

Amyloidosis News

CARING FOR PATIENTS AND THEIR FAMILIES LIVING WITH AMYLOIDOSIS

April 2007

Welcome to the first edition of **Amyloidosis News**. We hope the articles included will be helpful to those being treated for amyloidosis and will raise awareness of this extremely serious group of diseases amongst family and friends, the general public and health professionals.

Until relatively recently, patients diagnosed with amyloidosis were offered little hope. Through worldwide research, improved treatments, team work and better assessment many patients are now leading busy lives.

However, because of the rarity of the amyloidoses and the fact that the symptoms mimic other illnesses, amyloidosis is all too often not diagnosed until the patient has visited a variety of specialists and their disease is well advanced. Early diagnosis is essential if patients are to be offered optimum treatment.

Over the last two and a half years, I have coordinated three monthly amyloidosis support luncheons in Brisbane. We have welcomed a number of guest speakers from Australia and overseas at these events. These well attended luncheons allow patients and families to share their experiences, learn more about their disease and treatment and have a good laugh. I am delighted that the South Australian staff are now also running support meetings.

Across the country the Leukaemia Foundation is offering support and practical help to amyloidosis patients and where more specific information is needed about the diseases the Foundation's state offices are referring patients to me.

Amyloidosis patients and their families are an important part of the services offered by the Leukaemia Foundation. Our aim is to offer practical and emotional support to patients and families, raise awareness of these diseases and ultimately find a cure.

Pat Neely
Amyloidosis Services Coordinator
Leukaemia Foundation

Recommended websites for further information

The National Amyloidosis Treatment Centre London: www.ucl.ac.uk/medicine/amyloidosis

The Amyloidosis Support Network: www.amyloidosis.org

Amyloidosis Australia: www.amyloidosisaustralia.org

Kidney Health: www.kidney.org.au

Learning to live with a dialysis machine



“Ten months after I started dialysis, I came off the machine with hissing in my ears. I felt hot and had a headache. I am not looking for sympathy but I am writing about my feelings because I want others starting dialysis to know that such feelings are not unusual. Even as I look back now I can say many of the awful feelings I had in the beginning now occur less frequently.

I have AA amyloidosis and my kidneys have gradually been deteriorating for a long time. On 2 March, 2005 I had an AV (arterial to vein) fistula put into my left arm. Within eight weeks my health had deteriorated dramatically and despite the fact my doctor had wanted the AV fistula to run for 12 weeks, he felt it was necessary to start dialysis immediately. Eight weeks later my health deteriorated dramatically. Despite the fact my doctor who made the AV fistula would have preferred a twelve week wait, dialysis treatment was started immediately.

Although I had mixed feelings about starting dialysis I had always been a confident person and felt I would cope well. How wrong I was.

“My body has failed me a little but my spirit is stronger than ever”

A dialysis machine is a very complex piece of equipment. Preventing contamination by germs requires constant diligence. I quickly learnt about the machine and all the tasks needed for “getting on”. The manuals were good but I had problems doing things in the right order.

Mentally I found I could not cope. My husband was also having difficulty accepting the blood, the machines and my sickness. He would drive me

backwards and forwards to all my appointments but could not cope when I tried to talk about how I was feeling. This led to a lot of anger on my behalf.

I found my anger towards my husband and the dialysis machine difficult to control. One morning as I approached my machine at the hospital, I burst into tears crying, “I don’t want to be here.”

The wonderful unit staff swept me into their arms and supported me through every thing I needed to do that day.

The support the staff gave me was just incredible. I had lots of problems in allowing the nurses to put a needle into my immature vein and they all showed incredible patience. I have little feeling in the end of my fingers because of my AA amyloidosis and this made feeling the veins very difficult. Thanks to one of the wonderful male nurses I had the pleasure of dealing with, I stopped popping the vein so often, gained confidence and eventually learnt to needle myself.

I then had to learn to get on and off the machine on my own. I was driven to do this by my ambition to be able to dialyse at home. I have an 11-year-old daughter and I have better things to do than travel to hospital three times a week. There were days of tears and anger over the next few months but I found after a bit of shouting at my machine I often felt a bit better and with the support of the staff I learnt to manage my treatment.

