

# Amyloidosis News

CARING FOR PATIENTS AND THEIR FAMILIES LIVING WITH AMYLOIDOSIS

We were delighted with the positive feedback for the first Amyloidosis News. I hope this edition, with its mixture of medical articles and patient stories, will be equally informative. I would welcome any suggestions for future articles or letters to the editor.

2007 has been a very busy year with many new amyloidosis patients referred to the Foundation from around Australia.

In July I was delighted to visit Steve Marshall and his hard working team in the Adelaide Leukaemia Foundation office. It was a great privilege to meet and talk to the enthusiastic members of the South Australian support group led by Maureen Powell and Steve. The stories I hear about patients visiting a number of specialists over many months before being correctly diagnosed, reflects the sad situation world wide and illustrates how important raising awareness about amyloidosis is.



The support and education luncheons have continued to be well attended in Queensland. We have enjoyed enlightening presentations on "Renal Amyloidosis" by Dr John Burke and "Understanding the free light chain assay" by Dr Peter Mollee. In October we were delighted to welcome haematologist, Dr Hugh Goodman, now working in New Zealand after several years spent at the National Amyloidosis Centre, London. Dr Goodman gave a very helpful overview on old and new treatments. Patients from around Queensland and interstate attended and left with a feeling of hope.

In August I was able to catch up with all the Leukaemia Foundation state managers attending a Brisbane based conference. I look forward to continuing to work closely with them offering practical and emotional help to amyloidosis patients and families across the nation.

The amyloidosis T-shirts have arrived for sale. I would like to thank Allan Andrews, a Brisbane patient, for all his ideas and Leukaemia Foundation of Queensland for their support in getting this awareness building project off the ground. To order a t-shirt please contact me on 07 33786361 email [pneely@leukaemia.org.au](mailto:pneely@leukaemia.org.au) or Noeleen on 07 30403844.

This will be the last newsletter for 2007. We have exciting plans for 2008 including the production of a Leukaemia Foundation amyloidosis booklet. We already have a wonderful fundraiser in Victoria working hard to raise the \$5000 needed for this project. Her courageous story will appear in the Amyloidosis News Spring edition.

My thanks to the Leukaemia Foundation staff, doctors and health professionals, patients and families for their continuing support throughout this year. I send seasons greetings and best wishes to you all.

Pat Neely  
Amyloidosis services coordinator  
Leukaemia Foundation

## Useful websites for further information

National Amyloidosis Centre London [www.ucl.ac.uk/medicine/amyloidosis/nac/index.html](http://www.ucl.ac.uk/medicine/amyloidosis/nac/index.html)

Amyloidosis Support Network [www.amyloidosis.org](http://www.amyloidosis.org)

Amyloidosis Australia [www.amyloidosisaustralia.org](http://www.amyloidosisaustralia.org)

Heart Foundation [www.heartfoundation.org.au](http://www.heartfoundation.org.au)

# The use of the free light chain assay in AL Amyloidosis

Dr Peter Mollee, Dept of Haematology, QHPS, Princess Alexandra Hospital.

The amyloidoses are an uncommon group of diseases caused by the deposition of protein as abnormal fibrillar aggregates. It is a disorder of abnormal protein folding where eventually the abnormal deposited protein, known as amyloid, accumulates and disrupts organ failure.

There are many, many different types of proteins in the body. These proteins, which do many different jobs to keep the body running, are synthesized in cells as a long string of amino acids joined together to form the protein. Normally that protein folds up in a particular way to perform its particular function. In amyloid the protein does not fold the way it is supposed to, but it is not known why this happens. The protein folds in an abnormal manner resulting in the proteins lining up next to each other forming fibrils. More and more fibrils twist around each other getting progressively larger and forming the amyloid deposits in the tissues. These amyloid deposits have a unique appearance when tissue biopsies are examined to make the diagnosis of amyloidosis. The amyloid will stain red with the Congo Red stain, but using a polarizer light under a microscope the red will be seen to turn to green.

Amyloidosis can be due to many different proteins that have in common the ability to form this particular fibrillar structure. The main protein that constitutes the amyloid defines the type of amyloidosis.

Those proteins can be:

- completely normal proteins in normal concentrations in the body. One type of amyloidosis formed this way is senile amyloidosis affecting the heart.
- normal proteins but in high concentrations. This happens in AA amyloidosis, also known as secondary amyloidosis. Typically seen in people with chronic infections or inflammatory diseases.
- abnormal proteins where there is a mistake in the protein that is inherited. There are a number of types of inherited amyloidosis. The commonest forms are ATTR and AFib
- an abnormal protein that is not inherited but develops in later life. This is light chain amyloid, also known as primary amyloidosis or AL amyloidosis.

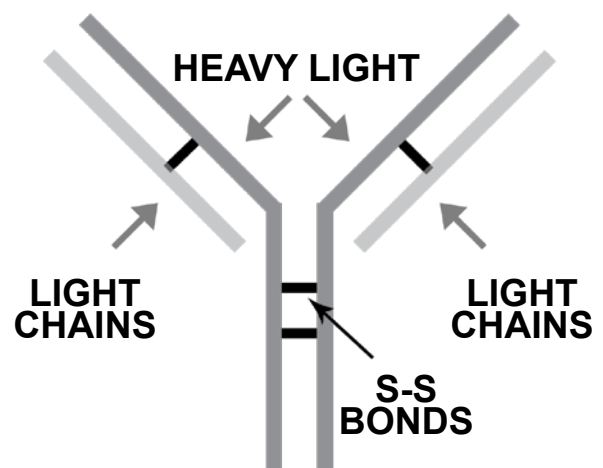
## What is AL amyloidosis?

