Alexander Disease

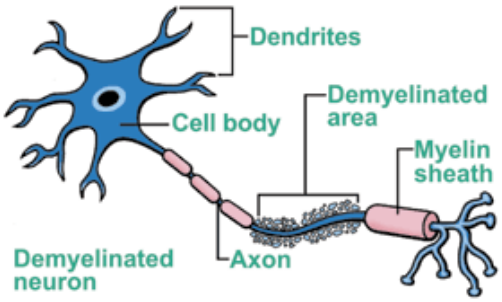
1. What do I need to know about Alexander Disease?

Alexander disease is a rare genetic disorder that mainly affects the nervous system and belongs to a group of conditions known collectively as leukodystrophies, or white matter degenerative diseases. It is a progressive disorder that primarily affects infants and children, but occasionally presents during adolescence or adulthood.

Alexander disease is a demyelinating disease. Demyelination means that the individual is unable to maintain myelin, a white, fatty tissue layer that protects the nerve cells (neurons) of the brain and spinal cord and speeds up the electrical messages between interconnected cells.

Alexander disease is further classified by time of onset into a neonatal, infantile, juvenile, and adult form. The infantile form comprises about 42% of affected individuals, the juvenile form about 22%, and the adult form about 33%. The neonatal form is relatively rare.

Image 1: Demyelination in Neurons



Source: Dpuadweb.depauw.edu

2. What Happens to People with Alexander Disease?

The symptoms associated with a case of Alexander disease depend largely on when the individual began experiencing them.

The neonatal form of Alexander disease, which typically presents *shortly after childbirth*, includes symptoms such as seizures, abnormal cerebrospinal fluid (CSF) accumulation in the brain, severe motor and intellectual disability, and elevated CSF protein concentration. Such early-onset Alexander disease typically leads to severe disability or death *within two years*.

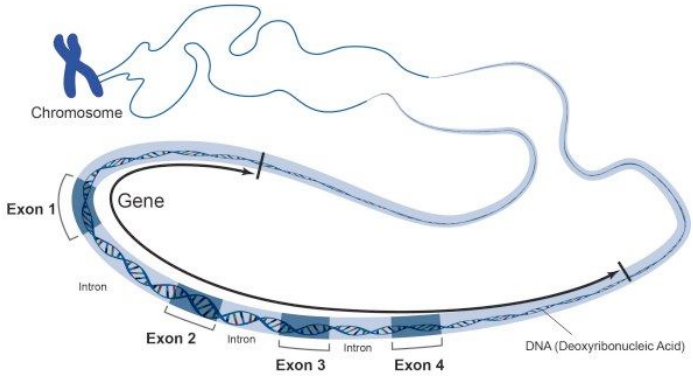
Type I Alexander Disease presents in *the first two years of life*. Symptoms typically include an enlarged brain and head, seizures, stiffness in the arms and/or legs, mental retardation, and delayed physical development. Affected individuals with infantile onset typically survive *weeks to several years.*

Type II Alexander Disease presents between *ages four and ten years*, and occasionally in the *mid-teens.* Type II Alexander Disease may also present during adulthood. Common symptoms for this category of Alexander Disease include speech abnormalities, swallowing difficulties, and poor coordination. Survival for juvenile onset ranges from the *early teens to the 20s-30s*, whereas survival for adult onset is *highly variable*.

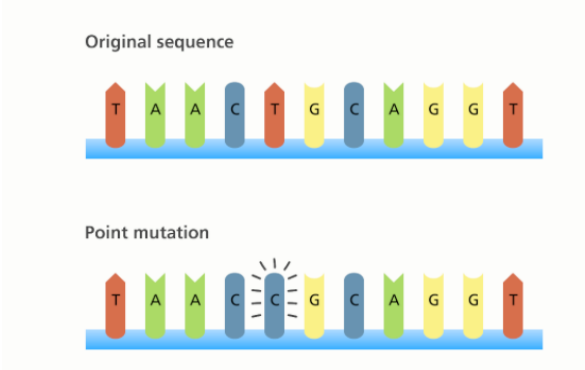
3. What Causes Alexander Disease?

Alexander disease is caused by a mutation or "change" in the DNA. DNA is the hereditary material in our bodies that is, in effect, the language of genetic information. DNA is what makes up our genes, which are the individual instructions that tell our body how to grow and develop. We have genes that provide instructions for heart and brain development and genes that determine unique traits such as eye and hair color. It is estimated that we have *30,000 different genes* and almost every cell in our body has a complete set of genes. Our genes come in pairs; we receive one copy from our mother and one copy from our father. Genes are made of two parts, the exons and the introns. Exons make the instructions and introns are not used to make the instructions but used in other ways not yet fully understood by scientists.

