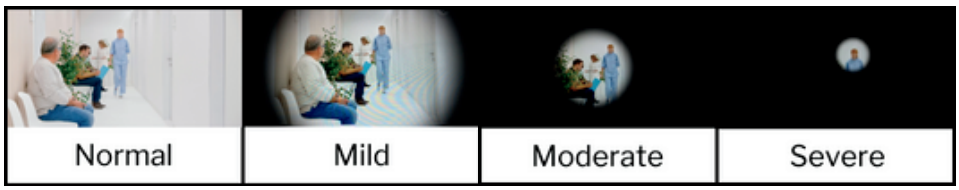
USHER SYNDROME EXPLAINED

What is Usher syndrome?

Usher syndrome (USH) is a rare, genetically inherited disease and its main symptoms are, sensorineural hearing loss and retinitis pigmentosa (RP) which causes a slow progressive loss of sight. For some USH types, there are also vestibular (balance) issues too. Usher syndrome is the leading genetic cause for combined hearing and sight loss. It is estimated that over 400,000 people worldwide have Usher syndrome. Since the data on the number of USH patients in Ireland is limited, it's our estimate there could be around 200-260 people living with the condition here.

How does Usher syndrome affect the eyes?

Inside the eye, there is a thin layer of tissue that lines the back of the eye called the retina. This layer is made up of millions of light-sensitive photoreceptor cells called rods and cones. The function of these cells is to take in the visual information and process it to the brain via the optical nerve helping us to see. Rods are essential for night-vision helping us to see in the dark and dull lighting, while cones are needed for day vision, colour and sharp vision. Retinitis pigmentosa (RP) associated with USH affects these photoreceptors cells causing these cells to degenerate slowly over time. The rods are usually the first to be affected and this explains why night-blindness is often the first sign of RP. Over time, there is a slow loss of the peripheral vision leading to tunnel vision. Central vision often remains intact until end-stage RP, as this area of the retina is heavily populated with cones. Many people with Usher syndrome retain some useable vision well into older age, however some do experience a full loss of sight. Unfortunately, there is no way to predict the onset of symptoms, how it will progress, and how severe it may be for each person with this condition.



Stages of RP

How does Usher syndrome affect the ears?

In the inner ear, the cochlea contains thousands of tiny hair cells. It is the role of these hair cells to respond to the different sounds coming into the ear by sending electrical impulses to the brain via the auditory nerve to help us hear. In Usher syndrome, these tiny hair cells are damaged thus impacting hearing. This is known as sensorineural hearing loss. Some are born with little to no hearing (profound loss) as typically seen in those with USH type 1. Those with USH type 2 usually have some but not all of these hair cells completely damaged, resulting in a moderate-severe loss and with the help of hearing aids, which amplifies sounds, they can access sound and speech. Some people with USH type 2, and people with USH type 3 and USH type 4, experience a progressive loss of hearing over time. For those who are born with a severe to profound loss, or for those who experience a progressive hearing loss, cochlear implants can be an option giving good access to sound and speech. These are electronic devices that replaces the function of the damaged tiny hair cells by sending electrical impulses to the brain.

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How does Usher syndrome affect balance?

USH type 1 may also be accompanied by balance issues due to damage of the vestibular system In the inner ear which determines balance, motion and location. This is especially noted where babies/toddlers with USH type 1 are slower to sit up, and/or are later to walk than their peers. However, these hurdles can be overcome in time as the brain learns to adapt alongside rehab exercises provided by occupational therapists and physiotherapists.

The different types of Usher syndrome

Usher syndrome is catergorised into four major types, 1,2,3, and 4. This chart shows the typical onset of hearing, sight, and balance loss experienced by those with a certain type of Usher syndrome. However, this is not representative of all those with Usher syndrome as the symptoms can sometimes vary in onset and severity.

