prescribe. Despite this lack of consensus, all schools of therapy agree that exercise must be tailored to individual patient tolerance. Conventional wisdom suggests that the common prohibition against lifting more than 5 or 10 pounds with an affected extremity must be altered to take into account differences among individual patients.

Compression
External pressure applied around the affected limb decreases the amount of interstitial fluid production and enhances the efficiency of the “muscle pump” as the muscles contract against a relatively inelastic barrier. Not only can compression prevent the stretching of the skin that can occur as a result of increased pressure, it may also protect the limb from trauma. A variety of types of compression options are currently available, with each method having advantages and disadvantages.

Compression garments—which work by providing gradient pressure, thus preventing the backflow of
lymphatic fluid distally—represent the most widely used form of compression. Both prefabricated and custom-made garments are available, and proper fitting of these garments is crucial to their efficacy. Patients vary in their tolerance of amounts of compression as well as the types of materials from which compression garments are fabricated. In general, garments should be comfortable, not cause any allergic reactions, and not create a tourniquet effect that increases edema proximal or distal to the end of the garment. Although garments are relatively simple to apply and easy to use during normal activities, they may be expensive, require replacement every 6 months, and not be covered by insurance. Studies indicate that garments are effective in reducing and/or maintaining lymphedema.\textsuperscript{19,20}

Wrapping the limb with low-stretch bandages in conjunction with padding and foam provides the ideal type of compression in many ways. This allows for a low resting pressure and a high working pressure, which work with the “muscle pump” to encourage lymphatic flow. These bandages have the potential to help reshape the limb because each application is “custom-made” compression. However, bandaging has a few disadvantages. Difficult to apply, these bandages require training to ensure proper technique. Improperly applied bandages may cause constrictions and consequently provoke additional swelling. Finally, using bandages during daily activities can be somewhat cumbersome.

A recent study used a randomized, controlled design to compare the effectiveness of treatment with compression bandaging followed by use of a garment and the use of a garment alone. One group of patients was treated with compression bandaging for 18 days. The bandages were left in place all day and replaced once a day. This group was then fitted with a garment for the remainder of the trial (24 weeks). The second group was treated only with a garment for 24 weeks. The statistically significant results indicate that use of compression bandaging for a limited period followed by use of a garment achieves greater reduction in limb volume than use of a garment alone.\textsuperscript{21}

Static compression devices have been promoted as an alternative to bandaging the arm. Constructed from foam, covered by an inelastic outer casing, and fastened with Velcro to adjust the pressure, these devices range from being flexible and useful during an exercise program to being rigid and only used at rest. Compared with garments and bandages, these devices are costly and may not be covered by insurance.

The use of prophylactic compression during airplane flights for asymptomatic patients who are at risk for developing lymphedema remains controversial. Given that the use of compression does not necessarily prevent the development of lymphedema and that the use of improperly fitting garments may cause a tourniquet effect at the proximal or distal portions of a limb, patients who use compression prophylactically incur some risk. Despite this, some patients feel more secure taking proactive steps to prevent the onset of lymphedema.

**Pneumatic Pumps**

Although at one time pneumatic compression pumps represented the standard treatment for lymphedema in the United States, controversy about their use exists today. Some studies corroborate their usefulness in treatment of lymphedema,\textsuperscript{22,23} while another randomized study discounts their effectiveness.\textsuperscript{24} Schools that support the utilization of pumps generally suggest using relatively low pressures (40 millimeters of mercury [mmHg] maximum distal pressure) as part of a comprehensive program.\textsuperscript{25,26} Other schools of lymphedema therapy are opposed to their use.\textsuperscript{27–29} In short, no clear guidelines exist in the selection or use of pumps. A variety of pumps, with single or multiple chambers and various maximal pressures, lengths of pumping time, and frequencies of use, have been recommended.\textsuperscript{23,30} One study indicated that pressures greater than 50–60 mmHg may injure superficial lymphatic vessels.\textsuperscript{31} Although some patients report ongoing benefit in the use of a pump as part of a home program, others experience little benefit. Some report swelling in the base of the limb or in an adjacent trunk quadrant, or the development of genital edema,\textsuperscript{32} following use of this device. This is due to the fact that the adjacent trunk quadrant drains toward the same group of lymph nodes as the limb itself and therefore has similarly compromised lymphatic drainage. Despite this risk, the utilization of pumps followed by the application of compression garments or bandages continues to be a component of treatment in some lymphedema clinics.