In AL amyloidosis, the abnormal light chain protein can be deposited locally, made from local cells. This is seen typically in the bladder or the upper part of the lung and is known as localised AL amyloidosis. More commonly,

however, is systemic AL amyloidosis where the light chains are made in the bone marrow, circulate in the blood and deposit in various tissues. In systemic AL amyloidosis, the amyloid can deposit almost anywhere in the body except the brain. There is thus a huge variation in the clinical manifestations that people with AL amyloidosis can have.

## What are free light chains?

In AL amyloidosis the protein comes from the light chain of an antibody. An antibody is a type of protein, known also as immunoglobulin, which our body makes to help us fight off infections. It is made of two "heavy" chains and two "light" chains (see picture).



Antibodies are made by plasma cells in the bone marrow and usually each plasma cell makes a slightly different antibody which has a unique light chain. Normally the body is making lots of different antibodies which have different heavy chains and lots of different light chains. The plasma cells makes light chains in excess of the amount needed to produce an antibody and those excess light chains circulate around in the blood as free light chains. There are two main types of light chains, kappa and lambda. Thus, everyone has small amounts of normal kappa and lambda free light chains in their blood.

In AL amyloidosis and myeloma one single plasma cell proliferates abnormally and builds up in the bone marrow. It makes large amounts of a single type of free light chain which may or may not have the ability to form amyloid deposits. Most people have free light chains that do not form amyloid.

Diseases that can result from these plasma cells which multiply and become abnormal

Plasma cell proliferation	Does the free light chain form amyloid?	Disease
Cancerous (=malignant)	No	Multiple myeloma
Cancerous	Yes	Multiple myeloma + AL amyloidosis
Non-malignant	No	MGUS (Monoclonal Gammopathy of Undetermined Significance)
Non-malignant	Yes	AL amyloidosis

## What is the free light chain assay?

The Free light chain assay is an automated test carried out in the laboratory. It is specific to the kappa and lambda free light chains recognising the free light chains that cause AL amyloidosis but not the light chains that are bound to the heavy chains. This test was developed by a biochemist in Birmingham UK and has been available in Queensland since 2002.

Why is the free light chain assay (FLC) so useful in AL amyloidosis?

1. The assay is much better than traditional methods at detecting small amounts of the light chains.
2. As measurable abnormal light chains are present in the blood in nearly all cases of AL amyloidosis, the assay is very useful in diagnosis.
3. The assay can be used to monitor response to therapy to see if the treatment is working or not. Changes in the serum free light chain assay also occur faster than the traditional methods of monitoring AL amyloidosis. This is because light chains only last for a few hours in the circulation as opposed to the antibodies that last about a month in the circulation. Therefore, if the treatment is working, reductions in the light chains occur quickly. Treatments can then be changed if there is no response.
4. As organ improvement in AL amyloidosis can take many months to years it was traditionally difficult to know if the treatment was working. Now, although there may not be immediate organ improvement, the drop in the FLC level can indicate the treatment is working before organ improvement is seen.

5. Data from the National Amyloidosis Centre in London showed that a 50% reduction in patients' free light chains correlated with an improvement in the amyloid load in the patients' organs shown by the SAP scan, a scan not available in this country. The data also showed a dramatic improvement in the number of patients alive at 5 years if the free light chains could be reduced by 50%.

Every patient with amyloidosis is different. The height of the FLC assay at diagnosis does not always correlate with the extent of the disease. Different patients need different amounts of reduction in their FLC assay result to improve the amyloid deposition in their organs. What is important in treatment is to reduce the FLC in the individual patient.

## As with all tests the FLC assay is not perfect.

It is not an easy test to do and is very time consuming. There are some problems with laboratory aspects of the test that can sometimes result in inaccurate results. Thus, there may be blimps in the FLC assay results from time to time and patients should not worry too much if suddenly one result is slightly higher. Similarly, the FLC assay result should not be used in isolation of the other more traditional tests and assessments of the affected organ function.

In spite of not being 100% correct the free light chain assay has certainly changed diagnosis, assessment and treatment in patients with AL amyloidosis and is an important part of the management of these patients.

# What shall we tell the children?

It would be normal for families facing a diagnosis of amyloidosis to be very upset. When there are young children or teens in the family there is the added concern of how the children will react and what they should be told.

Obviously the way this is handled will depend on the age of the child, the family relationships and the circumstances. But adults often underestimate the way children can cope with the truth if it is given in a loving environment in language they can understand.

Parents, who are often in shock themselves, may have concerns about being seen to be upset by their children or to burden them with worries and fears. However the children themselves usually sense that something is wrong. Often how they react to a worrying diagnosis will depend on how their parents and close adults handle the crisis. If they are not told anything they may fear that things are worse than they are, or that they are not wanted. Small children may even think they have caused the parent to be sick because they have misbehaved.

Children and many teenagers depend on adults for their nurturing and safety. They need to know that they are still very much part of the family and understand why their routine may change a little for a while. A few tears and hugs and some explanation given in a reassuring way can help them feel included without overly worrying them at first. This also means that the parents do not have to use energy hiding everything from their children.

Every family will deal with their children differently. Deciding how to handle this dilemma is far from easy. Some may seek advice from their general practitioner or other health professionals or one of the numerous websites available. Others will use family members for advice.

