



Understanding Amyloidosis

A guide for patients and families



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Foundation

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CONTENTS

	PAGE
Acknowledgements	2
Introduction	3
The Leukaemia Foundation	4
What is amyloidosis?	8
What are the different types of amyloidosis?	9
Organ involvement	10
What are the symptoms of amyloidosis?	11
Who is at risk of developing amyloidosis?	12
How common is amyloidosis?	12
How is amyloidosis diagnosed?	13
Can amyloidosis be treated?	14
AL amyloidosis	15
AA amyloidosis	35
Hereditary amyloidosis	37
Senile amyloidosis	40
What is a clinical trial?	41
Taking care of yourself	43
How can I understand my illness and treatment better?	44
What should we tell the children?	47
Glossary	48
Useful Information Sources	58

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INTRODUCTION

A diagnosis of amyloidosis may leave many of you feeling shocked, anxious, and confused. That is quite understandable as you will probably have never heard of the word amyloidosis before and you will find that most people you talk with have not heard of it either.

A great deal of information can be found on the internet but some of this may be confusing and difficult to understand and much of it may not apply to your situation. It is hoped that this booklet will help you begin to understand your particular disease a little better.

Please remember that the information in this booklet is written in very general terms. Your disease is unique to you. The treatment you will be offered will be decided only after your doctors make a definite diagnosis on the type of amyloidosis you have and fully assess your disease status. This booklet is written to supplement any information given to you by your doctors and the rest of your treatment team.

The first part of this booklet gives a very general overview of amyloidosis, symptoms, diagnosis, and treatment. The following sections discuss in more detail the main types of amyloidosis. All the sections may not apply to you. It may be useful to look at the list of contents and read the sections you feel most useful at the time.

Some medical terms have been used which may not be familiar to you. See the back of this booklet for a glossary of terms.

Some of you may require more information than the booklet covers. We have therefore included internet addresses and other links that may be useful. Your doctors and nurses may also give you written information as you proceed through diagnosis and treatment.

It is not the intention of this booklet to recommend any particular form of treatment. Your treating doctor will discuss your particular medical circumstances with you at all times. However we have taken the liberty of including a list of questions on page 45 in this booklet which may help you to think about questions you may wish to ask.

THE LEUKAEMIA FOUNDATION

The Leukaemia Foundation is the only national not-for-profit organisation dedicated to the care and cure of patients and families living with amyloidosis, leukaemias, lymphomas, myeloma, and related blood disorders. Since its establishment in 1975, the Foundation has been committed to improving survival rates of patients and providing much needed support. It does not receive direct ongoing government funding, relying instead on the continued and generous support of individuals, corporations, and community groups to develop and expand its services.

The Foundation provides a range of free support services to patients and their carers, family, and friends. This support may be offered over the telephone, face to face at home, in hospital, or at the Foundation's accommodation centres, depending on the needs of each person. Support may include giving information, patient education seminars and programs that provide a forum for peer support and consumer representation, practical assistance, accommodation, transport, and emotional support and counselling.

The Leukaemia Foundation funds leading research into better treatments and cures for amyloidosis, leukaemias, lymphomas, myeloma, and related blood disorders. Through its National Research Program, the Foundation has established the Leukaemia and Lymphoma Tissue Bank at the Princess Alexandra Hospital; and the Leukaemia Foundation Research Laboratory at the Queensland Institute of Medical Research. The Foundation also funds research grants, scholarships, and fellowships for talented researchers and rural health professionals.

The Leukaemia Foundation of Queensland made a contribution of \$30,000 towards the cost of Australia's first clinical trial in systemic amyloidosis, which was completed in 2009. This was conducted under the auspices of the Australasian Leukaemia and Lymphoma Group. Dr Peter Mollee of the Princess Alexandra Hospital in Brisbane was the chief investigator.

Support Services



"Foundation staff provide patients and their families with information and support across Australia"

The Leukaemia Foundation has a team of highly trained and caring Support Services staff with qualifications and experience in nursing or allied health that work across the country. They can offer individual support and care to you and your family when it is needed.

Support Services may include:

Information

The Leukaemia Foundation has a range of booklets, fact sheets, newsletters and other resources that are available free of charge. These can be ordered via the form at the back of this booklet or downloaded from the website (www.leukaemia.org.au). Translated versions (in languages other than English) of some booklets are also available from our website.

Education & support programs

The Leukaemia Foundation offers you and your family general education and support programs throughout Australia. These programs are designed to empower you with information about various aspects of diagnosis and treatment and how to support your general health and well being.

Emotional support

A diagnosis of amyloidosis can have a dramatic impact on a person's life. At times it can be difficult to cope with the emotional stress involved. The Leukaemia Foundation's Support Services staff can provide you and your family with much needed support during this time. They may refer you or a loved one to a specialist health professional eg psychologist if required.

Online discussion forum

The Foundation has established an on-line information and support group for people living with amyloidosis, leukaemia, lymphoma, myeloma, or a related blood disorder. Registration is free and participants can remain anonymous, see www.talkbloodcancer.com

Telephone Discussion Forums

This support service enables anyone throughout Australia who has or has had amyloidosis to share their experiences, provide tips, education and support others in a relaxed forum. Each discussion is facilitated by a member of the Leukaemia Foundation Support Services Team who has a background in haematology nursing.

Young adults

A website for young adults has been developed called "Revive". This site has information specifically designed for young adults and contains a discussion forum to allow patient to patient interaction and support. The site is www.teamrevive.com

Accommodation

Some patients and carers need to relocate for treatment and may need help with accommodation. The Leukaemia Foundation staff can help you to find suitable accommodation close to your hospital or treatment centre. In many areas, the Foundation's fully furnished self-contained units and houses can provide a 'home away from home' for you and your family.

Transport

The Foundation also assists with transporting patients and carers to and from hospital for treatment. Courtesy cars and other services are available in many areas throughout the country.

Practical assistance

The urgency and lengthy duration of medical treatment can affect you and your family's normal way of life and there may be practical things the Foundation can do to help. In special circumstances, the Leukaemia Foundation provides financial support for patients who are experiencing financial difficulties or hardships as a result of their illness or its treatment. This assistance is assessed on an individual basis.

Contacting us

The Leukaemia Foundation provides services and support in every Australian state and territory. Every person's experience of living with amyloidosis is different. It may not be easy, but you don't have to do it alone. Please call **1800 620 420** (Freecall) to speak to a local Support Service staff member or to find out more about the services offered by the Foundation. Alternatively, contact us via email by sending a message to info@leukaemia.org.au or visit www.leukaemia.org.au

WHAT IS AMYLOIDOSIS?

Amyloidosis is the general term given to a relatively rare and serious group of disorders in which an abnormal *protein* known as *amyloid* is produced.

Amyloid is an unusually stable material, which has a unique chemical structure, formed when certain proteins fold in an abnormal way. These *protein fibrils* progressively deposit and accumulate in organs and tissues of the body, disrupting normal function. Without treatment this may lead to organ damage and eventually failure.

Amyloid (the word means “starch-like”) proteins are not recyclable or biodegradable and cannot be broken down easily. Therefore the body finds it difficult to remove these proteins. As a result they accumulate in tissues and organs. At this time it is not known what triggers the initial formation of the amyloid protein and why this happens in such a small proportion of the population.

Amyloidosis can be acquired (develops over time due to unknown reasons) or hereditary (occurs due to a faulty *gene* passed on within families). It can be localised (amyloid protein produced and deposited only in one small area of the body), or systemic (amyloid protein circulates in the blood and deposits in one or several organs of the body).

Amyloidosis is not a *cancer* but it is equally as serious. Over the past 10 years there has been a much greater understanding of these diseases. With earlier diagnosis, great improvements in assessment and treatment regimens, many patients are now experiencing long remissions and living full lives.

Much research is being done around the world to develop drugs, which will hopefully inhibit the development of the protein amyloid in all types of systemic amyloidoses.

WHAT ARE THE DIFFERENT TYPES OF AMYLOIDOSIS?

Over 20 different types of amyloidosis have been identified at this time. Many of these are obscure and cause few problems. Each type of amyloidosis is different, requiring different treatments.

The abnormal amyloid protein occurs as a result of a number of different protein triggers. Each protein trigger (or *precursor* protein) has the ability to form the *fibrillar* structure called amyloid. Previously the amyloidoses were classified as either primary (occurring on their own) or secondary (occurring secondary to another underlying condition). Now amyloidosis is classified according to the main protein trigger that causes that particular type of amyloidosis. Each type is given an abbreviation where the first letter “A” stands for amyloid and the subsequent initials stand for the amyloid protein.

For example, in AL amyloidosis the A stands for amyloid and L for the type of fibril protein, *light chain*.

This booklet features the types of amyloidosis listed below:

- **AL amyloidosis** is a light chain amyloid caused by a bone marrow disorder.
- **AA amyloidosis** occurs when the SAA protein increases substantially in response to a long-term inflammatory disorder such as rheumatoid arthritis.
- **Hereditary amyloidosis** occurs when a gene mutation is inherited, leading to the life-long production of an abnormal protein. The most common types of hereditary amyloidosis are ATTR (*transthyretin gene mutation*) and AFib (fibrinogen alpha chain gene mutation).
- **Senile amyloidosis** occurs when transthyretin amyloid deposits in the heart, but this is NOT an inherited disease.