**Self-Massage**

Patients are sometimes taught a gentle form of self-massage that is designed to stimulate lymphatic flow. When possible, family members or friends are included in the training in order to reach areas that the patient cannot massage alone, and to help encourage compliance with this part of the home program.

**Intensive Treatment Followed by Home Management**

Intensive treatment of the superficial lymphatic system using a manual massagelike technique in conjunction with skin care, compression bandaging, and exercise is now considered a mainstay of lymphedema
therapy. This four-part approach to the treatment of lymphedema has been known by a variety of acronyms promulgated by different schools of lymphedema therapy. These have included MLD (manual lymphatic drainage), MLT (manual lymphatic therapy or manual lymphedema treatment), CLT (complex lymphatic therapy), CPT (complex physical therapy or combination of physical therapies), CDP (complex decongestive physiotherapy), and CDT (complete decongestive therapy). At a meeting in New York in February 1998, the various schools reached a consensus that DLT (decongestive lymphatic therapy) should be used to refer to this combination of therapies; however, the lymphatic massage part of the treatment is still referred to as MLT or MLD by some schools.33

Lymphatic massage—in contrast to high-pressure massage, which has been shown to damage initial lymphatics34—is applied gently in order to stimulate the initial lymphatics and stretch the lymphatic collectors. Proximal areas are cleared prior to distal areas. In addition, significant time is spent clearing the anastomoses along the watersheds that connect adjacent trunk quadrants in order to reroute lymphatic flow and facilitate drainage of lymph to uncompromised areas. Following lymphatic massage, patients must wear compression bandages all day and night until the next treatment. They are instructed in skin care, exercises, self-massage, and self-bandaging; these are continued on the weekends and into the second phase of home management, which begins at the conclusion of the intensive phase of treatment. Patients must continue to manage their condition on an ongoing basis in order to prevent reaccumulation of edema in the affected limb.

The goal of this intensive four-part approach to the management of lymphedema is to decongest the limb. There is no agreement as to the optimal frequency and duration of the intensive phase of treatment. Some clinics provide treatment 1–3 times per week over the course of 4–6 weeks or more, while other clinics provide treatment once or twice per day for 2–4 weeks or more. The number of weeks of treatment is usually dependent on the severity of the patient’s lymphedema. The transition from the intensive to the maintenance phase is preferably made sometime after the patient’s progress has reached a plateau. This is because the clinician hopes to maximize lymph drainage before transitioning to the home maintenance phase. Periodic maintenance treatments or retreatment for another intensive phase may be indicated for some patients if fluid begins to reaccumulate.

The intensive treatment protocol has been shown in numerous studies to be an effective treatment for lymphedema.35–41 Variable outcomes with this protocol may result from factors including individual physiology, the skill of the treating therapist, and patient compliance. More studies are needed to determine the efficacy of various treatment protocols. Other research options include comparison of different exercise protocols, duration of the intensive treatment protocol, or number of treatments per week.

Drug Therapy
Benzopyrones in general, and coumarin specifically, represent the class of drugs used most frequently to treat lymphedema. They work by stimulating macrophage activity and thereby enhancing the breakdown of proteins in the affected extremity. Although prior studies suggested the effectiveness of this drug in reducing edema,42 current research indicates that not only is coumarin ineffective in treating lymphedema, but it may have hepatotoxic effects.43 Diuretics, commonly used for treating a variety of edematous conditions, are not recommended for long-term use in treating lymphedema.