Three families have generously agreed to share their stories of how they coped at such a difficult time in their lives.

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In 2000, Coral Verhoeven from Brisbane was diagnosed with AL amyloidosis. She describes being completely overwhelmed and numb at the time of diagnosis but remembers her thoughts quickly turning to how her girls of 13 and eight years might manage without her. Would she live to see them grow up, graduate and marry?

She and her husband Patrick decided to involve both girls from the very beginning, including them in every decision.

“We gave them the opportunity to ask questions and discuss how they felt. We talked to them about mum perhaps dying and let them know that it was all right to feel sad and angry. I constantly told them how much I loved them and how I was writing birthday cards and letters to them for later in case I was not there. I remember my daughter, just 13, saying to me before I started chemo ‘mum you know that you do not have to do this for us, it will make you very sick and you will be hurting and suffering, we understand you love us.’ It was such a brave and teary moment from one so young.”

“During my four month stay in hospital my renal physician even had a desk moved into my room so that my girls could do their home work close to me. It made such a difference. I felt I hadn’t left them alone and they felt they were still part of my care. I also got the chance to have each of them sleep overnight in my ward. As sick as I was it was wonderful to be able to listen to their separate needs. They felt very special and it raised my soul.”

“The girls are now 18 and 14. We still share how things are going and they are very protective of me. They can still feel angry if things are not going to plan.”

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Jackie Forster from Victoria says that telling their five children ranging in age from nine to 22 that their father was sick was something she had never contemplated.

“When the children’s father is ill you have to deal with their pain and anxiety as well as your own. My husband found it extremely difficult to speak with the children and initially tried to walk away as he didn’t want them to see him cry. I grabbed him and called them over and we had a big group hug all crying. I just told them that dad was going to need treatment in a hospital four hours away. All he could say was ‘I am sorry’.”

“When we spoke with the haematology staff and understood the situation better we were able to explain it to the little ones in quite simple language. Our eldest daughter was working in Melbourne studying myotherapy and she spent a lot of time with her father when he was in hospital.”



“On occasions our nine year old daughter sometimes asks, ‘are you still better Dad?’. His response is ‘yes, I am well at the moment and I might stay well for a very long time!’ Call it denial but I believe he is cured and we lead a very normal life. Every three months we get very nervous when we visit his fantastic haematologist but for now the prognosis is good.”

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Michelle Taylor from Tasmania recalls that the day she heard the news that she had amyloidosis was the most difficult she had ever had to face. She and her husband were to attend their son’s primary school graduation that evening.

“I got home from the doctors feeling absolutely sick, I just wanted to go to bed and wake up from the bad dream.”

Michelle recalls the emotional roller coaster she and her husband experienced that evening as they put on brave faces and tried to share in their 12-year-old son’s excitement. As they fell into bed exhausted she recalls them saying to each other “shall we tell him or not?”

“After talking with our doctor we decided not to tell Sam too much at first but just to try and keep his routine as normal as possible and to answer his questions as they arose. Over the next 18 months as he saw me improving after being very sick his questions increased and he now knows a great deal about my disease and prognosis. As I felt better my husband and I suggested that Sam should write down the way he felt. This has enabled us to understand our son’s needs and feelings so much better.”

Sam has agreed to share his writings with us too and we thank him sincerely for this.

## My Happiness

Nan passed on and went to heaven  
Didn’t think life could treat me worse  
Mum saw a doctor called Tom a good lad  
but some bad news  
Mum was really sick with amyloidosis.

My happiness is slowly creeping back now  
you’re getting so much better  
I wish this thing didn’t happen but what can  
we do.

My happiness is slowly creeping back  
now with all that love  
I can’t wait until you get so much better so we  
can have fun and games with each other.

Holidays were not great we didn’t  
do the things we did before  
Saw some friends and looked after you  
with Dad.

Hated all the stare bares that looked at you like  
you were different  
But you are great and any normal person can  
see that.

When you finished chemo you were  
not great in hospital for weeks at a time  
I felt alone you gave me hope when you  
came home to me.

You’re so much better now we have fun in the  
holidays, but you’re still not great,  
You took me places and let me do things.  
Gave me a great time, you got a big bug which  
made you feel so bad, so you couldn’t do much  
again, but you went on and gave me hope.

So here we are, people took Mum for granted I  
don’t think they really knew  
How sick you were, as you didn’t have cancer  
But most have been kind, loving and generous,  
I just wish that everyone could  
See my Mum is the greatest in the world and  
my Mum is getting better, lucky, lucky me.

# Returning to work

As treatments for amyloidosis improve many patients are becoming well enough to consider returning to their paid occupation or their normal life. However thinking about returning to work after treatment for a life threatening illness can be daunting.

Many patients find their diagnosis and treatment quite traumatic. Often treatment decisions are made rapidly on diagnosis. Patients have to face the fact that if they do not receive treatment they will get worse and perhaps die quickly but that the treatment itself is not without its dangers. All of this takes its emotional toll and patients often emerge from treatment with lowered self-esteem and ongoing fatigue.

They may long to return to work or have to for financial reasons but they worry about when the right time would be and whether they are able to perform to the acceptable level.

Von Rydes, a Brisbane secondary school teacher who was diagnosed with AL amyloidosis in February 2006 likens returning to work after treatment to returning from war.

