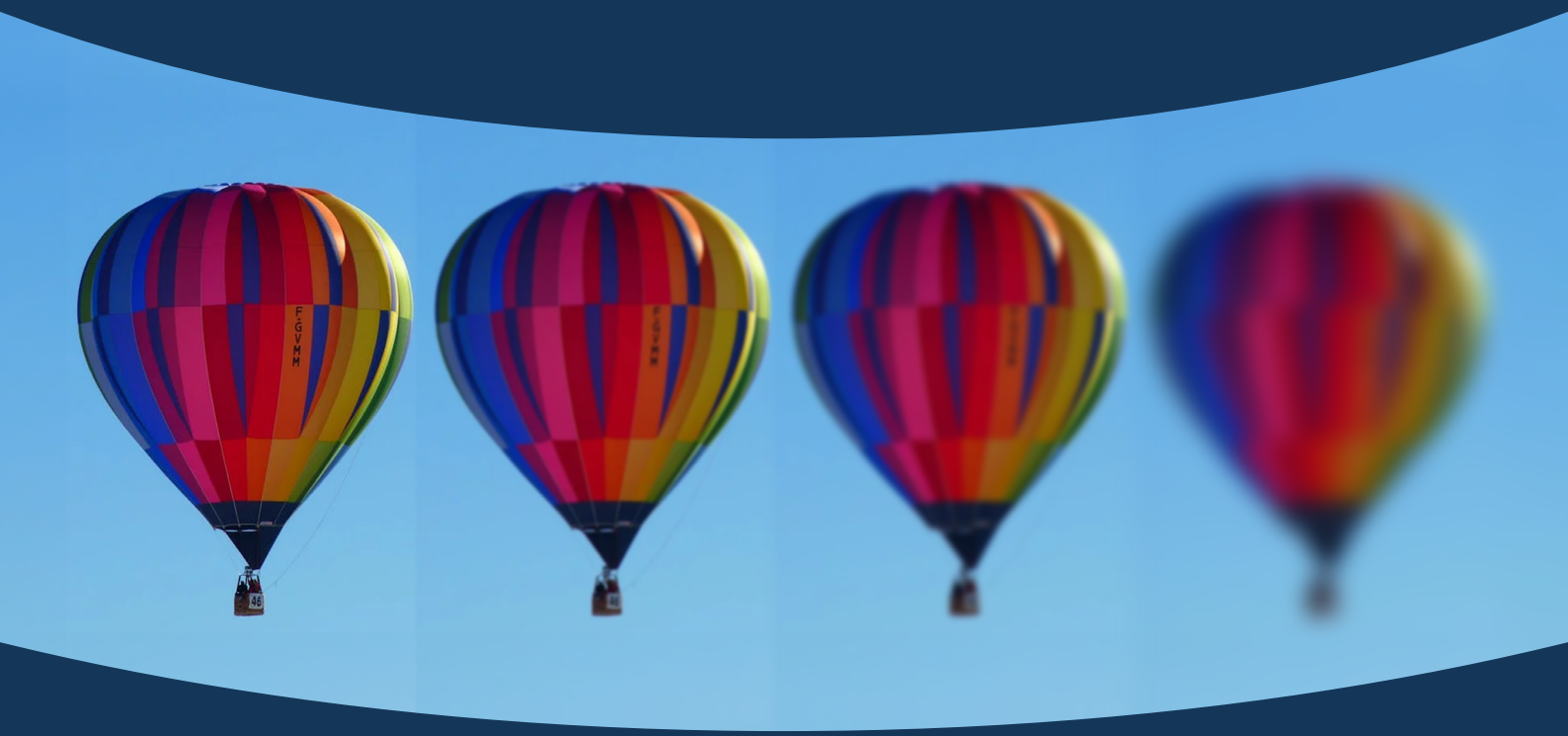
All about ADOA-plus (for patients)



CURE ADOA FOUNDATION

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Visio Foundation

1. What is ADOA-plus?

Autosomal dominant optic atrophy (ADOA) is a very rare inherited eye condition. It is caused by damage to the optic nerve. Some people are only slightly affected. Most experience a gradual decline in vision. Others become almost completely blind. In ADOA-plus, symptoms also occur in other parts of the body.

ADOA is not common. The condition affects approximately 1 in 30,000 people . As there is no comprehensive register of all patients, this remains an estimate. Approximately 1 in 5 people with ADOA develop ADOA-plus.

