# Genetics and Paget's Disease of Bone

**National Institutes of Health**
**Osteoporosis and Related Bone Diseases ~ National Resource Center**

2 AMS Circle
Bethesda, MD
20892-3676

**Tel:** (800) 624-BONE or
(202) 223-0344
**Fax:** (202) 293-2356
**TTY:** (202) 466-4315

**Internet:** www.niams.nih.gov/bone
**E-mail:** NIAMSBONEINFO@mail.nih.gov

The NIH Osteoporosis and Related Bone Diseases ~ National Resource Center is supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases with contributions from: National Institute on Aging, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institute of Dental and Craniofacial Research, National Institute of Diabetes and Digestive and Kidney Diseases, NIH Office of Research on Women's Health, DHHS Office on Women's Health.

*The National Institutes of Health (NIH) is a component of the U.S. Department of Health and Human Services.*

## What Is Paget's Disease of Bone?

Paget's disease of bone is a treatable chronic disease that results in enlarged and misshapen bones in one or more areas of the skeleton.

Healthy bone goes through a continuous renewal process in which old bone is broken down by cells called osteoclasts and new bone is formed by cells called osteoblasts. In Paget's disease, these two cells do not interact normally. Instead, bone breakdown and formation are excessive and produce bone that is enlarged and has a weaker structure. Some of the symptoms and complications that can result from Paget's disease include bone pain, osteoarthritis, misshapen bone, and broken bones.

Scientists and doctors do not fully understand what causes Paget's disease of bone.

## How Does Genetics Relate to Paget's Disease of Bone?

Genetics is the branch of biology that deals with heredity and variations in people and other living things. It is an exciting area of research for Paget's disease.

Recent studies suggest that genetics plays a role in at least some cases of Paget's disease. For example, Paget's disease can run in families. When this happens, it is referred to as **familial** or hereditary Paget's disease. However, the majority of people with Paget's disease do not have any affected relatives and do not appear to have familial Paget's disease. When there is no family history, the disease is referred to as **sporadic**.

Scientists are studying genetic factors in both familial and sporadic Paget's disease to better understand the causes and possible treatments.

## Have Any Genes Related to Paget's Disease Been Discovered?

Yes. So far, one gene has been discovered that, when altered, predisposes people to develop Paget's disease. It is called sequestosome 1. Scientists first discovered that this gene was altered in several families with familial Paget's disease, mainly living in Canada. Since then, scientists have found the same altered gene in other families with familial Paget's disease from many parts of the world, including the United States, Australia, the United Kingdom, Belgium, and Italy.

This gene is also altered in people who appear to have sporadic Paget's disease. Scientists are not sure whether these people have new alterations in the gene or whether they inherited them from parents who carried the altered gene but were not affected by Paget's disease. Not everyone with an alteration in this gene develops Paget's disease.

Scientists have also identified two other genes that are associated with Paget's disease. One is the RANK gene. Specific alterations in RANK cause a disease called familial expansile osteolysis (FEO). FEO has some similarities to Paget's disease, but usually involves the entire skeleton and is associated with several symptoms that are not typical of Paget's disease. Scientists also have found RANK in one family whose members developed Paget's disease, but at a younger age than most Paget's patients. VCP is the third gene that scientists have linked to Paget's disease. This gene is found in some people with Paget's disease who also have a muscle-weakening disease.

## Do Scientists Think That Genes Are the Only Cause of Paget's Disease?

No. It is likely that environmental factors, such as viruses, as well as genetic factors, may be involved in the development of Paget's disease. Scientists believe that the number of new cases of Paget's disease has been declining by almost 50 percent in some parts of the world over the last several decades. This decline is too rapid to be caused by a gene.

## Are Scientists Continuing to Do Research on Genetics and Paget's Disease?

Yes. The three genes associated with Paget's disease of bone have only been identified recently. Scientists are studying how these genes are altered in people with Paget's disease in order to begin to understand how the alterations actually

cause the disease. In addition, scientists have evidence that there are other, as-yet-unidentified Paget's disease genes. Their efforts to find these genes continue.

## If a Person Has a Parent or Sibling with Paget's Disease, Are There Any Special Medical Tests That Should Be Done?

Currently, no tests are available to screen for alterations in Paget's disease genes. This type of screening is only done for research purposes to better understand the relationship between Paget's disease and the gene alterations. However, tests are available to diagnose Paget's disease, and family members who are concerned about inheriting the disease may wish to discuss testing options with their doctor.

There is a simple blood test to determine if the level of serum alkaline phosphatase (SAP) is above normal. This may be a sign of Paget's disease, although high levels of SAP can also indicate liver disease and cancer, which need to be ruled out before diagnosing Paget's disease. In addition, a normal SAP test may not always rule out Paget's disease if only a small change in the bone, called a pagetic lesion, is involved.

Family members may wish to get a SAP test every 2 to 3 years after the age of 40 to screen for Paget's disease, since early diagnosis and treatment are important. Doctors do not recommend testing before age 40 because the disease is rare in younger people.

Another test doctors can use to detect Paget's disease is a bone scan. For this test, the doctor injects into the patient's bloodstream a safe amount of a radioactive substance that circulates through the blood and localizes in any areas where Paget's disease is found. When the bone scanner takes a picture of the bones, those with the localized radioactive substance appear darker, telling the doctor not only that the disease may be present but also which bones are affected. If a bone scan suggests Paget's disease, the doctor will need to x ray the affected bone or bones to confirm the diagnosis.

## Will Every Person Who Has a Parent or Sibling with Paget's Disease Develop Paget's Disease?

No. Most people with Paget's disease do not have any relatives who are affected by the disease. In addition, there are elderly people who carry a gene mutation linked to Paget's disease and never develop the disease in their lifetime.

## Where Can I Go to Get More Information About Paget's Disease?

There are many good sources of information about Paget's disease. These include:

**NIH Osteoporosis and Related Bone Diseases ~ National Resource Center**
2 AMS Circle, Bethesda, MD 20892-3676
Telephone: 1-800-624-BONE (1-800-624-2663, free of charge) or 202-223-0344
Fax: 202-293-2356
TTY: 202-466-4315
Internet: www.niams.nih.gov/bone
E-mail: NIAMSBONEINFO@mail.nih.gov

**National Institute of Arthritis and Musculoskeletal and Skin Diseases**
National Institutes of Health
1 AMS Circle, Bethesda, MD 20892-3675
Telephone: 1-877-22-NIAMS (1-877-226-4267, free of charge) or 301-495-4484
Fax: 301-718-6366
TTY: 301-565-2966
Internet: www.niams.nih.gov

**National Library of Medicine**
8600 Rockville Pike, Bethesda, MD 20894
Telephone: 1-888-FIND-NLM (1-888-346-3656, free of charge) or 301-594-5983
Fax: 301-402-1384
Internet: www.nlm.nih.gov
E-mail: custserv@nlm.nih.gov

**The Paget Foundation for Paget's Disease of Bone and Related Disorders**
120 Wall Street, Suite 1602, New York, NY 10005-4001
Telephone: 1-800-23-PAGET (1-800-237-2438, free of charge) or 212-509-5335
Fax: 212-509-8492
Internet: www.paget.org
E-mail: PagetFdn@aol.com

*The National Resource Center acknowledges the assistance of The Paget Foundation in the preparation of this publication.*

Revised December 2005