"I felt like a battle casualty that everyone recognised but didn't understand. I had just begun to feel really well again after treatment for breast cancer in 2004. I was back working full time and pursuing my love of ballroom dancing when I began to develop aches and pains, swelling in my legs and extreme tiredness. Six months later after a wrong diagnosis my world fell apart again when I was diagnosed with AL amyloidosis. Would I ever work again, I asked myself. Well I did!"

"Along the way there were many times when I almost lost my spirit. The road back was a physical and emotional nightmare at times. Undergoing the gruelling and frightening experience of three rounds of chemotherapy, two stem cell harvests and a stem cell transplant, left me without hair, little energy and a lowered self-esteem. However by November I had returned to work as if nothing had happened!"

"In my heart I had always hoped to return but driving the 38 kilometres to and from work presented a problem. Negotiations with my employer finally led to a five week placement closer to home before returning to my old school with a slightly reduced workload. Strangely, I really resented this, as I desperately wanted to be seen as normal in every way."

"Amyloidosis, which is not a cancer, is little understood by the community. I felt no one understood what I had

been through. I wondered whether my colleagues were questioning my ability to work and professional credibility when they asked, "do you feel tired?" "How are you?" I purposely hid the fact that I had doctor's appointments, always arranging them for after school. Sometimes this meant a 12 hour day. "

"One of my greatest concerns was my absence of hair. Teenagers are inquisitive and critical and sometimes they can be cruel. I worried about my own emotions. Teachers are public figures. As professionals we must give the appearance of strength, endurance and reliability. Fortunately the five weeks in the school where I was not known helped me regain some of my self esteem but I still hated my wig in the heat of the summer and could not wait to rip it off at the end of the school day."

"Re-entering the world of work has been a very mixed experience for me but I feel pleased that I have achieved it successfully by treading carefully and slowly. I do not look too far ahead. My experience has taught me not to take life quite as seriously. I am now just grateful for being alive and able to enjoy every day and the beauty around me. How long this will last I cannot say but I am just so grateful to be feeling well again.

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"I have to say returning to work 18 months after being off for AL amyloidosis was one of the hardest things I have ever done" Michelle Taylor from Tasmania, married with one son recounts. "I had been working as a roster clerk before I became sick. I was very nervous about whether I could do the job again.

I didn't want peoples' pity, I needed to be able to walk in and it be business as usual (I did cry to myself when I went through the doors initially).

I had thought about returning to work for months, but I really wanted to go somewhere that people didn't know my story.

We needed the money, as being unwell can be very expensive, so I must say my return was very money driven which was sad. In the back of mind I kept thinking, OK how long will I be able to work, I might get sick again, should I be making the most of my time and enjoying life.

I felt anxious about seeing people that hadn't made contact with me when I was sick. I was disappointed with some staff's reactions and very pleased with others. Let's face it, it doesn't take much to send a card or pick up the phone.

# Adam Gardiner Foundation & The Westmead Amyloidosis Clinic



With the support of many people, I established The Adam Gardiner Foundation, in memory of my husband who passed away 16 months ago at the young age of 35.

The Foundation's mission is to raise funds and awareness for amyloidosis while working within the structure of Westmead Hospitals Immunology Department and its Institute for Immunology & Allergy Research (IIAR).

We have joined forces to establish a lasting legacy in Adam's memory through the development of a specialised clinical service for patients with amyloidosis, the devastating disease from which Adam died in the prime of his life.

The aim of the clinic is to provide, through a team approach, integrated care for people with amyloidosis. Important aspects include rapid diagnosis of patients suspected of having amyloidosis, and an assessment of the extent of their disease involvement for those who have already been diagnosed. All patients will be provided with advice on treatment options (that may be then taken up at Westmead or by their own doctors closer to where they live) and educational material to assist with their decisions on treatment and other aspects of care.

The Westmead team includes each of the specialists needed to provide assessment and care for all of the potential problems caused by amyloidosis including haematologists, immunologists, neurologists, nephrologists (kidney specialists), cardiologists, nuclear medicine physicians (for diagnostic scans) and pathologists (to examine biopsies). Each of the Clinic doctors has a special interest in amyloidosis.

An important aspect of the Clinic is the ability to carry out genetic testing for the rare forms of amyloidosis that are inherited. This is the only genetic service for this disorder in Australia.

Appointments may be made through Mavis Billinge and phone enquiries should be directed to the clinic coordinator, Dr Ming-Wei Lin on (02) 9845 6933. Patients will require a referral letter from their GP or specialist and will be billed Medicare schedule fees.

We are appealing to all who can become a supporter of The Adam Gardiner Foundation through a donation or sponsorship. Donations will fund medical research for The Westmead Amyloidosis Clinic, and are tax deductible.

Please do not hesitate to contact me if you require any further information regarding The Adam Gardiner Foundation at PO Box 3179, Rhodes Westside, NSW 2138, or phone 0416 462 356 (mobile) or email [trisha@agf.org.au](mailto:trisha@agf.org.au).

Trisha Gardiner

I felt that I wasn't sharp enough to return to my old job, but I was wrong and after two months of working, the old Michelle was back. Things like driving myself to work became a great achievement.

I am now working full time again and I must say getting out of bed to be somewhere is very rewarding. I think my family are pleased too. On my first day back at work my son said "do you realise you haven't worked since I started high school eighteen months ago".

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Stan Forster from Victoria, married with a family was diagnosed with AL amyloidosis on 3 November and underwent an SCT on 7 December. Very weak but determined to be home for Christmas he was discharged from hospital on 22 December. "The first few weeks after returning home were difficult?" he says. "I was fighting the results of treatment but slowly my endurance improved and I began to feel human again. I spent as much time as I could fishing with my eldest son. He had to help me pull the boat in and out of the river!"