ORGAN INVOLVEMENT

Amyloidosis is usually a systemic disease, meaning that any of the tissues and organs of the body may be affected by the amyloid protein except the brain. There is no pattern in the way organs or tissues are affected but many patients will have more than one organ affected.

In a few cases amyloidosis may be localised, meaning the disease is confined to just one area of the body such as the bladder or skin.

Major organs involved in the most common types of 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

The way amyloid affects the organs is discussed in more detail in the section on AL amyloidosis on page 15.

WHAT ARE THE SYMPTOMS OF AMYLOIDOSIS?

Symptoms depend on which tissues and organs are affected and to what degree. Symptoms vary greatly from patient to patient and between the different types of amyloidosis.

Symptoms are often vague, mimicking other medical conditions. The most common symptoms are:

- Fatigue
- Unexplained weight loss
- Swelling of the ankles and legs due to fluid accumulation (oedema)

Other symptoms vary depending on the organ or tissues most affected and may include:

- Shortness of breath
- Loss of appetite
- Enlarged tongue (macroglossia)
- Unexplained bruising around the eyes (raccoon eyes)
- Numbness or tingling in the hands and feet (peripheral neuropathy)

Due to the rarity of the disease and vagueness of symptoms, diagnosis may be delayed.

WHO IS AT RISK OF DEVELOPING AMYLOIDOSIS?

Anyone can develop amyloidosis but certain factors increase the risk.

- Being over 50 years of age
- Males appear to be at a slightly higher risk
- About 15—20% of patients with multiple myeloma also develop AL amyloidosis
- Patients with a long-term chronic infectious or inflammatory disease are at risk of developing AA amyloidosis
- People who inherit a certain gene mutation may develop hereditary amyloidosis
- Patients who require kidney dialysis for a long period of time may be at increased risk of dialysis-associated amyloidosis, although this is rare with modern dialysis techniques

HOW COMMON IS AMYLOIDOSIS?

The amyloidoses are a rare group of diseases, which means that accurate statistics are difficult to collect.

In Australia amyloidosis is not a disease that is required to be reported on a state or national register, so we have no accurate way of knowing how many people are diagnosed with the disease each year. Nor do we know how many people are living in the community with the disease.

HOW IS AMYLOIDOSIS DIAGNOSED?

Amyloidosis can be difficult to diagnose. There is no specific blood test and results of investigations vary greatly from patient to patient. The diagnosis of amyloidosis starts when a doctor becomes suspicious of the patient's symptoms. A definite diagnosis is then made through a biopsy.

A biopsy involves taking a small piece of tissue. This may be taken from the organ that is causing the symptoms: or, as amyloid deposits are often present throughout the body, a less invasive biopsy of abdominal fat tissue, rectum, or lip may be performed.

This tissue biopsy is then sent to the laboratory for analysis where it is stained with a dye called *congo red*. If the amyloid protein is present, the biopsy will appear red under normal light and green (so called apple green *birefringence*) under special polarised light confirming the diagnosis of amyloidosis.

Once a diagnosis of amyloidosis has been made, further tests will be undertaken in the laboratory to establish which type of amyloidosis the patient has. This is important, as the treatment is very different for the various types of systemic amyloidosis.

Sometimes the tests determining the type of amyloidosis are not conclusive and a *DNA test* may be suggested.

When AL amyloidosis is suspected, a bone marrow biopsy may also be performed to establish the presence of abnormal *plasma cells*.

Further tests will then usually be arranged to establish whether the heart and kidneys or other organs of the body have been affected by the collection of the amyloid protein and by how much.

These tests include blood and *urine tests*, *echo cardiograms (ECHO)*, *electrocardiogram (ECG)*, and sometimes other *scans* and *nerve conduction tests*. Not all of these will be necessary for every type of amyloidosis.

CAN AMYLOIDOSIS BE TREATED?

There is a range of treatments available for the amyloidoses with much research being carried out around the world to find new treatments.

Once a diagnosis has been made and the *subtype* of amyloidosis identified, the doctors caring for you will discuss the recommended treatment regime with you.

Regardless of the type of amyloidosis you have, the goals of treatment are:

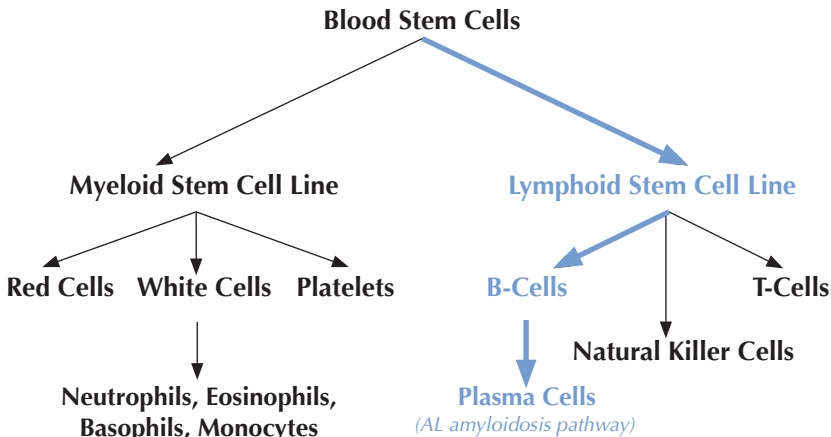
- To stop or slow the production of the amyloid protein
- To preserve and support affected organs and tissues
- To improve your quality of life

AL AMYLOIDOSIS

AL amyloidosis is the most commonly diagnosed form of systemic (found in any organs or tissues) amyloidosis in the western world. It is usually seen in people over the age of 50 but can occur in younger people. It is not inherited or *contagious*.

AL amyloidosis is caused by an abnormal protein (the “light chain” of an *immunoglobulin* or antibody protein) made by abnormal plasma cells found in the bone marrow. The bone marrow contains *stem cells*, which divide and produce red and white blood cells and *platelets*.

Plasma cells are a special type of white blood cell and are part of the body’s immune system. They are responsible for making antibodies, also called immunoglobulins, which are proteins involved in the body’s defence against infection. Normally once these proteins have served their purpose they are broken down and recycled in the body.



In AL amyloidosis a clone or single population of plasma cells grows excessively and produces an abnormal protein called an immunoglobulin light chain. These light chains build up in the blood stream and are progressively deposited as amyloid fibres (*fibrils*) in the tissues and organs of the body. The amyloid fibrils cannot easily be broken down. They stop the organs functioning normally and can lead to organ failure and eventually death unless treated.

AL amyloidosis is a complex and individual disease and there is great variation in the way the amyloid protein is laid down in the individual's organs and tissues, leading to variation in the symptoms experienced. Often more than one organ is affected.

The abnormal light chain protein can occasionally be deposited locally (in one specific area). These localised deposits are distinct from systemic forms of amyloidosis that deposit amyloid throughout the body.

SYMPTOMS

The symptoms experienced by each individual depend on the organs involved. Non-specific symptoms include weakness, tiredness, weight loss, and poor appetite. Organ-specific involvement may cause swollen ankles (kidney or heart), shortness of breath (heart), and tingling in the fingers and toes (nerves).

WHAT ORGANS MAY BE AFFECTED?

Any organ apart from the brain can be affected but the most commonly affected organs are the kidneys, heart, nerves and liver.

Kidney

The kidney is the organ most commonly involved in AL amyloidosis. It may be easier to think of the kidney as a sieve that filters your blood. When your sieve/kidneys are working well waste fluid can filter from your blood. This waste fluid becomes your urine. As the waste fluid passes through the sieve/kidneys, the sieve traps the normal products, such as proteins, and keeps them in your blood stream where they belong.

When the sieve/kidneys are affected by the amyloid protein the holes in the sieve are damaged and get bigger. As a result normal *blood proteins* leak through the holes. This can be proven by a simple urine test, which can show that protein is now present in the urine. This damage to the kidneys is known as *nephrotic syndrome*.

There are a number of consequences of this loss of protein.

- Blood protein in the urine can raise blood *cholesterol* level to very high levels.
- Protein in the blood is necessary for retaining fluid in the blood vessels. When this protein is lost, fluid leaks out of the blood vessels into tissues of the body. This fluid may build up to cause swelling (oedema). This is common in hands and feet.
- If this process goes on over a long period of time the filtering system of the kidney is damaged and the patient may develop kidney failure which may require dialysis.

Heart

The second most commonly involved organ in AL amyloidosis is the heart. The amyloid deposits change the way the heart muscle relaxes. The consequence of the amyloid infiltration is that the heart becomes stiff and relaxes poorly. Normally, after the heart beats and pumps blood out, it needs to relax to let more blood in. If the heart does not fill with blood appropriately in between beats when the heart is resting, there will not be enough blood to be pumped out. This may result in loss of heart function causing:

- lethargy and extreme tiredness
- shortness of breath on exertion
- swelling of the ankles and legs
- chest pain, mimicking angina

Some patients feel light-headed when standing due to low blood pressure.

