

Is LAM why she's breathless?

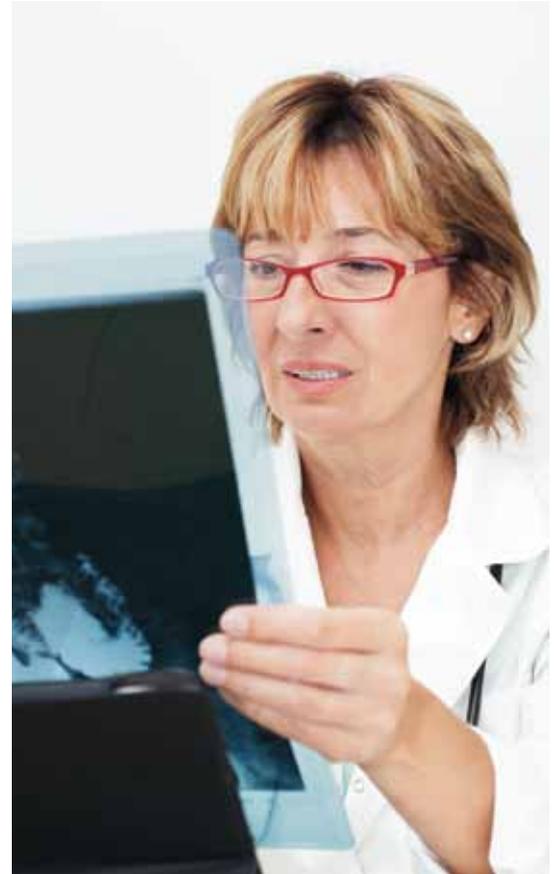
Lymphangiomyomatosis (LAM) is a progressive and devastating cystic lung disease. Symptoms typically appear in women in their 20s and 30s. Because LAM is rare and shares some symptoms with other conditions, correct diagnosis is often delayed.

LAM in the lungs

- LAM produces multiple air-filled cysts up to 5cm in diameter. These cause varying degrees of dyspnoea, especially on exertion. Smooth muscle proliferates, causing the bronchial wall to thicken and obstruct the airways. Lymphatic blockage may cause chylothorax. Vascular obstruction or invasion may cause haemoptysis.
- Asthma-like signs, such as coughing, wheezing and low FEV1, may be present. FEV1 may improve with a bronchodilator.
- CXR is often normal. A high resolution CT scan may be necessary to detect cysts.

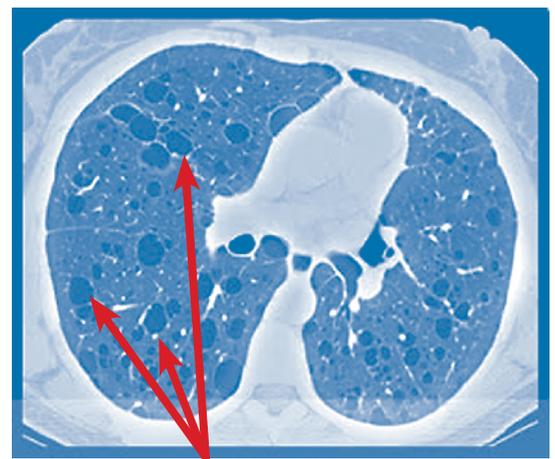
LAM in the kidneys

- Women with LAM may have angiomyolipomas or lymphangiomas within the retroperitoneal space. Unless these bleed, encroach on adjacent structures, or are associated with chylous ascites, they are usually symptom free.
- Angiomyolipomas and lymphangiomas can be diagnosed by US or CT without biopsy.



