

What is Ataxia?

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What is Ataxia

The word “ataxia” means “absence or loss of order.”

Ataxia does not refer to a specific disease or disorder. Rather, it is a set of symptoms caused by a dysfunction in the cerebellum and the connections that transfer information to and from the cerebellum. People who have ataxia have uncontrolled, uncoordinated movements in the way they walk, move their arms or eyes, or talk. If a person has these symptoms, they are said to have ataxia. Ataxia can have many different underlying causes.

- Some types of ataxia are considered to be “non-genetic.” These types of ataxia can be caused by diseases such as multiple sclerosis, strokes, brain tumors, heat stroke, or infections. Other types of non-genetic ataxia may be caused by exposure to alcohol, drugs, medicines, or other chemicals. Some types of non-genetic ataxias may be due to vitamin deficiencies or problems with the immune system. Doctors will often look for these non- genetic causes first because some types of non-genetic ataxia may be treatable.
- Some ataxias are hereditary. Hereditary means that the ataxia is caused by a change in the genetic instructions that tell our cerebellum how to work. These genetic changes can be passed through families. The different types of hereditary ataxia are discussed in more detail on following pages.

- Some ataxias are considered “sporadic.” Sporadic means that there is no single genetic or environmental cause of the ataxia. Sporadic ataxias may be due to the interaction of many genetic risk factors with many environmental exposures. While we do not understand the causes of sporadic ataxias today, many people are working to understand the genetic risk factors and environmental exposures that can cause sporadic ataxia.

The word ataxia itself does not denote a specific disease or disorder that affects all people in the same way. Ataxia, regardless of cause, affects every person differently. Even for inherited ataxias, the condition may affect various parts of the body in different ways, and may vary in severity. For example, many family members may be afflicted with the same type of inherited ataxia, but they may all have unique symptoms and/or severities.

Diagnosis

Ataxia is diagnosed by observing symptoms and evaluating the medical history and family history. Common symptoms of ataxia include lack of coordination in the arms or legs, slurred speech, or stiff movements. (For more information on diagnosis of specific types of ataxia, see Types of Ataxia.) These symptoms may also be caused by other conditions, such as stroke or multiple sclerosis.

Treatment

Depression is common in patients with cerebellar ataxia. This is understandable in terms of the disability resulting from the condition. Recent research also indicates that patients with cerebellar ataxia maybe prone to depression because of dysfunction of the cerebellum. Medication and emotional support are usually effective in treatment of depression in cerebellar ataxia.

Physical therapy, including stretching, conditioning and strengthening exercise, is also important. People who are not overweight, well conditioned, and flexible cope better with ataxia symptoms. Physical therapy and occupational therapy can also help evaluate the need for mobility and safety aids and help choose the appropriate aid for a particular patient. Home safety evaluations and recommendations for modifications are also performed more effectively by occupational therapists.

Speech therapy can help with evaluating swallowing and teaching the patient about how to speak clearly and avoid choking.

Hereditary Ataxia

What are genes?

Genes are chemical instructions that are passed through families. Genes encode many important functions for our body. Some genes act like blueprints and tell our body how to make brain structures, such as the cerebellum. Other genes act like instruction manuals for our body. They may tell parts of our body how to communicate with one another, how to get rid of toxic chemicals, or how to turn the food we eat into energy. We have two copies of most of our genetic instructions because we inherit one copy from our mother and another copy from our father.

Genes are spelled out with a chemical code. The chemical is called “DNA.” There are 4 different chemical “letters” in the DNA alphabet. Scientists have labeled the four different DNA letters “A,” “C,” “G,” and “T.”

The spelling of a particular genetic instruction can vary from person to person. Some of these variations are normal and don’t cause disease. For example, differences in eye color are due to differences in the DNA code. These types of spelling changes are considered to be benign (they don’t cause a problem). These benign spelling changes are sometimes called “polymorphisms.”

Types of Hereditary Ataxia

Hereditary ataxias are caused by changes in genes that can be passed through families. Genes are chemical blueprints for our body. Changes in these genetic blueprints can cause ataxia in some families. Ataxias can be inherited in several different patterns:

- **Autosomal dominant** - Autosomal means that both males and females are affected. Dominant means that each child of an affected individual has a 50% chance of inheriting the genetic change that causes ataxia. The dominant ataxias are labeled as spinocerebellar ataxias (SCA) and they are numbered in order of their discovery (i.e. SCA1 was the first dominant ataxia discovered and SCA32 is the most recent ataxia discovered in 2010).
- **Autosomal recessive** - Autosomal means that both males and females can be affected. Recessive means that in order to have the disease, a person must inherit a genetic change (mutation) from both of their parents. While affected individuals have two mutations, other family members may carry one copy of the mutation but are unaffected. These family members are called “carriers” of the disease. These carriers could potentially have children with ataxia only if they have children with another carrier. The most common recessive ataxias are Friedreich’s ataxia, AOA1, and AOA2.

- **X-linked** - X-linked conditions are caused by genetic changes that are found on the sex chromosomes. Sex chromosomes determine if we are male or female. Males usually have one X-chromosome and Y-chromosome, while females have two X-chromosomes. X-linked conditions tend to affect males more often than females. The most common X-linked form of ataxia is Fragile X tremor ataxia syndrome (FXTAS).
- **Mitochondrial** - Mitochondria are small structure found inside the cells. Mitochondria are the energy factories of our bodies. Mitochondria have their own set of genetic blueprints. Some types of ataxia may be caused by changes in the genes found in the mitochondria. These types of ataxias are usually passed to all children by females, but they are not passed to any children by males. Mitochondrial diseases can also be transmitted by autosomal dominant, autosomal recessive, or X-linked patterns of inheritance.

Genetic Testing for Ataxia

Hereditary forms of ataxia are often suspected when there is a family history of ataxia, or if the age of onset is very young. There are two types of genetic changes that can cause ataxia:

- **Repeat expansions** - Some parts of our genetic code contain repeated letters of DNA sequence. If there are too many of these repeats, then the gene may begin to malfunction and cause ataxia. Ataxias that are caused by abnormal numbers of DNA repeats include: SCA1, SCA2, SCA3, SCA6, SCA7, SCA8, SCA10, SCA12, SCA17, Friedreich's ataxia, and DRPLA.

- **DNA sequence changes** - Some types of ataxia are caused by single-letter misspellings in the genetic code. For these types of ataxia, laboratories need to examine all of the letters of the genetic code to see if there is a spelling change. The types of ataxia that are diagnosed by DNA sequence change include: SCA5, SCA13, SCA14, AOA1, AOA2, Ataxia with vitamin E deficiency and others.
- **“Variance of unknown significance”** - Some gene tests (especially SCA 14 gene) may show a “variation of unknown significance”. It is important that these types of results be interpreted very carefully because they do not mean that the individual has SCA14 in most cases.

