

Sporadic Genetic Mutations

By definition, a sporadic genetic disease is not inherited from parents, but arises via a mutation. However, a sporadic genetic disease becomes inheritable to children of the person who has acquired the genetic disease via mutation. A person with a sporadic genetic disease did not get it from their parents, but they can pass it to their children, according to the inheritance patterns that apply for the particular type of genetic disease.

Denoting either a genetic disorder that occurs for the first time in a family due to a new mutation

A spontaneous mutation is one that occurs as a result of natural processes in cells. We can distinguish these from induced mutations; those that occur as a result of interaction of DNA with an outside agent or mutagen. Since some of the same mechanisms are involved in producing spontaneous and induced mutations, we will consider them together. Some so-called "spontaneous mutations" probably are the result of naturally occurring mutagens in the environment; nevertheless there are others that definitely arise spontaneously, for example, DNA replication errors.

More commonly, the mutation arises as a spontaneous change in the genetic material of the affected person. These cases are called "sporadic" and do not affect parents or siblings, although each child of a person with sporadic achondroplasia has a 50% risk to inherit the condition.

What causes achondroplasia?

Achondroplasia is a genetic disease. This means that a gene that directs a specific process in the body does not work properly. In this particular condition, a protein in the body called the "Fibroblast Growth Factor Receptor" begins to function abnormally. The result is that the growth of bones, which normally occurs in the cartilage of the growth plate, is slowed. This leads to shorter bones, abnormally shaped bones, and shorter stature.

The genetic defect can be passed from a parent to his or her child. In the case of achondroplasia, however, it more commonly is the result of a spontaneous mutation (a sudden genetic defect) that occurs in the developing embryo.

Causes of achondroplasia

Mutations (chemical changes) within a single gene cause achondroplasia. The condition may be passed from one generation to the next or it may result from a new mutation in a gene from average-sized parents. Nine out of ten children born with achondroplasia have average-sized parents, and no other family member is affected. A person with this mutation has achondroplasia; it is not possible to have a little bit of achondroplasia, or "only a touch of it" -- a person either has it or not. In 1994 Dr. John Wasmuth and his colleagues discovered that a mutation of the fibroblast growth factor receptor-3 (FGFR3) gene on human chromosome 4 causes achondroplasia. The exact way in which mutations in FGFR3 cause achondroplasia is not yet known. Much research is being done in this area.

Two average-statured parents have little or no chance of having more than one child with achondroplasia.

My spouse and I do not have short stature. We have a child with achondroplasia.

- *What is the probability that our next baby will have this condition?* Answer: less than 0.1 percent, or less than 1 in 1,000.
- *What is the probability that our unaffected children will have this disorder?* Answer: less than 0.01 percent, or less than 1 in 10,000.

about seven-eighths of cases are due to a new mutation (a new change in the gene). This means that most cases of achondroplasia occur sporadically (out of the blue) and are the result of a new mutation in a sperm or ovum of one of the normal- appearing parents.