LAM pathophysiology

- LAM cells spread like a cancer. A spontaneous mutation in a single gene occurs in a cell somewhere in the body, possibly in the uterus. Mutant cells metastasise to the lungs, kidneys and abdomen via the lymphatics. They proliferate in these target organs, producing cysts and parenchymal destruction.
- Tuberous sclerosis associated LAM (TSC-LAM) is more common, but possibly less aggressive, than sporadic LAM. Tuberous sclerosis is a disease associated with seizures, skin lesions and kidney, brain and heart tumours. It is due to mutations on either chromosome 9 or 16, but more commonly 16.
- Sporadic LAM, the rarer, more rapid, and more destructive version of LAM, occurs in patients who do not have tuberous sclerosis complex (TSC), and results from a mutation on chromosome 16.
- Both forms of LAM result from deregulation of the mTOR pathway which controls cell division. Antiproliferative drugs such as rapamycin (sirolimus) and everolimus have shown promising results in recent trials. Drugs in the mTOR inhibitor class are effective in reducing the rate of lung function decline in LAM.
- LAM is progressive, irreversible and debilitating, but the rate and degree of progression vary enormously.
- Lung transplantation is a last resort, but can have excellent long-term results.



High-resolution CT scan shows bilateral lung cysts (arrowed) distributed randomly throughout the lungs.





When to suspect lymphangioleiomyomatosis (LAM)

- A woman, typically young or middle aged, presents with pneumothorax, chylothorax, or progressive shortness of breath without clear explanation.
- A woman has been diagnosed with COPD despite having no history of smoking or asthma, and without exacerbation or remission.
- Lung cysts consistent with LAM are discovered on CT scans done for other reasons.
- Incidental discovery on CT or US of an angiomyolipoma, a fatty kidney tumour.



What to do if you think she may have LAM

- Order a high resolution thoracic CT.
- Order a lung function test including spirometry, lung volumes and diffusing capacity.

What to do if LAM is confirmed

- Reassure your patient. She is likely to be shocked at being diagnosed with an incurable disease. Living with LAM can be challenging, but many women lead long and full lives following diagnosis. A study in *Lung* (12 Sep 2012) reported that median transplant-free survival was 29 years from onset of symptoms.
- Chronic debilitating conditions can negatively affect sexual and relationship dynamics and need to be addressed early as part of good holistic patient care.
- Recommend alternatives to medications containing oestrogen, including contraceptive pills and vaginal lubricants.
- Encourage your patient to take care of herself physically and psychologically by: maintaining a healthy lifestyle within the physical limitations of impaired lung function; maintaining a healthy diet and weight; and keeping flu and pneumovax vaccinations up to date. Recommend activities such as yoga, pilates, meditation and singing, which can be good for the body and the mind.
- Refer your patient to a respiratory specialist with expertise in LAM. The specialist will evaluate treatment options. Recommendations may include an mTOR inhibitor and, in some advanced cases, preparation for lung transplantation.
- Advise your patient that LAM Australia Research Alliance maintains a voluntary register of women with LAM and provides information, support, and contacts.

Future directions

- Research into biomarkers for LAM may develop a blood test which will facilitate diagnosis and treatment decisions.
- Rapamycin/sirolimus and a similar drug, everolimus, are being used in specialist units to treat some women with LAM. The MILES trial (*NEJM* 28 Apr 2011) found "...sirolimus stabilized lung function and was associated with a reduction in symptoms and improvement in quality of life". Everolimus may also improve lung function and other aspects of LAM.
- Researchers in Australia and worldwide are endeavouring to find tailored treatments and, ultimately, a cure for LAM.

Medical enquiries

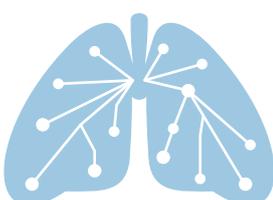
LAM Australia Research Alliance's Medical & Scientific Advisory Panel comprises Australian researchers and physicians with expertise in LAM. They can provide accurate, up-to-date information on LAM, its treatment and management.

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Together we can conquer LAM

LAM Australia Research Alliance is a not-for-profit organisation dedicated to funding research to find tailored treatments and a cure for LAM, raising awareness and knowledge of LAM, and supporting women living with LAM.

For further information including contact details of LAM specialists in Australia, see www.lamaustralia.org.au