

# **Amyloidosis Information**

## **A General Overview for Patients**



**Amyloidosis Foundation**



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**Amyloidosis was first discovered 150 years ago by the well know German pathologist, Dr. Rudolf Virchow. Although the disease has been recognized for many years, treatment has only been available for the past 15 years. And for some types of amyloidosis, treatment is not even yet available. Amyloidosis is a very complicated disease which accounts for why it has taken so long to develop treatments.**

**This booklet is provided to offer information and understanding of the amyloidoses diseases in a general manner.**

***This pamphlet is dedicated to the patients who have participated and are currently participating in clinical trials for amyloidosis. Their involvement is an important element in discovering new treatments, and to our goal of a cure.***

## **What is Amyloidosis?**

The amyloidoses are rare diseases first described over 150 years ago. The disease manifests itself when amyloid proteins deposit and accumulate in the body's organs and tissue. This accumulation may happen systemically (throughout the body) or locally (in one tissue).

Each year over 3000 cases of amyloidosis are diagnosed in the United States. Amyloidosis is generally a disease of middle-aged people and older, although the disease has been seen in individuals in their thirties. Other diseases can increase the risk of amyloidosis, and family history of the disease may indicate a hereditary version. Ten to 15% of people with multiple myeloma develop the amyloidosis. Long-term kidney dialysis may increase the risk of dialysis-associated amyloidosis.

Symptoms of the disease could include the following; fatigue, weight loss, a feeling of fullness, tingling and numbness in the lower extremities, shortness of breath, irregular heart rhythm and possibly an enlarged tongue.

### **Systemic Amyloidosis**

Systemic amyloidosis involves the deposition of amyloid throughout various tissues; including muscles, connective tissues, organs and peripheral nerves. There are a number of types of systemic amyloidosis. They include AL amyloidosis, hereditary amyloidosis and AA amyloidosis.

### **Localized Amyloidosis**

Localized amyloidosis involves tumor-like nodules that can be found on the lung, larynx, skin, bladder, small bowel and tongue. Localized amyloidosis may affect people with type II diabetes, people with certain cancers of the thyroid or endocrine system, and many people over the age of 80.

The ratio of systemic to localized amyloidosis is 9:1.

### **AL Amyloidosis (Primary)**

AL amyloidosis is the most common form of the disease. AL amyloidosis is a plasma cell disorder the cause of which is unknown. The bone marrow produces many cells, red and white blood cells, platelets and antibodies (which are proteins). In the case of AL amyloidosis, the bone marrow plasma cells produce mis-folded proteins (parts of antibodies called "light chains") that travel through the body and self-assemble and deposit in various organs, ultimately causing organ failure if the deposition is not stopped.

AL amyloidosis can affect a single organ or multiple organs. Common combinations of organ involvement include; heart/kidney, heart/GI tract and kidney/peripheral nerves, but almost any combination may present. About one third of people with AL have a high level of protein in the urine with few symptoms of organ involvement. Another third have symptoms of protein accumulation in the heart and in one quarter of AL patients the protein builds up in the liver and gastrointestinal tract.

### **AA Amyloidosis (Secondary)**

AA amyloidosis may occur in the course of a chronic inflammatory disease or chronic infection such as rheumatoid arthritis, familial Mediterranean fever (FMF), osteomyelitis, tuberculosis or inflammatory bowel disease. In the United States, this form of amyloidosis is rarely seen. This is because the medical treatment available for inflammatory diseases and chronic infection keeps them in check thus not triggering the development of AA. AA is much more prevalent in third world countries. The kidneys are the most common organ affected by AA amyloidosis

### **AF Amyloidosis (Familial)**

As the name implies, this form of amyloidosis can be inherited, is the only form that is hereditary and is not as rare as originally thought. Presence of the disease is due to inheriting an abnormal gene (a mutation) which leads to production of proteins that have the potential of forming amyloid. Symptoms of this disease normally do not present themselves until middle age or later. If a particular person has the mutated gene, each of their children has a 50% chance of inheriting the mutation. Not all people with one of the mutations will necessarily get sick. Some individuals only develop a small amount of amyloid in their body and some people may not accumulate any amyloid at all.

