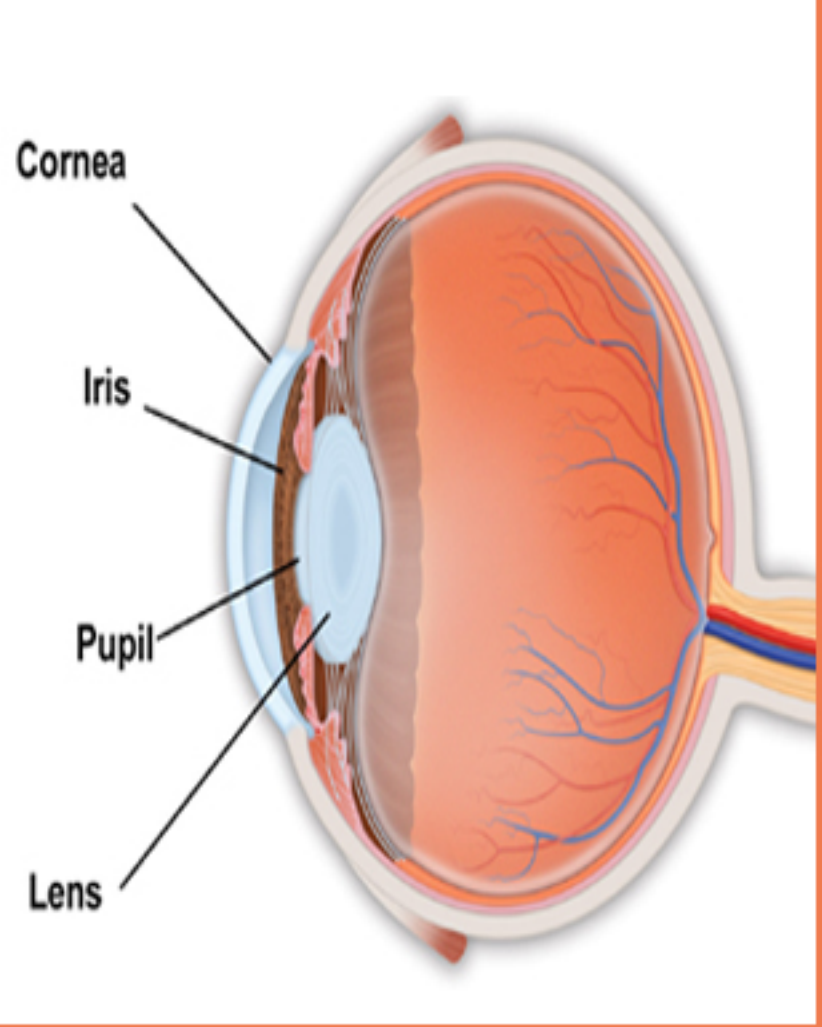

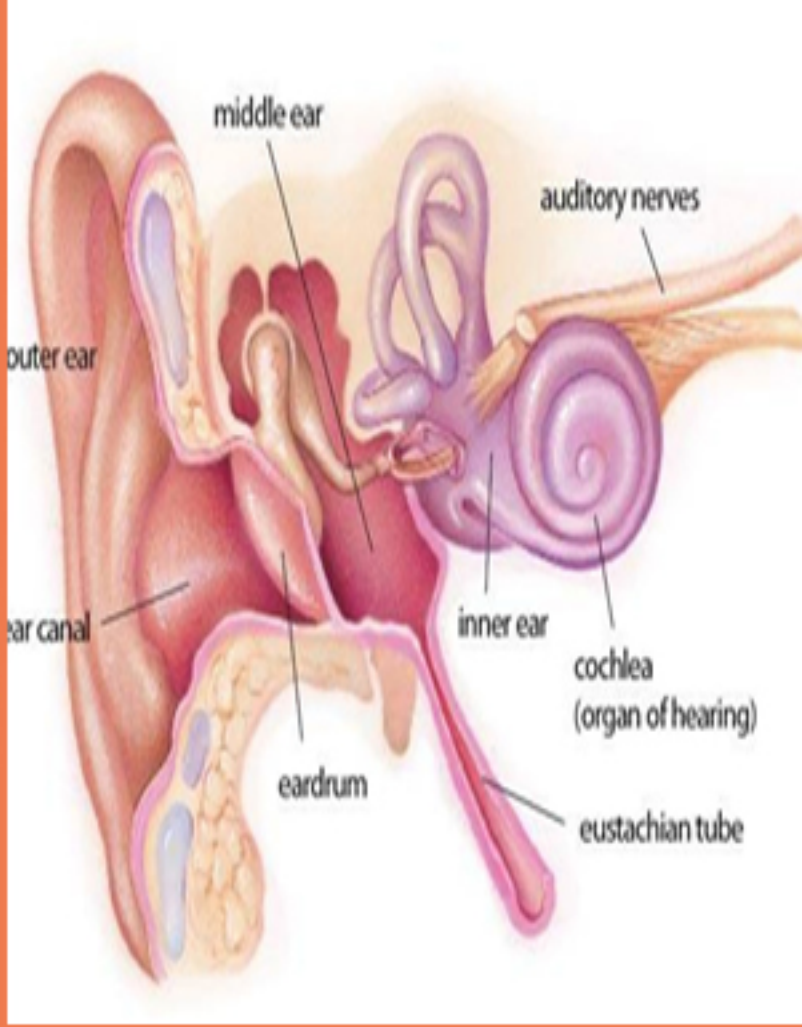

Eye and Ear Anatomy

London Ligon

Krysta Corrigan

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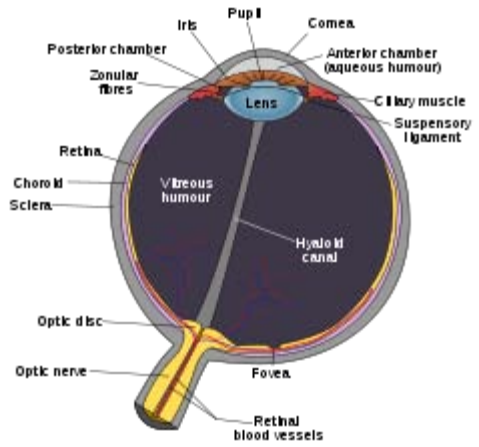
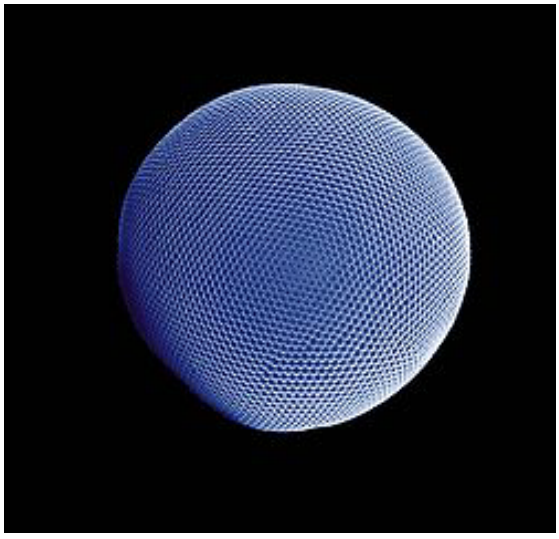
Chapter 1

Eye

Eye



Schematic diagram of the vertebrate eye



Compound eye of Antarctic krill

Eyes are organs that detect light, and convert it to electro-chemical impulses in neurons. The simplest photoreceptors in conscious vision connect light to movement. In higher organisms the eye is a complex optical system which collects light from the surrounding environment; regulates its intensity through a diaphragm; focuses it through an adjustable assembly of lenses to form an image; converts this image into a set of electrical signals; and transmits these signals to the brain, through complex neural pathways that connect the eye, via the optic nerve, to the visual cortex and other areas of the brain. Eyes with resolving power have come in ten fundamentally different forms, and 96% of animal species possess a complex optical system. Image-resolving eyes are present in molluscs, chordates and arthropods.

The simplest "eyes", such as those in microorganisms, do nothing but detect whether the surroundings are light or dark, which is sufficient for the entrainment of circadian rhythms. From more complex eyes, retinal photosensitive ganglion cells send signals along the retinohypothalamic tract to the suprachiasmatic nuclei to effect circadian adjustment.

Overview

Eye of the wisent, the European bison

Complex eyes can distinguish shapes and colours. The visual fields of many organisms, especially predators, involve large areas of binocular vision to improve depth perception; in other organisms, eyes are located so as to maximize the field of view, such as in rabbits and horses, which have monocular vision.

The first proto-eyes evolved among animals 600 million years ago, about the time of the Cambrian explosion. The last common ancestor of animals possessed the biochemical toolkit necessary for vision, and more advanced eyes have evolved in 96% of animal species in six of the thirty-plus main phyla. In most vertebrates and some molluscs, the eye works by allowing light to enter and project onto a light-sensitive panel of cells, known as the retina, at the rear of the eye. The cone cells (for colour) and the rod cells (for low-light contrasts) in the retina detect and convert light into neural signals for vision. The visual signals are then transmitted to the brain via the optic nerve. Such eyes are typically roughly spherical, filled with a transparent gel-like substance called the vitreous humour, with a focusing lens and often an iris; the relaxing or tightening of the muscles around the iris change the size of the pupil, thereby regulating the amount of light that enters the eye, and reducing aberrations when there is enough light.

The eyes of most cephalopods, fish, amphibians and snakes have fixed lens shapes, and focusing vision is achieved by telescoping the lens—similar to how a camera focuses.

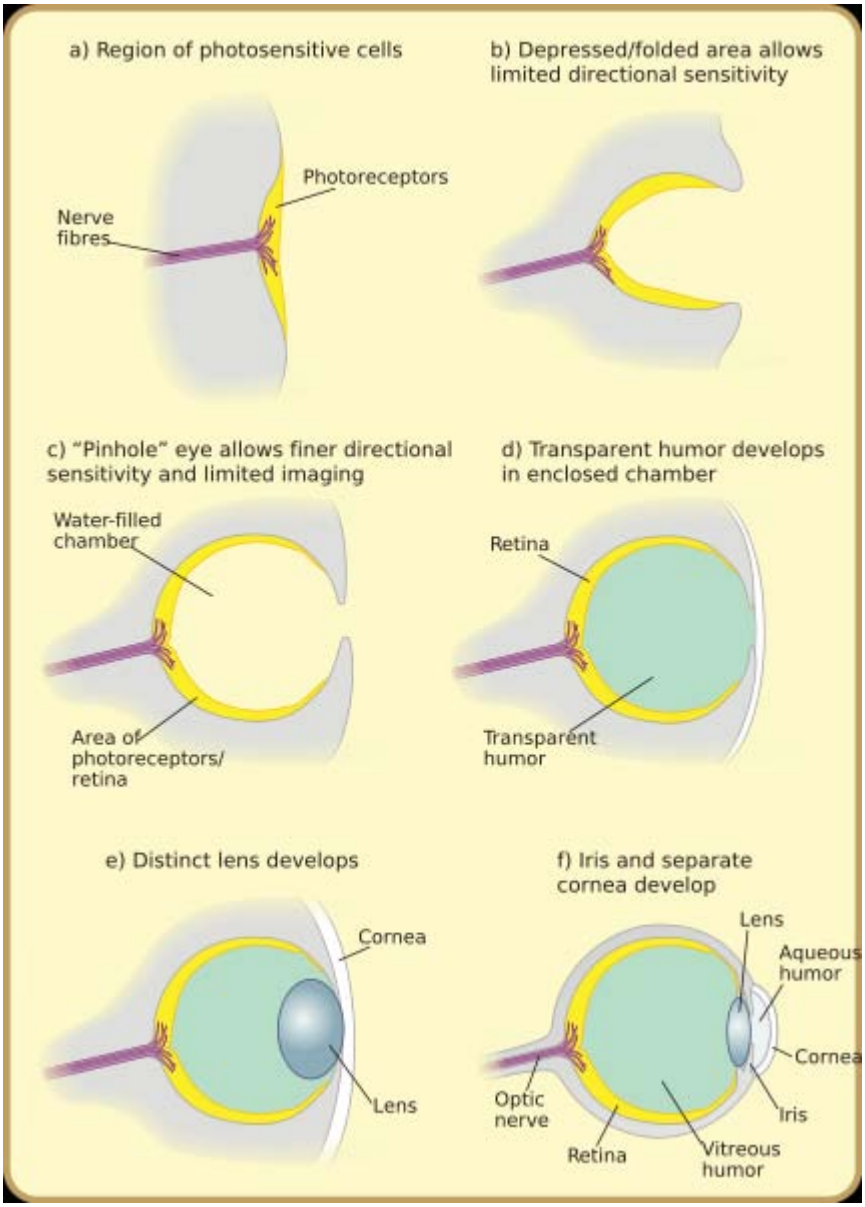
Compound eyes are found among the arthropods and are composed of many simple facets which, depending on the details of anatomy, may give either a single pixelated image or multiple images, per eye. Each sensor has its own lens and photosensitive cell(s). Some eyes have up to 28,000 such sensors, which are arranged hexagonally, and which can give a full 360-degree field of vision. Compound eyes are very sensitive to motion. Some arthropods, including many Strepsiptera, have compound eyes of only a few facets, each with a retina capable of creating an image, creating vision. With each eye viewing a different thing, a fused image from all the eyes is produced in the brain, providing very different, high-resolution images.

Possessing detailed hyperspectral colour vision, the Mantis shrimp has been reported to have the world's most complex colour vision system. Trilobites, which are now extinct, had unique compound eyes. They used clear calcite crystals to form the lenses of their eyes. In this, they differ from most other arthropods, which have soft eyes. The number of lenses in such an eye varied, however: some trilobites had only one, and some had thousands of lenses in one eye.

In contrast to compound eyes, simple eyes are those that have a single lens. For example, jumping spiders have a large pair of simple eyes with a narrow field of view, supported by an array of other, smaller eyes for peripheral vision. Some insect larvae, like caterpillars, have a different type of simple eye (stemmata) which gives a rough image. Some of the simplest eyes, called ocelli, can be found in animals like some of the snails, which cannot actually "see" in the normal sense. They do have photosensitive cells, but no lens and no other means of projecting an image onto these cells. They can distinguish between light and dark, but no more. This enables snails to keep out of direct sunlight. In

organisms dwelling near deep-sea vents, compound eyes have been secondarily simplified and adapted to spot the infra-red light produced by the hot vents–in this way the bearers can spot hot springs and avoid being boiled alive.

Evolution



Evolution of the eye

Photoreception is phylogenetically very old, with various theories of phylogenesis. The common origin (monophyly) of all animal eyes is now widely accepted as fact. This is based upon the shared anatomical and genetic features of all eyes; that is, all modern eyes, varied as they are, have their origins in a proto-eye believed to have evolved some 540 million years ago. The majority of the advancements in early eyes are believed to

have taken only a few million years to develop, since the first predator to gain true imaging would have touched off an "arms race". Prey animals and competing predators alike would be at a distinct disadvantage without such capabilities and would be less likely to survive and reproduce. Hence multiple eye types and subtypes developed in parallel.

Eyes in various animals show adaption to their requirements. For example, birds of prey have much greater visual acuity than humans, and some can see ultraviolet light. The different forms of eye in, for example, vertebrates and mollusks are often cited as examples of parallel evolution, despite their distant common ancestry.

The very earliest "eyes", called eyespots, were simple patches of photoreceptor protein in unicellular animals. In multicellular beings, multicellular eyespots evolved, physically similar to the receptor patches for taste and smell. These eyespots could only sense ambient brightness: they could distinguish light and dark, but not the direction of the lightsource.

Through gradual change, as the eyespot depressed into a shallow "cup" shape, the ability to slightly discriminate directional brightness was achieved by using the angle at which the light hit certain cells to identify the source. The pit deepened over time, the opening diminished in size, and the number of photoreceptor cells increased, forming an effective pinhole camera that was capable of dimly distinguishing shapes.

The thin overgrowth of transparent cells over the eye's aperture, originally formed to prevent damage to the eyespot, allowed the segregated contents of the eye chamber to specialize into a transparent humour that optimized color filtering, blocked harmful radiation, improved the eye's refractive index, and allowed functionality outside of water. The transparent protective cells eventually split into two layers, with circulatory fluid in between that allowed wider viewing angles and greater imaging resolution, and the thickness of the transparent layer gradually increased, in most species with the transparent crystallin protein.

The gap between tissue layers naturally formed a bioconvex shape, an optimally ideal structure for a normal refractive index. Independently, a transparent layer and a nontransparent layer split forward from the lens: the cornea and iris. Separation of the forward layer again formed a humour, the aqueous humour. This increased refractive power and again eased circulatory problems. Formation of a nontransparent ring allowed more blood vessels, more circulation, and larger eye sizes.

Types of eye

There are ten different eye layouts—indeed every way of capturing an optical image commonly used by man, with the exceptions of zoom and Fresnel lenses. Eye types can be categorized into "simple eyes", with one concave photoreceptive surface, and "compound eyes", which comprise a number of individual lenses laid out on a convex surface. Note that "simple" does not imply a reduced level of complexity or acuity.

Indeed, any eye type can be adapted for almost any behaviour or environment. The only limitations specific to eye types are that of resolution—the physics of compound eyes prevents them from achieving a resolution better than 1°. Also, superposition eyes can achieve greater sensitivity than apposition eyes, so are better suited to dark-dwelling creatures. Eyes also fall into two groups on the basis of their photoreceptor's cellular construction, with the photoreceptor cells either being cilliated (as in the vertebrates) or rhabdomeric. These two groups are not monophyletic; the cnidaria also possess cilliated cells, and some annelids possess both.

Non-compound eyes

Simple eyes are rather ubiquitous, and lens-bearing eyes have evolved at least seven times in vertebrates, cephalopods, annelids, crustacea and cubozoa.

Pit eyes

Pit eyes, also known as stemma, are eye-spots which may be set into a pit to reduce the angles of light that enters and affects the eyespot, to allow the organism to deduce the angle of incoming light. Found in about 85% of phyla, these basic forms were probably the precursors to more advanced types of "simple eye". They are small, comprising up to about 100 cells covering about 100 μm. The directionality can be improved by reducing the size of the aperture, by incorporating a reflective layer behind the receptor cells, or by filling the pit with a refractile material.

Pit vipers have developed pits that function as eyes by sensing thermal infra-red radiation, in addition to their optical wavelength eyes like those of other vertebrates.

Spherical lensed eye

The resolution of pit eyes can be greatly improved by incorporating a material with a higher refractive index to form a lens, which may greatly reduce the blur radius encountered—hence increasing the resolution obtainable. The most basic form, seen in some gastropods and annelids, consists of a lens of one refractive index. A far sharper image can be obtained using materials with a high refractive index, decreasing to the edges; this decreases the focal length and thus allows a sharp image to form on the retina. This also allows a larger aperture for a given sharpness of image, allowing more light to enter the lens; and a flatter lens, reducing spherical aberration. Such an inhomogeneous lens is necessary in order for the focal length to drop from about 4 times the lens radius, to 2.5 radii.

Heterogeneous eyes have evolved at least eight times: four or more times in gastropods, once in the copepods, once in the annelids and once in the cephalopods. No aquatic organisms possess homogeneous lenses; presumably the evolutionary pressure for a heterogeneous lens is great enough for this stage to be quickly "outgrown".

This eye creates an image that is sharp enough that motion of the eye can cause significant blurring. To minimize the effect of eye motion while the animal moves, most such eyes have stabilizing eye muscles.

The ocelli of insects bear a simple lens, but their focal point always lies behind the retina; consequently they can never form a sharp image. This capitulates the function of the eye. Ocelli (pit-type eyes of arthropods) blur the image across the whole retina, and are consequently excellent at responding to rapid changes in light intensity across the whole visual field; this fast response is further accelerated by the large nerve bundles which rush the information to the brain. Focusing the image would also cause the sun's image to be focused on a few receptors, with the possibility of damage under the intense light; shielding the receptors would block out some light and thus reduce their sensitivity. This fast response has led to suggestions that the ocelli of insects are used mainly in flight, because they can be used to detect sudden changes in which way is up (because light, especially UV light which is absorbed by vegetation, usually comes from above).

Multiple lenses

Some marine organisms bear more than one lens; for instance the copepod *Pontella* has three. The outer has a parabolic surface, countering the effects of spherical aberration while allowing a sharp image to be formed. Another copepod, *Copilia'*s eyes have two lenses, arranged like those in a telescope. Such arrangements are rare and poorly understood, but represent an interesting alternative construction. An interesting use of multiple lenses is seen in some hunters such as eagles and jumping spiders, which have a refractive cornea (discussed next): these have a negative lens, enlarging the observed image by up to 50% over the receptor cells, thus increasing their optical resolution.

Refractive cornea

In the eyes of most mammals, birds, reptiles, and most other terrestrial vertebrates (along with spiders and some insect larvae) the vitreous fluid has a higher refractive index than the air. In general, the lens is not spherical. Spherical lenses produce spherical aberration. In refractive corneas, the lens tissue is corrected with inhomogeneous lens material, or with an aspheric shape. Flattening the lens has a disadvantage; the quality of vision is diminished away from the main line of focus. Thus, animals that have evolved with a wide field-of-view often have eyes that make use of an inhomogeneous lens.

As mentioned above, a refractive cornea is only useful out of water; in water, there is little difference in refractive index between the vitreous fluid and the surrounding water. Hence creatures that have returned to the water—--penguins and seals, for example---lose their highly curved cornea and return to lens-based vision. An alternative solution, borne by some divers, is to have a very strongly focusing cornea.

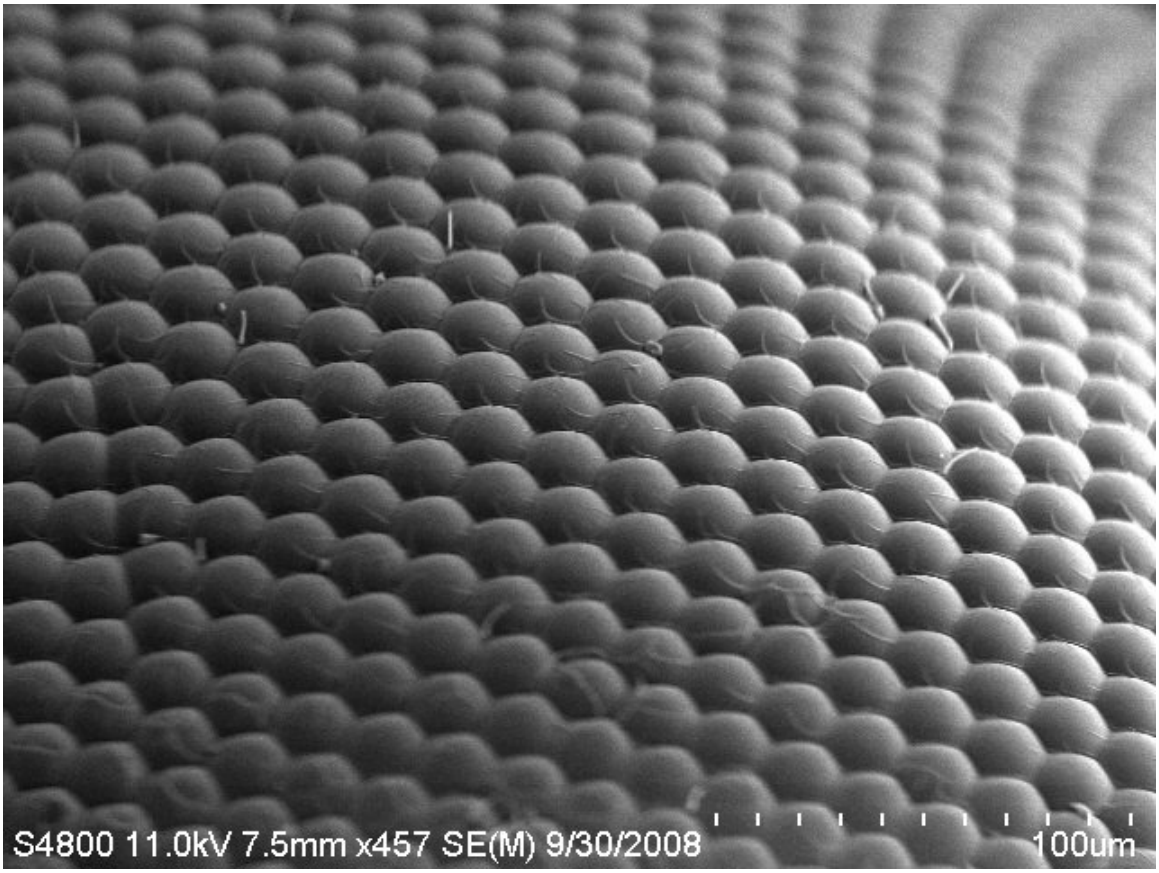
Reflector eyes

An alternative to a lens is to line the inside of the eye with " mirrors", and reflect the image to focus at a central point. The nature of these eyes means that if one were to peer into the pupil of an eye, one would see the same image that the organism would see, reflected back out.

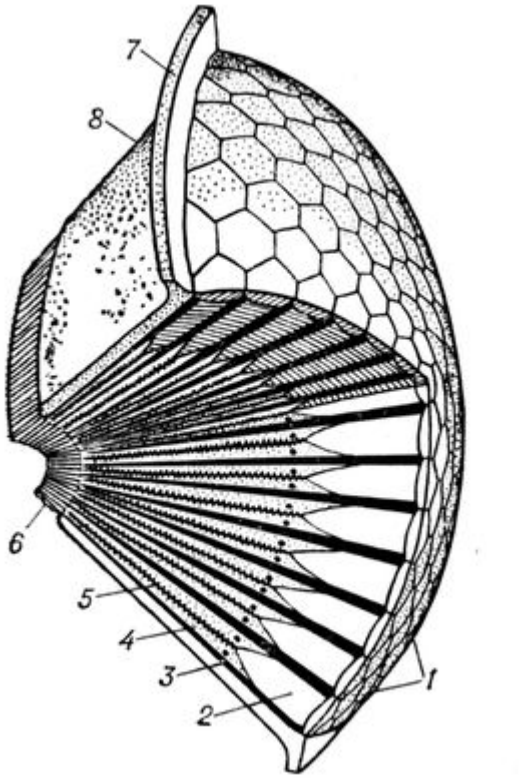
Many small organisms such as rotifers, copeopods and platyhelminths use such organs, but these are too small to produce usable images. Some larger organisms, such as scallops, also use reflector eyes. The scallop *Pecten* has up to 100 millimeter-scale reflector eyes fringing the edge of its shell. It detects moving objects as they pass successive lenses.

There is at least one vertebrate, the spookfish, whose eyes include reflective optics for focusing of light. Each of the two eyes of a spookfish collects light from both above and below; the light coming from above is focused by a lens, while that coming from below, by a curved mirror composed of many layers of small reflective plates made of guanine crystals.

Compound eyes



An image of a house fly compound eye surface by using Scanning Electron Microscope



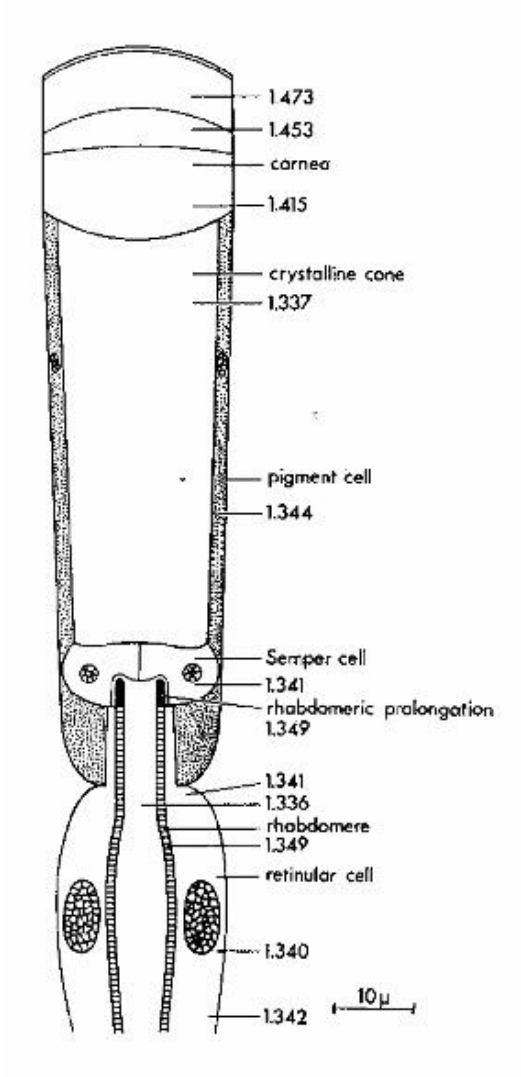
Anatomy of the compound eye of an insect

Arthropods such as this Calliphora vomitoria fly have compound eyes

A compound eye may consist of thousands of individual photoreceptor units or ommatidia (ommatidium, singular). The image perceived is a combination of inputs from the numerous ommatidia (individual "eye units"), which are located on a convex surface, thus pointing in slightly different directions. Compared with simple eyes, compound eyes possess a very large view angle, and can detect fast movement and, in some cases, the polarization of light. Because the individual lenses are so small, the effects of diffraction impose a limit on the possible resolution that can be obtained (assuming that they do not function as phased arrays). This can only be countered by increasing lens size and number. To see with a resolution comparable to our simple eyes, humans would require compound eyes which would each reach the size of their head.

Compound eyes fall into two groups: apposition eyes, which form multiple inverted images, and superposition eyes, which form a single erect image. Compound eyes are common in arthropods, and are also present in annelids and some bivalved molluscs.

Compound eyes, in arthropods at least, grow at their margins by the addition of new ommatidia.



Structure of the ommatidia of apposition compound eyes

Apposition eyes

Apposition eyes are the most common form of eye, and are presumably the ancestral form of compound eye. They are found in all arthropod groups, although they may have evolved more than once within this phylum. Some annelids and bivalves also have apposition eyes. They are also possessed by *Limulus*, the horseshoe crab, and there are suggestions that other chelicerates developed their simple eyes by reduction from a compound starting point. (Some caterpillars appear to have evolved compound eyes from simple eyes in the opposite fashion.)

Apposition eyes work by gathering a number of images, one from each eye, and combining them in the brain, with each eye typically contributing a single point of information.

The typical apposition eye has a lens focusing light from one direction on the rhabdom, while light from other directions is absorbed by the dark wall of the ommatidium. In the other kind of apposition eye, found in the Strepsiptera, lenses are not fused to one another, and each forms an entire image; these images are combined in the brain. This is called the schizochroal compound eye or the neural superposition eye. Because images are combined additively, this arrangement allows vision under lower light levels.

Superposition eyes

The second type is named the superposition eye. The superposition eye is divided into three types; the refracting, the reflecting and the parabolic superposition eye. The refracting superposition eye has a gap between the lens and the rhabdom, and no side wall. Each lens takes light at an angle to its axis and reflects it to the same angle on the other side. The result is an image at half the radius of the eye, which is where the tips of the rhabdoms are. This kind is used mostly by nocturnal insects. In the parabolic superposition compound eye type, seen in arthropods such as mayflies, the parabolic surfaces of the inside of each facet focus light from a reflector to a sensor array. Long-bodied decapod crustaceans such as shrimp, prawns, crayfish and lobsters are alone in having reflecting superposition eyes, which also have a transparent gap but use corner mirrors instead of lenses.

Parabolic superposition

This eye type functions by refracting light, then using a parabolic mirror to focus the image; it combines features of superposition and apposition eyes.

Other

Good fliers like flies or honey bees, or prey-catching insects like praying mantis or dragonflies, have specialized zones of ommatidia organized into a fovea area which gives acute vision. In the acute zone the eyes are flattened and the facets larger. The flattening allows more ommatidia to receive light from a spot and therefore higher resolution.

There are some exceptions from the types mentioned above. Some insects have a so-called single lens compound eye, a transitional type which is something between a superposition type of the multi-lens compound eye and the single lens eye found in animals with simple eyes. Then there is the mysid shrimp *Dioptromysis paucispinosa*. The shrimp has an eye of the refracting superposition type, in the rear behind this in each eye there is a single large facet that is three times in diameter the others in the eye and behind this is an enlarged crystalline cone. This projects an upright image on a specialized retina. The resulting eye is a mixture of a simple eye within a compound eye.

Another version is the pseudofaceted eye, as seen in Scutigera. This type of eye consists of a cluster of numerous ocelli on each side of the head, organized in a way that resembles a true compound eye.

The body of *Ophiocoma wendtii*, a type of brittle star, is covered with ommatidia, turning its whole skin into a compound eye. The same is true of many chitons.

Nutrients of the eye

The **ciliary body** is triangular in horizontal section and is coated by a double layer, the ciliary epithelium. The inner layer is transparent and covers the vitreous body, and is continuous from the neural tissue of the retina. The outer layer is highly pigmented, continuous with the retinal pigment epithelium, and constitutes the cells of the dilator muscle.

The **vitreous** is the transparent, colorless, gelatinous mass that fills the space between the lens of the eye and the retina lining the back of the eye. It is produced by certain retinal cells. It is of rather similar composition to the cornea, but contains very few cells (mostly phagocytes which remove unwanted cellular debris in the visual field, as well as the hyalocytes of Balazs of the surface of the vitreous, which reprocess the hyaluronic acid), no blood vessels, and 98-99% of its volume is water (as opposed to 75% in the cornea) with salts, sugars, vitrosin (a type of collagen), a network of collagen type II fibers with the mucopolysaccharide hyaluronic acid, and also a wide array of proteins in micro amounts. Amazingly, with so little solid matter, it tautly holds the eye.

Relationship to life requirements

Eyes are generally adapted to the environment and life requirements of the organism which bears them. For instance, the distribution of photoreceptors tends to match the area in which the highest acuity is required, with horizon-scanning organisms, such as those that live on the African plains, having a horizontal line of high-density ganglia, while tree-dwelling creatures which require good all-round vision tend to have a symmetrical distribution of ganglia, with acuity decreasing outwards from the centre.

Of course, for most eye types, it is impossible to diverge from a spherical form, so only the density of optical receptors can be altered. In organisms with compound eyes, it is the number of ommatidia rather than ganglia that reflects the region of highest data acquisition.[:23-4] Optical superposition eyes are constrained to a spherical shape, but other forms of compound eyes may deform to a shape where more ommatidia are aligned to, say, the horizon, without altering the size or density of individual ommatidia. Eyes of horizon-scanning organisms have stalks so they can be easily aligned to the horizon when this is inclined, for example if the animal is on a slope. An extension of this concept is that the eyes of predators typically have a zone of very acute vision at their centre, to assist in the identification of prey. In deep water organisms, it may not be the centre of the eye that is enlarged. The hyperiid amphipods are deep water animals that feed on organisms above them. Their eyes are almost divided into two, with the upper region thought to be involved in detecting the silhouettes of potential prey—or predators—against the faint light of the sky above. Accordingly, deeper water hyperiids, where the light against which the silhouettes must be compared is dimmer, have larger "upper-eyes", and may lose the lower portion of their eyes altogether. Depth perception can be

enhanced by having eyes which are enlarged in one direction; distorting the eye slightly allows the distance to the object to be estimated with a high degree of accuracy.

Acuity is higher among male organisms that mate in mid-air, as they need to be able to spot and assess potential mates against a very large backdrop. On the other hand, the eyes of organisms which operate in low light levels, such as around dawn and dusk or in deep water, tend to be larger to increase the amount of light that can be captured.

It is not only the shape of the eye that may be affected by lifestyle. Eyes can be the most visible parts of organisms, and this can act as a pressure on organisms to have more transparent eyes at the cost of function.

Eyes may be mounted on stalks to provide better all-round vision, by lifting them above an organism's carapace; this also allows them to track predators or prey without moving the head.

Visual acuity

A hawk's eye

Visual acuity, or resolving power, is "the ability to distinguish fine detail" and is the property of cones. It is often measured in *cycles per degree* (CPD), which measures an angular resolution, or how much an eye can differentiate one object from another in terms of visual angles. Resolution in CPD can be measured by bar charts of different numbers of white/black stripe cycles. For example, if each pattern is 1.75 cm wide and is placed at 1 m distance from the eye, it will subtend an angle of 1 degree, so the number of white/black bar pairs on the pattern will be a measure of the cycles per degree of that pattern. The highest such number that the eye can resolve as stripes, or distinguish from a gray block, is then the measurement of visual acuity of the eye.

For a human eye with excellent acuity, the maximum theoretical resolution is 50 CPD (1.2 arcminute per line pair, or a 0.35 mm line pair, at 1 m). A rat can resolve only about 1 to 2 CPD. A horse has higher acuity through most of the visual field of its eyes than a human has, but does not match the high acuity of the human eye's central fovea region.

Spherical aberration limits the resolution of a 7 mm pupil to about 3 arcminutes per line pair. At a pupil diameter of 3 mm, the spherical aberration is greatly reduced, resulting in an improved resolution of approximately 1.7 arcminutes per line pair. A resolution of 2 arcminutes per line pair, equivalent to a 1 arcminute gap in an optotype, corresponds to 20/20 (normal vision) in humans.

Perception of colours

"Colour vision is the faculty of the organism to distinguish lights of different spectral qualities." All organisms are restricted to a small range of electromagnetic spectrum; this varies from creature to creature, but is mainly between 400 and 700 nm. This is a rather small section of the electromagnetic spectrum, probably reflecting the submarine evolution of the organ: water blocks out all but two small windows of the EM spectrum, and there has been no evolutionary pressure among land animals to broaden this range.

The most sensitive pigment, rhodopsin, has a peak response at 500 nm. Small changes to the genes coding for this protein can tweak the peak response by a few nm; pigments in the lens can also filter incoming light, changing the peak response. Many organisms are unable to discriminate between colours, seeing instead in shades of grey; colour vision necessitates a range of pigment cells which are primarily sensitive to smaller ranges of the spectrum. In primates, geckos, and other organisms, these take the form of cone cells, from which the more sensitive rod cells evolved. Even if organisms are physically capable of discriminating different colours, this does not necessarily mean that they can perceive the different colours; only with behavioural tests can this be deduced.

Most organisms with colour vision are able to detect ultraviolet light. This high energy light can be damaging to receptor cells. With a few exceptions (snakes, placental mammals), most organisms avoid these effects by having absorbent oil droplets around their cone cells. The alternative, developed by organisms that had lost these oil droplets in the course of evolution, is to make the lens impervious to UV light — this precludes the possibility of any UV light being detected, as it does not even reach the retina.

Rods and cones

The retina contains two major types of light-sensitive photoreceptor cells used for vision: the rods and the cones.

Rods cannot distinguish colours, but are responsible for low-light (scotopic) monochrome (black-and-white) vision; they work well in dim light as they contain a pigment, rhodopsin (visual purple), which is sensitive at low light intensity, but saturates at higher (photopic) intensities. Rods are distributed throughout the retina but there are none at the fovea and none at the blind spot. Rod density is greater in the peripheral retina than in the central retina.

Cones are responsible for colour vision. They require brighter light to function than rods require. In humans, there are three types of cones, maximally sensitive to long-wavelength, medium-wavelength, and short-wavelength light (often referred to as red, green, and blue, respectively, though the sensitivity peaks are not actually at these colours). The colour seen is the combined effect of stimuli to, and responses from, these three types of cone cells. Cones are mostly concentrated in and near the fovea. Only a few are present at the sides of the retina. Objects are seen most sharply in focus when their images fall on the fovea, as when one looks at an object directly. Cone cells and rods are connected through intermediate cells in the retina to nerve fibres of the optic nerve. When rods and cones are stimulated by light, the nerves send off impulses through these fibres to the brain.

Pigmentation

The pigment molecules used in the eye are various, but can be used to define the evolutionary distance between different groups, and can also be an aid in determining which are closely related – although problems of convergence do exist.

Opsins are the pigments involved in photoreception. Other pigments, such as melanin, are used to shield the photoreceptor cells from light leaking in from the sides. The opsin protein group evolved long before the last common ancestor of animals, and has continued to diversify since.

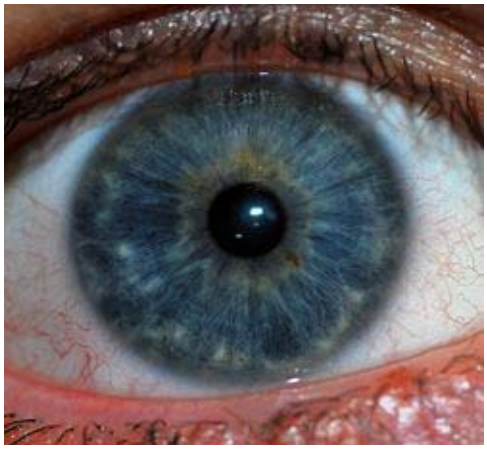
There are two types of opsin involved in vision; c-opsins, which are associated with ciliary-type photoreceptor cells, and r-opsins, associated with rhabdomeric photoreceptor cells. The eyes of vertebrates usually contain cilliary cells with c-opsins, and (bilaterian) invertebrates have rhabdomeric cells in the eye with r-opsins. However, some *ganglion* cells of vertebrates express r-opsins, suggesting that their ancestors used this pigment in vision, and that remnants survive in the eyes. Likewise, c-opsins have been found to be expressed in the *brain* of some invertebrates. They may have been expressed in ciliary cells of larval eyes, which were subsequently resorbed into the brain on metamorphosis to the adult form. C-opsins are also found in some derived bilaterian-invertebrate eyes, such as the pallial eyes of the bivalve molluscs; however, the lateral eyes (which were presumably the ancestral type for this group, if eyes evolved once there) always use r-

opsins. Cnidaria, which are an outgroup to the taxa mentioned above, express c-opsins - but r-opsins are yet to be found in this group. Incidentally, the melanin produced in the cnidaria is produced in the same fashion as that in vertebrates, suggesting the common descent of this pigment.

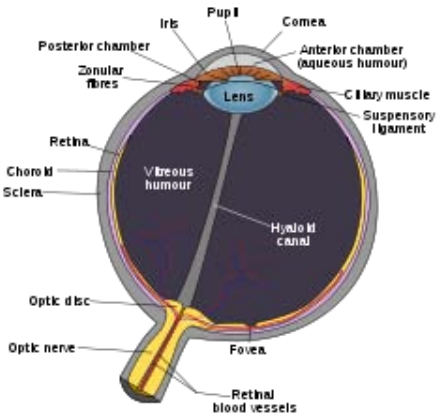
Chapter 2

Iris (Anatomy)

Iris



The **iris** is the blue area. The other structures visible are the pupil center and the white sclera surrounding the iris. The overlying cornea is pictured, but not visible, as it is transparent.



Schematic diagram of the human eye. (Iris labeled at upper left.)

Gray's	*subject #225 1012*
Artery	long posterior ciliary arteries
Nerve	long ciliary nerves, short ciliary nerves
MeSH	*Iris*

Dorlands/Elsevier *Iris*

The **iris** (plural: ***irides***, or rarely, irises) is a thin, circular structure in the eye, responsible for controlling the diameter and size of the pupils and thus the amount of light reaching the retina. "Eye color" is the color of the iris, which can be green, blue, or brown. In some cases it can be hazel (a combination of light brown, green and gold) or grey. In response to the amount of light entering the eye, muscles attached to the iris expand or contract the aperture at the center of the iris, known as the pupil. The larger the pupil, the more light can enter.

General structure

The iris consists of two layers: the front pigmented fibrovascular tissue known as a stroma and, beneath the stroma, pigmented epithelial cells.

The stroma connects to a sphincter muscle (sphincter pupillae), which contracts the pupil in a circular motion, and a set of dilator muscles (dilator pupillae) which pull the iris radially to enlarge the pupil, pulling it in folds. The back surface is covered by a heavily pigmented epithelial layer that is two cells thick (the iris pigment epithelium), but the front surface has no epithelium. This anterior surface projects as the dilator muscles. The high pigment content blocks light from passing through the iris to the retina, restricting it to the pupil. The outer edge of the iris, known as the root, is attached to the sclera and the anterior ciliary body. The iris and ciliary body together are known as the anterior uvea. Just in front of the root of the iris is the region referred to as the trabecular meshwork, through which the aqueous humour constantly drains out of the eye, with the result that diseases of the iris often have important effects on intraocular pressure, and body provide a lesser secondary pathway for the aqueous humour to drain from the eye.

The iris is divided into two major regions:

1. The **pupillary zone** is the inner region whose edge forms the boundary of the pupil.
2. The **ciliary zone** is the rest of the iris that extends to its origin at the ciliary body.

The **collarette** is the thickest region of the iris, separating the pupillary portion from the ciliary portion. The collarette is a rudiment of the coating of the embryonic pupil. It is typically defined as the region where the sphincter muscle and dilator muscle overlap.

Radial ridges extend from the periphery to the pupillary zone, to supply the iris with blood vessels. The root of the iris is the thinnest and most peripheral.

The muscle cells of the iris are smooth muscle in mammals and amphibians, but are striated muscle in birds and reptiles. Many fish have neither, and, as a result, their irises are unable to dilate and contract, so that the pupil always remains of a fixed size.

Histological features

From anterior (front) to posterior (back), the layers of the iris are:

- Anterior limiting layer
- Stroma of iris
- Iris sphincter muscle
- Iris dilator muscle
- Anterior pigment myoepithelium
- Posterior pigment epithelium

Anterior surface features

- The **Crypts of Fuchs** are a series of openings located on either side of the collarette that allow the stroma and deeper iris tissues to be bathed in aqueous humor. Collagen trabeculae that surround the border of the crypts can be seen in blue irides.
- The **pupillary ruffs** (crenations) are a series of small ridges at the pupillary margin formed by the continuation of the pigmented epithelium from the posterior surface.
- The **Circular contraction folds**, also known as **contraction furrows**, are a series of circular bands or folds about midway between the collarette and the origin of the iris. These folds result from changes in the surface of the iris as it dilates.
- **Crypts at the base of the iris** are additional openings that can be observed close to the outermost part of the ciliary portion of the iris.

Posterior surface features

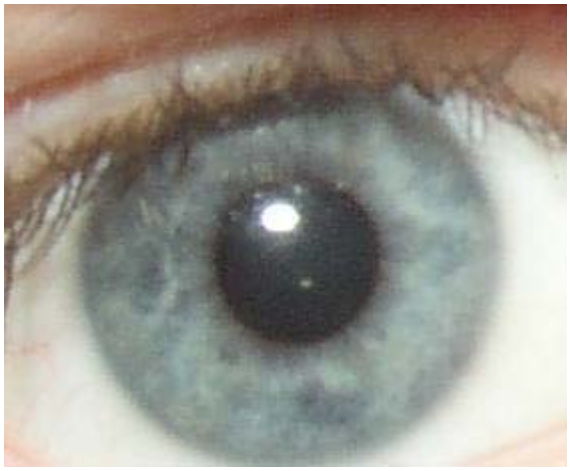
- The **Radial contraction folds of Schwalbe** are a series of very fine radial folds in the pupillary portion of the iris extending from the pupillary margin to the collarette. They are associated with the scalloped appearance of the pupillary ruff.
- The **Structural folds of Schwalbe** are radial folds extending from the border of the ciliary and pupillary zones that are much broader and more widely-spaced, continuous with the "valleys" between the ciliary processes.
- Some of the **Circular contraction folds** are a fine series of ridges that run near the pupillary margin and vary in thickness of the iris pigment epithelium; others are in ciliary portion of iris. It changes colors like a rainbow.

Among human phenotypes, Blue-Green-Grey eyes are a relatively rare eye color and the exact color is often perceived to vary according to its surroundings.

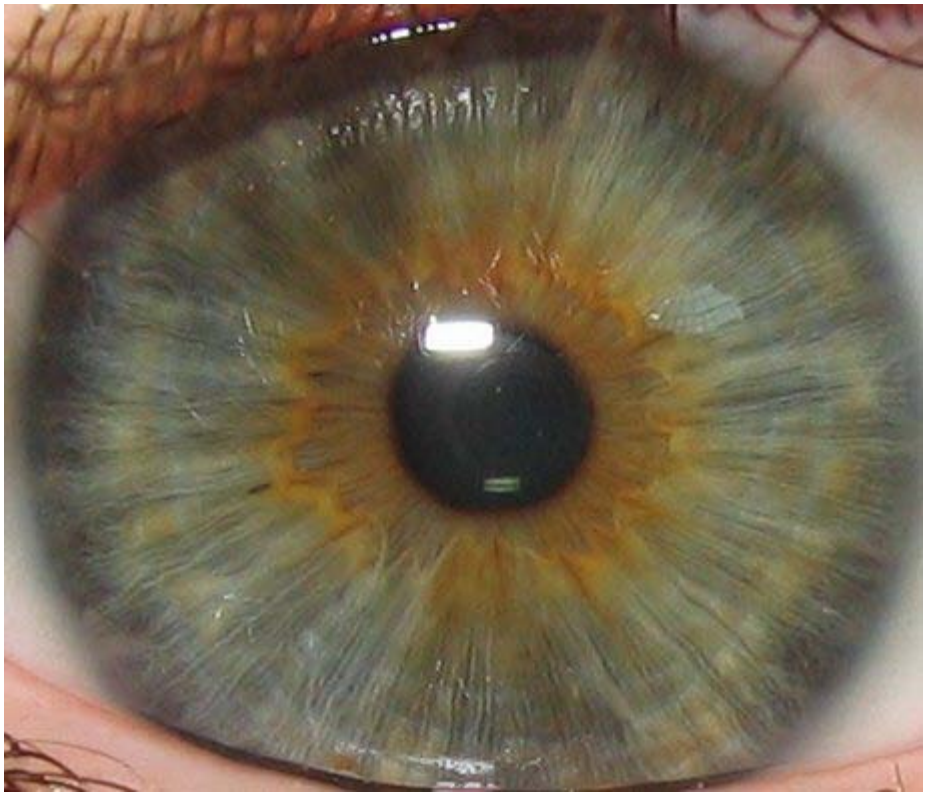
The iris is usually strongly pigmented, with colors ranging from brown to green, blue, grey, and hazel (which is how it earned its name, iris being Greek for "rainbow"1). Occasionally its color is due to lack of pigmentation, as in the pinkish-white of oculo-cutaneous albinism, or to obscuration of its pigment by blood vessels, as in the red of an abnormally vascularised iris. Despite the wide range of colors, there is only one pigment that contributes substantially to normal human iris color, the dark pigment called melanin. Structurally, this huge molecule is only slightly different from its equivalent found in skin and hair.

Genetic and physical factors determining iris color

Iris color is a highly complex phenomenon consisting of the combined effects of texture, pigmentation, fibrous tissue and blood vessels within the iris stroma, which together make up an individual's epigenetic constitution in this context. A person's "eye color" is actually the color of one's iris, the cornea being transparent and the white sclera entirely outside the area of interest. It is a common misconception that the iris color is entirely due to its melanin pigment; this varies only from brown to black.



