holding

THE SILENT DISEASE THAT'S KILLING YOUNG MUMS

It most commonly strikes women of child-bearing age and leaves them, literally, gasping for breath. **Bettina Arndt** talks to the courageous Australian women living with LAM – a rare, yet fatal, lung disease.

THE FIRST SIGN OF TROUBLE came when Shani Eldridge was pregnant with her first son. Her lung collapsed. No one knew what caused it. However, she went through her second pregnancy without a problem. Then, three years later, she started getting very short of breath.

"When I went to functions at my son's schools, I'd run out of breath walking up the hill to their classrooms. I'd pretend to talk into my mobile so people wouldn't notice something was wrong," says Shani.

She made repeated visits to doctors, who eventually diagnosed emphysema. "That seemed strange," she says, "because I'd never smoked."

It took a late-night phone call from her mother, Adrienne Chubb, to one of the world's experts on emphysema at the UK's Manchester University to find out the awful truth. Adrienne described Shani's symptoms and he immediately knew what was wrong. He told her Shani was suffering from a rare lung disease called lymphangioleiomyomatosis. It's pronounced lim-fan-gio-lio-mio-matosis, but is referred to as LAM. The disease is fatal.

So began their struggle to find out what they could about this little-known disease. Yet knowledge brought scant comfort. There is no cure and no effective treatment. LAM strikes only women and is usually diagnosed between the ages of 30 and 40. Their lung tissue is invaded by an unusual smooth muscle cell that proliferates and slowly smothers the lungs. The first symptoms are usually shortness of breath, coughing, sometimes with blood, lung collapse and chest pain. Some women have only four years before their lungs give out.

The last resort of these women is a lung transplant. Yet that's a prospect that makes the 40 Australian women currently diagnosed with the disease very nervous. In the past three years, they have lost two of the key women responsible for setting up LAM Australia, their support foundation. Both had had lung transplants.

Shani Eldridge, 43, was desperate to avoid having a lung transplant. "My children [Jordan, now 13, and Taylor, 11] were >>>

"MY CHILDREN WERE SO YOUNG … I COULDN'T BEAR THE THOUGHT OF THEM GROWING UP WITHOUT A MOTHER."

LAM sufferer Shani Eldridge, 43, surrounded by her family – husband Mark, 43, Jordan, 13 (top), and Taylor, 11.

PHOTOGRAPHY BY EAMON GALLAGHER.

their breath

so young," she says. "I didn't want to leave them. I couldn't bear the thought of them growing up without a mother."

After struggling with breathlessness for years, she finally had no choice. Her doctor told her she had to go on the transplant list – she didn't have long to live.

"I did worry about how much time there really was left in the old lungs," Shani says. "I don't think there was too much, actually."

Donor lungs are in short supply, so it was a huge shock when, after a mere eight weeks on the list, an early morning phone call announced lungs had come through for her. That was three months ago. Her husband, Mark, 43, was away on a work trip to London. "The flight back was the longest 24 hours of my life," he says.

He arrived a day after the operation to discover her sitting up in bed, talking to her family. "To see her like that – nothing could have made me happier," he says.

While Shani was trying out her new lungs, talking to her husband, a team of researchers at Sydney University was already working on her discarded lungs to seek further clues to the cause of this disease. Sarah Boustany, a PhD student, was carefully dissecting airway tubes out of the dark mass of lung.

"It usually looks more like strawberry mousse," says lab manager Jo Thompson, comparing it to a segment of non-diseased lung, which is lighter coloured and far less dense. "You can see from this section of the LAM lung that it hasn't had air pass through it for a long time."

"There's an overgrowth of smooth, muscle-like cells which wrap themselves around all the tubes in the lungs, such as the airways, blood and lymph vessels," explains Professor Judy Black, leader of the team conducting the pioneering LAM research. "This blocks airways, trapping air in pockets or cysts, which means the woman has difficulty moving air in and out. The lungs run out of airspace and gradually shut down. That's why the tissue looks so dark."

In trying to understand why these cells proliferate, the researchers are focusing on proteins produced by them which make the airway tubes thicker and stiffer, inhibiting the normal breathing process. They have already made interesting discoveries about abnormalities in lung tissue, which one day may hold the key to future treatments for LAM and, perhaps, also for diseases such as asthma.

That one day can't come soon enough for the LAM sufferers and their families. "Science works so slowly," fumes Shani's mother, Adrienne. "I know you've got to go through these trials and procedures, but you do feel as though you'd like to shake them and say, 'Get a move on. My daughter's dying!' "

Many of the scientists working on LAM have met the women dying of the disease and understand the urgency to come up with the answers. Some have even been specifically recruited by these families to get involved in the research.