## **How Amyloidosis is Diagnosed**

The diagnosis starts with a thorough physical examination and establishment of the patient's medical history. The symptoms presented will help to determine tests that may be performed.

Monoclonal light chains found in the blood serum or urine by immunofixation electrophoreses (IFE) or free light chain (FLC) assay indicate the precursor protein to AL amyloid may be present. Free light chain assays are only 80-90% sensitive and many facilities do not have them or use them as an initial screening test. Additional testing including a bone marrow biopsy may be required to confirm the presence and nature of the underlying plasma cell disease.

BNP, a hormone produced when the heart is stressed, is measured via a blood test. If elevated, it may indicate heart involvement with amyloid. An echocardiogram may show the thickening of the heart walls, which could also indicate cardiac involvement. If urinary protein levels are markedly elevated, it may indicate kidney involvement with amyloid. Elevated alkaline phosphatase is an indicator of possible liver involvement with amyloid. As some of these tests are indicators of several forms of the disease it is important that the results be reviewed in conjunction with all the other test results to assure a proper diagnosis and not be looked at alone.

Any diagnosis of amyloidosis must be confirmed with a positive biopsy. Tissue samples for the biopsy can be taken from abdominal fat or the rectum. Biopsy of the suspected organ is not always necessary but can be useful.

If a hereditary form of amyloidosis is suspected, genetic testing is required to confirm the type. This is a simple blood test where the genes are analyzed to determine which mutation is present.

If the initial diagnosis indicates AL amyloidosis, it is very important to also investigate a potential for a hereditary form of the disease, especially in the case of African Americans, patients who have dominant peripheral neuropathy and those with kidney involvement without amyloid in the bone marrow. The genetic testing is required as the course of treatment is completely different for these two forms of the disease.

## Treatment of Amyloidosis

The treatments for each type of amyloidosis differ. Extension of life and improved quality of life are the major outcomes that are sought.

**AL Amyloidosis** – The treatment target for AL therapies is to eliminate the precursor protein of the amyloid that is depositing in the body. The first thing that needs to be done for these patients once diagnosed is to assess the extent of organ involvement. This will steer the proper treatment option. In most cases a patient with more than two major organs involved will not be a candidate for an autologous stem cell transplant.

Autologous stem cell transplant involves utilizing the patient's own stem cells. The process begins with mobilizing the stem cells from the bone marrow into the blood stream so that they can be collected. The next step is to administer a pre-determined dose of IV melphalan (chemotherapy) to kill off all of the cells in the bone marrow. At this point the collected stem cells are re-infused into the blood stream to allow for them to migrate back into the bone marrow where they generate the red and white blood cells and platelets needed for normal blood counts.

For patients who are not candidates for stem cell transplant there are a number of chemotherapy treatments that are effective options. They include combinations of dexamethasone and oral melphalan or the proteasome-inhibitor Bortezomib (Velcade®) or the immunomodulatory drugs such as Thalidomide or Lenalidomide (Revlimid®) or thalidomide (Thalomid®). Interferon and other chemotherapy combinations including prednisone and cyclophosphamide have also been used. New agents are being investigated in recently developed clinical trials that will prove useful in the future.

Dexamethasone and prednisone are steroids. It has been found that in some patients with AL amyloidosis the use of steroids reduces the serum free light chains and slows the deposition of amyloid in the body. The other drugs mentioned are various chemotherapy immunomodulator agents that have shown to have some effect. Sometimes it may be necessary to use a number of the different protocols in succession. Throughout treatment, the serum free light chains and other blood counts are monitored to determine the effectiveness of the treatment.

**AF Amyloidosis** – In hereditary amyloidosis, the amyloid forming protein is usually produced in the liver. With this in mind, liver transplants are sometimes performed in patients with the intention of preventing further amyloid deposition. Recent research has found that there may be drug therapy options for patients with the disease caused by the mutated transthyretin protein and clinical trials are on-going.

**AA Amyloidosis** – Since AA amyloidosis is caused by an underlying inflammatory or infectious disease treatment involves eliminating the source of the inflammation and/or infection.

### **Clinical Trials**

Clinical trials are an important aspect in developing new treatments for amyloidosis. Patients may be asked to be part of a clinical trial and will be provided with extensive information on the treatment plan, its purpose, eligibility criteria and potential side effects. The decision to enroll in a clinical trial is strictly up to the patient. Patients can inquire at the various specialty centers to see if they are eligible to enroll in a clinical trial.