Image 4: DNA



Source: www.genome.gov



Source: Genome Research Limited

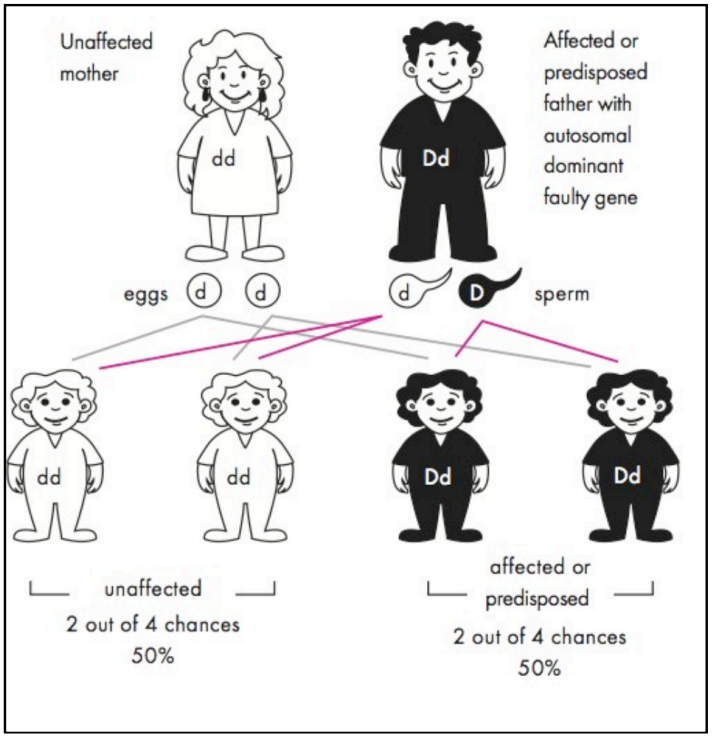
Different alterations in our DNA can affect how our body works. These alterations include too much or too little DNA, or a mutation in a gene such as a misspelling in the DNA code. If a gene has a serious mutation, then the gene will not work properly. If there is the incorrect amount of DNA or a gene is not working properly, then this can cause problems or disease. The exact problems or disease depends on the genes that are affected by the change in DNA.

Alexander disease is caused by a change, or mutation, in the *GFAP* gene, which contains the instructions the body needs to make glial fibrillary acidic protein (GFAP). When formed properly, GFAP is important for supporting the myelin sheaths that insulate neurons in the brain. However, in the case of Alexander disease, a mutated *GFAP* gene causes *overproduction* of the protein, which is ultimately toxic to cells and interferes with the proper formation and maintenance of myelin.

4. How is Alexander Disease Inherited?

Alexander disease follows an autosomal dominant pattern of inheritance. This means that when two parents have a child together, and one of the parents has Alexander disease, their child will have a 50% chance of developing Alexander disease as well. These odds remain the same regardless of how many children the couple has together.

Image 5: Autosomal Dominant Inheritance



Source: www.genetics.edu.au

All humans carry *two* copies of every gene in their body. When a baby is conceived, each parent passes on just one copy of each gene to the baby. Therefore, the baby is basically a "mixture" of the genetic information from its parents. When one parent is affected by a disease that follows autosomal dominant inheritance (such as Alexander disease), he/she will pass on either the "good" working copy or "bad" faulty copy of the gene to their child. This is why the child ultimately has a 50% chance of inheriting the disease.

However, many cases of Alexander disease occur because of a spontaneous mutation. In such situations, both parents can be completely healthy and still have a child that develops Alexander disease. Spontaneous mutations are rare, and it is extremely unlikely that this couple would have a second child with Alexander disease.

5. Is there a Chance that a Future Child May Have Alexander Disease?

Alexander Disease is an autosomal dominant condition and in most cases, the underlying genetic change is brand new in the affected person. This means that neither mom nor dad are carriers and the chance to have another affected child is less than 1%.

However, if one parent is a carrier, then the chance to have another affected child is 50%.

6. How can you Test for Alexander Disease?

The initial diagnosis is based on the symptoms and the results of an **MRI** (Magnetic Resonance Imaging), a medical imaging technique that can show if there is a specific pattern of brain tissue that is characteristic of Alexander disease. Genetic testing, using a blood sample, can identify changes in the *GFAP* gene to confirm the diagnosis of Alexander disease. A small proportion of patients who have symptoms and MRI findings consistent with Alexander disease have no identifiable changes in the GFAP gene, and so there may be other causes of the disease.

7. Is there treatment for Alexander Disease?

While there may not be a cure for Alexander Disease syndrome, treatment options may be available to manage its symptoms and improve quality of life.

Additionally, clinical trials may be an option. Please visit www.clinicaltrials.gov to see a list of ongoing studies, which may be targeting Alexander Disease.

Note: *Treatment options are unique to every person and some of these may or may not be healthy for your family. If you have any questions about treatment options please discuss these with your doctor.*

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