Surgery
Surgical intervention provides an alternative for patients whose lymphedema has been refractory to more conservative treatment.44 Modified versions of the Charles procedure involve radical excision of the skin and subcutaneous tissue. Other surgical options include creating lympho-lymphatic or lymphovenous anastomoses.45–47 Some argue that conservative treatment postsurgery helps to maintain the benefit derived from the procedures.45,48 However, these surgical options are not without consequence; various complications, including shunt failure, hypertrophic scarring, sensory loss, aggravation of edema distal to the resection, and gross deformity of the limb, have been reported as results.49

Psychologic Factors
For many women, lymphedema represents yet another cruel surprise resulting from their treatment for breast cancer. Although, thankfully, lymphedema is an uncommon phenomenon, its development is associated with significant psychologic distress; these patients report greater anxiety, depression, and adjustment problems than patients without lymphedema.50–52 In addition to psychologic distress, lymphedema patients report more dysfunction in vocational, domestic, social, and sexual arenas.52

Although not all women who develop lymphedema will have difficulty adjusting to this chronic condition, a variety of factors have been reported to be predictors of greater dysfunction in the patient with
lymphedema, including the presence of pain, the absence of social support, and a coping style characterized by avoiding problems rather than dealing with them directly. As a complication of lymphedema, pain causes significant distress, is usually poorly managed, and is correlated with decreased social and physical functioning. The presence of painful edema triggers women’s fears that something is wrong with their bodies and leads to intrusive thoughts about cancer and the fear of recurrence. The absence of social support has also been correlated with increased psychologic distress, functional impairment, and sexual dysfunction in the patient with lymphedema. Lack of meaningful social contact increases the sense of isolation and withdrawal and prevents women from obtaining assistance with daily activities, developing a sense of worth, or gaining new perspectives or practical strategies that may be helpful. Passive or avoidant coping styles are also associated with increased morbidity in patients with lymphedema. Women who used these coping strategies reported greater psychologic distress and physical dysfunction as well as an increase in body image concerns.

The psychologic management of patients with lymphedema optimally begins prior to surgery, when information about the possibility of lymphedema development is first broached in discussions between physician and patient. The goal of these discussions as well as those following surgery is to engage patients in being proactive in the management of their own health, rather than imposing on patients what may seem like an onerous set of restrictions. For patients who develop lymphedema, a thorough assessment of not only psychologic factors but also pain, social functioning, and sexual functioning comprises the appropriate evaluation. Compliance, the most important patient factor in the success of lymphedema management, can be compromised by the presence of debilitating anxiety or depression. The early recognition and management of these symptoms is essential.

Psychologic interventions such as individual or group psychotherapy, especially those which utilize a cognitive behavioral approach, assist lymphedema patients in addressing negative thoughts and developing strategies for coping with the management of lymphedema. Group psychotherapy can provide the patient with an opportunity to derive benefit from the experience of others. For patients experiencing significant sexual dysfunction, sexual therapy conducted by a therapist conversant in issues related to cancer can be beneficial. In cases where significant depression or anxiety exist and interfere with patients’ functioning, psychopharmacologic interventions should be considered. Although most of the newer antidepressants do not have significant side effects, the older tricyclic antidepressants, which have weight gain as a side effect, should be avoided.

CONCLUSIONS
As quality-of-life and survival issues have moved toward center stage for cancer patients, the prevention and treatment of lymphedema has become increasingly important. The increased utilization of sentinel lymph node biopsies in surgeries for breast cancer and malignant melanoma attest to the growing concern about lymphedema. Given the greater likelihood that treatment will be effective when initiated early, health care workers need to have a high index of suspicion about lymphedema and make referrals to appropriate treatment settings. Because psychologic distress, an all-too-common sequela of lymphedema, can lead to diminished quality of life as well as lack of compliance with the demands of lymphedema treatment, clinicians should monitor these symptoms and make appropriate referrals. As interest in the management of lymphedema increases, hopefully research into the efficacy of existing treatments and the development of new management techniques will follow suit.

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