This is different from normal heart failure where the heart muscle is weak. In the amyloid heart the heart muscle is normal but it pumps poorly and therefore many drugs used for heart failure may not be effective for amyloidosis patients. Generally *diuretics* are the most effective way of relieving symptoms.

Cardiac amyloidosis may also affect the way electrical signals move through the heart (conduction system). This can lead to *arrhythmias* (irregular heart beat) resulting in palpitations (a racing heart) and blackouts.

The degree of cardiac involvement will influence the type of treatment offered to the patient.

Nervous system

Together the brain and the spinal cord are called the central nervous system (CNS). The CNS can send signals to the rest of the body via the peripheral nerves to ensure the body works normally.

Amyloid deposits can affect the nerves in the hands, lower legs, and feet. These peripheral nerves act like electrical wiring carrying signals caused by touch, pain, heat/cold, from the feet and hands to the CNS which interprets the signs.

When the amyloid protein affects the nerves it can cause a short circuit in this wiring resulting in numbness, tingling, and loss of

light touch and temperature perception. This is known as peripheral neuropathy.

Nerves that control heart rate, blood pressure, and movement of the gut that allows us to digest food may also be affected.

Nerves that service the body organs, such as the gut, are known as “autonomic” nerves, and when they are affected by amyloidosis this is known as autonomic neuropathy. Symptoms may include nausea, abdominal bloating or pain, *diarrhoea*, inability to absorb nutrients from food in the gut, weight loss, impotence, and dizziness upon standing.

Digestive system and gastrointestinal tract (Gut)

Amyloid deposits may infiltrate the gastrointestinal tract (Gut). The main role of the gut is to break down the food you eat into small components so that you can absorb the nutrients into your body. Amyloid infiltration can prevent the regular movement of the gut, which helps break down the food particles, and can make it very difficult for the nutrients to pass from your gut into your body. This can cause *diarrhoea*, weight loss and disruption to the normal working of the gut

Amyloid proteins can also deposit in the tongue causing it to swell and become rubbery (*macroglossia*) resulting in problems with speech and eating.

Liver

Amyloid deposits in the liver can result in an enlargement of the liver (*hepatomegaly*) and disruption of its normal functioning. This will be picked up in routine blood tests, which measure liver function. Sometimes liver involvement may be very severe and lead to liver failure.

WHAT TESTS WILL I NEED?

Once it has been fully established that you have AL amyloidosis further tests will be performed to:

- Establish which organs are affected and the severity of damage
- Detect any other medical problems that may affect treatment
- Determine a treatment plan

Many of these tests will be repeated to monitor organ function and the effects of treatment. Some of these tests are listed below:

Blood Tests

This involves taking blood from a vein to:

1. Measure the number of red and white blood cells and platelets.
 - A low red blood count indicates *anaemia*
 - A low white count increases the risk of infection
 - A low platelet count increases the risk of bleeding or bruising
2. Measure the serum (blood fluid) free light chains. (See further information on What is the free light chain assay on page 32)
- 3 Identify markers that indicate kidney liver and heart function
4. Assess levels of normal protein (*albumin*) in the blood.

Urine tests

Are used to assess if the amyloid proteins are affecting the kidneys by measuring whether normal protein (albumin) is being lost into the urine, as well as to measure any free light chains in the urine (*Bence Jones protein*).

Bone marrow biopsy

A needle is inserted into a bone (usually the back of the pelvic bone) under a local anaesthetic and a sample of bone marrow is taken from the inside of the bone to establish the presence of abnormal *plasma cells*. A light sedative may also be given to the patient while this procedure is being done.

Echocardiogram

A scan using ultrasound technology to look at the function and structure of the heart and to see how the heart is pumping blood.

Electrocardiogram

A test used to measure the electrical activity in the heart.

CT scan

A computerised X-ray to look at images of organs and tissues of the body.

MRI scan

A scan using a powerful magnet to look at images of the organs and tissues of the body.

HOW IS AL AMYLOIDOSIS TREATED?

AL amyloidosis is a serious condition, which, in the absence of treatment, inevitably progresses. Over the past 10 years an increasing range of therapies has been developed. Although at this time therapy for AL amyloidosis is still not thought to lead to a cure, many patients are living long and active lives.

In deciding on the best treatment for you, your medical team will take into account a number of factors including your age, general health and the extent to which your organs have been affected by the disease. They will also consider potential complications of therapy.

Information gathered from hundreds of other people around the world who have had the same disease helps to guide your doctor in recommending the best treatment for you. It must be remembered however that no two people are the same.

The aim of treatment is to rapidly reduce the *free light chains* that are causing the production of amyloid. Targeting the plasma cells within the *bone marrow*, which are producing the free light chains, achieves this. Once the production of the amyloid protein is slowed or stopped, the amyloid fibrils already deposited in the organs may slowly move out of the affected organs. The function of the affected organs may then slowly improve.

Sometimes, however, the organs may be damaged to the point where the organ function does not improve greatly. At this time there are no specific treatments that can directly clear amyloid deposits from organs and tissues of the body.

Treatments for AL amyloidosis include:

- Chemotherapy
- Steroids such as dexamethasone and prednisolone
- Novel treatments, such as Thalidomide, Bortezomib/Velcade, and Lenalidomide/Revlamid
- *Autologous* stem cell transplant (A separate booklet on autologous transplantation is available from the Leukaemia Foundation)
- Treatments to preserve and support the function of affected organs that may be used in conjunction with the treatments above

These treatments have historically been borrowed from those proven to be beneficial in the treatment of the related disorder *myeloma*, also known as multiple myeloma.

Myeloma is also a disease of plasma cells although the plasma cells in myeloma are cancerous (malignant). Treatments that kill the cancerous plasma cells in myeloma are also effective in killing the *light chain* producing plasma cells in AL amyloidosis. Bone pain and fractures, high calcium levels, anaemia, kidney damage, and increased susceptibility to bacterial infection are common symptoms of people with myeloma.

Approximately 20% of patients with myeloma have or will develop AL amyloidosis. Fewer than 1% of patients with AL amyloidosis at diagnosis develop multiple myeloma at a future time. (Refer to the Leukaemia Foundation booklet *Understanding Myeloma*)

Other treatment may include:

- Organ transplantation
- Experimental treatments with drugs not yet available for general use through clinical trials

Amyloidosis is best treated by an experienced medical team. Members of this team may include a *haematologist*, *cardiologist*, *renal physician*, *gastroenterologist*, *neurologist*, and specialist nurses. Health professionals offering education, emotional, and practical support are also important team members.

What is chemotherapy?

Chemotherapy literally means therapy with chemicals.

Although amyloidosis is not a cancer, chemotherapy drugs are used in the treatment of AL amyloidosis to destroy the amyloid-producing plasma cells in the bone marrow.

Commonly used chemotherapy drugs in the treatment of AL amyloidosis include:

- Melphalan
- Cyclophosphamide
- Vincristine
- Doxorubicin (Adriamycin)

Chemotherapy may involve the use of a single drug or combinations of drugs (combination chemotherapy) and other medications such as steroids and novel agents. These drugs are usually given in several cycles (or courses) with a rest period of a few weeks in between each cycle. This is to allow the body to recover from the side effects of the drugs.

The names of the different treatment regimes are commonly derived from the first letters of each of the drugs given. Some examples of treatment combinations used to treat AL amyloidosis are listed below.

- MDex - **M**elphalan and **D**examethasone
- M&P - **M**elphalan and **P**rednisolone
- CTD - **C**yclophosphamide, **T**halidomide, and **D**examethasone
- VAD - **V**incristine, **A**driamycin, and **D**examethasone
- RevDex - **R**evlimid (Lenolidomide) and **D**examethasone
- VD - **V**elcade (Bortezomib) and **D**examethasone
- MDT - **M**elphalan, **D**examethasone, and **T**halidomide

Chemotherapy may be given in tablet (oral) form or by *intravenous (into the vein) injection*. Patients receiving oral treatment can usually take these drugs at home, visiting their doctor regularly for blood tests. Patients receiving chemotherapy into a vein may have their treatment administered in the haematology day-patient area or as an inpatient on a hospital ward.

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 to 18 months. In addition to chemotherapy, supportive measures can help to reduce symptoms, maintain general wellbeing, and assist the function of affected organs.

Chemotherapy side effects

Although the treatment is targeted to destroy abnormal plasma cells, it may also affect normal cells in the bone marrow, and other areas of the body. These side effects from treatment vary from one patient to another and vary depending on the drugs used. Most side effects are short term and will usually settle when the treatment ceases.

Common side effects some of you may experience.

- Hair loss (temporary)
- Lowering of red cell count (anaemia) may cause fatigue and shortness of breath when exerting yourself and may require a blood transfusion.
- Lowering the white cell count causing *neutropenia*. White cells are important in fighting infection so patients with a low white cell count are more at risk of infection. During this time sensible precautions should be taken such as avoiding crowds and people with infections. You will be asked to report any rise in temperature to your doctor.
- Lowering of platelet count which may lead to bruising and bleeding problems. Precautions should be taken to avoid physical injuries. Platelet transfusion may be required.
- Nausea, which is usually well controlled by medication
- Changes in taste and smell (temporary)
- Sore mouth - you may get mouth ulcers (mucositis). Use a soft toothbrush, do not use commercial mouth washes as they may contain an alcohol base which may cause your mouth ulcers to deteriorate. Eat soft foods and see your doctor if your sore mouth affects your ability to eat properly.
- Diarrhoea or constipation which is usually controlled by medication
- Fatigue - most people feel a degree of tiredness in the days and weeks following treatment. Gentle exercise when you feel you are able is a good way to improve your feeling of wellness and may reduce your fatigue.
- *Infertility* can be a concern. If so, you should speak with your doctor preferably before treatment starts.

