



Key Facts About Lymphangiomyomatosis

Patient Copy

WHAT IS PULMONARY LYMPHANGIOLEIOMYOMATOSIS (LAM)?

Lymphangiomyomatosis is pronounced lim-fan je-o-lio-mi o-ma-to sis. Lymph and angio refer to the lymph and blood vessels. Leiomyomatosis refers to the formation of the bundles of the unusual muscle cells.

Lymphangiomyomatosis (LAM) is a rare lung disease that was first described in the medical literature by von Stossel in 1937. The disease is characterized by an unusual type of muscle cell that invades the tissue of the lungs, including the airways, and blood and lymph vessels. Over time, these muscle cells form into bundles and grow into the walls of the airways, and blood and lymph vessels, causing them to become obstructed.

Although these cells are not considered cancerous, they grow without the usual controls within the lungs. Over time, the muscle cells block the flow of air, blood, and lymph vessels to and from the lungs, preventing the lungs from providing oxygen to the rest of the body.

An unusual, frequently asymptomatic, kidney tumor called angiomyolipoma is found in up to 50% of patients with LAM.

About 40-50% of female patients with tuberous sclerosis, a genetic disorder, develop a lung disease that is identical to that which occurs in LAM. These patients often have angiomyolipomas of the kidney as well. Although patients with LAM do not develop the central nervous system and skin changes of tuberous sclerosis, the similarities in the lung and kidney manifestations of the two diseases have led some investigators to postulate that they may have common causes. For more information contact the National Tuberous Sclerosis Foundation.

HOW COMMON IS LAM?

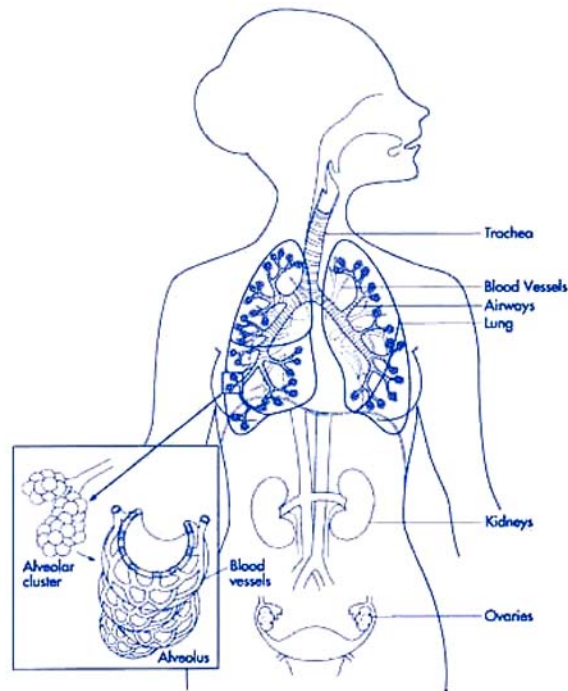
LAM affects almost exclusively women, usually between the onset of puberty and menopause. Several cases have been reported in older women, but it is not clear when the disease developed in these patients. The precise number of people who have LAM is not known.

It also has been suggested that LAM has become more common during the past 5 to 10 years, although it may be that doctors are doing a better job of diagnosing the disease.

WHAT ARE THE SYMPTOMS OF LYMPHANGIOLEIOMYOMATOSIS?

A common symptom of LAM is shortness of breath (dyspnea) with physical activity. In the early stages of disease, the person with LAM may experience shortness of breath only during strenuous exercise, but as the disease advances, there may be shortness of breath even at rest. Another common symptom is chest pain, and occasionally patients cough up small amounts of blood.

The symptoms associated with LAM are caused by the excessive growth of the muscle cells around the airways, and blood and lymph vessels. The excess muscle cells can block the airways, trapping air in the smallest air compartments in the lung (alveoli) and causing the person with LAM to have difficulty moving air out of the lungs. This results in a breakdown of the lung tissue and the formation of small cysts (air filled cavities).



Cysts near or on the surface of the lung (blebs) can rupture and, as air leaks from the lung into the chest cavity (pneumothorax), the lung or a part of the lung can collapse, causing pain. If the amount of air that leaks out is small, the lung may seal over the space and re-expand itself. If air continues to leak into the chest cavity, however, it may be necessary to re-expand the collapsed portion of the lung by removing the air that has leaked into the chest cavity. This is an in-patient procedure, done using a tube inserted through the chest wall into the chest cavity.

The excessive muscle growth may also block blood vessels in the lung, causing them to become distended with blood and even to rupture. This can result in the patient coughing up blood-stained sputum or blood (hemoptysis).

