

What is geographic atrophy?

Geographic atrophy (GA) is an advanced form of age-related macular degeneration (AMD).⁽¹⁾⁽²⁾

AMD is a disease that occurs in those above 50 years of age⁽³⁾ that causes the gradual and permanent loss of sight due to blurring or loss of central vision which affects the ability to read and see faces.

There are different stages of AMD. These are categorised using the Beckmann classification⁽³⁾ based on the clinical examination or evaluation of a fundus photo, which is a photo taken of the rear of the eye to identify lesions.

AMD has 3 distinct stages, early, intermediate, and advanced.⁽⁴⁾ The early and intermediate stages of AMD are less likely to cause changes in the vision. There are two forms of advanced AMD.⁽³⁾

1. Geographic atrophy (GA) ('dry' AMD) occurs when the photoreceptors and retinal pigment epithelium (RPE) cells at the macula die over time, causing a gradual, painless but permanent loss of central vision. The macula is the central part of the retina that processes what you see directly in front of you, that is, your central vision. It allows you to achieve high-resolution vision and accounts for your ability to read, recognise faces and to see the world in detail and colour.

- GA is a progressive disease that leads to irreversible central blindness over time.⁽⁵⁾ The severity of the visual disability associated with GA secondary to AMD is evidenced by the median time to progression to legal blindness estimated at 6.2 years.⁽⁴⁾

2. Neovascular AMD ('wet' AMD) occurs where new blood vessels grow into and under the retina, which can leak and cause bleeds leading to sudden vision loss and distorted vision.

How many people live with GA?

It is estimated that there are up to 100,000 Australians living with GA. This is based on an average 1-2% population estimate of late-stage AMD and that GA appears to occur in a proportion equal to that of those with wet or neovascular AMD.^{(6)(7) (8)(9)} Worldwide, there are an estimated 5 million people living with GA.⁽¹⁰⁾

- The incidence of GA is also more prevalent in the European population compared to the Asian, African, and Hispanic populations.⁽¹⁰⁾⁽¹¹⁾
- The incidence of GA has been shown to increase four-fold every ten years from the ages 50 to 80 in the European population.^{(12) (13)}
- As the aging population globally is estimated to increase over the coming decades, and the incidence of GA is therefore also projected to rise.⁽¹⁰⁾

How is GA identified

Through a retinal examination by an optometrist or ophthalmologist, GA is identified by areas of retinal thinning associated with loss of photoreceptors and retinal pigment epithelium (RPE). Over time, this damage to crucial parts of the retina can eventually lead to the loss of these retinal structures, resulting in the sharply defined areas of cell loss characteristic of GA.

These areas may have a scalloped or geographic border, which is the reason for the name “geographic atrophy.”⁽¹³⁾



Source image: Courtesy of Macular Research Unit, Centre for Eye Research Australia

What are the symptoms of GA

- GA often develops gradually over time and may not cause noticeable symptoms in its early stages. This is particularly so if it is only present in one eye to start with as the other eye will mask the problem. However, as the condition progresses, common symptoms may include:
 - Gradual central vision loss which affects the ability to see fine details, read, drive, and recognise faces. This vision loss typically worsens over time as the atrophic areas in the macula expand.
 - Blurred or distorted central vision. Straight lines may appear wavy or distorted, and objects may appear less clear or sharply defined.
 - Visual distortions such as seeing blind spots or missing areas in their central field of vision. These can interfere with daily tasks that require clear central vision.
 - Difficulty with low-light vision or experience reduced night vision. This can make it challenging to see in dimly lit environments or at night.

- Decreased contrast sensitivity making it harder to distinguish between objects of similar shades or colours. This can impact activities such as reading, driving, and navigating unfamiliar environments.
- It is important to note that the symptoms of GA can vary from person to person, and some individuals may experience more severe vision loss than others. Regular eye examinations and monitoring by an eye care professional are essential for detecting and managing GA, as early intervention (once approved and available in Australia) may help slow the progression of vision loss and preserve remaining vision.

What is the cause?

The development of GA is complex and influenced by various genetic, environmental, and age-related factors.