Interpreting Results of Genetic Testing

Ataxias caused by repeat expansions

- **Normal results** - Both copies of the gene have a normal number of repeats. People with normal results would not be expected to develop that type of ataxia.
- **Intermediate/indeterminate results** - These results can be very difficult to interpret. Repeat numbers in this range may or may not cause ataxia. In some types of ataxia (SCA1 for example), additional testing may help to determine if an intermediate repeat number could cause ataxia. Some individuals with intermediate repeat numbers will not develop ataxia, but they may be at risk for passing ataxia to their children. These types of results should be very carefully interpreted by a professional who is familiar with the genetics of ataxia.

- **Abnormal results** - One copy of the genes has an abnormal number of repeats. In these cases, there is very clear evidence that having this many repeats in one copy of the gene is enough to cause ataxia. If a person already has symptoms, then this result confirms the diagnosis. If they are asymptomatic, then they would be expected to develop this type of ataxia in the future.

Ataxias caused by sequence changes (spelling errors) in genes

- Normal results - Both copies of the gene have a normal sequence. There are no changes that would cause ataxia.
- Indeterminate results - A variation or variations were detected in the spelling of one copy of the genes. It is not clear if this is a normal variation, or if it is a variation that could cause ataxia. These types of changes are frequently found in ataxia testing and they can cause much confusion. It is important to note that finding these types of changes does not confirm the diagnosis of ataxia. There are some ways to help determine if one of these changes is significant-
- If there are other family members with ataxia, they can be tested to see if the genetic variation is present in everyone with ataxia.
- There may be physicians or researchers who are interested in investigating these new variants.

- With time, we will likely better understand how these genes can vary normally and what types of changes cause disease. Therefore, it is important to have your health care provider review the medical literature from time to time to see if there is additional information about your variation.
- Abnormal results - A sequence change or changes were detected that are be clearly associated with ataxia. These sequence changes may have been described before in other individuals with ataxia, or they may disrupt the function of the gene in such a way that they are clearly abnormal.



Types of Hereditary Ataxia

Dominant Spinocerebellar Ataxias (SCA)

There are many different types of Spinocerebellar Ataxia (SCA). These ataxias are all characterized by autosomal dominant inheritance. The primary feature of these disorders is ataxia (problems with balance, speech, and eye movements).

The spinocerebellar ataxias are labeled using the acronym “SCA” and then numbered in the order of their discovery.

SCA1

SCA1 was the first genetic form of dominant ataxia that was discovered in 1993 in two large families from Minnesota and Texas. SCA1 is an autosomal dominant form of ataxia that is caused by a repeat expansion. While symptoms most often develop in the mid 30's, they can begin in childhood or late in life. The first symptoms are usually problems with walking and coordinating hand movements. Normal repeat numbers in both copies of this gene are usually less than 36. If one gene has 45 or more repeats, the person will develop SCA1. If one gene has between 36-44 repeats, then additional testing may be required to interpret the result.

SCA2

SCA-2 is sometimes called “Cuban ataxia” because some of the first described families were from Cuba. This form of ataxia was the second form of dominant ataxia described. The inheritance pattern is autosomal dominant and it is caused by a repeat expansion. One common feature of SCA2 is slowness and paralysis of eye movements. Some individuals may have peripheral neuropathy or reduced reflexes. SCA2 can cause problems with memory in some individuals. Repeat numbers in both copies of the SCA2 gene are usually 31 or smaller. If one gene has 32 or more repeats, then the person will develop SCA2. Smaller repeat numbers (32 or 33) may be associated with later onset, while larger repeats (100 or more) may be seen in infants with SCA2.

SCA3

SCA-3 is also known as Machado-Joseph disease— named after affected families of Azorean ancestry who were descendants of William Machado (Portuguese immigrants living in England) and Antone Joseph (Portuguese sailors who went to California in 1845). The disease has also been identified in other ethnic groups, nationalities, and races.

SCA-3 is an autosomal dominant form of ataxia caused by a repeat expansion. SCA3 can show a variety of symptoms beside ataxia including tremor and stiff muscles (resembling Parkinson disease) and neuropathy. Some individuals may have twitching movements of the face and tongue (resembling Lou Gherig's disease or ALS). There may be abnormal movements of the eye. SCA3 is the most common dominant ataxia in many parts of the world.

If both copies of the gene have 44 or fewer repeats, then the individual will not develop SCA3. If one copy of the SCA3 genes has 45-51 repeats, the individual might develop SCA3. All individuals who have 52 or more repeats will develop SCA3. The repeat number may predict, to a limited degree, the type of symptoms that an individual experiences (ataxia vs. neuropathy vs. Parkinsonism).

SCA4

SCA-4 was first described in an American family from Utah. This family had Scandinavian ancestry. Since that time, the disease has also been described in a large German family. The hallmarks of this disease are late age of onset, difficulty with coordinating arms and legs, difficulty with speaking, and peripheral neuropathy. While this is one of the first ataxias that was mapped, the exact genetic cause has still not been determined. That is why there is currently no gene test for SCA4. Because the SCA4 and the SCA31 genes are located very close to one another in the genome, scientists have wondered whether or not these may be different forms of the same condition. At the present time, it appears that these are two distinct diseases that are caused by different genes that just happen to be located very closely to one another in our genome.

SCA5 (Lincoln's ataxia)

This form of ataxia was found in one branch of Abraham Lincoln's family. It is not known whether or not Abraham Lincoln actually had the disease gene. SCA5 is an autosomal dominant condition caused by sequence changes in a gene called "SPTBN2." SCA5 is often associated with a young age of onset and slowly progressive symptoms. SCA5 is usually

described as a “pure cerebellar ataxia” because other neurological problems are not commonly seen. Results of genetic testing for SCA5 need to be very carefully interpreted because the testing may identify sequence variations of unknown significance.

SCA6

SCA-6 is an autosomal dominant progressive cerebellar ataxia characterized by slurred speech, changes in eye movements, and lack of coordination in gait and extremities. Age of onset varies considerably, even within the same family, and ranges from 19 to 71 years of age. SCA6 may initially present as an episodic disorder (symptoms occur intermittently) and may be associated with migraine headaches. SCA6 is caused by a repeat expansion. Individuals who have 18 or fewer repeats in both copies of the gene do not have SCA6. If one repeat number is 20 or more, then the individual will develop SCA6. If one or both copies of the gene have 19 repeats, these results may be difficult to interpret.