Obstruction of the lymphatic vessels by the excess muscle growth can lead to leakage of fluid into the chest cavity (pleural effusion). The fluid may be straw-colored (lymph), or fat-containing, milky white (chyle), or pinkish-red if it contains blood. A physician can remove some of this fluid with a needle and syringe to determine its composition and origin. If large amounts of fluid accumulate in the chest cavity, it may have to be removed through a tube surgically inserted into the chest.

It is estimated that 30 to 50 percent of LAM patients will develop leakage of air into the chest cavity (pneumothorax), and up to 80 percent will have leakage of fluid into the chest cavity (pleural effusions). Coughing up blood-stained sputum or blood (hemoptysis) occurs less frequently.

WHAT IS THE COURSE OF LYMPHANGIOLEIOMYOMATOSIS?

LAM is generally progressive, leading to increasingly impaired lung function. The rate of development can vary considerably among patients. As the disease advances, there can be more extensive growth of muscle cells throughout the lung and repeated leakage of fluid into the chest cavity (pleural effusions). As an increasing number of cysts are formed, the lung takes on a honeycomb appearance.

HOW IS LYMPHANGIOLEIOMYOMATOSIS DIAGNOSED?

The diagnosis of LAM can be difficult because many of the early symptoms are similar to those of other lung diseases, such as asthma, emphysema, or bronchitis. Often the person with LAM first goes to the physician

complaining of chest pain and shortness of breath that was caused by a pneumothorax. Some patients first consult their physician because of shortness of breath upon exertion.

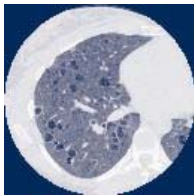
There are a number of tests the physician can do to confirm or rule out the existence of LAM.

Chest X-ray: This is a simple procedure that provides a picture of the lungs and other tissue in the chest. The chest x-ray is used to diagnose a pneumothorax or presence of fluid in the chest cavity (pleural effusion). The cysts that are suggestive of LAM can be difficult to see on a routine chest x-ray and this test is often not diagnostic.

Pulmonary Function Tests: The patient breathes through a mouthpiece into a machine (spirometer) that measures the volume of air in the lungs, the movement of air into and out of the lungs, and the movement of oxygen from the lungs into the blood. This test can be used to determine the effect that LAM has had on lung performance over time, but cannot be used to make a diagnosis.

Blood Tests: The patient's blood is analyzed to determine whether the lungs are providing an adequate supply of oxygen to the blood. This is also a useful test for following LAM patients.

Computed Tomography (CT): This test is the most useful imaging test for diagnosing LAM. The patient lies inside a long, cylindrical structure, and x-ray beams pass through the body from different angles producing multiple images. A computer combines all of these images and provides a multiple two-dimensional picture of the inside of the lungs and chest. This is called a CT scan.



On a CT scan, the presence of thin-walled cysts spread relatively uniformly throughout the lungs can indicate LAM. If an angiomyolipoma is also present on the abdominal cuts of the chest CT, the diagnosis of LAM can be made with reasonable certainty. In up to 50% of patients with LAM the finding of an angiomyolipoma on an abdominal CT is diagnostic of LAM. Up to 50% of patients with pulmonary LAM will have this uncommon benign kidney tumor. (Symptoms of LAM such as lung collapse, fluid in the lungs, shortness of breath, and chest pain, can also aid in the diagnosis of LAM without performing an open lung biopsy.)

Lung Biopsy: An open lung biopsy should be performed as a last resort to diagnose LAM. In this procedure, a few small pieces of lung tissue are removed through an incision made in the chest wall between the ribs.

Another procedure, thoracoscopy, is also being used in some patients to obtain lung tissue. In this procedure, tiny incisions are made in the chest wall and a small lighted tube (endoscope) is inserted so that the interior of the lung can be viewed, and small pieces of tissue are removed.

Both procedures must be done in the hospital under general anesthesia. Recovery from an open lung biopsy takes longer than the less invasive but usually completely adequate thoracoscopic procedure.

Another technique, called transbronchial biopsy, may also be used to obtain a small amount of lung tissue. A long, narrow, flexible, lighted tube (bronchoscope) is inserted down the windpipe (trachea), and into the lungs. Bits of lung tissue are sampled using a tiny forceps. This procedure is usually done in a hospital on an outpatient basis under local anesthesia. However, the amount of tissue that can be sampled is usually inadequate for diagnostic purposes in LAM.

After the lung tissue is removed, it is examined in a pathology laboratory for the presence of the abnormal muscle cells and cystic changes characteristic of LAM.