Your treatment team will talk with you about the treatment side effects you may experience but if you are experiencing anything out of the ordinary which has not been mentioned you should contact your local doctor or your treatment team.

It is important that you contact your doctor or the nursing team for advice immediately (at any time of the day or night) if you are feeling very unwell, or if you experience **any** of the following:

- a **temperature** of 38°C or over and/or an episode of uncontrolled shivering (also called a rigor)
- **bleeding** or **bruising**, for example blood in your urine, bowel motions, coughing up blood, bleeding gums or a persistent nose bleed
- **nausea** or **vomiting** that prevents you from eating or drinking or taking your normal medications
- **diarrhoea, stomach cramps** or **severe constipation**
- **persistent coughing** or **shortness of breath**
- the presence of a new **rash, reddening** of the skin itching
- a persistent **headache**
- a new severe **pain** or persistent unexplained soreness anywhere
- if you **cut** or otherwise injure yourself
- if you notice **pain, swelling, redness** or **pus** anywhere on our body

Cortico-steroids

Cortico-steroids are *hormones*, that are produced naturally by the body. They can also be made in the laboratory and they play an important role in treatment. Manufactured cortico-steroids such as prednisolone, dexamethasone, and methylprednisolone are commonly used alone or in combination with chemotherapy in the treatment of AL amyloidosis.

Side effects seen with cortico-steroids depend largely on how long they are used and the dose given. If they are used for a short time, you may notice that your appetite increases or you may feel more restless than usual. It is not uncommon for steroids to cause mood alterations with periods of feeling restless and hyperactive on the days you take them. This may be followed by periods of fatigue, low mood, and aches and pains on the days immediately after you stop taking the steroids. Some people find it more difficult to get to sleep at night and sleeping tablets are sometimes recommended.

Cortico-steroids can cause a rise in the blood sugar. *Diabetics* may find they need more of their anti-diabetic medication while they are taking these drugs. Some people who are not normally diabetic may require treatment to keep their blood sugar at acceptable levels. It is important to keep a check on the blood sugar and to keep a diary of the levels and the amount of diabetic medication being taken. Diabetics will already know how to do this.

People whose blood sugar only goes up when they are on cortico-steroids will be given information on diet and taught how to measure their blood sugar and adjust their medication. Many of the side effects of cortico-steroids are temporary and should pass once you finish taking them.

In patients with AL amyloidosis, cortico-steroid use may cause some other effects such as fluid retention (you may be asked to monitor your weight if this is an issue), worsening heart failure, and an increased susceptibility to infections. Aching joints such as the knees and hips have also been reported.

People taking steroids as part of their treatment may find that it heightens feelings of anxiety or depression. If you have ever had episodes of anxiety or depression, it is important to tell your treatment team before commencing steroid therapy and ask your friends and family to monitor your moods.

Patients need to be encouraged to inform their doctor about any worrying side effects they may be experiencing, including mood changes, so that help can be offered to minimise the impact of treatment. Keeping a diary recording when side effects are experienced and noting the severity and patterns of symptoms can be useful.

Novel Agents

Thalidomide

Thalidomide is a drug that works in a number of ways to interfere with the growth and survival of the light chain-producing plasma cells in the bone marrow.

Thalidomide is taken daily in tablet form. It can cause several side effects including:

- drowsiness - it is recommended that you take thalidomide in the evening
- lack of concentration
- dizziness
- constipation - a high fibre diet and when necessary laxatives may prevent complications
- skin rash
- heart problems
- nerve damage (peripheral neuropathy)
- blood clotting - your doctor may prescribe a blood thinning medication

Nerve damage is usually felt as tingling and loss of sensation in the hands and feet. It is important that you tell your doctor if you experience these as the dose of Thalidomide may need to be reduced or stopped.

Thalidomide is harmful to babies developing in the womb and should never be taken by pregnant women. It is important to avoid becoming pregnant and to use a suitable form of contraception, if necessary, while taking Thalidomide and for some time afterwards. There are special government regulations relating to the prescribing and dispensing of Thalidomide by which you and your doctor have to abide. Your doctor will explain these regulations to you.

Bortezomib (also known as Velcade)

Bortezomib is a new type of drug called a *proteasome inhibitor*. It causes the abnormal cells to die by altering their internal processes while leaving the normal healthy cell less affected.

Bortezomib is given by intravenous injection. While patients do not need to be admitted overnight for this treatment, it does require frequent visits to the hospital. The main side effects of Bortezomib are nausea, vomiting, diarrhoea, low platelet count, peripheral neuropathy and autonomic neuropathy. It also lowers immunity to certain viruses especially herpes zoster which increases the risk of shingles. Medications to prevent virus related illnesses are often used with Bortezomib.

Lenalidomide (also known as Revlimid)

Lenalidomide is a new drug derived by modifying the structure of Thalidomide. It is given in tablet form for three weeks out of four and often in combination with dexamethasone and sometimes with chemotherapy. Lenalidomide's main side effect is the lowering of blood counts (causing anaemia and risk of infection) and an increased risk of blood clots. Therapy with a blood-thinning agent may be used to help reduce the risk.

Lenalidomide may be harmful to babies developing in the womb and should never be taken by pregnant women. It is important to avoid becoming pregnant and to use a suitable form of contraception, if necessary, while taking Lenalidomide, and for some time afterwards. There are special government regulations relating to the prescribing and dispensing of Lenalidomide by which you and your doctor have to abide. The doctor will explain this to you.

Autologous stem cell transplantation (ASCT)

(Also refer to Leukaemia Foundation's booklet on (Understanding *Autologous transplantation*)

This treatment involves collecting stem cells from your blood stream, storing them, and then giving them back to you after you have received high-dose chemotherapy. An autologous stem cell transplant enables a larger dose of *chemotherapy* to be administered than would be given during a usual cycle of treatment.

This procedure requires admission to hospital. A high dose of chemotherapy is given intravenously to destroy the bone marrow. This is followed by the *infusion* of your own previously collected stem cells to “rescue” your bone marrow function. These stem cells will repopulate the bone marrow and restart the production of blood cells. You will remain in hospital for approximately three to four weeks following this procedure. The benefits in reduction of amyloid protein and improvement of organ function after an autologous stem cell transplant can be slow to occur, often taking 12—18 months to become apparent.

ASCT is an intensive procedure with a number of significant risks in patients with AL amyloidosis so it is usually considered only for younger patients with good heart and kidney function. If your medical team feels the risk of you undertaking an ASCT may be too high at diagnosis they may still suggest that your stem cells are collected and stored in case a stem cell transplant becomes an appropriate treatment choice in the future.

Collecting/harvesting stem cells

You will receive a course of injections of a stem cell stimulating drug (GCSF) several days before stem cell collection takes place. Most people can give these subcutaneous injections at home

Stem cells are collected or harvested from the blood by a process called apheresis once your blood tests have shown that that you have enough stem cells in your blood to collect. The patient’s blood is taken from a vein in the arm or through a special tube (Hickman catheter) and passed continuously through a special apheresis machine for some hours. This machine separates and collects the stem cells and returns the remainder of the blood back to the patient.

This procedure may take place in an outpatient or inpatient setting and sometimes in coronary care. Patients are monitored constantly throughout this procedure. The stem cells are frozen and can be preserved for a long period of time.

Allogeneic transplant

An Allogeneic Transplant uses another persons stem cells (usually a sibling) and is rarely used in treating AL amyloidosis. (The Leukaemia Foundation has a booklet “Understanding Allogeneic Transplants” if you would like more information about this treatment)

Supportive treatments

These treatments are an important part of your overall treatment plan. They are given to alleviate problems caused by the amyloid build-up in the various organs.

For example:

- *Diuretics* are often used to get rid of any build-up of fluid when the kidney or heart is affected
- Salt may be restricted in the diet as a high salt intake will encourage your body to hold excess fluid
- Elastic stockings and elevating feet and legs when sitting may be suggested to reduce fluid build-up
- Drugs may be given for low blood pressure, diarrhoea and nausea.
- Drugs may be given to preserve bones.

Organ transplantation

Slowing or stopping the production of amyloid may not be sufficient in itself to repair a damaged organ. When the damage is considered permanent an organ transplant may be considered. Kidney and heart transplants are sometimes offered in some treatment centres. Following a successful organ transplant the AL patient will need to undergo a stem cell transplant to stop the amyloid protein depositing in the new organ.

How will I know whether the treatment is working?

Your medical condition will be closely monitored throughout your treatment and after treatment has ceased. The aim of treatment is to reduce the production of the free light chains, which form the amyloid proteins. Tests will be performed to see whether there is evidence that this is being achieved.