- Genetic Factors: Certain gene variants are linked to a higher risk of developing GA and other forms of AMD. These include those in complement factor H (CFH), complement factor I (CFI), complement component 2 (C2), and complement factor B (CFB). These genes help regulate the immune system and inflammation, which are crucial in the development of AMD.⁽¹⁴⁾
- Environmental Factors: Smoking is the greatest modifiable risk factor ⁽¹⁵⁾ associated with an increased risk of GA. Other lifestyle and environmental risk factors include diet ⁽¹⁶⁾ and exposure to ultraviolet (UV) light.⁽¹⁷⁾
- Ageing: Ageing is the primary risk factor for GA, however it is non-modifiable, meaning that it is unable to be changed or controlled. As people age, cellular processes in the retina, including the function and maintenance of RPE cells, become less efficient. The accumulation of cellular damage and oxidative stress over time contributes to the degenerative changes seen in AMD, including GA.⁽¹⁸⁾⁽¹⁹⁾⁽²⁰⁾
- Inflammation in the retina can lead to RPE dysfunction, photoreceptor damage, and ultimately the formation of GA lesions.⁽¹³⁾

Social impact of GA

Geographic atrophy (GA) can make it difficult for individuals to perform everyday tasks independently, significantly affecting their daily functioning and quality of life.⁽²¹⁾

People with GA may find certain activities challenging such as reading, driving, watching television, completing household chores, recognising faces,⁽¹³⁾ and the ability to perceive non visual communications.

More light may be needed for tasks such as reading, typing, or sewing, and may experience blurred vision, sensitivity to light, colour vision defects, progressive visual loss, a restricted visual field, and poor contrast vision. ⁽²¹⁾ GA may also impact a person's ability to work, including volunteering which may lead to reduced community participation.

The impact of visual impairment goes beyond daily tasks. GA can cause emotional distress or even depression, anxiety about the future, frustration, and a sense of dependency on others. In addition, older adults with vision loss often have poorer physical and cognitive abilities, making them more susceptible to comorbidities, disability, and increased mortality.

Visual impairment, particularly the near vision impairment characteristic of GA, is also a risk factor for frailty and increases the incidence of falls among the elderly. Falls are a significant public health concern worldwide, with a substantial portion attributed to visual impairment, including GA and AMD. ⁽²¹⁾

What treatments are available

Emerging treatments

There are now two treatments for GA which have been approved in the USA. These aim to slow progression of the disease rather than stop or reverse it. They both use complement inhibitors that target the complement pathway, which plays a role in the immune response. By reducing the activity of this pathway, the medicine aims to reduce inflammation and retinal damage in order to slow down GA progression and preserve vision.

1. Pegcetacoplan (Syfovre, Apellis Pharmaceuticals)

Pegcetacoplan involves monthly or every-other-month intravitreal injections, which uses a fine needle to deliver the medication directly into the eye.

Pegcetacoplan was approved for use in the US by the Food and Drug Administration (FDA) in February 2023. It is currently being evaluated for use in Australia by the Therapeutic Goods Administration (TGA). ⁽²²⁾

2. Avacincaptad pegol (Izervay, Iveric Bio)

Avacincaptad pegol was approved for use in the US by the Food and Drug Administration (FDA) in August 2023. It is also administered via monthly intravitreal injections.

Late-stage clinical trials in progress

There are several late-stage clinical trials in progress for other GA treatments with one in Phase 3 testing an oral capsule called ALK-001 (Alkeus Pharmaceuticals).

In Australia, there is also one trial in Phase 3 called the Phoenix trial testing an oral tablet called Tnlarebant (Belite Bio). Also domestically, there is a trial in Phase 2 called ALXN2040-GA-201 testing an oral medication called Danicopan (Alexion Pharmaceuticals) and a Phase 2 trial called Parasol testing a gene therapy vector called JNJ-81201887 (Janssen).

There are other international Phase 2 studies and several earlier stage clinical trials targeting the complement system, using neuroprotective agents, and testing ocular gene therapy and stem cell therapy that may provide alternative treatments for GA in the future.⁽²³⁾

Clinical care

It is recommended that patients see their optometrist or ophthalmologist for further information. In preparation for potential new treatments coming to Australia for GA, The Royal Australian and New Zealand College of Ophthalmology (RANZCO) recently updated its [referral pathway for AMD management](#) (April 2024). It advises referral to an ophthalmologist if patients with GA are interested in learning more about potential GA treatments to enable them to make an informed decision.

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