2. What are the symptoms?

As well as eye problems, people with ADOA-plus may also suffer from:

- Problems with the brain, nerves and muscles (neurological problems):
- Hearing loss or deafness: usually in both ears (damage to the auditory nerve)
- Balance problems
- Muscle weakness, particularly in the upper legs and arms
- Muscle pain or cramps
- Difficulty moving and controlling your movements (ataxia)
- Tingling, reduced sensation or pain due to nerve damage (sensory neuropathy)
- High muscle tone (spasticity)
- Epilepsy

Other symptoms:

- Severe and persistent fatigue
- Problems with thinking and understanding (cognitive). For example, difficulty with memory or concentration
- Problems with the autonomic nervous system; this regulates, among other things, heart rate and blood pressure

3. How do you get ADOA-plus?

A fault in the OPA1 gene causes an energy deficiency

ADOA and ADOA-plus are caused by a fault in the DNA, the genetic material. Such a fault is also known as a genetic variant or gene mutation. In ADOA and ADOA-plus, the fault lies in the OPA1 gene.

The OPA1 gene is responsible for producing substances (proteins) that are important for the energy powerhouses in the cell (mitochondria). If these do not work properly, the cells receive too little energy. This often leads to problems with organs or tissues that require a lot of energy. In ADOA, this affects the optic nerves. In ADOA-plus, there are also problems with the auditory nerves, muscles or other organ systems.

There are several types of mutations in the OPA1 gene. With some mutations, there is a higher chance of developing ADOA-plus.

Inheritance

ADOA and ADOA-plus are rare inherited conditions. Both men and women can carry the genetic predisposition for ADOA and ADOA-plus and pass it on. Every child of a parent with ADOA or ADOA-plus has a 50% chance (1 in 2) of inheriting this genetic predisposition. This applies to both sons and daughters.

Of the children born with a defect in the OPA1 gene, approximately 95% (19 out of 20) develop symptoms. These often begin in the first ten years of life. Approximately 5% (1 in 20) of people who have the defect do not develop symptoms. However, they can still pass the defect on to their children.

4. How is it determined whether you have ADOA-plus?

The diagnosis of ADOA has often already been made by an ophthalmologist.

Genetic testing

A doctor specializing in genetic disorders (clinical geneticist) can carry out DNA testing to confirm a diagnosis of ADOA or ADOA-plus. Whether you wish to undergo this testing is a personal choice.

The clinical geneticist can discuss the pros and cons with you. This is known as a discussion about heredity and choices (genetic counselling).

DNA testing can also reveal whether people who do not (yet) have any symptoms still carry the genetic mutation in their DNA. We call this predictive DNA testing. Read more about genetic testing

Good to know:
- The costs of a counselling session and DNA testing vary by country.
- A counselling session or test may also affect the options and costs of life insurance or disability insurance. This also varies by country.

If you are planning to have children, there are various options available if you or your partner has a genetic defect. Read more under ***'What can you do yourself?'***.

Diagnosing ADOA-plus

In people with ADOA, the doctor may consider ADOA-plus if other symptoms are present, such as hearing loss, loss of strength, balance problems and (severe) fatigue. Fatigue alone as an additional symptom is insufficient for a diagnosis of ADOA-plus.

An ophthalmologist and a neurologist can make this diagnosis. Your own doctor (for example, an ophthalmologist, neurologist, clinical geneticist or GP) can refer you to a centre of expertise; a hospital with extensive experience of ADOA-plus. Before making the referral, your doctor may first consult with this team.

What happens after the diagnosis?
Once it has been established that you have ADOA-plus, you will agree on a care plan with your doctor. This can vary from person to person. Often, your own doctor can help you further. Sometimes you will remain under the care of the centre of expertise, for example once a year.

How the condition progresses in your life varies from person to person. It can even differ within a single family, including between parent and child. For most people, the symptoms get worse over the years. How much and how quickly this happens depends, among other things, on the type of error in the DNA.

Ultimately, ADOA-plus progresses differently in everyone. This is important for treatment and support.

5. What treatments are available?

Unfortunately, there is currently no treatment that cures ADOA-plus. This chapter focuses on the treatment of the 'plus' symptoms.

Treatment for hearing problems

The combination of poor vision and hearing problems in ADOA-plus makes life particularly difficult. That is why it is important that hearing problems are detected early. An ENT specialist and an audiologist can work together to find the best way to support hearing.