Treatment regimes may be changed or started at any time if the required results are not achieved or if you are experiencing severe side effects of the treatment. The medical team will regularly check any affected organs to see how they are coping with the treatment and whether their performance is improving.

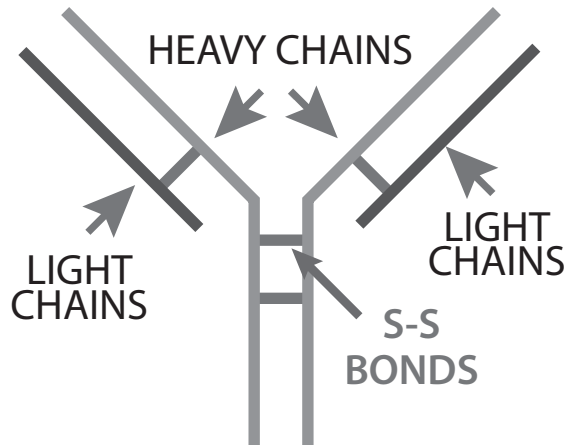
A test called the “free light chain assay”, which indicates whether your light chain numbers are rising or falling, is used by many doctors to help measure whether your treatment is working.

WHAT IS THE FREE LIGHT CHAIN (FLC) ASSAY?

The free light chain assay is a blood test used to detect monoclonal (single type) light chains in virtually all patients with AL amyloidosis. The free light chain assay is a test carried out in the laboratory. It recognises the kappa and lambda free light chains that cause AL amyloidosis but not the light chains that are bound to heavy chains. Reduction in the serum free light chains following treatment appears to correlate with reduction in the amyloid throughout the body

What are free light chains?

In AL amyloidosis the amyloid protein comes from the light chain of an antibody. An antibody is made of two “heavy” chains and two “light” chains (see diagram below)



Antibodies are made by plasma cells (activated B-cells) in the bone marrow. Normally the body makes lots of different antibodies, which have different heavy chains and lots of different light chains. The plasma cells make 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 abnormal plasma cells proliferate and build up in the bone marrow. They make large amounts of a single type of free light chains, which may or may not have the ability to form amyloid deposits. Most people have free light chains that do not

form amyloid. Although more patients with AL amyloidosis appear to have lambda light chains, the type of light chains does not seem to alter prognosis.

Diseases that can result from these plasma cells multiplying and becoming 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

Why is the FLC assay so useful?

The assay is much better than traditional methods at detecting small amounts of the free light chains in the blood, which form the AL amyloid protein.

The assay is very useful in diagnosis as measurable abnormal light chains are present in the blood in nearly all cases of AL amyloidosis.

The assay can be used to monitor response to therapy and 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. Treatments can then be changed if there is no response.

Organ improvement in AL amyloidosis can take many months to years making it traditionally difficult to know if the treatment is 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.

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 serum amyloid P (*SAP*) scan, a scan not currently available in Australia. The data also showed a dramatic improvement in the number of patients alive at five years if the free light chains could be reduced by 50%.

Every patient with amyloidosis is different. The measurement of the FLC assay at diagnosis does not always correlate with the extent of the disease and different patients need different amounts of reduction in their FLC assay result to improve the amyloid deposit 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.

There may be blips in the FLC assay results from time to time and patients should not worry too much if suddenly one result is slightly higher than before. Similarly, the FLC assay result should not be used in isolation from the other more traditional tests and assessments of the affected organ function.

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

What happens if treatment does not work?

It is very upsetting and disappointing to hear that the treatment you have been given is not achieving the hoped-for results. This may happen after a few months of treatment or after a period of remission when the AL amyloid is found to be active again.

Options at relapse — if the disease has come back.

Don't despair because at this point your medical team will fully assess the situation and probably discuss a different type of treatment with you. There may be a different combination of drugs with one of the newer drugs such as Velcade/Bortezomib or Revlimid/Lenalidomide. Sometimes an autologous stem cell transplant may be suggested.

There are some patients where the disease may have progressed to a point where supportive care may be the best way of proceeding. The treatment team may introduce the *palliative care team* who specialise in symptom management without adversely impacting the treatment.

AA AMYLOIDOSIS

AA amyloidosis which used to be known as “reactive or secondary” amyloidosis, occurs in patients who have long standing inflammatory disorders. These may include rheumatoid arthritis (children and adults), bronchiectasis, inflammatory bowel disease infections, and Familial Mediterranean Fever.

A small number of patients are unaware they have an underlying inflammatory disease. The number of people with this type of amyloidosis seems to be declining in the western world with better treatment and control of these inflammatory diseases.

How is the SAA (serum amyloid protein) produced?

The inflammatory disease causes changes in the blood chemistry. Healthy levels of the blood protein serum amyloid protein (SAA) can increase from normal levels to excessive levels and remain elevated as long as the inflammatory disease remains active. In a very small number of patients, the SAA proteins begin to be converted to AA amyloidosis fibrils and then deposit in various tissues and organs of the body over time. No one knows why this will happen in some people and not in others.

Symptoms

The underlying inflammatory disease often obscures symptoms experienced in AA amyloidosis.

Symptoms and signs are nonspecific but commonly include:

- swelling of the ankles and legs
- stomach problems.

Organ involvement

The spleen, kidneys, *adrenal glands*, and *gastrointestinal tract (gut)* appear to be the organs most affected by the SAA amyloid deposits. Deposits in the spleen may cause few symptoms although the spleen may be enlarged and rubbery. Damage in the kidneys from the SAA deposits may cause proteinuria and *nephrotic syndrome*.

Over time this can lead to kidney failure requiring dialysis. Vascular involvement may be widespread but involvement of the heart and nervous system is rare.

For more information on how the amyloid affects the organs see page 17.

Diagnosis

Amyloidosis can only be definitely proven through a *tissue biopsy* (Refer to introductory section on “diagnosing amyloidosis” on page 13).

Treatment

AA amyloidosis is managed by controlling the underlying inflammatory disease and therefore reducing the production of the amyloid protein SAA. If the SAA level can be reduced to almost normal and remains there for a long time there is a chance that the existing amyloid will eventually reduce, improving the organ function.

Prognosis

Once the underlying inflammatory disease has been controlled, the outlook for those with AA amyloidosis is often good with patients surviving for many years. Some patients may require a kidney transplant to return to good health.

HEREDITARY AMYLOIDOSIS

Hereditary amyloidosis is less common than AL and AA amyloidosis. It is caused by the inheritance of an abnormal (mutated) gene. This mutation leads to the production of the abnormal protein. This amyloid protein deposits in the organs and tissues of the body in the form of an amyloid *fibril*. Because the protein is not easily broken down it gradually builds up in the organs and tissues of the body, disrupting their function.

This mutant gene can be passed from one generation to another. Hereditary amyloidosis is known as an autosomal dominant disease, meaning that someone with the mutant gene may have inherited it from their father or mother and they in turn are capable of passing the gene to their children, who each have a 50% chance of inheriting it.

If you have not inherited the gene yourself you cannot pass it to your children.

Even if you have inherited one of these mutations you may not develop any clinical problems. If you do develop symptoms this usually will not be until middle age.

Diagnosing hereditary amyloidosis

Amyloidosis can be diagnosed conclusively only through a tissue biopsy. (Refer to the section *Diagnosing amyloidosis* on page 13). After a diagnosis of amyloidosis has been established further tests will be done in the laboratory to establish the type of amyloidosis.

The genes associated with all known forms of hereditary amyloidosis can be analysed through *genetic (DNA) testing*. This test can be performed from your blood sample in a specialised laboratory.

Healthy individuals who are at risk of having inherited a potentially amyloid-causing mutation may choose to undergo such DNA tests. However, this is not advised without discussing it with your doctor. Genetic counselling may be recommended.

Types of hereditary amyloidosis

The two main types of hereditary amyloidosis are ATTR and AFib although there are many others.

Symptoms

Symptoms vary depending on the type of hereditary amyloidosis the patient has, however many of the symptoms are similar to those experienced by people with AL amyloidosis (see page 15). It is therefore vital that the type of amyloidosis is diagnosed correctly before treatment is started.

Each family will have its own pattern of organ involvement with the various types of hereditary amyloid affecting individuals differently.

The progression of this group of diseases, which usually do not produce symptoms until middle age, is often very slow.

ATTR

ATTR is the most common form of hereditary amyloidosis. It is associated with mutations of the *transthyretin* protein. Rare mutations of other proteins can also be the cause.

The ATTR abbreviation consists of an A standing for amyloidosis and the other letters standing for the *precursor protein* transthyretin (TTR). The TTR is formed in the liver.

Treatment

The two main goals of your treatments will be:

- to stop or slow the production of the abnormal amyloid-forming protein
- to support and preserve organ function

Liver transplantation may be considered to remove the source of the abnormal amyloid-forming TTR. However, transplantation can be limited by the presence of amyloid in the heart, especially in the older patient.

Drugs are being trialled at this time to stop or interfere with the formation of the amyloid protein.

OTHER FORMS OF HEREDITARY AMYLOIDOSIS

Other types of hereditary systemic amyloidosis are uncommon. In these diseases nerve damage is not usually experienced. The liver and heart are sometimes affected but in general patients present with kidney disease and high blood pressure in middle age.