An example of a Blue-Grey Iris



An example of a Grey/Green-Brown Iris

An example of a Brown iris

Melanin is yellowish-brown to dark brown in the stromal pigment cells, and black in the iris pigment epithelium, which lies in a thin but very opaque layer across the back of the iris. Most human irises also show a condensation of the brownish stromal melanin in the thin anterior border layer, which by its position has an overt influence on the overall color. The degree of dispersion of the melanin, which is in subcellular bundles called melanosomes, has some influence on the observed color, but melanosomes in the iris of humans and other vertebrates are not mobile, and the degree of pigment dispersion cannot be reversed. Abnormal clumping of melanosomes does occur in disease and may lead to irreversible changes in iris color. Colors other than brown or black are due to selective reflection and absorption from the other stromal components. Sometimes lipofuscin, a yellow "wear and tear" pigment also enters into the visible eye color, especially in aged or diseased green eyes (but not in healthy green human eyes).

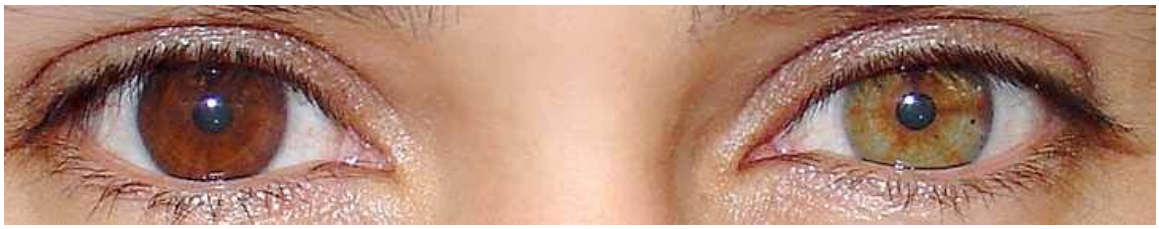
The optical mechanisms by which the non-pigmented stromal components influence eye color are complex, and many erroneous statements exist in the literature. Simple selective absorption and reflection by biological molecules (hemoglobin in the blood vessels, collagen in the vessel and stroma) is the most important element. Rayleigh scattering and

Tyndall scattering, (which also happen in the sky) and diffraction also occur. Raman scattering, and constructive interference, as in the feathers of birds, do not contribute to the color of the human eye, but interference phenomena are important in the brilliantly colored iris pigment cells (iridophores) in many animals. Interference effects can occur at both molecular and light microscopic scales, and are often associated (in melanin-bearing cells) with quasi-crystalline formations which enhance the optical effects. Interference is recognised by characteristic dependence of color on the angle of view, as seen in eyespots of some butterfly wings, although the chemical components remain the same.

Caucasian babies are born blue-eyed since there is no pigment in the stroma, and appear blue due to scattering and selective absorption from the posterior epithelium. If melanin is deposited substantially, there will be brown or black color, if not, they will remain blue or grey.

Blue is one of the possible eye colors in humans. The "blue" allele, existing in the Bey2 and Gey genes of chromosome 15, is recessive. This means that both genes must have both blue alleles i.e. "blue-blue", in a person with blue eyes. If one of the alleles were not "blue" ("green" for Gey or "brown" for Bey2) then the person would have those colored eyes respectively. As either allele (though not both) can be passed on to offspring it is perfectly possible for someone who does not have blue eyes to have blue-eyed children. In general, blue eyed parents have blue eyed children; rare exceptions occur due to genes which control the pathway to determining eye color. Though this explanation gives an idea of eye color delineation, it is incomplete, and all the contributing factors towards eye color and its variation are not fully understood. Autosomal recessive/dominant traits in iris color are inherent in other species but coloration can follow a different pattern.

Different colors in the two eyes



An example of heterochromia. The subject has a brown and hazel eye.

Heterochromia (also known as a *heterochromia iridis* or *heterochromia iridium*) is an ocular condition in which one iris is a different color from the other iris (complete heterochromia), or where the part of one iris is a different color from the remainder (partial heterochromia or sectoral heterochromia). Uncommon in humans, it is often an indicator of ocular disease, such as chronic iritis or diffuse iris melanoma, but may also occur as a normal variant. Sectors or patches of strikingly different colors in the same iris are less common. Alexander the Great and Anastasios the First were dubbed **dikoro*s** (*dikoros*, "with two pupils") for their patent *heterochromias*. In their case, this was not a true *dicoria* (two pupils in the same iris). Real polycoria can be due to disease but is most often due to previous trauma or surgery.

In contrast, heterochromia and variegated iris patterns are common in veterinary practice. Siberian Huskies show heterochromia, possibly analogous to the genetically-determined Waardenburg syndrome of humans. Some white cat fancies (e.g., white Turkish Angora or white Turkish van cats) may show striking heterochromia, with the most common pattern being one uniformly blue, the other copper, orange, yellow or green. Striking variation within the same iris is also common in some animals, and is the norm in some species. Several herding breeds, particularly those with a blue merle coat color (such as Australian Shepherds and Border Collies) may show well-defined blue areas within a brown iris as well as separate blue and darker eyes. Some horses (usually within the white, spotted, palomino or cremello groups of breeds) may show amber, brown, white, and blue all within the same eye, without any sign of eye disease.

One eye with a white or bluish-white iris is also known as a *walleye*.

Conjunctivitis

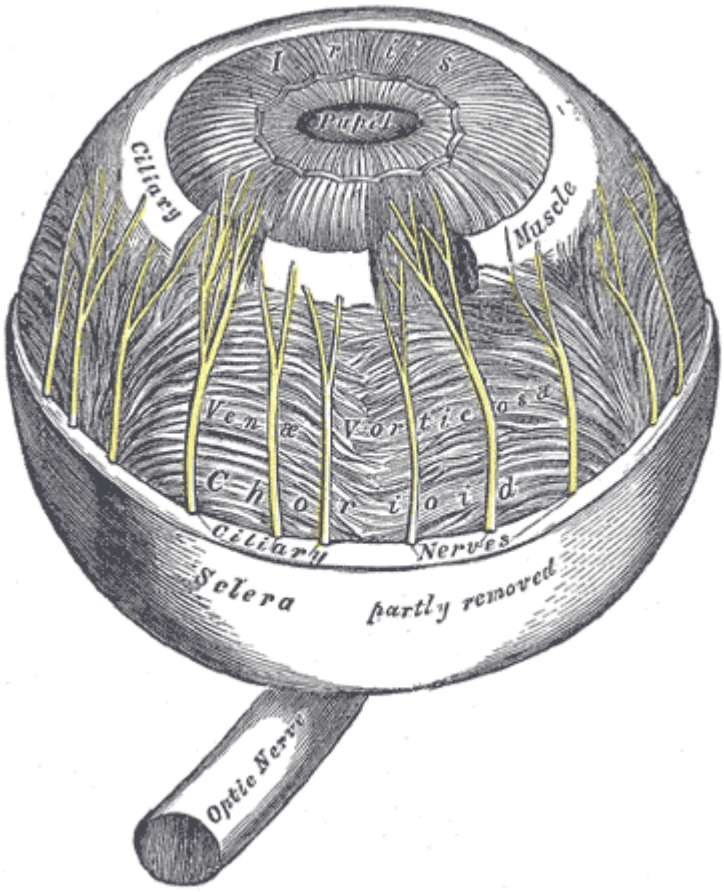
When photographed with a flash, the iris constricts but not fast enough to avoid the red-eye effect. This represents reflection of light from the back of the eye, and is closely related to the term *red reflex*, used by ophthalmologists and optometrists in describing appearances on fundal examination. "Red eye" is also commonly visible in photographs, giving them the "vampire effect."

When used as a descriptive term in medicine, the meaning of "**red eye**" is quite different, and indicates that the bulbar conjunctiva is reddened due to dilatation of superficial blood vessels. Leaving aside rarities, it indicates surface infection (conjunctivitis), intraocular inflammation (e.g., iridocyclitis) or high intraocular pressure (acute glaucoma or occasionally severe, untreated chronic glaucoma). This use of "red eye" implies disease. The term is therefore not used in medicine for ocular albinism, in which the eye is otherwise healthy despite an obviously red pupil and a translucent pinkish iris due to reflected light from the fundus. "Red eye" is used more loosely in veterinary practice, where investigation of eye diseases can be difficult, but even so albinotic breeds are easily recognised and are usually described as having "pink eye" rather than "red eye".

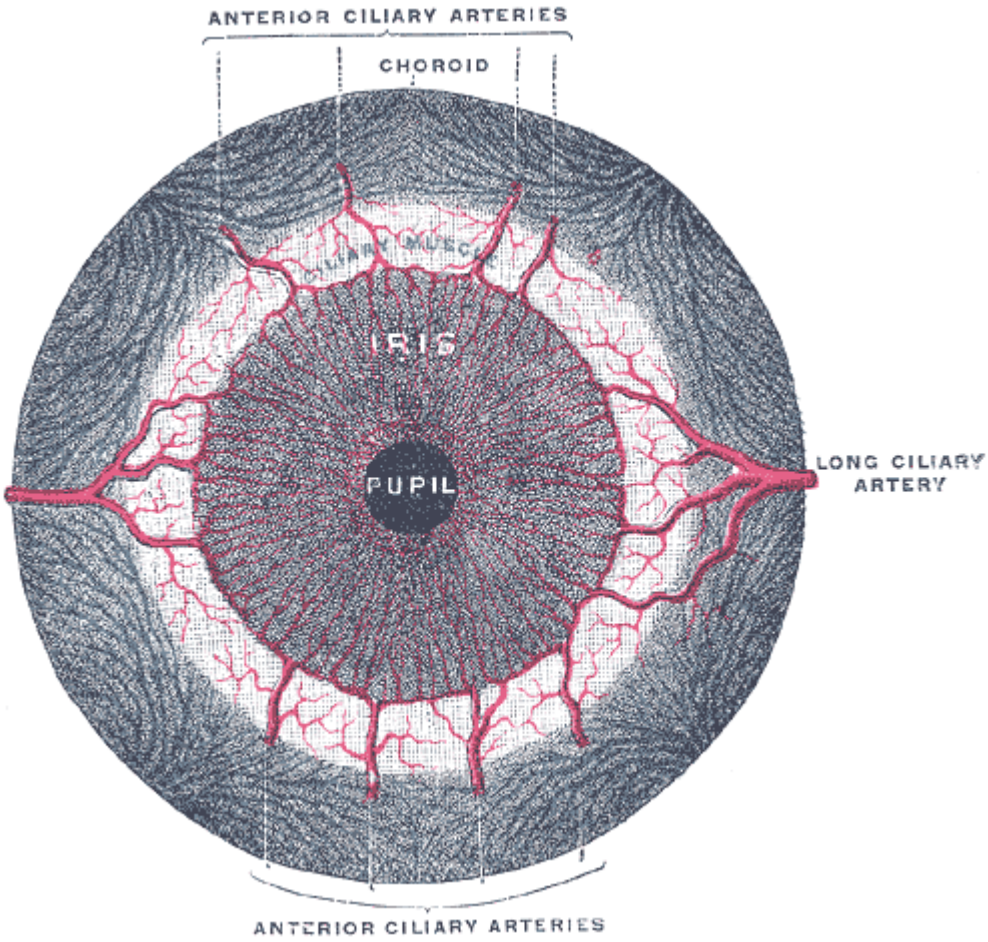
Alternative medicine

Iridology (also known as **iridodiagnosis**) is an alternative medicine technique whose proponents believe that patterns, colors, and other characteristics of the iris can be examined to determine information about a patient's systemic health. Practitioners match their observations to *iris charts* which divide the iris into zones corresponding to specific parts of the human body. Iridologists see the eyes as "windows" into the body's state of health.

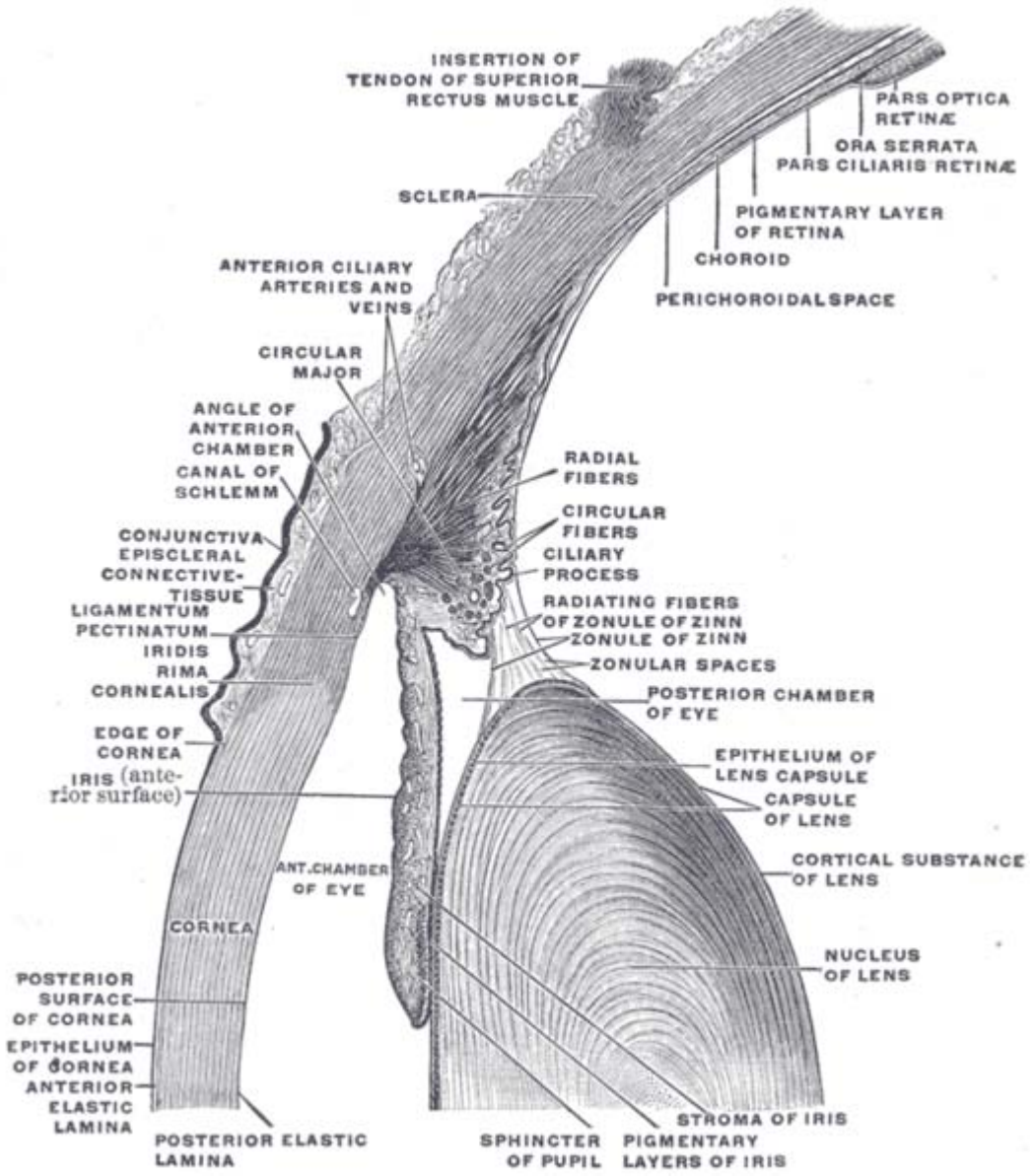
Iridology is not supported by quality research studies and is considered pseudoscience and quackery by most medical practitioners and eye care professionals.



The choroid and iris



Iris, front view

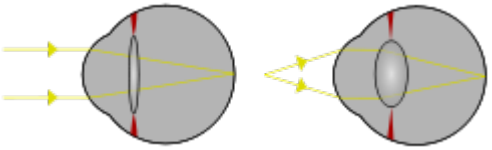


The upper half of a sagittal section through the front of the eyeball

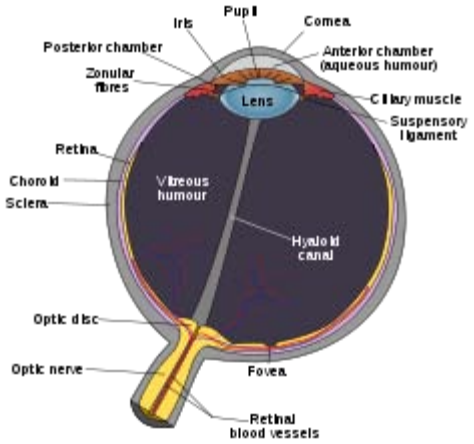
Chapter 3

Lens (Anatomy)

Lens (anatomy)



Light from a single point of a distant object and light from a single point of a near object being brought to a focus by changing the curvature of the lens.



Schematic diagram of the human eye.

Latin	*lens crystallina*
Gray's	*subject #226 1019*
MeSH	*Crystalline+lens*

The **lens** is a transparent, biconvex structure in the eye that, along with the cornea, helps to refract light to be focused on the retina. The lens, by changing shape, functions to change the focal distance of the eye so that it can focus on objects at various distances,

thus allowing a sharp real image of the object of interest to be formed on the retina. This adjustment of the lens is known as accommodation. It is similar to the focusing of a photographic camera via movement of its lenses. The lens is flatter on its anterior side.

The lens is also known as the *aquula* (Latin, *a little stream*, dim. of *aqua*, *water*) or *crystalline lens*. In humans, the refractive power of the lens in its natural environment is approximately 18 dioptres, roughly one-third of the eye's total power.

Position, size, and shape

The lens is part of the anterior segment of the eye. Anterior to the lens is the iris, which regulates the amount of light entering into the eye. The lens is suspended in place by the zonular fibers, which attach to the lens near its equatorial line and connect the lens to the ciliary body. Posterior to the lens is the vitreous body, which, along with the aqueous humor on the anterior surface, bathes the lens. The lens has an ellipsoid, biconvex shape. The anterior surface is less curved than the posterior. In the adult, the lens is typically circa 10 mm in diameter and has an axial length of about 4 mm, though it is important to note that the size and shape can change due to accommodation and because the lens continues to grow throughout a person’s lifetime.

Variations among vertebrates

In many aquatic vertebrates, the lens is considerably thicker, almost spherical, to increase the refraction of light. This difference compensates for the smaller angle of refraction between the eye's cornea and the watery medium, as they have similar refractive indices. Even among terrestrial animals, however, the lens of primates such as humans is unusually flat.

In reptiles and birds, the ciliary body touches the lens with a number of pads on its inner surface, in addition to the zonular fibres. These pads compress and release the lens to modify its shape while focusing on objects at different distances; the zonular fibres perform this function in mammals. In fish and amphibians, the lens is fixed in shape, and focusing is instead achieved by moving the lens forwards or backwards within the eye.

In cartilaginous fish the zonular fibres are replaced by a membrane, including a small muscle at the underside of the lens. This muscle pulls the lens forward from its relaxed position when focusing on nearby objects. In teleosts, by contrast, a muscle projects from a vascular structure in the floor of the eye, called the *falciform process*, and serves to pull the lens backwards from the relaxed position to focus on distant objects. While amphibians move the lens forward, as do cartilaginous fish, the muscles involved are not homologous with those of either type of fish. In frogs, there are two muscles, one above and one below the lens, while other amphibians have only the lower muscle.

In the most primitive vertebrates, the lampreys and hagfish, the lens is not attached to the outer surface of the eyeball at all. There is no aqueous humour in these fish, and the vitreous body simply presses the lens against the surface of the cornea. To focus its eyes,

a lamprey flattens the cornea using muscles outside of the eye, and pushes the lens backwards.

Lens structure and function

The lens has three main parts: the lens capsule, the lens epithelium, and the lens fibers. The lens capsule forms the outermost layer of the lens and the lens fibers form the bulk of the interior of the lens. The cells of the lens epithelium, located between the lens capsule and the outermost layer of lens fibers, are found only on the anterior side of the lens.

Lens capsule

The lens capsule is a smooth, transparent basement membrane that completely surrounds the lens. The capsule is elastic and is composed of collagen. It is synthesized by the lens epithelium and its main components are Type IV collagen and sulfated glycosaminoglycans (GAGs). The capsule is very elastic and so causes the lens to assume a more globular shape when not under the tension of the zonular fibers, which connect the lens capsule to the ciliary body. The capsule varies from 2-28 micrometres in thickness, being thickest near the equator and thinnest near the posterior pole.' The lens capsule may be involved with the higher anterior curvature than posterior of the lens.

Lens epithelium

The lens epithelium, located in the anterior portion of the lens between the lens capsule and the lens fibers, is a simple cuboidal epithelium. The cells of the lens epithelium regulate most of the homeostatic functions of the lens. As ions, nutrients, and liquid enter the lens from the aqueous humor, Na+/K+ ATPase pumps in the lens epithelial cells pump ions out of the lens to maintain appropriate lens osmolarity and volume, with equatorially positioned lens epithelium cells contributing most to this current. The activity of the Na+/K+ ATPases keeps water and current flowing through the lens from the poles and exiting through the equatorial regions.

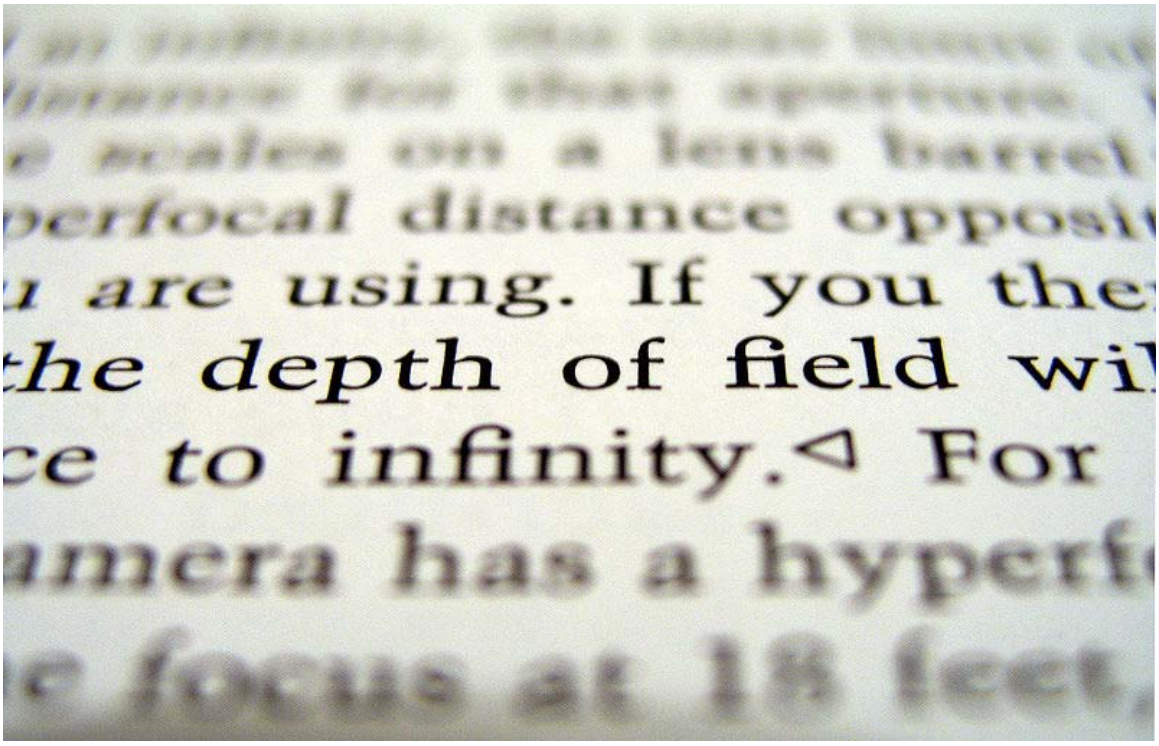
The cells of the lens epithelium also serve as the progenitors for new lens fibers. It constantly lays down fibers in the embryo, fetus, infant, and adult, and continues to lay down fibers for lifelong growth.

Lens fibers

The lens fibers form the bulk of the lens. They are long, thin, transparent cells, firmly packed, with diameters typically between 4-7 micrometres and lengths of up to 12 mm long. The lens fibers stretch lengthwise from the posterior to the anterior poles and, when cut horizontally, are arranged in concentric layers rather like the layers of an onion. If cut along the equator, it appears as a honeycomb. The middle of each fiber lies on the equator. These tightly packed layers of lens fibers are referred to as laminae. The lens fibers are linked together via gap junctions and interdigitations of the cells that resemble “ball and socket” forms.

The lens is split into regions depending on the age of the lens fibers of a particular layer. Moving outwards from the central, oldest layer, the lens is split into an embryonic nucleus, the fetal nucleus, the adult nucleus, and the outer cortex. New lens fibers, generated from the lens epithelium, are added to the outer cortex. Mature lens fibers have no organelles or nuclei.

Accommodation: changing the power of the lens



An image that is partially in focus, but mostly out of focus in varying degrees

The lens is flexible and its curvature is controlled by ciliary muscles through the zonules. By changing the curvature of the lens, one can focus the eye on objects at different distances from it. This process is called accommodation. At short focal distance the ciliary muscle contracts, zonule fibers loosen, and the lens thickens, resulting in a rounder shape and thus high refractive power. Changing focus to an object at a greater distance requires the relaxation of the ciliary muscle, which in turn increases the tension on the zonules, flattening the lens and thus increasing the focal distance.

The refractive index of the lens varies from approximately 1.406 in the central layers down to 1.386 in less dense cortex of the lens. This index gradient enhances the optical power of the lens.

Aquatic animals must rely entirely on their lens for both focusing and to provide almost the entire refractive power of the eye as the water-cornea interface does not have a large enough difference in indices of refraction to provide significant refractive power. As such, lenses in aquatic eyes tend to be much rounder and harder.

Crystallins and transparency

Crystallins are water-soluble proteins that compose over 90% of the protein within the lens. The three main crystallin types found in the human eye are α-, β-, and γ-crystallins. Crystallins tend to form soluble, high-molecular weight aggregates that pack tightly in lens fibers, thus increasing the index of refraction of the lens while maintaining its transparency. β and γ crystallins are found primarily in the lens, while subunits of α -crystallin have been isolated from other parts of the eye and the body. α-crystallin proteins belong to a larger superfamily of molecular chaperone proteins, and so it is believed that the crystallin proteins were evolutionarily recruited from chaperone proteins for optical purposes. The chaperone functions of α -crystallin may also help maintain the lens proteins, which must last a human for his/her entire lifetime.

Another important factor in maintaining the transparency of the lens is the absence of light-scattering organelles such as the nucleus, endoplasmic reticulum, and mitochondria within the mature lens fibers. Lens fibers also have a very extensive cytoskeleton that maintains the precise shape and packing of the lens fibers; disruptions/mutations in certain cytoskeletal elements can lead to the loss of transparency.

Development and growth

Development of the human lens begins at the 4 mm embryonic stage. Unlike the rest of the eye, which is derived mostly from the neural ectoderm, the lens is derived from the surface ectoderm. The first stage of lens differentiation takes place when the optic vesicle, which is formed from outpocketings in the neural ectoderm, comes in proximity to the surface ectoderm. The optic vesicle induces nearby surface ectoderm to form the lens placode. At the 4 mm stage, the lens placode is a single monolayer of columnar cells.

As development progresses, the lens placode begins to deepen and invaginate. As the placode continues to deepen, the opening to the surface ectoderm constricts and the lens cells forms a structure known as the lens vesicle. By the 10 mm stage, the lens vesicle has completely separated from the surface ectoderm.

After the 10 mm stage, signals from the developing neural retina induces the cells closest to the posterior end of the lens vesicle begin to elongate toward the anterior end of the vesicle. These signals also induce the synthesis of crystallins. These elongating cells eventually fill in the lumen of the vesicle to form the primary fibers, which become the embryonic nucleus in the mature lens. The cells of the anterior portion of the lens vesicle give rise to the lens epithelium.

Additional secondary fibers are derived from lens epithelial cells located toward the equatorial region of the lens. These cells lengthen anteriorly and posteriorly to encircle the primary fibers. The new fibers grow longer than those of the primary layer, but as the lens gets larger, the ends of the newer fibers cannot reach the posterior or anterior poles of the lens. The lens fibers that do not reach the poles form tight, interdigitating seams with neighboring fibers. These seams are readily visible and are termed sutures. The

suture patterns become more complex as more layers of lens fibers are added to the outer portion of the lens.

The lens continues to grow after birth, with the new secondary fibers being added as outer layers. New lens fibers are generated from the equatorial cells of the lens epithelium, in a region referred to as the germinative zone. The lens epithelial cells elongate, lose contact with the capsule and epithelium, synthesize crystallin, and then finally lose their nuclei (enucleate) as they become mature lens fibers.From development through early adulthood, the addition of secondary lens fibers results in the lens growing more ellipsoid in shape; after about age 20, however, the lens grows rounder with time.

Nourishment

The lens is metabolically active and requires nourishment in order to maintain its growth and transparency. Compared to other tissues in the eye, however, the lens has considerably lower energy demands.

By nine weeks into human development, the lens is surrounded and nourished by a net of vessels, the tunica vasculosa lentis, which is derived from the hyaloid artery. Beginning in the fourth month of development, the hyaloid artery and its related vasculature begin to atrophy and completely disappear by birth. In the postnatal eye, Cloquet's canal marks the former location of the hyaloid artery.

After regression of the hyaloid artery, the lens receives all its nourishment from the aqueous humor. Nutrients diffuse in and waste diffuses out through a constant flow of fluid from the anterior/posterior poles of the lens and out of the equatorial regions, a dynamic that is maintained by the Na+/K+ ATPase pumps located in the equatorially positioned cells of the lens epithelium.

Glucose is the primary energy source for the lens. As mature lens fibers do not have mitochondria, approximately 80% of the glucose is metabolized via anaerobic respiration. The remaining fraction of glucose is shunted primarily down the pentose phosphate pathway. The lack of aerobic respiration means that the lens consumes very little oxygen as well.

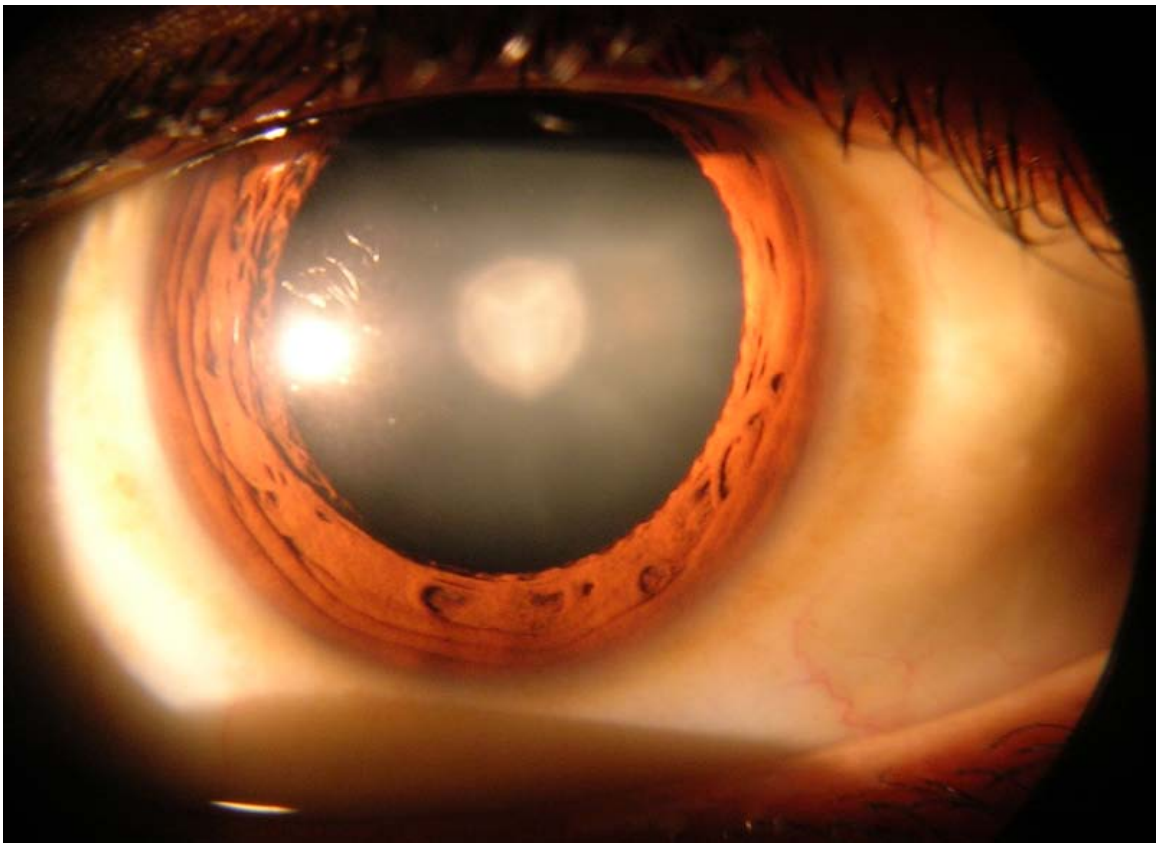
Diseases and disorders

- Cataracts are opacities of the lens. While some are small and do not require any treatment, others may be large enough to block light and obstruct vision. Cataracts usually develop as the aging lens becomes more and more opaque, but cataracts can also form congenitally or after injury to the lens. Diabetes is also a risk factor for cataract.

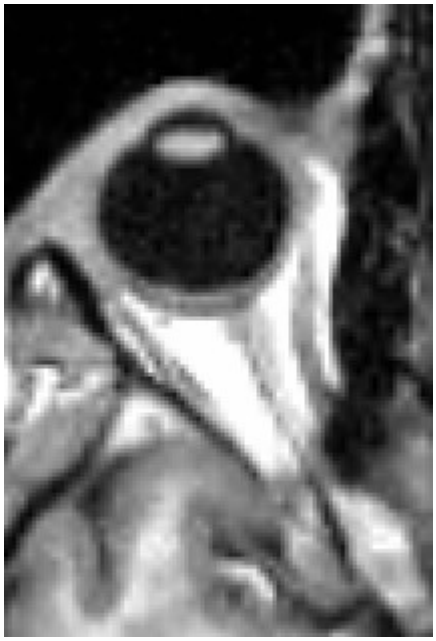
- Presbyopia is the age-related loss of accommodation, which is marked by the inability of the eye to focus on nearby objects. The exact mechanism is still

unknown, but age-related changes in the hardness, shape, and size of the lens have all been linked to the condition.

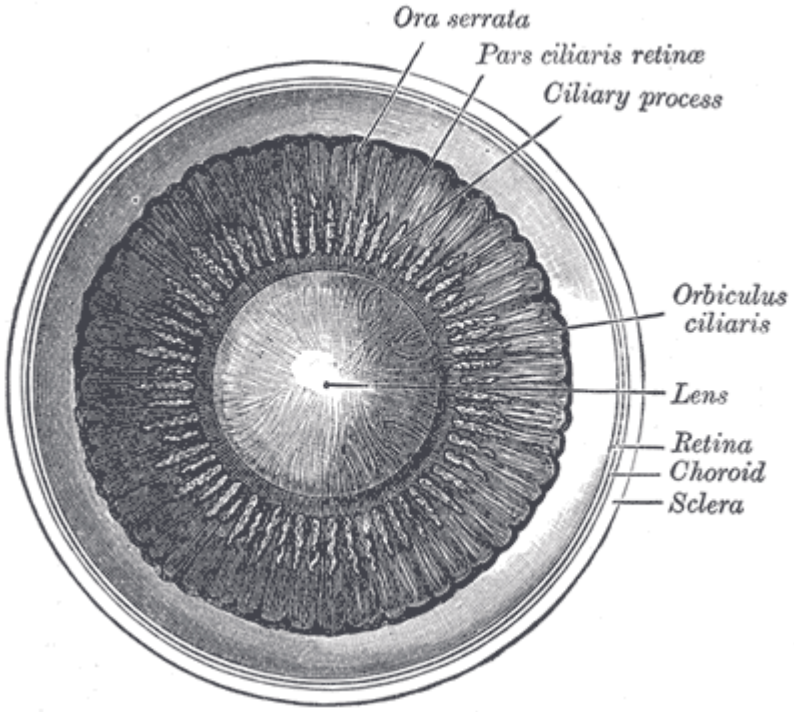
- Ectopia lentis is the displacement of the lens from its normal position.
- Aphakia is the absence of the lens from the eye. Aphakia can be the result of surgery or injury, or it can be congenital.
- Nuclear sclerosis is an age-related change in the density of the lens nucleus that occurs in all older animals.



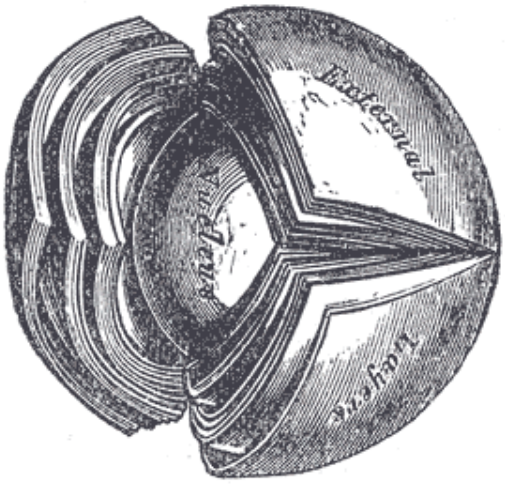
Cataract in Human Eye- Magnified view seen on examination with a slit lamp



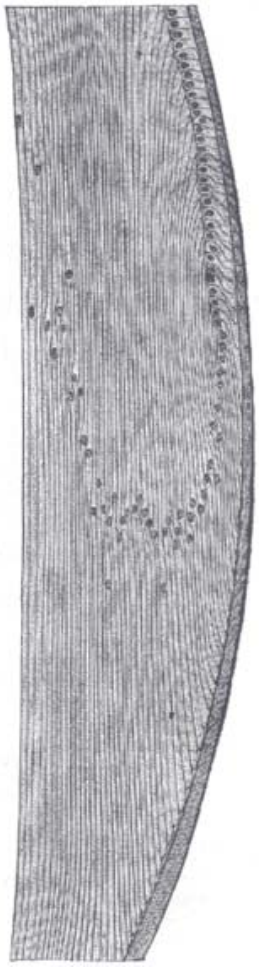
MRI scan of human eye showing lens



Interior of anterior chamber of eye



The crystalline lens, hardened and divided

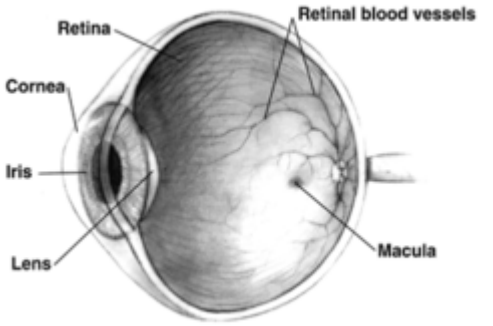


Section through the margin of the lens, showing the transition of the epithelium into the lens fibers.

Chapter 4

Retina

Retina



Right human eye cross-sectional view. Courtesy NIH National Eye Institute. Many animals have eyes different from the human eye.

Gray's	*subject #225 1014*
Artery	central retinal artery
MeSH	*Retina*
Dorlands/Elsevier	*Retina*

The vertebrate **retina** is a light-sensitive tissue lining the inner surface of the eye. The optics of the eye create an image of the visual world on the retina, which serves much the same function as the film in a camera. Light striking the retina initiates a cascade of chemical and electrical events that ultimately trigger nerve impulses. These are sent to various visual centers of the brain through the fibers of the optic nerve.

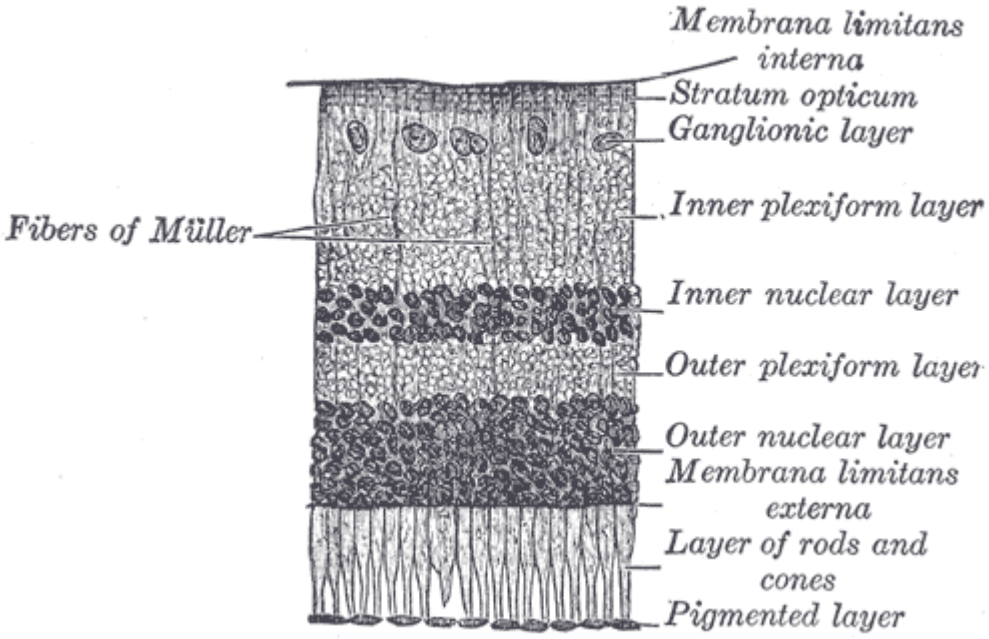
In vertebrate embryonic development, the retina and the optic nerve originate as outgrowths of the developing brain, so the retina is considered part of the central nervous system (CNS). It is the only part of the CNS that can be visualized non-invasively.

The retina is a complex, layered structure with several layers of neurons interconnected by synapses. The only neurons that are directly sensitive to light are the photoreceptor

cells. These are mainly of two types: the rods and cones. Rods function mainly in dim light and provide black-and-white vision, while cones support daytime vision and the perception of colour. A third, much rarer type of photoreceptor, the photosensitive ganglion cell, is important for reflexive responses to bright daylight.

Neural signals from the rods and cones undergo complex processing by other neurons of the retina. The output takes the form of action potentials in retinal ganglion cells whose axons form the optic nerve. Several important features of visual perception can be traced to the retinal encoding and processing of light.

Anatomy of vertebrate retina



Section of retina

The vertebrate retina has ten distinct layers. From closest to farthest from the vitreous body, they include:

1. *Inner limiting membrane* – Müller cell footplates
2. *Nerve fiber layer* – essentially the axons of the ganglion cell nuclei
3. *Ganglion cell layer* – layer that contains nuclei of ganglion cells, the axons of which become the optic nerve fibers for messages
4. *Inner plexiform layer* – contains the synapse between the bipolar cell axons and the dendrites of the ganglion and amacrine cells.
5. *Inner nuclear layer* – contains the nuclei and surrounding cell bodies (perikarya) of the bipolar cells, which correspond to heat and touch sensory skin receptors transmitting signals to the spinal cord or its continuation, the medulla.

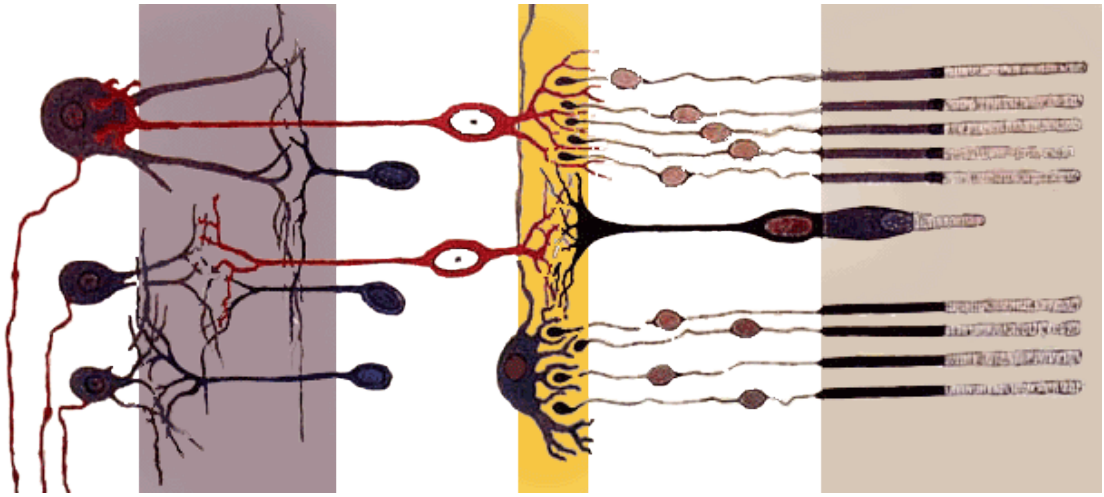
6. *Outer plexiform layer* – projections of rods and cones ending in the rod spherule and cone pedicle, respectively. These make synapses with dendrites of bipolar In the macular region, this is known as the *Fiber layer of Henle*.
7. *Outer nuclear layer* – cell bodies of rods and cones
8. *External limiting membrane* – layer that separates the inner segment portions of the photoreceptors from their cell nucleus
9. *Photoreceptor layer* – rods/cones
10. *Retinal pigment epithelium*

Of these the four main layers of the ten, from outside in: pigment epithelium, the photoreceptor layer for sight, bipolar cells, and finally, the ganglion cell layer which also contains photoreceptors, the photosensitive ganglion cells.

Therefore, the optic nerve is less a nerve than a central tract, connecting the bipolars to the lateral geniculate body, a visual relay station in the diencephalon (the rear of the forebrain). Additional structures, not directly associated with vision, are found as outgrowths of the retina in some vertebrate groups. In birds, the pecten is a vascular structure of complex shape that projects from the retina into the vitreous humour; it supplies oxygen and nutrients to the eye, and may also aid in vision. Reptiles have a similar, but much simpler, structure, referred to as the *papillary cone*.

Physical structure of human retina

In adult humans the entire retina is approximately 72% of a sphere about 22 mm in diameter. The entire retina contains about 7 million cones and 75 to 150 million rods. The optic disc, a part of the retina sometimes called "the blind spot" because it lacks photoreceptors, is located at the optic papilla, a nasal zone where the optic-nerve fibers leave the eye. It appears as an oval white area of 3mm². Temporal (in the direction of the temples) to this disc is the macula. At its center is the fovea, a pit that is responsible for our sharp central vision but is actually less sensitive to light because of its lack of rods. Human and non-human primates possess one fovea as opposed to certain bird species such as hawks who actually are bifoviate and dogs and cats who possess no fovea but a central band known as the visual streak. Around the fovea extends the central retina for about 6 mm and then the peripheral retina. The edge of the retina is defined by the ora serrata. The length from one ora to the other (or macula), the most sensitive area along the horizontal meridian is about 3.2 mm.



Retina's simplified axial organization. The retina is a stack of several neuronal layers. Light is concentrated from the eye and passes across these layers (from left to right) to hit the photoreceptors (right layer). This elicits chemical transformation mediating a propagation of signal to the bipolar and horizontal cells (middle yellow layer). The signal is then propagated to the amacrine and ganglion cells. These neurons ultimately may produce action potentials on their axons. This spatiotemporal pattern of spikes determines the raw input from the eyes to the brain. (Modified from a drawing by Ramón y Cajal.)

In section the retina is no more than 0.5 mm thick. It has three layers of nerve cells and two of synapses, including the unique ribbon synapses. The optic nerve carries the ganglion cell axons to the brain and the blood vessels that open into the retina. The ganglion cells lie innermost in the retina while the photoreceptive cells lie outermost. Because of this counter-intuitive arrangement, light must first pass through and around the ganglion cells and through the thickness of the retina, (including its capillary vessels, not shown) before reaching the rods and cones. However it does not pass through the epithelium or the choroid (both of which are opaque).

The white blood cells in the capillaries in front of the photoreceptors can be perceived as tiny bright moving dots when looking into blue light. This is known as the blue field entoptic phenomenon (or Scheerer's phenomenon).

Between the ganglion cell layer and the rods and cones there are two layers of neuropils where synaptic contacts are made. The neuropil layers are the outer plexiform layer and the inner plexiform layer. In the outer the rods and cones connect to the vertically running bipolar cells, and the horizontally oriented horizontal cells connect to ganglion cells.

The central retina is cone-dominated and the peripheral retina is rod-dominated. In total there are about seven million cones and a hundred million rods. At the centre of the macula is the foveal pit where the cones are smallest and in a hexagonal mosaic, the most efficient and highest density. Below the pit the other retina layers are displaced, before building up along the foveal slope until the rim of the fovea or parafovea which is the thickest portion of the retina. The macula has a yellow pigmentation from screening

pigments and is known as the macula lutea. The area directly surrounding the fovea has the highest density of rods converging on single bipolars. Since the cones have a much lesser power of merging signals, the fovea allows for the sharpest vision the eye can attain.

Though the rod and cones are a mosaic of sorts, transmission from receptors to bipolars to ganglion cells is not the case, Since there are about 150 million receptors and only 1 million optic nerve fibers, there must be convergence and thus mixing of signals. Moreover, the horizontal action of the horizontal and amacrine cells can allow one area of the retina to control another (e.g., one stimulus inhibiting another). This inhibition is key to the sum of messages sent to the higher regions of the brain. In some lower vertebrates, (e.g., the pigeon) there is a "centrifugal" control of messages, that is, one layer can control another, or higher regions of the brain can drive the retinal nerve cells, but in primates this does not occur.

Vertebrate and cephalopod retina differences

The vertebrate retina is *inverted* in the sense that the light sensing cells sit at the back side of the retina, so that light has to pass through layers of neurons and capillaries before it reaches the rods and cones. By contrast, the cephalopod retina has the photoreceptors at the front side of the retina, with processing neurons and capillaries behind them. Because of this, cephalopods do not have a blind spot.

The cephalopod retina does not originate as an outgrowth of the brain, as the vertebrate one does. It was originally argued that this difference shows that vertebrate and cephalopod eyes are not homologous but have evolved separately. The evolutionary biologist Richard Dawkins cites the imperfect structure of the human retina as confounding claims by creationists or intelligent design theorists that the human eye is so perfect it must have a designer.

In 2009 Kröger anatomically showed in Zebrafish that though the inverted arrangement is nonadaptive in that it creates avoidable scattering of light (and thus loss of light and image blur), it has space-saving advantages for small-eyed animals in which there is a minimal vitreous body, as the space between the lens and the photoreceptors' light-sensitive outer segments is completely filled with retinal cells.

Physiology

An image is produced by the patterned excitation of the cones and rods in the retina. The excitation is processed by the neuronal system and various parts of the brain working in parallel to form a representation of the external environment in the brain.