One person collaborating with Judy Black on recent LAM investigations is Mervyn Merrilees, a New Zealand heart researcher. Professor Merrilees was working on smooth muscle cells involved in coronary heart disease when he was hunted down by Bronwyn Gray, whose daughter, Lisa, a young lawyer, had just been diagnosed with LAM.

Bronwyn was determined not to allow her daughter to die without a fight and recruited eminent New Zealanders, including Prime Minister Helen Clark, for a LAM foundation. Another mother of a LAM sufferer, Sue Byrnes, has raised more than $7.8million in the US to fund research.

It is extraordinary what these women have achieved. "Bronwyn Gray is amazing. After spending a few hours with her, you feel you have to dedicate every waking moment to LAM research," says Professor Black, who is a leading asthma researcher, but is now also focusing on LAM.

Anna Lazic, 41, and husband Michael have had to face the fact they can never safely have children together.

EAMON GALLAGHER.

LEARNING ABOUT LAM

Sydney chest physician Dr Deborah Yates is medical adviser to LAM Australia. Last year, with her colleague Dr Alessandra Sandrini, she conducted a survey of 29 of Australia's LAM patients which revealed the following:

- **It is not clear if there are two forms of LAM, with one far more aggressive than the other, or whether some women with LAM have a long stable period when they are not diagnosed.**
- **Pregnancy appears to accelerate LAM, probably due to the flood of female hormones circulating at the time. Dr Yates' survey found that 76 per cent of LAM mothers had their first lung collapse during pregnancy (but only 9 per cent were diagnosed at that time). It appears oestrogen is the major culprit in accelerating the disease. Women without children are usually advised against pregnancy. Dr Yates points out that some LAM women choose to risk pregnancy and some deteriorate more significantly than others. LAM women are also advised against taking oestrogen-based contraceptive pills and HRT. Doctors sometimes remove the ovaries of LAM women, or give them progesterone, but Professor Allan Glanville says there is no good evidence that such treatments are effective. LAM can also appear in the reproductive organs, such as the uterus and fallopian tubes, affecting fertility.**
- **There is no overall, effective way to treat LAM and the complications of the disease need careful monitoring. The lung collapses and haemorrhaging from the kidney tumours can be avoided – if LAM has been diagnosed. Yet experts, such as Dr Deborah Yates, fear that misdiagnosis is common.**

"You can't help but want to do something to provide hope for these women. It is so awful watching them losing their struggle to breathe."

A mighty struggle it is. Jeanann Coleman, 47, is a woman who likes to talk. The warm, friendly mother of three and grandmother of four took over as president of LAM Australia in 2002, following the death of founding president Virginia Northwood. She talks non-stop about her "Lamies". Every few minutes, though, she has to stop and draw breath, or has a coughing fit. She's had to give up working, is on oxygen every night and some days even battles to get out of bed.

Jeanann was 20, picking tomatoes to support her three children, when she had her first lung collapse (pneumothorax). "It hurt like hell," she recalls. She ended up in hospital for a week, but within a few months, her lungs collapsed twice more. »»

"No one knew why this was happening. They couldn't give me any answers," she says. It took more than 20 years for Jeanann to discover she had LAM. By then, her lungs had collapsed 13 times and doctors had discovered she had tumours in her kidneys – a known complication of LAM. Yet her breathing problems were still put down to asthma or emphysema – despite the fact she'd never smoked. In 1998, she ended up in Sydney's Royal North Shore Hospital with pneumonia, and a CT scan revealed the cysts indicative of LAM. Doctors told her that if she was lucky, she'd have 10 years to live.

Life is certainly becoming tougher for Jeannan, who is now having difficulty with everyday tasks, such as vacuuming or food shopping, in her small, NSW Central Coast town. Yet it helps to talk to other LAM women facing similar struggles. The foundation regularly holds lunches for LAM sufferers to get together and most find this a great support, but it does have its downside. "You meet people who have the same disease as you and then they get really sick," says one of the women.

"So many have died. It's scary. You worry so much about your friends and then you think, 'Hang on a minute, this is my thing, too. It could be me!' "

At a recent gathering at a Sydney cafe, the women joked about the difficulties they face. "What I hate is I can't try on lots of clothes any more. I get too out of breath and have to keep sitting down," says one woman. "I miss being able to paint my toenails," says another, giggling.

"You've got all these young women in the prime of life. It takes so much away from them," says Allan Glanville, medical director of the lung transplant team at St Vincent's Hospital Sydney. "They should be depressed and devastated, but it's remarkable how well many of them cope."

