



## Heredity and Arthritis

**Note:** Because of the technical nature of this topic, you may wish to consult with your physician if you have questions after reading this information.

Like most human diseases, the many forms of arthritis or rheumatic diseases have genetic components. Each disease, however, has its own unique degree and pattern of heredity, as well as different genes which influence not only susceptibility to, but also severity of, the disease.

### Fast facts

- Each rheumatic disease has its own specific cause(s), including a certain inherited background.
- Rheumatological diseases are caused by the interplay of multiple genes and environmental factors.
- Studying twins has proven very helpful in examining the genetic and environmental influences that may cause disease.

### What are genetics and genes?

Part of the study of genetics is a focus on how human characteristics are inherited from one's ancestors. The means by which these characteristics appear in descendants is attributed to genes. These genes, which are a small portion of a chromosome, are considered a unit of heredity and are randomly passed from parents to offspring.

In reality, there are approximately 25,000 genes, all varying from person to person, all influencing human traits like appearance, personality and susceptibility to different diseases. Mutations, which are usually harmful changes in the genes, or even mild and usually harmless variations in genes, can result in diseases in offspring.



### How do unifactorial and multifactorial diseases differ?

The diseases resulting from mutating or normal variations in genes are typically classified as either unifactorial or multifactorial. Unifactorial diseases are caused by the passing of a mutated gene or pair of genes to a child by one or both parents. For example, sickle cell anemia is a unifactorial disease in which, if the same harmful mutated gene is passed to a child by both parents, the child has the disease. If the child inherits one mutated (sickle cell) gene from one parent and a normal gene from the other, the child has what is called "sickle cell trait" but not the disease. However, with other unifactorial diseases, such as Marfan syndrome, the child can receive the abnormal gene from only one parent and inherit the disease, meaning one gene is enough to pass on the disease.

Multifactorial diseases are caused by a complicated interaction of multiple genes and environmental factors such as age, gender, infection or nutrition. Most diseases, including [osteoarthritis](#) and adult-onset diabetes, are thought to be multifactorial. Because the predisposition to these diseases is caused by several genes, they are also called polygenic diseases. Most forms of arthritis are thought to be multifactorial and polygenic.

### How twin studies help

Studying twins has proven very helpful in examining the genetic and environmental influences that may cause disease. Identical (monozygotic) twin pairs possess exactly the same genes, while non-identical (dizygotic) twin pairs, like any other siblings, typically mirror only half of their genes.

Regardless of their genetic background, however, both identical and non-identical twins usually grow up in the same environment and share similar exposures during childhood. Therefore, a simple comparison of how frequently a disease affects identical versus non-identical twin pairs can provide valuable information about to what extent a disease is influenced by genetic versus environmental factors.

If the disease is unifactorial, both identical twins nearly always will be affected, while a much smaller percentage of non-identical twins will both develop the disease. In multifactorial diseases, the frequency of both identical twins getting the disease is 5 to 70%, and for non-identical pairs, even lower.

### Genetics and ankylosing spondylitis

Each rheumatic disease has its own specific cause(s), including a certain genetic background. One of the strongest examples of this genetic influence on a rheumatic disease is the connection between ankylosing spondylitis (AS) and a gene called HLA-B27. Ankylosing spondylitis is an inflammatory arthritis affecting primarily the spine that begins in teenagers and young adults.

More than 90% of Caucasian AS patients have the HLA-B27 gene, compared to the approximately 7% of the general population who carry this gene. This means only a small portion of the general population (approximately 5%) who carries the gene will develop the disease.

On the other hand, first-degree family members (parents, siblings and children) of AS patients with the HLA-B27 gene have a 20% chance of developing the disease. This is probably because they are exposed to the same environmental factors as the patient and have inherited certain other important genes in addition to the HLA-B27 gene. ARTS 1 and IL23R are two newly identified non-HLA B27 susceptibility genes for ankylosing spondylitis.