Organ damage in the different types of amyloidosis are summarised in the table below.

TYPE	USUAL CLINICAL FEATURES
Transthyretin	neuropathy, heart failure, diarrhoea, kidney failure
Fibrinogen	hypertension, kidney failure
Apolipoprotein A1	kidney failure
Lysozyme	kidney failure, liver failure
Gelsolin	corneal changes (eye), occasionally heart and kidney disease
Cystatin C	intra-cranial (brain) hemorrhage
Apolipoprotein AII	kidney failure

Fibrinogen A alpha chain amyloidosis

A number of mutations of a gene called the fibrinogen A alpha chain are known to cause amyloid. Patients usually present with kidney disease at age 50-60.

As the abnormal fibrinogen is produced solely in the liver, a liver transplant can prevent further amyloid deposition. A kidney transplant can also be used to replace the failed organ.

Apolipoprotein A1

Several mutations in the gene for apolipoprotein A1 cause amyloidosis. Half of the abnormal protein is produced in the liver. The kidneys are the main organs affected but the heart, liver, and other organs can be affected. Transplant to replace any of these organs may improve the situation.

Lysozyme amyloidosis

This type of hereditary amyloidosis is very rare. There is no specific treatment except for liver and kidney transplants to replace the failing organs. Progression of this disease is usually extremely slow.

SENILE AMYLOIDOSIS

Senile ATTR amyloidosis is NOT a hereditary disease. It is caused by overproduction of the normal protein TTR (transthyretin). This condition, which mainly affects the heart, is becoming more common as the average age of the population increases.

Senile amyloidosis of the heart can coexist with some bone marrow disorders creating the false impression that AL amyloidosis is the diagnosis.

Treatment is generally aimed at treating the symptoms of the disease. Because the heart is the most commonly affected organ, this disease will be monitored and treated by a cardiologist. As chemotherapy may actually disadvantage these patients, careful review is required to clarify the diagnosis particularly if the amyloid is found only in the heart.

WHAT IS A CLINICAL TRIAL?

Clinical trials are research studies in which patients and researchers help find ways to improve health care. Each clinical trial sets out to answer specific questions about new therapies or new ways of using known treatments. Carefully conducted clinical trials are the fastest and safest way to find treatments that work.

A clinical trial is one of the final stages of long and careful research processes which usually begin with scientists first developing and testing new ideas in the laboratory. Before the clinical research stage is reached there has to be evidence of benefit to patients.

Clinical trials contribute to the knowledge and progress of treating disease. If a new treatment is proven effective in a trial it may become a new standard treatment for many patients.

What is a protocol?

All clinical trials are based on a set of rules called a protocol. A protocol sets out:

- What types of people may participate in the trial
- The schedule of tests, procedures, medications, dosages, and how the participant should be monitored
- The length of the study

This protocol will be fully discussed with the participating patient by their doctors.

While in a clinical trial, participants are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment.

Clinical trials proceed through four phases.

- **Phase 1** trials determine the proper amount of a drug to be given to a patient (dosing) and major side effects.
- **Phase 2** trials gather data on a treatment's safety and benefits.
- **Phase 3** trials test the treatment's effectiveness, monitor side effects and compare the new product to an existing treatment to determine which is better.

- **Phase 4** trials are conducted after a treatment has been approved by the Therapeutic Goods Administration in Australia. During this phase, researchers study the long-term risks, benefits and optimal use of the therapy.

Why participate in a trial?

Clinical trials ensure high levels of quality control within a clinical treatment unit as results are independently monitored and verified. Participating patients are more closely monitored and may need to visit hospital more frequently than a person undergoing standard treatment. However, it must be emphasised that a clinical trial may not always result in improved outcomes and may occasionally result in an unexpected less favourable outcome. Participation in clinical trials is the main way that doctors learn how to better treat illness.

You can choose to leave a clinical trial at any time for any reason. You are not obliged to stay on a trial should you change your mind.

TAKING CARE OF YOURSELF

Coping with a diagnosis of amyloidosis can be very demanding physically and psychologically.

Many patients and carers experience feelings of depression, fear, anxiety, and sadness mixed with periods of optimism. These feelings and emotions are nothing to be ashamed of but it is important to tell your doctor if your depressive or anxious feelings last any length of time or are interfering with your life. There is help available and your doctor may refer you for counselling or offer some medication.

Anxiety, fear, and exhaustion can change all relationships. Sexual relationships may seem unimportant as you try to cope with the disease and the treatment. Treatments themselves can reduce sexual desire and AL amyloidosis can cause impotence. It is usually helpful to discuss the way you feel with your partner and look for a level of closeness that suits you both.

Talking about your illness with family and friends can help you reduce anxiety.

It may also be helpful to talk with others who are undergoing treatment for amyloidosis. There are amyloidosis support groups in Australia or you may wish to join a chat line on the internet. (See page 58)

Learning about your disease is important so that the relationship with your multidisciplinary care team can be one of collaboration. There may be more than one option for treatment and being able to ask questions and discuss these options will help you to feel more in control of your life.

Looking after yourself is important. You may need to accept help and let friends and families take over some of your duties for a while.

It is important to eat well, continue with some exercise, and get the rest you need. Your care team are there to help you and you can ask to speak with a dietician, exercise therapist or physiotherapist. Talking with other patients about how they have coped with problems such as a lack of appetite and inability to sleep may help.

HOW CAN I UNDERSTAND MY ILLNESS AND TREATMENT A LITTLE BETTER?

Coping with the shock of the diagnosis of a life-threatening disease such as amyloidosis can leave you and your family feeling numb, out of control, and unable to think properly. However good the doctors may be at talking about the disease and treatment, many patients say they have difficulty retaining any information they have been given, except perhaps how serious amyloidosis is.

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 doctors for doctors and can be difficult to understand. Many patients turn to the internet where much of the information will not apply to you. Some people will join chat lines or attend support meetings. This may give a good general overview about amyloidosis, however everyone's disease is slightly different and after full assessment your doctor will suggest treatment designed specifically for you.

People vary in how much they want to know and what they can understand. Some people want to know as much as possible about their disease from the beginning and will ask many questions. Other people would rather not know very much at first or are overwhelmed when they meet their doctor and are unable to ask questions.

In the course of the diagnosis and assessment of your disease you may see a number of specialists. They will try to be sensitive to your needs and give the information they perceive you want. 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 the doctor whether he/she is happy with this. Always carry a pen and paper to make notes.

Think about and write down your questions before your doctor's appointment. The mind tends to go blank when we enter the doctor's consulting room.

A diagnosis of amyloidosis means that you will be quickly learning a new vocabulary. Asking the questions that are relevant to you can help you understand these new terms and build a better understanding between you and your doctor.

In their publication '*AL amyloidosis — your essential guide*', Myeloma UK suggests questions to help you understand your disease and treatment. We have used many of these questions and added a few of our own.

Obviously you may not want to ask all these questions at one time and the relevant questions will change as you move through your treatment.

Example questions to ask your doctor and treatment team

The disease

- What is amyloidosis?
- What type of amyloidosis do I have?
- How serious is this disease?
- How can I learn more about my disease? Do you have any written material I can read?
- Are there many other people you know with this disease?
- Are there any support groups or people I could 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?
- Will I have to stay in hospital?
- Will I be able to work or look after my children during treatment?
- How do people usually feel during 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?
- Are there any costs attached to the drugs recommended for my treatment?
- What happens if this treatment does not work?

Past experience

- How many patients have you treated with this treatment regime?
- How much experience is there with this treatment in Australia and around the world?
- What is the likelihood of achieving a complete or partial remission?
- How long have other people remained in remission?
- In the event of the disease coming back, would there be other treatments I could have?
- What factors influence 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 affective might the alternative treatment be for me?

WHAT WILL WE TELL THE CHILDREN AND GRANDCHILDREN?

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. However, adults often underestimate the way children can cope with the truth if it is given in a loving way 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. But 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 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 handle the way they deal with their children differently. Deciding how to handle this dilemma is far from easy for many families. 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 help.

GLOSSARY

Adrenal glands

A pair of small glands, which sit on top of the kidneys. These glands produce hormones that help control the heart rate, blood pressure; the way the body uses food, and other vital functions. They also secrete steroid (cortisone-related) hormones and mineralocorticoids that regulate the levels of minerals such as sodium and potassium in the blood.

Albumin

A simple water-soluble protein found in many animal tissues and liquids. Albumin helps to keep fluid in the blood stream. People with low albumin often have fluid build-up in the tissues, especially in the hands and feet.

Allogeneic transplant

A procedure in which stem cells are collected from a compatible donor, often a sibling, stored and given to the patient following high-dose chemotherapy. The risks associated with this procedure increase with age and so it may not be suitable for older patients.

Amyloid

An abnormal, insoluble protein, which deposits in organs and tissues of the body.

Amyloidosis

A general term for a group of diseases in which an abnormal protein called amyloid is produced and distributed in organs and tissues of the body.

Antibodies

Proteins found in the blood and produced by specialised white blood cells (plasma cells) to fight infection and disease

Apheresis

A procedure in which a machine separates and collects stem cells from the patient's blood, returning the remainder of the blood components to the patient.