SCA7

SCA-7 is an **autosomal dominant** ataxia caused by a **repeat expansion**. One of the most striking features of SCA7 is the vision-loss, which often begins in the late teens or early 20’s. Visual symptoms often begin with decreased visual acuity and decreased color vision. Progressive ataxia usually follows the onset of visual symptoms. Patients should be evaluated for the use of medications to treat eye symptoms and use of dark glasses to limit retinal damage from ultraviolet light. If both copies of the gene have 19 or fewer repeats, then the individual does not have SCA7. If one copy of the gene has more than 36 repeats,

then an individual will develop SCA7. Borderline repeat numbers between 28- 36 repeats may be difficult to interpret. The size of the repeat sometimes grows dramatically in SCA7, leading to younger ages of onset in each generation. Infantile onset SCA7 has been reported in several families with as many as 460 repeats reported.

SCA8

SCA-8 is a slowly progressive ataxia resulting in poor coordination of limbs, especially lower extremities, and poor coordination of gait and speech. SCA-8 is officially described as an **autosomal dominant** ataxia, however, many people who inherit abnormal SCA8 genes never develop the disease. This is called reduced penetrance. It is not known why some people develop ataxia and others do not. SCA8 is caused by a **repeat expansion**. Repeat numbers larger than 71 are considered abnormal, but it is important to remember that many people with abnormal repeat numbers do not develop ataxia.

SCA9

Evidence for SCA-9 was first reported in 1997. Scientists described a large family and traced the ataxia back to a British couple who emigrated to the United States in 1685. The clinical findings in this family were reported to be similar to SCA3 families. Some individuals had symptoms similar to Parkinson disease or multiple sclerosis. No other work has been published on SCA9 since 1997. Therefore, the gene that causes SCA9 is unknown and genetic testing is not available for this condition.

SCA10

SCA-10 is a slowly progressive ataxia, that is found primarily in people with Mexican, or Brazilian ancestry. In addition to the typical symptoms of ataxia, patients with SCA-10 may also develop epilepsy (seizures), weakness, and loss of sensation. SCA-10 is an **autosomal dominant** condition that is caused by a **repeat expansion**. If both copies of the gene have 10-29 repeats, then the individual will not develop SCA10. If one copy of the gene has more than 800 repeats, then the individual will develop SCA10. Additional interpretation may be required if one of the repeat numbers is between 29 and 800. Some, but not all, individuals in this range will develop SCA10. Management includes anti-seizure medications to control seizures.

SCA11

SCA11 has been genetically confirmed in a family from England and in a family from Pakistan. SCA11 appears to be caused by sequence changes in a gene called “TTBK2.” Individuals with SCA11 have difficulties with balance and eye movements. The symptoms begin in later adulthood and appear to progress more slowly than other types of ataxia. Genetic testing for this type of ataxia is not currently available in the United States.

SCA12

SCA12 is a very rare form of **autosomal dominant** ataxia that has been described in families with German, American, or Asian-Indian ancestry. The first symptoms are often tremor, rather than true ataxia. Patients later develop symptoms of ataxia. Patients may also develop slowness of movement, similar to Parkinson’s disease, and exaggerated tendon reflexes

and loss of sensation. Tremor in SCA-12 might respond to medications used for essential tremor. SCA12 is caused by a **repeat expansion**. If both genes have 4-32 repeats, then the individual does not have SCA12. If one repeat has 51-78 repeats in one copy of the SCA12 gene, then they will develop SCA12. If one gene has 32-50 repeats, it is not clear if the person will develop SCA12.

SCA13

SCA13 is a very variable form of ataxia. In some families, the disease may begin in childhood and be accompanied by mental subnormality. In other families, the disease may have a very late age of onset without cognitive manifestations. SCA13 is inherited in an autosomal dominant pattern and it is caused by sequence changes in a gene called "KCNC3." Sometimes, testing for SCA13 may show a variation of unknown significance. It is important that these types of results be interpreted very carefully because they do not necessarily mean that the individual has SCA13.

SCA14

SCA14 is a rare form of autosomal dominant ataxia and it is caused by sequence changes in a gene called "PRKCG."

Commonly, testing for SCA14 gene may show a "variation of unknown significance." It is important that these

types of results be interpreted very carefully because they do not mean that the individual has SCA14 in most cases.

SCA-14 is characterized by poor coordination of the arms, legs, gait, and

speech and jerky movements that affect the trunk of the body. The jerky movements are called myoclonus. Tremor, sensory loss, twitches of facial muscles, and slowness and stiffness similar to that seen in Parkinson's disease have been observed in SCA-14.

SCA15

SCA15 was first described in an Australian family. It has since been described in families from the UK and Japan. This type of ataxia appears to be a slowly progressive form of ataxia. Symptoms may begin as early as childhood, or as late as the 60's. There are usually no other neurological symptoms, with the exception of occasional tremors. SCA15 is caused by either sequence changes or deletions of a gene called "ITPR1." Gene testing for SCA15 is currently not available in the United States.

SCA16

SCA16 was first described in Japanese families. It was later discovered that SCA16 and SCA15 are actually the same disease.

SCA17

SCA-17 is associated with abnormal movements twitching/fidgety movements (chorea) and abnormal posturing (dystonia), as well as problems with memory and ataxia. Patients may also develop mental health problems such as mood disorders. Many patients also have features resembling Parkinson's disease, including muscle stiffness and tremor. Age of onset is between 3 to 55 years. SCA17 is an **autosomal dominant** condition caused by a **repeat expansion**. If both genes have repeat numbers between 25-42, then the individual will not develop SCA17. If one copy of the gene has between 43-

48 repeats, then that individual might develop SCA17, i.e. some individuals with 43-48 repeats do not develop SCA17. If one copy of the gene has 49 or more repeats, then the individual will develop SCA17. Specific treatment for mental health problems and seizures is recommended. Treatment for dystonia (such as botulinum toxin injections) and stiffness can also be given.

SCA18 (SMNA)

SCA18 is more commonly called “sensory/motor neuropathy with ataxia” (SMNA). This type of ataxia was described in a large Irish-American family. In addition to ataxia, individuals with this condition have problems with the nerves in their arms and legs (peripheral nerves). These peripheral nerve problems include weakness and problems with sensation. In 2009, researchers reported that they may have found the gene that causes SMNA, but further research is needed to confirm this finding. Until that time, testing for SCA18 (SMNA) is not available.

SCA19

SCA19 was first described in a large Dutch family. Symptoms usually begin between the ages of 20 and 45. In addition to ataxia, individuals with SCA19 may have myoclonus (very fast jerking movements) and cognitive changes (problems with memory). The gene causing SCA19 has not yet been discovered. SCA19 and SCA22 may actually be the same disease, but this is not yet clear.