The cones respond to bright light and mediate high-resolution colour vision during daylight illumination (also called photopic vision). The rods are saturated at daylight levels and don't contribute to pattern vision. However, rods do respond to dim light and mediate lower-resolution, monochromatic vision under very low levels of illumination

(called scotopic vision). The illumination in most office settings falls between these two levels and is called mesopic vision. At these light levels, both the rods and cones are actively contributing pattern information to that exiting the eye. What contribution the rod information makes to pattern vision under these circumstances is unclear.

The response of cones to various wavelengths of light is called their spectral sensitivity. In normal human vision, the spectral sensitivity of a cone falls into one of three subgroups. These are often called red, green, and blue cones but more accurately are short, medium, and long wavelength sensitive cone subgroups. It is a lack of one or more of the cone subtypes that causes individuals to have deficiencies in colour vision or various kinds of colour blindness. These individuals are not blind to objects of a particular colour but experience the inability to distinguish between two groups of colours that *can* be distinguished by people with normal vision. Humans have three different types of cones (trichromatic vision) while most other mammals lack cones with red sensitive pigment and therefore have poorer (dichromatic) colour vision. However, some animals have four spectral subgroups, e.g., the trout adds an ultraviolet subgroup to short, medium and long subgroups that are similar to humans. Some fish are sensitive to the polarization of light as well.

When light falls on a receptor it sends a proportional response synaptically to bipolar cells which in turn signal the retinal ganglion cells. The receptors are also 'cross-linked' by horizontal cells and amacrine cells, which modify the synaptic signal before the ganglion cells. Rod and cone signals are intermixed and combine, although rods are mostly active in very poorly lit conditions and saturate in broad daylight, while cones function in brighter lighting because they are not sensitive enough to work at very low light levels.

Despite the fact that all are nerve cells, only the retinal ganglion cells and few amacrine cells create action potentials. In the photoreceptors, exposure to light hyperpolarizes the membrane in a series of graded shifts. The outer cell segment contains a photopigment. Inside the cell the normal levels of cyclic guanosine monophosphate (cGMP) keep the Na+ channel open and thus in the resting state the cell is depolarised. The photon causes the retinal bound to the receptor protein to isomerise to trans-retinal. This causes receptor to activate multiple G-proteins. This in turn causes the Ga-subunit of the protein to bind and degrade cGMP inside the cell which then cannot bind to the Na+ cyclic nucleotide-gated ion channels (CNGs). Thus the cell is hyperpolarised. The amount of neurotransmitter released is reduced in bright light and increases as light levels fall. The actual photopigment is bleached away in bright light and only replaced as a chemical process, so in a transition from bright light to darkness the eye can take up to thirty minutes to reach full sensitivity.

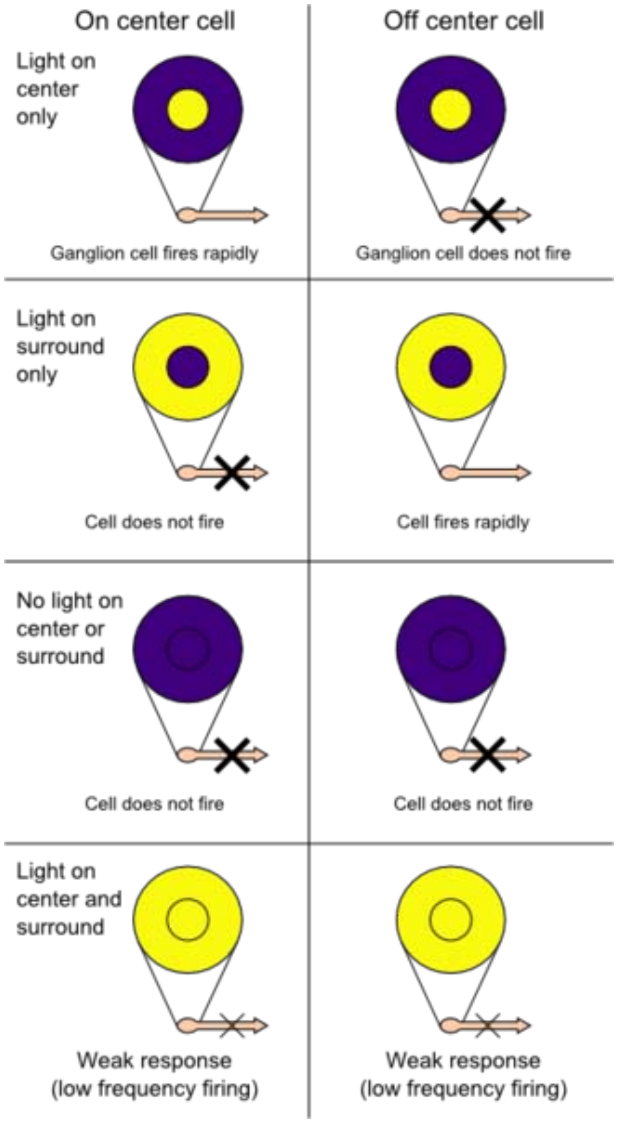
In the retinal ganglion cells there are two types of response, depending on the receptive field of the cell. The receptive fields of retinal ganglion cells comprise a central approximately circular area, where light has one effect on the firing of the cell, and an annular surround, where light has the opposite effect on the firing of the cell. In ON cells, an increment in light intensity in the centre of the receptive field causes the firing rate to

increase. In OFF cells, it makes it decrease. In a linear model, this response profile is well described by a Difference of Gaussians and is the basis for edge detection algorithms. Beyond this simple difference ganglion cells are also differentiated by chromatic sensitivity and the type of spatial summation. Cells showing linear spatial summation are termed X cells (also called parvocellular, P, or midget ganglion cells), and those showing non-linear summation are Y cells (also called magnocellular, M, or parasol retinal ganglion cells), although the correspondence between X and Y cells (in the cat retina) and P and M cells (in the primate retina) is not as simple as it once seemed.

In the transfer of visual signals to the brain, the visual pathway, the retina is vertically divided in two, a temporal (nearer to the temple) half and a nasal (nearer to the nose) half. The axons from the nasal half cross the brain at the optic chiasma to join with axons from the temporal half of the other eye before passing into the lateral geniculate body.

Although there are more than 130 million retinal receptors, there are only approximately 1.2 million fibres (axons) in the optic nerve; a large amount of pre-processing is performed within the retina. The fovea produces the most accurate information. Despite occupying about 0.01% of the visual field (less than 2° of visual angle), about 10% of axons in the optic nerve are devoted to the fovea. The resolution limit of the fovea has been determined at around 10,000 points. The information capacity is estimated at 500,000 bits per second without colour or around 600,000 bits per second including colour.

Spatial encoding



On-centers and off-centers of the retina

The retina, unlike a camera, does not simply send a picture to the brain. The retina spatially encodes (compresses) the image to fit the limited capacity of the optic nerve. Compression is necessary because there are 100 times more Photoreceptor cells than ganglion cells as mentioned above. The retina does so by "decorrelating" the incoming images in a manner to be described below. These operations are carried out by the center surround structures as implemented by the bipolar and ganglion cells.

There are two types of center surround structures in the retina—on-centers and off-centers. On-centers have a positively weighted center and a negatively weighted surround. Off-centers are just the opposite. Positive weighting is more commonly known as excitatory and negative weighting is more commonly known as inhibitory.

These center surround structures are not physical in the sense that you cannot see them by staining samples of tissue and examining the retina's anatomy. The center surround structures are logical (i.e., mathematically abstract) in the sense that they depend on the connection strengths between ganglion and bipolar cells. It is believed that the connection strengths between cells is caused by the number and types of ion channels embedded in the synapses between the ganglion and bipolar cells. Stephen Kuffler in the 1950s was the first person to begin to understand these center surround structures in the retina of cats.

The center surround structures are mathematically equivalent to the edge detection algorithms used by computer programmers to extract or enhance the edges in a digital photograph. Thus the retina performs operations on the image to enhance the edges of objects within its visual field. For example, in a picture of a dog, a cat and a car, it is the edges of these objects that contain the most information. In order for higher functions in the brain (or in a computer for that matter) to extract and classify objects such as a dog and a cat, the retina is the first step to separating out the various objects within the scene.

As an example, the following matrix is at the heart of the computer algorithm that implements edge detection. This matrix is the computer equivalent to the center surround structure. In this example, each box (element) within this matrix would be connected to one photoreceptor. The photoreceptor in the center is the current receptor being processed. The center photoreceptor is multiplied by the +1 weight factor. The surrounding photoreceptors are the "nearest neighbors" to the center and are multiplied by the -1/8 value. The sum of all nine of these elements is finally calculated. This summation is repeated for every photoreceptor in the image by shifting left to the end of a row and then down to the next line.

-1/8	-1/8	-1/8
-1/8	+1	-1/8
-1/8	-1/8	-1/8

The total sum of this matrix is zero if all the inputs from the nine photoreceptors are the same value. The zero result indicates the image was uniform (non-changing) within this small patch. Negative or positive sums mean something was varying (changing) within this small patch of nine photoreceptors.

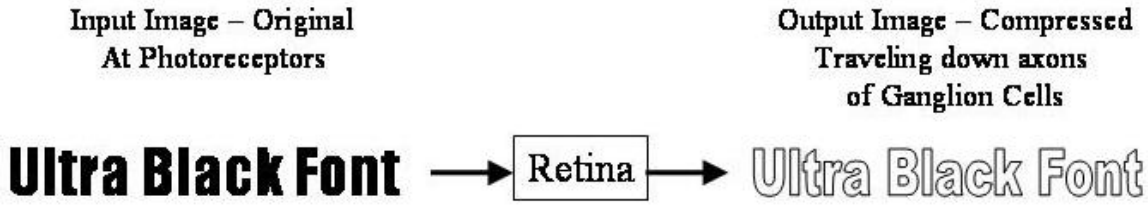
The above matrix is only an approximation to what really happens inside the retina. The differences are:

1. The above example is called "balanced". The term balanced means that the sum of the negative weights is equal to the sum of the positive weights so that they cancel out perfectly. Retinal ganglion cells are almost never perfectly balanced.
2. The table is square while the center surround structures in the retina are circular.
3. Neurons operate on spike trains traveling down nerve cell axons. Computers operate on a single Floating point number that is essentially constant from each

input pixel. (The computer pixel is basically the equivalent of a biological photoreceptor.)

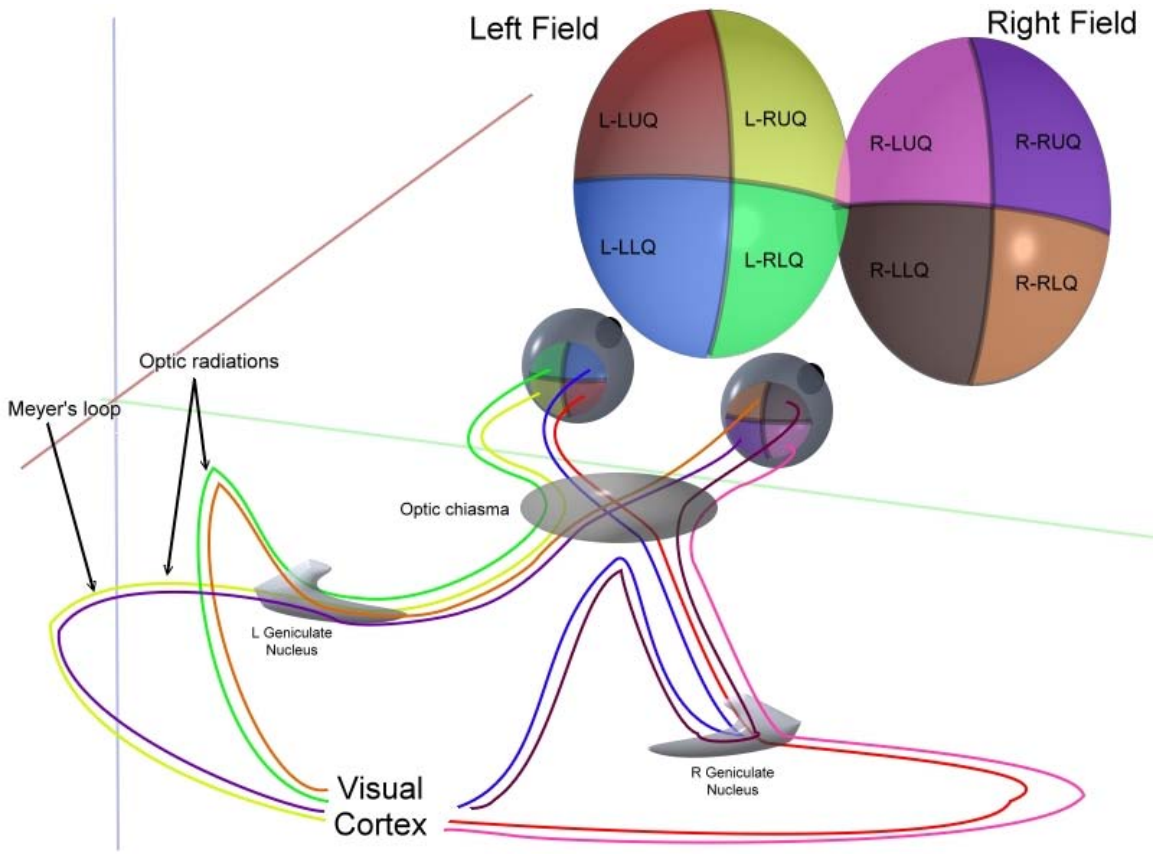
4. The retina performs all these calculations in parallel while the computer operates on each pixel one at a time. There are no repeated summations and shifting as there would be in a computer.
5. Finally, the horizontal and amacrine cells play a significant role in this process but that is not represented here.

Here is an example of an input image and how edge detection would modify it.



Once the image is spatially encoded by the center surround structures, the signal is sent out the optical nerve (via the axons of the ganglion cells) through the optic chiasm to the LGN (lateral geniculate nucleus). The exact function of the LGN is unknown at this time. The output of the LGN is then sent to the back of the brain. Specifically the output of the LGN "radiates" out to the V1 Primary visual cortex.

Simplified Signal Flow: Photoreceptors → Bipolar → Ganglion → Chiasm → LGN → V1 cortex



Diseases and disorders

There are many inherited and acquired diseases or disorders that may affect the retina. Some of them include:

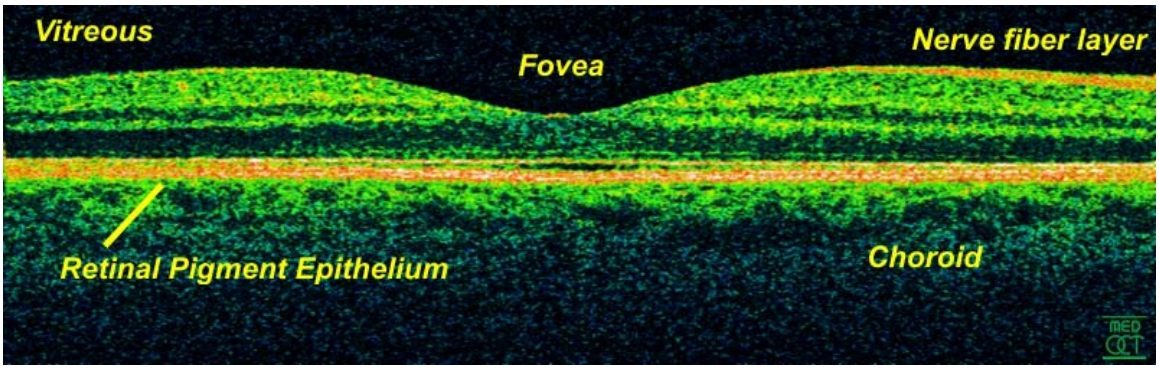
- Retinitis pigmentosa is a group of genetic diseases that affect the retina and causes the loss of night vision and peripheral vision.
- Macular degeneration describes a group of diseases characterized by loss of central vision because of death or impairment of the cells in the macula.
- Cone-rod dystrophy (CORD) describes a number of diseases where vision loss is caused by deterioration of the cones and/or rods in the retina.
- In retinal separation, the retina detaches from the back of the eyeball. Ignipuncture is an outdated treatment method. The term retinal detachment is used to describe a separation of the neurosensory retina from the retinal pigment epithelium. There are several modern treatment methods for fixing a retinal detachment: pneumatic retinopexy, scleral buckle, cryotherapy, laser photocoagulation and pars plana vitrectomy.
- Both hypertension and diabetes mellitus can cause damage to the tiny blood vessels that supply the retina, leading to hypertensive retinopathy and diabetic retinopathy.
- Retinoblastoma is a cancer of the retina.

- Retinal diseases in dogs include retinal dysplasia, progressive retinal atrophy, and sudden acquired retinal degeneration.
- *Lipemia retinalis* is a white appearance of the retina, and can occur by lipid deposition in lipoprotein lipase deficiency.

Diagnosis and treatment

A number of different instruments are available for the diagnosis of diseases and disorders affecting the retina. An ophthalmoscope is used to examine the retina. Recently, adaptive optics has been used to image individual rods and cones in the living human retina and a company based in Scotland have engineered technology that allows physicians to observe the complete retina without any discomfort to patients.

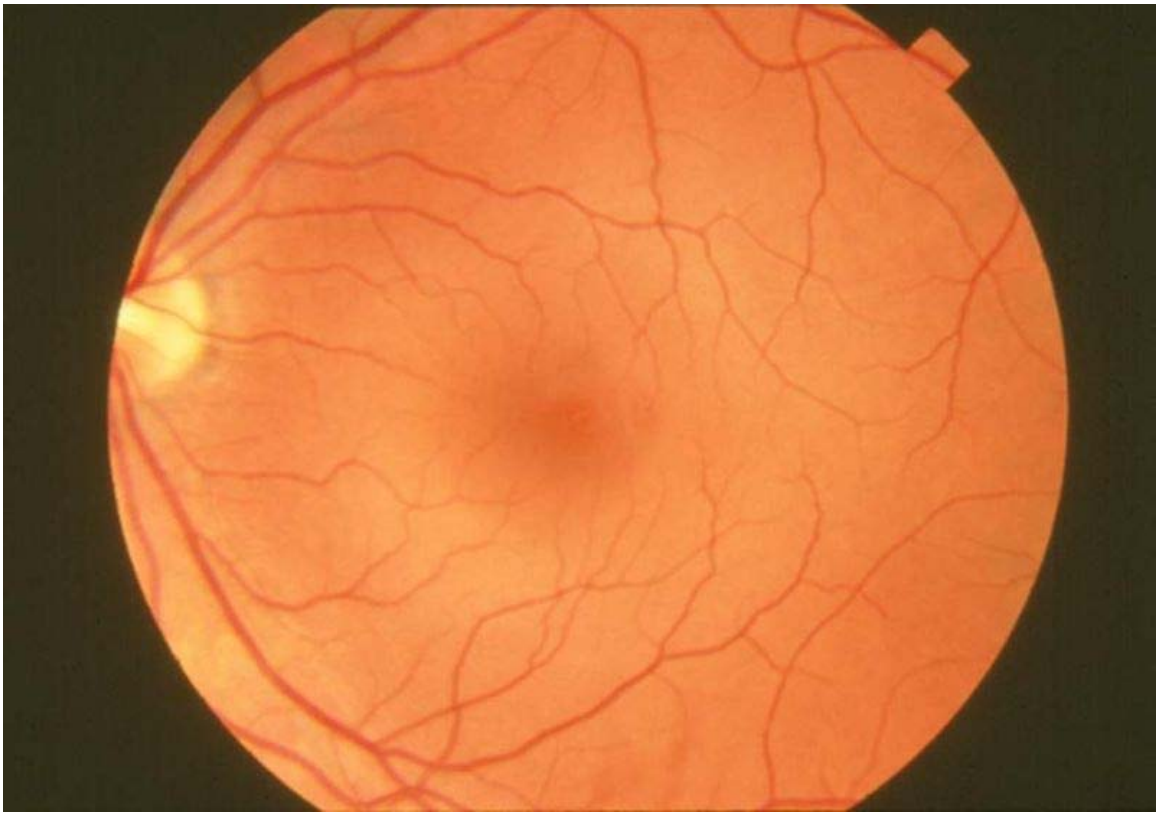
The electroretinogram is used to measure non-invasively the retina's electrical activity, which is affected by certain diseases. A relatively new technology, now becoming widely available, is optical coherence tomography (OCT). This non-invasive technique allows one to obtain a 3D volumetric or high resolution cross-sectional tomogram of the retinal fine structure with histologic-quality.



OCT scan of a retina at 800nm with an axial resolution of 3µm

Treatment depends upon the nature of the disease or disorder. Transplantation of retinas has been attempted, but without much success. At MIT, The University of Southern California, and the University of New South Wales, an "artificial retina" is under development: an implant which will bypass the photoreceptors of the retina and stimulate the attached nerve cells directly, with signals from a digital camera.

Retinal blood supply



The blood vessels in a normal human retina. The optic disk is at extreme left, and the macula lutea is near the center.

There are two circulations, both supplied by the ophthalmic artery. The uveal circulation consists of arteries entering the globe outside the optic nerve, these supply the uvea and outer and middle layers of the retina. The retinal circulation, on the other hand, supplies the inner layer of the retina and passes with the optic nerve as a branch of the ophthalmic artery called the central artery of the retina. The unique structure of the blood vessels in the retina has been used for biometric identification.

Research

George Wald, Haldan Keffer Hartline and Ragnar Granit won the 1967 Nobel Prize in Physiology or Medicine for their scientific research on the retina.

A recent University of Pennsylvania study calculated the approximate bandwidth of human retinas is 8.75 megabits per second, whereas guinea pig retinas transfer at 875 kilobits.

MacLaren & Pearson and colleagues at University College London and Moorfields Eye Hospital in London showed in 2006 that photoreceptor cells could be transplanted successfully in the mouse retina if donor cells were at a critical developmental stage.

Recently Ader and colleagues in Dublin showed using the electron microscope that transplanted photoreceptors formed synaptic connections.

Retinal gene therapy

Gene therapy holds promise as a potential avenue to cure a wide range of retinal diseases. This involves using a non-infectious virus to shuttle a gene into a part of the retina. Recombinant adeno-associated virus (rAAV) vectors possess a number of features that render them ideally suited for retinal gene therapy, including a lack of pathogenicity, minimal immunogenicity, and the ability to transduce postmitotic cells in a stable and efficient manner. rAAV vectors are increasingly utilized for their ability to mediate efficient transduction of retinal pigment epithelium (RPE), photoreceptor cells and retinal ganglion cells. Each cell type can be specifically targeted by choosing the appropriate combination of AAV serotype, promoter, and intraocular injection site.

The unique architecture of the retina and its relatively immune-privileged environment help this process. Tight junctions that form the blood retinal barrier separate the subretinal space from the blood supply, thus protecting it from microbes and most immune-mediated damage, and enhancing its potential to respond to vector-mediated therapies. The highly compartmentalized anatomy of the eye facilitates accurate delivery of therapeutic vector suspensions to specific tissues under direct visualization using microsurgical techniques. In the sheltered environment of the retina, AAV vectors are able to maintain high levels of transgene expression in the retinal pigmented epithelium (RPE), photoreceptors, or ganglion cells for long periods of time after a single treatment. In addition, the eye and the visual system can be routinely and easily monitored for visual function and retinal structural changes after injections with noninvasive advanced technology, such as visual acuities, contrast sensitivity, fundus auto-fluorescence (FAF), dark-adapted visual thresholds, vascular diameters, pupillometry, electroretinography (ERG), multifocal ERG and optical coherence tomography (OCT).

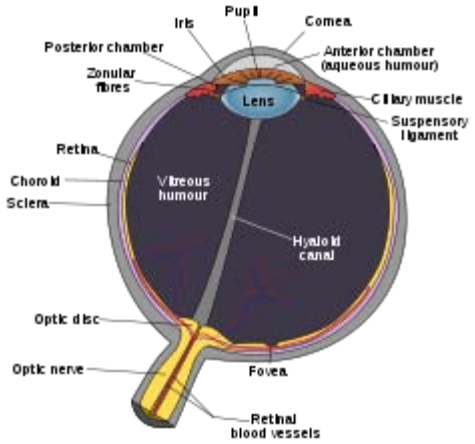
This strategy is effective against retinal diseases that have been studied including neovascular diseases that are features of age-related macular degeneration, diabetic retinopathy and retinopathy of prematurity. Since the regulation of vascularization in the mature retina involves a balance between endogenous positive growth factors, such as vascular endothelial growth factor (VEGF) and inhibitors of angiogenesis, such as pigment epithelium-derived factor (PEDF), rAAV-mediated expression of PEDF, angiostatin, and the soluble VEGF receptor sFlt-1, which are all antiangiogenic proteins, have been shown to reduce aberrant vessel formation in animal models. Since specific gene therapies cannot readily be used to treat a significant fraction of patients with retinal dystrophy, there is a major interest in developing a more generally applicable survival factor therapy. Neurotrophic factors have the ability to modulate neuronal growth during development to maintain existing cells and to allow recovery of injured neuronal populations in the eye. AAV encoding neurotrophic factors such as fibroblast growth factor (FGF) family members and GDNF either protected photoreceptors from apoptosis or slowed down cell death.

However, treatment of inherited retinal degenerative diseases such as retinitis pigmentosa and Leber congenital amaurosis (LCA) via gene replacement therapy constitutes the most straightforward and therefore the most promising approach for treating the autosomal recessive retinal disease. Leber Congenital Amaurosis (LCA2) is a defect of the *RPE65* gene, which is responsible for the synthesis of 11-cis retinal, an important molecule in the visual phototransduction, and gene replacement therapy studies utilizing *rpe65*-encoding AAV have yielded hopeful results in animal models. Based on several encouraging reports from animal models, at least three clinical trials are currently underway for the treatment of LCA using modified AAV vectors carrying the RPE65 cDNA and have reported positive preliminary results.

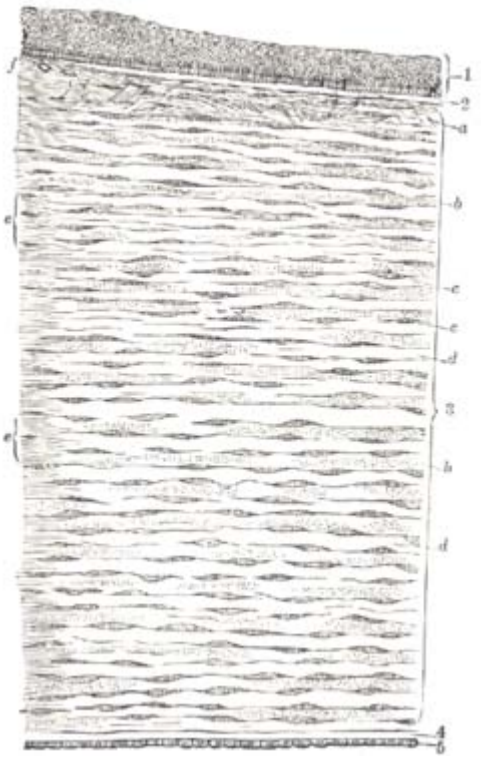
Chapter 5

Cornea

Cornea



Schematic diagram of the human eye. (Cornea labeled at center top.)



Vertical section of human cornea from near the margin. (Waldeyer.) Magnified.

1. Epithelium.

2. Anterior elastic lamina.

3. substantia propria.

4. Posterior elastic lamina.

5. Endothelium of the anterior chamber.

a. Oblique fibers in the anterior layer of the substantia propria.

b. Lamellæ the fibers of which are cut across, producing a dotted appearance.

c. Corneal corpuscles appearing fusiform in section.

d. Lamellæ the fibers of which are cut longitudinally.

e. Transition to the sclera, with more distinct fibrillation, and surmounted by a thicker epithelium.

f. Small bloodvessels cut across near the margin of the cornea.

The **cornea** is the transparent front part of the eye that covers the iris, pupil, and anterior chamber. Together with the lens, the cornea refracts light, with the cornea accounting for approximately two-thirds of the eye's total optical power. In humans, the refractive power of the cornea is approximately 43 dioptres. While the cornea contributes most of the eye's focusing power, its focus is fixed. The curvature of the lens, on the other hand, can be adjusted to "tune" the focus depending upon the object's distance. Medical terms related to the cornea often start with the prefix "*kerat-*" from the Greek word κέρας, *horn*.

Structure

The cornea has unmyelinated nerve endings sensitive to touch, temperature and chemicals; a touch of the cornea causes an involuntary reflex to close the eyelid. Because transparency is of prime importance the cornea does not have blood vessels; it receives nutrients via diffusion from the tear fluid at the outside and the aqueous humour at the inside and also from neurotrophins supplied by nerve fibres that innervate it. In humans, the cornea has a diameter of about 11.5 mm and a thickness of 0.5–0.6 mm in the center and 0.6–0.8 mm at the periphery. Transparency, avascularity, the presence of immature resident immune cells, and immunologic privilege makes the cornea a very special tissue. The cornea has no blood supply; it gets oxygen directly through the air. Oxygen first dissolves in the tears and then diffuses throughout the cornea to keep it healthy.

It borders with the sclera by the corneal limbus.

The most abundant soluble protein in mammalian cornea is albumin.

In lampreys, the cornea is solely an extension of the sclera, and is separate from the skin lying above it, but in more advanced vertebrates it is always fused with the skin to form a single structure, albeit one composed of multiple layers. In fish, and aquatic vertebrates in general, the cornea plays no role in focusing light, since it has virtually the same refractive index as water.

Layers

The human cornea, like those of other primates, has five layers; the corneas of cats, dogs, wolves, and other carnivores only have four. From the anterior to posterior the five layers of the human cornea are:

1. **Corneal epithelium**: a thin epithelial multicellular tissue layer (non-keratinized stratified squamous epithelium) of fast-growing and easily-regenerated cells, kept moist with tears. Irregularity or edema of the corneal epithelium disrupts the smoothness of the air-tear film interface, the most significant component of the total refractive power of the eye, thereby reducing visual acuity. It is continuous with the conjunctival epithelium is composed of about 6 layers of cells which are shed constantly on the exposed layer and are regenerated by multiplication in the basal layer.

2. **Bowman's layer** (also erroneously known as the *anterior limiting membrane*, when in fact it is not a membrane but a condensed layer of collagen): a tough layer that protects the corneal stroma, consisting of a similar irregularly-arranged collagen fibers, essentially a type of stroma. It is eight to 14 micrometres thick. This layer is absent in carnivores.
3. **Corneal stroma** (also *substantia propria*): a thick, transparent middle layer, consisting of regularly-arranged collagen fibers along with sparsely distributed interconnected keratocytes, which are the cells for general repair and maintenance. They are parallel and are superimposed like book pages The corneal stroma consists of approximately 200 layers of type I collagen fibrils. Each layer is 1.5 to 2.5 micrometres. Up to 90% of the corneal thickness is composed of stroma. There are 2 theories of how transparency in the cornea comes about:
    1. The lattice arrangements of the collagen fibrils in the stroma. The light scatter by individual fibrils is cancelled by destructive interference from the scattered light from other individual fibrils.(Maurice)
    2. The spacing of the neighbouring collagen fibrils in the stroma must be < 200 nm for there to be transparency. (Goldman and Benedek)
4. **Descemet's membrane** (also *posterior limiting membrane*): a thin acellular layer that serves as the modified basement membrane of the corneal endothelium, from which the cells are derived (but in a different collagen structure. It is 5-10 micrometres thick
5. **Corneal endothelium**: a simple squamous or low cuboidal monolayer of mitochondria-rich cells responsible for regulating fluid and solute transport between the aqueous and corneal stromal compartments. (The term *endothelium* is a misnomer here. The corneal endothelium is bathed by aqueous humour, not by blood or lymph, and has a very different origin, function, and appearance from vascular endothelia.) Unlike the corneal epithelium the cells of the endothelium do not regenerate. Instead, they stretch to compensate for dead cells which reduces the overall cell density of the endothelium and has an impact on fluid regulation. If the endothelium can no longer maintain a proper fluid balance, stromal swelling due to excess fluids and subsequent loss of transparency will occur.

The mnemonic "**EBSDE**in", read as "Ebstein" can be used to remember the layers in sequence.

Keeping the cornea transparent

Upon death or removal of an eye the cornea absorbs the aqueous humor, thickens, and becomes hazy. Transparency can be restored by putting it in a warm, well-ventilated chamber at 31 °C (88 °F, the normal temperature), allowing the fluid to leave the cornea and become transparent. The cornea takes in fluid from the aqueous humor and the small blood vessels of the limbus, but a pump ejects the fluid immediately upon entry. When energy is deficient the pump may fail, or works too slowly to compensate, causing swelling. This could arise at death, but a dead eye can be placed in a warm chamber and the reservoirs of sugar and glycogen can keep the cornea transparent for at least 24 hours.

The endothelium controls this pumping action, and as discussed above, damage thereof is more serious, and is a cause of opaqueness and swelling. When damage to the cornea occurs, such as in a viral infection, the collagen used to repair the process is not regularly arranged, leading to an opaque patch (leukoma). When a cornea is needed for transplant, as from an eye bank, the best procedure is to remove the cornea from the eyeball, preventing the cornea from absorbing the aqueous humor.

Innervation

The cornea is one of the most sensitive tissues of the body, as it is densely innervated with sensory nerve fibres via the ophthalmic division of the trigeminal nerve by way of 70–80 long ciliary nerves and short ciliary nerves. The ciliary nerves run under the endothelium and exit the eye through holes in the sclera apart from the optic nerve (which transmits only optic signals).

The nerves enter the cornea via three levels; *scleral, episcleral and conjunctival*. Most of the bundles give rise by subdivision to a network in the stroma, from which fibres supply the different regions. The three networks are *midstromal, subepithelial/Bowman's layer, and epithelium*. The receptive fields of each nerve ending are very large, and may overlap.

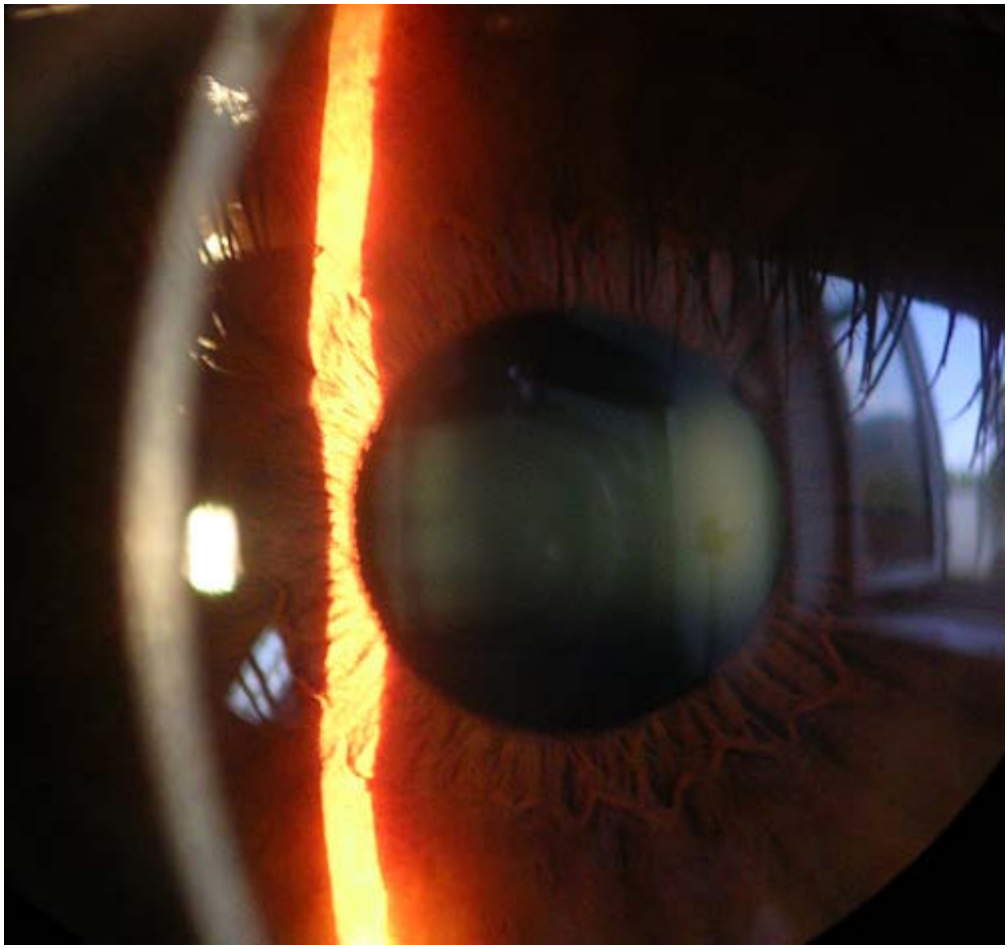
Corneal nerves of the subepithelial layer terminate near superficial epithelial layer of the cornea in a logarithmic spiral pattern.

Refractive nature

The optical component is concerned with producing a reduced inverted image on the retina. The eye's optical system consists of not only two but four surfaces—two on the cornea, two on the lens. Rays are refracted toward the midline. Distant rays, due to their parallel nature, converge to a point on the retina. The cornea admits light at the greatest angle. The aqueous and vitreous humors both have a refractive index of 1.336, whereas the cornea has a refractive index of 1.376. Because the change in refractive index between cornea and aqueous humor is relatively small compared to the change at the air–cornea interface, it has a negligible refractive effect, typically -6 diopters.

Diseases and disorders

Treatment and management



Slit lamp image of the cornea, iris and lens

Surgical procedures

Various refractive eye surgery techniques change the shape of the cornea in order to reduce the need for corrective lenses or otherwise improve the refractive state of the eye. In many of the techniques used today, reshaping of the cornea is performed by photoablation using the excimer laser.

If the corneal stroma develops visually significant opacity, irregularity, or edema, a cornea of a deceased donor can be transplanted. Because there are no blood vessels in the cornea, there are also few problems with rejection of the new cornea.

There are also synthetic corneas (keratoprostheses) in development. Most are merely plastic inserts, but there are also those composed of biocompatible synthetic materials

that encourage tissue ingrowth into the synthetic cornea, thereby promoting biointegration.

Non-surgical procedures

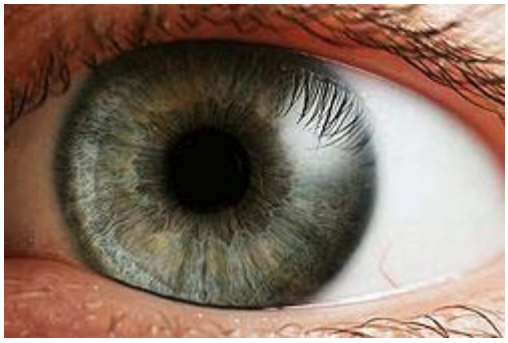
Orthokeratology is a method using specialized hard or rigid gas-permeable contact lenses to transiently reshape the cornea in order to improve the refractive state of the eye or reduce the need for eyeglasses and contact lenses.

In 2009, researchers at the University of Pittsburgh Medical center demonstrated that stem cells collected from human corneas can restore transparency without provoking a rejection response in mice with corneal damage.

Chapter 6

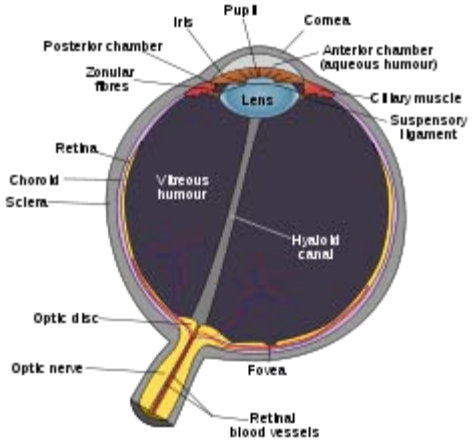
Pupil

Pupil



The human eye

The pupil is the central transparent area (showing as black). The grey/blue area surrounding it is the iris. The white outer area is the sclera, the central transparent part of which is the cornea.



Schematic diagram of the human eye.

The **pupil** is a hole located in the center of the iris of the eye that allows light to enter the retina. It appears black because most of the light entering the pupil is absorbed by the tissues inside the eye. In humans the pupil is round, but other species, such as some cats, have slit pupils. In optical terms, the anatomical pupil is the eye's aperture and the iris is the aperture stop. The image of the pupil as seen from outside the eye is the entrance pupil, which does not exactly correspond to the location and size of the physical pupil because it is magnified by the cornea. On the inner edge lies a prominent structure, the collarette, marking the junction of the embryonic pupillary membrane covering the embryonic pupil.

Controlling

The iris is a contractile structure, consisting mainly of smooth muscle, surrounding the pupil. Light enters the eye through the pupil, and the iris regulates the amount of light by controlling the size of the pupil. In humans the pupil is round, but other species, such as some cats, have slit pupils. The iris contains two groups of smooth muscles; a circular group called the sphincter pupillae, and a radial group called the dilator pupillae. When the sphincter pupillae contract, the iris decreases or constricts the size of the pupil. The dilator pupillae, innervated by sympathetic nerves from the superior cervical ganglion, cause the pupil to dilate when they contract. These muscles are sometimes referred to as intrinsic eye muscles. The sensory pathway (rod or cone, bipolar, ganglion) is linked with its counterpart in the other eye by a partial crossover of each eye's fibers. This causes the effect in one eye to carry over to the other. If the drug pilocarpine is administered, the pupils will constrict and accommodation is increased due to the parasympathetic action on the circular muscle fibers, conversely, atropine will cause paralysis of accommodation (cycloplegia) and dilation of the pupil. The sympathetic nerve system can dilate the pupil in two ways: by the stimulation of the sympathetic nerve in the neck, or by influx of adrenaline.

Optic effects

When bright light is shone on the eye light sensitive cells in the retina, including rod and cone photoreceptors and melanopsin ganglion cells, will send signals to the oculomotor nerve, specifically the parasympathetic part coming from the Edinger-Westphal nucleus, which terminates on the circular iris sphincter muscle. When this muscle contracts, it reduces the size of the pupil. This is the pupillary light reflex, which is an important test of brainstem function. Furthermore, the pupil will dilate if a person sees an object of interest.

The pupil gets wider in the dark but narrower in light. When narrow, the diameter is 3 to 4 millimeters. In the dark it will be the same at first, but will approach the maximum distance for a wide pupil 4 to 9 mm. In any human age group there is however considerable variation in maximal pupil size. For example, at the peak age of 15, the dark-adapted pupil can vary from 4 mm to 9 mm with different individuals. After 25 years of age the average pupil size decreases, though not at a steady rate. At this stage the pupils do not remain completely still, therefore may lead to oscillation, which may

intensify and become known as hippus. When only one eye is stimulated, both eyes contract equally. The constriction of the pupil and near vision are closely tied. In bright light, the pupils constrict to prevent aberrations of light rays and thus attain their expected acuity; in the dark this is not necessary, so it is chiefly concerned with admitting sufficient light into the eye.

A condition called *bene dilitatism* occurs when the optic nerves are partially damaged. This condition is typified by chronically widened pupils due to the decreased ability of the optic nerves to respond to light. In normal lighting, people afflicted with this condition normally have dilated pupils, and bright lighting can cause pain. At the other end of the spectrum, people with this condition have trouble seeing in darkness. It is necessary for these people to be especially careful when driving at night due to their inability to see objects in their full perspective. This condition is not otherwise dangerous.

Psychological effects

The pupil dilates in response to extreme emotional situations such as fear, or to contact of a sensory nerve, such as pain. Task-evoked pupillary response is the tendency of pupils to dilate slightly in response to loads on working memory, increased attention, sensory discrimination, or other cognitive loads.

Facial expressions of sadness with small pupils are judged significantly more intensely sad with decreasing pupil size though the brainstem pupillary control Edinger-Westphal nucleus in proportion to a person's pupil size change response to that in another. The greater degree to which a person's pupil dilation mirrors another person's coincides with that person having a greater empathy score.

Effect of drugs

The sphincter muscle has a parasympathetic innervation, and the dilator has a sympathetic innervation. In pupillary constriction induced by pilocarpine, not only is the sphincter nerve supply activated but that of the dilator is inhibited. The reverse is true, so control of pupil size is controlled by differences in contraction intensity of each muscle.

Certain drugs cause constriction of the pupils, such as alcohol and opioids. Other drugs, such as atropine, LSD, MDMA, mescaline, psilocybin mushrooms, cocaine and amphetamines may cause pupil dilation.

Another term for the constriction of the pupil is miosis. Substances that cause miosis are described as miotic. Dilation of the pupil is mydriasis. Dilation can be caused by mydriatic substances such as an eye drop solution containing tropicamide.

Chapter 7

Eyelid

Eyelid

Upper and lower eyelids
Latin *palpebra inferior, palpebra superior*
Gray's *subject #227 1025*
Artery lacrimal, superior palpebral, inferior palpebral
Nerve *upper:* infratrochlear, supratrochlear, supraorbital, lacrimal *lower:* infratrochlear, branches of infraorbital
MeSH *Eyelids*

An **eyelid** is a thin fold of skin that covers and protects an eye. With the exception of the prepuce and the labia minora, it has the thinnest skin of the whole body. The levator palpebrae superioris muscle retracts the eyelid to "open" the eye. This can be either voluntarily or involuntarily. The human eyelid features a row of eyelashes which serve to heighten the protection of the eye from dust and foreign debris, as well as from perspiration. "Palpebral" (and "blepharo") means relating to the eyelids. Its key function is to regularly spread the tears and other secretions on the eye surface to keep it moist, since the cornea must be continuously moist. They keep the eyes from drying out when asleep. Moreover, the blink reflex protects the eye from foreign bodies.

Anatomy

Layers

The eyelid is made up of several layers; from superficial to deep, these are: skin, subcutaneous tissue, orbicularis oculi, orbital septum & tarsal plates, and palpebral conjunctiva. The meibomian glands lie within the eyelid and secrete the lipid part of the tearfilm.

Skin

The skin is similar to areas elsewhere, but has more pigment cells. In diseased persons these may wander and cause a discoloration of the lids. It contains sweat glands and hairs, the latter becoming eyelashes as the border of the eyelid is met.

Innervation

In humans, the sensory nerve supply to the upper eyelids is from the infratrochlear, supratrochlear, supraorbital and the lacrimal nerves from the ophthalmic branch (V1) of the trigeminal nerve (CN V). The skin of the lower eyelid is supplied by branches of the infratrochlear at the medial angle, the rest is supplied by branches of the infraorbital nerve of the maxillary branch (V2) of the trigeminal nerve.

Blood supply

In humans, the eyelids are supplied with blood by two arches on each upper and lower lid. The arches are formed by anastamoses of the lateral palpebral arteries and medial palpebral arteries, branching off from the lacrimal artery and ophthalmic artery, respectively.

Death

After death, it is common in many cultures to pull the eyelids of the deceased down to close the eyes. This is a typical part of the last offices.

Eyelid disorders

Any condition that affects the eyelid is called eyelid disorder. The most common eyelid disorders, their causes, symptoms and treatments are the following:

• **Styes** are infections of the sebaceous glands of Zein usually caused by Staphylococcus Aureus bacteria. They are characterized by an acute onset of symptoms and they look like a red bump that is placed underneath the eyelid. The main symptoms of styes include pain, redness of the eyelid and sometimes swollen eyelids. Styes usually disappear within a week without treatment. Otherwise, antibiotics may be prescribed and home remedies

such as warm water compresses may be used to promote faster healing. Styes are normally harmless and do not cause long lasting damage.

• **Chalazion** is caused by the obstruction of the oil glands and can occur in both upper and lower eyelids. Chalazia may be mistaken as styes due to the similar symptoms. This condition is however less painful and it tends to be chronic. Chalazia heals within few months if treatment is administered and otherwise it can resorb within two years. Chalazia that do not respond to topical medication is usually treated with surgery as a last resort.

• **Blepharitis** is a common condition that causes inflammation of the eyelids and which is quite difficult to manage because it tends to recur. This condition is mainly caused by staphylococcus infection and scalp dandruff. Blepharitis symptoms include burning sensation, the feeling that there is something in the eye, excessive tearing, blurred vision, redness of the eye, light sensitivity, red and swollen eyelids, dry eye and sometimes crusting of the eyelashes on awakening. Treatment normally consists in maintaining a good hygiene of the eye and holding warm compresses on the affected eyelid to remove the crusts. Gently scrubbing the eyelid with the warm compress is recommended as it eases the healing process. In more serious cases, antibiotics may be prescribed.

• **Entropion** usually results from aging, but sometimes can be due to a congenital defect, a spastic eyelid muscle, or a scar on the inside of the lid that could be from surgery, injury, or disease. It is an asymptomatic condition that can rarely lead to trichiasis which requires surgery. It mostly affects the lower lid and it is characterized by the turning inward of the lid, toward globe.

• **Ectropion** is another aging-related eyelid condition that causes chronic eye irritation and scarring. It may also be the result of allergies and its main symptoms are excessive tearing and hardening of the eyelid conjunctiva.

• **Eyelid edema** is a condition in which the eyelids are swollen and contain excessive fluid. It may be serious when it increases the intraocular pressure. Eyelid edema is caused by an allergic reaction that one has to food, drugs, plan allergens, trichinosis or infections. The main symptoms are swollen red eyelids, pain, and itching. Treatment may vary depending on what is causing the condition. Whereas infections are fought against with antibiotics, allergic edemas treatments consists in staying away from the allergen. Chronic bouts of eyelid edema can lead to blepharochalasis.

• **Eyelid tumors** may also occur. Basal cell carcinomas are the most frequently encountered kind of cancer affecting the eyelid, making up 85% to 95% of all malignant eyelid tumors. The tumors may be benign or malignant. Usually benign tumors are localized and removed before becoming a cancerous threat and before they become large enough to impair one's vision. Malignant tumors on the other hand tend to spread to surrounding areas and tissues.

• **Eyelid twitching** is an involuntary spasm of the eyelid muscle. The most common factors that make the muscle in the eyelid twitch are fatigue, stress, and caffeine. Eyelid twitching is not considered a harmful condition and therefore there is no treatment available. Patients are however advised to get more sleep and drink less caffeine.

• **Eyelid dermatitis** is the inflammation of the eyelid skin. It is mostly a result of allergies or it is triggered by contact dermatitis of the eyelid. Symptoms that one may experience are dry and flaky skin on the eyelids and swollen eyelids. The affected eyelid may itch. Treatment consists in proper eye hygiene and avoiding the allergens that trigger the condition. In rare cases, topical creams may be used but only under a doctor's supervision.