HOW IS LAM TREATED?

Because LAM affects almost exclusively women of childbearing age, physicians have thought that the hormone estrogen might be involved in the abnormal muscle cell growth that characterizes the disease, just as it is in the growth of smooth muscle in the uterus in a woman's childbearing years.

Although there is no direct evidence that there is a relationship between estrogen and LAM, the treatment of LAM has focused on reducing the production or effects of estrogen. The response to treatment has been highly individual, and no therapy has been found to be effective for all LAM patients. Treatments vary in effectiveness from patient to patient, and none have yet been scientifically proven. Oxygen therapy may become necessary if the disease continues to worsen and lung function is impaired. Lung transplantation is considered as a last resort.

A treatment trial is presently being conducted at the University of Cincinnati using a new drug called rapamycin. In 2005, a second trial called The Sirolimus Multicenter International Lymphangiomyomatosis Efficacy and Safety (SMILES) Trial will be conducted for LAM patients worldwide.

WHAT IS THE EFFECT OF LAM ON THE PATIENT'S LIFESTYLE?

In the early stages of the disease, most patients can go about their daily activities, including attending school, going to work, and performing common physical activities. In more advanced stages, the patient may have very limited ability to move around and may require oxygen. Patients with LAM should follow the same healthy lifestyle recommended for the general population, including eating a healthy diet, getting as much exercise as they can, as well as plenty of rest, and, of course, not smoking. Traveling to remote areas where medical attention is not readily available or to high altitudes where the blebs can expand and rupture should be considered carefully before undertaking. Some doctors and LAM patients feel that pregnancy accelerates the disease.

LAM RESEARCH PROGRAMS

Some LAM patients may be eligible to participate in clinical studies at the Warren Grant Magnuson Clinical Center of the National Institutes of Health in Bethesda, Maryland. Participants must meet specific LAM Patient Protocol requirements.

INTRAMURAL RESEARCH

LAM research is being conducted presently through the Intramural Research Program at the National Heart, Lung, and Blood Institute (NHLBI) at the National Institutes of Health (NIH). The study is headed by Dr. Joel Moss.

ORGAN DONATION

The LAM Foundation urges you to encourage your family and friends to become organ donors. Remember to (1) sign your donor card and (2) notify your family of your wishes to become a donor, so that precious gifts of life don't go unused. If you would like to know more about organ donation, you may call your local Organ Procurement Office or visit one of many websites. The Second Wind Organization focuses on the needs of lung transplant recipients. Another excellent resource can be found at www.organdonor.gov. We hope that you will join with us in this tremendously important mission

TISSUE DONATIONS NEEDED

The most valuable resource for our LAM researchers is human tissue donated at the time of surgery or lung transplantation. If you are a LAM patient planning to have any type of surgery and are interested in donating tissue, please contact The LAM Foundation at 513-777-6889 or email lam@one.net.

ORGANIZATIONS

United Network for Organ Sharing (UNOS)

1100 Boulders Parkway, Suite 500
Richmond, VA 23225-8770

Second Wind National Lung Transplant Patients Association

16393 E. Duran Blvd.
Loxahatchee, FL 33470
(407) 793-7480
<http://www.2ndwind.org>

American Lung Association (ALA)

1740 Broadway
New York, NY 10019-4374
(800) 586-4872 (Voice)
(800) 528-2971 (Living Bank)

American Thoracic Society (ATS)

1740 Broadway
New York, NY 10019-4374
(212) 315-8804

OTHER LUNG TRANSPLANT WEB SITES

Lung Transplantation Program Columbia University
The International Society For Heart and Lung Transplantation
(This site does not have patient resources or information for non-medical professionals)
The Brigham and Women's Hospital's Lung Transplantation Program
Daily Lung Transplant 1
Daily Lung Transplant 2
John Hopkins Comprehensive Transplant Center *(not active)*
University of Utah Transplant Center
Cystic L Handbook
The University of Maryland Medical Center's Transplantation Program
Chest Surgeons
Pulmonary Re-transplant Registry
The National Transplant Assistance Fund
National Foundation for Transplants

OTHER SOURCES OF INFORMATION

National Organization for Rare Disorders, Inc. (NORD)

100 Rt. 37, P.O. Box 8923
New Fairfield, CT 06812-1783
Phone: (203) 746-6518, (800) 999-6673

Office of Research on Women's Health

Building 1, Room 202
Bethesda, MD 20892-0161
Phone: (301) 402-1770
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Office of Rare Disease Research

Federal Building, Room 618
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