SCA21

SCA20 has only been described in a single Australian family with ancestry in the British Isles. In addition to ataxia, problems with speaking are very prominent in SCA20. Individuals with SCA20 often have a tremor in their palate (the roof of the mouth). A genetic change was recently identified in the Australian family, but it is not yet clear if this genetic change is truly causing the ataxia. This genetic change is a large duplication of a piece of genetic code. Until the exact cause of SCA20 is confirmed, there will not be genetic testing for this condition.

SCA21

SCA21 is characterized by a young age of onset compared to some other dominant forms of ataxia (age 6-30 years). SCA21 was first reported in a large family from France. In addition to ataxia, individuals with SCA21 may have some symptoms similar to Parkinson disease (tremor and stiffness). The gene that causes SCA21 has not been identified. Genetic testing for this condition is not available.

SCA22

This form of ataxia was first described in a large Chinese family. It is now suspected that SCA22 and SCA19 are actually the same condition. The Chinese family with SCA22 did not have some of the features reported in the SCA19 family (myoclonus and cognitive changes). Therefore, it is not completely clear that SCA19 and SCA22 are the same disease.

SCA23

SCA23 has been described in a single Dutch family. Symptoms generally began in the 40's and 50's. In addition to typical symptoms of ataxia, there are pronounced problems with eye movements. The exact gene that causes SCA23 has not been identified. Therefore, there is no genetic testing for this condition at the present time.

SCA24 (SCAR4)

This condition is no longer called SCA24. The autosomal recessive pattern of inheritance is different from the other SCA's. SCA24 is now called spinocerebellar ataxia autosomal recessive type 4 (SCAR4). It is also called "spinocerebellar ataxia with saccadic intrusions." This condition was first described in a family from Slovenia and the most striking feature is the unusual sudden fast eye movements (saccades). There is no genetic testing for this condition at the present time.

SCA25

SCA25 has been described in a single family from South-Eastern France. The gene that causes this condition has not yet been identified. Symptoms typically begin between the ages of 17 and 39. There is no genetic testing for this condition at the present time.

SCA26

SCA26 has been described in a single family from the Upper-Midwest region of the United States. The family had Norwegian ancestry. On average, symptoms started in the 40's. Besides the typical problems associated with ataxia (balance, speech, eye movements), affected individuals had no other neurological symptoms. There is no genetic testing for this condition at the present time but will likely be available soon.

SCA27

SCA27 was originally described in a Dutch family. Several other families or individuals with SCA27 have now been identified. SCA27 is caused by **sequence changes** in a gene called “FGF14.” In addition to ataxia, individuals with SCA27 may have developmental delays or mental retardation. Testing for SCA27 is not yet available.

SCA28

SCA28 was first described in an Italian family, and later in a German family. SCA28 is caused by **sequence changes** in a gene called “AFG3L2.” Symptoms of SCA28 often begin in childhood. In addition to problems with balance, individuals with SCA28 can have paralysis of the muscles that move the eyes. Clinical testing for SCA28 is not yet available.

SCA29

SCA29 is a type of ataxia that presents very early in life, but is not progressive. That means that the symptoms do not appear to grow worse over time. A specific gene for SCA29 has not yet been found.

SCA30

At the time this booklet was written, no information has yet been published in the medical literature about SCA30. The name SCA30 has been reserved, which means that a group of scientists believes that they found a family with a unique genetic form of SCA.

SCA31

The gene that causes SCA31 is very close to the gene that is believed to cause SCA4. There has been some discussion as to whether these might be the same condition. SCA31 is caused by a **repeat expansion**. Due to the very recent discovery of the SCA31 gene, the range of normal and abnormal repeat numbers is not yet known. Genetic testing is not yet available.

SCA32

The gene for SCA32 has now been identified in a family from the Upper-Midwest region of the United States. Information about SCA32 has not been published.

Other Forms of SCA

There are now at least 32 different forms of SCA (and counting). As new genes are discovered, tests for these new types of SCA will become available in laboratories. Even after new genes are discovered, it may take many years for scientists to understand the gene well enough to offer testing to patients. That is why there are many SCA's for which clinical testing is currently not available. It is important to remember that as many as half of SCA families will have normal genetic testing (as of 2010). This means that there are many more genes to be discovered.

Dominant Spastic Ataxias

Spastic ataxias are ataxias that have spasticity (muscle stiffness) in addition to ataxia. Some types of spastic ataxias are dominant and some are recessive. The dominant forms are described below, while the recessive forms are discussed later in this booklet. The acronym SPAX is used to name some of these ataxias (SPastic AtaXia).

SPAX1

SPAX1 is a type of dominant spastic ataxia that has so far been described in families from Newfoundland and Iran. The spasticity (muscle stiffness) primarily affects the legs. Symptoms begin in adulthood (50's) in the family from Iran, while symptoms began between ages 10-20 in the family from Newfoundland. The gene that causes this condition has not yet been identified.

Other Dominant Conditions That Include Ataxia as a Symptom

Haw River Syndrome-DRPLA

Haw River Syndrome, also called dentatorubral pallidolusian atrophy (DRPLA), is characterized by progressive ataxia, involuntary movements, and dementia. Some patients have epilepsy. Patients may have seizures and abnormal movements or jerks (myoclonus) that may require specific drug treatment. Psychiatric symptoms may also require specific treatment. Age of onset varies from young childhood to age 62. DRPLA is an **autosomal dominant** condition that is caused by a **repeat expansion**. If both repeat numbers are less than 35, then the individual will not develop DRPLA. If one repeat number is 48 or larger, the individual will develop DRPLA.

OPA1

OPA stands for Optic Atrophy. Optic nerve is the nerve of that eyes that allows vision. Patients with optic atrophy have shrunken optic nerves which interferes with vision. Some patients with OPA1 also have ataxia. Patients with OPA1 can also have hearing loss, paralysis of the muscles that move the eyes, and muscle weakness. OPA1 is caused by sequence changes in the OPA1 gene.

POLG1 Ataxias

This is a group of ataxias caused by sequence changes in the POLG1 gene. The POLG1 gene is very important because it is responsible for copying the DNA in our mitochondria. Mitochondria are found inside the cell and are the energy factories in our bodies. Mitochondria have their own genetic instructions. When we need to make new mitochondria, these genetic instructions have to be copied. If the POLG1 gene is not functioning correctly, the genetic instructions in the mitochondria are copied incorrectly. This leads to malfunctioning mitochondria, which can cause several types of ataxia. Some of these ataxias are autosomal recessive and some are autosomal dominant. Some of these ataxias are pure (no other symptoms), while others are complicated (with many other neurological symptoms in addition to ataxia). Additional symptoms may include infertility, paralysis of the eye muscles, seizures, problems with the liver, and other findings.