Research looks at Melphalan treatment for AL amyloidosis patients

AL amyloidosis is a rare and devastating disease. It is a bone marrow disorder where abnormal proteins (free light chains) are produced and deposit in the tissues, disrupting organ function and ultimately leading to death if left untreated. The amyloid protein may be deposited in any organ of the body but most often is found in the kidneys, heart, liver, bowel, and nerves. The care of patients with AL amyloidosis has often been difficult due to its rarity, the diversity of organ (and therefore specialist) involvement, and until recently a lack of treatment options.

This trial is examining treatment with a type of chemotherapy called melphalan. It is known that melphalan delivered at intermediate-dose or at high-dose with stem cell transplantation has considerable activity in AL amyloidosis, although the toxicity of the transplant procedure remains concerning. Therefore, there is a pressing need to identify the optimal mode of delivery of melphalan for individual patients.

The trial is evaluating a risk-adapted melphalan dosing strategy to deliver a safe stem cell transplant

to those who can tolerate the procedure reserving the less toxic intermediate-dose melphalan for patients who are not candidates for transplantation. The reduction in free light chains measured six months after treatment will be the main outcome measure of this strategy as patients who achieve a reduction in their free light chains are known to live longer. Attached to the trial are other scientific studies which will help us learn more about amyloidosis and the information patients need at diagnosis and throughout treatment.

This study is funded by the Leukaemia Foundation, Amgen Australia and the Princess Alexandra Hospital Foundation. It is being conducted under the auspices of the Australasian Leukaemia and Lymphoma Study Group and is currently enrolling new patients on the trial. Further information can be obtained from the Trial Coordinator (**Jan Alexander 07 3240 5112**) or **from the Principle Investigator (Dr Peter Mollee 07 3240 2396)**.

In July I moved to Southport where I was taught to really survive alone with my machine. Again there were many mistakes and many down days but by September 2005 I was at home with my machine plumbed in. With a nurse by my side I ventured into my new life undergoing dialysis treatment at home.

By February 2006 life was improving greatly. The whole family were coping better I was undergoing dialysis for eight hours overnight and this left me with the time I needed to live a much more normal life.

My kidneys had been failing for 20 years as the result of amyloidosis. I thought about dialysis a lot as a treatment option but I fought hard to keep myself reasonably well so that I would not need it. When it happened it was a huge blow and I felt as though I had failed. Failure had not been in my vocabulary before.

I gave myself two weeks to grieve my loss and then turned my thoughts around. I had not failed. I had a disease called AA amyloidosis caused by the bronchiectasis I suffered since child hood. This disease eventually caused my kidneys to fail. My body has failed me a little but my spirit is stronger than ever. I am alive. I am living a busy life. I have not failed at all. I have won.

I would like to thank my doctors and the staff at the Robina and Southport Dialysis Centres on the Gold Coast for all their support in helping me to get my life back again."

Ann Beecroft

About amyloidosis

What is amyloidosis?

Amyloidosis is a rare and devastating disease. The term amyloidosis covers a spectrum of diseases where protein fibrils, which have in common a particular abnormal chemical structure called a beta-pleated sheet, are deposited within the tissues and organs of the body. These abnormal protein deposits (or amyloid) are relatively insoluble and therefore cannot be easily broken down by the body. They build up in the tissues leading to progressive organ failure and, in the absence of effective treatment, eventually to death.

Are there different types of amyloidosis?

The many different types of amyloidosis are now classified according to the type of protein fibril that the amyloid deposits are made up of (see Table 1). Each type of amyloid is given a "name" consisting of a capital A (for Amyloid) followed by an abbreviation for the fibril protein. For example: in AL amyloid, the L refers to the light chain component of the immunoglobulin protein; in AFib, the Fib refers to the fibrinogen protein. Amyloidosis can be due to the overproduction of a normal protein (e.g. AA, seen with long-term inflammatory illness) or due to inheritance of an abnormal (or mutated) protein (e.g. AFib, ATTR). The most common type of amyloidosis, however, is AL. Correctly diagnosing the type of amyloidosis is critical as

treatment is very different for the various types of amyloid (e.g. chemotherapy and stem cell transplantation will not work for hereditary types of amyloid).