	HEARING	SIGHT	BALANCE
USH1	Profound at birth	Tend to experience decreased night vision by the age of 10, progressing to severe vision loss by midlife.	Issues present from birth
USH2	Moderate to severe at birth	Decreased night vision typically begins during teens, progressing to severe vision loss by midlife.	No issues
USH3	Normal at birth. Loss begins in childhood	Decreased night vision typically begins during teens, progressing to severe vision loss by midlife.	Issues varies
USH4	Normal at birth. Loss begins in adulthood	Vision loss begins later in life	No issues

Usher syndrome types and subtypes

USH type one and two are the most common types of Usher syndrome with USH type three representing only about 2-5% of overall USH cases. In USH type one, USH1B is the most common subtype representing between 33 – 50% of all USH type 1 cases, followed by USH1D. In USH type 2, USH2A is believed to represent up to 85% of all USH type 2 cases. The following chart shows each USH subtype with their respective USH gene.

USH1	USH1B (MYO7A)	USH1C (USH1C)	USH1D (CDH23)	USH1F (PCDH15)	USH1G (SANS)	USH1J (CIB2)
USH2	USH2A (USH2A)	USH2C (ADGRV1)	USH2D (WHRN)			
USH3	USH3A (CLRN1)	USH3B (HARS)				
USH4	USH4 (ARSG)					

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How is Usher syndrome diagnosed?

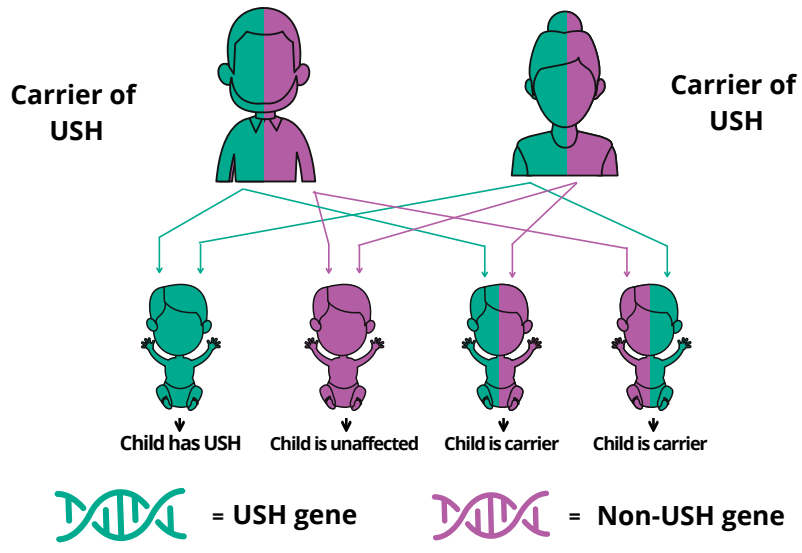
Usher syndrome may be clinically diagnosed by carrying out a range of tests for hearing, vision, and balance. To confirm a clinical USH diagnosis, genetic testing must be performed to find the causative USH gene.

How is Usher syndrome inherited?

Every person has two copies of each gene, one inherited from each parent. Usher syndrome is inherited when both parents have passed a gene with the same Usher syndrome mutation to their child. This inheritance pattern is known as autosomal recessive, and the symptoms of this condition are only evident when the person has two copies of the same mutated USH gene.

Where both parents carry the same USH mutation:

- there is a one-in-four (25%) chance of their child having Usher syndrome
- there is a one-in-four (25%) chance of their child not being affected
- there is a one-in-two (50%) chance of their child being a carrier of Usher syndrome



Usher Syndrome Inheritance Pattern

Research

While there is currently no treatment or cure for Usher syndrome, research into this condition is moving forward faster than ever before. There is currently one ongoing trial for RP associated with USH2A (exon 13) with many other potential therapies currently being explored with the hope that they too will progress to human trials. Please visit our 'Research' hub for all the latest information: ***https://usherireland.org/usher-syndrome-research***

Life with Usher syndrome

With a good support network and the right accommodations provided when necessary, people with Usher syndrome lead independent and fulfilling lives with careers and families of their own. The USH community is a diverse and large community where many individuals and families have made connections worldwide providing encouragement and support to each other. We strongly encourage anyone feeling alone or looking for support to reach out to us. We can help you to make connections, and provide support where possible.

For further information please visit our website
www.usherireland.org