Recessive forms-

- MIRAS - Mitochondrial Recessive Ataxia Syndrome
- ANS - Ataxia Neuropathy Spectrum
- SANDO - Sensory Ataxic Neuropathy Dysarthria and Ophthalmoparesis
- SCAE - SpinoCerebellar Ataxia with Epilepsy
- There are several more beyond this listing
- PEO-Progressive External Ophthalmoplegia

Episodic Ataxia

Episodic ataxias are characterized by intermittent symptoms or episodes that can vary in duration, lasting from minutes to days, consisting of slurred speech, a feeling of dizziness, ringing in the ears, abnormal posturing, unsteadiness and sometimes paralysis of one side of the body. Many patients with episodic ataxia complain of migraine headaches. Attacks can be as frequent as several times a week, but may occur much less frequently, once or twice a year. Precipitating causes for episodic ataxia attacks are unknown, though sometimes are attributed to ingestion of alcohol or caffeine, stress, fatigue, exposure to some paint thinners (toluene), and some medications such as phenytoin. The disease is usually **autosomal dominant**. Episodic ataxia may be caused by **sequence changes** in several different genes. There are many different types of episodic ataxia.

Using a numbering system similar to the SCA disorders, episodic ataxias are labeled using the acronym “EA” and then numbered in the order of their discovery.

Episodic ataxias are often called “channelopathies.” Channels are proteins in our brain cells that provide a pathway for certain chemicals to move in and out of brain cells. This transmission of chemicals in and out of brain cells is an important part of how our brain sends signals.

EA1

This type of ataxia is caused by **sequence changes** in a gene called KCNA1. This gene encodes a channel for Potassium to move in and out of brain cells. The chemical abbreviation for

potassium is “K” which accounts for the “K” in KCNA1. Symptoms often begin in childhood or teenage years. Episodes of ataxia may last from several seconds to several minutes. The episodes can rarely last for hours. Episodes may occur several times in a day, or only a few times per month. During the episodes, individuals experience ataxia (loss of balance and coordination), contractions and tightening of muscles, double vision, nausea, headache, and difficulty speaking or breathing. In between episodes, patients may experience “myokymia” which is a twitching or rippling of certain muscles.

EA2

This type of ataxia is caused by **sequence changes** in a gene called CACNA1A. This gene encodes a channel for calcium to move in and out of brain cells. The chemical abbreviation for calcium is “Ca” which explains the “Ca” in CACNA1A. The symptoms during the episodes are very similar to the episodes described above for EA1. One main difference is the episodes in EA2 may last much longer (sometimes lasting for days). In between episodes, individuals may have problems with eye movements and ataxia. Symptoms may grow worse and MRI sometimes shows the middle part of the cerebellum (the vermis) shrinking. Episodes may be triggered by stress, caffeine, alcohol, or exertion.

It is interesting to note that the CACNA1A gene is also involved in SCA6 and in a condition called familial hemiplegic migraine. About half of individuals with EA2 have migraines.

EA3

EA3 has been described in some Canadian Mennonite families. During episodes, patients may experience vertigo (dizziness) and tinnitus (ringing in the ears). No gene has been identified for this condition.

EA4

This type of episodic ataxia has been described in 2 Caucasian families from North Carolina. No gene has yet been identified.

EA5

This type of episodic ataxia is caused by sequence changes in a gene called CACNB4. This gene encodes a channel that allows calcium to move in and out of nerve cells. This type of ataxia has been described in Caucasian families from Germany and Canada. This same gene is also involved in some types of epilepsy.

EA6

EA6 is caused by sequence changes in a gene called SLC1A3. This gene encodes a channel that allows chemicals called “amino acids” in and out of brain cells. This type of episodic ataxia has only been described in a handful of families.

EA7

EA7 is the most recently described form of episodic ataxia. Symptoms generally begin before adulthood and episodes can last from hours to days in length. Attacks were infrequent (monthly to yearly) and may decrease in frequency with age. No gene testing is available.

Recessive Ataxias

Friedreich's ataxia

Friedreich's ataxia is the most common type hereditary ataxia and it is inherited in an autosomal recessive pattern. It is a slowly progressive ataxia with the age of onset in the first and second decades of life—usually below age 25. Some individuals with Friedreich's ataxia may not develop symptoms until very late in life. Weakness of the extremities and loss of sensation become more prominent as the disease progresses. Skeletal deformities, including scoliosis, are also common. Friedreich's Ataxia may also be associated with heart problems, including irregular heart beat and enlargement of the heart.

Most individuals with Friedreich's ataxia have **repeat expansions** in both of their copies of the Friedreich's ataxia gene. Some rare individuals may have a combination of a **repeat expansion** in one gene and a **sequence change** in their other copy of the gene. Carrier testing is available to family members. About 1-2% of the general population carries an abnormal gene for

Friedreich's ataxia, but these individuals do not have symptoms of Friedreich's ataxia. It is only when both parents are carriers, the offspring will have a 25% chance of having the disease.

Ataxia with oculomotor apraxia

There are two forms of recessive ataxia with oculomotor (muscles of eye movement) apraxia (difficulty in executing movement).

- **AOA1** - is often associated with other types of movement problems (chorea), neuropathy, and rarely changes in learning and memory. Symptoms of AOA1 usually develop early in childhood. Individuals with AOA1 may have high levels of cholesterol and low levels of a substance called “albumin” in their blood. AOA1 is an **autosomal recessive** form of ataxia caused by **sequence changes** in a gene called “APT_X.” In order to confirm a diagnosis of AOA1, sequence changes must be found in both copies of the gene. Carrier testing for family members may be available if sequence changes are identified in the individual with ataxia.
- **AOA2** - Usually has a later age of onset as compared to AOA1. Onset is still usually before 20 years of age. Individuals often have a high level of a protein called “Alpha Feto Protein or AFP” in their blood. Individuals with AOA2 may have problems with abnormal posture (dystonia), twitching movements (chorea), in addition to ataxia. Neuropathy is often found in this condition. AOA2 is an **autosomal recessive** condition caused by sequence changes in a gene called “SET_X.” In order to confirm a diagnosis of AOA2, sequence changes must be found in both copies of the gene. Carrier testing for family members may be available if sequence changes are identified in the individual with ataxia.

