



Amyloidosis and Kidney Disease

Proteins are important building blocks for all body parts, including muscles, bones, hair, and nails. Proteins circulate throughout the body in the blood and are normally harmless. Occasionally, cells produce abnormal proteins that can settle in body tissue, forming deposits and causing disease. When these deposits of abnormal proteins were first discovered, they were called *amyloid*, and the disease process *amyloidosis*.

In recent years, researchers have discovered that different kinds of proteins can form amyloid deposits and have identified several types of amyloidosis. Two of these types are closely related to kidney disease. In *primary amyloidosis*, abnormal protein production occurs as a first step and can lead to kidney disease. *Dialysis-related amyloidosis (DRA)*, on the other hand, is a result of kidney disease.

Primary Amyloidosis

Primary amyloidosis occurs when the body's antibody-producing cells do not function properly and produce abnormal protein fibers made of antibody fragments. Some people with primary amyloidosis have a condition called multiple myeloma. The antibody fragments come together to form amyloid deposits in different organs, including

the kidneys, where they cause serious damage. Injured kidneys can't function effectively and may be unable to remove urea and other wastes from the blood. Elevated levels of these protein fibers can also damage the heart, lungs, brain, and digestive system.

One common sign of kidney amyloidosis is the presence of abnormally high levels of protein in the urine, a condition known as *proteinuria*. Healthy kidneys prevent protein from entering the urine, so the presence of protein may be a sign that the kidneys aren't working properly. A physician who finds large amounts of protein in the urine may also perform a biopsy—take a small sample of tissue for examination under a microscope—to confirm amyloidosis.

No effective treatment has been found to reverse the effects of amyloidosis. Combination drug therapy with melphalan (a cancer drug) and prednisone (an anti-inflammatory steroid drug) may improve organ function and survival rates by interrupting the growth of the abnormal cells that produce amyloid protein. These are the same drugs used in chemotherapy to treat certain cancers (such as multiple myeloma), and they may have serious side effects, such as nausea and vomiting, hair loss, and fatigue.



Dialysis-Related Amyloidosis

Normal kidneys filter and remove excess small proteins from the blood, thus keeping blood levels normal. When the kidneys don't work properly, as in patients receiving dialysis, one type of small protein called *beta-2-microglobulin* builds up in the blood. When this occurs, beta-2-microglobulin molecules may join together, like the links of a chain, forming a few very large molecules from many smaller ones. These large molecules can form deposits and eventually damage the surrounding tissues and cause great discomfort. This condition is called *dialysis-related amyloidosis (DRA)*.

DRA is relatively common in patients who have been on hemodialysis for more than 5 years, especially among the elderly. Hemodialysis membranes that have been used for many years don't effectively remove the large, complex beta-2-microglobulin proteins from the bloodstream. Newer hemodialysis membranes, as well as peritoneal dialysis, remove beta-2-microglobulin more effectively, but not enough to keep blood levels normal. As a result, blood levels remain elevated, and deposits form in bone, joints, and tendons. DRA may result in pain, stiffness, and fluid in the joints. Patients with DRA may also develop hollow cavities, or cysts, in some of their bones; these may lead to unexpected bone fractures. Amyloid deposits may cause tears in ligaments and tendons (the tissue that connects the muscle to the bone). Most patients with these problems can be helped by surgical intervention.

Half of the people with DRA also develop a condition called carpal tunnel syndrome, which results from the unusual buildup of protein in the wrists. Patients with this disorder may experience numbness or tingling, sometimes



Amyloid may build up in the wrist and cause bone cysts or carpal tunnel syndrome.

associated with muscle weakness, in their fingers and hands. This is a treatable condition.

Unfortunately, no cure for DRA has been found, although a successful kidney transplant may stop the disease from progressing. However, DRA has caught the attention of dialysis engineers, who are attempting to develop new dialysis membranes that can remove larger amounts of beta-2-microglobulin from the blood.

Hope Through Research

In recent years, researchers have learned a great deal about kidney disease. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) sponsors several programs aimed at understanding kidney failure and finding treatments to stop its progression.

NIDDK's Division of Kidney, Urologic, and Hematologic Diseases supports basic research into normal kidney function and the diseases that impair normal function at the cellular and molecular levels, including amyloidosis. Recently, NIDDK-sponsored researchers have identified several genes that may contribute to a hereditary form of primary amyloidosis. In 2001, a team of researchers at the Indiana University School of Medicine located a mutation in the apolipoprotein A-II gene of a patient with kidney damage caused by amyloidosis. The researchers noted that the patient had reabsorbed most of the amyloid. They theorize that learning how this reabsorption occurs may point the way to possible therapies for all forms of amyloidosis.

For More Information

For information on primary amyloidosis:

National Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse

National Institutes of Health

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National Kidney and Urologic Diseases Information Clearinghouse

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Publications produced by the clearinghouse are carefully reviewed by both NIDDK scientists and outside experts. This fact sheet was reviewed by Glenn Chertow, M.D., University of California at San Francisco; and William J. Stone, M.D., Vanderbilt University.

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This fact sheet is also available at www.kidney.niddk.nih.gov.



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