Eyelid surgeries

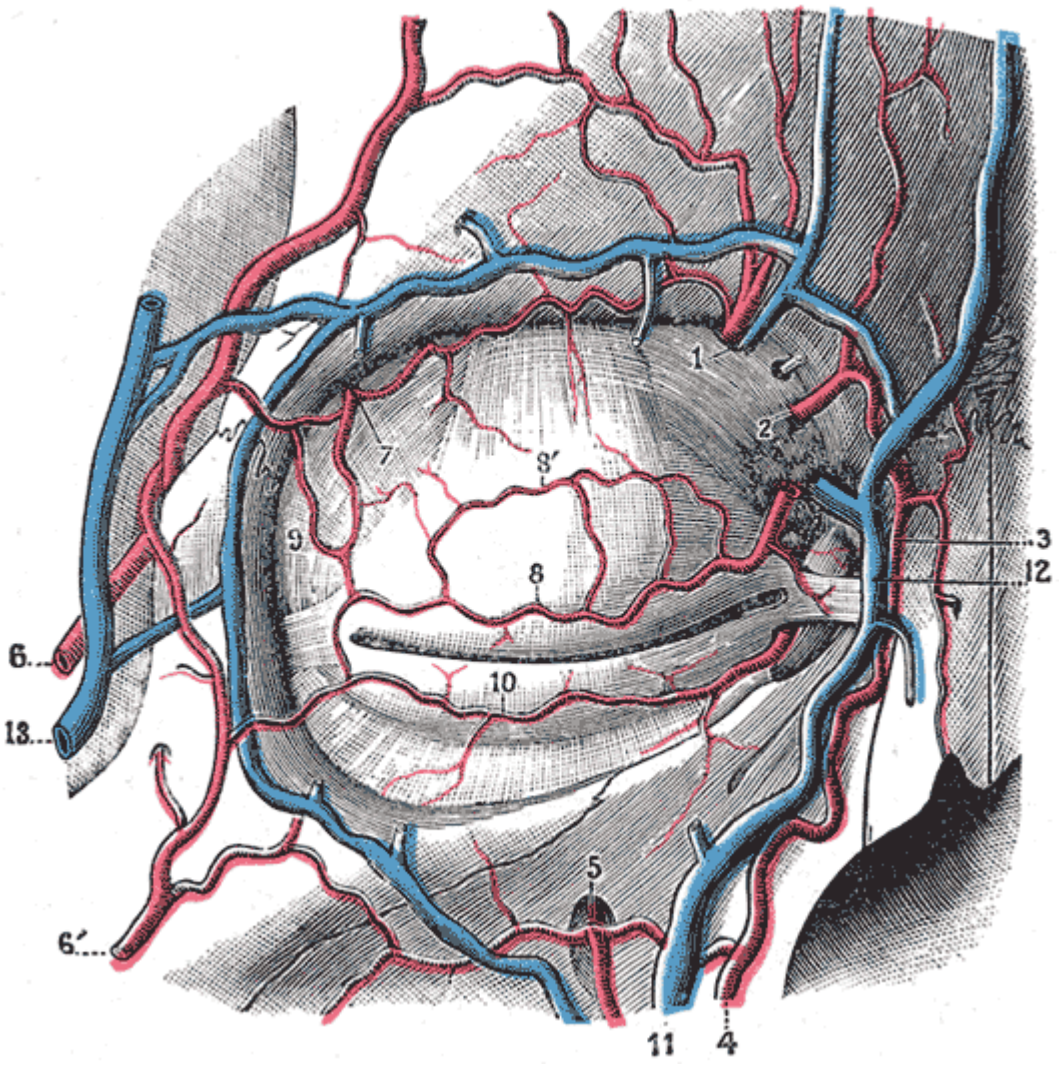
The eyelid surgeries are called blepharoplasties and are performed either out of medical reasons or to improve one's facial appearance.

Most of the cosmetic eyelid surgeries are aimed to enhance the look of the face and to boost one's self-confidence by restoring a youthful eyelid appearance. They are intended to remove fat and excess skin that may be found on the eyelids after a certain age. Cosmetic eyelid surgeries are mostly used to regain a younger and refreshed look but the costs are quite raised, so not everyone affords them.

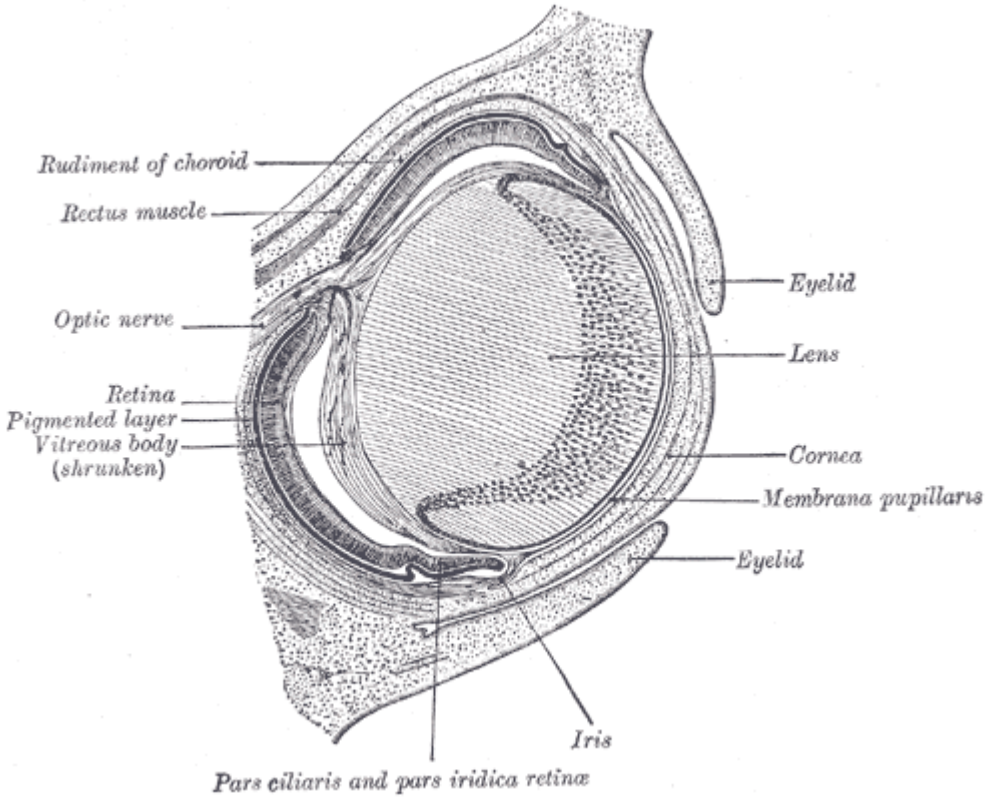
Eyelid surgeries are also performed to improve one's peripheral vision or to treat different eyelid related conditions such as chalazion, eyelid tumors, ptosis, trichiasis, and other.

Eyelid surgeries are overall safe procedures but they carry certain risks since the area on which the operation is performed is so close to the eye.

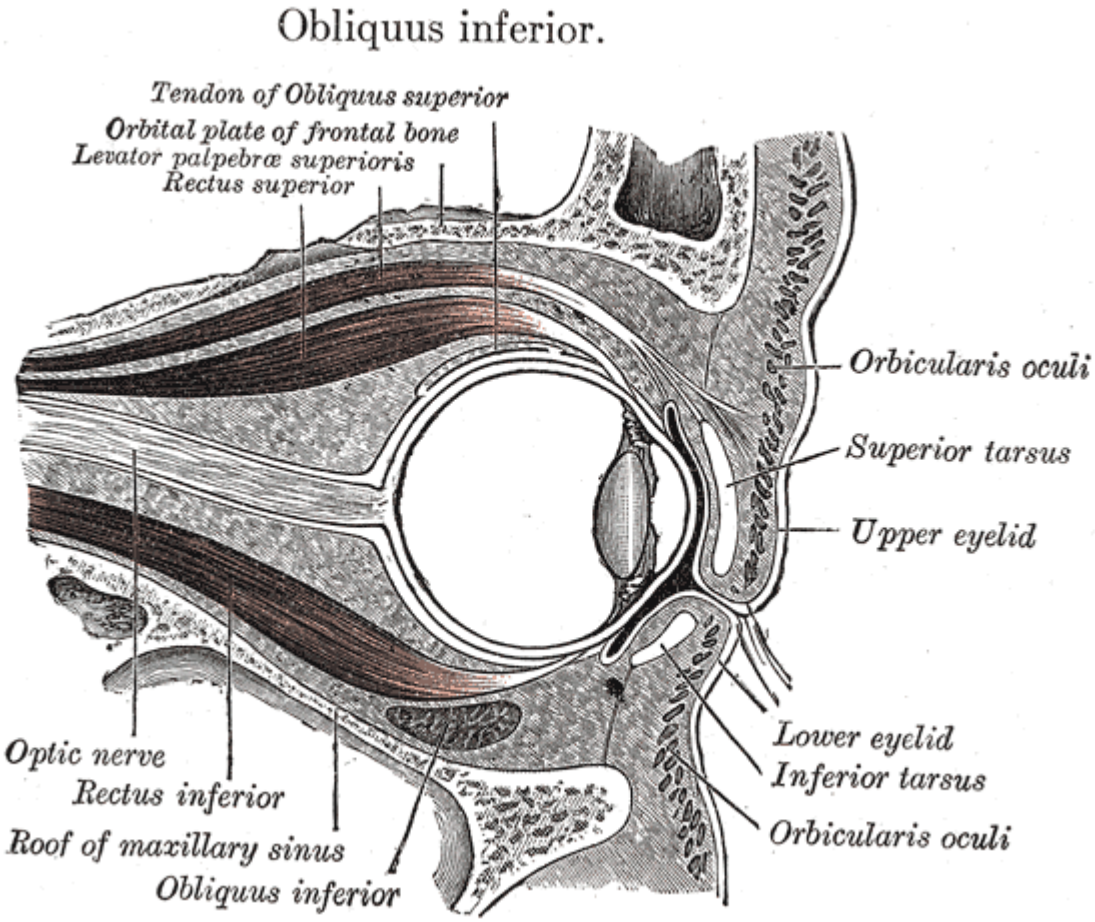
Eye makeup



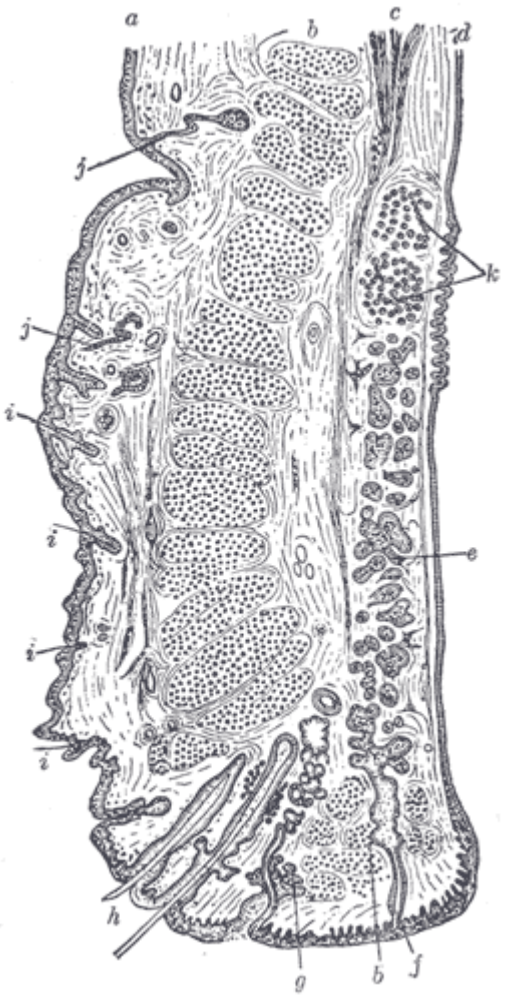
Bloodvessels of the eyelids, front view



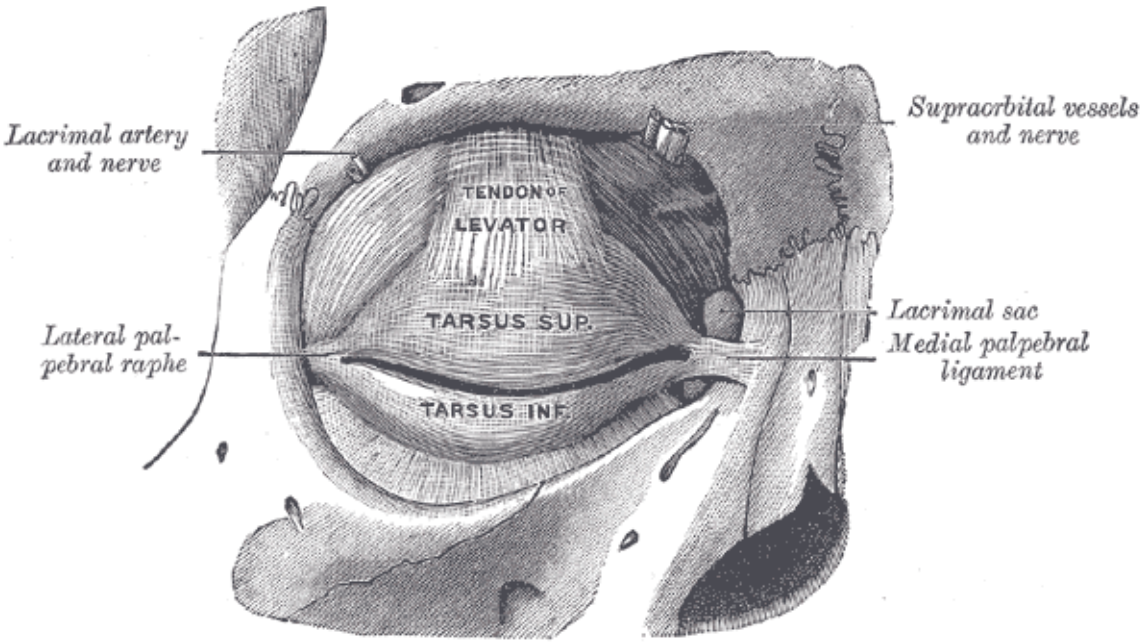
Horizontal section through the eye of an eighteen days' embryo rabbit



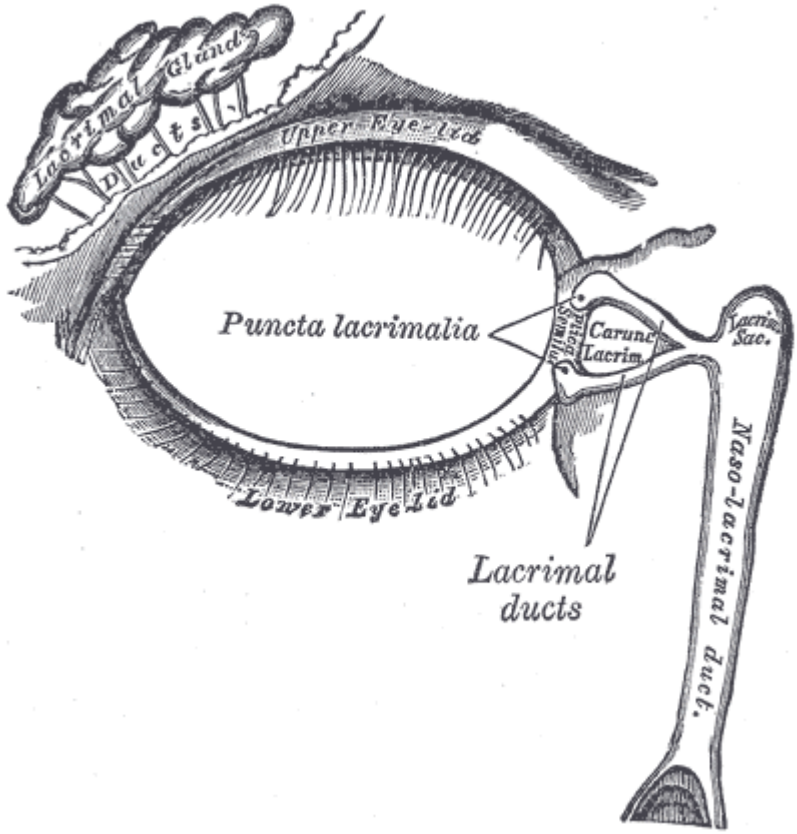
Sagittal section of right orbital cavity



Sagittal section through the upper eyelid



The tarsi and their ligaments. Right eye; front view



The lacrimal apparatus. Right side

Chapter 8

Eyebrow and Eyelash

Eyebrow

Eyebrow

A man's unmodified eyebrow and eye

Latin	*supercilium*
MeSH	*Eyebrows*

The **eyebrow** is an area of thick, delicate hairs above the eye that follows the shape of the lower margin of the brow ridges of some mammals. Their main function is to prevent sweat or water, and other debris, from falling down into the eye socket, but they are also important to human communication and facial expression. It is not uncommon for people – women in particular – to modify their eyebrows by means of hair addition, removal, make up, or piercings.

Functions

Physical

The main function of the eyebrow is to prevent moisture, mostly salty sweat and rain, from flowing into the eye. The typical curved shape of the eyebrow (with a slant on the side) and the direction in which eyebrow hairs are pointed, make sure that moisture has a tendency to flow sideways around the eyes, along the side of the head and along the nose. The slightly protruding brow ridges of modern humans could also still play a supporting role in this process in this way it helps them make expressions. Together with the brow ridges, the eyebrows also shade the eyes from sunlight. Eyebrows also prevent debris

such as dandruff and other small objects from falling into the eyes, as well as providing a more sensitive sense for detecting objects being near the eye, like small insects.The name for one hair of the eyebrow is the browy.

Psychological

Eyebrows also have an important facilitative function in communication, strengthening expressions, such as surprise or anger. Many makeup artists view eyebrows as a major feature in defining the face. The eyebrows shape the human face and give definition to one's eyes and forehead. Depending on the shape of the eyebrows, it sometimes can cause what is known as a false facial expression (such as a person's eyebrows shaped to seem as if the person was angry, but really isn't).

Identification

In a study published by MIT, where subjects were asked to identify celebrities with either their eyes or their eyebrows digitally edited out, the subjects were able to recognize the celebrity 46% of the time with their eyebrows edited out, compared to 60% of the time with their eyes edited out. The findings indicate the importance of eyebrows in providing cues to an individual's identity.

Eyebrow modification

A woman's eyebrow that has been modified via waxing

Eyebrows are a major facial feature. Several cosmetic methods have been developed to enhance the look of one's eyebrows, whether the goal is to add or remove hair, change the color, or change the position of the eyebrow.

Several options exist for removing hair in order to achieve a thinner or smaller eyebrow, or to "correct" a unibrow, including tweezing, waxing, threading and electronic tweezer. The most common method is to use tweezers to thin out and shape the eyebrow. Waxing is also becoming more popular in recent times. Lastly, there is the option of threading eyebrows, wherein a cotton thread is rolled over hair to pull it out. Small scissors are sometimes used to trim the eyebrows, either along with another method of hair removal or alone. All of these methods can be painful for some seconds or minutes due to the sensitivity of the area around the eye, but, often, this pain decreases over time as the individual becomes used to the sensation. After a certain period of time, hair that has

been plucked will stop growing back. There are some who completely wax or shave off their entire eyebrows, then, either leave them bare, stencil or draw them in with eye liner, or tattoo them on. In Western societies, it has become more common for men to pluck part of their eyebrows as well.

To create a fuller look, eyebrows can be cloned in an eyebrow transplant, wherein individual strands of the eyebrow are mimicked to create a natural looking eyebrow of the desired shape. Eyebrow brushes and shaders are also used to further define the eyebrow. A fairly recent trend in eyebrow modification is in the form of eyebrow tinting, in which permanent dye, similar to that of hair color, is used on the eyebrow, often to darken them.

An eyebrow-lift, a cosmetic surgery to raise the eyebrow, usually in order to create a more feminine or youthful appearance, is a new phenomenon. They can be affected during a face lift or an eye lift. More recently, doctors inject patients' eyebrows with botox or similar toxins to temporarily raise the eyebrow.

Shaving lines in eyebrows is another cosmetic alteration, more common among younger people in the 1990s and 2000s.

Eyelash

Eyelash

Human eyelashes

Latin *cilia*

An **eyelash** or simply **lash** is one of the hairs that grow at the edge of the eyelid. Eyelashes protect the eye from debris and perform some of the same function as whiskers do on a cat or a mouse in the sense that they are sensitive to being touched, thus providing a warning that an object (such as an insect or dust mite) is near the eye (which is then closed reflexively).

The Greek word for eyelash is "blepharis". This word is often used as a root in biological terms (*Blepharis*, Kathablepharis, etc.)

Human eyelashes

The eyelashes of the embryo develop between the 22nd and 26th week of pregnancy. Eyelashes take about seven to eight weeks to grow back if pulled out. Their color may differ from that of the hair, although they tend to be dark on someone with dark hair and lighter on someone with light hair.

The follicles of eyelashes are associated with a number of glands known as the Glands of Zeis and the Glands of Moll.

Cosmetics

Green mascara

Long eyelashes are considered a sign of femininity in many cultures. Accordingly, some women seek to enhance their eyelash length artificially, using eyelash extensions. On the other hand, Hadza women are known to trim their own eyelashes.

Kohl has been worn as far back as the Bronze Age to protect and enhance lashes. In Ancient Egypt it was used as well by the wealthy and the royal to protect their eyes from the sand, dust and bugs.

Modern eye makeup includes mascara, eyeliner, eye putty, and eye shadow to emphasize the eyes. The twentieth century saw the beginning of convincing-looking false eyelashes, popular in the 1960s.

Permanent eyelash tints and eyelash extensions have also become popular procedures, even in fairly basic salons.

It is also possible to get eyelash transplants, which are similar in nature to hair transplantation often done on the head. Since the hair is tranplanted from the hair on the head, the new eyelashes will continue to grow like head hair and will need to be trimmed regularly.

Latisse was introduced in the first quarter of 2009 by Allergan as the first drug to receive FDA approval for eyelash growth. Latisse is a solution of bimatoprost, the active component of the glaucoma medication Lumigan. According to Allergan, noticeable eyelash growth occurs within 16 weeks. Growth is reported to occur primarily on the upper eyelashes.

In addition, the past decade has seen the rapid increase in the development of eyelash conditioners. These conditioners are designed to increase the health and length of your lashes. Many utilize seed extract, minerals, and other chemicals to achieve these results.

Health

A stye

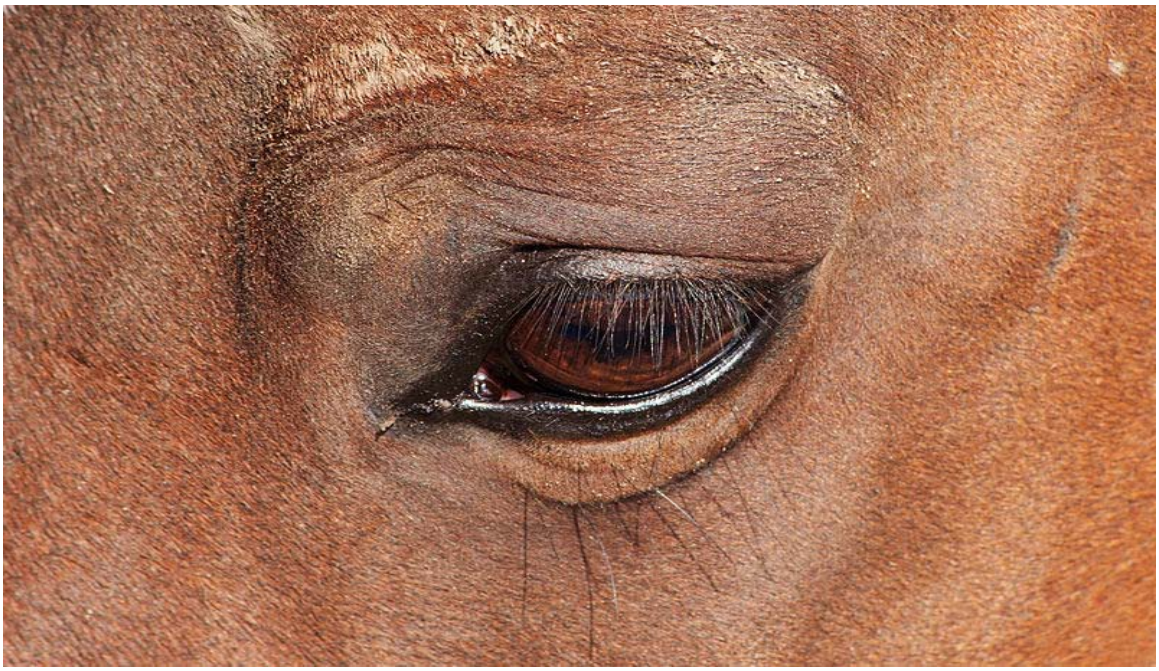
There are a number of diseases or disorders involving the eyelashes:

- Madarosis is the loss of eyelashes.
- Blepharitis is the irritation of the lid margin, where eyelashes join the eyelid. The eyelids are red and itching, the skin often becomes flaky, and the eyelashes may fall out.
- Distichiasis is the abnormal growth of lashes from certain areas of the eyelid.
- Trichiasis is ingrown eyelashes.
- Eyelashes may become infested with parasitic crab louse.

- An external hordeolum, or stye, is a purulent inflammation of infected eyelash follicles and surrounding sebaceous (Zeis) and apocrine (Moll) glands of the lid margin.
- Trichotillomania is a disorder that urges the sufferer to pull out scalp hair, eyelashes, etc.
- *Demodex folliculorum* (or the demodicid) is a small mite that lives harmlessly in eyelash and other hair follicles, and about 98% of people have these mites living on them. Occasionally they may cause blepharitis.

Eyelash and eyebrow transplant surgeries may be help to reconstruct or thicken lashes or eyebrow hair.

Nonhumans



A horse's eye, showing lashes

Lashes, being hair, are found in mammals. Camels' lashes are remarkably long and thick. Horses, cows, and also ostriches, (vestigial feathers without barbs) feature eyelashes as well.

Inherited eyelash problems are common in some breeds of dogs.

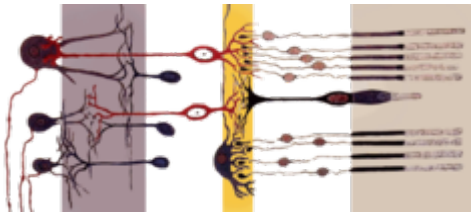
Eyelash vipers show a set of modified scales over the eyes which look much like eyelashes.

Hornbills have prominent feather eyelashes, an uncommon feature in birds.

Chapter 9

Rod Cell

Neuron: Rod cell



Cross section of the retina. Rods are visible at far right.

Location	Retina
Function	Low light photoreceptor
Morphology	rod shaped
Presynaptic connections	None
Postsynaptic connections	Bipolar Cells and Horizontal cells
NeuroLex ID	*sao1458938856*

Rod cells, or **rods**, are photoreceptor cells in the retina of the eye that can function in less intense light than can the other type of visual photoreceptor, cone cells. Named for their cylindrical shape, rods are concentrated at the outer edges of the retina and are used in peripheral vision. On average, there are approximately 92 million rod cells in the human retina. More sensitive than cone cells, rod cells are almost entirely responsible for night vision.

Structure and function

Rods are a little narrower than cones but have the same structural basis. The pigment is on the outer side, lying on the pigment epithelium. This end contains many stacked disks. Rods have a high area for visual pigment and thus substantial efficiency of light absorption. Because they have only one type of light-sensitive pigment, rather than the three types that human cone cells have, rods have little, if any, role in color vision.

Like cones, rod cells have a synaptic terminal, an inner segment, and an outer segment. The synaptic terminal forms a synapse with another neuron, for example a bipolar cell.

The inner and outer segments are connected by a cilium, which lines the distal segment. The inner segment contains organelles and the cell's nucleus, while the rod outer segment (abbreviated to ROS), which is pointed toward the back of the eye, contains the light-absorbing materials.

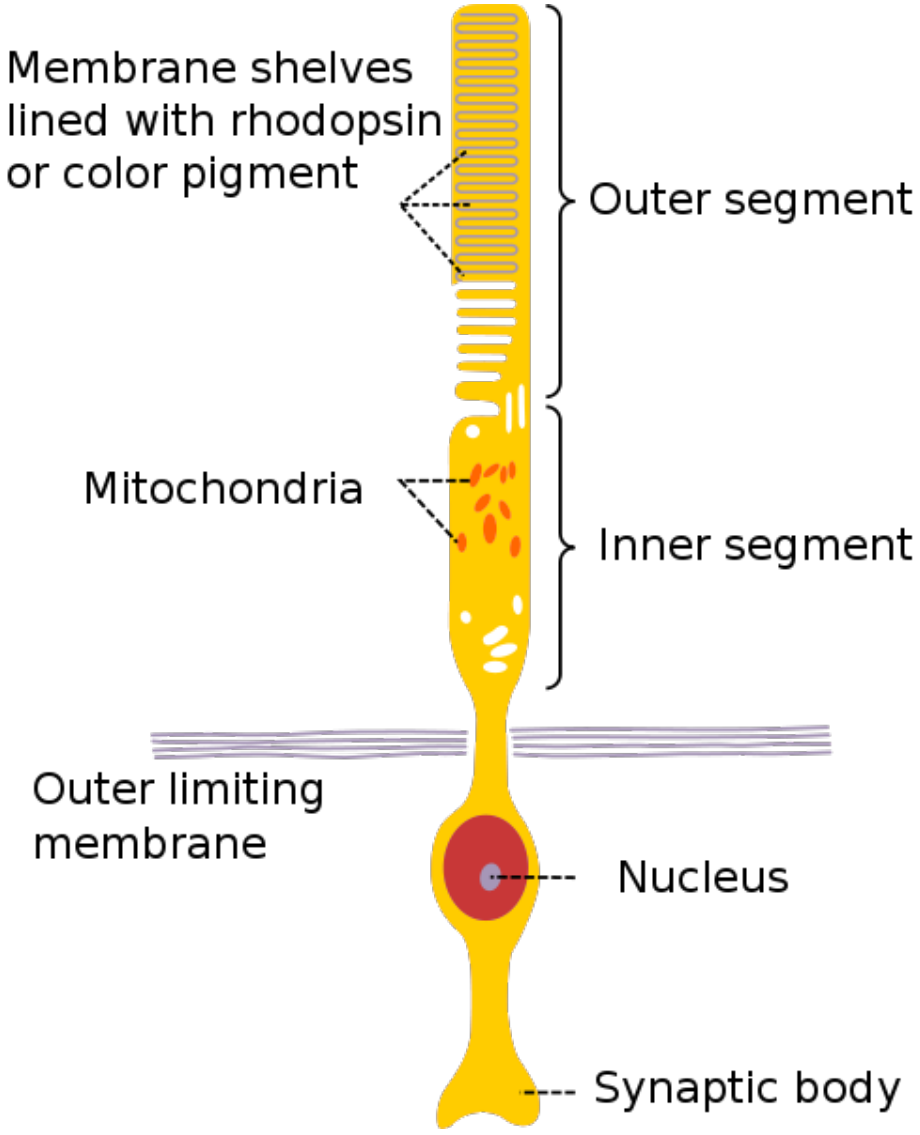
Sensitivity

A rod cell is sensitive enough to respond to a single photon of light, and is about 100 times more sensitive to a single photon than cones. Rods require less light to function than cones, they are therefore the primary source of visual information at night (scotopic vision). Cone cells, on the other hand, require tens to hundreds of photons to become activated. Additionally, multiple rod cells converge on a single interneuron, collecting and amplifying the signals. However, this convergence comes at a cost to visual acuity (or image resolution) because the pooled information from multiple cells is less distinct than it would be if the visual system received information from each rod cell individually. The convergence of rod cells also tends to make peripheral vision very sensitive to movement, and is responsible for the phenomenon of an individual seeing something vague occur out of the corner of his or her eye.

Rod cells also respond more slowly to light than cones do, so stimuli they receive are added over about 100 milliseconds. While this makes rods more sensitive to smaller amounts of light, it also means that their ability to sense temporal changes, such as quickly changing images, is less accurate than that of cones.

Experiments by George Wald and others showed that rods are most sensitive to wavelengths of light around 498 nm (green-blue), and less sensitive to wavelengths longer than about 640 nm (red). This fact is responsible for the Purkinje effect, in which blue colors appear more intense relative to reds at twilight, when rods take over as the cells responsible for vision.

Response to light



Anatomy of a Rod Cell

In vertebrates, activation of a photoreceptor cell is actually a hyperpolarization (inhibition) of the cell. When they are not being stimulated, such as in the dark, rod cells and cone cells depolarize and release a neurotransmitter spontaneously. This neurotransmitter hyperpolarizes the bipolar cell. Bipolar cells exist between photoreceptors and ganglion cells and act to transmit signals from the photoreceptors to the ganglion cells. As a result of the bipolar cell being hyperpolarized, it does not release its transmitter at the bipolar-ganglion synapse and the synapse is not excited.

Activation of photopigments by light sends a signal by hyperpolarizing the rod cell, leading to the rod cell not sending its neurotransmitter, which leads to the bipolar cell then releasing its transmitter at the bipolar-ganglion synapse and exciting the synapse.

Depolarization of rod cells (causing release of their neurotransmitter) occurs because in the dark, cells have a relatively high concentration of cyclic guanosine 3'-5' monophosphate (cGMP), which opens ion channels (largely sodium channels, though calcium can enter through these channels as well). The positive charges of the ions that enter the cell down its electrochemical gradient change the cell's membrane potential, cause depolarization, and lead to the release of the neurotransmitter glutamate. Glutamate can depolarize some neurons and hyperpolarize others, allowing photoreceptors to interact in an antagonistic manner.

When light hits photoreceptive pigments within the photoreceptor cell, the pigment changes shape. The pigment, called rhodopsin (photopsin is found in cone cells) comprises a large protein called opsin (situated in the plasma membrane), attached to which is a covalently-bound prosthetic group: an organic molecule called retinal (a derivative of vitamin A). The retinal exists in the 11-cis-retinal form when in the dark, and stimulation by light causes its structure to change to all-trans-retinal. This structural change causes a series of changes in the opsin that ultimately lead it to activate a regulatory protein called transducin (a type of G protein), which leads to the activation of cGMP phosphodiesterase, which breaks cGMP down into 5'-GMP. Reduction in cGMP allows the ion channels to close, preventing the influx of positive ions, hyperpolarizing the cell, and stopping the release of neurotransmitters (Kandel et al., 2000). Though cone cells primarily use the neurotransmitter substance acetylcholine, rod cells use a variety. The entire process by which light initiates a sensory response is called visual phototransduction.

Activation of a single unit of rhodopsin, the photosensitive pigment in rods, can lead to a large reaction in the cell because the signal is amplified. Once activated, rhodopsin can activate hundreds of transducin molecules, each of which in turn activates a phosphodiesterase molecule, which can break down over a thousand cGMP molecules per second (Kandel et al. 2000). Thus, rods can have a large response to a small amount of light.

As the retinal component of rhodopsin is derived from vitamin A, a deficiency of vitamin A causes a deficit in the pigment needed by rod cells. Consequently, fewer rod cells are able to sufficiently respond in darker conditions, and as the cone cells are poorly adapted for sight in the dark, blindness can result. This is night-blindness.

Revert to the resting state

Rods make use of three inhibitory mechanisms (negative feedback mechanisms) to allow a rapid revert to the resting state after a flash of light.

Firstly, there exists a rhodopsin kinase (RK) which would phosphorylate the cytosolic tail of the activated rhodopsin on the multiple serines, partially inhibiting the activation of transducin. Also, an inhibitory protein - arrestin then binds to the phosphorylated rhodopsins to further inhibit the rhodopsin's activity.

While arrestin shuts off rhodopsin, an RGS protein (functioning as a GTPase-activating proteins(GAPs)) drives the transducin (G-protein) into an "off" state by increasing the rate of hydrolysis of the bounded GTP to GDP.

Also as the cGMP sensitive channels allow not only the influx of sodium ions, but also calcium ions, with the decrease in concentration of cGMP, cGMP sensitive channels are then closed and reducing the normal influx of calcium ions. The decrease in the concentration of calcium ions stimulates the calcium ion-sensitive proteins, which would then activate the guanylyl cyclase to replenish the cGMP, rapidly restoring its original concentration. The restoration opens the cGMP sensitive channels and causes a depolarization of the plasma membrane.

Desensitization

When the rods are exposed to a high concentration of photons for a prolonged period, they become desensitized (adapted) to the environment.

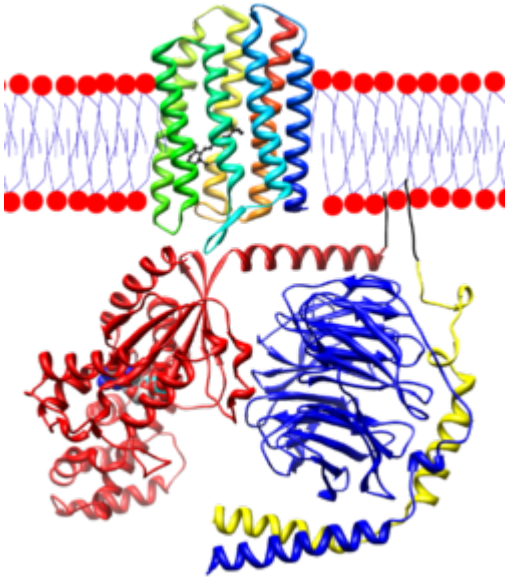
As rhodopsin is phosphorylated by rhodopsin kinase (a member of the GPCR kinases(GRKs)), it binds with high affinity to the arrestin. The bound arrestin can contribute to the desensitization process in at least two ways. First, it prevents the interaction between the G protein and the activated receptor. Second, it serves as an adaptor protein to aid the receptor to the clathrin-dependent endocytosis machinery (to induce receptor-mediated endocytosis).

Chapter 10

Rhodopsin and Drusen

Rhodopsin

Rhodopsin (opsin 2, rod pigment) (retinitis pigmentosa 4, autosomal dominant)

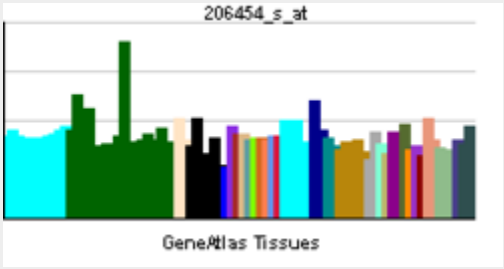


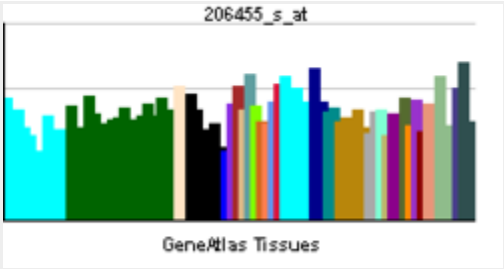
Sensory rhodopsin II (rainbow colored) embedded in a lipid bilayer (heads red and tails blue) with Transducin below it. $G_t\alpha$ is colored red, $G_t\beta$ blue, and $G_t\gamma$ yellow. There is a bound GDP molecule in the $G_t\alpha$-subunit and a bound retinal (black) in the rhodopsin. The N-terminus terminus of rhodopsin is red and the C-terminus blue. Presumed anchoring of transducin to the membrane has been drawn in black.

Identifiers

Symbols	RHO; MGC138309; MGC138311; OPN2; RP4
External IDs	OMIM: 180380 MGI: 97914 HomoloGene: 68068 GeneCards: RHO Gene

RNA expression pattern





More reference expression data

Orthologs

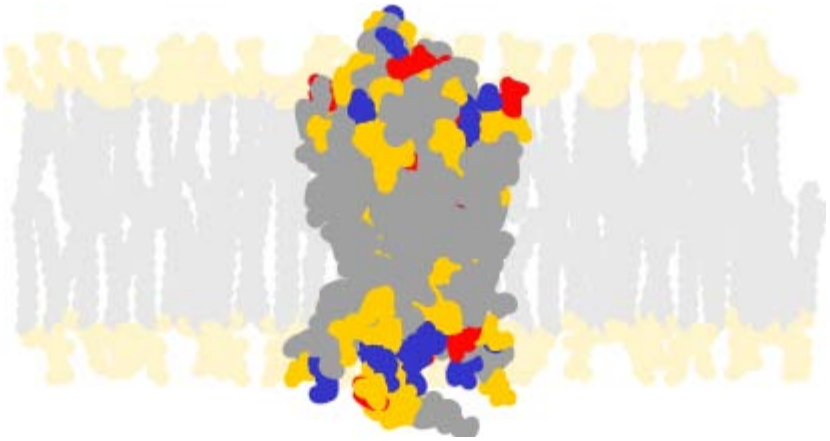
Species	Human	Mouse
Entrez	6010	212541
Ensembl	ENSG00000163914	ENSMUSG00000030324
UniProt	P08100	Q8K0D8
RefSeq (mRNA)	NM_000539	NM_145383
RefSeq (protein)	NP_000530	NP_663358
Location (UCSC)	Chr 3: 130.73 - 130.74 Mb	Chr 6: 115.9 - 115.9 Mb

Rhodopsin, also known as **visual purple**, is a pigment of the retina that is responsible for both the formation of the photoreceptor cells and the first events in the perception of light. Rhodopsins belong to the G-protein coupled receptor family and are extremely sensitive to light, enabling vision in low-light conditions. Exposed to light, the pigment immediately photobleaches, and it takes about 30 minutes to regenerate fully in humans.

Structure

Rhodopsin consists of the protein moiety **opsin** and a reversibly covalently bound cofactor, retinal. Opsin, a bundle of seven transmembrane helices connected to each other by protein loops, binds retinal (a photoreactive chromophore), which is located in a central pocket on the seventh helix at a lysine residue. Retinal lies horizontally with relation to the membrane. Each outer segment disc contains thousands of visual pigment molecules. About half the opsin is within the lipid bilayer. Retinal is produced in the retina from Vitamin A, from dietary beta-carotene. Isomerization of 11-*cis*-retinal into all-*trans*-retinal by light induces a conformational change (bleaching) in opsin continuing with metarhodopsin II, which activates the associated G protein transducin and triggers a second messenger cascade.

Rhodopsin of the rods most strongly absorbs green-blue light and therefore appears reddish-purple, which is why it is also called "visual purple". It is responsible for *monochromatic* vision in the dark.



Bovine rhodopsin

Several closely related opsins exist that differ only in a few amino acids and in the wavelengths of light that they absorb most strongly. Humans have four different other opsins beside rhodopsin. The photopsins are found in the different types of the cone cells of the retina and are the basis of color vision. They have absorption maxima for yellowish-green (photopsin I), green (photopsin II), and bluish-violet (photopsin III) light. The remaining opsin (melanopsin) is found in photosensitive ganglion cells and absorbs blue light most strongly.

The structure of rhodopsin has been studied in detail via x-ray crystallography on rhodopsin crystals. The photoisomerization dynamics has been investigated with time-resolved IR spectroscopy and UV/Vis spectroscopy. A first photoproduct called **photorhodopsin** forms within 200 femtoseconds after irradiation followed within picoseconds by a second one called **bathorhodopsin** with distorted all-trans bonds. This

intermediate can be trapped and studied at cryogenic temperatures. Several models (e.g. the *bicycle-pedal mechanism*, *hula-twist mechanism*) attempt to explain how the retinal group can change its conformation without clashing with the enveloping rhodopsin protein pocket.

Recent data supports that it is a functional monomer as opposed to a dimer, which was the paradigm of G-coupled protein receptors for many years.

Rhodopsin and retinal disease

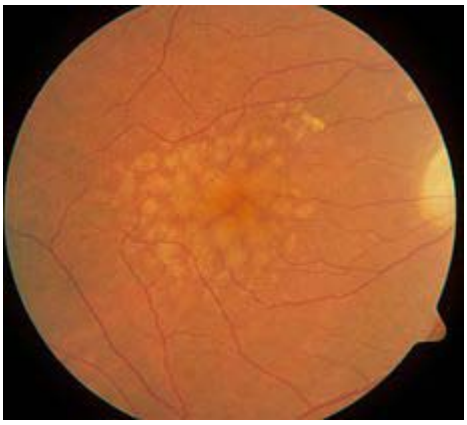
Mutation of the rhodopsin gene is a major contributor to various retinopathies such as retinitis pigmentosa. The disease-causing protein generally aggregates with ubiquitin in inclusion bodies, disrupts the intermediate filament network and impairs the ability of the cell to degrade non-functioning proteins which leads to photoreceptor apoptosis. Other mutations on rhodopsin lead to X-linked congenital stationary night blindness, mainly due to constitutive activation, when the mutations occur around the chromophore binding pocket of rhodopsin. Several other pathological states relating to rhodopsin have been discovered including poor post-Golgi trafficking, dysregulative activation, rod outer segment instability and arrestin binding.

Microbial rhodopsins

Some prokaryotes express proton pumps called bacteriorhodopsin, proteorhodopsin, xanthorhodopsin to carry out phototrophy. Like rhodopsin, these contain retinal and have seven transmembrane alpha helices; however they are not coupled to a G protein. Bacterial halorhodopsin is a light-activated chloride pump. Finally, an alga is known to have an opsin that contains its own monolithic light-gated ion channel, channelrhodopsin. While bacteriorhodopsin, halorhodopsin, and channelrhodopsin all have significant sequence homology to one another, they have no detectable sequence identity to G-protein coupled receptor (GPCR) family where rhodopsins belong. Nevertheless, bacterial rhodopsins and GPCR are possibly evolutionarily related, based on similarity of their three-dimensional structures. Therefore, they have been assigned to the same superfamily in Structural Classification of Proteins.

Drusen

Drusen



Macular soft Drusen in the right eye of a 70 year old male

ICD-10	H35.3, H47.3
OMIM	126700 126600 611040 603075 134370
DiseasesDB	29371
eMedicine	topic list

Drusen (singular, "druse") are tiny yellow or white accumulations of extracellular material that build up in Bruch's membrane of the eye. The presence of a few small ("hard") drusen is normal with advancing age, and most people over 40 have some hard drusen. However, the presence of larger and more numerous drusen in the macula is a common early sign of age-related macular degeneration (AMD).

Classification

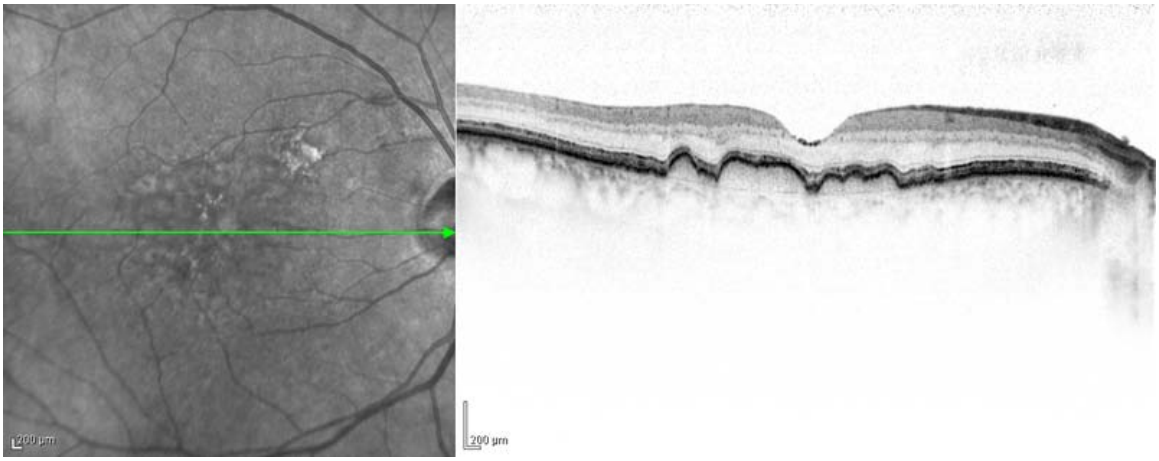
Drusen associated with aging and macular degeneration are distinct from another clinical entity, optic disc drusen, which is present on the optic nerve head. Both age-related drusen and optic disc drusen can be observed by ophthalmoscopy. On CT scans of the orbits or head, calcification at the head of the optic nerve without change in size of globe strongly suggests drusen in a middle-age or elderly patient.

Whether drusen promote AMD or are symptomatic of an underlying process that causes both drusen and AMD is not known, but they are indicators of increased risk of the complications of AMD.

'Hard drusen' may coalesce into 'soft drusen' which is a manifestation of macular degeneration.

Pathophysiology

Drusen were initially described by Franciscus Donders who called them "Colloidkugeln" (colloid spheres). Later, Heinrich Müller named them for the German word for geode, based on their glittering appearance. In view of their location between the retinal pigment epithelium (RPE) and its vascular supply, the choriocapillaris, it is possible that drusen deprive the RPE and photoreceptor cells of oxygen and nutrients. Interestingly, drusen always develop above the so called pillars of choriocapillaris that is the area between two microvessels.



Drusen in Optical Coherence Tomography

The source of the proteins and lipids in drusen is also not clear, with potential contributions by both the RPE and the choroid. Several trace elements are present in drusen, probably the most concentrated being zinc. The protein composition of drusen includes apolipoproteins and members of the complement system. Zinc in drusen have been suggested to play a role in drusen formation by precipitating and inhibiting the elements of the complement cascade, especially complement factor H.

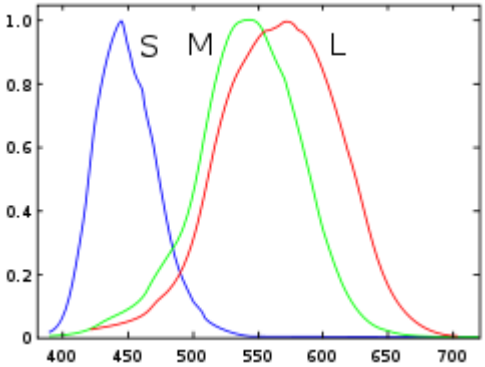
The presence of molecules that regulate inflammation in drusen has led some investigators to conclude that these deposits are product of the immune system.

