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Establishing Standards for Centers of Excellence for the Diagnosis and Treatment of Lymphatic Disease

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Abstract

Background: Lymphatic disease patients make up a significant proportion of the US and world populations. Due to inadequate medical school training and underestimation of the impact of lymphatic circulation, lymphatic disease patients often have difficulty finding competent diagnosis and care.
Methods and Results: The Lymphatic Education & Research Network has initiated a Centers of Excellence program to designate institutions that provide services for lymphatic disease patients. Committees of experts drafted standards for five types of Centers of Excellence.
Conclusions: The Centers of Excellence program is now launched, and the description of the formation process herein could provide other organizations guidance for similar ventures.

Keywords: Center of Excellence, lymphatic disease, lymphedema, lipedema

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Introduction

While the heart and blood vasculature are well studied and easily recognizable by the general public—most people know heart, artery, and vein anatomy basics—the lymphatic system is an unfamiliar topic to most. The lymphatic system consists of hundreds of lymph nodes connected by lymphatic vessels traversing the entire body.[1] Each time the heart pumps blood to tissues, cells use nutrients, fluids, and gases and excrete waste. Until ~10 years ago, this excreted/extracellular fluid, along with large proteins and immune cells (lymph), was believed to return to the blood circulation through venular capillaries. Levick and Michel, however, showed that nearly all extracellular fluid instead transits through lymphatics.[2] In fact, 4–8 L of lymph per day travels through the lymphatic ducts, so any malfunction in lymph flow can result in significant swelling and immune dysfunction.

The number of people affected by diseased lymphatics in the United States is estimated at 10 million,[3] ~3% of the population. Adding the estimated 11% of women with lipedema (LI),[4] a lymphatic/adipose disorder that is often mistaken for obesity or lymphedema (LE), increases the lymphatic patient population substantially to ~14 million. As the population of cancer survivors, a significant proportion of whom will encounter LE, continues to increase[5] and awareness of lymphatic diseases (LDs) grows, the total number of lymphatic patients may exceed 7% of the US population.

Accurate diagnosis of LD is often delayed or missed altogether because lymphatic dysfunction can be mistaken for blood vasculature failure and other disease symptoms. Studies have shown that treatment of LD in early stages significantly improves outcomes/quality of life,[6–8] yet the length of time for accurate diagnosis and treatment of LD often exceeds 13 years.[9]

Identifying an acute need to facilitate accurate early diagnosis and treatment of LDs, the Lymphatic Education & Research Network (LE&RN), an international consortium of LD patients, physicians, therapists, and researchers, initiated establishment of Centers of Excellence (COEs) for LDs. The objectives of COE designation are to (1) enable patients

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and primary care physicians to readily identify knowledgeable LD caretakers, (2) recognize health care professionals and organizations efficiently serving LD patients, (3) raise awareness of LDs within physician and patient populations, and (4) encourage health care institutions to aspire to serve lymphatic patients optimally. Herein, we describe the steps taken to establish standards for LE&RN COEs in the diagnosis and treatment of LDs.

The Start—Recognizing the Need for COEs

Deluged with phone calls and emails from patients seeking diagnosis and care for LDs, leadership at LE&RN identified the need for COEs. LE&RN was already requiring newly established chapters to identify LD health care professionals and institutions within their geographical areas; however, simply listing these resources on a website was not deemed the ideal way to guide patients to the best care for several reasons.

Lymphatic knowledge is off the radar for many physicians given that medical school education on lymphatics averages <30 minutes.[10] Unfamiliarity with lymphatics makes it difficult for many physicians to correctly diagnose LD. Diagnosis and treatment of LDs can be complicated and can require visiting different types of physicians and other health professionals. Simply knowing the name of a lymphatic physician can be insufficient information for most patients. For example, after diagnosis, standard-of-care treatment for LE requires multiple visits to specially trained, certified lymphedema therapists for complete decongestive therapy (CDT)—manual lymphatic drainage (MLD), fitting of compression garments, skin care education, and sometimes training in the use of pneumatic compression therapy. Often, patients need training for home/self-care of LE because MLD is expensive, inadequately covered by medical insurers, and often unavailable outside large metropolitan areas. If standard CDT care fails, patients may opt for lymphatic-sparing liposuction or lymphatic microsurgeries, which include lymphovenous bypass (LVB) and vascularized lymph node transfer (VLNT) procedures. The surgeons providing these intricate procedures are highly trained and should perform a minimum number of surgeries per year to maintain surgical skills. LE may have genetic origins (primary LE) or may occur after cancer treatment or trauma (secondary LE). Health care providers may excel at diagnosis with genetic testing, screening during and after cancer treatment, MLD, or lymphatic microsurgeries. Patients may not have sufficient knowledge for discerning which health care providers can best meet their needs and for finding tools to navigate webs of different health institutions. Recognized COEs could help guide patients through the maze of lymphatic caretakers.

