Canadian Lymphedema and Lymphatic-related Research

Highlighting projects by Canadian researchers

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By Pamela Hodgson

This sample of recent publications and projects highlights Canadian research in basic science, epidemiology, rehabilitation, surgery, and the social and nursing sciences. Greater understanding of the function and capacities of lymphatic vessels is emerging, as well as their important role in inflammation, adipose tissue metabolism, cancer, and other diseases, and of their ability to adapt after trauma. Surgical methods devised in part to prevent lymphedema may not yet be as effective as hoped. Treatments using different types of bandages and water-based exercise show promise, as do self-management techniques. Large population studies following breast cancer patients for 5 years are documenting the incidence and impact of lymphedema. A short film has been made on the experience of women with breast cancer related lymphedema. The need for reliable information for patients and physicians is being documented. Finally, but not least, Canadian researchers are collaborating with international teams to document and investigate how best to manage lymphedema.

Information needs

Information for patients with or at risk of cancer-related lymphedema.
Dubois S, Folch N. Clin J Oncol Nurs. 2013. Oct.
This University of Montreal team searched the Internet for information about cancer-related lymphedema (CRL). They found 19 web sites (of 120) that met inclusion criteria. 79% of the sites focused solely on CRL; 74% were in English. Content was incomplete and evaluation of web site impact and effectiveness was nonexistent. This review suggests that websites about CRL vary greatly in terms of structure and content.

The information needs and media preferences of Canadian cancer specialists regarding breast cancer treatment related arm morbidity.
Shaw R, Thomas R. European Journal of Cancer Care. 2014. 23(1) 98-110.
Providing specialists with summary information about arm morbidity does not suffice. An educational campaign that includes the importance of physician vigilance in regularly monitoring patients for early and latent indications of this morbidity may be necessary.

Treatment studies

Breast cancer-related lymphedema: a randomized controlled pilot and feasibility study.
Letellier M-E, Towers A, Shimony A, Tidhar D. Am J Phys Med Rehabil. 2014; 93(9) 751-63.
The authors compared Aqua Lymphatic Therapy (ALT) combined with home-based exercise with home-based exercise alone, among patients with breast cancer-related lymphedema. The ALT group showed significant changes after 12 weeks of treatment, compared to the control group. ALT may serve as a safe alternative to land-based treatments of breast cancer-related lymphedema.

A lymphedema self-management programme: a report on 30 cases.
Tidhar D, Hodgson P, Shay C, Towers A. Physiotherapy Canada. August 2014. Advance online article.
28 participants with lymphedema were taught self-bandaging at the McGill University Health Centre Lymphedema Clinic. The majority had moderate to severe lymphedema; all achieved reduction of edema from between 48% and 92%. A majority reported a global rate of change of 80%. For selected patients,

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a self-bandaging program can be a route to lymphedema reduction, independence, and self-efficacy.

A randomized trial of decongestive lymphatic therapy for the treatment of lymphedema in women with breast cancer.
Dayes IS, Whelan TJ, Julian JA, Parpia S, Pritchard KI, D'Souza DP, Kligman L, Reise D, LeBlanc L, McNeely ML, Manchul L, Wiernikowski J, and Levine MN. Journal of Clinical Oncology. 2013.
An interview with Dr. Dayes appeared in the Spring 2014 issue of *Pathways*.

Evaluation of the performance of a new compression system in patients with lymphoedema.
Franks PJ, Moffatt CJ, Murray S, Reddick M, Tilley A, Schreiber A. Int Wound J. 2013. 10 (2):203-9

A prospective study to identify factors that predict the performance of the 3M oedema reduction system (Coban) and standard compression used within decongestive lymphatic therapy in patients with lymphedema.
Tilley A.
A team including members from the previous study aims to enroll 264 participants overall from Japan, England, France and Canada (33). One Canadian site will use the 3M system and another will use the standard compression system.

Laboratory research

Inflammation-induced lymphangiogenesis and lymphatic dysfunction.
Liao S, von der Weid PY. Angiogenesis. 2014. 17 (2) 325-34.
This review provides a critical update on the role of the lymphatic system in disease processes such as chronic inflammation and cancer and examines the changes in lymphatic functions, the disease's cause and the influence these changes have on the progression of the disease.

