

# Diamond Blackfan Anemia, Genetics, and You



## Q Is Diamond Blackfan Anemia (DBA) a genetic disorder?

**A** Yes, DBA is a genetic disorder. In about half of families studied, only one person in the family has DBA. In these cases, DBA occurs as a new event, but it can be passed on to the children of the affected person. In fewer than half of families, more than one family member is affected. For example, two or more siblings or both a parent and a child may have DBA. Signs of the disorder can be very minor, and some people have no signs at all. In a family with one of the known genetic mutations, genetic tests can tell whether or not a family member is affected.

## Q What is a gene?

**A** A gene is made up of DNA (deoxyribonucleic acid), which is the hereditary material in humans and almost all other living things. Genes hold the instructions needed to make proteins that make the body function. Proteins do the work inside the body, based on the instructions in genes. Genes and proteins tell the cells of a person's body how to grow and work. Every cell in the body contains the same set of genes. Each person has two copies of every gene in each cell, one copy from his or her mother and one from his or her father.

## Q What is a genetic mutation?

**A** Genes are made up of a long strand of bases that are strung together in a certain order. If you think of the bases as letters (A, T, G, and C), the order or sequence of the letters tells the cells what to do. A genetic mutation is any change in a gene that makes it different from the usual sequence of letters that most people have, like a typo or a misspelling of a word in a book, or a missing or added sentence or set of sentences in a book. If the mutation causes a change in the way that the gene works, the person with the mutation could have a particular disorder (such as DBA).

## Q Why do genes matter to me?

**A** The body's failure to make enough red blood cells has been linked to genetic mutations in some people. In DBA, certain mutations affect the way the body is instructed to make red blood cells. In DBA, the bone marrow (the center of the bone where blood cells are made) does not make enough red blood cells, which carry oxygen from the lungs to the body.

## Q What type of mutation causes DBA?

**A** About half of DBA patients have been found to have a mutation in one of the genes that carries the instructions for making a certain kind of protein called a ribosomal protein.

DBA is caused by autosomal dominant mutations. This means a person, either male or female, needs only one copy of the mutated gene and one copy of the typical gene to have the disorder (see figure). The copy of the mutated gene can come from the mother or the father, or can be a new sporadic mutation (see definition below). If one parent has the gene mutation, there is a 50:50 chance that it will be passed to his or her child at conception.

## Q How many different genes have been linked to DBA?

**A** Scientists have linked mutations in several different genes to DBA. All of these genes carry the instructions for a family of proteins called ribosomal proteins. Researchers are working to identify more genes with mutations linked to DBA, because genetic mutations have not yet been found to explain more than half of the causes of the disorder.

## Q What is genetic testing?

**A** Genetic testing is typically done to check for mutations or changes in specific genes. Most of the time, genetic testing is used to find mutations linked with disorders that may be passed down from parent to child. If the results of genetic testing are conclusive, they can show a link between the mutation and a particular disorder. They may also be used to help find out a person's chance of developing or passing on a genetic disorder. However, fairly often results come back with no findings and the genetic tests cannot rule out or confirm a diagnosis.

## Q Can genetic testing be used to detect DBA mutations?

**A** Yes, genetic tests can be used to test for mutations found in DBA. These tests are done by studying a sample of blood. The blood sample is sent to a laboratory where technicians look for specific changes in DNA.

Genetic tests are costly and the results can be hard to read and explain. About half of the time, the genetic tests are "inconclusive" which means that the results do not provide exact information about the risks for or presence of disease. Anyone thinking about having genetic testing should talk to his or her doctor about a referral for genetic counseling to learn more about the benefits, risks, and limitations of genetic testing.