Initiation of Committee Work

LE&RN leadership gathered committee members from the lymphatic community willing to serve on two separate committees to provide a system of checks and balances for accountability. The first/steering committee was responsible for determining standards for health care providers to meet to qualify for COE designation and for drafting applications/proposals. The second/global oversight committee was responsible for assessing the standards and judging whether applicant health care providers/institutions met criteria for COE designation.

To draft a list of COE requirements, the first committee relied on a prominent, established lymphatic physician and researcher who provided guidance and a comprehensive list of criteria. Working with the resulting list, the committee discussed each benchmark through teleconferences, deciding which points were essential and how and whether to weight each. Several concerns were addressed. First, not every institution has resources to meet each requirement on the comprehensive list, but many institutions can meet subsets of the requirements very well. For example, cancer centers predominantly see and treat cancer-related LE, not congenital LE or LI, yet premier lymphatic bypass/lymph node transfer surgeons are often located within cancer centers, so the standards committee determined that specialized COEs could be designated. Second, many institutions exist as part of larger medical campuses, and while a single institution may not be able to fulfill every COE requirement, it is possible to build localized networks of referral that can collectively meet COE needs.

Potential Pitfalls Identified

The first/standard-setting committee recognized the need to avoid numerous stumbling blocks in drafting standards for COEs. COE status can be coveted by many institutions as a feather in one's cap and a lucrative patient recruitment tool. Allowing every physician hoping to increase patient base to be listed as a LE&RN COE denies patients the screening process that can result in best practices. Institution renown in nonlymphatic fields could mislead LD patients. Impartial judging of applicants, avoiding subjective cronyism and politics, was deemed as highest priority, so objective, measurable relevant qualifications were chosen for inclusion in the list of standards.

Legal liability concerns could paralyze efforts to guide patients to caretakers—what if a malpractice situation arises? This concern is not trivial—approximately one third of all physicians have been sued, according to an American Medical Association survey.[11] LE&RN joins many other disease support organizations to include website disclaimer language to caution users of limitations.

Many LD patients reside in areas that are underserved by appropriate caregivers. While the standards committee could not feasibly address this important limitation in the application/proposals, it is hoped that LE&RN chapters can work to share information about affordable housing and transportation options to patients needing to travel for care.

Another pitfall the committee wished to avoid was exclusivity—if an institution was not initially chosen for COE status, LE&RN wanted to encourage the institution to evolve to COE standards. Transparent, objective measurable criteria for application review ensure a level playing field so that institutions vying for COE status can easily discern steps needed to strengthen an application.

How to ascertain that each application is truthful and accurate? While this duty was assigned to the second/global oversight committee, the first/steering committee tried to choose metrics that would be easily verifiable.

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Table 1. Centers of Excellence Standards for Diagnosis and Care of Lymphatic Disease

	Comprehensive Center of Excellence	*Network of Excellence*	*Referral Network of Excellence*	*LD Surgery Center of Excellence*	*LD Conservative Care Center of Excellence*
Diagnosis					
Cancer-related or noncancer-related LE	✓	✓ or affiliate referral	✓ or local referral		
Lipedema	✓	✓ or affiliate referral	✓ or local referral		
Congenital vascular anomalies, including lymphatic malformations	✓	✓ or affiliate referral	✓ or local referral		
Systemic lymphatic disorders (pleural effusion, pulmonary, chylothorax, protein-losing enteropathy, lymphangiectasia, and genital)	✓	✓ or affiliate referral	✓ or local referral		
Protein-losing enteropathy	✓	✓ or affiliate referral	✓ or local referral		
Lymphangiectasia	✓	✓ or affiliate referral	✓ or local referral		
Lymphaticovenous disease	✓	✓ or affiliate referral	✓ or local referral		
Pediatric lymphatics	✓	✓ or affiliate referral	✓ or local referral		
Filariasis, podoconiosis	✓	✓ or affiliate referral	✓ or local referral		
Gorham's disease and lymphangiomatosis	✓	✓ or affiliate referral	✓ or local referral		
Collaboration with practitioner(s) or facility capable of accurate LD diagnosis				✓	✓
Imaging					
Radionuclide lymphoscintigraphy	✓	✓ or affiliate referral	✓ or local referral		
Near-infrared fluorescence lymphography	✓	✓ or affiliate referral	✓ or local referral	✓	
Direct contrast lymphography (for cisterna chyli and thoracic duct visualization)	✓	✓ or affiliate referral	✓ or local referral		
Venography	✓	✓ or affiliate referral	✓ or local referral		
Venous and lymphatic ultrasonography	✓	✓ or affiliate referral	✓ or local referral		
MRI imaging	✓	✓ or affiliate referral	✓ or local referral		
MR lymphography	✓	✓ or affiliate referral	✓ or local referral		
Conservative management services					
LE risk reduction and surveillance for high risk or collaboration with practitioner(s) who do so	✓	✓ or affiliate referral	✓ or local referral	✓	✓
Complete lymphatic decongestive therapy (intensive treatment—5×/week, 60-minute sessions), LANA-certified or equivalent practitioner(s), and short-stretch bandaging expertise	✓	✓ or affiliate referral	✓ or local referral		✓
Maintenance treatment, including garment fitting, dispensation of medical bandages, garments, pneumatic compression, and other medical goods	✓	✓ or affiliate referral	✓ or local referral		✓
Management and surveillance of head/neck LE	✓	✓ or affiliate referral	✓ or local referral		✓
Management of vascular and other complex malformations for overlapping vascular/lymphatic conditions	✓	✓ or affiliate referral	✓ or local referral		

