



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 with a microscope—to confirm amyloidosis.

Current treatments are aimed at slowing the progression of amyloid build-up. 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.

Some clinics have reported promising results treating amyloidosis by transplanting the patient's own blood stem



cells to replace diseased or damaged bone marrow. The therapy also requires high doses of melphalan, so side effects can be serious. Patients with heart problems may not be considered for this treatment.

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, especially older adults, who have been on hemodialysis for more than 5 years. 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 (the tissue that connects the muscle to the bone). 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. 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



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

results from the unusual buildup of protein in the wrists. Patients with this condition may experience numbness or tingling, sometimes 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.

The 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. The NIDDK is also supporting multiple efforts to develop a blood detoxification system that will eliminate beta-2-microglobulin.

For More Information

National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Institutes of Health
1 AMS Circle
Bethesda, MD 20892-3675
Phone: 1-877-226-4267 or 301-495-4484
TTY: 301-565-2966
Fax: 301-718-6366
Email: niamsinfo@mail.nih.gov
Internet: www.niams.nih.gov

Amyloidosis Support Network

1490 Herndon Lane
Marietta, GA 30062
Phone: 1-888-AMYLOID (269-5643)
or 713-466-4351
Support group information:
800-689-1238 x27
Email: info@amyloidosis.org
Internet: amyloidosis.org

About the Kidney Failure Series

The NIDDK Kidney Failure Series includes six booklets and seven fact sheets that can help you learn more about treatment methods for kidney failure, complications of dialysis, financial help for the treatment of kidney failure, and eating right on hemodialysis. For free single printed copies of this series, please contact the National Kidney and Urologic Diseases Information Clearinghouse.

National Kidney and Urologic Diseases Information Clearinghouse

3 Information Way
Bethesda, MD 20892-3580
Phone: 1-800-891-5390
Fax: 703-738-4929
Email: nkudic@info.niddk.nih.gov
Internet: www.kidney.niddk.nih.gov

The National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health under the U.S. Department of Health and Human Services. Established in 1987, the Clearinghouse provides information about diseases of the kidneys and urologic system to people with kidney and urologic disorders and to their families, health care professionals, and the public. The NKUDIC answers inquiries, develops and distributes publications, and works closely with professional and patient organizations and Government agencies to coordinate resources about kidney and urologic diseases.

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.

This publication is not copyrighted. The Clearinghouse encourages users of this fact sheet to duplicate and distribute as many copies as desired.

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



U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
National Institutes of Health

NIH Publication No. 06-4694
May 2006