Chapter 11

Cone Cell and Ciliary Body

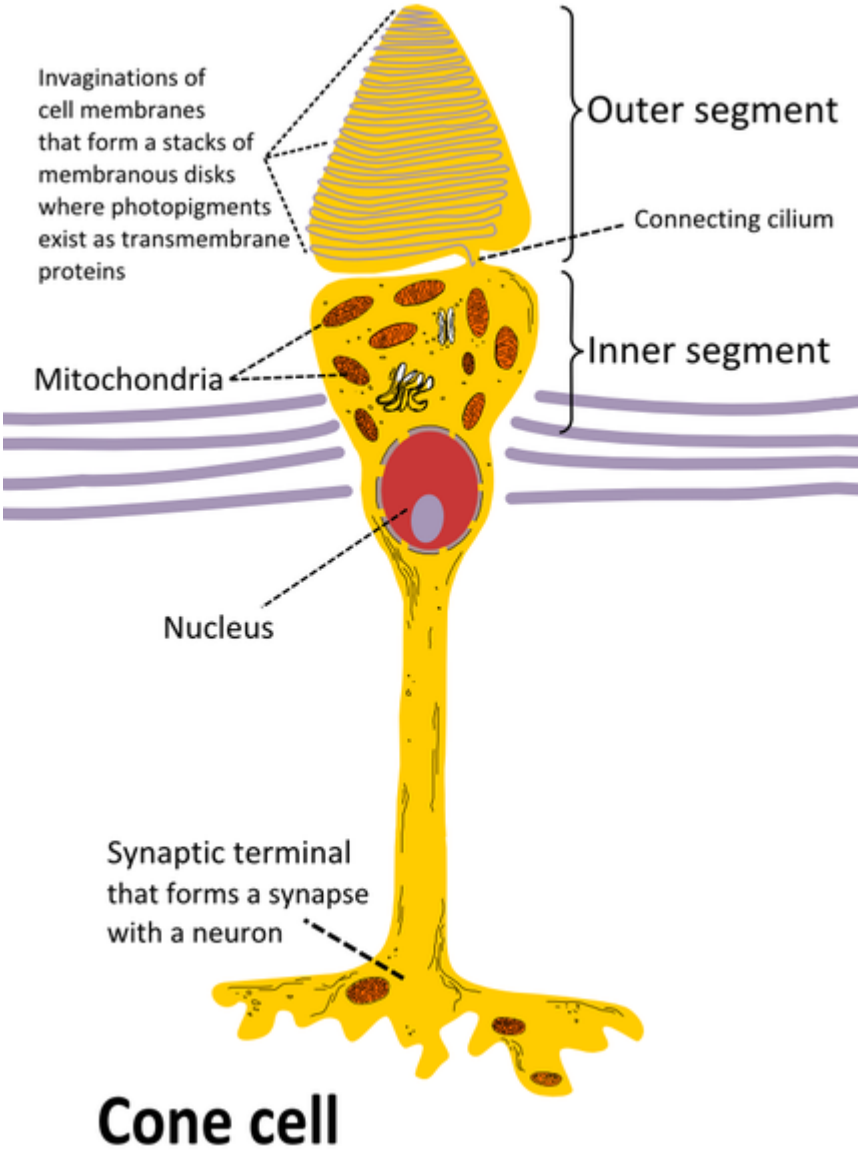
Cone cell

Neuron: Cone Cell



Normalized responsivity spectra of human cone cells, S, M, and L types

NeuroLex ID *sao1103104164*



Cone cell structure

Cone cells, or **cones**, are photoreceptor cells in the retina of the eye that are responsible for color vision; they function best in relatively bright light, as opposed to rod cells that work better in dim light. Cone cells are densely packed in the fovea, but gradually become sparser towards the periphery of the retina.

A commonly cited figure of six million in the human eye was found by Osterberg in 1935. Oyster's textbook (1999) cites work by Curcio et al. (1990) indicating an average closer to 4.5 million cone cells and 90 million rod cells in the human retina.

Cones are less sensitive to light than the rod cells in the retina (which support vision at low light levels), but allow the perception of color. They are also able to perceive finer

detail and more rapid changes in images, because their response times to stimuli are faster than those of rods. Because humans usually have three kinds of cones with different photopsins, which have different response curves and thus respond to variation in color in different ways, they have trichromatic vision. Being color blind can change this, and there have been reports of people with four or more types of cones, giving them tetrachromatic vision.

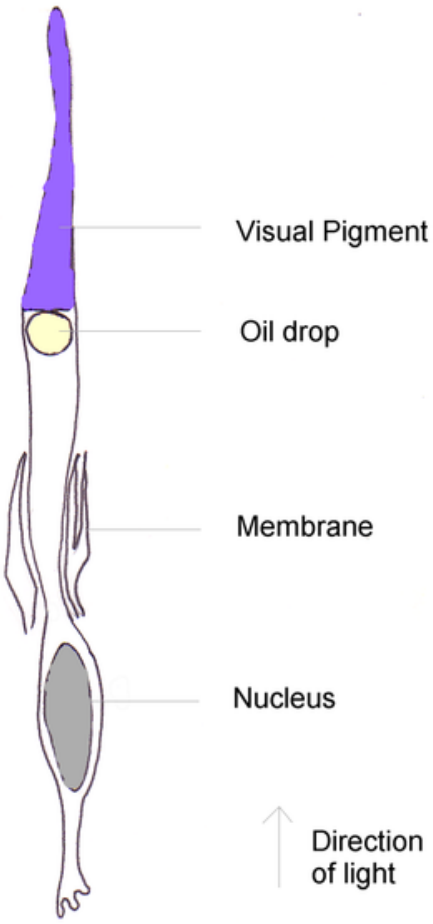
Types

Humans normally have three kinds of cones. The first responds most to light of long wavelengths, peaking at a greenish yellow color; this type is sometimes designated **L** for long. The second type responds most to light of medium-wavelength, peaking at a green color, and is abbreviated **M** for medium. The third type responds most to short-wavelength light, of a bluish color, and is designated **S** for short. The three types have peak wavelengths near 564–580 nm, 534–545 nm, and 420–440 nm, respectively. The difference in the signals received from the three cone types allows the brain to perceive all possible colors, through the opponent process of color vision. (Rod cells have a peak sensitivity at 498 nm, roughly halfway between the peak sensitivities of the S and M cones.)

The color yellow, for example, is perceived when the L cones are stimulated slightly more than the M cones, and the color red is perceived when the L cones are stimulated significantly more than the M cones. Similarly, blue and violet hues are perceived when the S receptor is stimulated more than the other two.

The **S** cones are most sensitive to light at wavelengths around 420 nm. However, the lens and cornea of the human eye are increasingly absorptive to smaller wavelengths, and this sets the lower wavelength limit of human-visible light to approximately 380 nm, which is therefore called 'ultraviolet' light. People with aphakia, a condition where the eye lacks a lens, sometimes report the ability to see into the ultraviolet range. At moderate to bright light levels where the cones function, the eye is more sensitive to yellowish-green light than other colors because this stimulates the two most common of the three kinds of cones almost equally. At lower light levels, where only the rod cells function, the sensitivity is greatest at a blueish-green wavelength.

Structure



Bird, reptilian, and monotreme cone cells contain a colored oil drop

Cone cells are somewhat shorter than rods, but wider and tapered, and are much less numerous than rods in most parts of the retina, but greatly outnumber rods in the fovea. Structurally, cone cells have a cone-like shape at one end where a pigment filters incoming light, giving them their different response curves. They are typically 40-50 µm long, and their diameter varies from 0.5 to 4.0 µm, being smallest and most tightly packed at the center of the eye at the fovea. The S cones are a little larger than the others.

Photobleaching can be used to determine cone arrangement. This is done by exposing dark-adapted retina to a certain wavelength of light that paralyzes the particular type of cone sensitive to that wavelength for up to thirty minutes from being able to dark-adapt making it appear white in contrast to the grey dark-adapted cones when a picture of the retina is taken. The results illustrate that **S** cones are randomly placed and appear much less frequently than the **M** and **L** cones. The ratio of **M** and **L** cones varies greatly among different people with regular vision (e.g. values of 75.8% **L** with 20.0% **M** versus 50.6% **L** with 44.2% **M** in two male subjects).

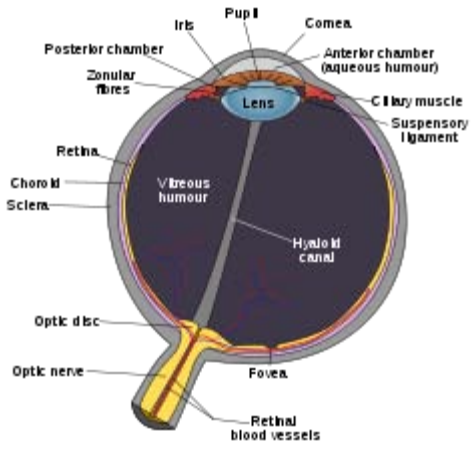
Like rods, each cone cell has a synaptic terminal, an inner segment, and an outer segment as well as an interior nucleus and various mitochondria. The synaptic terminal forms a synapse with a neuron such as a bipolar cell. The inner and outer segments are connected by a cilium. The inner segment contains organelles and the cell's nucleus, while the outer segment, which is pointed toward the back of the eye, contains the light-absorbing materials.

Like rods, the outer segments of cones have invaginations of their cell membranes that create stacks of membranous disks. Photopigments exist as transmembrane proteins within these disks, which provide more surface area for light to affect the pigments. In cones, these disks are attached to the outer membrane, whereas they are pinched off and exist separately in rods. Neither rods nor cones divide, but their membranous disks wear out and are worn off at the end of the outer segment, to be consumed and recycled by phagocytic cells.

The response of cone cells to light is also directionally nonuniform, peaking at a direction that receives light from the center of the pupil; this effect is known as the Stiles–Crawford effect.

Ciliary body

Ciliary body



Schematic diagram of the human eye

Latin	*corpus ciliare*
Gray's	*subject #225 1010*
Artery	long posterior ciliary arteries
MeSH	*Ciliary+Body*

The **ciliary body** is the circumferential tissue inside the eye composed of the ciliary muscle and ciliary processes. It is triangular in horizontal section and is coated by a double layer, the ciliary epithelium. This epithelium produces the aqueous humor. The inner layer is transparent and covers the vitreous body, and is continuous from the neural tissue of the retina. The outer layer is highly pigmented, continuous with the retinal pigment epithelium, and constitutes the cells of the dilator muscle. This double membrane is often regarded to be continuous with the retina and a rudiment of the embryological correspondent to the retina. The inner layer is unpigmented until it reaches the iris, where it takes on pigment. The retina ends at the ora serrata. It is part of the uveal tract— the layer of tissue which provides most of the nutrients in the eye. It extends from the ora serrata to the root of the iris. There are three sets of ciliary muscles in the eye, the longitudinal, radial, and circular muscles. They are near the front of the eye, above and below the lens. They are attached to the lens by connective tissue called the zonule of Zinn, and are responsible for shaping the lens to focus light on the retina. The ciliary body receives parasympathetic innervation from the oculomotor nerve.

Functions

The ciliary body has three functions: accommodation, aqueous humor production and the production and maintenance of the lens zonules. It also anchors the lens in place. Accomommodation essentially means that when the ciliary muscle contracts, the lens becomes more convex, generally improving the focus for closer objects. When it relaxes,it flattens the lens, generally improving the focus for farther objects. One of the essential roles of the ciliary body is also the production of the aqueous humor, which is responsible for providing most of the nutrients for the lens and the cornea and involved in waste management of these areas.

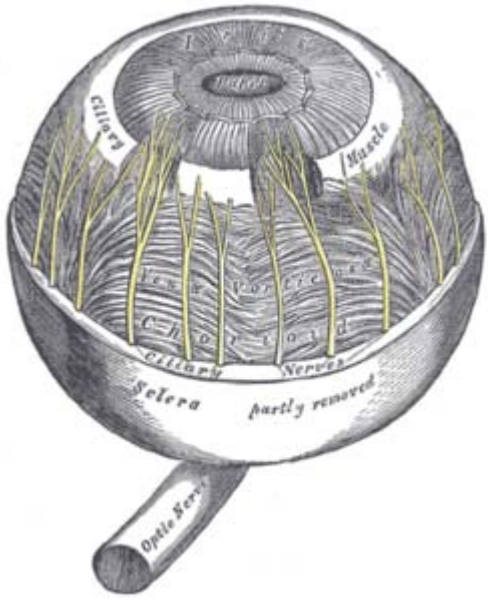
Clinical significance

The ciliary body is the main target of drugs against glaucoma (apraclonidine) as it is responsible for aqueous humor production. Its inhibition leads to the lowering of aqueous humor production and causes a subsequent drop in the intraocular pressure.

Chapter 12

Ciliary Muscle and Fovea Centralis

Ciliary muscle

Ciliary muscle	
	
The choroid and iris. (Ciliary muscle is labeled near top.)	
Latin	*musculus ciliaris*
Gray's	*subject #225 1011*
Origin	1) longitudinal fibers → scleral spur; 2) circular fibers → encircle root of iris
Insertion	1) longitudinal fibers → ciliary process, 2) circular fibers → encircle root of iris
Artery	long posterior ciliary arteries
Nerve	short ciliary

Actions	1) accommodation, 2) regulation of trabecular meshwork pore size

The **ciliary muscle** is a ring of striated smooth muscle in the eye's middle layer (vascular layer) that controls accommodation for viewing objects at varying distances and regulates the flow of aqueous humour into Schlemm's canal. The muscle has parasympathetic and sympathetic innervation.

Etymology

The word *ciliary* had its origins around 1685–1695. The term *cilia* originated a few years later in 1705–1715, and is the Neo-Latin plural of *cilium* meaning eyelash. In Latin, *cilia* means upper eyelid and is perhaps a back formation from *supercilium*, meaning eyebrow. The suffix *-ary* originally occurred in loanwords from Middle English (*-arie*), Old French (*-er*, *-eer*, *-ier*, *-aire*, -er), and Latin (*-ārius*); it can generally mean "pertaining to, connected with," "contributing to," and "for the purpose of." Taken together, *cili(a)-ary* pertains to various anatomical structures in and around the eye, namely the ciliary body and annular suspension of the lens of the eye.

Embryologic development

Forms from the mesoderm within the choroid and considered a cranial neural crest derivative.

Mode of action

Accommodation

The ciliary fibers have circular (Ivanoff), longitudinal (meridional) and radial orientations.

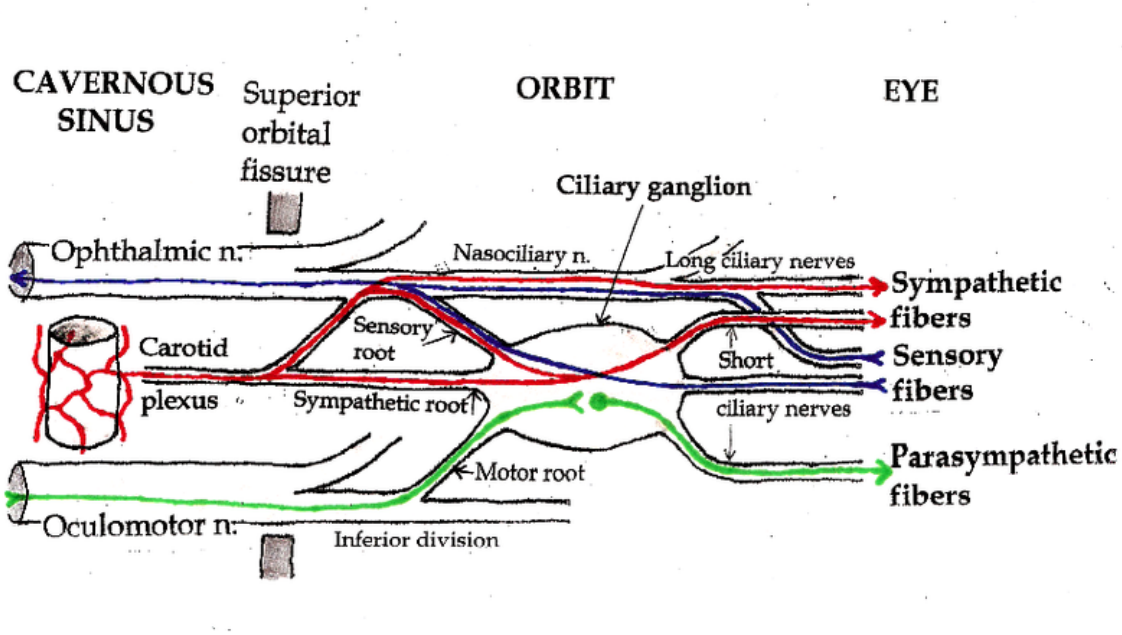
According to Hermann von Helmholtz's theory, the circular ciliary muscle fibers affect zonular fibers in the eye (fibers that suspend the lens in position during accommodation), enabling changes in lens shape for light focusing. When the ciliary muscle contracts, it pulls itself forward and moves the frontal region toward the axis of the eye. This releases the tension on the lens caused by the zonular fibers (fibers that hold or flatten the lens). This release of tension of the zonular fibers causes the lens to become more spherical, adapting to short range focus. The other way around, relaxation of the ciliary muscle causes the zonular fibers to become taut, flattening the lens, increasing the focal distance, increasing long range focus. Although Helmholtz's theory has been widely accepted since 1855, its mechanism still remains controversial. Alternative theories of accommodation have been proposed by others, including L. Johnson, M. Tscherning, and Ronald A. Schachar.

Trabecular meshwork pore size

Contraction and relaxation of the longitudinal fibers, which insert into the trabecular meshwork in the anterior chamber of the eye, cause an increase and decrease in the meshwork pore size, respectively, facilitating and impeding aqueous humour flow into the canal of Schlemm.

Innervation

The ciliary muscle receives both parasympathetic and sympathetic fibers from the ciliary ganglion called short ciliary nerves. These postganglionic fibers are part of cranial nerve III (Oculomotor nerve).



Ciliary ganglion with sympathetic and parasympathetic fibers of ciliary nerves

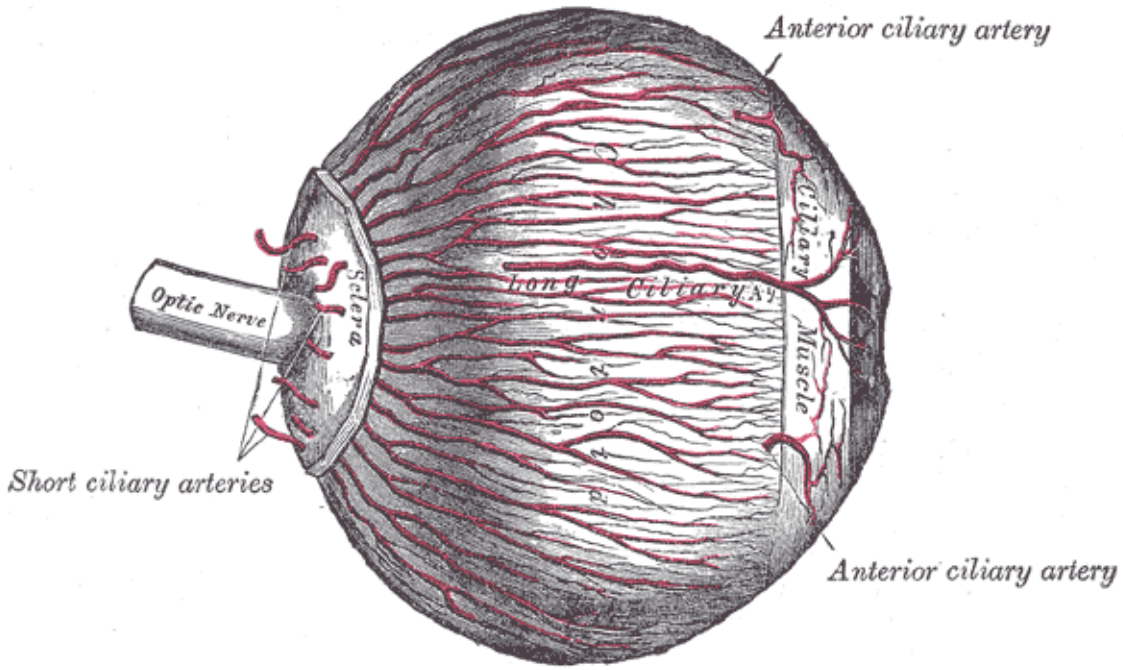
Postsynaptic sympathetic signals that originate in the superior cervical ganglion are carried by the nasociliary nerve or directly extend from the internal carotid plexus and pass through the ciliary ganglion. Sympathetic (adrenergic) activation of the muscle's beta-2 receptors result in relaxation and increase in ciliary body size.

Presynaptic parasympathetic signals that originate in the Edinger-Westphal nucleus are carried by cranial nerve III (the oculomotor nerve) and synapse on the ciliary ganglion. Parasympathetic activation of the M3 muscarinic receptors causes ciliary muscle contraction and consequent reduction in the size of the ciliary body.

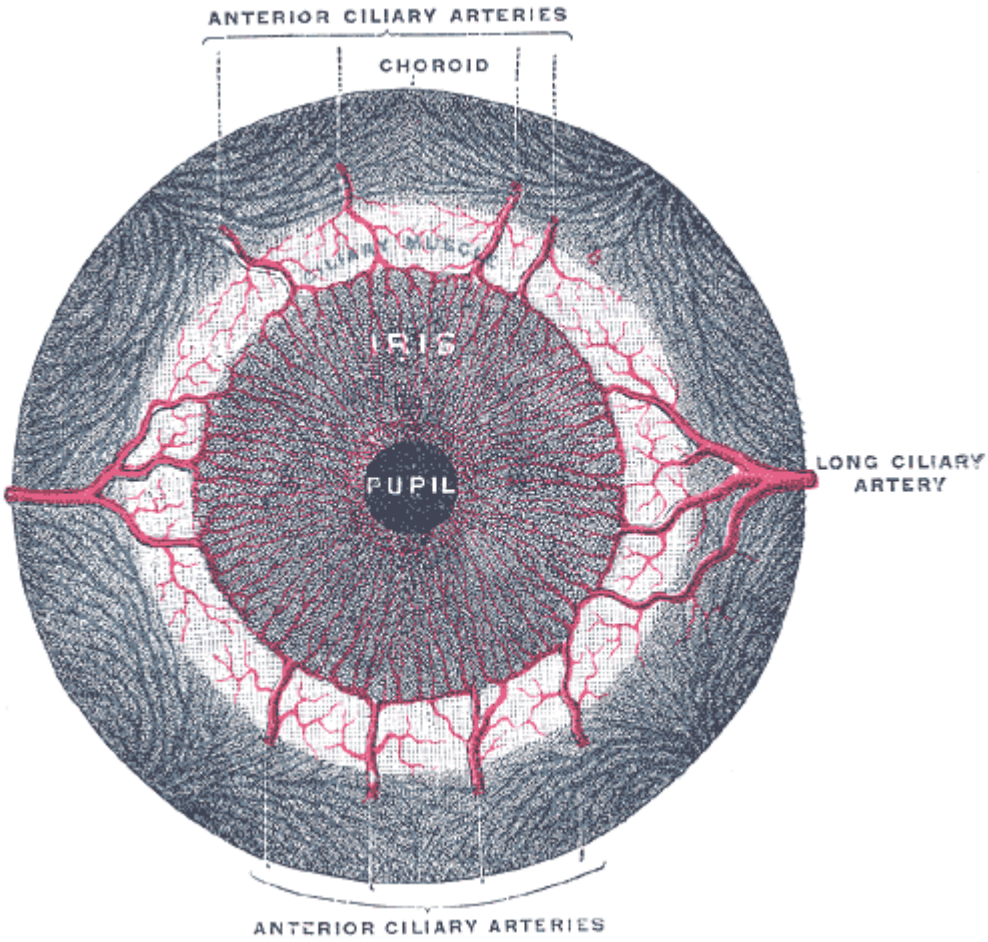
The adrenergic tone is dominant over the parasympathetic tone.

Role in the treatment of glaucoma

Open-angle glaucoma (OAG) and closed-angle glaucoma (CAG) may be treated by muscarinic receptor agonists (e.g., pilocarpine), which cause rapid miosis and contraction of the ciliary muscles, opening the trabecular meshwork, facilitating drainage of the aqueous humour into the canal of Schlemm and ultimately decreasing intraocular pressure.



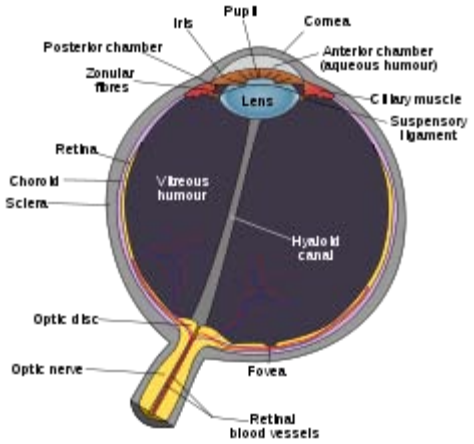
The arteries of the choroid and iris. The greater part of the sclera has been removed.



Iris, front view

Fovea centralis

Fovea centralis



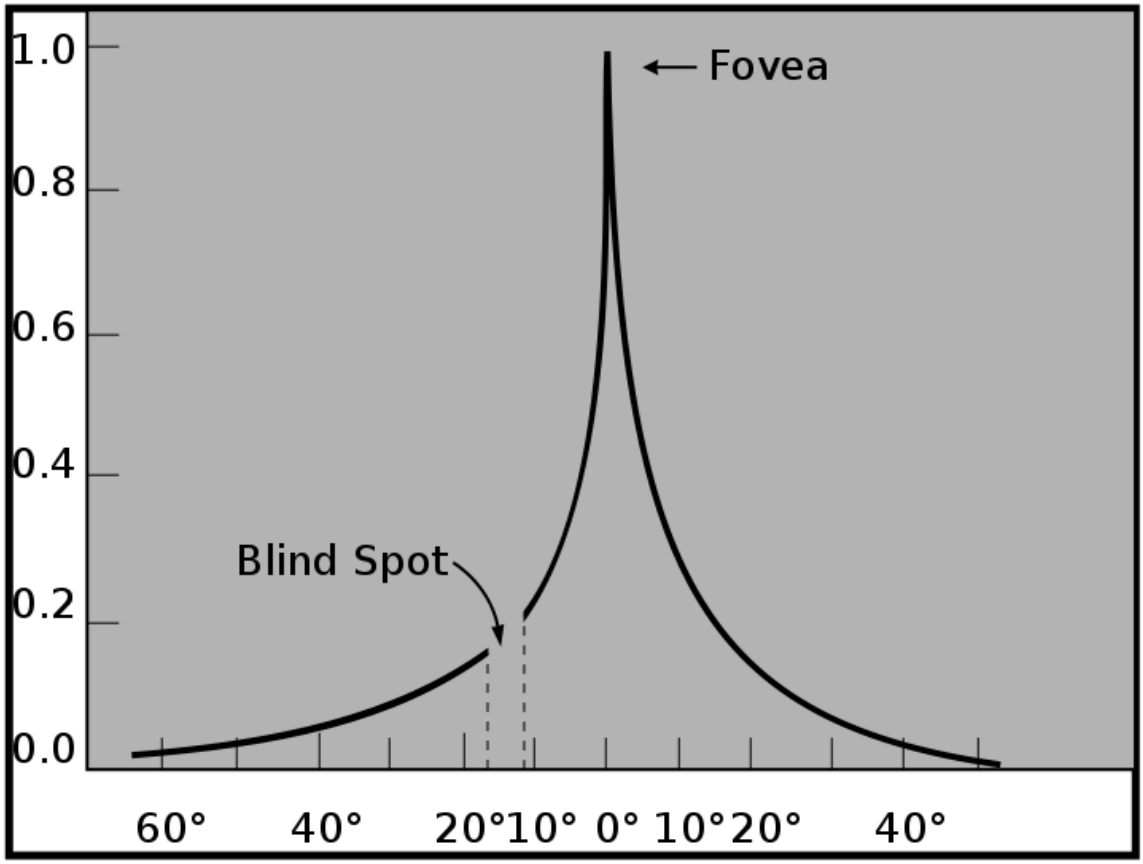
Schematic diagram of the human eye, with the fovea at the bottom. It shows a horizontal section through the right eye

Latin *fovea centralis*

The **fovea centralis**, also generally known as the **fovea** (the term *fovea* comes from the Latin, meaning *pit* or *pitfall*), is a part of the eye, located in the center of the macula region of the retina. The fovea is responsible for sharp central vision (also called foveal vision), which is necessary in humans for reading, watching television or movies, driving, and any activity where visual detail is of primary importance. The fovea is surrounded by the *parafovea* belt, and the *perifovea* outer region: The parafovea is the intermediate belt, where the ganglion cell layer is composed of more than five rows of cells, as well as the highest density of cones; the perifovea is the outermost region where the ganglion cell layer contains two to four rows of cells, and is where visual acuity is below the optimum. The perifovea contains an even more diminished density of cones, having 12 per 100 micrometres versus 50 per 100 micrometres in the most central fovea. This, in turn, is surrounded by a larger peripheral area that delivers highly compressed information of low resolution. Approximately 50% of the nerve fibers in the optic nerve carry information from the fovea, while the other 50% carry information from the rest of the retina. The parafovea extends to a distance of 1¼ mm from the central fovea, and the perifovea is found 2¾ mm away from the fovea centralis.

Description

In the human eye the term *fovea* (or *fovea centralis*) denotes the pit in the retina, which allows for maximum acuity of vision.



The diagram shows the relative acuity of the left human eye (horizontal section) in degrees from the fovea.

The human fovea has a diameter of about 1.0 mm with a high concentration of cone photoreceptors. The center of the fovea is the foveola – about 0.2 mm in diameter – where only cone photoreceptors are present and there are virtually no rods. The central fovea consists of very compact cones, thinner and more rod-like in appearance than cones elsewhere. Starting at the outskirts of the fovea, however, rods gradually appear, and the absolute density of cone receptors progressively decreases.

In the primate fovea (presumably including human) the ratio of ganglion cells to photoreceptors is about 2.5; almost every ganglion cell receives data from a single cone, and each cone feeds onto between 1 and 3 ganglion cells. Therefore, the acuity of foveal vision is limited only by the density of the cone mosaic, and the fovea is the area of the eye with the highest sensitivity to fine details.

Compared to the rest of the retina, the cones in the foveal pit have a smaller diameter and can, therefore, be more densely packed (in a hexagonal pattern). The high spatial density of cones accounts for the high visual acuity capability at the fovea. This is enhanced by the local absence of retinal blood vessels from the fovea, which, if present, would interfere with the passage of light striking the foveal cone mosaic. The absence of inner

retinal cells from the foveae of primates is assumed to contribute further to the high acuity function of the fovea.

The fovea centralis is a central pit, near the optic axis. It eliminates the necessity to pass through the inner, non-sensitive neurons and allows direct passage to the receptors. It is employed for accurate vision in the direction where it is pointed. If an object is large and thus covering a large angle, the eyes must constantly shift their gaze to subsequently bring different portions of the image into the fovea (as in reading).

Since the macula does not have a blood supply, the fovea must receive oxygen from the vessels in the choroid, which is across the retinal pigment epithelium and Bruch's membrane. This blood supply alone does not satisfy the metabolic needs of the fovea under conditions of bright light, and the fovea, thus, exists in a state of hypoxia when under bright illumination.

Since cones contain the pigmented opsins that allow humans to discriminate color, the fovea is largely responsible for the color vision in humans, which is superior to that of most other mammals.

The fovea comprises less than 1% of retinal size but takes up over 50% of the visual cortex in the brain. The foveal pit is not located exactly on the optical axis, but is displaced about 4 to 8 degrees temporal to it. The fovea sees only the central two degrees of the visual field, which is roughly equivalent to twice the width of your thumbnail at arm's length.

Surrounding the foveal pit is the foveal rim, where the neurons displaced from the pit are located. This is the thickest part of the retina.

Since the fovea does not have rods, it is not sensitive to dim lights. Astronomers know this; in order to observe a dim star, they use averted vision, looking out of "the side of their eyes".

The fovea is covered in a yellow pigment called xanthophyll, with the carotenoids zeaxanthin and lutein (Balashov and Bernstein, 1998), present in the cone axons of the Henle fibre layer. The pigment area absorbs blue light and is probably an evolutionary adaptation to the problem of chromatic aberration.

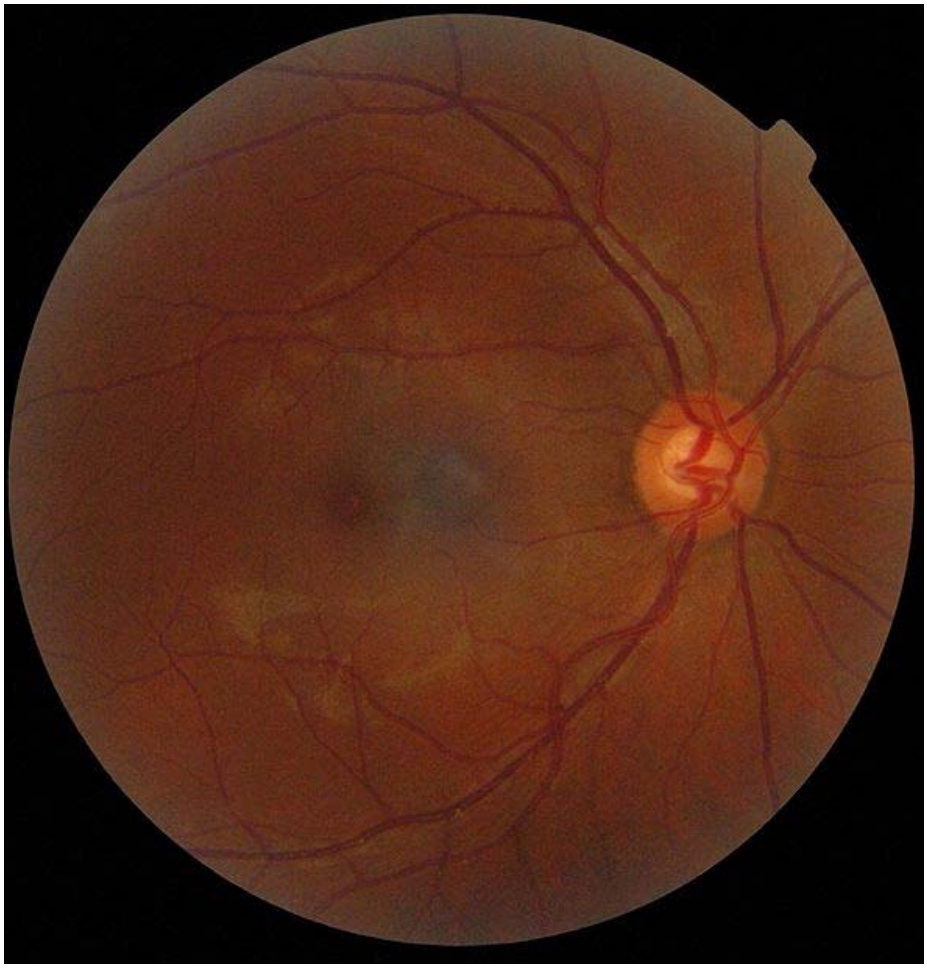
The fovea is also a pit in the surface of the retinas of many types of fish, reptiles, and birds. Among mammals, it is found only in simian primates. The retinal fovea takes slightly different forms in different types of animals. For example, in primates, cone photoreceptors line the base of the foveal pit, the cells that elsewhere in the retina form more superficial layers having been displaced away from the foveal region during late fetal and early postnatal life. Other foveae may show only a reduced thickness in the inner cell layers, rather than an almost complete absence.

The only photo-receptors located in the fovea of most humans are three kinds of cone photo receptors. The red, blue, and green allow the eye to see the colours that humans need for survival; however, some organisms are known to possess four independent channels for conveying color information, or possessing four different types of cone cells in the eye, a characteristic called *tetrachromacy*. Organisms with tetrachromacy are called tetrachromats. The rods are located on the fovea's periphery. This assists the eye in seeing in the dark.

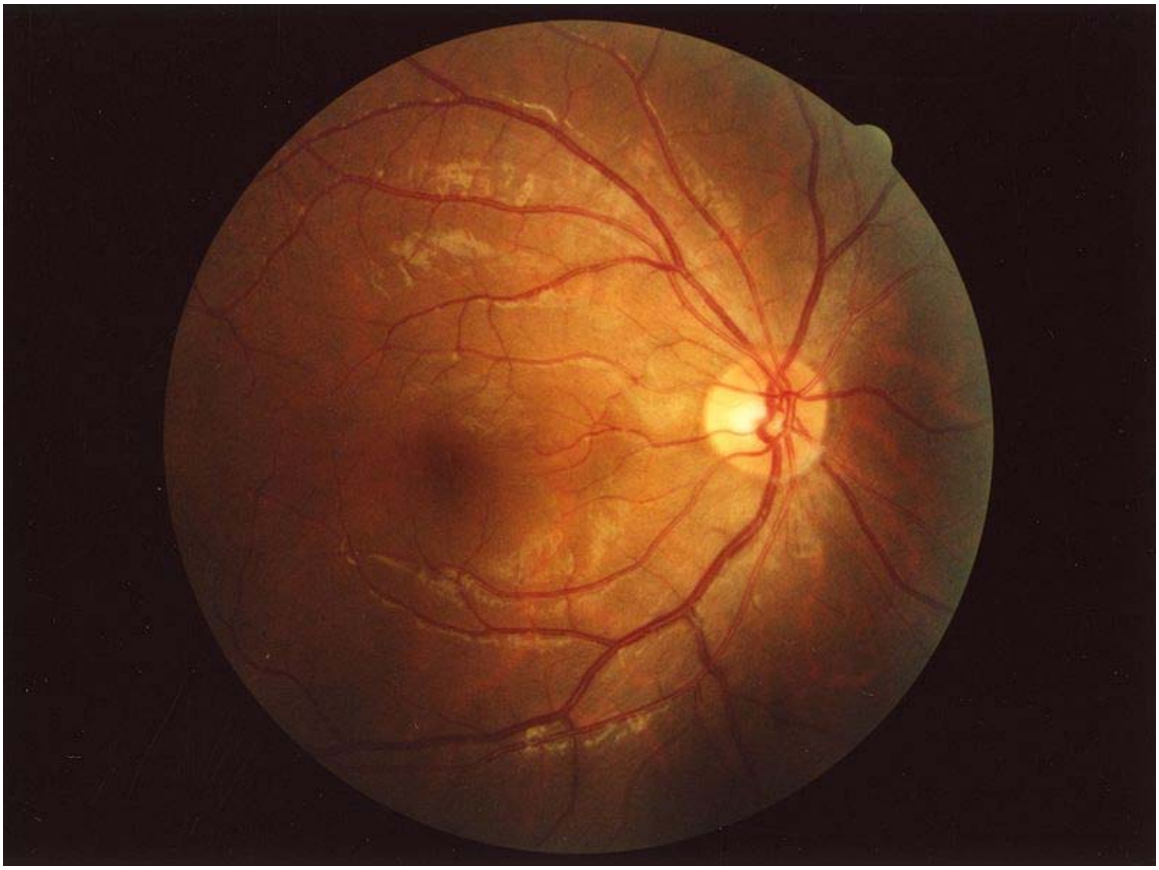
Chapter 13

Fundus (Eye) and Eye Color

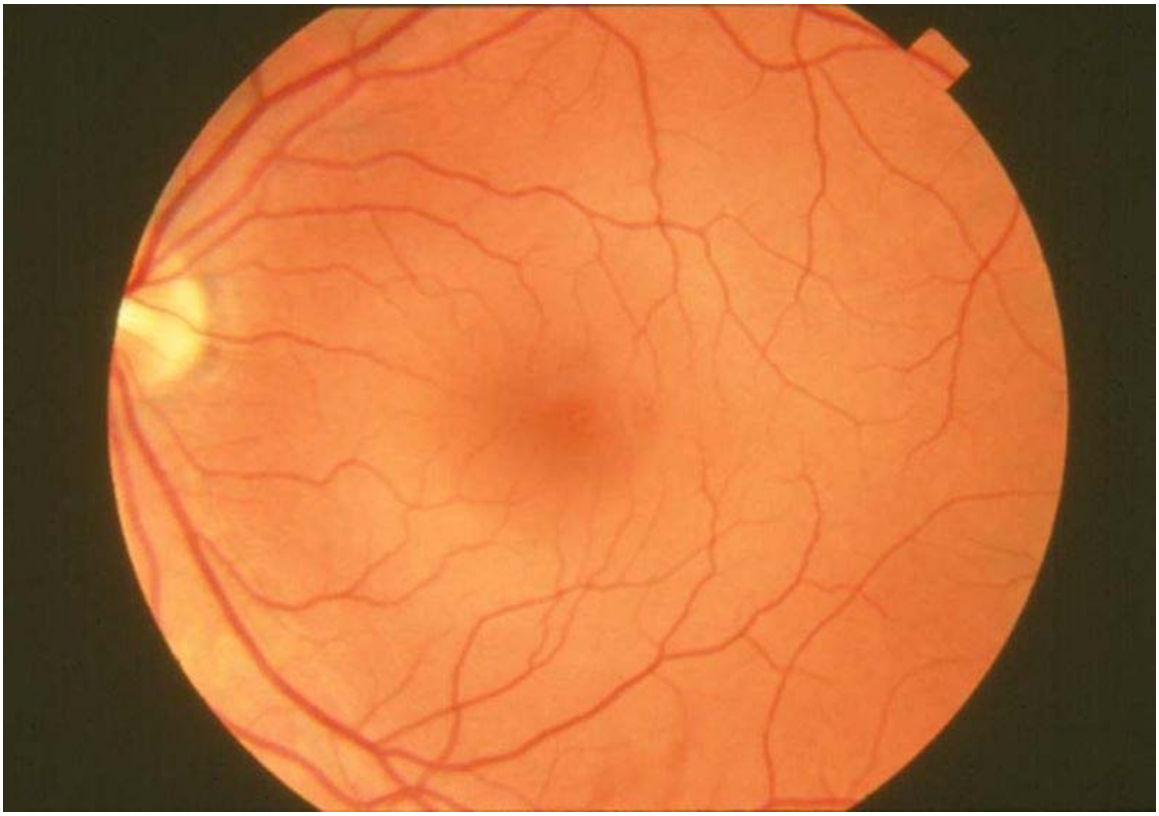
Fundus (eye)



An ophthalmogram, showing the optic disc as a bright area on the right where blood vessels converge. The spot to the left of the centre is the macula. The grey, more diffuse spot in the centre is a shadow artifact.



Fundus of human eye



Fundus of human eye

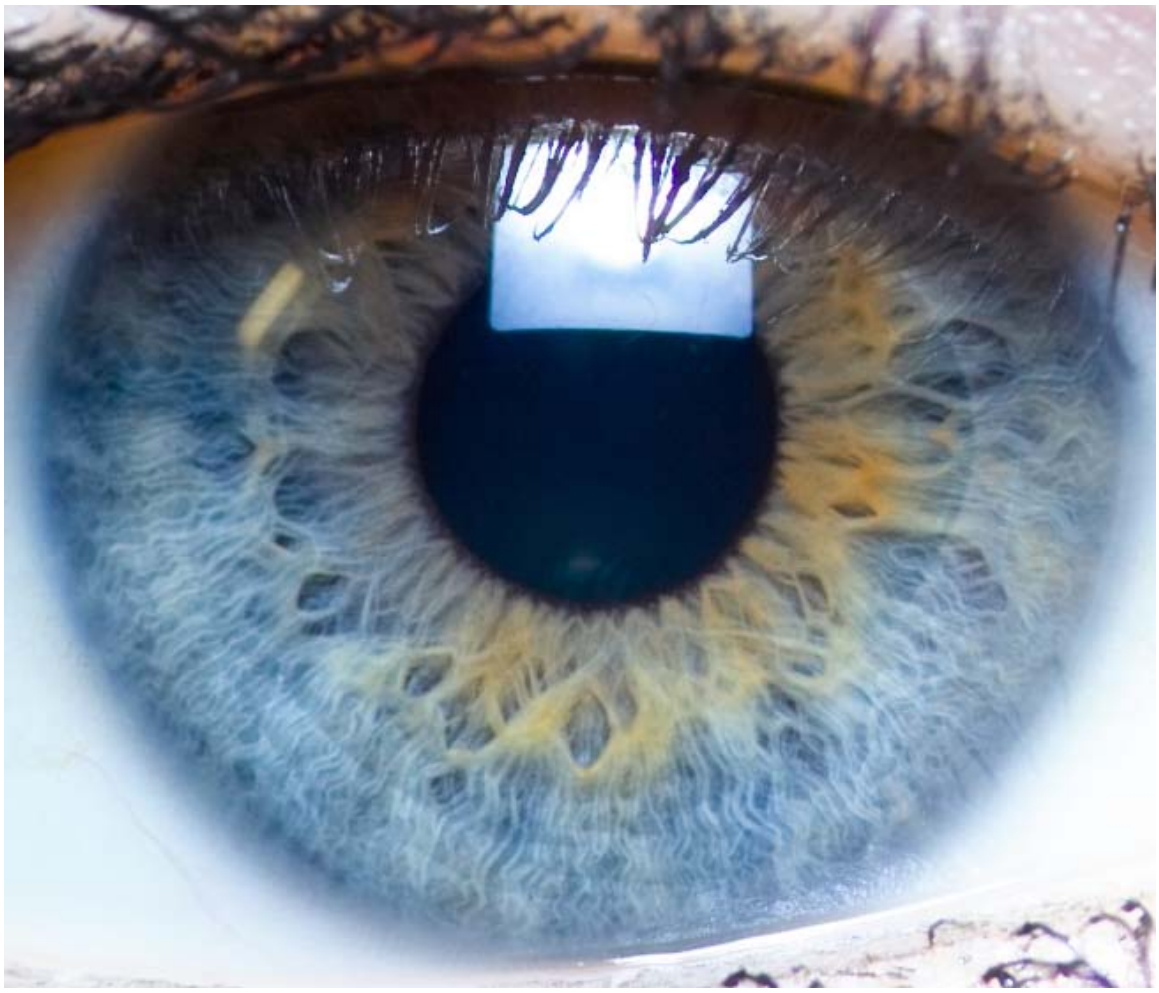
The **fundus** of the eye is the interior surface of the eye, opposite the lens, and includes the retina, optic disc, macula and fovea, and posterior pole. The fundus can be viewed with an ophthalmoscope. The term may also be inclusive of Bruch's membrane and the choroid.

The color of the fundus varies both between and within species. In one study of primates the retina is blue, green, yellow, orange, and red; only the human fundus (from a lightly pigmented blond person) is red. The major differences noted among the "higher" primate species were size and regularity of the border of macular area, size and shape of the optic disc, apparent 'texturing' of retina, and pigmentation of retina.

The eye's fundus is the only part of the human body where the microcirculation can be observed directly. The diameter of the blood vessels around the optic disc is about 150 μm, and an ophthalmoscope allows observation of blood vessels with diameters as small as 10 μm.

Medical signs that can be detected from observation of eye fundus include hemorrhages, exudates, cotton wool spots, blood vessel abnormalities (tortuosity, pulsation and new vessels) and pigmentation.

Eye color



Eye color is a polygenic phenotypic character and is determined by the amount and type of pigments in the eye's iris. Humans and other animals have many phenotypic variations in eye color, as blue, brown, gray, green, and others. These variations constitute phenotypic traits.

The genetics of eye color are complicated, and color is determined by multiple genes. Some of the eye-color genes include *EYCL1* (a green/blue eye-color gene located on chromosome 19), *EYCL2* (a brown eye-color gene) and *EYCL3* (a brown/blue eye-color gene located on chromosome 15). The once-held view that blue eye color is a simple recessive trait has been shown to be wrong. The genetics of eye color are so complex that almost any parent-child combination of eye colors can occur.

In human eyes, these variations in color are attributed to varying ratios of eumelanin produced by melanocytes in the iris. The brightly colored eyes of many bird species are largely determined by other pigments, such as pteridines, purines, and carotenoids.

Three main elements within the iris contribute to its color: the melanin content of the iris pigment epithelium, the melanin content within the iris stroma, and the cellular density of the iris stroma. In eyes of all colors, the iris pigment epithelium contains the black pigment, eumelanin. Color variations among different irides are typically attributed to the melanin content within the iris stroma. The density of cells within the stroma affects how much light is absorbed by the underlying pigment epithelium. OCA2 gene polymorphism, close to proximal 5′ regulatory region, explains most human eye-color variation.

Genetic determination of eye color

Eye colors can range from the most common color, brown, to the least common, green. Eye color is an inherited trait influenced by more than one gene. These genes are being sought using associations to small changes in the genes themselves and in neighboring genes. These changes are known as single-nucleotide polymorphisms or SNPs. The actual number of genes that contribute to eye color is currently unknown, but there are a few likely candidates. A study in Rotterdam (2009) found that it was possible to predict the color of eyes with more than 90% accuracy for brown and blue, using just six SNPs (from six genes).

The gene *OCA2* (OMIM: 203200), when in a variant form, causes the pink eye color and hypopigmentation common in human albinism. (The name of the gene is derived from the disorder it causes, oculocutaneous albinism type II.) Different SNPs within *OCA2* are strongly associated with blue and green eyes as well as variations in freckling, mole counts, hair and skin tone. The polymorphisms may be in an *OCA2* regulatory sequence, where they may influence the expression of the gene product, which in turn affects pigmentation. A specific mutation within the *HERC2* gene, a gene that regulates *OCA2* expression, is partly responsible for blue eyes. Other genes implicated in eye color variation are: *SLC24A4* and *TYR*.

Blue eyes with a brown spot, green eyes, and gray eyes are caused by an entirely different part of the genome. As Eiberg said: "The SNP rs12913832 [of the *Herc2* gene] is found to be associated with the brown and blue eye color, but this single DNA variation cannot explain all the brown eye color variation from dark brown over hazel to blue eyes with brown spots."

Classification of color

Iris color can provide a large amount of information about an individual, and a classification of various colors may be useful in documenting pathological changes or determining how a person may respond to various ocular pharmaceuticals. Various classification systems have ranged from a basic light or dark description to detailed gradings employing photographic standards for comparison. Others have attempted to set objective standards of color comparison.

As the perception of color depends on viewing conditions (e.g., the amount and kind of illumination, as well as the hue of the surrounding environment), so does the perception of eye color.

Eye colors range from the darkest shades of brown to the lightest tints of blue. To meet the need for standardized classification, at once simple yet detailed enough for research purposes, Seddon et al. developed a graded system based on the predominant iris color and the amount of brown or yellow pigment present. There are three pigment colors that determine, depending on their proportion, the outward appearance of the iris: brown, yellow, and blue. Green irides, for example, have blue and some yellow. Brown irides contain mostly brown. Eye color in animals other than *Homo sapiens* are differently regulated. For example, instead of blue as in humans, autosomal recessive eye color in the skink species: *Corucia zebrata* is black, and the autosomal dominant color is yellow-green.

Changes in eye color

In all populations, children are most commonly born with unpigmented eyes. However, most babies who have European ancestry have light colored eyes before the age of one. As the child develops, melanocytes (cells found within the iris of human eyes, as well as skin and hair follicles) slowly begin to produce melanin. Because melanocyte cells continually produce pigment, in theory eye color can be changed. Most eye changes happen when the infant is around one year old, although it can happen up to three years of age. Observing the iris of an infant from the side using only transmitted light with no reflection from the back of the iris, it is possible to detect the presence or absence of low levels of melanin. An iris that appears blue under this method of observation is more likely to remain blue as the infant ages. An iris that appears golden contains some melanin even at this early age and is likely to turn green or brown as the infant ages.

Changes (lightening or darkening) of eye colors during puberty, early childhood, pregnancy, and sometimes after serious trauma (like heterochromia) do represent cause for plausible argument to state that some eyes can or do change, based on chemical reactions and hormonal changes within the body.

Studies on Caucasian twins, both fraternal and identical, have shown that eye color over time can be subject to change, and major demelanization of the iris may also be genetically determined. Most eye-color changes have been observed or reported in the Caucasian population with hazel eyes.

