

Genetics and Lymphedema



FORWARD

The following excerpt is from a wonderful new book entitled, *100 Questions and Answers About Lymphedema*, (published by Jones and Bartlett, 2010) and has been reprinted with permission from the publisher. Chapter Seven explains “Genetics and Lymphedema”, describing the various types of Primary Lymphedema that children can be impacted by.

The authors, Saskia Thiadens, RN; Paul Stewart, MD; and Nicole Stout, MPT; are all well known experts and opinion leaders in the lymphedema community.

Is lymphedema a genetic condition?

The most common causes of lymphedema are surgical or trauma. Worldwide, the most common cause of lymphedema is filarial disease. Approximately 10% of all lymphedema cases in the United States are genetic. A variety of genetic abnormalities can result in lymphedema. Some of the most easily recognizable genetic conditions associated with lymphedema are discussed in the following list.

In **Milroy’s disease**, lymphedema is present at birth, and there is a congenital absence of lymphatic vessels. Recent work on the genetics of this disease indicates that mutations at the VEGFR-3 (vascular endothelial growth factor receptor 3) locus are responsible for the inheritance of Milroy’s disease. This is an **autosomal dominant** disease; thus, there is a 50% chance that parents with Milroy’s disease will pass the condition on to their child.

Another widely recognized genetic link to lymphedema is **Distichiasis syndrome**, in which there are two rows of eyelashes along the posterior border of the lid and associated hyperplasia of lymphatic vessels in the lower extremities, with reflux of lymphatic fluid. This condition can also be associated with problems with drooping eyelids, heart defects, cleft lip and palate, and venous abnormalities. The mutation responsible for this condition has been localized to the FOX C2 gene on chromosome 16.

There are other identified syndromes such as **lymphedema praecox**, in which the onset of lymphedema occurs before the age of 35, or, **lymphedema tarda**, in which the onset of lymphedema occurs after the age of 35. There are often strong family histories of lymphedema in these persons; however, no genetic focus has yet been identified in association with this condition, which on lymphoscintigraphy appears to be due to a lack of distal lymphatics (i.e., lymphatics near the far portions of the body).

Turner’s syndrome is a genetic condition in which females are born with only one X chromosome. Approximately 80% of these infants are born with lymphedema. Interestingly enough, 80% of these children will experience complete resolution of their lymphedema during puberty, which implies a delay in maturation of the lymphatic system as a cause of the lymphedema.

There are other conditions such as **Noonan’s syndrome**, which causes short stature, droopy eyes, low-set ears, and neck webbing, heart abnormalities with lymphedema that is present at birth or shortly after. It appears that lymphedema is related to the presence of a cystic hygroma in utero and is found in instances where the lymphatic vessels fail to mature or are slow to mature. It appears that this condition is related to abnormalities on chromosome 12.

Yellow nail syndrome is rare and is associated with the presence of yellow nails and upper airway problems, most often with chronic sinus problems, bronchiectasis, and pleural effusions. Lymphedema can be more or less associated with this syndrome.

Lymphography will typically show mega-lymphatics with pleural effusions (excess fluid around the lungs).

We are in our infancy in understanding the complexities of lymphatic genetics and vigorous research is currently underway in this fascinating area of lymphedema research.

This book can be purchased through the Lymphedema Association of Ontario.

Please note: The pictures featured on this page as well as the front cover of this newsletter are all actual children living with lymphedema in Canada. The Lymphedema Association of Ontario is grateful to their parents for sharing these wonderful photos.