"My employer agreed to initially let me return to work for a few hours a day when I felt I could handle it. I started on January 22 working mornings that first week. I then moved to three full days and then four".

"For the first two weeks I struggled physically. I had to gauge my condition and leave work before I felt totally flat otherwise I would have been unable to make it home. But I was determined as was my wife. In our minds returning to work meant that things were back to normal and I was getting better. I had always had extremely supportive co-workers. I needed their friendship and the support of people who really cared. One wonderful colleague even had a Sydney Swan's training shirt sent to me signed by Adam Goodes (my hero)".

"Sometimes I would become really agitated and too abrupt with some of my co-workers. At this time my assistant would talk to me and suggest I take a break. The frustration was simply me putting too much pressure on myself to get back to "normal". What a fantastic feeling it was five months later to be told that I had achieved the best result in the organisation and I was being sent to a Gold Coast conference!"

My family and I do not dwell on the future. We are very positive and I am just so grateful for the second chance I have been given.

# Cardiac Amyloidosis

Dr Elizabeth Donnelly M.B., B.S., B. Sc(Med), F.R.A.C.P. cardiologist.

Cardiac amyloidosis occurs when there is extracellular deposition of specific protein molecules in heart tissues. These proteins interfere in a progressive manner with contractile function and electrical properties of the heart. Cardiac amyloidosis is usually part of a systems disorder. Infiltration of the heart is associated with the worst prognosis in all amyloid patients, therefore, early diagnosis is very important as is appropriate selection of treatment.

While there are 25 different types of amyloid fibrous proteins, cardiac amyloidosis is classified into categories according to the protein and cardiac involvement:

- 1. Primary (AL) amyloidosis. Due to a light chain produced as a result of a plasma cell dyscrasia. The heart is involved in 22-34% of cases. Median survival is 13 months only, 4 months if the heart failure is present at the time of diagnosis.**
- 2. Hereditary transthyretin (ATTR) amyloidosis. Due to a mutant transthyretin protein produced by the liver. Patients usually have a severe neuropathy and cardiac involvement is variable.**
- 3. Senile systemic (ATTR) amyloidosis due to deposition of the transthyretin molecule, cardiac involvement is quite common.**
- 4. Reactive (AA) amyloidosis due to an amyloid A protein. Frequently these patients have renal failure with limited cardiac involvement to less than 10%.**
- 5. Isolated atrial amyloidosis and dialysis related amyloidosis are two rare forms of amyloidosis affecting the heart.**

Common to all these forms of amyloidosis is that biopsies stain with congo red showing apple-green birefringence under polarising light microscopy. There are Beta-pleated protein sheets within the extracellular tissues. While there is an exchange of soluble and insoluble protein between plasma and the tissue, deposition tends to be progressive and relentless.

## CLINICAL MANIFESTATIONS

Amyloid affects the heart in two major ways, through the deposition of proteins in the interstitium causing an impairment of contractile function and as a result of these deposits interrupting and destabilising electrical conduction. Amyloid deposits can also be found in the coronary arteries affecting coronary flow.

## SYMPTOMS AND SIGNS

These vary according to the distribution of the protein fibrils. First signs are the presence of impairment in the relaxation properties of the heart, i.e. diastolic dysfunction often resulting in pulmonary congestion, oedema and other symptoms of heart failure. Later in the disease, there is progression towards an intermediate form of diastolic dysfunction and finally there is a restrictive

form of filling with worsening oedema and heart failure. Further progression results in systolic dysfunction. Cardiac involvement is then usually severe and prognosis poor. Later manifestations include symptoms of angina from microvascular disease. The propensity to arrhythmias is variable. Patients can present with various forms of heart block associated with presyncope and syncope. Tachyarrhythmias including atrial fibrillation and malignant ventricular arrhythmias are also noted, sometimes early in the disease.

The identification of early cardiac amyloidosis is difficult. However, oedema, abdominal distension and fullness associated with hepatic enlargement and ascites can occur, and new onset of atrial fibrillation or other arrhythmias are clues. The deposits can affect the body's autonomic function and the response to low and high blood pressure so that patients may have presyncope and light-headedness due to autonomic dysfunction and difficulties with compensatory cardiac and neurohormonal reflexes. Patients sometimes present with normalisation of previous hypertension.

Whilst these symptoms are a clue to the diagnosis of amyloidosis, the preferable time for diagnosis would be before any signs or symptoms of cardiac involvement occur. The first signs of amyloidosis can include unexplained bruising, evidence of a peripheral neuropathy with tingling or numbness in the fingers or toes, unexplained swelling, tiredness, fatigue and weight loss. In the absence of diabetes nephrotic syndrome may be an early sign of systemic amyloidosis.

## PHYSICAL EXAMINATION

Examination of patients with amyloidosis reveals a wide variety of clinical signs. They may have a bradycardia with heart block, atrial or ventricular tachycardia or atrial fibrillation. There may be frequent atrial or ventricular ectopics noted. They may have postural hypotension. Jugular venous pressure will be raised particularly if right heart failure is present. Normally the heart sounds are unremarkable although a third or fourth heart sound can represent the presence of systolic or diastolic dysfunction. There may be associated atrioventricular valve incompetence if there is systolic dysfunction particularly. There will often be bibasal crepitations, signs of pleural effusions and frequently ankle and sacral oedema with abdominal distension and hepatic enlargement. Other signs may include macroglossia, peri-orbital purpura and peripheral neuropathy.