"I WAS DIAGNOSED THE DAY AFTER PRINCESS DI DIED. I SAT THERE SAYING TO MYSELF, 'I'M 37 AND I'M NOT DEAD. [I'M] A YEAR OLDER THAN SHE WAS, SO I'M LAUGHING."

Professor Glanville saw his first LAM patient more than 20 years ago, when he was working in England. Since he has been in Australia, he's seen more than 20 women with LAM – of those, six have died and eight have received lung transplants. Of the ones who have received transplants, he says some are doing well more than 10 years on, with about 60 per cent of his LAM transplant patients surviving more than five years.

Many women live with LAM symptoms for years before being correctly diagnosed. Melbourne woman Tracy Hughan, 45, was 18 weeks pregnant with her third child when she experienced a lung collapse. No one picked up the LAM until seven years later, when she had another collapse and a CT scan. "I was diagnosed the day after Princess Di died. I sat there saying to myself, 'I'm 37 and I'm not dead. That's a year older than she was, so I'm laughing, really'," says Tracy.

Since then, Tracy's whole family has become involved in LAM. Her brother helped set up the LAM Australia website and her father has been trying to put together a brochure on the disease. The problem is that every time he has it finished, complete with photographs of a number of LAM women, one of them dies and the whole project is put on hold.

Yet Tracy is one of the lucky ones. Her disease has been stable for eight years, but she's now noticing a few things are getting harder. "When I vacuum the house or walk up lots of stairs, I get puffed," she says. Yet her lung function has shown little deterioration. And there are a small number of LAM women who are similarly stable.

Melbourne teacher Anna Lazic, 41, was newly married and planning children when she started coughing up blood. The discovery four years ago that she had LAM came as a huge shock. "In the beginning, all I thought about was dying," she says. "I woke up, I went to bed every day with that thought in my mind."

Giving up the idea of having her own child was another major issue for Anna (pregnancy can be a risk for LAM sufferers). For years, she couldn't bear to tell her parents about the disease, but in the face of her mother's gentle nagging about the baby issue – "Have you seen a doctor, dear?" – she finally broke down.

"My dad was a blubbering mess," says Anna, but her mother has helped her move on from the baby issue. "Thank God, you've got a ready-made son," she tells her (Anna's husband Michael has a son aged 13 who lives with them), determined to keep her daughter from further risk.

Anna is doing well. She still works four days a week teaching in a high school, although "walking across campus makes me feel I've run a marathon". Recently, at one of her family's typical huge Greek weddings, she was determined to get up and join in the wild dancing. Not such a good idea, she discovered, as she ended up staggering back to her chair.

All agree it's time to get the LAM message out. The first real breakthrough >>>

COURTESY OF ERIC NORTHWOOD.

LAM ACTIVIST, VIRGINIA NORTHWOOD

"Virginia Northwood was the first person I talked to who had LAM. Until then, it felt like I was the only person in the world with the disease," says Claire Magee, a 60-year-old mother of four from Queensland's Gold Coast. She remembers she was cooking dinner one night – three years after she discovered she had the disease – when the phone rang. "It's someone called Virginia," a family member told her. "She says she has LAM!"

Two hours later, Claire finally put down the phone. It was the first time either of them had spoken to another woman with LAM. "It was just wonderful, being able to relate to someone else who knew what it was like," says Claire.

Virginia, a Sydney paediatric nurse, had found Claire through the LAM Foundation in the US. That was the start. Virginia went on to pull together all the other LAM women she could find and set up LAM Australia as a support group for them.

"She was incredible. She'd be on the phone at 11 o'clock at night asking us how we were. She was very, very supportive, kept us all together," says Claire.

Virginia was a woman with enormous energy. She met her husband, Eric, on a 2500km cycling tour of Britain. She'd climbed glaciers in Iceland, skied in France and thought nothing of swimming five kilometres after a tough day at work.

The 34-year-old was diagnosed with LAM in 1996 and, at first, went into complete denial, pushing herself to keep working and determined to stay fit.

When the disease started to take hold, however, she turned her energies to tackling LAM, working as president of the new support group, arranging lunches, fundraising, setting up a system to collect LAM lungs after transplants for research by Professor Judy Black and her team.

Towards the end, Virginia had to carry portable oxygen everywhere she went – even to the gym. "She'd always be at us to keep up our exercise," says Claire.

Virginia Northwood died four weeks after receiving a lung transplant in 2002, leaving her estate to be used for research into the causes of LAM.

Since her lung transplant, Claire Magee, 60, has travelled around the world and is now touring Australia.

in treating the disease has now appeared and LAM sufferers are needed to test its effectiveness. Preliminary trials in the US have shown that the drug Rapamycin – which is used as an immune suppressant in transplants – may be able to stop the growth of the smooth muscle cells.

