ELF EUROPEAN LUNG FOUNDATION

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Lymphangioleiomyomatosis (LAM)

Lymphangioleiomyomatosis (LAM) is a rare lung condition that mainly affects women of childbearing age. Although it has been reported in men, it is extremely rare.

It is estimated that three to five in every one million women will develop LAM.

This factsheet gives an overview of the symptoms of LAM, how it is diagnosed and treated, and tips for living with the condition. As healthcare professionals do not often come into contact with people with LAM, you might find it helpful to take this factsheet to your next appointment.

What is LAM?

LAM is characterised by lung cysts (air-filled sacs which gradually destroy the lung), changes to the lymphatic system and tumours in the kidneys.

It is a progressive condition, which means that symptoms will generally get worse over time.

LAM develops differently in each person. In some women, it can be quite mild so they stay very well for decades and do not need any treatment. However, for others, their lung function will decline more quickly over time, and they may require treatment with oxygen, treatment with drugs and/or a lung transplant.

For every one million women, around three to five will have LAM.

"LAM is not the same in everyone; in some women it progresses more slowly than in others, so do not compare yourself with other people as this can cause unnecessary stress." **Iris, Italy**

What causes LAM?

You can get LAM without any other condition. This is known as sporadic LAM. Or you can get it together with a condition called tuberous sclerosis. The causes of LAM are not fully understood.

Sporadic LAM

Sporadic LAM is not inherited and it is not passed on to children. One of two proteins (called tuberin and hamartin) are abnormal in LAM tissue. This is due to mutations (changes) in the genes responsible for these proteins. The proteins act as a brake on the growth of LAM cells and when they are abnormal there is excessive growth of these cells. Why this should happen is not clear, but stopping the growth of these cells is the main focus of research at the moment.

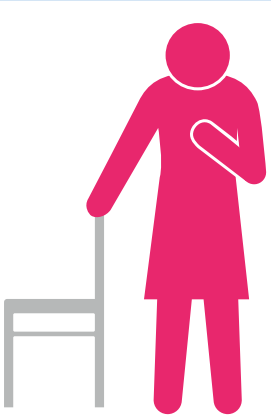
Tuberous sclerosis and LAM

Tuberous sclerosis is a hereditary condition. Individuals with tuberous sclerosis have the same gene mutation in all or most of their cells and so they are very likely to get LAM. By the age of 40 years, about 80% of women with tuberous sclerosis have LAM, although they may not go on to have lots of symptoms.

Oestrogen plays some part in LAM; although it does not appear to be the direct cause of LAM, higher levels of oestrogen can speed up the disease.

The average age at which people start to have symptoms of LAM is around 35 years, but now that healthcare professionals are getting better at recognising the condition it is being diagnosed earlier. LAM very seldomly affects children.

What are the main symptoms of LAM?



Symptoms vary, but the two that are most common are breathlessness and pneumothorax (lung collapse).

A pneumothorax refers to a collapse of one or both of the lungs, caused by air entering the pleural cavity. The pleural cavity is the space between your lungs and the chest wall.

Less common symptoms are cough, coughing up blood, kidney tumours (angiomyolipomas), which occur in about half of cases, and chylous effusions (when lymph that forms in the digestive system, called chyle, builds up in the thin cavity around your lungs and stops them expanding properly when you breathe).

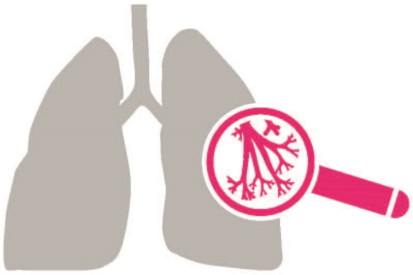
The course of LAM varies between individuals, but there are ways to manage the symptoms.

How is LAM diagnosed?

It can be difficult to diagnose LAM, as many symptoms are similar to other lung conditions (such as asthma, chronic obstructive pulmonary disease (COPD) and bronchitis).