### Genetics and rheumatoid arthritis

[Rheumatoid arthritis](#), a multifactorial disease, is a common type of inflammatory arthritis which affects many joints and occurs in approximately 1% of the population worldwide. In this case, the gene link with rheumatoid arthritis is to an immune system gene called HLA-DR4. In rheumatoid arthritis patients of European ancestry, as many as 60-70% carry the HLA-DR4 gene, compared with 30% in the general population.

Twin studies show that 12-15% of identical twins both develop rheumatoid arthritis compared to only 4% in non-identical twins. Further, the disease rate in first-degree family members of rheumatoid arthritis patients is only 0.8% compared to 0.5% in the general population. This indicates that genes only modestly increase the risk for rheumatoid arthritis and that the environment is likely to play a stronger role. Recent studies have indicated an interplay between smoking and DR4 that leads to an increased rheumatoid arthritis risk.

### Genetics and lupus

[Systemic lupus erythematosus](#) (SLE) is a chronic inflammatory disease that can affect skin, joints, kidneys, lungs and/or other organs of the body. A study showed 8% of patients with SLE had at least one first-degree family member (parents, siblings and children) with the same diagnosis compared to 0.08% of the general population. This suggests SLE recurs to a modest degree in families.

A twin study showed that SLE recurs in the other sibling in 24% of identical twins and 2% non-identical twins, implying both genetic and environmental factors are important. Researchers have identified multiple gene alterations that contribute to a modestly increased risk for this disease. It is thought that a combination of these genes leads to development of SLE.

### Do autoimmune diseases share some susceptibility genes?

The immune system protects us from harmful germs, but can become redirected and attack various parts of our own bodies. This state of affairs creates a biological basis for autoimmune diseases. Rheumatoid arthritis and SLE, along with a variety of other diseases—such as thyroid disorders, multiple sclerosis and juvenile diabetes mellitus—belong to this group of autoimmune diseases.

Frequently, multiple and different autoimmune diseases are observed in the same families. For example, 11% of SLE patients have one other relative with an autoimmune disease in their family, indicating these diseases may share some of the same susceptibility genes.

Also, certain immune system genes, like PTPN22 and STAT4 have been linked to multiple autoimmune diseases, including SLE, scleroderma and rheumatoid arthritis.



### Genetics and osteoarthritis

**Osteoarthritis** (OA) or degenerative joint disease (DJD) is the most common type of arthritis. OA and DJD are not autoimmune diseases and, therefore, are unlikely to share the same genes as ankylosing spondylitis, rheumatoid arthritis or SLE. In a study comparing identical to non-identical twins, an identical twin had a two-fold higher chance of developing OA of the hand or knee if the other twin had the same disease. This indicates genetics may play an important role in the development of OA or DJD.

Another study investigating the role of genetics in OA of the hand showed that sisters of women with this disease had a two-fold increased risk of developing hand OA when compared to the general population. This risk was increased by five- to seven-fold if the diseased sibling had severe disease. Certain gene mutations have been linked only to a particular site of OA (e.g., knee, hip or hand) implying that each site might have its own genetic basis.

These recent findings about the genes contributing to the many forms of arthritis are leading to new knowledge about their cause, as well as new treatment strategies to reduce pain and crippling, and possible means of disease prevention.

### Points to remember

- Ankylosing spondylitis and rheumatoid arthritis appear to have identifiable genes that play a substantial role in passing the disease to a child.
- Recent findings are leading to new knowledge about the causes of arthritis diseases, as well as new treatment strategies to reduce pain and crippling, and possibly disease prevention.
- The clustering of multiple and different autoimmune diseases is observed frequently in the same families, suggesting existence of shared susceptibility genes among these diseases.

### To find a rheumatologist

For a listing of rheumatologists in your area, [click here](#).

Learn more about [rheumatologists](#) and [rheumatology health professionals](#).

### For more information

If you want more information on this or any other form of arthritis, contact the Arthritis Foundation at (800)283-7800 or visit the Arthritis Foundation Web site at [www.arthritis.org](http://www.arthritis.org).



This illustration shows OA in the knee joint.



**Reviewed February 2012**

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