Assistive devices for hearing problems
People with hearing loss are usually fitted with hearing aids. In cases of severe hearing loss, surgery is often an option, involving the fitting of a cochlear implant (CI). A CI works differently from a hearing aid. It converts sound into an electrical signal that stimulates the auditory nerve. This enables people (usually) to hear again as they did with a hearing aid. The ENT specialist and audiologist will determine whether a CI is suitable.

When choosing a hearing aid, it is important to take into account the further progression of hearing loss caused by ADOA-plus. In addition to hearing loss caused by ADOA-plus, people often experience a decline in hearing as they get older due to age-related hearing loss.

A hearing aid or cochlear implant is an aid. It can still be difficult to understand people in noisy environments. Sometimes simple solutions, such as a quieter (work) environment or explaining the situation to classmates, teachers, colleagues, family and friends, can be a great help. There are also other aids to help you follow lessons, telephone conversations, TV, presentations or meetings more easily. These aids can also be helpful in places such as restaurants or the theatre.

Support
An occupational health and safety audiology centre and/or hearing care professional can assist with obtaining hearing aids or assistive devices, and can offer advice for work and social situations. The most important advice is not to wait too long before seeking help for hearing problems. Most people find that this improves their quality of life.

Hearing protection
To prevent further damage to your hearing as much as possible, the advice is not to listen to loud music (too often or for too long) or to be in noisy environments. Or, if necessary, to wear hearing protectors.

Communication in deafblindness
If someone has both hearing and vision impairments (deafblindness), new ways of communicating are needed. In cases of deafblindness, sign language conveyed through touch may be suitable. This is known as four-hand signing. This also includes finger spelling in the hand.

In this method, the conversation partners hold each other’s hands, allowing the deafblind person to feel what is being signed.

Some people can still see well enough to recognise gestures. They can use sign language.

It is important that the signs are made within the person's field of vision. Sometimes, support from a sign language interpreter can be helpful.

Through training, you can learn how the different methods of communication work. This helps you prepare for the future. What works best depends on the situation and the type of deafblindness. You can also attend these training sessions together with your loved ones.

Support in dealing with ADOA-plus

With diseases affecting the energy-producing structures in cells (mitochondrial disease) such as ADOA-plus, general statements are often inaccurate. For example, regarding how severe the condition is, how it will progress and what you should do. The extent of your symptoms varies from person to person, even within the same family.

That is why it is very important that the information, support and treatment are well suited to your situation. This way, you can work with your doctor or healthcare provider(s) to ensure you do not become overly burdened. It is also important to focus on what you can do, rather than just looking at the limitations. Read more under ***'What can you do yourself?".***

Points to consider regarding medication use

People with ADOA-plus need care that suits them ('tailored care'). It is important that healthcare providers pay attention to the medicines they prescribe. People with a mitochondrial disease, such as ADOA-plus, should avoid certain medicines.

A group of doctors and researchers from various countries has compiled a list of:

- medicines that may be harmful
- medicines that are safe

Tip: Always tell your doctors about this list.

Alternative treatments

Unfortunately, there are currently no medicines that can cure ADOA-plus. However, a great deal of research is being carried out in this area.

For people who eat too little or are malnourished, tablets containing extra vitamins and minerals (supplements) can be helpful, alongside a healthy diet.

See *'Healthy eating'* under 'What you can do yourself'.

Scientific research

Researchers are researching ADOA and ADOA-plus. Their initial aim is to find a medication that stabilises vision, preventing further deterioration. It may be years before a medication or other treatment is actually available.

New types of treatment are also being explored, such as gene therapy or stem cell therapy.

More research is important, because a cure for ADOA and ADOA-plus remains the ultimate goal of the Cure ADOA Foundation.

6. What can you do yourself?

It is important to live a healthy lifestyle: eat healthily, get enough exercise and manage your energy levels well.

Healthy diet: avoiding eating too little (malnutrition)

A healthy diet in line with official dietary guidelines is important for ADOA-plus. The parts of the cell that produce energy (mitochondria) do not function as well, and as a result, your body has different energy requirements. See *'How do you get ADOA-plus?'.*

It is important to get enough energy from your diet. If you do not manage to do this, malnutrition can develop. With malnutrition, your body is often too thin due to insufficient body fat and muscle mass. You then have a poor nutritional status.

To prevent malnutrition:
- Do not fast and do not follow a strict diet where you eat very little (crash diet).
- If you have a fever, bear in mind that your body needs more energy.
- A dietitian can advise you on which diet suits you best. The aim is for your diet to be healthy, your nutritional status to be good, and for you to enjoy a better quality of life.