It is very important that a proper diagnosis is made. European Respiratory Society (ERS) guidelines state that to diagnose LAM you need to have:

- a computerised tomography (CT) scan (where your body is X-rayed at a number of angles before a computer puts together a detailed image) showing lung cysts, plus
- another piece of evidence, e.g. tuberous sclerosis, kidney tumour, chylous effusion



A blood test showing a high level of a protein called vascular endothelial growth factor D (VEGF-D) in the blood can also help in diagnosing LAM.

In very rare cases, where a diagnosis cannot be made from a combination of the above symptoms, a biopsy may be needed. This is where some samples of the tissue from your lungs are taken and tested.

As LAM is such a rare condition, it is important to get a specialist opinion as early as possible and to discuss your individual case with an expert on the condition.

"Take your time and let the diagnosis sink in as it can feel very confusing at first." **Emer, Ireland**

"A diagnosis also hits the family of the person with LAM very hard and you all may be very protective of each other. Talking to an outside party can help." **Gill, UK**

"It is very important to raise awareness of LAM among family doctors, who are often the first point of contact." **Iris, Italy**

How does LAM progress?

Although there have been some major advances in LAM research, there is currently no cure.

Women with LAM tend to get increasing loss of lung function. This is usually slow, but it can happen more quickly for some people.

Most women with LAM live for decades from the start of their symptoms, but it can vary. Therefore, it is important to discuss your own case with a specialist.

"Today there are much better diagnosis methods, better treatment and better knowledge of LAM among health workers. And I am living proof of that you can live for many years with this condition. I was diagnosed aged 30 years and am 52 years now."
Lisbeth, Norway

What treatment is there?

Usually you will be monitored to see if your condition is stable or progressing, so that the best treatment and management can be offered to you.

Treating symptoms

You may receive supportive treatment at first. This could include the use of inhalers (bronchodilators), which make breathing easier. This may be the only treatment that some women need. Some women benefit from supplementary oxygen, which helps with breathlessness.

Pleurodesis or pleurectomy (for collapsed lung)

Some women with LAM will have more than one pneumothorax (lung collapse) during their lives, and the following procedures may be recommended to prevent this happening again. This can significantly improve the quality of life for women with LAM.

- Pleurodesis is a procedure that aims to stick the pleura together to prevent your lung from collapsing again.
- Pleurectomy is a procedure during which the surgeon strips the lining between the lung and the chest wall so that the lung sticks to the chest wall, preventing further lung collapse.

Medication

The main treatment for LAM is a drug called sirolimus (also called rapamycin). This drug helps to stop loss of lung function for many women. However, not every individual will need treatment with sirolimus. Others may not benefit from the drug and some can experience side-effects.

Lung transplant

A lung transplant may be an option for some women with advanced LAM, where there are no other treatment options. Many women with LAM have had successful lung transplants and improved quality of life as a result.

Managing symptoms

You can help manage common symptoms of LAM by:

- Keeping a healthy weight
- Not smoking
- Keeping active (supplementary oxygen, if required, may help you exercise more effectively)
- Doing a pulmonary rehabilitation programme to help with breathlessness
- Using inhalers, if your airways are narrowed
- Having vaccinations against influenza and pneumococcus
- Not taking the combined oral contraceptive pill (which contains oestrogen and progesterone)
- Discussing pregnancy with your specialist, as symptoms can get worse during pregnancy due to higher oestrogen levels
- Not having hormone replacement therapy (HRT) after the menopause

Your lung function should be monitored regularly for changes. If your lung function is decreasing, your physician may recommend other treatment.