## DIAGNOSTIC INVESTIGATIONS

A number of investigations are useful in assisting diagnosis. Sometimes the first clues occur on echocardiographic and electrocardiographic assessment in patients with lethargy or breathlessness.

## ECG

The key to electrocardiographic features in amyloidosis are that of a normal voltage or even reduced voltage in a setting of an echocardiogram demonstrating evidence of left ventricular hypertrophy. Other findings on the electrocardiograph include the presence of atrial fibrillation, ventricular and supraventricular ectopy, and conduction delay. Between 50 and 75% of patients will have evidence of ECG abnormalities.

## Echocardiography

There will be evidence of myocardial thickening without the presence of hypertension or a history of hypertrophic cardiomyopathy. The thickening tends to be concentric and diffuse. Even prior to the development of hypertrophy, the patient will have evidence of diastolic dysfunction with initially a pattern of abnormal relaxation, progressing to a “pseudo-normalisation” pattern, then to a restrictive pattern. Patients with restrictive diastolic filling have the most severe form of diastolic dysfunction with the poorest prognosis and the highest probability of symptoms and signs of diastolic heart failure. Doppler tissue imaging has been shown to be very useful in identifying amyloidosis, these patients demonstrate reduced S waves and classic elevations in the E/E prime ratio associated with elevated left atrial pressures. The degree of left ventricular hypertrophy is widely variable, particularly in senile amyloidosis and not necessarily related to the degree of diastolic dysfunction.

Systolic dysfunction occurs later in the disease and when present is indicative of a very poor prognosis. The classic findings in advanced amyloidosis are of atrial fibrillation, left atrial enlargement, left ventricular hypertrophy with restrictive diastolic dysfunction and systolic dysfunction, and a pericardial effusion. It should be noted that often there is thickening of the valves with abnormal regurgitation. There may be abnormal thickening of the right ventricle, often a clue to distinguishing these patients from those with hypertrophic cardiomyopathy or Fabry’s disease.

## Radiography

Radiography can be useful, confirming the presence of a normal heart size with evidence of oedema, pleural effusions and interstitial oedema.

Other investigations can include cardiac catheterisation, myocardial perfusion scans and MRIs. A coronary angiogram offers the opportunity to take a biopsy of the myocardium and to confirm the presence of a restrictive cardiomyopathy by measuring end diastolic pressures in the left and right ventricles. Myocardial perfusion imaging has not been shown to be particularly diagnostic. MRI scanning shows a decreased tissue signal intensity with late subendocardial tissue enhancing by Gadolinium.

## Laboratory Investigations

Laboratory data will vary significantly between patients depending on the presence of heart failure and other organ involvement. There may be an elevation in serum troponin or creatine kinase. Because of cardiac involvement, there may be an elevation in serum natriuretic peptide (nBNP) concentration and there may be elevations in creatinine, urea and eGFR if the patient has associated renal failure. A monoclonal spike on the serum electrophoretic protein pattern, the presence of a coagulopathy or anaemia associated with gut involvement or plasma cell dyscrasia may be evident. Urinary examination may reveal proteinuria. The more recently available “serum free light chain assay” is a very sensitive way of detecting amyloid protein and has prognostic utility when performed before and after treatment. Serum nBNP is also very useful in monitoring progress and response to treatment.

Biopsy is the diagnostic test of choice, four myocardial biopsy samplings allowing up to 100% sensitivity in detecting disease. Other biopsy sites include abdominal fat or rectal submucosa.

## TREATMENT

Management of cardiac amyloidosis has evolved significantly during the last decade. Early detection remains a priority.

### Objectives of treatment are to:

1. Slow or stop production of amyloid protein and prevent further organ tissue damage,
2. Control symptoms and provide supportive treatment to the damaged organs

## Medical Therapy

Symptom control is most important.

Diuretics are useful in treating the symptoms of diastolic dysfunction including oedema, pleural effusions and elevated left atrial pressures. Small doses of ACE inhibitors may be of some value particularly in patients with systolic dysfunction. There is no evidence that these will reduce the degree of left ventricular hypertrophy and they may further aggravate the patient’s symptoms of hypotension. In patients with restrictive cardiomyopathy it is important to be cautious with Beta-blockers as these patients are very dependant on their heart rate to provide cardiac output. Digoxin has been noted to bind to amyloid fibrils and this can result in toxicity, therefore, this drug is better avoided. There is no evidence to support the use of calcium channel blockers or AT2 blockers in these patients.

Patients may require a pacemaker or defibrillator for heart block, bradyarrhythmias and malignant ventricular arrhythmias. Supportive treatment is recommended for the symptoms of postural hypotension associated

[Cardiac Amyloidosis continues on pg 11.](#)

# How can I understand my illness and treatment better?

Coping with the shock of the diagnosis and treatment for a life threatening disease like amyloidosis can leave patients and families feeling numb. Patients talk about feeling out of control at this time and unable to think properly. However good their doctor may be at explaining every thing many patients say they feel only panic and have difficulty retaining the information they have been given.

If you or your family wish to make informed decisions about treatment you need to have the facts. Much of what is written about amyloidosis is written by the doctors and can be difficult to understand. Many patients learn about the disease from posting questions on the American amyloidosis listserv or chat on a chat line. This may help to give a good general overview of the medical problems but everyone's disease is slightly different and your doctor will suggest treatment that is specifically designed for your condition.