Electrophysiological properties of rat mesenteric lymphatic vessels and their regulation by stretch.
von der Weid PY, Lee S, Imitiaz MS, et.al. Lymphat Res Biol. 2014. 12(2) 66-75.
Researchers examined the properties of rat mesenteric lymphatic muscle (Vm) under resting conditions and when distended. In their experimental conditions, they found that rat lymphatic muscle has electrophysiological characteristics similar to that of other species. It responds to an increase in isometric tension with an increase in action potential frequency, but Vm is not significantly affected. 24 people with arm or leg lymphedema from clinics in England and Canada (Fredericton and St. John's) were treated with the two-layer system of bandaging for 19 days. Mean percentage changes in limb volume were 14.9% and 16.1% for legs and arms, respectively. The authors concluded that the new compression system provided good edema reduction and improvements in symptoms associated with lymphedema.

Atherosclerosis and transit of HDL through the lymphatic vasculature
Martel C, Randolph G J. Curr Artheroscler Rep. 2013. 15(9) 354.
Researchers focus on recent evidence that the lymphatic vasculature is critical for the removal of cholesterol, likely as a component of HDL, from tissues including skin and the artery wall. It is possible that progression of atherosclerosis might in part be linked to sluggish removal of cholesterol from the plaque.

Macrophage reverse cholesterol transport in mice relies on the lymphatic vasculature.
Martel C, Li W, Fulp B, et.al. J. Clin Invest. 2013; 123 (4) 1571–79.
The team found that macrophage reverse cholesterol transport (RCT) was markedly impaired in 2 models where lymphatic drainage was disrupted and found that RCT was mediated by lymphatic vessels from the aortic wall. The lymphatic vessel route is critical for RCT from multiple tissues, including the aortic wall. These results suggest that supporting lymphatic transport function may facilitate cholesterol clearance in therapies aimed at reversing atherosclerosis.

Lymphatic function is impaired following irradiation of a single lymph node.
Baker A, Semple JL, Moore S, Johnston M. Lymphat Res Biol. 2014. 12 (2) 76-88.
The aim of this controlled experimental study performed at the Sunnybrook Research Institute using a rabbit model was to quantify the impact of lymph node irradiation on lymph flow. The authors found that irradiation impaired lymph transport and increased the pressure required to maintain flow through the system. New vessel formation and the growth of lymph-venous anastomoses indicated the development of alternative drainage pathways as a compensatory response.

Mechanisms of VIP-induced inhibition of the lymphatic vessel pump.
von der Weid PY, Rehal S, Dyrda P, et.al. J Physiol. 2012. 590 (11) 2677-91.
This study found that vasoactive intestinal peptide (VIP) decreases the frequency of lymphatic contractions and hyperpolarizes the lymphatic muscle membrane potential in a concentration-dependent manner in the guinea pig. Inhibition of lymphatic pumping by VIP may compromise lymph drainage, oedema resolution and immune cell trafficking to the draining lymph nodes.

Lymphatic vessel function in atherosclerosis.
Martel C.
Researchers previously demonstrated that cholesterol gets out of tissues and reaches the bloodstream by first entering lymphatic vessels. This emerging research team aims to develop further understanding of the mechanisms connecting abnormal lymphatic function and atherosclerosis progression. Start-up funds have been awarded by the Montreal Heart Institute Foundation and grant submissions elsewhere are in process.

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Surgery

Axillary reverse lymphatic mapping in breast cancer surgery: a comprehensive review.
Seyednejad N, Kuusk U, Wiseman SM. Expert Rev Anticancer Ther. 2014. 14 (7) 771-81.
The authors found that the axillary reverse lymphatic mapping (ARM) technique had several limitations that include a poor success rate for identification of arm lymph nodes (ARM nodes) and lymphatics. The occurrence of common lymphatic drainage pathways of the arm and the breast in a subset of patients raises concerns regarding its oncological soundness. The effectiveness of the ARM procedure in reducing lymphedema risk in breast cancer patients who undergo a variety of treatments has yet to be clearly defined.