"Stay as healthy as possible and share your experiences with other women with LAM through patient organisations and support groups." **Iris, Italy**

"Exercise really helps me, both physically and mentally. I started taking oxygen to the gym and going on the treadmill." **Gill, UK**

"I try to find balance between taking things slowly – and to actually having a life." **Lisbeth, Norway**

Research and hopes for future

There is a lot of research going on and the most significant areas of research are focusing on:

Better tools to predict how LAM will develop – so healthcare professionals can know whether an individual is likely to remain stable or need treatment sooner rather than later. Various studies are looking for biomarkers (a biological marker in the blood that suggests that a person has a particular condition), to give information on how the condition is developing.

Finding a cure – sirolimus prevents LAM from getting worse, but only works while you are taking the drug. If you stop taking it, your lung function will decline again. New treatments are currently being evaluated which include new drugs as well as research into combining sirolimus with other drugs to see if LAM cells can be killed, rather than just stopped from growing.

Regenerative treatments – studies into regenerative treatments aim to mend the damaged lung tissue. This is still at a very early stage, and significant results are a long way off.

"It is vital to promote trials of new potential drugs at a European level and to communicate information to patients about these new therapies. This could accelerate the process of getting a cure. As LAM is a rare disease, it requires more effort from the LAM community and physicians." **Iris, Italy**

Daily living and support

Due to advances in LAM research, living with the condition is very different to how it used to be.

As living with LAM is very different for every woman, you should not compare yourself with others.

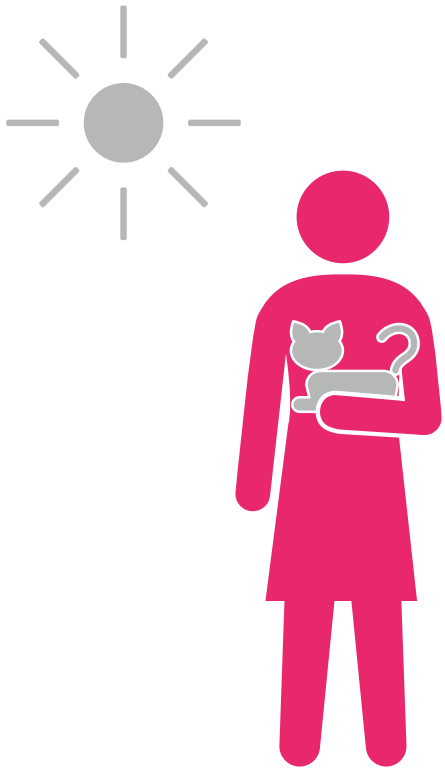
Many women feel desperate and anxious when they first get their diagnosis. It can be helpful to make contact with others diagnosed with LAM to talk and share information and practical tips on what helps.

"I have found Tai Chi and yoga helpful in reducing my anxiety." **Emer, Ireland**

"Never give up and never lose faith. Stay positive!" **Lisbeth, Norway**

"It can be lonely at times when there is little energy left to be social. Then it is good to have social media (such as Facebook) to keep in touch with friends and family." **Lisbeth, Norway**

"Try not to search the internet, and contact a local group within your own country instead." **Emer, Ireland**



Further reading

European Lung Foundation LAM website: **www.europeanlung.org/lam**

- Access information developed by people with experience of LAM and experts in the field
- Find LAM support networks, centres and specialists in Europe
- Read case studies from women with LAM

European Lung Foundation website: **www.europeanlung.org**

Access more information on lung health and factsheets relevant for people living with LAM, including:

- Primary spontanous pneumothorax (PSP)
- Pulmonary rehabilitation

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The European Lung Foundation (ELF) was founded by the European Respiratory Society (ERS), with the aim of bringing together patients, the public and respiratory professionals to positively influence respiratory medicine. ELF is dedicated to lung health throughout Europe, and draws together the leading European medical experts to provide patient information and raise public awareness about lung disease.

This material was compiled as part of the LAM patient priorities project with the help of Professor Simon Johnson, Dr Sergio Harari, Dr Marcel Veltkamp, Elma Zwanenburg and members of ELF's LAM patient advisory group.