**Table 1:** Comparison of TSC-LAM and Sporadic LAM

| | TSC-LAM | Sporadic LAM |
|---|---|---|
| Estimated # patients on earth | 250,000 | 30,000 - 50,000 |
| Reported in males | + | - |
| Reported in children | + | + |
| Ascertainment | mostly by screening | dyspnea and pueumothorax |
| Germ line TSC mutations | + | - |
| Both hits = somatic mutations | + | - |
| Inheritable | + | - |
| TSC1 / TSC2 mutations reported | 33% / 66% | 0% / 100% 40 - 50% |
| Angiomyolipomas | 70 - 80% multiple / bilateral | single / unilateral |
| MMPH | + | very rare |
| CNS / skin / eye / cardiac lesions | + | - |
| Retroperitoneal, thoracic adenopathy | + | - |
| Dyspnea | less common | more common |
| Chylothorax | less common | 33% |
| Pneumothorax | less common | 66% |
| Respriatory failure | less common | more common |

**ABBREVIATIONS - CNS;** central nervous system, **MMPH;** Multifocal micronodular pneumocyte

**Table 2:** Recommended interventions, studies and immunizations in patients with Lymphangioleiomyomatosis (LAM)

| | | |
|---|---|---|
| Stop smoking<br>No estrogen containing meds | Pulmonary | Head CT to r/o TSC |
| Yearly flu shot and pneumovax | Rest, sleep, exercise oximetry | Wood's lamp skin exam |
| Counsel re: pneumothorax and pregnancy | HRCT chest | Transplant eval for FEV1 < 30% |
| Pleurodesis on first pneumothorax | a 1-antitrypsin level | Refer for embolization if AML > 4cm |
| Base bone densitometry | Abdominal CT / USG | Oophorectomy rarely recommended |

*** Tables Courtesy of the American LAM Foundation**



# Lymphangioleiomyomatosis


2006 Abstract by S.R. Johnson,
Division of Therapeutics and Molecular Medicine, University Hospital,
Queens Medical Centre, Nottingham NG7 2UH UK.



Lymphangioleiomyomatosis (LAM) ia a rare disease of the lungs and lymphatics, which can occur sporadically or in association with tuberous sclerosis. LAM almost exclusively affects females, generally developing before menopause.

The disease is characterised by pulmonary cystic change, recurrent pneumothorax, chylous pleural collections and, in most cases, progressive respiratory failure. Abdominal manifestations include lymphadenopathy, cystic lymphatic masses (lymphangioleiomyomas), chylous ascites and angiomyolipoma (a benign tumour). Survival in LAM is < 70% at 10yrs, although this is highly variable since long-term survivors have been described.

Diagnosis is made by a combination of clinical features and computed tomography scanning or, in cases of doubt, lung biopsy. In patients with rapidly progressive disease, hormone treatment (predominantly progesterone) has been used, although no firm evidence supports its use. Otherwise, treatment is aimed at complications including pneumothorax, chylous collections and extrapulmonary manifestations. The only treatment for severe LAM is currently lung transplantation.

Recently developments in cell biology of Lymphangioleiomyomatosis have shown that these patients have somatic mutations in the genes linked to tuberous sclerosis and that rapamycin may correct the resulting cellular abnormality. Trials of rapamycin of fLymphangioleiomyomatosis are currently underway and offer hope of evidence-based treatment for the disease

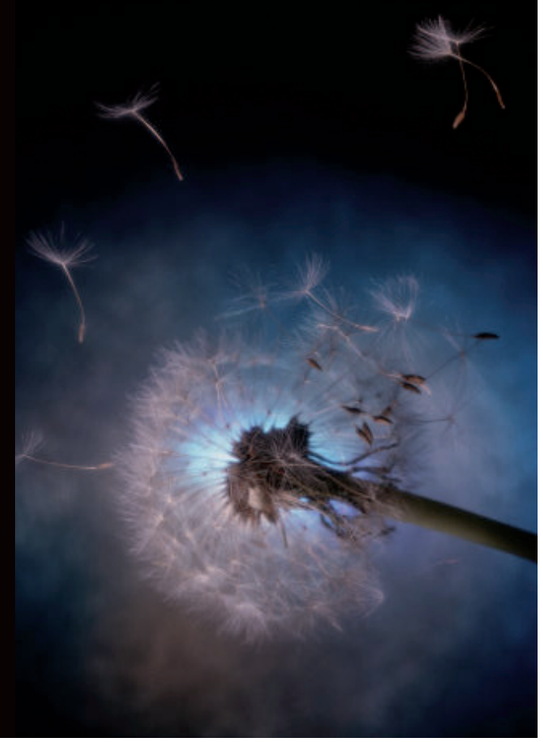


**KEYWORDS:** Angiomyolipoma, interstitial disease, orphan disease, tuberous sclerosis


*If you can't breathe nothing else matters*

THE NEW ZEALAND LAM CHARITABLE TRUST

Key Facts About Lymphangioleiomyomatosis (LAM)