AL amyloidosis

AL amyloidosis was previously known as "primary systemic amyloidosis". In AL amyloidosis, the amyloid forming protein is derived from the light chain component of a protein in the blood called monoclonal immunoglobulin. These light chains are produced by abnormal cells (called plasma or B cells) which are usually in the bone marrow. The underlying bone marrow disorder is known by many different names (MGUS - Monoclonal Gammopathy of Undetermined Significance, plasma cell dyscrasia, paraprotein disorder etc) and in most cases is very subtle. In about 20% of cases, the monoclonal plasma cells in the bone marrow behave in a cancerous fashion, in which case the underlying bone marrow disorder is multiple myeloma. A patient with myeloma may have or develop AL amyloidosis, but it is rare for a patient with AL amyloidosis (who does not have myeloma at presentation) to progress to full blown myeloma. Rarely, AL amyloidosis can be due to abnormal light chains produced by lymphomas or chronic lymphocytic leukaemia. AL amyloidosis is not inherited or contagious.

The symptoms of AL amyloidosis are multiple and reflect the

predominant organs involved. Kidney, heart, nerve and liver dysfunction most commonly arise, although any organ apart from the brain can be affected. Symptoms are often non-specific and include weakness, tiredness, weight loss and poor appetite. Other symptoms relate to specific organ involvement and include swollen ankles (kidney or heart), shortness of breath (heart), and tingling in the fingers and toes (nerve). It is a rare disease with an estimated age-adjusted incidence of 5.1 to 12.8 cases per million person-years in the United States, which equates to approximately 160 new cases per year in Australia.

AL amyloidosis is a serious condition, which in the absence of treatment, inevitably progresses leading ultimately to death, usually within five years. Amyloid deposition is a dynamic process, however, and treatments that reduce the production of monoclonal light chains frequently result in the stabilisation or regression of amyloid deposits, and subsequently, in the preservation and improvement of organ function.

Treatments utilised in AL amyloidosis have mirrored those that are used in the related plasma cell dyscrasia multiple myeloma, and range from low-dose chemotherapy to high-dose chemotherapy with autologous stem cell transplantation. Autologous stem cell transplantation is very effective at reducing the amyloid forming light chains,

but unfortunately is unsuitable for many patients due to the high rates of death associated with the procedure. Transplantation is too dangerous a procedure for most patients with advanced cardiac amyloidosis. Lower dose chemotherapy based around dexamethasone is also effective and a recent trial in France found that patients treated with tablet melphalan and dexamethasone did just as well as those treated with transplantation. Other drugs such as low-dose thalidomide, Velcade and Revlimid are also useful treatments or are currently being trialled in AL amyloidosis.

The aim of the various chemotherapy treatments is to reduce the production of the amyloid forming monoclonal free

light chains. A new test, the free light chain assay, is now available to monitor free light chains in the blood. It can detect monoclonal light chains in virtually all patients with AL amyloidosis. In addition, reduction in the serum free light chains following chemotherapy correlates with reduction in the whole body amyloid load and improved survival.

Whatever the type of chemotherapy, it is important to appreciate that improvement in amyloid related symptoms is often slow and may not be apparent for 12-18 months. The success rate varies between treatments but is about 40% to 60% on average. In addition to chemotherapy, supportive measures can help to reduce symptoms, maintain

general wellbeing and assist the function of affected organs.

Australia and New Zealand's first therapeutic trial in AL amyloidosis is currently underway in several major centres and is organised through the Australasian Leukaemia and Lymphoma Group. This study will evaluate a risk-adapted intravenous melphalan dosing strategy to deliver a safe stem cell transplant to those who can tolerate the procedure reserving the less toxic intermediate-dose melphalan and dexamethasone for patients who are not candidates for transplantation.

Table 1. Some common types of systemic amyloidosis

Amyloid type	Nature of amyloid forming protein	Other names	Major organs involved
AL	Immunoglobulin light chain	Primary systemic amyloidosis Myeloma-associated amyloidosis	Kidney Heart Nervous system Liver Gastrointestinal Soft tissues
AA	Amyloid A protein	Secondary amyloidosis	Kidney Liver
ATTR	Transthyretin	Familial amyloidotic polyneuropathy	Nervous System Heart
ATTR	Transthyretin	Senile amyloidosis	Heart
AFib	Fibrinogen alpha chain		Kidney

Renal amyloidosis – an overview

by Dr Peter Mollee

The amyloidoses are a group of diseases in which an abnormal protein called amyloid is deposited in one or several organs and tissues of the body.

