

# Amyloidosis and Its Impact on Patients With ESRD

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**P**roteins are the essential foundational tools for all body parts and processes and normally circulate throughout the body in the blood. Sometimes, cells in the body produce fragment or unusually shaped proteins that can settle as deposits in body tissues causing disease. These deposits of abnormal proteins are called *amyloids* and the disease process *amyloidosis*. There are different types of proteins that can form amyloid deposits, and two of them are closely related to kidney disease. In *primary amyloidosis*, abnormal protein production associated with plasma cell dyscrasia occurs as a first step and can lead to kidney disease. *Dialysis-related amyloidosis* (DRA), however, results from kidney disease (NIDDK, 2003).

## Primary Amyloidosis

Primary amyloidosis occurs when the body produces abnormal protein fibers, which join together to form amyloid deposits in different organs, including the kidneys, where they cause serious damage (NIDDK, 2003). The kidneys become unable to function to remove urea and other wastes from the blood, resulting in the need for a dialysis prescription and therapy.

The initial sign that amyloidosis is present is the abnormally high amounts of protein in the urine or proteinuria (NIDDK, 2003). A kidney biopsy may be used to confirm the diagnosis of amyloidosis. No treatment has been found to be effective in reversing the effects of amyloidosis, although the use of melphalan and prednisone may help improve organ function and survival rates by interrupting the growth of

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*Patients, like those with ESRD, who have lost the ability to filter excess proteins from their bodies are at risk to develop beta-2-microglobulin amyloidosis, also known as dialysis-related amyloidosis (DRA). When the kidneys do not work efficiently, a protein called beta-2-microglobulin can build up in the blood. Eventually, these molecules can form large deposits and potentially damage surrounding tissues. Currently, dialyzer membranes do not effectively remove these large molecules and, as the blood levels become elevated, deposits begin forming in bone, joints, and tendons resulting in pain and/or stiffness. Unfortunately, there is no known cure for DRA, although attempts are being made to develop dialyzer membranes that can more efficiently remove beta-2-microglobulin from the blood. Implications for practice include early diagnosis, patient teaching, optimal pain management, and fall risk management.*

## Goal

Compare and contrast primary and dialysis-related amyloidosis.

## Objectives

1. Discuss the cause, diagnosis, and prognosis of primary amyloidosis.
2. Describe the signs and symptoms of dialysis-related amyloidosis (DRA).
3. Cite implications for nursing practice in care of patients with amyloidosis.

cells that produce amyloid protein (NIDDK, 2003).

## Dialysis-Related Amyloidosis

Patients, like those on dialysis, who have lost the ability to filter excess small proteins from their bodies, are at risk to develop DRA. When the kidneys do not work efficiently, a protein called *beta-2-microglobulin* can build up in the blood. Eventually, these molecules can form large deposits by forming a chain of small molecules into a large molecule and potentially damage surrounding tissues (NIDDK, 2003). Unfortunately, dialyzer membranes do not effectively remove these

large molecules and as the blood levels become elevated, deposits begin forming in bone, joints, and tendons resulting in pain and/or stiffness.

## Incidence

DRA has been found to be relatively common in patients on hemodialysis who have been receiving treatment for longer than 5 years, and especially among the elderly (NIDDK, 2003). DRA has also been found in patients who have been treated exclusively with CAPD (Cornelius et al., 1989). The overall incidence of amyloidosis is 8 cases per million per year, representing

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The Nephrology Nursing Certification Commission (NNCC) requires 60 contact hours for each recertification period for all nephrology nurses. Forty-five of these 60 hours must be specific to nephrology nursing practice. This CE article may be applied to the 45 required contact hours in nephrology nursing.

**Table 1  
Amyloidosis Resources**

The following support groups and information sites exist for patients with amyloidosis, their families, and healthcare providers:

**Amyloidosis Support Network**

1490 Herndon Lane  
Marietta, GA 30062  
[www.amyloidosis.org](http://www.amyloidosis.org)

**Amyloidosis Network International, Inc**

7118 Cole Creek Drive  
Houston, TX 77092-1421  
1-888-AMYLOID

**Amyloid Treatment and Research Center**

<http://amyloid.bu.edu/amyloid/amyloid1.htm>

**Association for Neuro-Metabolic Disorders**

5223 Brookfield Lane  
Sylvania, OH 43560-1809  
1-419-885-1497  
<http://www.kumc.edu/gec/support/neuro-me.html>

**National Institutes of Health National Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse**

One AMS Circle  
Bethesda, MD 20892-3675  
1-301-495-4484  
[www.nih.gov/niams/healthinfo](http://www.nih.gov/niams/healthinfo)

**National Kidney and Urologic Diseases Information Clearinghouse**

3 Information Way  
Bethesda, MD 20892-3580  
1-800-891-5390  
[www.niddk.nih.gov](http://www.niddk.nih.gov)

**National Kidney Foundation**

30 East 33<sup>rd</sup> Street  
Suite 1100  
New York, NY 10016  
1-800-622-9010  
[www.kidney.org](http://www.kidney.org)

2,500 new cases annually in the United States. Peak occurrences of this disease are in ages 60-67 and are more common in males than females (Mayo, 2002).