The purpose of clinical trials is to determine the effectiveness and safety of new treatment protocols. Not all patients will benefit from participation in a clinical trial, but the information generated during the trial is very important in the development of treatments for future amyloidosis patients.

### **Supportive Care**

Supportive care is important to address specific problems and symptoms that are caused by the amyloid deposits in the body. In the case of cardiac or kidney involvement, edema (fluid buildup) may be a problem and a diuretic can be prescribed to help minimize the problem. In some cases, compression stockings can be of benefit and elevating the legs can help lessen the swelling. Patients with congestive heart failure due to amyloid in their heart need special diets and medication under the care of a cardiologist who understands the needs related to amyloid heart disease. If the gastrointestinal tract is involved, diet modifications and some medications can help with diarrhea and the feeling of fullness. Some patients with macroglossia (enlarged tongue) have difficulty swallowing and sometimes aspirate fluids into their lungs. Thickeners can be obtained to mix into everyday fluids that will help to minimize aspiration into the lungs.

## **Prognosis for an Amyloidosis Patient**

With early diagnosis, the outlook for patients with amyloidosis has shifted to hopeful in the last decade. The early diagnosis allows treatment to begin before the amyloid protein burden in the body becomes too great to overcome. Without treatment, the outlook for patients with AL amyloidosis is not good, many passing away within 18 – 24 months after diagnosis. Early diagnosis is the key to managing the disease.

In familial amyloidosis, the outlook varies depending on the type of gene mutation and when the condition is diagnosed. Some patients may survive up to 15 years after the disease presents.

Localized amyloid tumors can be surgically removed and generally do not recur.

## **Conclusion**

Although a cure for amyloidosis and a cause for some of the forms of the disease still have not been found, the outlook for amyloid patients has improved in the last decade especially if diagnosed early on. The information contained in this pamphlet is intended to provide a general overview of the disease and its treatment.

It is important to note that although advances in treatment options have progressed there is still much to be discovered. It is not known how certain proteins and immunoglobulin light chains form amyloid. How to stop the light chains from sticking together and forming amyloid, and the exact way that this makes patients sick is also unknown. The answers to these and many other questions are important for the continued development of treatments and will lead to our goal of a cure.

### **Major U.S. Amyloidosis Treatment Centers**

Boston University Medical Center – Boston, MA  
Amyloid Treatment and Research Program  
[www.bu.edu/amyloid](http://www.bu.edu/amyloid)  
617-638-4317

The Mayo Clinic – Rochester, MN  
[www.mayoclinic.org/amyloidosis/index.html](http://www.mayoclinic.org/amyloidosis/index.html)  
507-538-3270

Memorial Sloan-Kettering Cancer Center – New York, NY  
<http://www.mskcc.org/mskcc/html/8616.cfm>  
212-639-8088

Tufts Medical Center—Boston, MA  
[www.tuftsmedicalcenter.org](http://www.tuftsmedicalcenter.org)  
617-636-6454

### **Other U.S. physicians with specific clinical expertise in amyloidosis**

Familial Amyloidosis – Merrill Benson, MD. Amyloid Research Group, University of Indiana, Indianapolis, IN  
<http://www.iupui.edu/~amyloid/>  
317-278-3426

Cardiac Amyloidosis – Rodney H. Falk, MD.  
Harvard Vanguard Medical Associates, Harvard Medical School,  
Brigham and Women's Hospital. Boston, MA  
[rfalk@partners.org](mailto:rfalk@partners.org)  
617-421-6050

Cardiac Amyloidosis - Mathew Mauer, MD  
Columbia University Medical Center  
Presbyterian Hospital  
New York NY  
[msm10@columbia.edu](mailto:msm10@columbia.edu)  
212-932-6036

For other institutions that have experience with the disease please, contact us for information. 1-877-AMYLOID

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**Amyloidosis Foundation  
7251 N. Main St.  
Suite 2  
Clarkston, MI 48346**

**1-877-AMYLOID  
(toll free USA and Canada)  
1-248-922-9610 p  
1-248-922-9620 f**

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