Amyloidosis affecting the kidney is the most common and sometimes the most serious form of organ involvement associated with this disease. Clinically significant renal involvement usually occurs in AL (primary) and AA (secondary) amyloidosis. Rare hereditary forms of the disease exist as well as the different form of amyloid deposition called dialysis-associated amyloidosis, which occurs in patients on prolonged dialysis.

What does the kidney do?

Most people are born with two kidneys. The major function of the kidneys is to remove waste products and excess fluid from the body. These products and fluids are removed through the urine. Urine is produced through a highly complex filtering process in the kidneys. Each kidney contains millions of functioning units called nephrons. Each nephron consists of a filtering unit called a glomerulus attached to a tube.

In patients with renal amyloidosis the abnormal protein amyloid deposits in the kidneys causing damage and stopping the kidney functioning properly. The way the kidneys are affected varies depending where the amyloid is deposited. Damaged kidneys cannot function properly and may be unable to remove urea and other wastes from the blood.

What are the symptoms of renal amyloidosis?

Some patients experience swelling of their ankles, raised blood pressure, anaemia and raised cholesterol but many people do not experience symptoms until late in the disease process.

One common sign of amyloidosis in the kidney is the presence of high levels of protein in the urine. This condition is called proteinuria.

How is renal amyloidosis diagnosed?

A doctor who finds a large amount of protein in the urine may suggest a biopsy of the kidney or a fat pad biopsy from the tummy. A bone marrow biopsy

may also be performed. The biopsy will be sent to a pathologist to establish whether the patient has amyloidosis and if so what type.

If amyloid is present in the biopsy, congo-red staining will show apple green birefringence under polarised light. Immunofluorescent microscopy may be only weakly positive. Electron microscopy will reveal the characteristic extracellular fibrils.

Management of amyloidosis

The aim of treating any type of amyloidosis is two fold

- a) To stop the production of the amyloid protein.
- b) To preserve the damaged organs so that functioning does not get worse.

There is now some evidence that after successful treatment the amyloid protein may leech out of some organs improving the functioning of that organ.

Primary amyloidosis AL

Patients with renal amyloidosis will probably be managed by a renal physician, a haematologist and if any other organs are involved, the appropriate specialist.

Treatments used for AL amyloidosis are decided only after thorough assessment of amount of damage in any of the affected organs

Treatments range from low-dose chemotherapy to high-dose chemotherapy with autologous stem cell transplantation (SCT). Although SCT is very effective at reducing the amyloid forming light chains, it has proven to be unsuitable for many patients especially those with advanced cardiac amyloidosis, due to the high rates of death associated with this procedure.

Lower dose chemotherapy based around dexamethasone is also effective and a recent trial in France found that patients treated with tablet melphalan and dexamethasone did just as well as those treated with transplantation. Other drugs such as low-dose thalidomide, Velcade and Revlimid are also useful treatments or are currently being trialled in AL amyloidosis.

The aim of the chemotherapy treatments is to reduce

A problem with diagnosis actually saved my life.

After running 189 half marathons and 53 full marathons I prided myself on being fit at the age of 60. But 6 months after the last half marathon I began to lose my breath on effort. I had always been extremely fit. To find myself constantly out of breath was devastating. Heart failure was diagnosed but tests looking for a reason were inconclusive and a heart transplant was recommended.

Despite being a success the heart transplant revealed I had a rare blood related condition called AL amyloidosis which if not treated results in damage to the organs leading eventually to death.

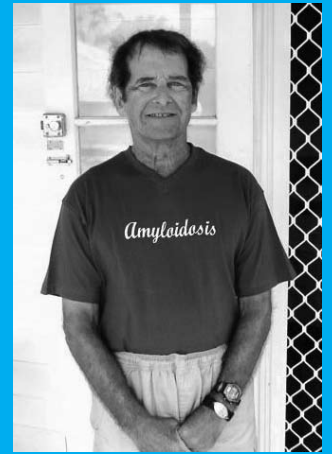
As soon as I was well enough from my heart transplant I had to undergo chemotherapy and a stem cell transplant to prevent the amyloid protein damaging my new heart. Following this procedure I was plagued with a series of unexpected infections causing tremendous suffering and major health problems. Now five years on with consistent hard work, care and perseverance I am feeling quite well and much of my energy has returned and both transplants seem to have been a success.