Eye colour chart (Martin–Schultz scale)

Carleton Coon created this chart by the Martin–Schultz scale often used in physical anthropology.

I. Light eyes

Eyes light and light mixed are 16–12 in Martin scale.

Light
Gray, blue, green.
Light-mixed

a. Very light-mixed (blue with gray or green or green with gray)
b. Light-mixed (light or very light-mixed with small admixture of brown pigment)

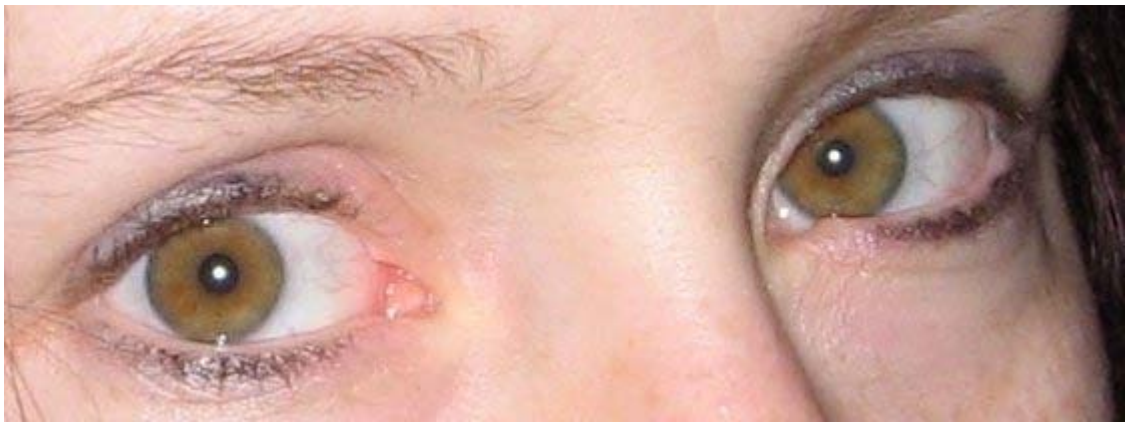
II. Mixed eyes

Mixed
12–6 in Martin scale. Mixture of light eyes (blue, gray or green) with brown pigment when light and brown pigment are the same level.

III. Dark eyes

Dark-mixed
6–4 in Martin scale. Brown with small admixture of light pigment.
Dark
4–1 in Martin scale. Brown (light brown and dark brown) and very dark brown (almost black).

Amber



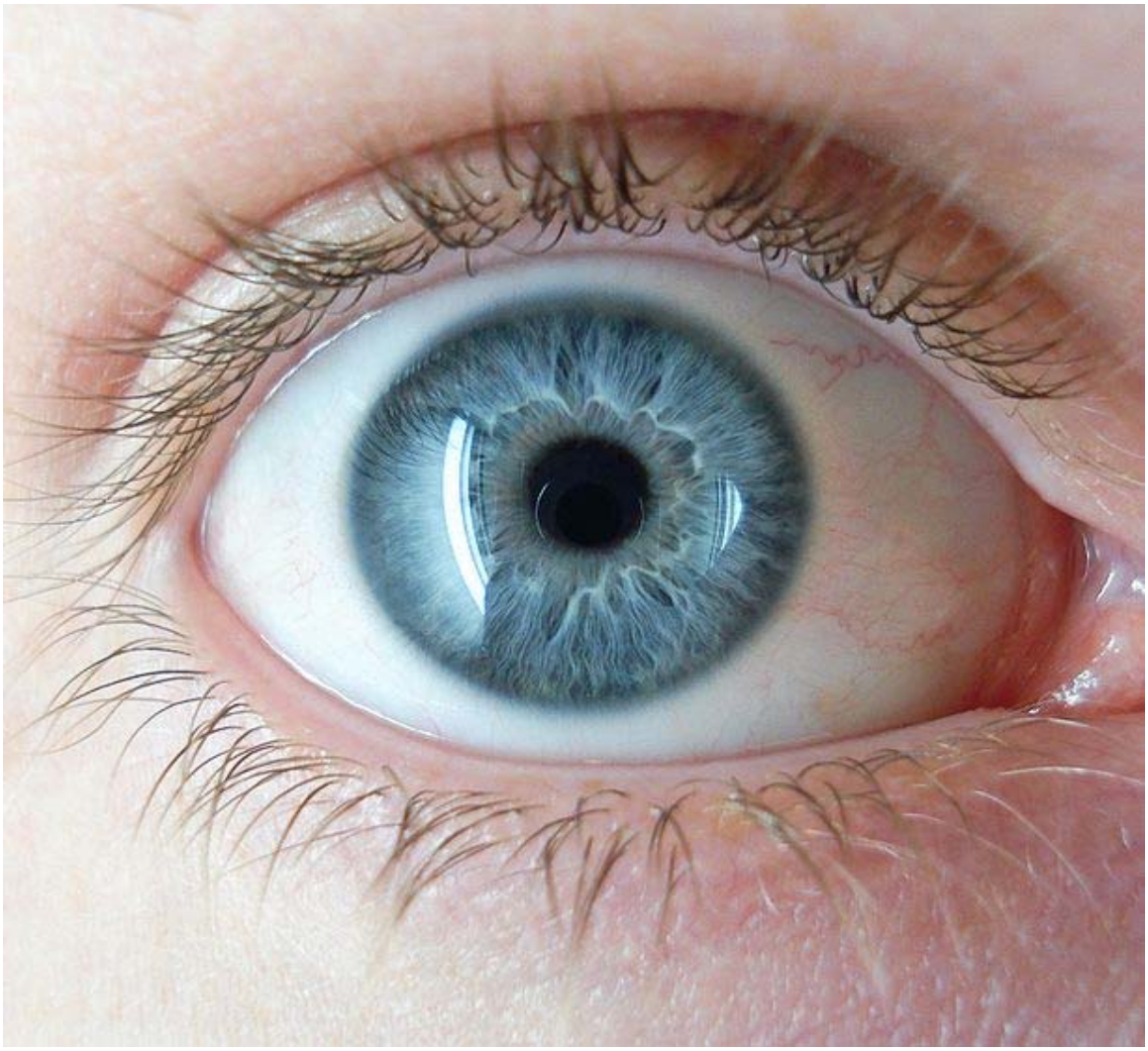
Amber eyes / Golden green-brown

Amber eyes are of a solid color and have a strong yellowish/golden and russet/coppery tint. This might be due to the deposition of the yellow pigment called lipochrome in the iris (which is also found in green eyes). Amber eyes should not be confused with hazel eyes; although hazel eyes may contain specks of amber or gold, they usually tend to comprise many other colors, including green, brown and orange. Also, hazel eyes may appear to shift in color and consist of flecks and ripples, while amber eyes are of a solid

gold hue. Even though amber is considered to be like gold, some people have russet or copper colored amber eyes which many people mistake for hazel, though hazel tends to be duller and contains green with red/gold flecks, like mentioned above. Amber eyes may also contain amounts of very light gold-ish gray, found in animals like wolves.

The eyes of some pigeons contain yellow fluorescing pigments known as pteridines. The bright yellow eyes of the Great Horned Owl are thought to be due to the presence of the pteridine pigment xanthopterin within certain chromatophores (called xanthophores) located in the iris stroma. In humans, yellowish specks or patches are thought to be due to the pigment lipofuscin, also known as lipochrome. Many animals such as canines, domestic cats, owls, eagles, pigeons and fish have amber eyes as a common color, whereas in humans this color occurs less frequently, more in places like Brazil and Asia, being rare in other regions.

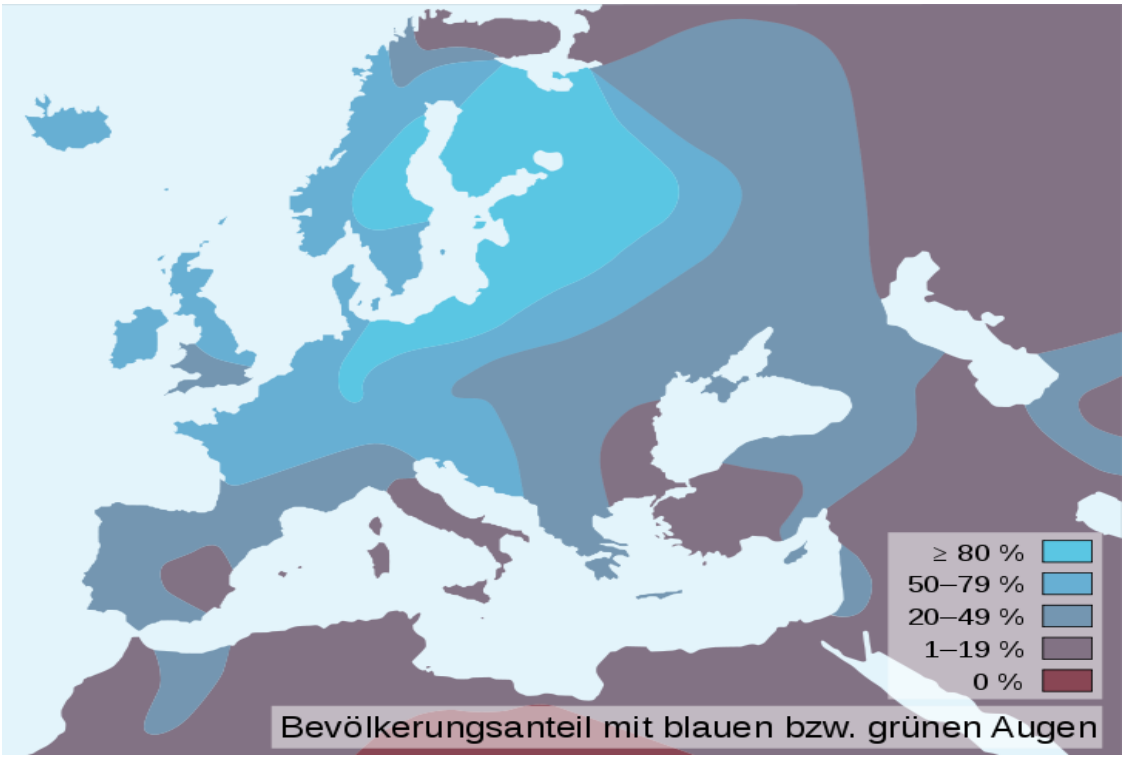
Blue



A blue iris

Blue eyes contain low amounts of melanin within the iris stroma; longer wavelengths of light tend to be absorbed by the underlying iris pigment epithelium, and shorter wavelengths are reflected and undergo Rayleigh scattering. The type of melanin present is eumelanin. The inheritance pattern followed by blue eyes is considered similar to that of a recessive trait (in general, eye color inheritance is considered a polygenic trait, meaning that it is controlled by the interactions of several genes, not just one). In 2008, new research revealed that people with blue eyes have a single common ancestor. Scientists tracked down a genetic mutation that leads to blue eyes. "Originally, we all had brown eyes," said Hans Eiberg from the Department of Cellular and Molecular Medicine at the University of Copenhagen. Eiberg and colleagues showed in a study published in *Human Genetics* that a mutation in the 86th intron of the *HERC2* gene, which is hypothesized to interact with the *OCA2* gene promoter, reduced expression of *OCA2* with subsequent reduction in melanin production. The authors concluded that the mutation may have arisen in a single individual in the Near East or around the Black Sea region 6,000–10,000 years ago during the Neolithic revolution. Eiberg stated, "A genetic mutation affecting the OCA2 gene in our chromosomes resulted in the creation of a 'switch,' which literally 'turned off' the ability to produce brown eyes."

The genetic switch is located in the gene adjacent to OCA2 and rather than completely turning off the gene, the switch limits its action, which reduces the production of melanin in the iris. In effect, the turned-down switch diluted brown eyes to blue. If the OCA2 gene had been completely shut down, our hair, eyes and skin would be melanin-less, a condition known as albinism.



Historic distribution of light-eyed persons in Europe

A 2009 study suggested that blue eyes were present in Siberia during the Bronze Age; 15 of 25 specimens (60%) from the Krasnoyarsk area had blue (or green) eyes.

Blue eyes are most common in the Baltic Sea region, Northern, Eastern and Central Europe, and to a lesser degree in Southern Europe and southern Central Asia; Afghanistan and Pakistan are a notable example. Blue eyes are found in the Levant and the Middle East, especially amongst the Jewish population of Israel. However, many modern Israeli Jews are of European Ashkenazi origin, among whom this trait is common (53.7% of Ukrainian Jews have blue eyes). They are also found in parts of North Africa, West Asia, and South Asia, in particular the northern areas of India, largely Kashmir. Pakistan and Iran also have a considerable population of blue eyed people. While blue eyes are thought to be exclusive to non-Black ethnic groups, the manifestation of blue eyes has been documented in pure-blooded, darkly complected tribal Africans, as well as people of mixed African and European ancestry; the former, usually the result of genetic mutation and the latter most often the manifestation of recessive European genes.

A 2002 study found that the prevalence of blue eye color among Caucasians in the United States to be 33.8 percent for those born from 1936 through 1951 compared with 57.4 percent for those born from 1899 through 1905. Another 2002 study concluded that almost one in nine Italian children had blue eyes. Blue eyes have become increasingly rare among American children, with only one out of every six or 16.6%, which is 49.8 million out of 300 million (22.4% of white Americans) of the total United States population having blue eyes.

The outer surface of the iris of a blue-eyed person is actually clear, lacking the outer layer of pigmentation that is found in brown eyes. Their color is caused by the inner layer of pigmentation and the semi-opaque fibrous tissues that lie between the two layers.

Brown

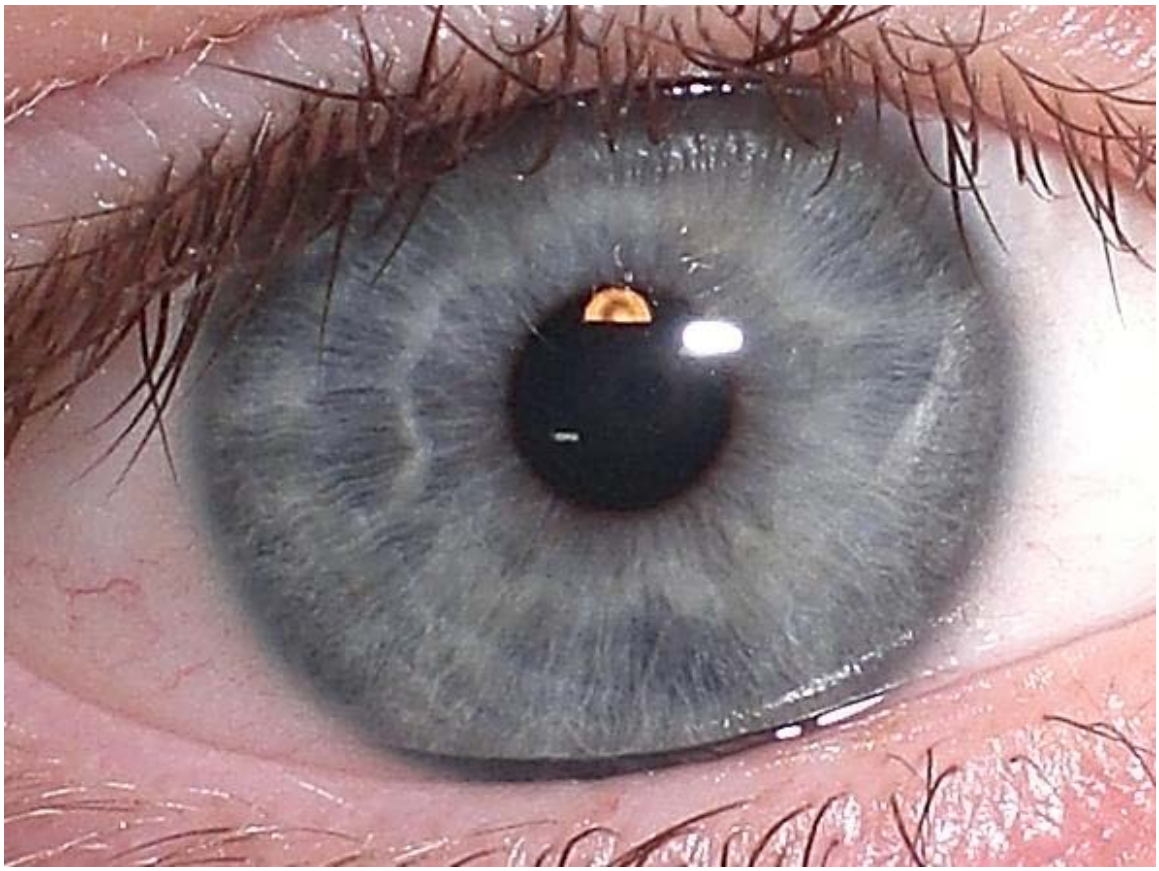
Brown iris

Brown eyes are dominant in humans and in many parts of the world, it is nearly the only iris color present. It is less common in countries around the Baltic Sea and in Scandinavia. Dark pigment of brown eyes are most common in East Asia, Southeast Asia, South Asia, West Asia, Oceania, Africa, and throughout the Americas.

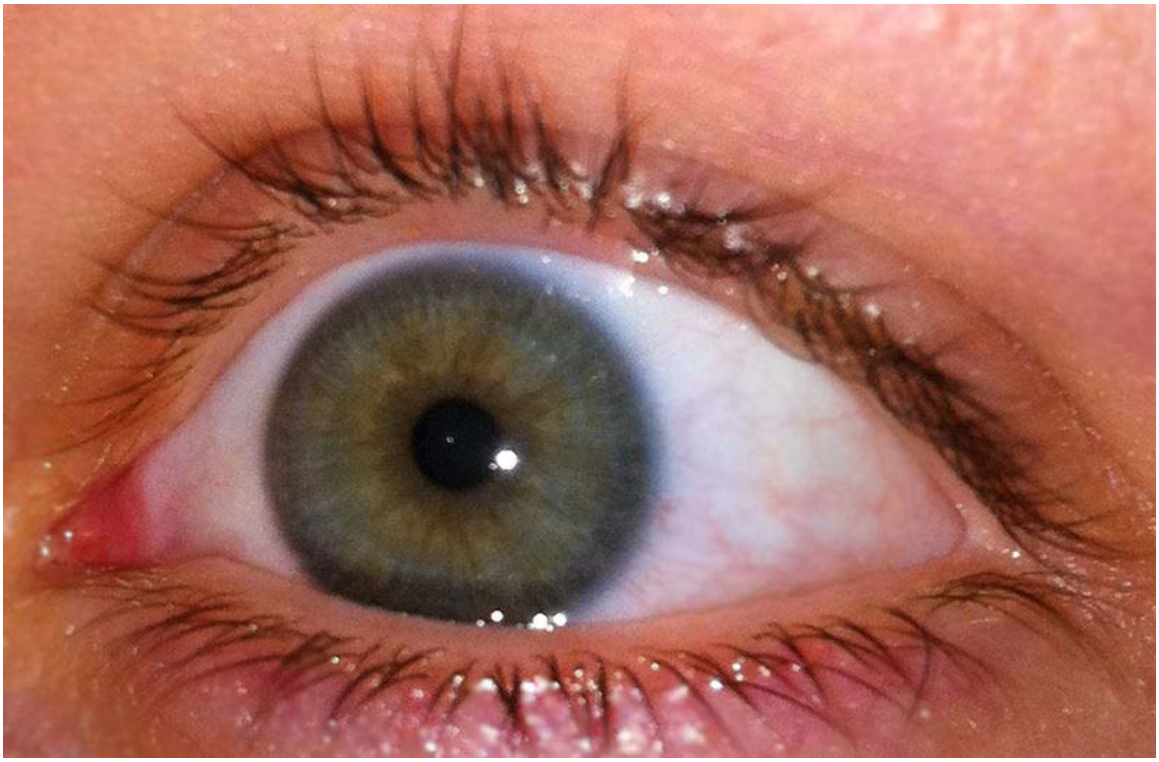
Light or medium-pigmented brown eyes are common in Europe, India, Iran, Armenia, Pakistan and Afghanistan, as well as some parts of the Middle East. Light-pigmented brown eyes are sometimes referred to as "honey eyes".

In humans, brown eyes contain large amounts of melanin within the iris stroma, which serves to absorb light at both shorter and longer wavelengths. Brown eyes are the most common eye color, with over half of the world's population having them.

Gray



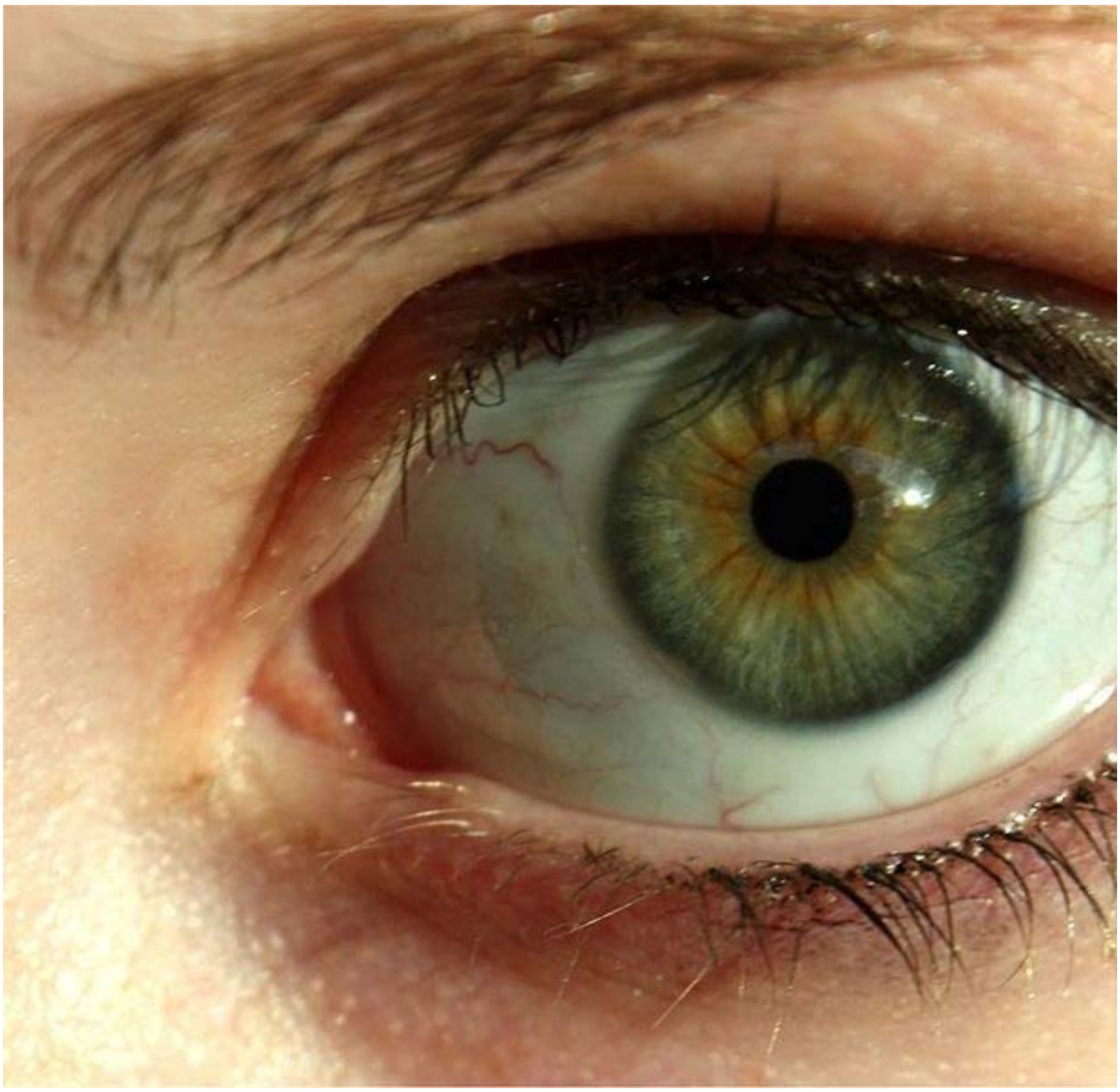
A steel blue-gray iris



Gray eyes are most common in Northern and Eastern Europe. Gray eyes are also common among North Africans. Under magnification, gray eyes exhibit small amounts of yellow and brown color in the iris. Ultimately, there are at least two things that could determine gray eye color. The first is the amount of melanin made, and the second is the density of the proteins in the stroma.

A gray iris may indicate the presence of a uveitis. However, other visual signs make a uveitis obvious. Gray iris color, as well as blue, are at increased risk of uveal melanoma.

Green

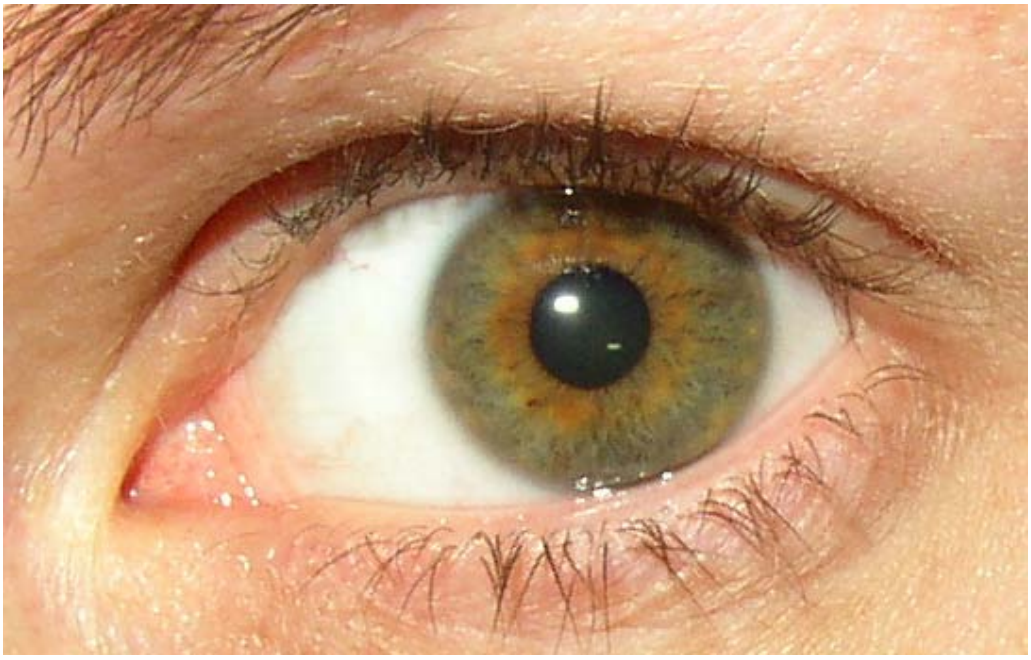


A light green iris with small amounts of brown

Olive green eyes

Green eyes are the product of low to moderate amounts of melanin and probably represent the interaction of multiple variants within the *OCA2* and other genes. Green eyes were present in south Siberia during the Bronze Age. They are most common in Northern and Central Europe. They can also be found in parts of Southern Europe and North Africa. In Iceland, 89% of women and 87% of men have either blue or green eye color. A study of Icelandic and Dutch adults found green eyes to be much more prevalent in women than in men. Among European Americans, green eyes are most common among those of Celtic and Germanic ancestry, about 16%.

Hazel

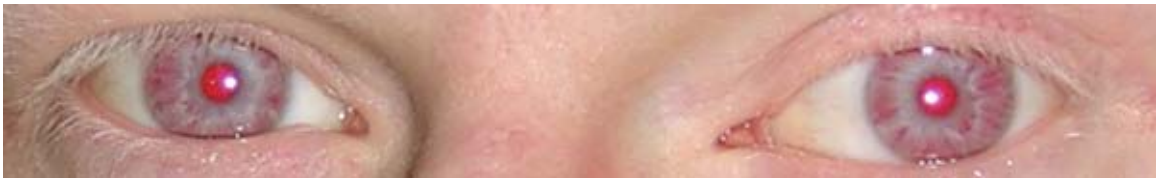


Hazel iris (Inner brown and outer green ring)

Hazel eyes are due to a combination of Rayleigh scattering and a moderate amount of melanin in the iris's anterior border layer. Hazel eyes often appear to shift in color from a light brown to a golden-green. Hazel mostly consists of brown and green. The dominant color in the eye can either be green or light brown/gold. This is how many people mistake hazel eyes to be amber and vice versa. This can sometimes produce a multicolored iris, i.e., an eye that is light brown/amber near the pupil and charcoal or dark green on the outer part of the iris (and vice versa) when observed in sunlight. Hazel eyes are common in the following countries and regions such as Romania, Czech Republic, Austria, Albania, France, Spain, Bulgaria, Greece, England, Portugal, Chile, Italy, Hungary, Eastern Germany, Serbia, Croatia, Slovenia, United States, West Asia, Eastern Russia, Estonia, Argentina, Brazil, and Montenegro.

Definitions of the eye color *hazel* vary: it is sometimes considered to be synonymous with light brown or gold, as in the color of a hazelnut shell.

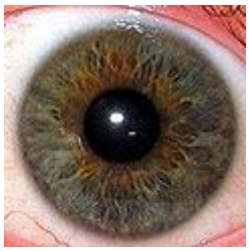
Red

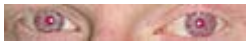


"Red" albino eyes

The eyes of people with severe forms of albinism may appear red under certain lighting conditions owing to the extremely low quantities of melanin, allowing the blood vessels to show through. In addition, flash photography can sometimes cause a "red-eye effect", in which the very bright light from a flash reflects off the back of the eyeball, which is abundantly vascular, causing the pupil to appear red in the photograph.

Spectrum of eye color





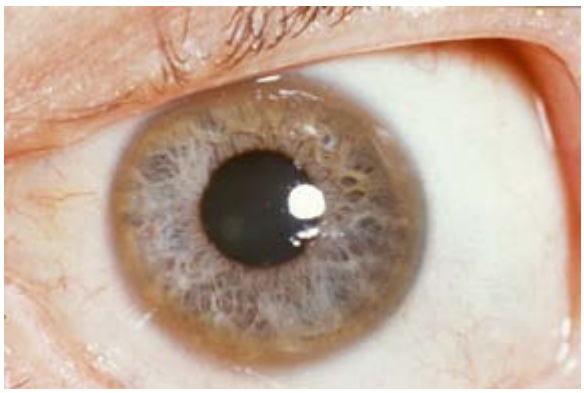
Medical implications

Those with lighter iris color have been found to have a higher prevalence of age-related macular degeneration (ARMD) than those with darker iris color; lighter eye color is also associated with an increased risk of ARMD progression. An increased risk of uveal

melanoma has been found in those with blue, green or gray iris color. However, a study in 2000 suggests that people with dark brown eyes are at increased risk of developing cataracts and therefore should protect their eyes from direct exposure to sunlight.

Eye color may also be symptomatic of disease. Aside from the iris, yellowing of the whites of the eyes is associated with jaundice and symptomatic of liver disease, including cirrhosis, hepatitis and malaria. Yellowing of the whites of the eyes in people with darker pigmented skin is often due to melanin being present in the whites of the eyes. However, any sudden changes in the color of the whites of the eyes should be addressed by a medical professional.

Wilson's disease



A Kayser–Fleischer ring in a patient with Wilson's disease

Wilson's disease involves a mutation of the gene coding for the enzyme ATPase7B, which prevents copper within the liver from entering the Golgi apparatus in cells. Instead, the copper accumulates in the liver and in other tissues, including the iris of the eye. This results in the formation of Kayser-Fleischer rings, which are dark rings that encircle the periphery of the iris.

Anomalous conditions

Aniridia

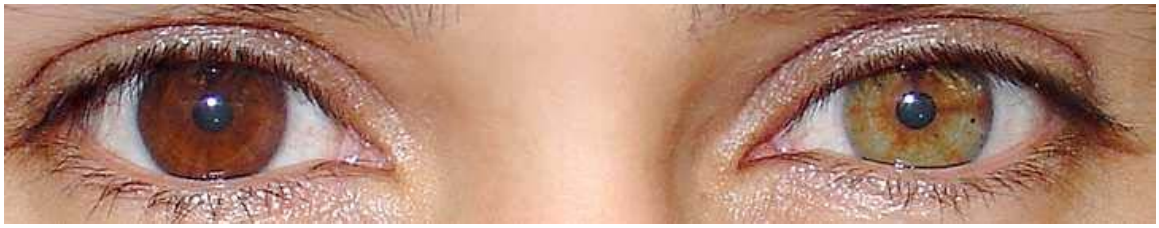
Aniridia is a congenital condition characterized by an extremely underdeveloped iris, which appears absent on superficial examination.

Ocular albinism and eye color

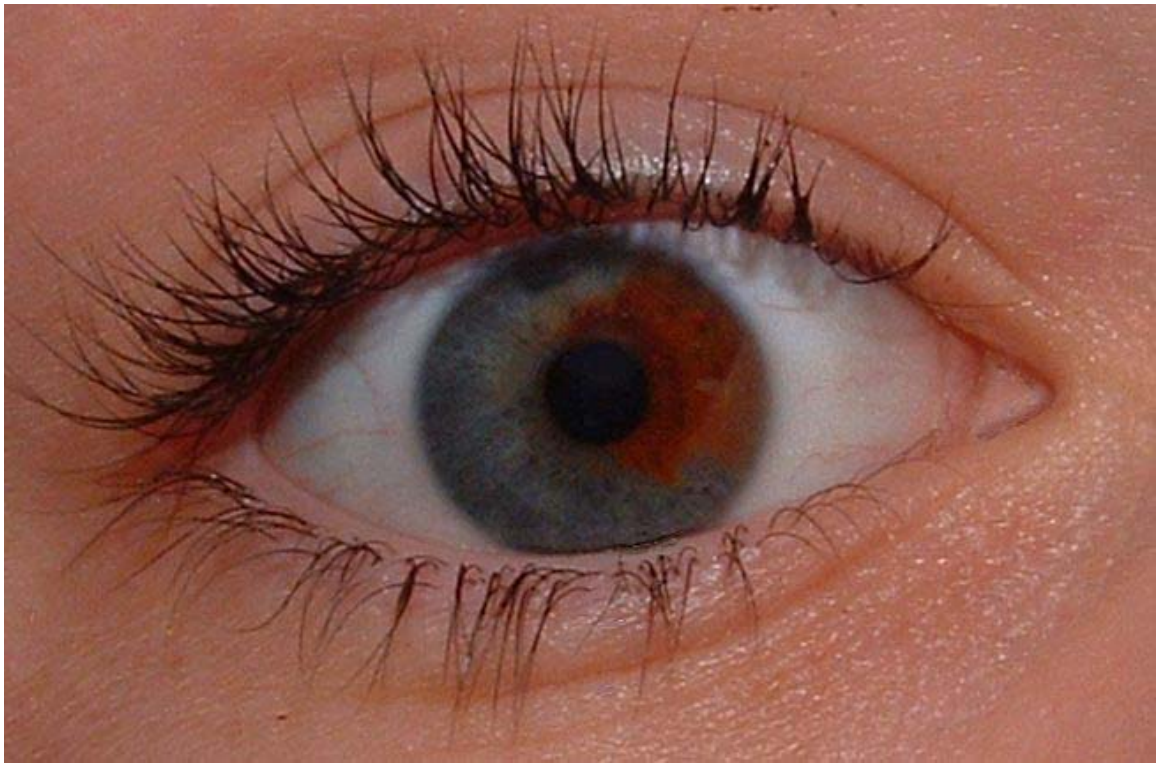
Normally, there is a thick layer of melanin on the back of the iris. Even people with the lightest blue eyes, with no melanin on the front of the iris at all, have dark brown coloration on the back of it, to prevent light from scattering around inside the eye. In those with milder forms of albinism, the color of the irides is typically blue but can vary from blue to brown. In severe forms of albinism, there is no pigment on the back of the

iris, and light from inside the eye can pass through the iris to the front. In these cases, the only color seen is the red from the hemoglobin of the blood in the capillaries of the iris. Such albinos have pink eyes, as do albino rabbits, mice, or any other animal with a total lack of melanin. Transillumination defects can almost always be observed during an eye examination due to lack of iridial pigmentation. The ocular albino also lacks normal amounts of melanin in the retina as well, which allows more light than normal to reflect off the retina and out of the eye. Because of this, the pupillary reflex is much brighter in the albino, and this can increase the red eye effect in photographs.

Heterochromia



An example of complete heterochromia. The subject has one brown eye and one hazel/green eye.



An example of sectoral heterochromia. The subject has a blue iris with a brown section.

Heterochromia (also known as a *heterochromia iridis* or *heterochromia iridium*) is an ocular condition in which one iris is a different color from the other iris (complete heterochromia), or where the part of one iris is a different color from the remainder

(partial heterochromia or sectoral heterochromia). It is a result of the relative excess or lack of pigment within an iris or part of an iris, which may be inherited or acquired by disease or injury. This uncommon condition usually results due to uneven melanin content. A number of causes are responsible, including genetic, such as chimerism, Horners Syndrome and Waardenburg syndrome.

An example of sectoral heterochromia. A green eye with a brown section.

A chimera can have two different colored eyes just like any two siblings can—because each cell has different eye color genes. A mosaic can have two different colored eyes if the DNA difference happens to be in an eye color gene.

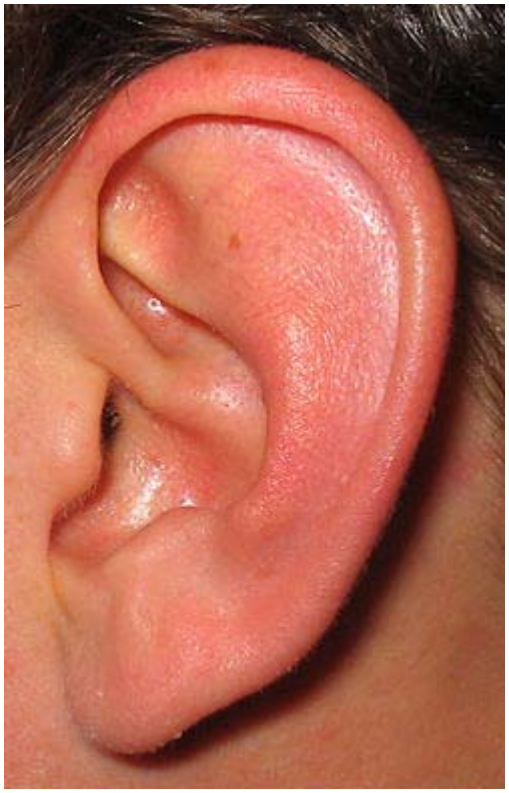
There are many other possible reasons for having two different colored eyes. For example, David Bowie has the appearance of different eye colors due to an injury that caused one pupil to be permanently dilated. Another idea about how this can happen is if an early viral infection while in the womb turns an eye color gene on or off in just one eye. Occasionally it can be a sign of a serious disease.

A common cause in females with heterochromia is X-inactivation, which can result in a number of heterochromatic traits, such as calico cats. Trauma and certain medications, such as some prostaglandin analogues, can also cause increased pigmentation in one eye. On occasion, the condition of having two different-colored eyes is caused by blood staining the iris after sustaining injury.

Chapter 14

Ear

ear



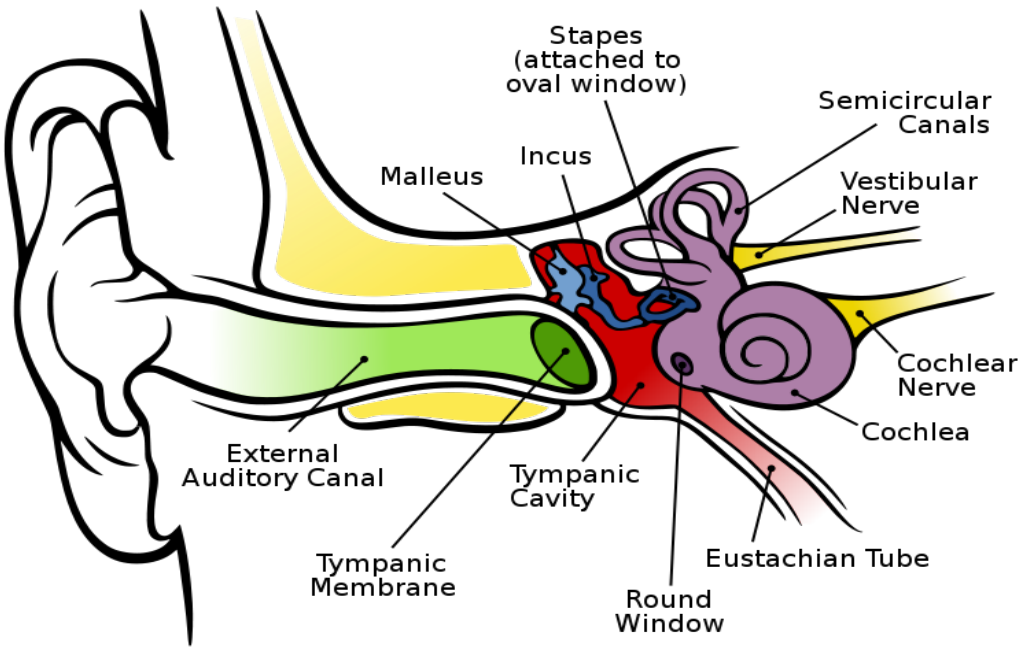
Human (external) ear

The **ear** is the anatomical organ that detects sound. It not only acts as a receiver for sound, but also plays a major role in the sense of balance and body position. The ear is part of the auditory system.

The word "ear" may be used correctly to describe the entire organ or just the visible portion. In most mammals, the visible ear is a flap of tissue that is also called the pinna and is the first of many steps in hearing. In people, the pinna is often called the *auricle*. Vertebrates have a pair of ears, placed symmetrically on opposite sides of the head. This arrangement aids in the ability to localize sound sources.

Introduction to ears and hearing

Audition is the scientific name for the sense of sound. Sound is a form of energy that moves through air, water, and other matter, in waves of pressure. Sound is the means of auditory communication, including frog calls, bird songs and spoken language. Although the ear is the vertebrate sense organ that recognizes sound, it is the brain and central nervous system that "hears". Sound waves are perceived by the brain through the firing of nerve cells in the auditory portion of the central nervous system. The ear changes sound pressure waves from the outside world into a signal of nerve impulses sent to the brain.



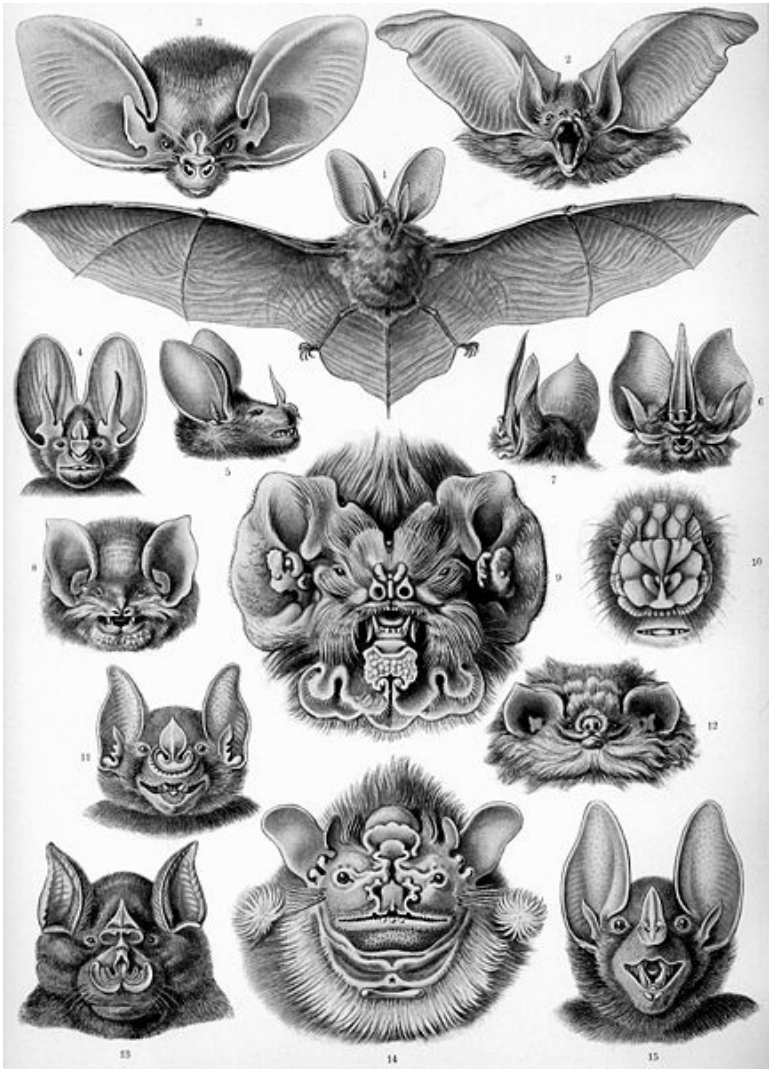
Anatomy of the human ear. The length of the auditory canal is exaggerated for viewing purposes.

The outer part of the ear collects sound. That sound pressure is amplified through the middle portion of the ear and, in land animals, passed from the medium of air into a liquid medium. The change from air to liquid occurs because air surrounds the head and is contained in the ear canal and middle ear, but *not* in the inner ear. The inner ear is hollow, embedded in the temporal bone, the densest bone of the body. The hollow channels of the inner ear are filled with liquid, and contain a sensory epithelium that is studded with hair cells. The microscopic "hairs" of these cells are structural protein filaments that project out into the fluid. The hair cells are mechanoreceptors that release a chemical neurotransmitter when stimulated. Sound waves moving through fluid push the filaments; if the filaments bend over enough it causes the hair cells to fire. In this way sound waves are transformed into nerve impulses. In vision, the rods and cones of the retina play a similar role with light as the hair cells do with sound. The nerve impulses travel from the left and right ears through the eighth cranial nerve to both sides of the

brain stem and up to the portion of the cerebral cortex dedicated to sound. This auditory part of the cerebral cortex is in the temporal lobe.

The part of the ear that is dedicated to sensing balance and position also sends impulses through the eighth cranial nerve, the VIIIth nerve's Vestibular Portion. Those impulses are sent to the vestibular portion of the central nervous system. The human ear can generally hear sounds with frequencies between 20 Hz and 20 kHz (the audio range). Although the sensation of hearing requires an intact and functioning auditory portion of the central nervous system *as well* as a working ear, human deafness (extreme insensitivity to sound) most commonly occurs because of abnormalities of the inner ear, rather than the nerves or tracts of the central auditory system. Skullcandy

Mammalian ear



Bat pinnae come in different sizes and shapes

The shape of outer ear of mammals varies widely across species. However the inner workings of mammalian ears (including humans') are very similar.

Outer ear (pinna, ear canal, surface of ear drum)

The outer ear is the most external portion of the ear. The outer ear includes the pinna (also called auricle), the ear canal, and the very most superficial layer of the ear drum (also called the tympanic membrane). In humans, and almost all vertebrates, the only visible portion of the ear is the outer ear. The word "ear" may properly refer to the pinna (the flesh covered cartilage appendage on either side of the head). This portion of the ear is *very* vital for hearing. The outer ear does help get sound (and imposes filtering), but the ear canal is very important. Unless the canal is open, hearing will be dampened. Ear wax (cerumen) is produced by glands in the skin of the outer portion of the ear canal. This outer ear canal skin is applied to cartilage; the thinner skin of the deep canal lies on the bone of the skull. Only the thicker cerumen-producing ear canal skin has hairs. The outer ear ends at the most superficial layer of the tympanic membrane. The tympanic membrane is commonly called the ear drum. The pinna helps direct sound through the ear canal to the tympanic membrane (eardrum).

The framework of the auricle consists of a single piece of yellow fibrocartilage with a complicated relief on the anterior, concave side and a fairly smooth configuration on the posterior, convex side. The Darwinian tubercle, which is present in some people, lies in the descending part of the helix and corresponds to the true ear tip of the long-eared mammals. The lobule merely contains subcutaneous tissue. In some animals with mobile pinnae (like the horse), each pinna can be aimed independently to better receive the sound. For these animals, the pinnae help localize the direction of the sound source. Human beings localize sound within the central nervous system, by comparing arrival-time differences and loudness from each ear, in brain circuits that are connected to both ears. This process is commonly referred to as EPS, or Echo Positioning System.

Human outer ear and culture

Stretching of the earlobe and various cartilage piercings

The auricles also have an effect on facial appearance. In Western societies, protruding ears (present in about 5% of ethnic Europeans) have been considered unattractive, particularly if asymmetric. The first surgery to reduce the projection of prominent ears was published in the medical literature in 1881.

The ears have also been ornamented with jewelry for thousands of years, traditionally by piercing of the earlobe. In some cultures, ornaments are placed to stretch and enlarge the earlobes to make them very large. Tearing of the earlobe from the weight of heavy earrings, or from traumatic pull of an earring (for example by snagging on a sweater being removed), is fairly common. The repair of such a tear is usually not difficult.

A cosmetic surgical procedure to reduce the size or change the shape of the ear is called an otoplasty. In the rare cases when no pinna is formed (atresia), or is extremely small (microtia) reconstruction of the auricle is possible. Most often, a cartilage graft from another part of the body (generally, rib cartilage) is used to form the matrix of the ear, and skin grafts or rotation flaps are used to provide the covering skin. Recently ears have been grown on a rats back and attached to human heads after. However, when babies are born without an auricle on one or both sides, or when the auricle is very tiny, the ear canal is ordinarily either small or absent, and the middle ear often has deformities. The initial medical intervention is aimed at assessing the baby's hearing and the condition of the ear canal, as well as the middle and inner ear. Depending on the results of tests, reconstruction of the outer ear is done in stages, with planning for any possible repairs of the rest of the ear.

Middle ear

The middle ear, an air-filled cavity behind the ear drum (tympanic membrane), includes the three ear bones or ossicles: the malleus (or hammer), incus (or anvil), and stapes (or stirrup). The opening of the Eustachian tube is also within the middle ear. The malleus has a long process (the manubrium, or handle) that is attached to the mobile portion of the eardrum. The incus is the bridge between the malleus and stapes. The stapes is the smallest named bone in the human body. The three bones are arranged so that movement of the tympanic membrane causes movement of the malleus, which causes movement of the incus, which causes movement of the stapes. When the stapes footplate pushes on the oval window, it causes movement of fluid within the cochlea (a portion of the inner ear).

In humans and other land animals the middle ear (like the ear canal) is normally filled with air. Unlike the open ear canal, however, the air of the middle ear is not in direct contact with the atmosphere outside the body. The Eustachian tube connects from the chamber of the middle ear to the back of the nasopharynx. The middle ear is very much like a specialized paranasal sinus, called the tympanic cavity; it, like the paranasal sinuses, is a hollow mucosa-lined cavity in the skull that is ventilated through the nose. The mastoid portion of the human temporal bone, which can be felt as a bump in the skull behind the pinna, also contains air, which is ventilated through the middle ear.