"I'M SO GRATEFUL THAT THERE WERE SOME LUNGS THAT WERE COMPATIBLE. AND I KNOW SOMEONE HAD TO LOSE THEIR LOVED ONE FOR ME TO HAVE THAT GIFT."

There's some evidence it works both on kidney tumours and the lungs. Controlled trials – aptly named the SMILES trials – should commence early in 2006 and involve women from the US and New Zealand, and as many Australian women as possible, ideally early in the onset of their disease.

Meanwhile, Professor Judy Black's lab in Sydney is investigating how the drug works on the smooth muscle cells. The researchers will use Shani Eldridge's lung tissue to investigate how the Rapamycin affects the lung cell. "The LAM women who have had transplants are so keen for us to have their lungs to do this work," says the busy Professor Black, who combines her research work with chairing the research committee of Australia's peak body, the National Health and Medical Research Council.

The LAM momentum is building and, in April next year, many of the scientists making these discoveries will gather in the Blue Mountains, outside Sydney, for the third Australian/New Zealand Virginia Northwood LAM Science Symposium.

There are scientists all over the world now investigating this puzzling disease. It has been discovered that LAM is triggered by the loss of a protein called tuberin and that Rapamycin mimics the function of tuberin in LAM cells. The genes triggering the smooth muscle proliferation have been identified and work is underway on possible gene therapy.

"It's all too late for my daughter," says Shani's mother, Adrienne, who is grateful her daughter was given a second chance at life through her lung transplant. Three months after the transplant, Shani is doing very well. "I'm so grateful that there were some lungs that were compatible," she says. "And I know someone had to lose their loved one for me to have that gift."

Although a lung transplant is a risky business, for some it offers a second chance. "It's so nice to be a normal person," says sufferer "Margaret". That's not her real name, but the South Australian mother of two has recently survived her first post-LAM spell in the workforce and she's nervous about missing out on future jobs if people discover her medical history.

She lived with LAM for seven years before her transplant in 2001. By the end, she was in a constant state of panic about whether she'd be able to reach her oxygen cylinder if she ran out of breath. She'd even take her mobile phone into the toilet in case she ran into trouble.

Her husband is a keen surfer and she'd sometimes spend hours in the cliff-top car park overlooking his surfing beach, ready to flash the headlights if she needed him.

Now that is all over. After years of having to live near a hospital, they are about to move to a beachside home where her husband can surf every day.

"He deserves it. He spent so many years looking after me," Margaret says.

Claire Magee is another woman who counts herself very lucky. This active 60-year-old mother of four from the Queensland Gold Coast discovered she had LAM in 1994, after she fell over while water skiing and then had trouble breathing. Her doctor told her very little about LAM and it was one of her 23-year-old twin boys who discovered that the disease is terminal. Claire had sent him to the library to investigate and he came back with the dreadful news. "It was just so traumatic for him," she recalls.

By the time she had her transplant, five years ago, Claire couldn't even walk to her mailbox and was on oxygen constantly. Six days after the operation, she was doing very well. "I was up, dancing to *Saturday Night Fever* in the ward, with all these tubes hanging from me," she says.

Since then, she's successfully travelled around the world with only a slight mishap – she stepped off the footpath at a jazz festival in Austria and broke her foot (one of her anti-rejection drugs has given her osteoporosis). Now she's on the move again – driving a motorhome around Australia, starting in outback Queensland.

"I've been blessed. Every day is a bonus," she says, mentally sending a big thank you to her unknown donor family. ■

GIVE THE GIFT OF LIFE

There's a young paediatrician in Sydney who's just spent a week in St Vincent's Hospital and she's very much hoping to return soon. This mother of two children, aged seven and 10, is desperately ill with LAM. She's been on the transplant list for nearly a year and time is running out.

Sadly, many LAM patients miss out on a lung transplant once it becomes their best chance of escaping the disease. Australia has the second worst organ donor rate in the developed world. It's not just that there aren't enough people willing to be donors, but that half the time grieving families refuse their consent.

This is about to become less of a problem – under new federal legislation, clinicians no longer have to ask families for consent, provided the donor is registered on the new Australian Organ Donor Register.

For information about donating organs, call 1800 777 203, or visit www.hic.gov.au, or any Medicare office.

■ Donations to LAM Australia Inc should be sent to PO Box 168, Rozelle, NSW 2039, or via the website at www.lam.org.au. Phone (02) 4393 1449 or 0414 768 751.

PHOTOGRAPHY BY ANDREW RANKIN.