Undergoing two transplants so close together was traumatic. The diagnosis of amyloidosis was devastating. I have learnt since then that just like me other patients are not diagnosed until the disease is well advanced and treatment is difficult—especially when the heart is affected.

However in my case I felt strangely grateful that my amyloidosis was not diagnosed. If it had been I probably would not have been offered a transplant and would not be alive today.

I am very grateful to all my doctors and to the Leukaemia Foundation for the practical and emotional support I have received. I am now working closely with Pat Neely and the Foundation to try and raise awareness of this devastating disease amongst the medical profession and the community in the hope that earlier diagnosis will lead to better outcomes.

Allan Andrews



the production of the amyloid forming monoclonal free light chains. These light chains can now be monitored by the free light chain assay, a fairly new test which monitors the free light chains in the blood. It can detect monoclonal light chains in virtually all patients with AL amyloidosis.

In addition, reduction in the serum free light chains following chemotherapy correlates with reduction in the whole body amyloid load and improved survival.

Secondary amyloidosis (AA)

The most important therapeutic goal is successful treatment of the underlying inflammatory process. This may be through the use of cytotoxic agents if the precipitating cause is rheumatoid arthritis or antibiotics if the precipitating cause is chronic infection. In these patients the hope is that treatment will lead to stabilisation of renal function, a reduction in protein excretion and partial resolution of amyloid deposits.

Colchicine delays the onset of nephropathy in patients with familial Mediterranean fever but has not been of proven use in other forms of amyloid nephropathy.

Dialysis and renal transplantation

Renal replacement therapy, dialysis, is an option for those patients who reach end stage renal failure. Haemodialysis and peritoneal dialysis appear to be equally effective. Many patients manage dialysis in their own homes.

Renal transplantation is a further option for patients with amyloidosis that has led to end stage renal disease. Prognosis of transplant recipients depends largely on the type of amyloidosis. This in turn affects a patient's suitability for renal transplantation.

Seminar Series dates

General meeting

Date: Tuesday, 24 May
Time: 12 noon start

Taking Control - Adapting to change

Presenter: Arthur Alexander
Date: Saturday, 23 June
Time: 9am - 3pm (lunch provided)

What is the free-light-chain-assay?

Guest Speaker: Dr Peter Mollee
Date: Tuesday, 4 September
Time: 12 noon start

Bookings are essential

Where: All seminars are held at the auditorium
Leukaemia Foundation of Queensland
ESA Village
64 Raymond Terrace
South Brisbane

RSVP: Noeleen on (07) 3840 3844

*Parking may be available in the Mater Hospital carpark across the street from ESA Village

News from South Australia

by Steve Marshall

In August 2000 an amyloidosis patient who had undergone extensive treatment including a stem cell transplant approached the Leukaemia Foundation in South Australia. She expressed her feeling that there was a need for a support network for amyloidosis patients in that state.

After discussions it was decided to invite amyloidosis patients and families known to the South Australian staff and any other patients to attend to an informal meeting in November 2006 to discuss what was needed. The meeting was a great success; eight patients and two carers attended and everyone was able to share in a supportive environment their experiences on living with amyloidosis.

There was unanimous agreement to continue with the meetings and invite guest speakers whenever possible. Dr Noemi Horvath from Royal Adelaide Hospital has kindly agreed to speak at the next meeting on April 12 and Pat Neely coordinator of amyloidosis services for the Leukaemia Foundation will address the group on July 18.

The South Australian staff continue to offer individual practical and emotional help to all amyloidosis patients and families who are referred or approach the Foundation for help.

Brisbane Support Services Team

Barbara Hartigan - Director of Support Services
Dean King - Support Services Coordinator
Kathryn Huntley - Support Services Coordinator
Kris Murphy - Support Services Coordinator
Maryanne Skarparis - Support Service Coordinator
Pat Neely - Amyloidosis Services Coordinator
Jenny Gallagher - Grief Support Services Coordinator
Shirley Cunningham - Grief Support Services Coordinator
Noeleen Schulte - Support Services Administration Officer

Townsville Support Services Team

Angela Daly - Support Services Coordinator

For help call...

Brisbane: 07 3840 3844

All other states: 1800 620 420

www.leukaemia.org.au



**Leukaemia
Foundation**

VISION TO CURE
MISSION TO CARE

GPO Box 9954
Brisbane QLD 4001
ph: 1800 620 420

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

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.