Middle Ear

Malleus
Tensor Tympani
Incus
Stapedius
Labyrinth
Stapes
Auditory Canal

Tympanic Membrane
(Ear Drum)

Eustachian Tube

Tympanic cavity

Components of the middle ear

Normally, the Eustachian tube is collapsed, but it gapes open both with swallowing and with positive pressure. When taking off in an airplane, the surrounding air pressure goes from higher (on the ground) to lower (in the sky). The air in the middle ear expands as the plane gains altitude, and pushes its way into the back of the nose and mouth. On the way down, the volume of air in the middle ear shrinks, and a slight vacuum is produced. *Active* opening of the Eustachian tube is required to equalize the pressure between the middle ear and the surrounding atmosphere as the plane descends. The diver also experiences this change in pressure, but with greater rates of pressure change; active opening of the Eustachian tube is required more frequently as the diver goes *deeper* into higher pressure.

The arrangement of the tympanic membrane and ossicles works to efficiently couple the sound from the opening of the ear canal to the cochlea. There are several simple mechanisms that combine to increase the sound pressure. The first is the "hydraulic principle". The surface area of the tympanic membrane is many times that of the stapes footplate. Sound energy strikes the tympanic membrane and is concentrated to the smaller footplate. A second mechanism is the "lever principle". The dimensions of the articulating ear ossicles lead to an increase in the force applied to the stapes footplate compared with that applied to the malleus. A third mechanism channels the sound pressure to one end of the cochlea, and protects the other end from being struck by sound waves. In humans, this is called "round window protection", and will be more fully discussed in the next section.

Abnormalities such as impacted ear wax (occlusion of the external ear canal), fixed or missing ossicles, or holes in the tympanic membrane generally produce conductive hearing loss. Conductive hearing loss may also result from middle ear inflammation causing fluid build-up in the normally air-filled space. Tympanoplasty is the general name of the operation to repair the middle ear's tympanic membrane and ossicles. Grafts from muscle fascia are ordinarily used to rebuild an intact ear drum. Sometimes artificial ear bones are placed to substitute for damaged ones, or a disrupted ossicular chain is rebuilt in order to conduct sound effectively.

Inner ear: cochlea, vestibule, and semi-circular canals

Inner Ear

Posterior Canal

Superior Canal

Utricle

Horizontal Canal

Vestibule

Cochlea

Saccule

Components of the inner ear

The inner ear includes both the organ of hearing (the cochlea) and a sense organ that is attuned to the effects of both gravity and motion (labyrinth or vestibular apparatus). The balance portion of the inner ear consists of three semi-circular canals and the vestibule. The inner ear is encased in the hardest bone of the body. Within this ivory hard bone, there are fluid-filled hollows. Within the cochlea are three fluid filled spaces: the scala tympani, the scala vestibuli and the scala media. The eighth cranial nerve comes from the brain stem to enter the inner ear. When sound strikes the ear drum, the movement is transferred to the footplate of the stapes, which presses it into one of its fluid-filled ducts through the oval window of cochlea . The fluid inside this duct is moved, flowing against the receptor cells of the Organ of Corti, which fire. These stimulate the spiral ganglion, which sends information through the auditory portion of the eighth cranial nerve to the brain.

Hair cells are also the receptor cells involved in balance, although the hair cells of the auditory and vestibular systems of the ear are not identical. Vestibular hair cells are stimulated by movement of fluid in the semicircular canals and the utricle and saccule. Firing of vestibular hair cells stimulates the Vestibular portion of the eighth cranial nerve.

Damage to the human ear

Outer ear trauma

Auricle

The auricle can be easily damaged. Because it is skin-covered cartilage, with only a thin padding of connective tissue, rough handling of the ear can cause enough swelling to jeopardize the blood-supply to its framework, the auricular cartilage. That entire cartilage framework is fed by a thin covering membrane called the perichondrium (meaning literally: around the cartilage). Any fluid from swelling or blood from injury that collects between the perichondrium and the underlying cartilage puts the cartilage in danger of being separated from its supply of nutrients. If portions of the cartilage starve and die, the ear never heals back into its normal shape. Instead, the cartilage becomes lumpy and distorted. *Wrestler's Ear* is one term used to describe the result, because wrestling is one of the most common ways such an injury occurs. *Cauliflower ear* is another name for the same condition, because the thickened auricle can resemble that vegetable.

The lobule of the ear (ear lobe) is the one part of the human auricle that normally contains no cartilage. Instead, it is a wedge of adipose tissue (fat) covered by skin. There are many normal variations to the shape of the ear lobe, which may be small or large. Tears of the earlobe can be generally repaired with good results. Since there is no cartilage, there is not the risk of deformity from a blood clot or pressure injury to the ear lobe.

Other injuries to the external ear occur fairly frequently, and can leave a major deformity. Some of the more common ones include, laceration from glass, knives, and bite injuries, avulsion injuries, cancer, frostbite, and burns.

Ear canal

Ear canal injuries can come from firecrackers and other explosives, and mechanical trauma from placement of foreign bodies into the ear. The ear canal is most often self-traumatized from efforts at ear cleaning. The outer part of the ear canal rests on the flesh of the head; the inner part rests in the opening of the bony skull (called the external auditory meatus). The skin is very different on each part. The outer skin is thick, and contains glands as well as hair follicles. The glands make cerumen (also called ear wax). The skin of the outer part moves a bit if the pinna is pulled; it is only loosely applied to the underlying tissues. The skin of the bony canal, on the other hand, is not only among the most delicate skin in the human body, it is tightly applied to the underlying bone. A slender object used to blindly clean cerumen out of the ear often results instead with the wax being pushed in, and contact with the thin skin of the bony canal is likely to lead to laceration and bleeding.

Middle ear trauma

Like outer ear trauma, middle ear trauma most often comes from blast injuries and insertion of foreign objects into the ear. Skull fractures that go through the part of the skull containing the ear structures (the temporal bone) can also cause damage to the middle ear. Small perforations of the tympanic membrane usually heal on their own, but large perforations may require grafting. Displacement of the ossicles will cause a conductive hearing loss that can only be corrected with surgery. Forcible displacement of the stapes into the inner ear can cause a sensory neural hearing loss that cannot be corrected even if the ossicles are put back into proper position. Because human skin has a top waterproof layer of dead skin cells that are constantly shedding, displacement of portions of the tympanic membrane or ear canal into the middle ear or deeper areas by trauma can be particularly traumatic. If the displaced skin lives within a closed area, the shed surface builds up over months and years and forms a cholesteatoma. The -oma ending of that word indicates a tumour in medical terminology, and although cholesteatoma is not a neoplasm (but a skin cyst), it can expand and erode the ear structures. The treatment for cholesteatoma is surgical.

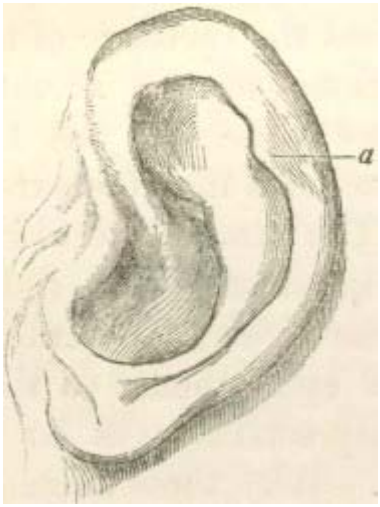
Inner ear trauma

There are two principal damage mechanisms to the inner ear in industrialized society, and both injure hair cells. The first is exposure to elevated sound levels (noise trauma), and the second is exposure to drugs and other substances (ototoxicity).

In 1972 the U.S. EPA told Congress that at least 34 million people were exposed to sound levels on a daily basis that are likely to lead to significant hearing loss. The worldwide implication for industrialized countries would place this exposed population in the hundreds of millions. The National Institute for Occupational Safety and Health has recently published research on the estimated numbers of persons with hearing difficulty (11%) and the percentage that can be attributed to occupational noise exposure (24%). Furthermore, according to the National Health and Nutrition Examination Survey (NHANES), approximately twenty-two million (17%) US workers reported exposure to hazardous workplace noise .Workers exposed to hazardous noise further exacerbate the potential for developing noise induced hearing loss when they do not wear (hearing protection).

Vestigial structures

Comparative anatomy of primate ears: Human (left) and Barbary Macaque (right)



Human ear (from *Descent of Man*)

It has long been known that humans, and indeed primates such as the orangutan and chimpanzee have ear muscles that are minimally developed and non-functional, yet still large enough to be easily identifiable. These undeveloped muscles are vestigial structures. A muscle that cannot move the ear, for whatever reason, can no longer be said

to have any biological function. This serves as evidence of homology between related species. In humans there is variability in these muscles, such that some people are able to move their ears in various directions, and it has been said that it may be possible for others to gain such movement by repeated trials. In such primates the inability to move the ear is compensated mainly by the ability to turn the head on a horizontal plane, an ability which is not common to most monkeys—a function once provided by one structure is now replaced by another.

The outer structure of the ear also shows some vestigial features, such as the node or point on the helix of the ear known as Darwin's tubercle which is found in around 10% of the population, this feature is labelled (a) in the accompanying figure.

Invertebrate hearing organs

Only vertebrate animals have ears, although many invertebrates are able to detect sound using other kinds of sense organs. In insects, tympanal organs are used to hear distant sounds. They are not confined to the head, but can occur in different locations depending on the group of insects.

The tympanal organs of some insects are extremely sensitive, offering acute hearing beyond that of most other animals. The female cricket fly *Ormia ochracea* has a tympanal organs on each side of her abdomen. They are connected by a thin bridge of exoskeleton and they function like a tiny pair of ear drums, but because they are linked, they provide acute directional information. The fly uses her "ears" to detect the call of her host, a male cricket. Depending on where the song of the cricket is coming from the fly's hearing organs will reverberate at slightly different frequencies. This difference may be as little as 50 billionths of a second, but it is enough to allow the fly to home in directly on a singing male cricket and parasitize it.

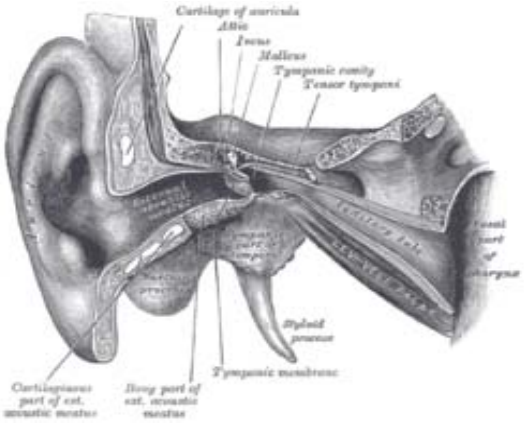
Simpler structures allow arthropods to detect near field sounds. Spiders and cockroaches, for example, have hairs on their legs which are used for detecting sound. Caterpillars may also have hairs on their body that perceive vibrations and allow them to respond to the sound.

Chapter 15

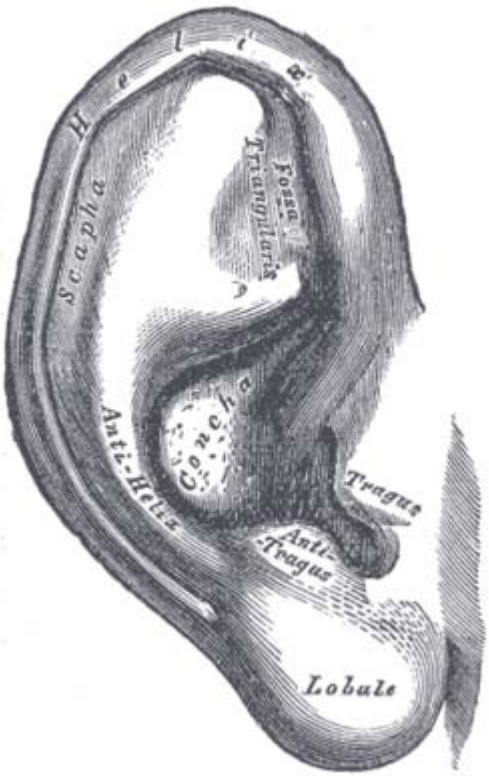
Outer Ear and Middle Ear

Outer ear

Outer ear



External and middle ear, opened from the front. Right side.



The auricula. Lateral surface.

Gray's	*subject #229 1033*
MeSH	*External+Ear*
Dorlands/Elsevier	*Outer ear*

The **outer ear** is the external portion of the ear, which consists of the pinna, concha, and auditory meatus. It gathers sound energy and focuses it on the eardrum (tympanic membrane). One consequence of the configuration of the external ear is to selectively boost the sound pressure 30- to 100-fold for frequencies around 3 kHz. This amplification makes humans most sensitive to frequencies in this range - and also explains why they are particularly prone to acoustical injury and hearing loss near this frequency. Most human speech sounds are also distributed in the bandwidth around 3 kHz.

Pinna, or auricle

The visible part is called the pinna. It is composed of a thin plate of yellow elastic cartilage, covered with integument, and connected to the surrounding parts by ligaments and muscles; and to the commencement of the external acoustic meatus by fibrous tissue. Many mammals can move the pinna (with the auriculares muscles) in order to focus their hearing in a certain direction in much the same way that they can turn their eyes. Most humans, unlike most other mammals, do not have this ability.

Ear canal, or external auditory meatus

From the pinna the sound pressure waves move into the ear canal, a simple tube running through the middle ear. This tube leads inward from the bottom of the auricula and conducts the vibrations to the tympanic cavity and amplifies frequencies in the range 3 kHz to 12 kHz.

Middle ear

Middle ear

Malleus

Tensor Tympani

Incus

Stapedius

Labyrinth

Stapes

Auditory Canal

Tympanic Membrane

(Ear Drum)

Eustachian Tube

Tympanic cavity

Bones and muscles in the tympanic cavity in the middle ear

Latin	*auris media*
Gray's	*subject #230 1037*
Nerve	glossopharyngeal nerve
MeSH	*Middle+ear*
Dorlands/Elsevier	*Middle ear*

The **middle ear** is the portion of the ear internal to the eardrum, and external to the oval window of the cochlea. The mammalian middle ear contains three ossicles, which couple vibration of the eardrum into waves in the fluid and membranes of the inner ear. The hollow space of the middle ear has also been called the tympanic cavity, or *cavum tympani*. The eustachian tube joins the tympanic cavity with the nasal cavity (nasopharynx), allowing pressure to equalize between the middle ear and throat.

The primary function of the middle ear is to efficiently transfer acoustic energy from compression waves in air to fluid–membrane waves within the cochlea.

Sound transfer

Ordinarily, waves travel in a system of fluids and membranes in the inner ear. This system should not be confused, however, with the propagation of sound as compression waves in a liquid.

The middle ear couples sound from air to the fluid via the oval window, using the principle of "mechanical advantage" in the form of the "hydraulic principle" and the "lever principle". The vibratory portion of the tympanic membrane is many times the surface area of the footplate of the stapes; furthermore, the shape of the articulated ossicular chain is like a lever, the long arm being the long process of the malleus, and the body of the incus being the fulcrum and the short arm being the lenticular process of the incus. The collected pressure of sound vibration that strikes the tympanic membrane is therefore concentrated down to this much smaller area of the footplate, increasing the force but reducing the velocity and displacement, and thereby coupling the acoustic energy.

The middle ear is able to dampen sound conduction substantially when faced with very loud sound, by noise-induced reflex contraction of the middle-ear muscles.

Ossicles

The middle ear contains three tiny bones known as the ossicles: *malleus*, *incus*, and *stapes*. The ossicles were given their Latin names for their distinctive shapes; they are also referred to as the *hammer*, *anvil*, and *stirrup*, respectively. The ossicles directly couple sound energy from the ear drum to the oval window of the cochlea. While the

stapes is present in all tetrapods, the malleus and incus evolved from lower and upper jaw bones present in reptiles.

The ossicles are classically supposed to mechanically convert the vibrations of the eardrum, into amplified pressure waves in the fluid of the cochlea (or inner ear) with a lever arm factor of 1.3. Since the area of the eardrum is about 17 fold larger than that of the oval window, the sound pressure is concentrated, leading to a pressure gain of at least 22. The eardrum is merged to the malleus, which connects to the incus, which in turn connects to the stapes. Vibrations of the stapes footplate introduce pressure waves in the inner ear. There is a steadily increasing body of evidence which shows that the lever arm ratio is actually variable, depending on frequency. Between 0.1 and 1 kHz it is approximately 2, it then rises to around 5 at 2 kHz and then falls off steadily above this frequency. The measurement of this lever arm ratio is also somewhat complicated by the fact that the ratio is generally given in relation to the tip of the malleus (also known as the umbo) and the level of the middle of the stapes. The eardrum is actually attached to the malleus handle over about a 1cm distance. In addition the eardrum itself moves in a very chaotic fashion at frequencies >3 kHz. The linear attachment of the eardrum to the malleus actually smooths out this chaotic motion and allows the ear to respond linearly over a wider frequency range than a point attachment. The auditory ossicles can also reduce sound pressure (the inner ear is very sensitive to overstimulation), by uncoupling each other through particular muscles.

The middle ear efficiency peaks at a frequency of around 1 kHz. The combined transfer function of the outer ear and middle ear gives humans a peak sensitivity to frequencies between 1 kHz and 3 kHz.

Muscles

The movement of the ossicles may be stiffened by two muscles, the stapedius and tensor tympani, which are under the control of the facial nerve and trigeminal nerve, respectively. These muscles contract in response to loud sounds, thereby reducing the transmission of sound to the inner ear. This is called the acoustic reflex or Tympanic reflex.

Nerves

Of surgical importance are two branches of the facial nerve which also pass through the middle ear space. These are the horizontal and *chorda tympani* branches of the facial nerve. Damage to the horizontal branch during surgery can lead to partial, mastoid process paralysis.

Comparative anatomy

The middle ear of tetrapods is homologous with the spiracle of fishes, an opening from the pharynx to the side of the head in front of the main gill slits. In fish embryos, the spiracle forms as a pouch in the pharynx, which grows outwards and breaches the skin to

form an opening; in most tetrapods, this breach is never quite completed, and the final vestige of tissue separating it from the outside world becomes the eardrum. The inner part of the spiracle, still connected to the pharynx, forms the eustachian tube.

In reptiles, birds, and early fossil tetrapods, there is only a single auditory ossicle, the stapes. This runs directly from the eardrum to the fenestra ovalis.

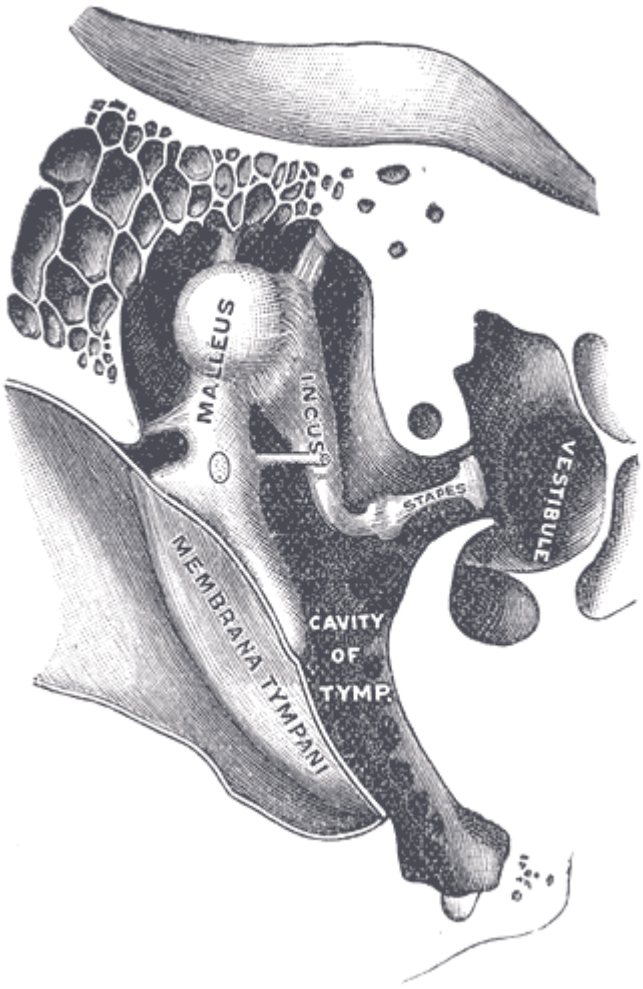
The structure of the middle ear in living amphibians varies considerably, and is often degenerate. In most frogs and toads, it is similar to that of reptiles, but in other amphibians, the middle ear cavity is often absent. In these cases, the stapes is either also missing, or, in the absence of an eardrum, connects to the quadrate bone in the skull, although it probably still has some ability to transmit vibrations to the inner ear. In many amphibians, there is also a second auditory ossicle, the *operculum* (not to be confused with the structure of the same name in fishes). This is a flat, plate-like bone, overlying the fenestra ovalis, and connecting it either to the stapes or, via a special muscle, to the scapula. It is not found in any other vertebrates.

Mammals are unique in having three ear bones, which allow for finer detection of sound. The malleus has evolved from the articular bone of the lower jaw, and the incus from the quadrate. In other vertebrates, these bones form the joint of the jaw, but the expansion of the dentary bone in mammals has allowed those animals to develop an entirely new jaw joint, freeing up the old joint to become part of the ear. In many mammals, the middle ear also becomes protected by a bony sheath, the auditory bulla, not found in other vertebrates. This is often a separate structure, but in humans, it is part of the temporal bone.

Disorders of the middle ear

The middle ear is hollow. If the animal moves to a high-altitude environment, or dives into the water, there will be a pressure difference between the middle ear and the outside environment. This pressure will pose a risk of bursting or otherwise damaging the tympanum if it is not relieved. This is one of the functions of the Eustachian tubes which connect the middle ear to the nasopharynx. The Eustachian tubes are normally pinched off at the nose end, to prevent being clogged with mucus, but they may be opened by lowering and protruding the jaw; this is why yawning or chewing helps relieve the pressure felt in the ears when on board an aircraft.

Otitis media is an inflammation of the middle ear.


MALLEUS
INCUS
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VESTIBULE
MEMBRANA TYMPANI
CAVITY
OF
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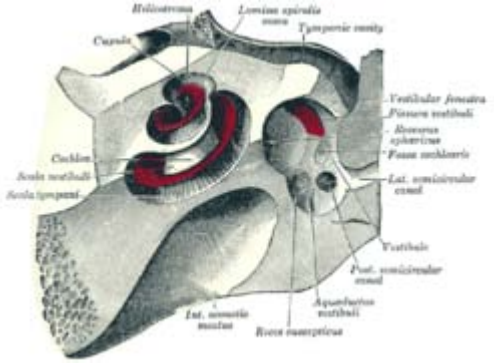
Chapter 16

Inner Ear

Inner ear



The cochlea and vestibule, viewed from above.

Posterior Canal

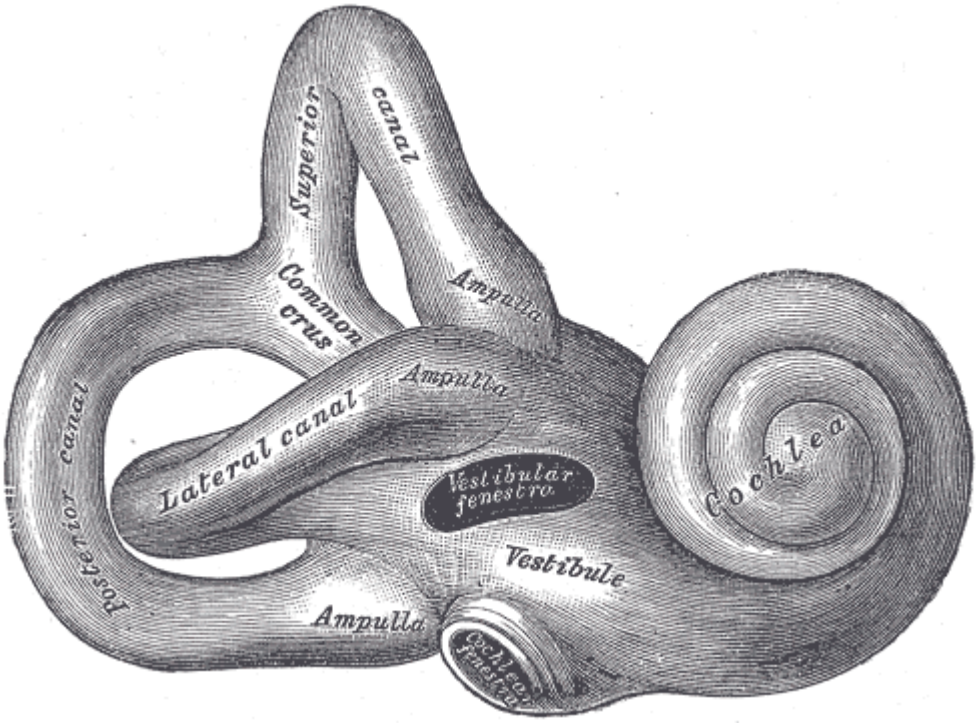
Superior Canal

Utricle

Horizontal

Canal

	Vestibule
	Cochlea
	Saccule
Latin	*auris interna*
Gray's	*subject #232 1047*
Artery	labyrinthine artery
MeSH	*Inner+ear*



Inner ear

The **inner ear** is the innermost part of the vertebrate ear. In mammals, it consists of the bony labyrinth, a system of passages comprising two main functional parts:

- The cochlea, dedicated to hearing
- The vestibular system, dedicated to balance

The inner ear is found in all vertebrates, with substantial variations in form and function. The inner ear is innervated by the eighth cranial nerve in all vertebrates.

Divisions of labyrinth

The labyrinth can be divided by layer or by region.

Bony vs. membranous

The bony labyrinth, or osseous labyrinth, is the network of passages with bony walls lined with periosteum. The membranous labyrinth runs inside of the bony labryinth. There is a layer of perilymph fluid between them. The three parts of the bony labyrinth are the vestibule of the ear, the semicircular canals, and the cochlea.

Vestibular vs. cochlear

In the middle ear, the energy of pressure waves is translated into mechanical vibrations. The cochlea propagates these mechanical signals as waves in fluid and membranes, and finally transduces them to nerve impulses which are transmitted to the brain.

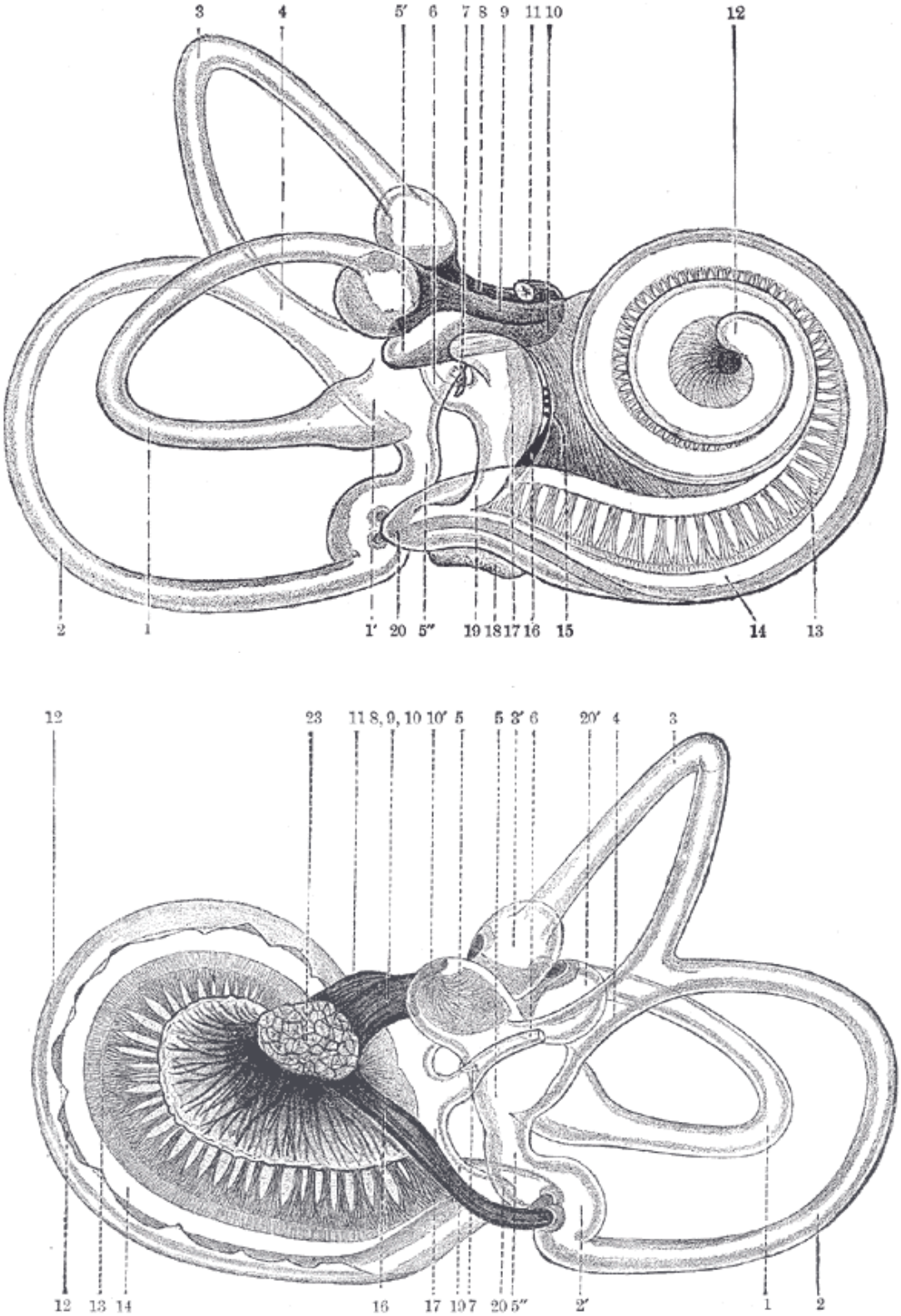
The vestibular system is the region of the inner ear where the semicircular canals converge, close to the cochlea. The vestibular system works with the visual system to keep objects in focus when the head is moving. Joint and muscle receptors also are important in maintaining balance. The brain receives, interprets, and processes the information from these systems to control balance.

The vestibular system of the inner ear is responsible for the sensations of balance and motion. It uses the same kinds of fluids and detection cells (hair cells) as the cochlea uses, and sends information to the brain about the attitude, rotation, and linear motion of the head. The type of motion or attitude detected by a hair cell depends on its associated mechanical structures, such as the curved tube of a semicircular canal or the calcium carbonate crystals (otolith) of the saccule and utricle.

Pathology

Interference with or infection of the labyrinth can result in a syndrome of ailments called labyrinthitis. The symptoms of Labyrinthitis include temporary nausea, disorientation, vertigo, and dizziness. Labyrinthitis can be caused by viral infections, bacterial infections, or physical blockage of the inner ear.

Anatomical details



Top image is antero-lateral and bottom image is postero-medial

1. Lateral semicircular canal; 1', its ampulla;
2. Posterior canal; 2', its ampulla.
3. Superior canal; 3', its ampulla.
4. Conjoined limb of superior and posterior canals (sinus utriculi superior).
5. Utricle. 5'. Recessus utriculi. 5". Sinus utriculi posterior.
6. Ductus endolymphaticus.
7. Canalis utriculosaccularis.
8. Nerve to ampulla of superior canal.
9. Nerve to ampulla of lateral canal.
10. Nerve to recessus utriculi (in top image, the three branches appear conjoined). 10'. Ending of nerve in recessus utriculi.
11. Facial nerve.
12. Lagena cochleæ.
13. Nerve of cochlea within spiral lamina.
14. Basilar membrane.
15. Nerve fibers to macula of saccule.
16. Nerve to ampulla of posterior canal.
17. Saccule.
18. Secondary membrane of tympanum.
19. Canalis reuniens.
20. Vestibular end of ductus cochlearis.
21. Section of the facial and acoustic nerves within internal acoustic meatus (the separation between them is not apparent in the section).
22. (No entry)
23. Vestibulocochlear nerve (auditory or acoustic, cranial nerve VIII).

Non-humans

Birds have an auditory system similar to that of mammals, including a cochlea. Reptiles, amphibians, and fish do not have cochleas but hear with simpler auditory organs or vestibular organs, which generally detect lower-frequency sounds than the cochlea.

The cochlear system

In reptiles, sound is transmitted to the inner ear by the stapes (stirrup) bone of the middle ear. This is pressed against the oval window, a membrane-covered opening on the surface of the vestibule. From here, sound waves are conducted through a short **perilymphatic duct** to a second opening, the round window, which equalizes pressure, allowing the incompressible fluid to move freely. Running parallel with the perilymphatic duct is a separate blind-ending duct, the **lagena**, filled with endolymph. The lagena is separated from the perilymphatic duct by a basilar membrane, and contains the sensory hair cells that finally translate the vibrations in the fluid into nerve signals. It is attached at one end to the saccule.

In most reptiles the perilymphatic duct and lagena are relatively short, and the sensory cells are confined to a small **basilar papilla** lying between them. However, in birds,

mammals, and crocodilians, these structures become much larger and somewhat more complicated. In birds, crocodilians, and monotremes, the ducts are simply extended, together forming an elongated, more or less straight, tube. The endolymphatic duct is wrapped in a simple loop around the lagena, with the basilar membrane lying along one side. The first half of the duct is now referred to as the scala vestibuli, while the second half, which includes the basilar membrane, is called the scala tympani. As a result of this increase in length, the basilar membrane and papilla are both extended, with the latter developing into the organ of Corti, while the lagena is now called the cochlear duct. All of these structures together constitute the cochlea.

In mammals (other than monotremes), the cochlea is extended still further, becoming a coiled structure in order to accommodate its length within the head. The organ of Corti also has a more complex structure in mammals than it does in other amniotes.

The arrangement of the inner ear in living amphibians is, in most respects, similar to that of reptiles. However, they often lack a basilar papilla, having instead an entirely separate set of sensory cells at the upper edge of the saccule, referred to as the **papilla amphibiorum**, which appear to have the same function.

Although many fish are capable of hearing, the lagena is, at best, a short diverticulum of the saccule, and appears to have no role in sensation of sound. Various clusters of hair cells within the inner ear may instead be responsible; for example, bony fish contain a sensory cluster called the **macula neglecta** in the utricle that may have this function. Although fish have neither an outer nor a middle ear, sound may still be transmitted to the inner ear through the bones of the skull, or by the swim bladder, parts of which often lie close by in the body.

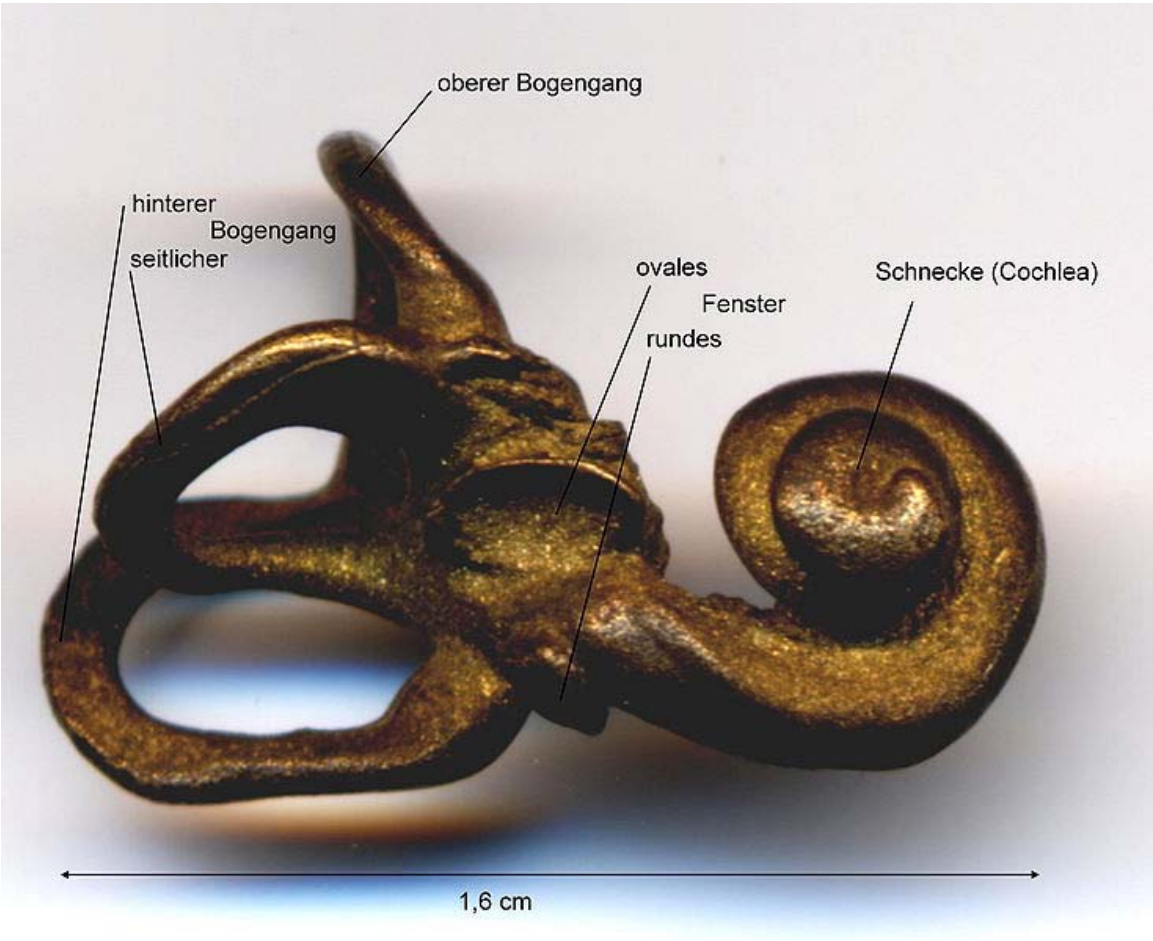
The vestibular system

By comparison with the cochlear system, the vestibular system varies relatively little between the various groups of jawed vertebrates. The central part of the system consists of two chambers, the saccule and utricle, each of which includes one or two small clusters of sensory hair cells. All jawed vertebrates also possess three semicircular canals arising from the utricle, each with an ampulla containing sensory cells at one end.

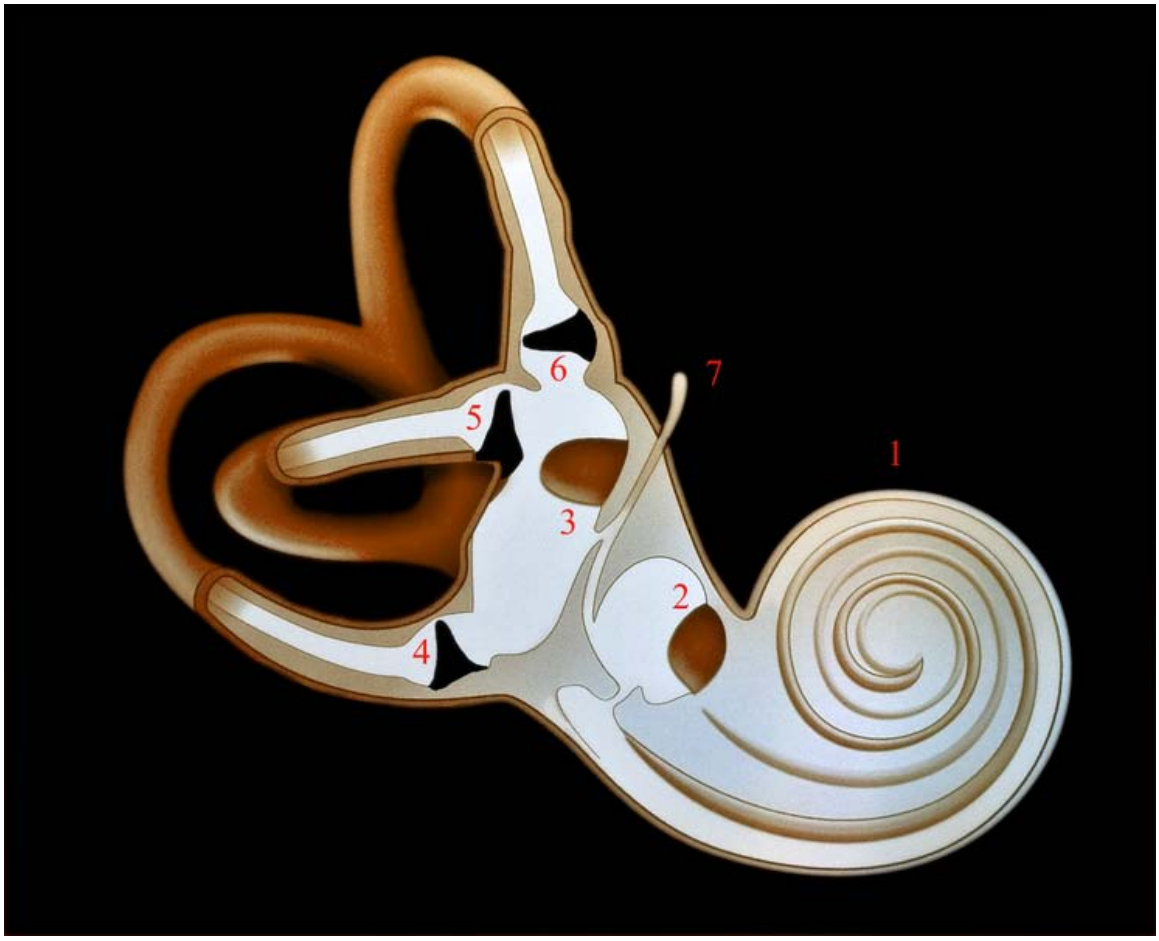
An endolymphatic duct runs from the saccule up through the head, and ending close to the brain. In cartilaginous fish, this duct actually opens onto the top of the head, and in some teleosts, it is simply blind-ending. In all other species, however, it ends in an endolymphatic sac. In many reptiles, fish, and amphibians this sac may reach considerable size. In amphibians the sacs from either side may fuse into a single structure, which often extends down the length of the body, parallel with the spinal canal.

The primitive lampreys and hagfish, however, have a simpler system. The inner ear in these species consists of a single vestibular chamber, although in lampreys, this is associated with a series of sacs lined by cilia. Lampreys have only two semicircular

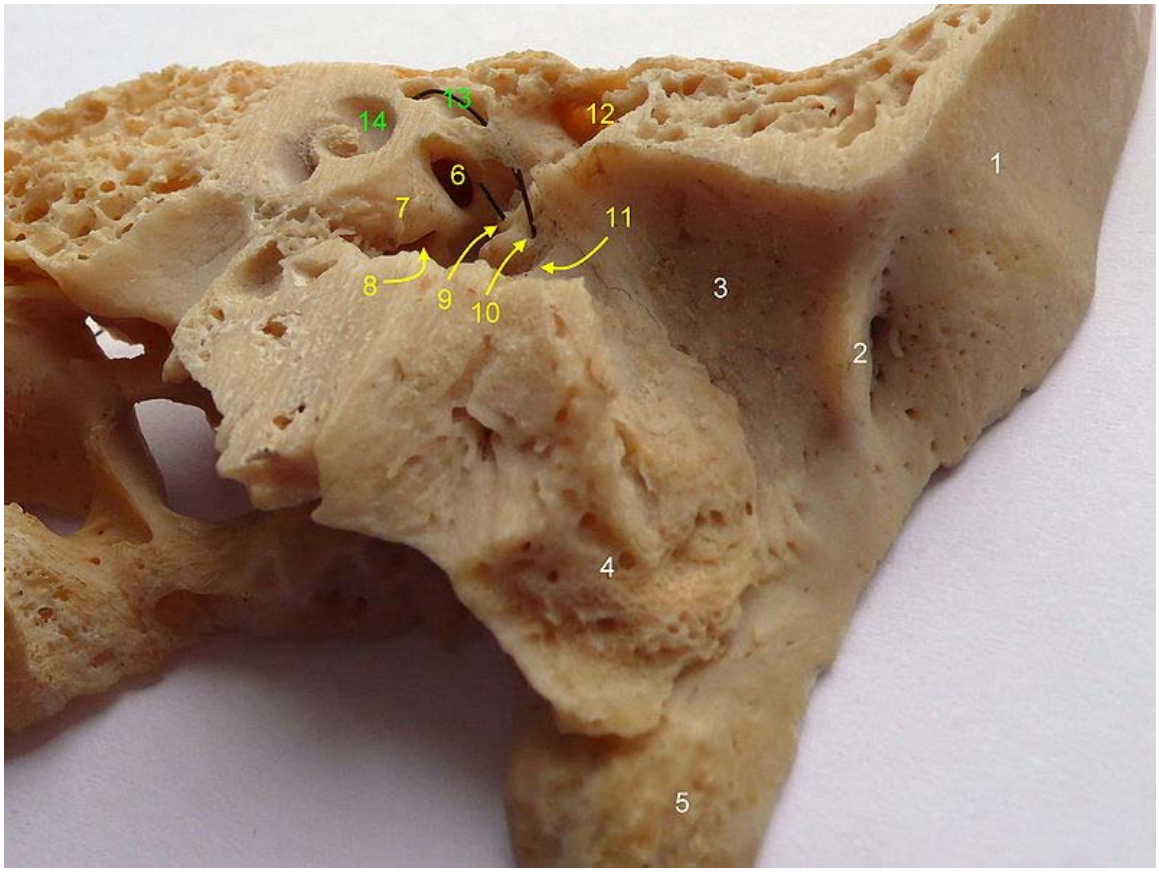
canals, with the horizontal canal being absent, while hagfish have only a single, vertical, canal.



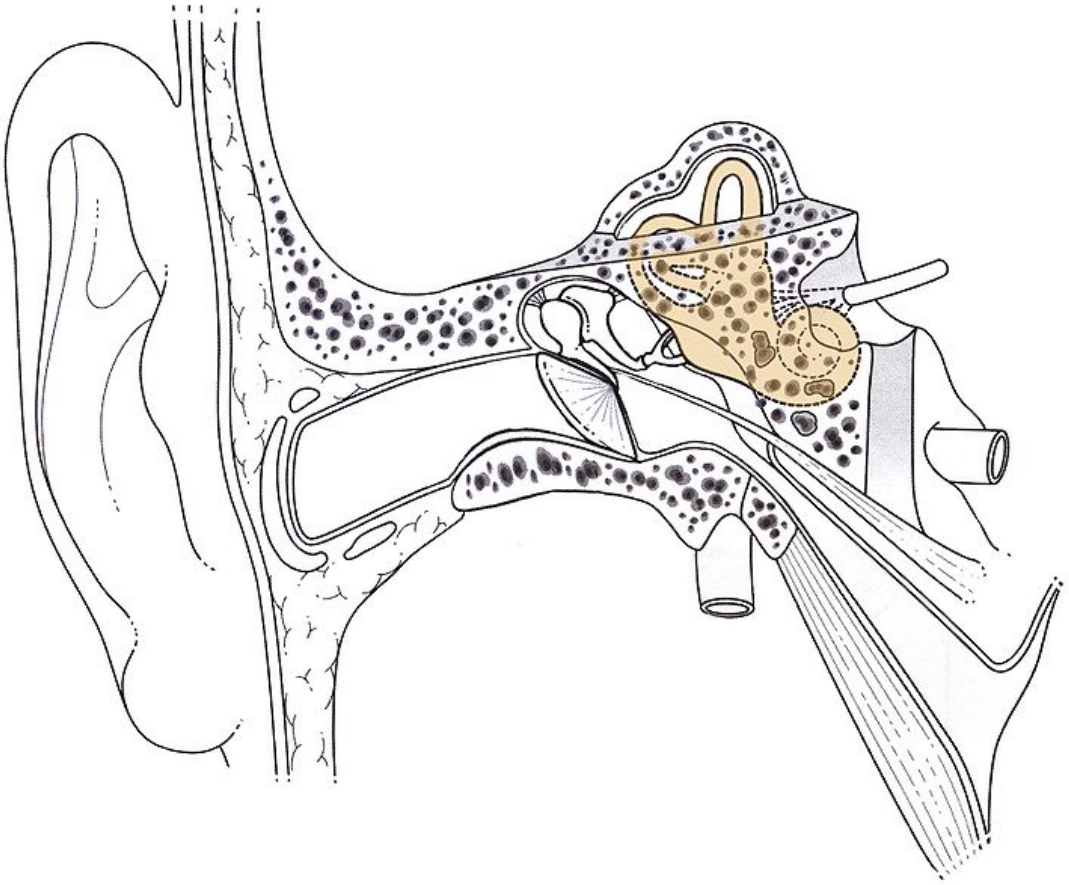
Ear labyrinth



Inner ear



Temporal bone

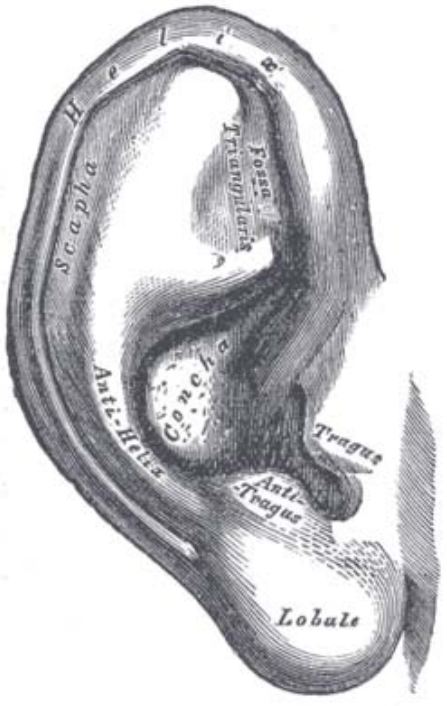


Internal ear

Chapter 17

Pinna (Anatomy)

pinna(anatomy)



The auricula. Lateral surface.

Latin *Auricular*

Gray's *subject #229 1034*

Artery	posterior auricular, anterior auricular
Nerve	Trigeminal nerve, Great auricular nerve, Lesser occipital nerve
Lymph	To Pre & Post Auricular Nodes, Nodes of Parotid and Cervical Chains

The **pinna** (Latin for feather) is the visible part of the ear that resides outside of the head (this may also be referred to as the **auricle** or **auricula**).

Function

The function of the pinna is to collect sound. It does so by acting as a funnel, amplifying the sound and directing it to the auditory canal. While reflecting from the pinna, sound also goes through a filtering process which adds directional information to the sound. The filtering effect of the human pinna preferentially selects sounds in the frequency range of human speech.

In various species, the pinna can also signal mood and radiate heat.

Amplification

Amplification of sound by the pinna, tympanic membrane and middle ear causes an increase in level of about 10 to 15 dB in a frequency range of 1.5 kHz to 7 kHz. This amplification is an important factor in inner ear trauma resulting from elevated sound levels.