All patients are different in how much they want to know and in what they can understand. Some patients want to know a lot about their disease and will ask many questions while other people are overwhelmed when they meet their doctor.

In the course of the diagnosis and assessment of your disease you may see a number of doctors. They will more than likely try to be sensitive to your needs and give the information they perceive you want. However doctors are very busy people and being able to understand your needs when they may have only met you once or twice may not be easy.

It is often a good idea to take your partner or a friend to your appointments. Some people like to tape the consultation. It is wise to ask first whether the doctor is happy with this.

Thinking through and writing down the questions you feel you want to ask before the appointment can be helpful as so often our memories go blank when we actually enter the doctors consulting room.

A diagnosis of amyloidosis means that you will be having considerable contact with your doctors for some while. Asking the questions that are relevant to you can help to build a better understanding between you and your doctor.

Myeloma UK, previously the International Myeloma Foundation UK, in their publication "AL amyloidosis - Your essential Guide" suggest questions that may help you understand your disease and treatment better. We have

used many of these questions below and added a few more! Obviously the questions you ask will change as you move through your treatment.

## The disease

- What is amyloidosis?
- What type of amyloidosis do I have?
- How can I learn more about my disease?
- Are there many other people with this disease?
- Are there any support groups or people I can talk with?

## Treatment program

To gain a complete idea about your treatment some or all of the following questions may be useful

- What exactly is the treatment?
- What are the objectives of treatment?
- Over what period would it be given?
- How will the treatment be given?
- How often would I have to visit hospital?
- Would I have to stay in hospital?
- Would I be able to work or look after my children during treatment?
- How do people usually feel during this treatment?
- How long would the treatment last?
- How long would I take to get over it?
- What will happen after the treatment is finished?
- Why have you chosen this treatment for me?

## Past experience

To find out how well the treatment has worked for others in similar situations remembering of course effectiveness can be measured in a number of ways.

- How many patients have you treated with this treatment regime?
- How much experience is there with this treatment in Australia and around the world?
- How long have people been followed after their treatment?
- How well have they done and is there the likelihood of achieving a complete or partial remission?
- How long have other peoples remission lasted?
- In the event of the disease coming back would there be other treatments I could have?
- What factors are seen as an influence on outcomes.
- If I should develop any pain, nausea or other problems through the treatment would there be medicines to help me?
- How will you know whether the treatment is working?



### Side effects

- What side effects do people usually get on the treatment you have suggested?
- When would I begin to experience any side effects?
- Could any side effects be life threatening or cause pain and permanent damage?
- Will I be offered treatment for any side effects?

### Alternatives

- What are the alternatives to the treatment you are recommending?
- What would be the good and bad things about the alternative treatment?
- How effective might the alternative treatment be for me?
- How can I help myself?

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### Cardiac Amyloidosis continued from pg9.

with sympathetic nervous system dysfunction. Routine monitoring of fluid intake and salt consumption are useful as well as monitoring weight daily.

### Chemotherapy

Chemotherapy regimes are useful in treating patients with AL amyloidosis. The role of high dose chemotherapy with autologous stem cell transplantation is evolving. Its use varies between institutions. Cardiac amyloidosis universally adversely affects mortality rates in patients undergoing this treatment. The risk of transplant related mortality is five times higher in amyloidosis when compared with other haematological malignancies, this has been attributed to both the presence of extensive cardiac involvement and amyloid deposits in the kidneys, gut and arteries. However, some studies have shown an up to 63%, 2 year survival in patients with cardiac involvement IF they survive SCT.

A recent French trial demonstrated no significant difference in survival between patients receiving high dose Melphalan and stem cell rescue versus standard dose Melphalan and Dexamethasone. The role of chemotherapy and preferred treatments varies according to disease expression and remains a controversial area.

There is evidence that amyloid deposition in the myocardium may be reversible although this is a slow

process and depends to an extent on the disease activity and response to therapy. Frequently this reduction in wall thickness does not translate into clinical improvement. However, there are some reports indicating a significant reversal in both objective and clinical findings in these patients. The serum nBNP is a particularly useful marker in monitoring patient response.

Senile amyloidosis often results in more dramatic echocardiographic findings with greater myocardial thickening. This disease of the elderly is associated with a better prognosis. There is no evidence that these patients respond to chemotherapy or transplantation. The difference between these two conditions suggests that there may be a toxic component to the circulating proteins in AL amyloidosis.

Liver and heart transplantation surgery in patients with hereditary transthyretin (ATTR) amyloidosis with severe cardiac involvement has been used successfully. The liver transplantation removes the source of the abnormal transthyretin protein and essentially allows a cure. Patients need to be treated early however.

Recently the “free light chain assay” has been found to be useful in assessing amyloidosis patients prior to the onset of treatment and throughout treatment and in providing prognostic information. Patients who achieve a greater than 50% reduction in their pathological free light chain levels have been shown to have an improved overall survival.

### SUMMARY

Suspicion of the disease and early diagnosis is the best treatment strategy in patients with amyloidosis, particularly AL amyloidosis. Suspecting amyloidosis when a normal or low voltage ECG is seen in patients with symptoms of heart failure who has left ventricular hypertrophy on their echocardiogram may allow for early diagnosis. Thinking of the diagnosis in patients with non-specific symptoms including fatigue, weight loss, unexplained heart failure, oedema or bruising may lead to early detection.

Clearly in cardiac amyloidosis prognosis and response to treatment will always be better when the patient has milder involvement with lower free light chain concentrations. While this condition continues to have a grave prognosis, any small improvement in detection and screening has the potential to improve treatment options and outcomes for patients.