Apolipoprotein A1

APOA-I is instrumental in promoting the transfer of cholesterol into the liver where it is metabolised and then excreted via the intestine from the body.

Arrhythmias

A disturbance of rhythm in the heartbeat.

Autologous transplant

A procedure whereby stem cells are collected from the patient, stored, and returned to the patient following high-dose chemotherapy. As these stem cells do not create any problems with tissue matching, this procedure can be successfully used in older patients. Age will be a consideration in AL amyloidosis patients.

Autonomic neuropathy

Symptoms that occur when there is damage to nerves that regulate body organs.

Autosomal

Pertaining to a chromosome that is not a sex chromosome. People normally have 22 pairs of autosomes (44 autosomes) in each cell together with two sex chromosomes (XY in the male and XX in the female).

Bence Jones Protein

Free light chains filtered from the blood by the kidney and found in the urine.

Biodegradable

A substance or object able to be broken down by a biological agent.

Biopsy

The removal of a sample of tissue from a living body for diagnostic purposes.

Birefringence

Birefringence is the splitting of a light ray, generally by a crystal, into two components that travel at different velocities and are polarised at right angles to each other.

Blood count (also called a complete blood count or CBC)

This is one of the most commonly ordered clinical laboratory tests. It is a basic evaluation of the cells (red blood cells, white blood cells, and platelets) suspended in the liquid part of the blood (plasma). It involves determining the numbers, concentrations, and conditions of the different types of blood cells.

Blood pressure

Blood pressure is the pressure of the blood within the arteries produced primarily by the contraction of the heart muscle. Two numbers record the measurement. The first (systolic pressure) is measured after the heart contracts and 'blood pressure is at its highest'. The second (diastolic pressure) is measured when the heart is at rest and blood pressure is at its lowest. Blood pressure varies with the strength of the heartbeat, the elasticity of the arterial walls, the volume and viscosity of the blood, and a person's health, age, and physical condition.

Blood proteins

Blood proteins, also called serum proteins, are proteins found in the blood plasma

Bone marrow

The red area inside your bones where the platelets and red and white blood cells are produced.

Bone marrow biopsy

A needle is inserted into a bone (usually the back of the pelvic bone) under a local anaesthetic and a sample of bone marrow is taken from the inside of the bone to establish the presence of abnormal *plasma cells*. A light sedative may also be given to the patient while this procedure is being done.

Bronchiectasis

A disease that causes localised, irreversible dilation of part of the bronchial tree (branches of the windpipe in the lungs).

Cancer

A disease characterised by uncontrolled growth, division, accumulation and invasion of genetically damaged cells into other tissues. It causes problems in the body because its cells acquire abnormal functions or lose the ability to perform normal functions.

Cardiologist

A doctor who specialises in treating heart disorders.

Cell

The smallest unit of life, which make up the tissues and organs of our bodies. They can be seen with a microscope and can be grown in culture in a laboratory.

Chemotherapy

Treatment with drugs intended to kill dividing cells, particularly cancer and cancer-like cells.

Cholesterol

A fatty substance that occurs naturally in the body and which is necessary for hormone production, cell metabolism, and other vital processes

Complementary therapies

A wide range of therapeutic disciplines used alongside conventional medicine.

Complete remission (CR)

The disappearance of all detectable signs of amyloidosis.

Congo Red Dye

Congo red dye shows a fluorescent activity when bound to amyloid fibrils. It is used as a sensitive diagnosis tool for amyloidosis.

Amyloid is stained a light orange-red with Congo red and exhibits apple green birefringence under polarised light.

Contagious

Can be spread from one person to another.

Creatinine

A chemical waste molecule that is generated from muscle metabolism. The kidneys filter out most of the creatinine and dispose of it in the urine. A high level of creatinine in the blood may indicate poor kidney function.

CT Scan (computerised tomography)

A scan that shows three-dimensional images of organs and the structures of the body.

Diabetic

A condition in which a person has a high blood sugar (glucose) level as a result of the body either not producing enough insulin, or because body cells do not properly respond to the insulin that is produced.

Diarrhoea

The frequent passing of watery faeces.

Diuretics

A substance or drug to increase the production of urine to rid the body of excess fluid.

DNA testing

This is a simple blood test where the genes are analyzed to determine if a mutation is present.

Echocardiogram

A scan using ultrasound technology to image the heart. It measures the fraction of blood pumped out of your heart with each heart beat.

Ejection fraction

The amount of blood pumped out of the heart each time it beats.

Electrocardiogram (ECG)

A test measuring the electrical currents of the heart.

Enzyme

A protein that speeds up chemical reactions in the body.

Fatigue

A feeling of extreme tiredness, lethargy and exhaustion, which may be caused by the disease and or the treatments. It can be made worse by poor nutrition, anaemia, pain, stress and some treatments. Fatigue is common in amyloidosis.

Fibril

A fibril is a fine fibre approximately one millimetre in diameter.

Free light chain

Part of an antibody (immunoglobulin) that circulates freely in the blood stream.

Gastroenterologist

A doctor who specialises in diseases of the gastrointestinal tract (gut).

Gastrointestinal tract

The digestive tract, which includes the oesophagus, stomach, small and large intestines and rectum.

Gene

Genes are collections of DNA on a chromosome, which direct the activities of cells. They are responsible for the inherited characteristics that distinguish one individual from another.

Gene mutation

A change in the DNA of a gene which may be caused by exposure to a hazardous substance or a mistake during cell division. Mutations can affect normal cell functions leading to disease development. This happens through loss of a function or the development of abnormal functions in the cell.

Haematologist

A doctor who specialises in the diagnosis, treatment, and prevention of diseases of the blood and bone marrow.

Hickman's catheter

A type of central venous catheter used for the long-term administration of substances into the veins. It may also be used to draw blood for blood tests.

Hormone

The secretion of a gland that is transported by the blood to target cells. The hormone will stimulate the target to perform a specific action.

Immune system

Cells responsible for defending an organism against infections.

Immunoglobulins

Also known as antibodies. They are proteins found in the blood, which are produced by plasma cell (specialised white cells) to fight infections.

Immunomodulatory drugs

Drugs that suppress the immune system.

Intravenous injection

An injection into a vein.

Light chains

There are 2 main types of light chains Kappa and Lambda. Light chains help form antibodies.

Lysozyme

An enzyme present in saliva, tears, egg white, and many animal fluids, functioning as an antibacterial agent.

MRI Scan (magnetic resonance imaging)

A scan, which uses a powerful magnet to image the organs and tissues of the body.

Myeloma

A cancer of the bone marrow where plasma cells become malignant. Healthy plasma cells produce antibodies, which help to protect us from infections.

Nephrotic syndrome

Damage to the kidney resulting in the loss of a normal blood protein known as albumin into the urine. This causes water to leak out of the blood vessels into the tissues causing swelling (oedema). This occurs particularly in the hands and feet.

Nerve conduction test

An electrical test used to detect nerve conditions.

Neurologist

A doctor who specialises in the diagnosis and treatment of disorders of the nervous system.

Neutropenia

An abnormally low number of white blood cells. (neutrophils). It may be caused by high dose chemotherapy and carries risk of increased infection.

Oedema

Swelling in the tissues due to fluid retention.

Oncologist

A doctor who specialises in the diagnosis and treatment of cancer and the use of chemotherapy and other drugs to treat cancer.

Palliative care

Care that concentrates on disease symptoms with the goal of preventing and relieving suffering and improving quality of life. Palliative care aims to complement any ongoing treatment for disease.

Paraprotein

Abnormal accumulation of antibody protein (immunoglobulin produced by mature B cells (usually plasma cells).

Peripheral neuropathy

Damage in the peripheral nerves particularly in the hands and feet causing pain, tingling, and loss of sensation. Peripheral neuropathy may also be caused by some of the treatments used in amyloidosis.

PICC line

Peripherally inserted tube used for infusion of medicine, usually chemotherapy.

Plasma cells

Specialised white blood cells that produce antibodies (immunoglobulins) to fight infection. Derive from B-cells.

Platelets

Small blood cell fragments which are involved in blood clotting.

Precursor

A substance from which another substance is formed.

Prognosis

The likely course of the disease.

Proteasome inhibitor

A drug that interferes with the normal functioning of the part of the cell called the proteasome causing abnormal cells to die while leaving normal cells less affected.

Proteins

A molecule made up of amino acids that are needed for the body to function properly. Proteins are the basis of body structures such as skin and hair and of substances such as enzymes and antibodies.

Proteinuria

The presence of excessive protein in the urine.

Red blood cells

Blood cells which contain the red pigment and transport oxygen around the body. This oxygen is required to make the body's energy.

Relapse

A term used when amyloidosis has responded to previous treatment but there are signs that the disease is active again.

Renal dialysis

The process of filtering the blood, the way kidneys normally do, using a machine.

Renal failure

A term used when the kidneys are losing the ability to cleanse blood.

SAP scan

This scan is available only at the National Amyloidosis Centre in London.