Ataxia telangiectasia

Ataxia telangiectasia is an autosomal recessive form of ataxia that is associated with enlarged and prominent blood vessels in the eyes (telangiectases), ataxia, problems with the immune system, and an increased risk for some types of cancers. Age of onset is usually in the first decade of life, although milder later-onset cases have been reported. Ataxia telangiectasia is caused by sequence changes in a gene called “ATM.” Diagnosis of ataxia telangiectasia can be very tricky and may involve many specialized laboratory tests that can only be performed in specific labs. Management includes cancer surveillance. Unaffected family members who carry a single sequence change might also have a higher risk for some types of cancer.

Other Autosomal Recessive Ataxias

Autosomal recessive ataxias are now classified using a similar system to the autosomal dominant SCA's. The ataxias are numbered by the order of their discovery. The acronym “SCAR” is used rather than “SCA,” which is used for dominant ataxias. The acronym SCAR stands for Spinocerebellar ataxia autosomal recessive. Many of these ataxias are quite rare and have only been reported in one family in the world. To make matters more confusing, some autosomal recessive ataxias used to be named with the acronym ARCA (Autosomal Recessive Cerebellar Ataxia).

SCAR1 (AOA2)

SCAR 1 is now used to indicate ataxia with oculomotor apraxia type 2 (AOA2). Usually has a later age of onset as compared to AOA1. Onset is still usually before 20 years of age. Individuals often have a high level of a protein called “Alpha Feto Protein or AFP” in their blood. Individuals with AOA2 may have problems with abnormal posture (dystonia), twitching movements (chorea), in addition to ataxia. Neuropathy is often found in this condition. AOA2 is an **autosomal recessive** condition caused by sequence changes in a gene called “SETX.” In order to confirm a diagnosis of AOA2, sequence changes must be found in both copies of the gene. Carrier testing for family members may be available if sequence changes are identified in the individual with ataxia.

SCAR2

This is a severe form of recessive ataxia that is also associated with mental subnormality. Affected individuals may not survive until adulthood. Families from Italy and Lebanon have been reported. The gene that causes this type of ataxia has not been discovered. Therefore, no gene testing is available.

SCAR3

This type of ataxia is also associated with blindness and deafness. Two families have been reported, one of which was from Israel. The gene that causes this type of ataxia has not been identified. No gene testing is available.

SCAR4

SCAR4 was originally called SCA24. Because the pattern of inheritance is autosomal recessive, the name was changed to SCAR4. This type of ataxia has been described in a single family from Slovenia. There is no gene testing for SCAR4.

SCAR5

SCAR5 has been described in a single family from Lebanon. There is no gene testing for this type of ataxia. Affected family members often have problems with the optic nerve in the eye (optic atrophy).

SCAR6

This type of ataxia begins in infancy and is slowly progressive. The one family described is from Norway. There is no gene testing available.

SCAR7

SCAR7 is a slowly progressive form of ataxia described in a single Dutch family. There is no gene testing available.

SCAR8 (ARCA1)

SCAR8 has been described in some French Canadian families. This condition is also called ARCA1 (autosomal recessive ataxia 1) or Ataxia of Beauce. Beauce is the region of Quebec where this ataxia is seen. SCAR8 is caused by sequence changes in a gene called SYNE1. Four different sequence changes in the SYNE1 gene have been found in this part of Canada.

These sequence changes appear to be specific to the French Canadian population.

SCAR9

This type of ataxia was identified in a family from Algeria. The symptoms begin in childhood and in some cases, there may be mental subnormality or learning difficulties. This type of ataxia is caused by sequence changes in a gene called CABP1. This type of ataxia has also been called ARCA2 (autosomal recessive cerebellar ataxia type 2).

Ataxia with vitamin E deficiency (AVED)

Ataxia with vitamin E deficiency has symptoms that resemble Friedreich's ataxia. This type of ataxia can be non-genetic or genetic. Individuals with non-genetic AVED either lack vitamin E in their diet, or they don't absorb vitamin E from their diet. Individuals with the genetic form of AVED have sequence changes in a gene called TTPA. This genetic instruction normally tells the body how to process and use vitamin E.

Symptoms often begin around puberty and often involve problems with sensation. Affected individuals have difficulty sensing where their joints, arms, legs, feet etc. are in space. This makes it very difficult for them to coordinate movements.

AVED often responds to treatment with vitamin E. Because this type of ataxia is treatable, neurologists should screen all ataxia patients to make sure they have normal vitamin E levels. If the levels are low, patients must be evaluated to see if the vitamin E deficiency is due to dietary reasons or genetic reasons.

IOSCA

IOSCA stands for Infantile Onset SpinoCerebellar Ataxia. This type of ataxia has only been identified in people from Finland. Symptoms often begin around the age of 2 and include ataxia, muscle weakness, abnormal twisting movements, hearing loss, vision loss, and paralysis of the muscles that move the eyes. Females often have problems with hormones that may affect their fertility. Later in the disease, seizures may develop. These seizures can be severe and life-threatening. This type of ataxia is caused by sequence changes in a gene called C10ORF2. IOSCA has not yet been found in people without Finnish ancestry.

Marinesco-Sjogren Syndrome

This type of ataxia usually begins in early childhood. The first symptoms include ataxia, muscle weakness, mental retardation, and cataracts. Adults with Marinesco Sjogren syndrome often have significant mental retardation, but usually have a normal life-span. Marinesco Sjogren syndrome is caused by sequence changes in a gene called SIL1.

Coenzyme Q10 deficiency

Coenzyme Q10 is a very important chemical in the body. It is critical in the process that our body uses to make energy. Some individuals with ataxia have very low levels of coenzyme Q10 in their muscle tissue. There are many different genes that can cause coenzyme Q10 deficiency. All of the different forms of coenzyme Q10 deficiency appear to be inherited in an autosomal recessive manner. The clinical findings in people with coenzyme Q10 deficiency are extremely variable and can include ataxia, infertility, blindness, seizures, muscle disease, kidney disease, and other symptoms. The diagnosis is initially suspected by finding low hormones in the blood and confirmed by measuring coenzyme Q10 on a muscle biopsy. If there is a deficiency, genetic testing for some genes that cause coenzyme Q10 deficiency is available. Coenzyme Q10 is available as a medication in the form of pills (anti-oxidant).

Recessive Spastic Ataxias

Spastic ataxias are ataxias that have spasticity (muscle stiffness) in addition to ataxia. Some types of spastic ataxias are dominant and some are recessive. The recessive forms are described below. The acronym SPAX is used to name some of these ataxias (**SP**astic **AtaX**ia).

Autosomal recessive spastic ataxia of Chalevois-Saguenay (ARSACS)

ARSACS, which usually manifests in childhood, occurs in individuals born in Quebec Province in Canada and rarely in patients of Japanese descent. ARSACS is characterized by ataxia, muscle wasting and neuropathy, with weakness in the arms and legs, eye movement abnormalities, and yellow streaks in the retina of the eyes.