(*continued*)

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Table 1. (Continued)

	Comprehensive Center of Excellence	*Network of Excellence*	*Referral Network of Excellence*	*LD Surgery Center of Excellence*	*LD Conservative Care Center of Excellence*
Management of protein-losing enteropathies, chylothorax, chyloperitoneum, and management of mTOR inhibitors/other pharmacotherapies for lymphatic malformations and complex vascular lesions	✓	✓ or affiliate referral	✓ or local referral		
Assessment tools					
Perometer, bioimpedance, truncated cone/tape measurement, or other serial measurement modality expertise	✓	✓ or affiliate referral	✓ or local referral		
Risk assessment using perometry or bioimpedance spectroscopy	✓	✓ or affiliate referral	✓ or local referral		
Interventional therapies					
Venoplasty and stenting for venous lesions presenting as LE (including ovarian vein ablation)	✓	✓ or affiliate referral	✓ or local referral		
Venous and lymphatic sclerotherapy	✓	✓ or affiliate referral	✓ or local referral		
Thoracic duct embolization for plastic bronchitis, chylothorax, and chyloperitoneum	✓	✓ or affiliate referral	✓ or local referral		
Sclerotherapy for macrocystic lymphatic malformations	✓	✓ or affiliate referral	✓ or local referral		
Surgical					
Suction-assisted lipectomy (including surgical follow-up)	✓	✓ or affiliate referral	✓ or local referral	✓	
Tumescent liposuction for lipedema	✓	✓ or affiliate referral	✓ or local referral	✓	
Lymphaticovenous anastomosis	✓	✓ or affiliate referral	✓ or local referral	✓	
Vascularized lymph node transfer	✓	✓ or affiliate referral	✓ or local referral	✓	
Pleurodesis and shunts for chronic effusive disorders	✓	✓ or affiliate referral	✓ or local referral	✓	
Collaboration with a facility or practitioner meeting conservative care COE criteria					
Genetics					
Screening for known genes and mutations	✓	✓ or affiliate referral	✓ or local referral		
Genetic counseling to patients and families	✓	✓ or affiliate referral	✓ or local referral		
Consultative					
Psychiatric/psychological services for depression	✓	✓ or affiliate referral	✓ or local referral		
Pulmonary medicine	✓	✓ or affiliate referral	✓ or local referral		
Gastroenterology	✓	✓ or affiliate referral	✓ or local referral		
Gynecology	✓	✓ or affiliate referral	✓ or local referral		
Oncology	✓	✓ or affiliate referral	✓ or local referral		
Diagnostic and interventional radiology	✓	✓ or affiliate referral	✓ or local referral		
Dermatology	✓	✓ or affiliate referral	✓ or local referral		
Urology	✓	✓ or affiliate referral	✓ or local referral		
Radiation oncology	✓	✓ or affiliate referral	✓ or local referral		
Nutrition (particularly for protein-losing enteropathy and lipedema patients)	✓	✓ or affiliate referral	✓ or local referral		
Neurology	✓	✓ or affiliate referral	✓ or local referral		
Plastic surgery	✓	✓ or affiliate referral	✓ or local referral		

(*continued*)