## Q Can a parent who has DBA pass the mutation on to their children?

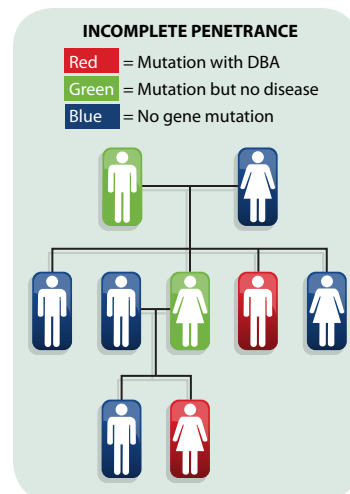
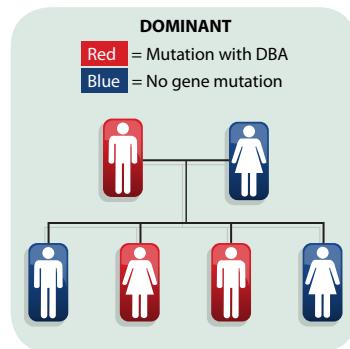
**A** Yes, a parent who has a DBA mutation has a 50:50 chance of passing the mutation on to each of his or her children.

## Q If you have DBA, does there have to be a family history of DBA?

**A** No. Sometimes, the mutation that causes DBA is not found in either parent and is new to the family. This new mutation is called “sporadic” or “de novo”. Sporadic mutations, like any mutation, have a 50:50 chance of being passed on to the affected person’s children. It is also possible that a parent of an affected individual does have a mutation, but has not developed signs of DBA.

## Q Does everyone with a mutation in a DBA gene have the disorder?

**A** No, the mutations that cause DBA have “incomplete penetrance.” That means some people with the mutation will not have DBA (see figure). But even people without signs of the disorder can pass on the DBA mutation to their children. These children with the mutation may or may not have DBA. The severity of the disorder can vary, even within families.



## Q Is there any way to prevent having a pregnancy affected by DBA?

**A** Yes, it is possible to do preimplantation genetic diagnosis (PGD) for a known family mutation. In this testing, a woman’s eggs are fertilized in a lab with her partner’s sperm in a process known as in vitro fertilization (IVF). The resulting embryos are then tested for the known mutation. Only embryos without the mutation will be implanted in the woman’s uterus. This process may be discussed with your doctor, a genetic counselor, or a fertility specialist.

## Q Can DBA be tested for prenatally?

**A** Yes, when there is a known genetic mutation in a parent, it is possible to do prenatal testing. In this case, tests called chorionic villus sampling (CVS) or amniocentesis can be done during the first or second trimesters of pregnancy to see whether the baby has the known DBA mutation.

## Q Is prenatal testing dangerous to the fetus and/or the mother?

**A** Before deciding to undergo prenatal testing, prospective parents should talk with a genetic counselor to make sure they understand the risks, benefits, and limitations of these procedures. Both CVS and amniocentesis have a risk for miscarriage of approximately 1/300 to 1/500. The timing of these procedures is also an important consideration and should be discussed with your obstetrician or genetic counselor.

## Q This sounds very complicated. How can I learn more about how the genetics of DBA works in my family?

**A** DBA is very complicated, and there is still a lot to learn. The best way to find out about how DBA runs in your family is to see a genetic counselor working with your hematologist. These professionals have experience with genetic blood disorders. They also specialize in prenatal genetic counseling. The genetic counselor will look at your family history and discuss with you what is known about DBA in your family. The counselor will also discuss potential genetic testing including preimplantation and prenatal testing. It is best to learn all you can about this before deciding to have children.

## The following resources might also be helpful in understanding genetics:

**Genetics Home Reference: Your Guide to Understanding Genetic Conditions** U.S. National Library of Medicine, National Institutes of Health, <http://ghr.nlm.nih.gov>

**Frequently Asked Questions About Genetic Testing** National Human Genome Research Institute, National Institutes of Health, <http://www.genome.gov/19516567>

**Talking Glossary of Genetic Terms** National Human Genome Research Institute, National Institutes of Health, <http://www.genome.gov/10002096>

**U.S. Surgeon General’s Family History Initiative** U.S. Department of Health & Human Services, <http://www.hhs.gov/familyhistory>

**My Family Health Portrait: A Tool from the Surgeon General** U.S. Department of Health & Human Services, <https://familyhistory.hhs.gov/fhh-web/home.action>

**Genetics Home Reference: Genetic Consultation** U.S. National Library of Medicine, National Institutes of Health, <http://ghr.nlm.nih.gov/info=consultation>

**National Society of Genetic Counselors: Find a Counselor** <http://www.nsgc.org/resource/cfm>