SPAX2

This type of spastic ataxia has been described in a single family from Morocco. Symptoms began at age 14 and included difficulty speaking, difficulty walking, and spasticity (stiffness) in the legs and arms. There are three other families in the world that may also have this type of spastic ataxia. The gene that causes this type of ataxia has not yet been discovered.

SPAX3

This type of ataxia has only been seen in individuals with French Canadian ancestry. This type of ataxia is also called **ARSAL** (Autosomal Recessive Spastic Ataxia with Leukoencephalopathy). Leukoencephalopathy literally means a disease of the white matter in the brain. The white matter is the part of the brain that connects brain cells to each other. Symptoms of ARSAL can begin anywhere between age 2 and 59.

Other Recessive Ataxias

There many other recessive forms of ataxia and there are many recessive conditions that include ataxia as one of the symptoms. The complete list would be too much to include in this booklet.

X-linked Ataxia

Fragile X tremor ataxia syndrome

Fragile X tremor ataxia syndrome (FXTAS) is believed to be a common cause of ataxia in males. This condition shows **X-linked** inheritance, which means that males show symptoms much more often than females. The disease is caused by a repeat expansion. There are several diseases associated with **repeat expansions** in the fragile X gene including FXTAS, fragile X mental retardation syndrome, and premature ovarian failure in females. The repeat numbers that are usually associated with FXTAS are in the 55-200 range. Individuals with FXTAS are NOT mentally retarded, but family members may be at risk for having a child with fragile X mental retardation.

SCAX syndromes

Several types of ataxia are believed to be caused by genes on the X-chromosome. These ataxias are called “X-linked” and they tend to affect males more often and more severely than females. These types of ataxia are named in a similar pattern to SCA ataxias (Spino Cerebellar Ataxia X-linked). The ataxias are numbered in the order of their discovery.

At the present time, SCAX1-SCAX5 have been reported, but no genes have been identified for any of these conditions.

Mitochondrial Ataxias

Mitochondrial ataxias are caused by problems in the mitochondria (the energy factories in our cells). Mitochondria have their own set of DNA that is kept separate from the rest of the genes in our genome. Mutations in this mitochondrial DNA are usually passed from women to all of their children.

Mitochondria also use some genes in our regular genome and these conditions are passed in an autosomal dominant or autosomal recessive manner. Mitochondrial diseases can be very difficult to diagnose because they can have such variable symptoms. The diagnosis is often made by performing a muscle biopsy to look for evidence that the mitochondria are not working in the muscle. Some of the dominant and recessive conditions that affect mitochondria were described in other sections (POLG1, OPA1). In order to diagnose diseases caused by changes in the mitochondrial genes, we need to look at the actual DNA in the mitochondria. There are many mitochondrial diseases that include ataxia as a symptom or feature.

Hereditary Dominant



Sporadic Ataxia

Olivo-Ponto-Cerebellar Atrophy (OPCA)

This is a degenerative disease similar to Parkinson's disease but affects the cerebellum and brain stem (pons and medulla). The name currently used is MSA-C (multi-system atrophy-cerebellar type) to differentiate from the Parkinson's type (MSA-P). MSA-C is a progressive disease, however progression rate varies considerably from person to person. Symptoms include ataxia with incoordination of the arms and gait, poor balance slurred speech and difficulty swallowing. The diagnosis is made after ruling out other causes of ataxia. Similar to ataxia, treatment is supportive.

Common Causes of Sporadic Ataxia Secondary to an Underlying Disease

Multiple Sclerosis (MS)

Multiple sclerosis is a common cause of ataxia. MS is believed to result from an abnormal immune response causing damage to myelin which is a fatty material that covers the nerve fibers (similar to wire insulating material) to improve the conduction of nerve impulses. MS affects myelin in the brain, brain stem and spinal cord. The areas affected are called plaques. These lesions can occur anywhere in the central nervous system and if the cerebellum or brain stem are affected, patients may present with ataxia. Indeed sometimes inherited ataxias are misdiagnosed as MS. On many occasions, ataxia patients indicate that their older family members were misdiagnosed with MS. MS diagnosis is primarily made by MRI and further supported by results of spinal tap.

Wheat allergy

The classic form of wheat allergy usually occurs as celiac disease (derived from Greek word *koiiliakós*, "abdominal"). Patients with celiac disease develop loose stools and abdominal cramps when they ingest wheat. The active substance that causes this reaction is gluten, which is the protein of wheat. Other substances in rye, barley, and perhaps oats cause the same reaction in patients with celiac disease. When patients with celiac disease stop eating gluten their symptoms resolve, usually completely and immediately. These patients, usually children, are instructed to continue a strict gluten-free diet for life. There are specialized grocery stores, or sections of grocery stores with gluten-free foods, such as rice bread and rice pasta.

The relationship of celiac disease to ataxia has been known for several decades. Patients with celiac disease may develop cerebellar ataxia and their symptoms and findings cannot be distinguished from patients with inherited ataxia. The cerebellar ataxia in celiac disease does not seem to be the result of poor absorption of nutrients. Celiac disease patients do develop deficiencies in essential nutrients because the inflammation of the lining of the gut tissue prevents the absorption of nutrients and vitamins. Deficiency of such nutrients and vitamins is not the cause for ataxia, but it seems that the allergy to wheat is responsible for ataxia. This is believed to be due to an immune reaction of the human body to wheat protein which inadvertently damages the cerebellum.

Recent research has shown that a person does not have to have the classic symptoms of celiac disease to develop ataxia. An individual may have ataxia symptoms initially and later test

positive for celiac disease. One test for wheat allergy is to detect gliadin antibodies, which are proteins in the blood that react with gluten components. Gliadins are components of gluten and are the targets for these antibodies. If the gliadin antibodies are high, doctors conduct further tests to confirm celiac disease. These tests include more specific blood tests or a biopsy, in which an endoscope is used to remove a small piece of tissue from the gut to be examined under the microscope. This often shows specific inflammation of the lining of the gut that helps to diagnose celiac disease. More recent research, however, shows that patients may have ataxia without gut abnormalities. Studies have also shown that people with hereditary ataxia may have high gliadin antibodies. It is not clear whether gliadin antibodies in hereditary ataxia contribute to the ataxia syndrome or make it worse. A strict gluten-free diet is recommended for people who have high gliadin antibodies and ataxia. The hope is that the antibodies are causing the cerebellar ataxia or contributing to ataxia caused by other factors. Because a gluten-free diet is a safe endeavor, trying the diet is risk-free. Before beginning this type of diet, consultation with a dietitian is necessary to learn about the types of foods that contain gluten. For patients with celiac disease, it is easy to follow the strict diet because ingesting gluten- contaminated foods leads to stomach pain, cramps, and/or diarrhea. However, these symptoms do not always occur in ataxia with wheat allergy. Usually a trial of the diet is recommended for at least six months, before reevaluation and possible continuation of the diet. The gluten-free diet requires great commitment by patients and their families.