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Table 1. (Continued)

	Comprehensive Center of Excellence	*Network of Excellence*	*Referral Network of Excellence*	*LD Surgery Center of Excellence*	*LD Conservative Care Center of Excellence*
Research					
Basic/animal lymphatic science, publications	✓ preferred				
Applied/clinical studies or trials, reporting in ClinicalTrials.gov					
Recruitment of patients to the International Lymphatic Disease Registry and Biorepository	✓	✓	✓	✓	✓
Infrastructure to support future research endeavors					
Accountability					
Participation in patient experience survey network					
Reporting of patient outcomes, at least short-term outcomes					
Collegiality					
Attendance/participation in at least one LE&RN-associated event/year	✓	✓	✓	✓	✓
Attendance/participation in other lymphatic/scientific meetings					
Patient education					
Vascular surgeon education					
Physician/therapist education/workshops	✓	✓			
Administration					
Sufficient administrative resources to handle phone calls/emails inquiring of services					
Participation in LE&RN collaborative administration of COEs					
Community					
Resources/referrals for need-based financial assistance					
Pro bono services, where appropriate					
Resources/referrals for patient travel assistance					

LD, lymphatic disease; LE, lymphedema; MRI, magnetic resonance imaging; MR, magnetic resonance; LE&RN, Lymphatic Education and Research Network; COE, Center of Excellence; LANA, Archaeology Association of North America.

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Perspective Is Everything

Throughout the standard-drafting activity, the first committee attempted to see COE status from a patient's perspective—how easy would an institution or network make a patient's quest for accurate timely diagnosis and optimal care?

The committee also strived to see COEs from the perspective of doctors and other health care professionals. Physicians and institutions are subject to review by insurers and governing agencies for effectiveness of care given and avoidance of misdiagnosis, failed care, and other medical mistakes.

While cherry picking of patients can be used by physicians to facilitate best reviews, a properly structured COE designation process could ensure that the right patients seek out the right doctors and therapists to the benefit of everyone. Physicians do not want patients who have inaccurately attempted to self-diagnose and demand inappropriate treatment. An example would be an LE patient with established disease, with significant subdermal adipose accumulation, noncompliant with compression use, and who demands lymphatic microsurgery. Studies have proven that LVB and VLNT microsurgeries work best for early not-as-established LE, while lymphatic-sparing liposuction may work best for those with long-standing, adipose-prevalent established LE.[12–15] The committee attempted to present COE standards that help guide patients to the appropriate, not merely desired, treatment.

The Standards Committee's Recommendations

Table 1 lists suggested expertise requirements in multiple categories. Proper diagnosis of LD necessitates consideration of complex syndromes, accurate physical assessment, and knowledge of genetic and environmental contributions to LD. Imaging is an important part of an examination workup, and magnetic resonance lymphography, lymphoscintigraphy, near-infrared fluorescence lymphography, and other modalities should be parts of a physician's toolbox. Genetic screening and counseling may be required for discerning a hereditary basis for LD in some cases.

After diagnosis, proper treatment and patient compliance are crucial to satisfactory outcomes. Conservative management, including MLD/CDT, pharmacotherapies, and compression garment fitting, may be sufficient for many LD patients. Physician expertise in interventional and surgical therapies, such as sclerotherapy, thoracic duct embolization, tumescent liposuction, pleurodesis/shunts, and lymphatic microsurgeries, is essential for treatment of lymphovascular anomalies, as well as lymphatic-only diseases.

Treating only physiological LD symptoms is not sufficient for best patient outcomes. LE patients, for example, experience depression at higher than average rates and may need counseling and/or medication for this concern. LE patients experience cellulitis also at higher-than-average rates and may require dermatological services or, in the case of sepsis development, hospitalization. LI and protein-losing enteropathy patients can benefit from nutrition counseling.[16]

Basic science and clinical research in LDs is now increasing. Advances in understanding the science behind LDs depend on dissemination of research findings and cooperative efforts within the communities of caretakers and researchers. LE&RN established the International Lymphatic Disease and Lymphedema Patient Registry and Biorepository in 2009,[17] and recruitment of patients who will provide health information and biological samples to this bank for future research endeavors is included as a COE criterion. Collegiality, as judged by attendance at LE&RN-associated events, physician/therapist education workshops, and other lymphatic-related conferences, is also included in the list of criteria.