## Defining LAM

Lymphangioleiomyomatosis, or LAM, is an uncommon, progressive, cystic lung disease that occurs almost exclusively in young women. Pulmonary parenchymal changes consistent with LAM are found in about one third of women with tuberous sclerosis complex (TSC). LAM also occurs in a sporadic form that is not associated with germline mutations in TSC genes. Sporadic LAM, (S.LAM) has never been reported in a male.

## Characteristics of LAM

The most common presentation of LAM is progressive dyspnea on exertion, often in association with a history of pneumothorax or chylothorax. Other symptoms of LAM include chest pain and coughing. The histopathological hallmarks of the disease are dilated distal airspaces and diffuse infiltration of the pulmonary interstitium with atypical smooth muscle cells, including spaces surrounding airways, vessels, and lymphatics.

## Clinical Presentation of LAM

Most women complain of dyspnea on exertion, coughing and wheezing, chest pain and less commonly hemoptysis. Figures from the American LAM Foundation show that pneumothorax occurs in 66% of registered LAM patients. Angiomyolipomas are present in most patients with LAM, including 70-80% of patients with TSC-LAM and 40-50% of patients with S-LAM. The average age at diagnosis of S-LAM is about 35 years, after an average symptomatic period of 3-5 years. However, more recent reports include patients ranging from age 12-75 years.

## Renal Angiomyolipomas

Kidney tumors (angiomyolipomas), unusual hamartomas containing fat, smooth muscle and blood vessels, are present in about 70-80% of patients with TSC related LAM and 50% of Sporadic LAM **(Table 1)**.

## Laboratory Findings & Radiology

There are no consistent laboratory findings that are helpful in the diagnosis or management of LAM

The chest radiograph in LAM can be surprisingly unremarkable, even in the presence of moderately advanced disease.

High resolution CT scanning of the chest is the most helpful radiologic modality in LAM, and usually demonstrates profuse thin walled cysts in all lung fields.

## Pregnancy and LAM

Patients should be advised that pregnancy has been reported to result in exacerbations of LAM and pneumothorax. However, the risk of pregnancy in LAM has not been rigorously studied. The physician and patient should discuss the risks of pregnancy carefully and decisions should be made on an individual basis.

## Diagnosis

Diagnostic dilemmas in LAM fall into two major categories; 1) How to identify LAM with progressive dyspnea and/or pneumothorax, 2) How to make the diagnosis of LAM in a woman with diffuse cystic changes on a CT scan of the chest with or without other corroborating evidence of LAM or TSC.
The first scenario presents major challenges; how to identify a rare, life threatening disease in a sea of common, less morbid obstructive diseases such as asthma and COPD. LAM is not usually part of the differential diagnosis for emergency and primary care physicians faced with a dyspneic patient, nor is it realistic to think that it will become so in the foreseeable future. Physical examination of the thorax and the chest radiograph can be surprisingly devoid of clues. Even severe cystic disease can be radiographically invisible on a chest radiograph. High resolution CT scanning should be obtained on all young nonsmoking women who present with dyspnea and a history of pneumothorax.

## Prevalence

The prevalence of Sporadic LAM is roughly estimated to be approximately 3-5 per million people (30,000-50,000 patients worldwide), based on organized attempts to identify LAM patients in England, the United States and France by saturation mailings to all pulmonary physicians identified in each country.

In New Zealand and Australia the numbers of women registered with LAM patient organisations (2006) is 16 in New Zealand and 60 in Australia.

## New Zealand and Australia survey

A 2002 study of 36 women with LAM in New Zealand and Australia showed that the average time from presentation of respiratory symptoms to diagnosis of LAM was seven years (Dr Debbie Yates and Dr Alessandra Sandrini St Vincents Hospital, Sydney Australia).

LYMPHANGIOLEIOMYOMATOSIS

nothing else matters

If you can't breathe

**Rt Hon. Helen Clark,**

Patron of the New Zealand LAM Charitable Trust.

I am proud to be involved with the LAM Charitable Trust which is dedicated to giving hope to women with this rare and tragic disease.

The Trust's fundamental belief is that the cause of this disease will be uncovered by basic scientific research. I totally support activities that seek to raise funds to support research on LAM and I fully support the Trust as a symbol of hope for LAM patients and their families.

Helen Clark