**Signs and Symptoms**

Most symptoms of amyloidosis are nonspecific and often not recognized initially. Weight loss, fatigue, and weakness appear to be the most common symptoms reported. Others include: dyspnea, edema, and pares-

thesias. The primary signs and symptoms of DRA revolve around joint pain, fluid, and stiffness; neuropathy; nephropathy; bone fractures; ligament and tendon tears; and GI abnormalities (Sprague & Moe, 1996; Zingraff, 1990). Carpal tunnel syndrome is the most common complaint, occurring in about half of the patients who have DRA (NIDDK, 2003). Shoulders, back, hips, and neck joints are also affected in 20%-30% of patients with DRA (Calal, Pavlovici, Mrzljak, & Jankovis, 1993).

**Tests and Exams**

Amyloidosis is uncommon and primary care physicians may not recognize when and how to test for the disease. Biopsy tissue that shows amyloid deposits on “Congo-red staining” is the only definitive confirmation of amyloidosis (NKF, 2003). Tissue that can be used for the biopsy includes: stomach fat aspirate, oral or rectal mucosa, bone marrow, or the specific organ affected (Mayo, 2002). Other tests commonly ordered to diagnose or prognose include: abdominal ultrasound, ECG, echocardiogram, nerve conduction tests, and renal function tests. BUN, serum creatinine, and urinary casts all act as predictors of disease and survival rates. Cystatin C. Serum #82994 is a recently introduced test that provides a more sensitive indicator of glomerular filtration rate (GFR) and is proving very useful in diagnosing and monitoring nephritic syndrome caused by amyloidosis (Mayo, 2002).

**Treatment**

Unfortunately, no cure has been found, although a successful kidney transplant may stop DRA from progressing, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK, 2003). The National Kidney Foundation’s K/DOQI Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease suggests the use of high-flux dialyzers to slow the progression of the disease. Attempts are being made to develop membranes that can more efficiently remove *beta*-2-microglobulin from the blood during hemodialysis (NKF, 2003).

Primary amyloidosis is treated with combination drug therapy. Currently, melphalan (a common chemotherapy drug) and prednisone are used to slow progression of the disease (NIDDK, 2003). Clinical trials are presently underway using such drugs as dexamethasone, interferons, and thalidomide. Stem cell transplantation is also under investigation. Symptomatic treatment is the only

option in many cases. Dialysis, renal transplantation, carpal tunnel release, and heart transplantation (in very selected cases) are some of the treatments available to relieve symptoms of amyloidosis.

### Prognosis and Survival Rates

Drug therapy and good management may potentially slow the progression of the disease, but the prognosis remains bleak. Congestive heart failure is the single greatest prognostic indicator in patient survival (Mayo, 2002). Echocardiogram results are abnormal in one-third of patients at diagnosis, and almost one-half of patients have septal thickness of 15 mm or more. The thickness apparently reflects the amount of amyloid that has deposited in the myocardium and is also a predictor of patient survival. Patients who do not exhibit congestive heart failure have up to a 5-fold increase in estimated survival time (Mayo, 2002). Recent studies have demonstrated that high counts and percentages of peripheral blood plasma cells (PBPC) are associated with shorter survival in amyloidosis.

While mortality from DRA is rare, the disease can cause significant morbidity and is a major cause of immobility in patients on long-term dialysis. The K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease recognize the lack of quality studies in this area and suggest that it is a reflection of the slow progressive nature of the disease as well as the difficulty in diagnosing when symptomatology is vague (NKF, 2003). The guidelines do not recommend rou-

tine screening of the patients for the presence of *beta-2*-microglobulin.

### Implications for Practice

Implications for practice include patient teaching, optimal pain management, fall risk management, and early diagnosis. Patient teaching for amyloidosis needs to be specific to the disease process, appropriate pharmacological and nonpharmacological pain management alternatives, musculoskeletal concerns, and appropriate lab tests. Patients also need to be aware of current options in treatment management: use of high flux dialyzers, transplantation, surgery, etc. Safety concerns for this population would include a fall risk plan and interventions due to the musculoskeletal pain and weaknesses. Safety equipment for the home and/or work area are recommended. The impact of carpal tunnel syndrome on an arm that already contains a graft or fistula for hemodialysis should be explored with the patient and lifestyle alterations considered.

Pain management techniques include teaching on a pain assessment scale, evaluation of interventions, and the use of safety devices. Teaching on appropriate pain relief medications is imperative, especially if it is dialysis-related amyloidosis. The medications must also be kidney friendly.

Finally, early diagnosis is essential but difficult. Since many symptoms are vague, the diagnosis can be easily missed. Community education and education in the dialysis arena could trigger earlier lab tests and the use of preventive techniques (such as

type of dialyzer). Patients and family members need to be aware of resources (see Table 1) and support groups available to them for more information on current clinical trials, treatment modalities, and emotional reinforcement.

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