Several categories of COE designation allow expertise in specialized areas to be recognized when an institution cannot meet all of the Comprehensive COE requirements. In addition to the Comprehensive COE designation, four other COE categories are recognized: (1) Network of Excellence for affiliated institutions; (2) Referral Network of Excellence for nonaffiliated, but neighboring institutions; (3) LD Surgery COE for institutions at which LD microsurgeries and liposuction procedures are the focus of treatment; and (4) LD Conservative Care COE for institutions delivering quality CDT/MLD.

Conclusions

Recognition of LDs and the quest for care are mushrooming areas of health care. The cost for caring for lymphatic patients is significant—treatments for LE were the 13th most often reimbursed procedures ($498 million) in 2012 by the Centers for Medicare and Medicaid Services.[18] Especially, as LI becomes more and more recognized as distinct from (regular) obesity, demand for accurate diagnosis and effective care for this and other LDs will possibly rival that of blood vasculature disorders. There is an urgent need to set standards for optimal LD diagnosis and care. LE&RN, by establishing COE designation standards for health care institutions, is addressing this need and pushing optimal LD patient care forward.

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References

1. Foldi M, Foldi E. *Foldi's Textbook of lymphology*, 3rd edition. Munich, Germany: Elsevier GmbH; 2012.
2. Levick JR, Michel CC. Microvascular fluid exchange and the revised Starling principle. Cardiovasc Res 2010; 87:198–210.
3. Lymphatic Education & Research Network. Lymphedema and lymphatic diseases affect miillions and concern us all. Available at: https://lymphaticnetwork.org. Accessed January 25, 2021.
4. National Institutes of Health, National Center for Advancing Translational Sciences, Lipedema. Available at: https://rarediseases.info.nih.gov/diseases/10542/lipedema. Accessed January 25, 2021.

5. Siegel RL, Miller KD, Jemal A. Cancer statistics. CA Cancer J Clin 2020; 70:7–30.
6. Shah C, Arthur DW, Wazer D, Khan A, Ridner S, Vicini F. The impact of early detection and intervention of breast cancer-related lymphedema: A systematic review. Cancer Med 2016; 5:1154–1162.
7. Stout Gergich NL, Pfalzer LA, McGarvey C, Springer B, Gerber LH, Soballe P. Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. Cancer 2008; 112:2809–2819.
8. Johnson AR, Kimball S, Epstein S, Recht A, Lin SJ, Lee BT, James TA, Singhal D. Lymphedema incidence after axillary lymph node dissection: Quantifying the impact of radiation and the lymphatic microsurgical preventive healing approach. Ann Plast Surg 2019; 82(4S Suppl 3):S234–S241.
9. Blome C, Sandner A, Herberger K, Augustin M. Lymphedema—the long way to diagnosis and therapy. Vasa 2013; 42:363–369.
10. Granger DN, Skeff KM, Chaite W, Rockson SG. Lymphatic biology and disease: Is it being taught? Who is listening? Lymphatic Res Biol 2004; 2:86–95.
11. Guardado JR. Policy research perspectives: Medical liability claim frequency among U.S. physicians. 2016. Available at: https://www.ama-assn.org/sites/default/files/media-browser/public/government/advocacy/policy-research-perspective-medical-liability-claim-frequency.pdf. Accessed January 25, 2021.
12. Chang DW, Suami H, Skoracki R. A prospective analysis of 100 consecutive lymphovenous bypass cases for treatment of extremity lymphedema. Plast Reconstr Surg 2013; 132:1305–1314.
13. Dayan JH, Ly CL, Kataru RP, Mehrara BJ. Lymphedema: Pathogenesis and novel therapies. Annu Rev Med 2018; 69: 263–276.
14. Schaverien MV, Coroneos CJ. Surgical treatment of lymphedema. Plast Reconstr Surg 2019; 144:7388–7758.
15. Gould DJ, Mehrara BJ, Neligan P, Cheng MH, Patel KM. Lymph node transplantation for the treatment of lymphedema. J Surg Oncol 2018; 118:736–742.
16. Ehrlich C, Iker E, Herbst KL, Kahn L-A, Sears DD, Kenyon M, McMahon E. *Lymphedema and Lipedema Nutrition Guide*. San Francisco, CA: Lymph Notes; 2016.
17. Lymphatic Education & Research Network. The International Lymphatic Disease and Lymphedema Patient Registry & Biorepository. Available at: https://lernregistry.stanford.edu. Accessed January 25, 2021.
18. Centers for Medicare & Medicaid Services. Physician and Other Supplier Data CY 2012. Available at: cms.gov/Research-Statistics-Data-and-Systems/Statistic-Trends-and-Reports/Medicare-Provider-Charge-Data/Physician-and-Other-Supplier2012. Accessed January 25, 2021.

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