Thyroid disease

The thyroid gland is located in the neck in front of the windpipe. Inflammation of the thyroid gland may occur as an autoimmune disease, in which the immune system produces a response against one of its own tissues. This immune response may be in the form of antibodies that target the thyroid gland and cause inflammation. The inflammation of the thyroid gland usually results in an underactive thyroid. When the thyroid is underactive, it does not secrete enough thyroid hormones, which are important for burning of nutrients, regulation of temperature, and body fat. An underactive thyroid may result in slowness of heart rate, weight gain, and feeling of being unduly cold. Patients with an underactive thyroid have been known to develop cerebellar ataxia. Recent research shows that cerebellar ataxia may be specifically related to the presence of antibodies against the thyroid rather than the lack of thyroid hormones themselves. These antibodies are believed to damage the cerebellum. Laboratory tests are available to test for these antibodies, and patients with cerebellar ataxia of unknown etiology should be tested for thyroid antibodies. If antibodies are detected, prednisone or other corticosteroid medication may be recommended to reduce the inflammation and autoimmunity. The onset of cerebellar ataxia with thyroid antibodies may vary. It can be chronic, with an onset of months or years, or it may occur subacutely—in a matter of days or weeks.

Anti-glutamic acid decarboxylase (GAD) antibodies

Anti-GAD antibodies target an enzyme called Glutamic Acid Decarboxylase. This enzyme is responsible for converting glutamic acid to GABA, a chemical found in high concentrations in the cerebellum. It is believed that the lack of GABA results in cerebellar ataxia. Patients with cerebellar ataxia of an unknown

cause should have an anti-GAD test. The anti-GAD antibodies have also been associated with a disease characterized by stiffness of the muscles, called "stiff person syndrome". The stiff person syndrome and cerebellar ataxia do not necessarily occur together in patients with anti-GAD antibodies. Anti-GAD antibodies are particularly common in diabetes mellitus and autoimmune diseases such as thyroid disease and rheumatoid arthritis. The treatment for anti-GAD antibodies is corticosteroids or prednisone to reduce the abnormal immune response. If this is ineffective infusion of immunoglobulin intravenously (IVIG) or a procedure called plasma exchange can be used.

Chronic hypoglycemia

Chronic low blood sugar, such as that resulting from insulin-producing tumors, can rarely produce cerebellar ataxia.

Paraneoplastic syndromes Paraneoplastic syndrome is a disorder that accompanies tumors and may include symptoms of cerebellar ataxia. In this case, the body produces an immune response against the cancer cells. These antibodies may damage the cerebellum or other nervous system tissues, causing cerebellar ataxia. Paraneoplastic syndrome may occur rather rapidly, within a few days or few weeks, and ataxia may indeed be the first symptom of cancer. In this case, ataxia of rapid onset can be considered an important signal for hidden cancer.

Diagnosis of paraneoplastic syndrome is made by measuring known antibodies in the blood in patients with cerebellar ataxia of short duration. Patients with ataxia for several years are unlikely to have cancer. The treatment is directed towards removing the cancer or treating it with chemotherapy.

Corticosteroids can be used to reduce the abnormal immune response.

Infections

Ataxia that is caused by infection usually comes on quickly. It may be caused by inflammation of the cerebellum either by an infectious agent itself (usually virus) or as an immune response against the infectious agent.

Stroke

Cerebellar ataxia may occur because of a blockage in an artery that supplies blood to the cerebellum or to the connections of the cerebellum. The blockage of an artery results in damage of the cerebellar tissue in the area supplied by that particular artery. These infarcts or strokes are easily and readily seen on a magnetic resonance image (MRI) of the brain. Another type of stroke is a bleed, in which an artery or a vein ruptures, causing an area of blood collection and damage of tissue. A bleed is seen readily on computed tomography (CT) scan or MRI. Cerebellar ataxia from strokes occurs abruptly and is often associated with other symptoms such as eye, arm, or leg paralysis or loss of sensation on the face or the body. Cerebellar ataxia from strokes may also be confined to one side of the body. The ataxia symptoms may improve to some extent in few weeks after the stroke. Rarely, a stroke in a particular part of the brain stem may result in ataxia that is of delayed onset, occurring several weeks or even several months after the stroke. In this case, the ataxia may actually progress. These types of ataxia can also be detected with brain imaging. The main management of a stroke involves preventing further strokes by using blood thinners such as aspirin when appropriate.

Vitamin deficiencies

Deficiencies of vitamins E and B1 (thiamin) can produce symptoms of cerebellar ataxia. Indeed a rare autosomal recessive ataxia with symptoms similar to Friedreich's Ataxia may have low levels of vitamin E. Therefore, vitamin levels (especially vitamin E) should be measured in all ataxia patients. Treatment is directed to the specific deficiency.

Medications

Many medications can be toxic to the cerebellum. These include seizure medications such as carbamazepine (Tegretol), phenytoin (Dilantin), and chemotherapy agents such as cyclosporine. Some medications that produce sedative effects on the brain worsen the cerebellar ataxia. These include medications such as diazepam (e.g., Valium) and similar medications in that class (benzodiazepines). Alcohol may have the same effect.

Environmental toxins

Ataxia can be caused by exposure to environmental toxins, in particular toluene and methylmercury. People at risk of toluene toxicity are those exposed to organic solvents such as car mechanics and painters. Chronic toxicity results in headache, cerebellar ataxia, irritability, loss of concentration, and memory loss. Kidney problems may also occur. The main way that people are exposed to methylmercury is through accidental exposure—for example, by eating fish that contain the chemical.

Alcohol

Patients with cerebellar ataxia very quickly learn that consuming alcohol worsens their symptoms. It is not unusual for patients with cerebellar ataxia to be questioned by the police, especially when driving. Most patients are allowed to drive after evaluation. A letter from a doctor can be provided to patients (who are safe drivers) stating that they suffer from cerebellar ataxia, which may resemble alcohol intoxication. Shrinkage of the cerebellum from prolonged use of alcohol (along with deficiencies in nutrients, such as thiamin) can also result in permanent cerebellar ataxia.

Notes

Notes

*We acknowledge with thanks the permission to reproduce this
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