Get enough exercise without overexerting yourself

A physiotherapist (a specialist in exercise) can advise you on a training programme that suits you. This helps to improve your fitness and strength. Strength training focuses mainly on how long you can sustain an effort (endurance) rather than on becoming as strong as possible.

Examples of good exercises include walking/running with a buddy, tandem cycling, swimming, gym workouts, and dancing.

Managing your energy

An occupational therapist can teach you how to manage your energy effectively. For example, by using practical methods or aids. This helps prevent you from becoming overburdened and allows you to discover what you can manage.

What should you avoid?

There are also things you should avoid if you have ADOA-plus.
The advice is:
- Do not engage in very strenuous physical activities.
- Avoid stress or overexertion, for example if you are ill or have a fever.
- Do not fast and do not follow a strict diet where you suddenly eat very little (crash diet).
- Do not smoke or use e-cigarettes (vapes).
- Do not drink alcohol.
- Do not use drugs.
- Do not take any medicines that are harmful to people with ADOA-plus.

Coping with your disability

The symptoms of ADOA-plus have a significant impact on your daily life. Poor vision, hearing difficulties and getting tired easily affect your school life, your choice of work, your social life and your hobbies.

In some cases, you can request a consultation with a social worker or psychologist. They can help you learn to cope with your dual disability. They can also offer advice on how to make your daily life easier, such as using assistive technology to watch TV, making calls with headphones, using a special travel card on public transport, or arranging taxi transport where necessary, etc.

Peer support

It can be helpful to share experiences with people who have the same condition. This is known as peer support. It helps you realise you are not alone. You can exchange tips and practical solutions.

There is a special ADOA-plus day every year. There is also a separate group in the ADOA app. And a WhatsApp group consisting solely of people with ADOA-plus. Please contact Gabriëlle to sign up for this.

Community

We have our own app for anyone connected to ADOA and ADOA-plus. With this app, you can chat with each other in group chats or have one-to-one conversations.
We also share news updates and activities via the app. So, with this app, you can stay up to date with all the latest news.
Read more about the Cure ADOA Foundation app

Desire to have children

If you (or your partner) have a hereditary condition, this may influence your decision on whether or not to have children. It also means there are options to reduce the risk of a child inheriting ADOA and ADOA-plus.

With ADOA and ADOA-plus, you know that every child has a 50% (1 in 2) chance of inheriting the mutation in the OPA1 gene. If a child inherits this mutation, around 95% (19 out of 20) will actually develop symptom.

Decisions regarding having children vary from person to person. They may also depend on how someone experiences life with ADOA and ADOA-plus. It is important to note that the severity of symptoms in the child may differ from that of the parent.

Not wanting to have a child with ADOA or ADOA-plus does not mean that having a child is impossible. There are various options, including PGT. This is a test carried out on embryos before they are transferred to the womb (embryo selection, pre-implantation genetic testing).

Read more about ADOA and desire to have children

Tip: Discuss your desire to have children with your doctor before conception.

Insurance

It is good to know that a genetic defect in your DNA can sometimes have consequences if you wish to take out insurance. For example, life insurance and/or disability insurance (insurance for if you are no longer able to work). The impact on insurance policies varies from country to country.

7. What does the Cure ADOA Foundation do?

Since November 2018, the Cure ADOA Foundation has been working to support people with ADOA or ADOA-plus and their families. It is a recognised patient organisation.

The foundation has four objectives:
1. Supporting scientific research
2. Advocacy
3. Raising awareness of ADOA(-plus)
4. Connecting peers

The ultimate goal is to prevent and cure ADOA and ADOA-plus. Questions about ADOA-plus? Send us an email!

8. Want to know more? You might also find this interesting:

- Information by country
- What is ADOA – digital patient leaflet
- ADOA-plus Day 29 March: learnt a lot from Dr Janssen and from each other!
- ADOA podcast Episode #13: Dr Mirian Janssen on ADOA-plus
- Gabrielle's story
- The road to treatment 21 on heredity
- Overview of 'The road to treatment'
- Lifestyle tips
- List of medicines for ADOA/ADOA-plus (downloads)
- ADOA and the desire to have children (PGD)
- Other potentially useful links

Connecting with others

- The Cure ADOA Foundation app: staying in touch!

A WhatsApp group exclusively for people with ADOA-plus. Send an email to Gabriëlle to sign up.

About the Cure ADOA Foundation
Since November 2018, the Cure ADOA Foundation has been committed to supporting people with ADOA(-plus) and their families.

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