Axillary reverse mapping in breast cancer: A Canadian experience.
Kuusk U1, Seyednejad N, McKevitt EC, Dingee CK, Wiseman SM. J Surg Oncol. 2014 Jul [Epub ahead of print].
37 women received sentinel node dissection (SNL) and 15 received axillary node dissection. The authors concluded that the axillary reverse mapping technique did not prevent identification of the SLN and they identified much greater crossover than previously reported.

Impact of lymphedema

The New Normal: Living with Lymphedema after Breast Cancer.
Quinlan E, Thomas R, Ahmed S, Fichtner P, McMullen L, Block J, Juxtapose Productions (producer). 2014. Peer-review: CES4Health http://www.ces4health.info/find-products/view-product.aspx?code=DLFLZP5W
This educational YouTube Video features an ethnodrama performance of the lived experiences of breast cancer survivors with arm problems along with interviews with the researchers and participants involved in the production. (French or English)

Lymphedema trajectories among breast cancer survivors.
Quinlan E, Thomas R, Hack T, Towers A, Kwan W, Miedema B, Tatemichi S, Tilley A. Journal of Lympheodema. 2014.9 (1) 12-19
Researchers followed women for two years and found that lymphoedema increased over time and that there was a confounding effect of arm dominance. This emphasizes the need for pre-operative measurement of both arms.

Illustrating the (in) visible: Understanding the impact of loss in adults living with secondary lymphedema after cancer.
Thomas R, Hamilton R. Int J Qual Stud Health Well-being. 2014 Aug 21;9:24354.
This research indicates that timely diagnosis, increased awareness and the development of new resources and psychosocial supports are needed to enhance quality of life for those living with secondary lymphedema.

Loss, adaptation and new directions: The impact of arm morbidity on leisure activities following breast cancer.
Hack T, Quinlan E, Tatemichi S, Towers A, Kwan W, Miedema B, Tilley A, Hamoline R, Morrison T. Under review. Canadian Journal of Nursing Oncology. Aug 2014

Beyond the body: Insights from an iyengar yoga program for women with disability after breast cancer.
Thomas R, Quinlan E, Kowalski K, Spriggs P, Hamoline R. Holist Nurs Pract. 2014 Nov-Dec; 28(6):353-61.
Qualitative interviews and participants' journals show that there were a number of benefits to the yoga program.

Other

Determining the precision of dual energy x-ray absorptiometry and multi-frequency bioelectric impedance spectroscopy in the assessment of breast cancer-related lymphedema.
Newman AL, Rosenthall L, Towers A, Hodgson P, Shay C, Tidhar D, Vigano A, Kilgour RD. Lymphatic Research and Biology. 2013, 11(2): 104-109.
The team determined that the two measurement instruments provide acceptable levels of precision for the measurement of arm lean mass, fat mass and extracellular fluid volume.

The Alberta moving beyond breast cancer (AMBER) cohort study: a prospective study of physical activity and health-related fitness in breast cancer survivors.
Courneya KS1, Vallance JK, Culos-Reed SN, McNeely ML, Bell GJ, Mackey JR, Yasui Y, Yuan Y, Matthews CE, Lau DC, Cook D, Friedenreich CM. BMC Cancer.2012.12.525.
This study aims to enroll, in Alberta, 1500 newly diagnosed patients with breast cancer and to follow them for 5 years. This will provide comprehensive data on the outcomes, determinants, mechanisms, and moderators of physical activity and health-related fitness in breast cancer survivors.

Effect of early compression therapy on incidence of lymphedema in patients treated for gynecological cancer
Shallwani S, Towers A, Hodgson P, Yung A, Salvador S, Gotlieb W, Gilbert L, Khan S, Kham L.
The aim of this prospective randomised trial is to investigate the effect of early compression therapy with individualized education and exercise on the incidence of lymphedema in patients surgically treated for gynecological cancer. LP

Editor's Note:
This list of studies is not exhaustive. *Pathways* welcomes information about any research. Readers can learn how to access the details of some of these studies by visiting **www.lymphedemapathways.ca**.