## The South Australia Support group – how it came about?

Six years ago I went to bed exhausted and rose eight to 10 hours later feeling no better. I couldn't work out why I was feeling like this.

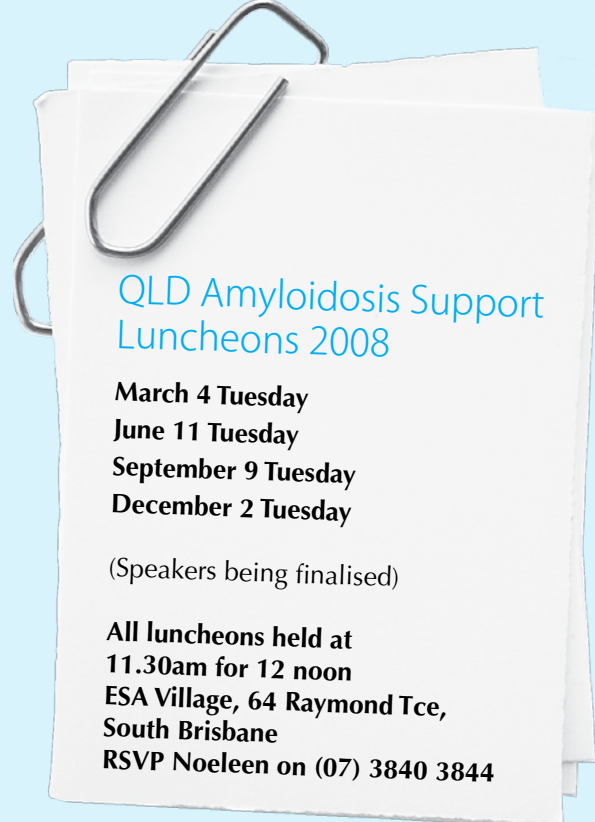
My legs were always swollen, like tree trunks and the tablets the G.P prescribed made little difference. Then it was an appointment with a physician, then a urologist. A kidney biopsy revealed a disease that I, a registered nurse, had never even heard of - AL Amyloidosis. What was it? Who else had it? Who could I talk to when even initially the doctors appeared nonplussed?

The internet held a variety of articles, some informative, but others I would have rather not read as they were so negative. Seeing a haematologist was the next step and then things began to move at a fast rate - x-ray this, biopsy that - and then at last I knew that this rare disease was primarily in my kidneys. A chemotherapy regime and then a stem cell transplant followed and now here I am comparatively well and very privileged to have met so many wonderful doctors and nursing staff.

However, after meeting up with several other amyloidosis patients I felt that a support group where people could talk freely and have the support and encouragement of others would be beneficial. After speaking to Allan and Steve at the Leukaemia Foundation it was decided to contact those who were known Amyloidosis patients to ascertain their interest in an association linked to the Leukaemia Foundation. The response has been wonderful and we have a very special group of people with a common bond who meet three monthly. Next meeting is a fun one at the zoo! I would personally like to acknowledge the assistance and support offered to myself and other patients with an illness that they could not fight alone.

### Maureen Powell

Regular support meetings will be held throughout 2008. If you would like more information phone Steve Marshall on 08 8273 3555



### QLD Amyloidosis Support Luncheons 2008

**March 4 Tuesday**  
**June 11 Tuesday**  
**September 9 Tuesday**  
**December 2 Tuesday**

(Speakers being finalised)

**All luncheons held at  
11.30am for 12 noon  
ESA Village, 64 Raymond Tce,  
South Brisbane  
RSVP Noeleen on (07) 3840 3844**

### Support Services team

#### Amyloidosis services coordinator

Pat Neely

#### Support Services team coordinators

**Queensland** – Barbara Hartigan

**Townsville** – Angela Daly

**Victoria/Tasmania** – Sam Schembri

**New South Wales/ACT** – Gabrielle Prest

**South Australia/Northern Territory** – Steve Marshall

**Western Australia** – Sandy McKiernan

### For help call...

**Brisbane: 07 3840 3844**

**All other states: 1800 620 420**

**[www.leukaemia.org.au](http://www.leukaemia.org.au)**

## Our vision to cure and mission to care.

The Leukaemia Foundation of Queensland is a not for profit organisation focused on the care and support of patients and their families living with leukaemias, lymphomas, myeloma and related blood disorders.

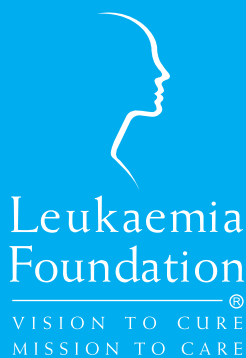
The Foundation does this by providing emotional support, accommodation, transportation and practical assistance for patients and their families. The Leukaemia Foundation also funds research into cures and better treatments for leukaemias, lymphomas, myeloma and related blood disorders.

The Leukaemia Foundation receives no direct ongoing government funding, and relies on the continuous support of individuals and corporate partners to expand its services.

To find out more about the work of the Leukaemia Foundation of Queensland and how you can help, phone 1800 620 420 or visit the Foundation's website: [www.leukaemia.org.au](http://www.leukaemia.org.au)

Disclaimer: No person should rely on the contents of this publication without first obtaining advice from their treating specialist.

If you do not wish to receive future editions of this publication please contact the Leukaemia Foundation Support Services Division on 07 3840 3840.



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