Lymphangioleiomyomatosis (LAM)

Lymphangioleiomyomatosis (LAM) is a rare lung disease that almost always affects women, usually during the reproductive years. The average age it starts is around 34 years. Abnormal tissue growth in the lungs causes cysts, which lead to breathing problems. Other affected organs may include the kidneys, uterus and lymphatic system.

The cause of LAM is unknown. Sporadic LAM (sLAM) occurs in about one woman in a million, although the exact incidence is not known. LAM can also occur in women who have a condition known as tuberous sclerosis complex (TSC). To date, there is no known cure for LAM.

Abnormal growth of lung cells

LAM usually targets the lungs. The smooth muscle cells of the lungs begin to ‘overgrow’, forming clumps and cysts (fluid-filled sacs) around the airways, blood vessels and lymph vessels. As the disease progresses, these abnormal growths damage healthy lung tissue and interfere with breathing.

Symptoms

In the early stages, the symptoms of LAM resemble those of more common respiratory conditions such as asthma, bronchitis or emphysema. The symptoms of LAM may include:

- Shortness of breath
- Breathlessness during physical exertion
- Chest pain
- Cough
- Coughing up viscous white sputum
- Coughing up blood (haemoptysis)
- Progressive worsening of symptoms over time.

Other body parts may be affected

LAM can cause problems in other areas of the body, such as:

- **Kidneys** – benign (non-cancerous) growths. About one woman in three who has LAM has kidney tumours, which are called angiomyolipomas (AMLS).
- **Abdomen and pelvis** – cysts or tissue masses called lymphangioleiomyomas that develop behind the lining of the abdomen (peritoneum).
- **Lymph nodes** – enlargement, which is usually harmless.

LAM complications

LAM may cause serious complications including:

- **Collapsed lung (pneumothorax)** – caused by changes in air pressure inside the chest. Typically, a cyst bursts and leaks air from the lungs into the chest cavity. In mild cases of partial collapse, the lung may reinflate by itself. In other cases, surgery is needed. Sometimes, the condition is chronic and the affected lung may collapse over and over again. Pneumothorax is relatively common in people with LAM.
• **Pleural effusion** – build-up of fluid in the space between the lungs and the lung membrane (pleura). The fluid may be an unusual type called chyle, producing a chylothorax. About one woman in three affected by LAM has an abnormal leakage of lymphatic fluid into the chest cavity.

• **Bleeding tumours** – the kidney tumours (angiomyolipomas, or AMLs) may bleed. Symptoms include back pain and blood in the urine.

### The link with tuberous sclerosis complex (TSC)

LAM develops in about 40 per cent of women who have a disease called tuberous sclerosis complex (TSC). It also occasionally develops in men with this disease. TSC is a rare genetic disorder that involves the formation of root-like growths in the brain and, occasionally, other organs such as the kidneys, heart, liver and lungs. These growths begin to form in the brain prior to birth and interfere with brain functioning. In most cases, the cause is a spontaneous gene mutation within the developing baby. In about 20 per cent of cases, the mutated gene is inherited.

LAM is a different condition to TSC. It is not thought to be inherited or passed on through genes in the same way, but its association with TSC suggests that genetics may still play an important role. Doctors believe that the cause of both LAM and TSC is a genetic mutation in one of the two tumour suppression genes known as TSC1 and TSC2. The reason for the genetic mutation is a mystery.

### Oestrogen may be involved

LAM almost always affects women. The condition tends to develop before the onset of menopause and usually slows down after menopause. Pregnancy is also known to speed the progression of disease. That’s why doctors think the female hormone oestrogen is an important risk factor. Be guided by your doctor but, generally, women with LAM are advised against taking medicines that contain oestrogen such as the combined contraceptive pill, hormone replacement therapy and fertility treatments.

### Diagnosis

Since LAM is extremely rare, it can be easily mistaken for another respiratory condition such as asthma, bronchitis or emphysema. Indeed, asthma occurs in about 30 per cent of women with LAM.

Tests used to diagnose LAM may include:

- Physical examination
- Medical history
- Lung function tests, to check the amount of air that the lungs can inhale and exhale
- Blood tests
- Pulse oximetry, a non-invasive test that checks the levels of oxygen in the blood
- Chest x-ray
- Computed tomography (CT) scans of the chest and abdomen
- Ultrasound of the kidneys
- Lung biopsy, performed under local or general anaesthesia.

### Treatment

LAM is a progressive disease, which means it gets worse over time. However, the rate of progression differs from one person to the next, for reasons unknown. There is currently no cure nor have any treatments been definitely proved to stop or slow the formation of cysts in the lungs or elsewhere in the body. Treatment aims to ease the symptoms and reduce the risk of complications.

Treatment options may include:

- **Medicines** – such as bronchodilators to open the airways and improve airflow or water tablets (diuretics) to remove excess fluid.
- **Flu (influenza) vaccination** – to reduce the risk of respiratory infection.
- **Supplemental oxygen** – oxygen that is breathed through a tube or mask to increase the oxygen supply to the lungs.
• **Surgery** – to reinflate a collapsed lung (repair a pneumothorax) or prevent recurrence of fluid. A biopsy may be used to make a diagnosis.

• **Lung transplantation** – the diseased lungs are surgically removed and replaced with healthy lung tissue from a deceased donor. This is a major operation with serious risks. Doctors consider a lung transplant as the last resort in the treatment of a potentially life-threatening case of LAM.

### Possible treatments for the future

Because LAM is rare, it is difficult for doctors to find enough people to participate in trials to test the effectiveness of new treatments. Drugs currently under consideration for the treatment of LAM include:

- **Doxycycline** – an antibiotic that it is thought may decrease the spread of LAM cells in lung tissue.
- **Rapamycin** – an immunosuppressant drug that may decrease LAM cell growth.
- **Progestosterone** – a female hormone.

Other trials are being considered to test the effectiveness of a range of other treatments, including statins, metformin (an oral anti-diabetic drug), lymphangiogenesis inhibitors and autophagy inhibitors.

### Where to get help

- Your doctor
- Referral for specialist treatment – this may be provided by a pulmonologist, endocrinologist, obstetrician-gynecologist or urologist
- St Vincent’s Hospital LAM Clinic, Sydney Tel. (02) 8382 2330 or (02) 8382 3150
- LAM Clinic Victoria Tel. (03) 9276 2867
- Australasian Tuberous Sclerosis Society Tel. (02) 9630 3147 or 1300 733 435

### Things to remember

- Lymphangioleiomyomatosis (LAM) is a rare lung disease that can affect women during their reproductive years.
- Other areas of the body that may be affected include the kidneys, abdomen and pelvis, and lymphatic system.
- The cause is unknown and there is no cure; treatment aims to ease symptoms and reduce the risk of complications.

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