Serum amyloid P component (SAP) is a normal protein found in the blood that binds to amyloid deposits in proportion to the amount of

amyloid present. A small amount of SAP is tagged with a radioactive iodine tracer and is injected intravenously. The tagged SAP then binds to amyloid deposited within the organs of the body. A gamma camera scan is then performed six to 24 hours later to image these deposits and show the amount and distribution of amyloid within the body. The scanner is an open device on which patients lie, fully clothed for about 40 minutes. It is not necessary to avoid any food, drinks or medications before the scan. Unfortunately, hollow or moving organs such as the gastrointestinal tract and heart cannot be assessed reliably by the SAP scan.

Stem cells

The most primitive cells in the bone marrow from which all blood cells develop.

Stem cell transplant

Stem cell transplant or bone marrow transplant is a procedure in which high-dose chemotherapy is used to destroy bone marrow cells. Stem cells previously collected from the patient or donor are infused to restore healthy bone marrow.

Systemic

Meaning any of the tissues and organs of the body may be affected by the amyloid protein except the brain.

Transthyretin

A protein component of blood serum that functions especially in the transport of thyroxine - also called prealbumin

Uraemia

Accumulation in the blood of nitrogenous waste products (urea) that are usually excreted in the urine.

Virus

A minute infective particle smaller than a bacteria, which cannot grow or reproduce outside a living cell. Sometimes they behave like a "wild gene" and become part of the genes in our cells.

White blood cells

Blood cells (leucocytes) formed in the bone marrow and are involved in the body's immune system. They consist of several different cell types.

USEFUL INFORMATION SOURCES

The Leukaemia Foundation

The Leukaemia Foundation produces a number of booklets and pamphlets.

- Understanding amyloidosis
- Understanding myeloma
- Understanding autologous transplants
- Living with leukaemias, lymphomas, myeloma and other related disorders (such as AL amyloidosis)
- Eating well

In addition, Amyloidosis News is a newsletter produced by the Leukaemia Foundation twice a year specifically to provide information about amyloidosis for patients, carers, and medical practitioners. It also contains information about the services offered by the Leukaemia Foundation.

Copies of these publications can be downloaded from www.leukaemia.org.au

Or you can ring 1800 620 420 from anywhere in Australia to obtain copies or further information.

Myeloma UK

www.myeloma.org.uk/amyloidosis

Myeloma UK has a number of booklets or articles available, including:

- Living with AL amyloidosis – your essential guide
- AL amyloidosis an introduction
- AL amyloidosis - your essential guide
- High dose chemotherapy and stem cell transplantation
- Mel/dex
- Revlimid
- CTD
- Understanding Myeloma
- Understanding Revlimid
- Understanding Thalidomide Therapy
- Understanding Dexamethazone and other steroids

Links to other Australian and overseas amyloidosis organisations

Adam Gardiner Foundation & The Westmead Amyloidosis Assessment and Treatment Clinic Westmead Hospital, Sydney

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. www.agf.org.au

Amyloidosis Treatment and Assessment Centre

Princess Alexandra Hospital, Brisbane, Queensland

The clinic provides a diagnostic and management advice service for patients with amyloidosis. (07) 3240 5095

- Amyloidosis Research Foundation USA
www.amyloidosisresearchfoundation.org
- Boston University Amyloid Treatment and Research Program, USA
www.bu.edu/amyloid/
- Myeloma Foundation of Australia Inc
www.myeloma.org.au
- Mayo Clinic Amyloidosis Centre, USA
www.mayoclinic.org/amyloidosis/
- National Amyloidosis Treatment and Assessment Centre, London
www.ucl.ac.uk/medicine/amyloidosis/nac

Other helpful organisations

- Amyloidosis Australia
www.amyloidosisaustralia.org
- Australian Centre for Grief and Bereavement
www.grief.org.au
- Beyondblue
www.beyondblue.org.au
- Cancer Council Australia
www.cancer.org.au

- Centrelink
www.centrelink.gov.au
- Kidney Health Australia
www.kidney.org.au
- Look Good feel better
www.lgfb.org.au
- Palliative Care Australia
www.pallcare.org.au
- The Heart Foundation
www.heartfoundation.org.au



Leukaemia
Foundation
VISION TO CURE
MISSION TO CARE

A bequest

Your planned gift to the Leukaemia Foundation

A wonderful way to make a significant gift is through a bequest in your will. After making due allowance for loved ones, a bequest of a specific amount or a proportion of the residue of your estate, is a way of leaving a real and lasting legacy to the future.

Your bequest to the Leukaemia Foundation will be used to support our mission to care for patients, carers and families and help us achieve our vision to find a cure for leukaemias, lymphomas, myeloma and related blood disorders.

Wording your bequest to the Leukaemia Foundation

You may choose to make a general bequest and allow the Leukaemia Foundation to decide how your bequest will be used, or you may prefer to make that decision yourself e.g. direct your bequest to patient support or research. Your legal adviser can provide further information on the different types of bequests, and on the appropriate wording for a bequest.

As a guide, the following wording may be useful:

'I give and bequeath free of all duties (here state the amount/percentage or share/residue or assets to be gifted) to the Leukaemia Foundation of (here insert the address) absolutely -

- for the general charitable purposes of the said Foundation (this is the Leukaemia Foundation's preferred option); or
- for the purpose of patient and family support; or
- for the purpose of research into the cause, cure or treatment of leukaemia, lymphoma, myeloma and related blood disorders

and I direct that a receipt of the proper officer for the time being of the Leukaemia Foundation shall be a good and sufficient discharge to my trustee/s'.

Please see the next page for the response form.

Response Form

- I have already made a bequest to the Leukaemia Foundation in my will
- I am considering/it is my intention to make (please circle) a bequest to the Leukaemia Foundation
- I would like more information about making a bequest and/or where to direct my bequest
- I would like to speak to the Planned Giving Manager about appropriate recognition for my bequest
- I would like to receive invitations to functions

Dr/Mr/Mrs/Ms/Miss:

Address:

..... Postcode.....

Telephone: (h).....

(w)

Email:

Please return this form to the:

Planned Giving Manager,
The Leukaemia Foundation,
GPO Box 9954,
in your Capital City
(marked Private & Confidential)

If you are interested in leaving a bequest to the Leukaemia Foundation in your will and you would like further information, without any obligation, in strictest confidence, please contact the Planned Giving Manager in your state on Freecall 1800 620 420 .





Leukaemia
Foundation

VISION TO CURE
MISSION TO CARE

Making a donation

The Leukaemia Foundation is the only national not-for-profit organisation dedicated to the care and cure of patients and families living with leukaemias, lymphomas, myeloma and related blood disorders.

You can help by making a donation. Please fill out the form below or visit www.leukaemia.org.au to make your gift online.

Dr/Mr/Mrs/Ms/Miss:

Address:

..... Postcode.....

Telephone: (h).....

(w)

Email:

Please accept my tax deductible donation for \$

My cheque, made payable to the Leukaemia Foundation, is enclosed, or please charge \$..... to my credit card:

Bankcard Visa Mastercard Amex Diners

_____/_____/_____/_____

Cardholder's name:

Cardholder's signature:

Expiry date:/.....

Contact Telephone number:

Please send to:

The Leukaemia Foundation

GPO Box 9954

in your Capital City.



Please send me a copy of the following information booklets:

- Eating Well: A practical guide for people living with leukaemias, lymphomas and myeloma
- Living with Leukaemias, Lymphomas, Myeloma & Related Blood Disorders: Information & Support
- Understanding Leukaemias, Lymphomas, Myeloma and Related Blood Disorders
- Understanding Acute Lymphoblastic Leukaemia in Adults
- Understanding Acute Lymphoblastic Leukaemia in Children
- Understanding Acute Myeloid Leukaemia
- Understanding Allogeneic Transplants
- Understanding Amyloidosis
- Understanding Autologous Transplants
- Understanding Chronic Lymphocytic Leukaemia
- Understanding Chronic Myeloid Leukaemia
- Understanding Hodgkin Lymphoma
- Understanding Non-Hodgkin Lymphomas
- Understanding Myelodysplastic Syndromes
- Understanding Myeloma
- Understanding Myeloproliferative Disorders
- Young Adults with a Blood Cancer

Or information about:

- The Leukaemia Foundation's Support Services
- Workplace giving
- Regular deduction scheme
- National fundraising campaigns
- Volunteering
- Receiving the Foundation's newsletters

Name:

Street or Postal Address:.....

Suburb.....

State/Postcode

Email: Tel: (.....).....

Please send to:

Leukaemia Foundation, GPO Box 9954, In Your Capital City

or Freecall 1800 620 420

or email: info@leukaemia.org.au

Further information is available on the Leukaemia Foundation's website

www.leukaemia.org.au



Leukaemia Foundation

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VISION TO CURE
MISSION TO CARE

This information booklet is produced by the Leukaemia Foundation and is one in a series on leukaemias, lymphomas, myeloma and related blood disorders.

Some booklets are also available in other languages. Copies of this booklet and the other booklets can be obtained from the Leukaemia Foundation in your state by contacting us on

Freecall: 1800 620 420
Email: info@leukaemia.org.au
Website: www.leukaemia.org.au

The Leukaemia Foundation is a non-profit organisation that depends on donations and support from the community.

Please support our work by calling 1800 620 420
or by mailing your donation to:
The Leukaemia Foundation
GPO Box 9954
in your capital city

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