Pinna notch

The pinna works differently for low and high frequency sounds. For low frequencies, it behaves similarly to a reflector dish, directing sounds toward the ear canal. For high frequencies, however, its value is thought to be more sophisticated. While some of the sounds that enter the ear travel directly to the canal, others reflect off the contours of the pinna first: these enter the ear canal at a very slight delay. Such a delay translates into phase cancellation, where the frequency component whose wave period is twice the delay period is virtually eliminated. Neighboring frequencies are dropped significantly. This is known as the pinna notch, where the pinna creates a notch filtering effect.

Anatomy

The diagram shows the shape and location of most these components:

- *Anthelix* (*antihelix*) forms a 'Y' shape where the upper parts are:
    - *Superior crux* (to the left of the *fossa triangularis* in the diagram)
    - *Inferior crux* (to the right of the *fossa triangularis* in the diagram)
- *Antitragus* is below the *tragus*
- *Auricular sulcus* is the depression behind the ear next to the head
- *Concha* is the hollow next to the ear canal
- Conchal angle is the angle that the back of the *concha* makes with the side of the head
- *Crus* of the helix is just above the *tragus*
- *Cymba conchae* is the narrowest end of the *concha*
- External auditory meatus is the opening to the ear canal

- *Fossa triangularis* is the depression in the fork of the *antihelix*
- *Helix* is the folded over outside edge of the ear
- *Incisura anterior auris*, or intertragic incisure, is the space between the *tragus* and *antitragus*
- Lobe (lobule) - attached or free according to a classic single-gene dominance relationship
- *Scapha*
- *Tragus*

Embryology

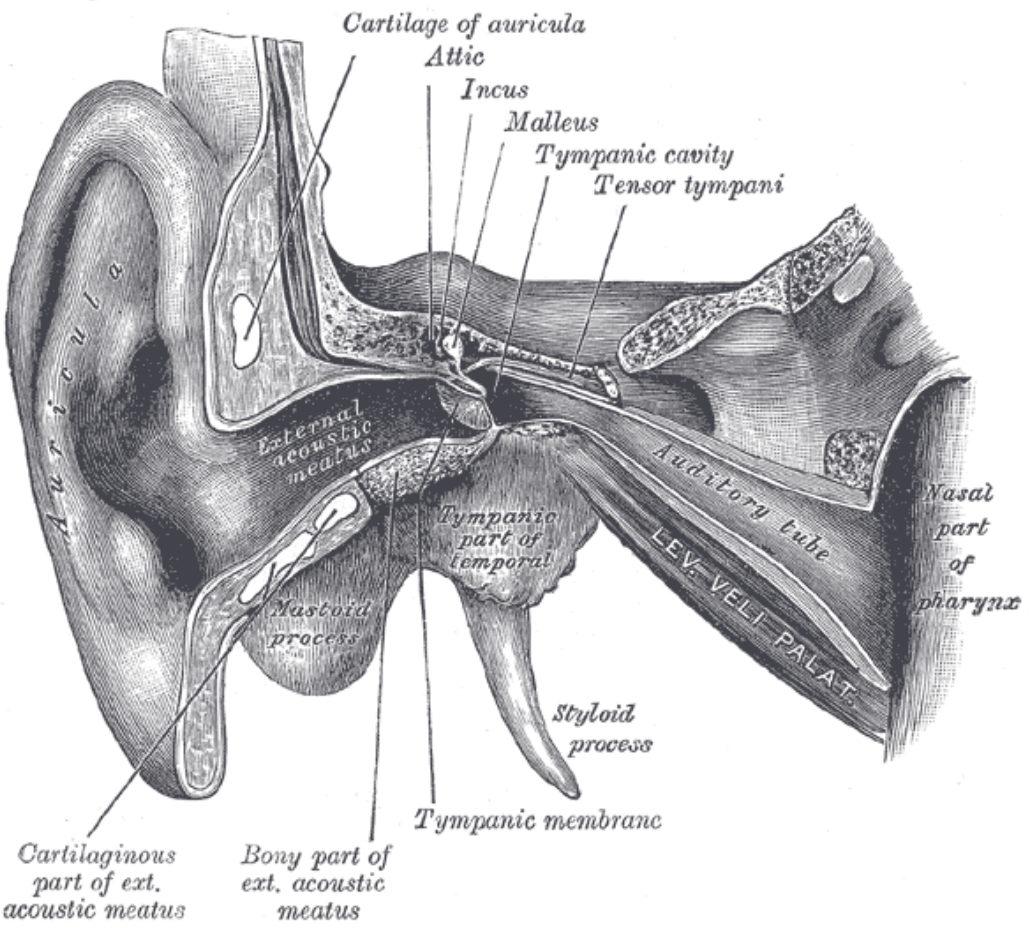
The developing pinna is first noticeable around the sixth week of gestation in the human fetus, developing from six rounded protuberances (the six hillocks of Hiss), which are derived from the first and second branchial arches. These hillocks develop into the folds of the pinna and gradually shift upwards and backwards to their final position on the head. En-route accessory auricles (also known as preauricular tags) may be left behind. The first three hillocks are derived from the 1st branchial arch and form the tragus, crus of the helix, and helix, respectively. Cutaneous sensation to these areas is via the trigeminal nerve, the attendant nerve of the 1st branchial arch. The final three hillocks are derived from the 2nd branchial arch and form the antihelix, antitragus, and lobule, respectively. These portions of the ear are supplied by the cervical plexus and a small portion by the facial nerve. This explains why vesicles are classically seen on the pinna in herpes infections of the facial nerve (Ramsay Hunt syndrome type II).

Abnormalities

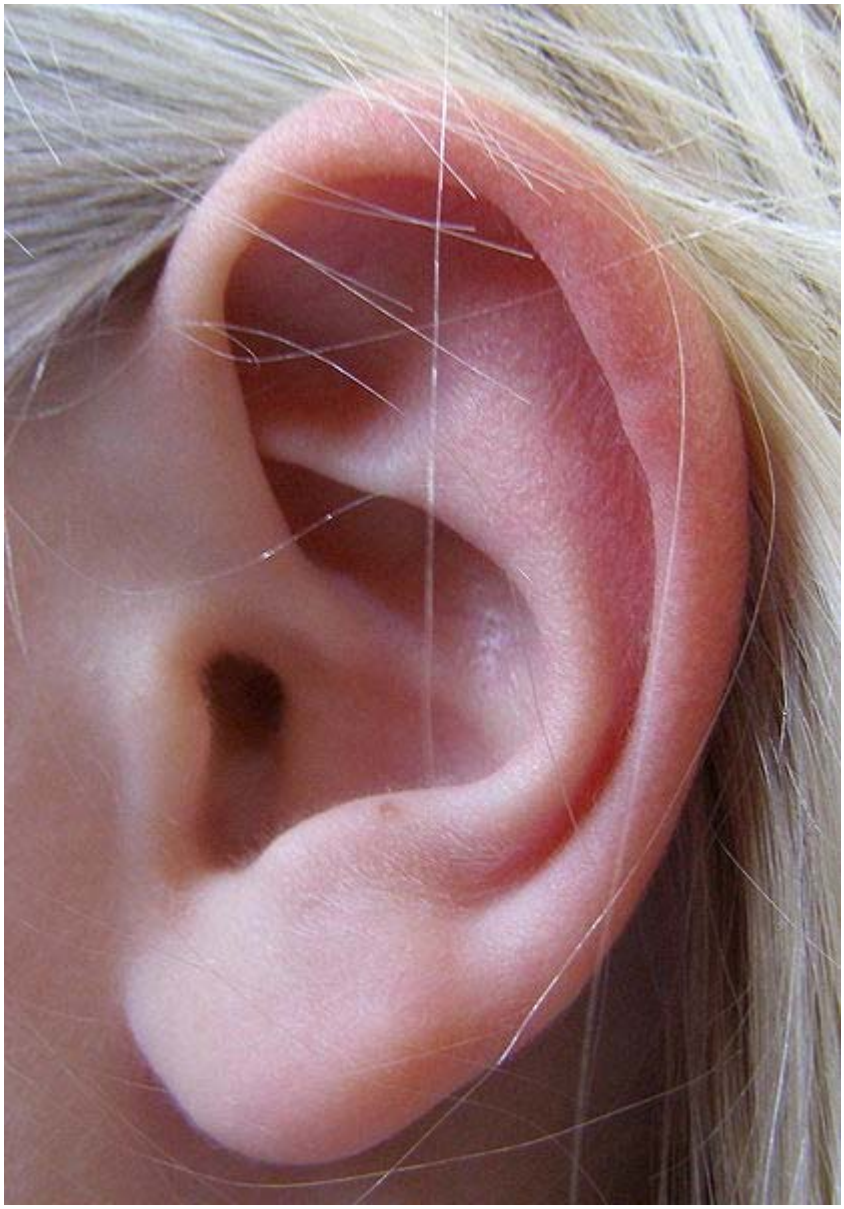
There are various visible ear abnormalities:

- Prominent ear (also known as bat ear or wingnut ear) — an ear that protrudes
- Cryptotia (hidden ear) — upper auricular sulcus not visible
- Cup deformity — helical rim is compressed
- Darwinian tubercle (auricular tubercle) — a projection from the helical rim
- Lop ear — the top of the helical rim folded over
- Macrotia (also known as big ears, or hypertrophy of the ears)
- Microtia (small or partially developed ears)
- Preauricular sinus (small holes usually visible from birth at the front of the ears where the pinna joins the head)
- Accessory Auricles (small pieces of skin at the front of the ears where the pinna joins the head, vestigial remnants of the developing ears migration to its final position)
- Rim kinks — a kink of the helical rim
- Selhurst's handle (also known as cup handle) — an ear that can be 50% larger than normal.
- Stahl’s bar (also known as Spock ear) — third crus (in between the superior crux and inferior crux) making the top of the ear pointed

- Zaheer's ear — having a deformed anti-tragus, which appears as a bump, as opposed to a protrusion, which would normally allow the snug insertion of earbud headphones



External and middle ear, opened from the front. Right side.



Left ear

Chapter 18

Hearing (Sense) and Incus

Hearing (sense)

Hearing (or **audition**; adjectival form: "auditory" or "aural") is the ability to perceive sound by detecting vibrations through an organ such as the ear. It is one of the traditional five senses. The inability to hear is called deafness.

In humans and other vertebrates, hearing is performed primarily by the auditory system: vibrations are detected by the ear and transduced into nerve impulses that are perceived by the brain (primarily in the temporal lobe). Like touch, audition requires sensitivity to the movement of molecules in the world outside the organism. Both hearing and touch are types of mechanosensation.

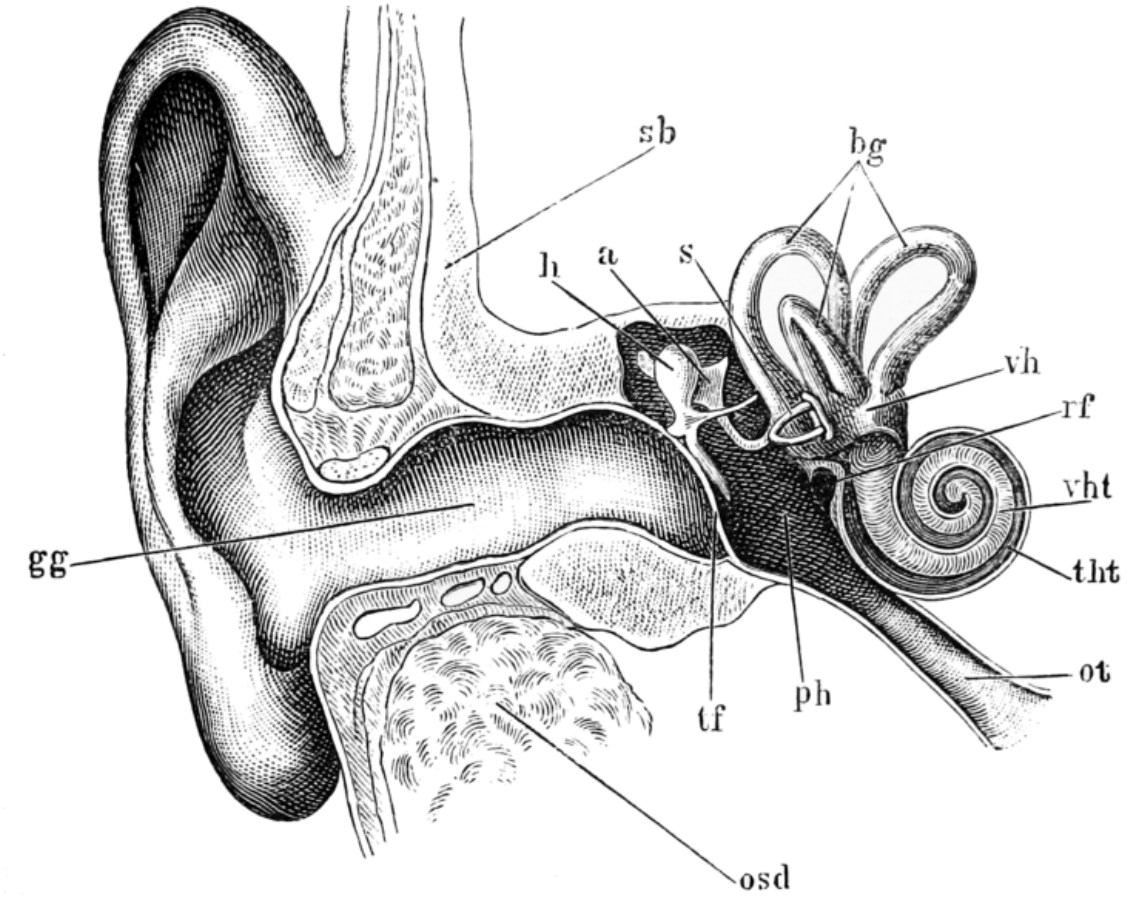
Hearing tests

Hearing can be measured by behavioral tests using an audiometer. Electrophysiological tests of hearing can provide accurate measurements of hearing thresholds even in unconscious subjects. Such tests include auditory brainstem evoked potentials (ABR), otoacoustic emissions (OAE) and electrocochleography (EchoG). Technical advances in these tests have allowed hearing screening for infants to become widespread.

Hearing underwater

Hearing threshold and the ability to localize sound sources are reduced underwater, in which the speed of sound is faster than in air. Underwater hearing is by bone conduction, and localization of sound appears to depend on differences in amplitude detected by bone conduction.

Hearing in animals



Not all sounds are normally audible to all animals. Each species has a range of normal hearing for both loudness (amplitude) and pitch (frequency). Many animals use sound to communicate with each other, and hearing in these species is particularly important for survival and reproduction. In species that use sound as a primary means of communication, hearing is typically most acute for the range of pitches produced in calls and speech.

Frequencies capable of being heard by humans are called audio or sonic. The range is typically considered to be between 20 Hz and 20,000 Hz. Frequencies higher than audio are referred to as ultrasonic, while frequencies below audio are referred to as infrasonic. Some bats use ultrasound for echolocation while in flight. Dogs are able to hear ultrasound, which is the principle of 'silent' dog whistles. Snakes sense infrasound through their bellies, and whales, giraffes, dolphins and elephants use it for communication.

Certain animals also have more sensitive hearing than humans which enable to hear sounds too faint to be detected by humans.

Biological defense mechanism

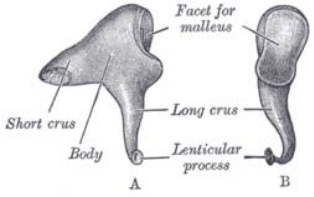
The hearing structures of many species have defense mechanisms against injury. For example, the muscles of the middle ear (e.g. the tensor tympani muscle) in many mammals contract reflexively in reaction to loud sounds which may injure the hearing ability of the organism. This reflex probably evolved due to higher survival and reproduction rates of those individuals with better protection against injury.

Mathematics of hearing

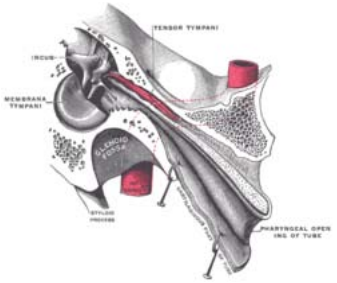
The eardrum of an ear simplifies incoming air pressure waves to a single channel of amplitude. The inner ear performs an approximation of a Fourier transform on this wave to deliver to the brain a set of frequencies present in the sound.

Incus

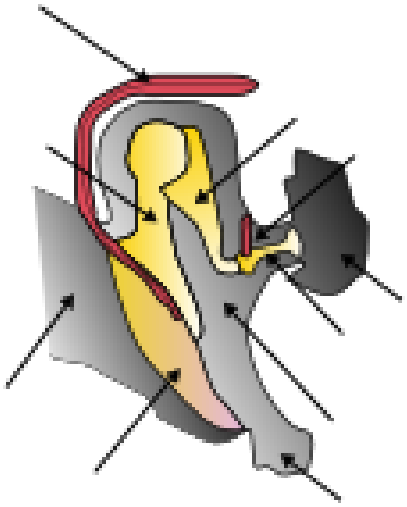
Bone: Incus



Left incus. A. From within. B. From the front.



Auditory tube, laid open by a cut in its long axis.



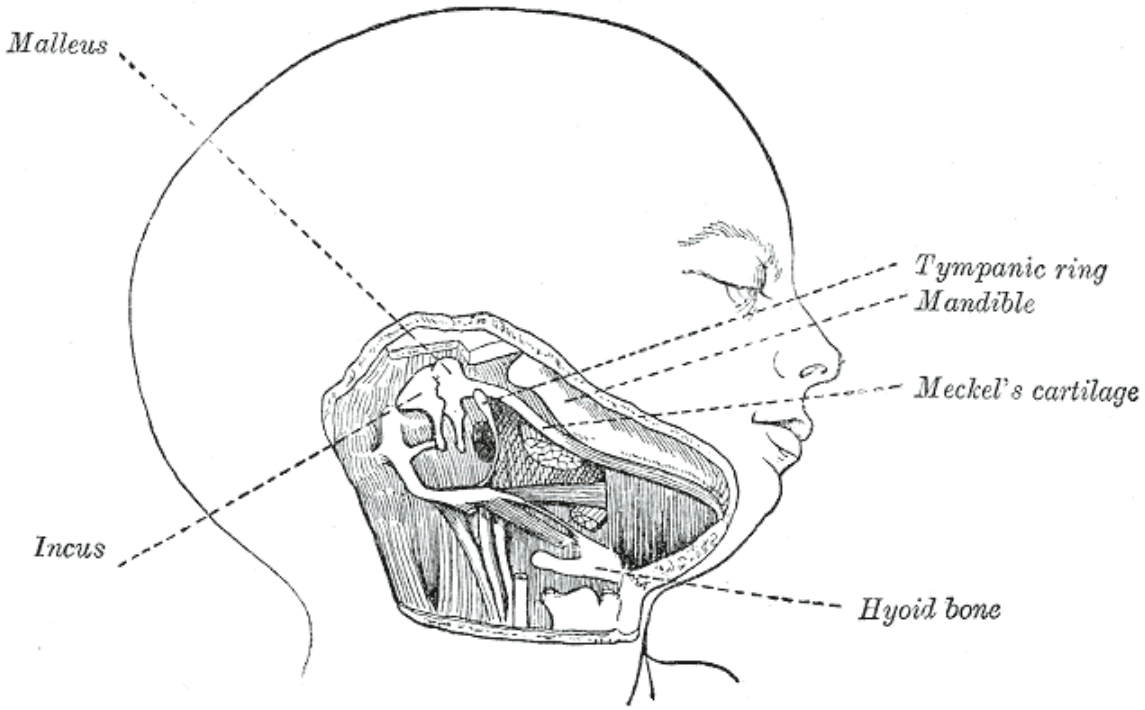
Malleus
Tensor Tympani
Incus
Stapedius
Labyrinth
Stapes
Auditory Canal
Tympanic Membrane
(Ear Drum)
Eustachian Tube
Tympanic cavity

Bones and muscles in the tympanic cavity in the middle ear

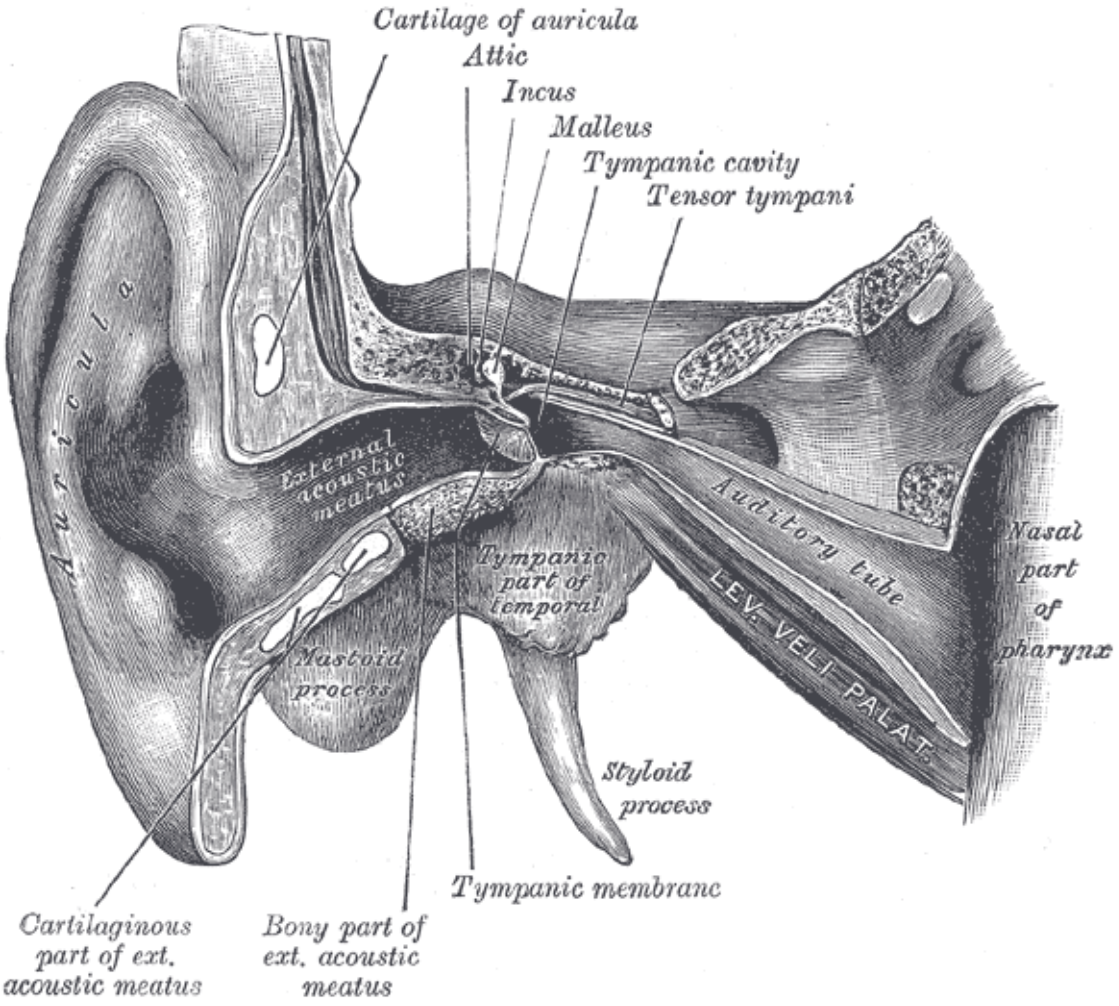
Gray's	*subject #231 1044*
Precursor	1st branchial arch
MeSH	*Incus*

The **incus** or **anvil** is the anvil-shaped small bone or ossicle in the middle ear. It connects the malleus to the stapes. It was first described by Alessandro Achillini of Bologna.

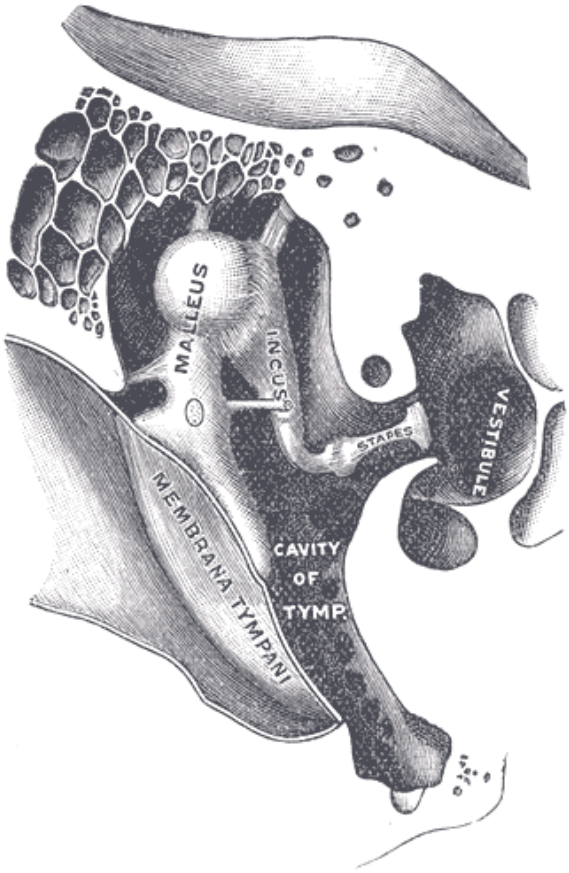
The incus transmits sound vibrations from the malleus to the stapes. The incus only exists in mammals, and is derived from a reptilian upper jaw bone, the quadrate bone. Embryologically it is derived from the first pharyngeal arch along with the rest of the bones of mastication, such as the maxilla and mandible.



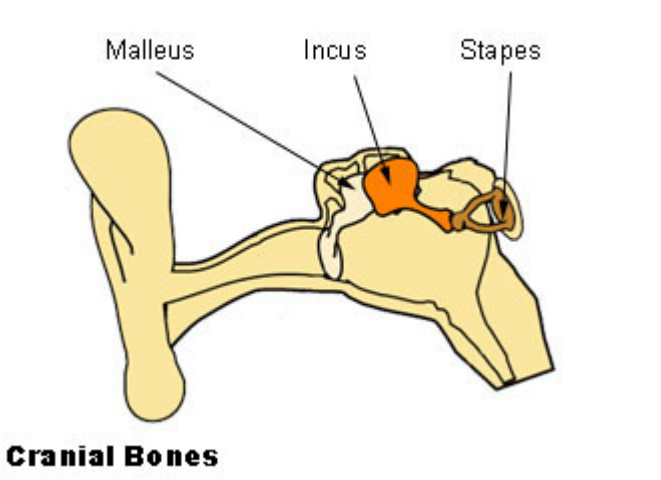
Head and neck of a human embryo eighteen weeks old, with Meckel's cartilage and hyoid bar exposed.



External and middle ear, opened from the front. Right side.



Chain of ossicles and their ligaments, seen from the front in a vertical, transverse section of the tympanum.

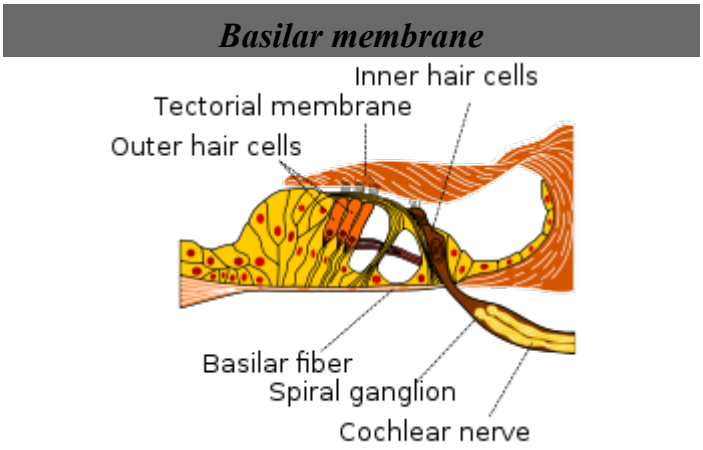


Ossicles

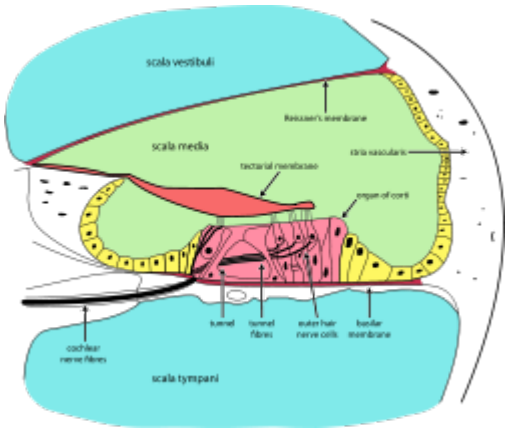
Chapter 19

Basilar Membrane and Ear Canal

Basilar membrane



Section through organ of corti, showing basilar membrane

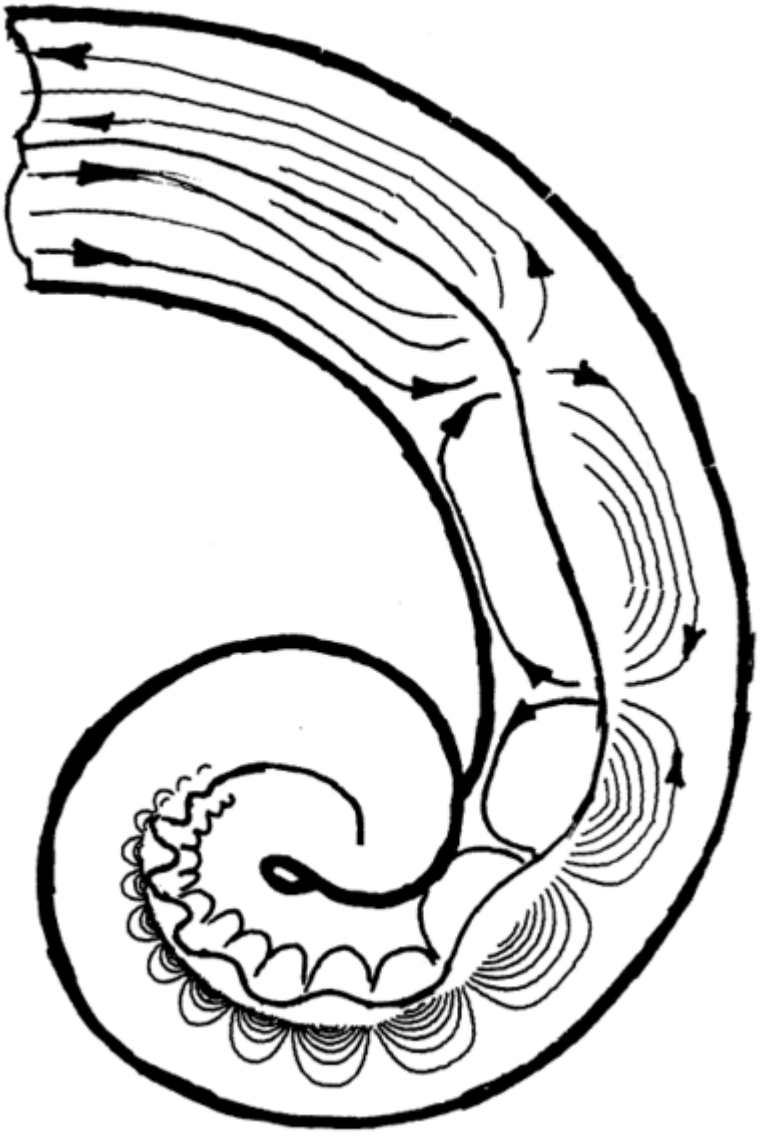


Cross section of the cochlea.

Latin	*lamina basilaris ductus cochlearis*
Gray's	*subject #232 1056*
MeSH	*Basilar+membrane*

The **basilar membrane** within the cochlea of the inner ear is a stiff structural element that separates two liquid-filled tubes that run along the coil of the cochlea, the scala media and the scala tympani.

Function



Sinusoidal drive through the oval window (top) causes a traveling wave of fluid flow (snapshot of fluid streamlines as shown) in the cochlear ducts, with corresponding displacement and velocity waves on the basilar membrane. The wavelength is long compared to the duct height near the base, in what is called the long-wave region, and very short near the place where the displacement and velocity are maximized, just before cutoff, in the short-wave region.

Endolymph/perilymph separation

The fluids in these two tubes, the endolymph and the perilymph are very different chemically, biochemically, and electrically. Therefore they are kept strictly separated. This separation is the main function of Reissner's membrane (between scala vestibuli and scala media), and is erroneously believed to be one of the functions of the basilar membrane in the hearing organ of all land vertebrates. However, the basilar membrane is in fact permeable to perilymph, thus the second border between endolymph and perilymph occurs at the reticular lamina.

A *base* for the sensory cells

The basilar membrane is also the *base* for the sensory cells of hearing, the hair cells or "Stereocilia" of which there are approximately 30,000 (see figure), and hence plays a crucial role in the transfer of sound waves to the brain. This function gave the *basilar* membrane its name, and it is again present in all land vertebrates. Due to its location, the basilar membrane places the hair cells in a position where they are adjacent to both the endolymph and the perilymph, which is a precondition of hair cell function.

Frequency dispersion

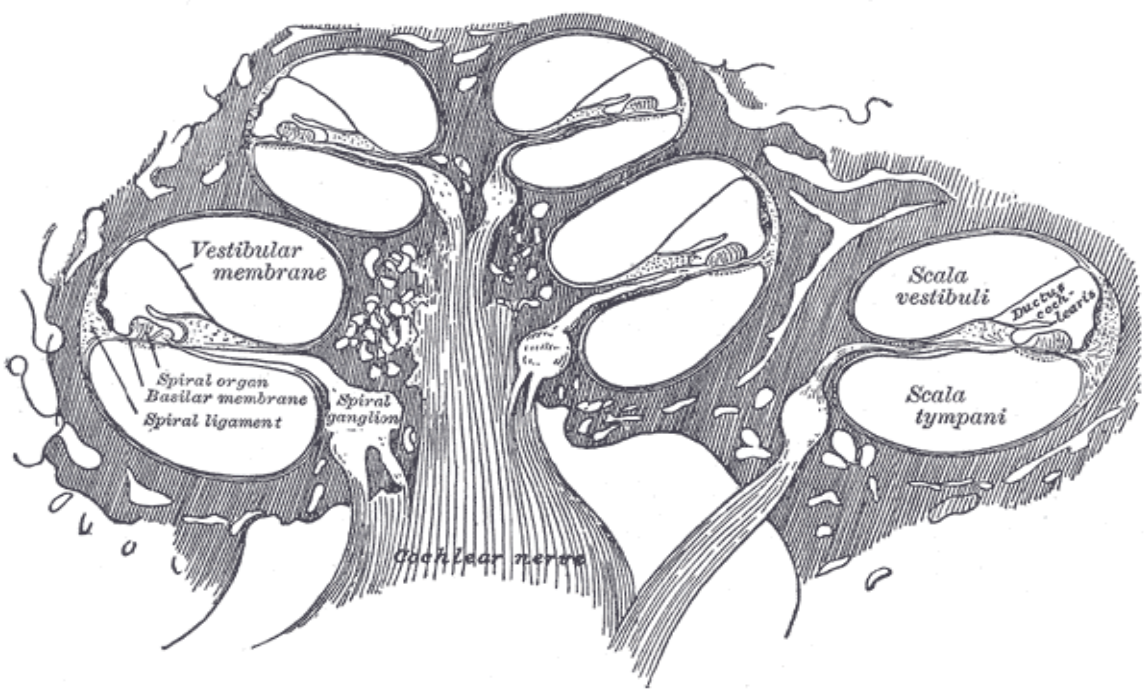
A third, evolutionarily younger, function of the basilar membrane is strongly developed in the cochlea of most mammalian species and weakly developed in some bird species: the dispersion of incoming sound waves to separate frequencies spatially. In brief, the membrane is tapered and it is stiffer at one end than at the other. The dispersion of fluid waves causes sound input of a certain frequency to vibrate some locations of the membrane more than other locations. As shown in experiments by Nobel Prize laureate Georg von Békésy, high frequencies lead to maximum vibrations at the basal end of the cochlear coil, where the membrane is narrow and stiff, and low frequencies lead to maximum vibrations at the apical end of the cochlear coil, where the membrane is wider and more compliant. This "place–frequency map" can be described quantitatively by the Greenwood function and its variants.

Sound-driven vibrations travel as waves along this membrane, along which, in humans, lie about 7,500 inner hair cells spaced in a single row. Each cell is attached to a tiny triangular frame. The 'hairs' are minute processes on the end of the cell, which are very sensitive to movement. When the vibration of the membrane rocks the triangular frames, the hairs on the cells are repeatedly displaced, and that produce streams of corresponding pulses in the nerve fibers, which are transmitted to the auditory pathway. The outer hair cells feed back energy to amplify the traveling wave, by up to 65 dB at some locations.

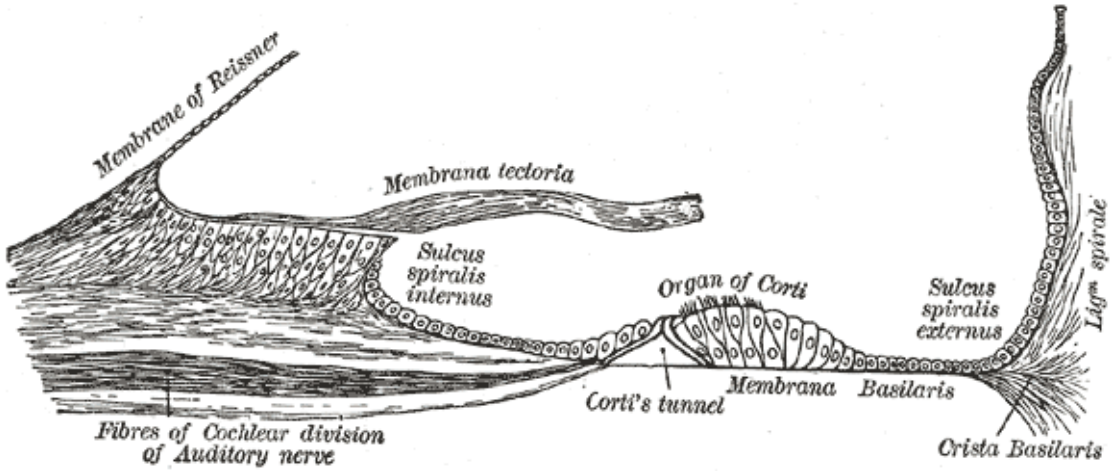
Anatomy

The basilar membrane is a pseudo-resonant structure that, like strings on an instrument, varies in width and stiffness. The "string" of the basilar membrane is not a set of parallel strings, as in a guitar, but a long structure that has different properties (width, stiffness,

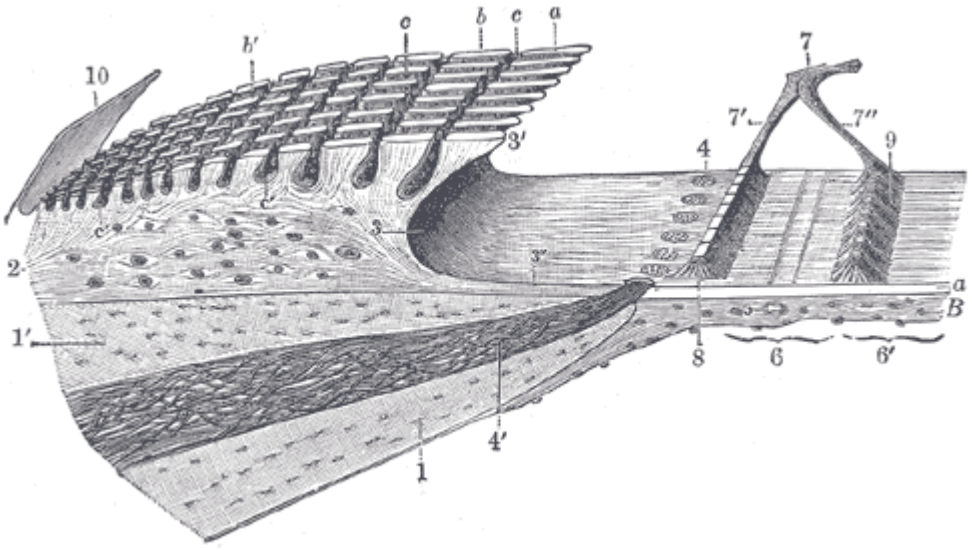
mass, damping, and the dimensions of the ducts that it couples to) at different points along its length. The motion of the basilar membrane is generally described as a traveling wave. The parameters of the membrane at a given point along its length determine its characteristic frequency (CF), the frequency at which it is most sensitive to sound vibrations. The Basilar membrane is widest (0.42–0.65 mm) and least stiff at the apex of the cochlea, and narrowest (0.08–0.16 mm) and most stiff at the base. High-frequency sounds localize near the base of the cochlea (near the round and oval windows), while low-frequency sounds localize near the apex.



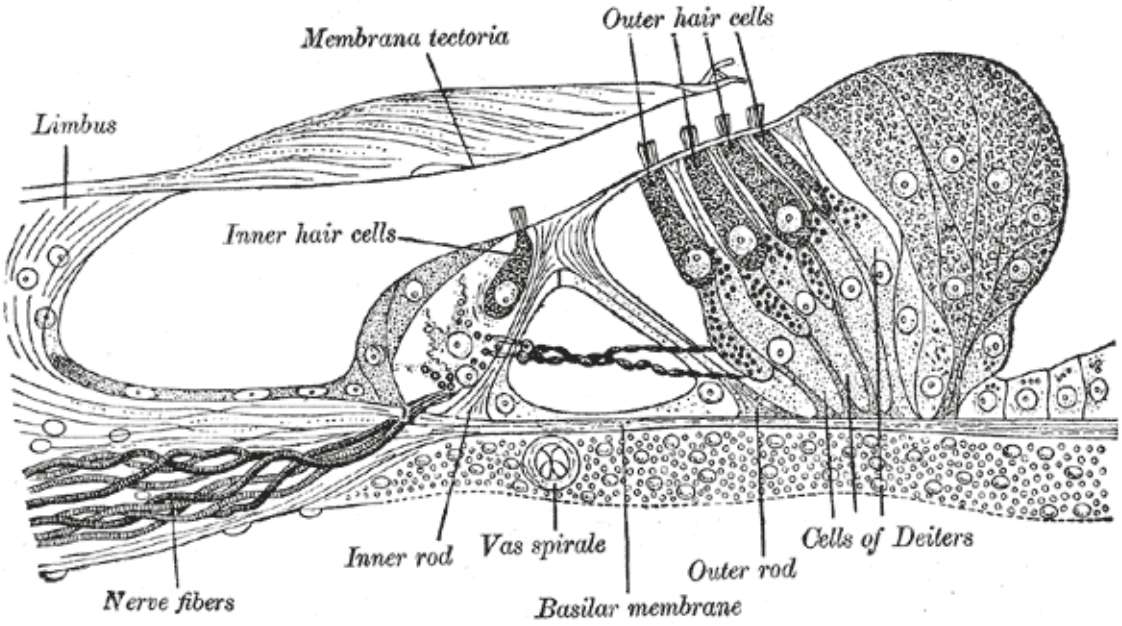
Diagrammatic longitudinal section of the cochlea



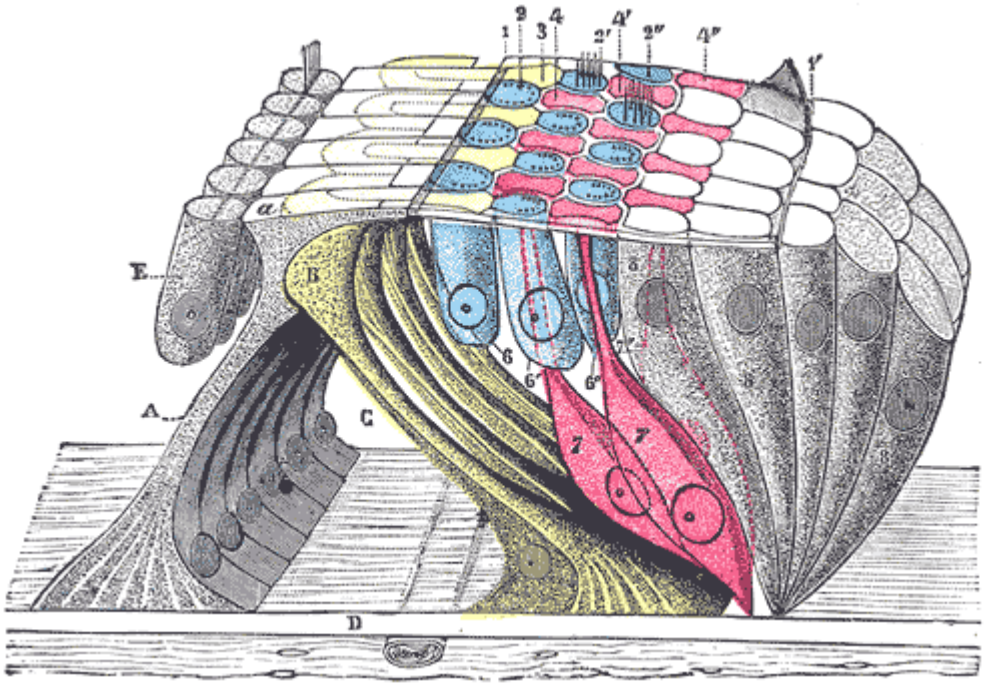
Floor of cochlear duct



Spiral limbus and basilar membrane



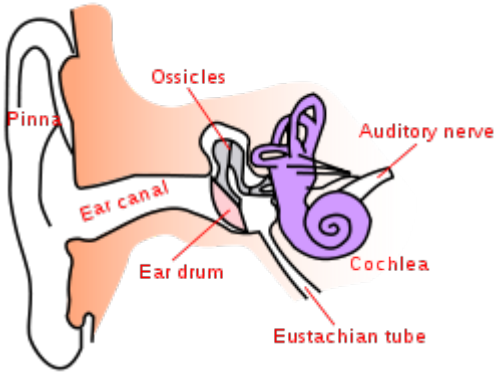
Section through the spiral organ of Corti (magnified)



The reticular lamina and subjacent structures

Ear canal

External acoustic meatus	



Anatomy of the human ear.

Latin	*meatus acusticus externus*
Gray's	*subject #229 1036*
Artery	anterior part: superficial temporal artery

	posterior part: posterior auricular artery
Vein	superficial temporal veins, external jugular vein, pterygoid plexus
Nerve	auriculotemporal nerve, great auricular nerve, auricular branch of vagus nerve
Lymph	superficial cervical lymph nodes, deep cervical lymph nodes
Precursor	groove (cleft) of the first branchial arch.

The **ear canal** (**external auditory meatus**, **external acoustic meatus**) (Latin: *meatus acusticus externus*) , is a tube running from the outer ear to the middle ear. The human ear canal extends from the pinna to the eardrum and is about 35 mm in length and 5 to 10 mm in diameter.

Structure

The human ear canal is divided into two parts. The fibrocartilaginous part forms the outer third of the canal, Its anterior and lower wall are cartilaginous, whereas its superior and back wall are fibrous. The cartilage is the continuation of the cartilage framework of pinna. The bony part forms the inner two thirds. The bony part is much shorter in children and is only a ring (*annulus tympanicus*) in the newborn.

Size and shape of the canal vary among individuals. The canal is approximately 35 mm long and 5 to 10 mm in diameter. It has a sigmoid form and runs from behind and above downward and forward. On the cross-section, it is of oval shape. These are important factors to consider when fitting earplugs.

Disorders

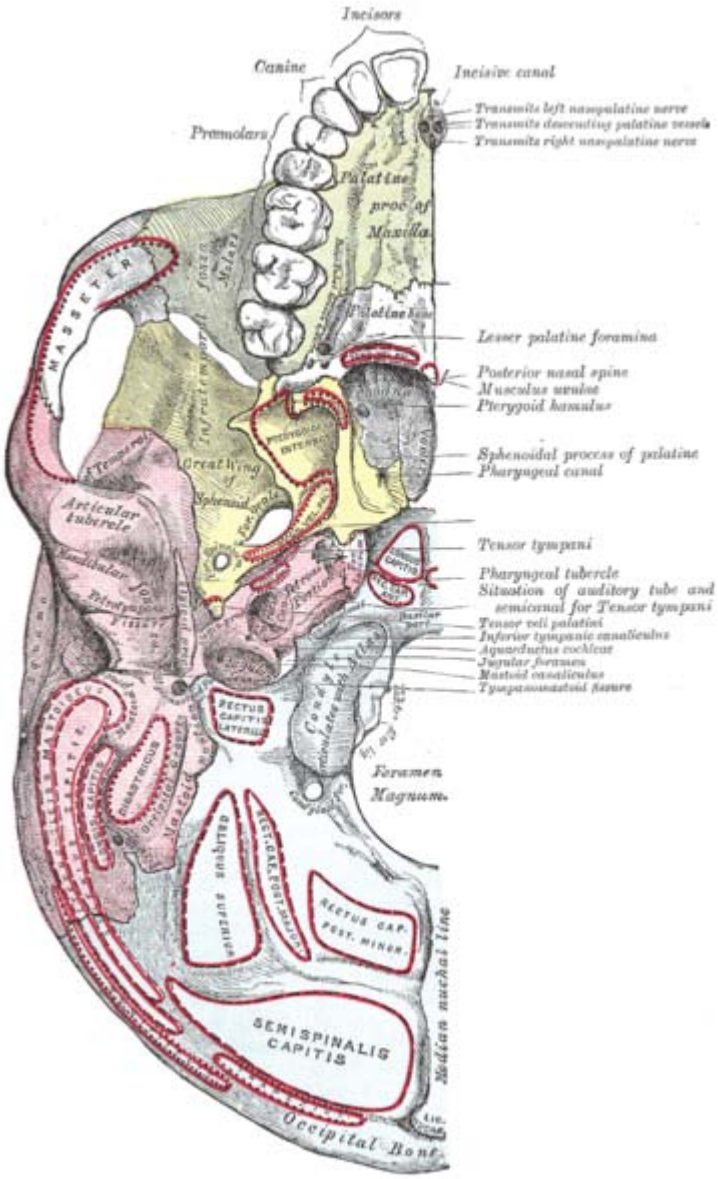
The ear canal, because of its relative exposure to the outside world, is a common victim of diseases and other disorders. Some disorders include:

- Atresia of the ear canal
- Otitis externa (swimmer's ear), bacteria-caused inflammation of the ear canal
- Contact dermatitis of the ear canal
- Ear fungus
- Ear myiasis, an extremely rare infestation of maggots
- Bone exposure, caused by the wearing away of skin in the canal
- Granuloma, a scar usually caused by tympanostomy tubes
- Stenosis, a gradual closing of the canal
- Foreign body in ear
- Cholesteatoma

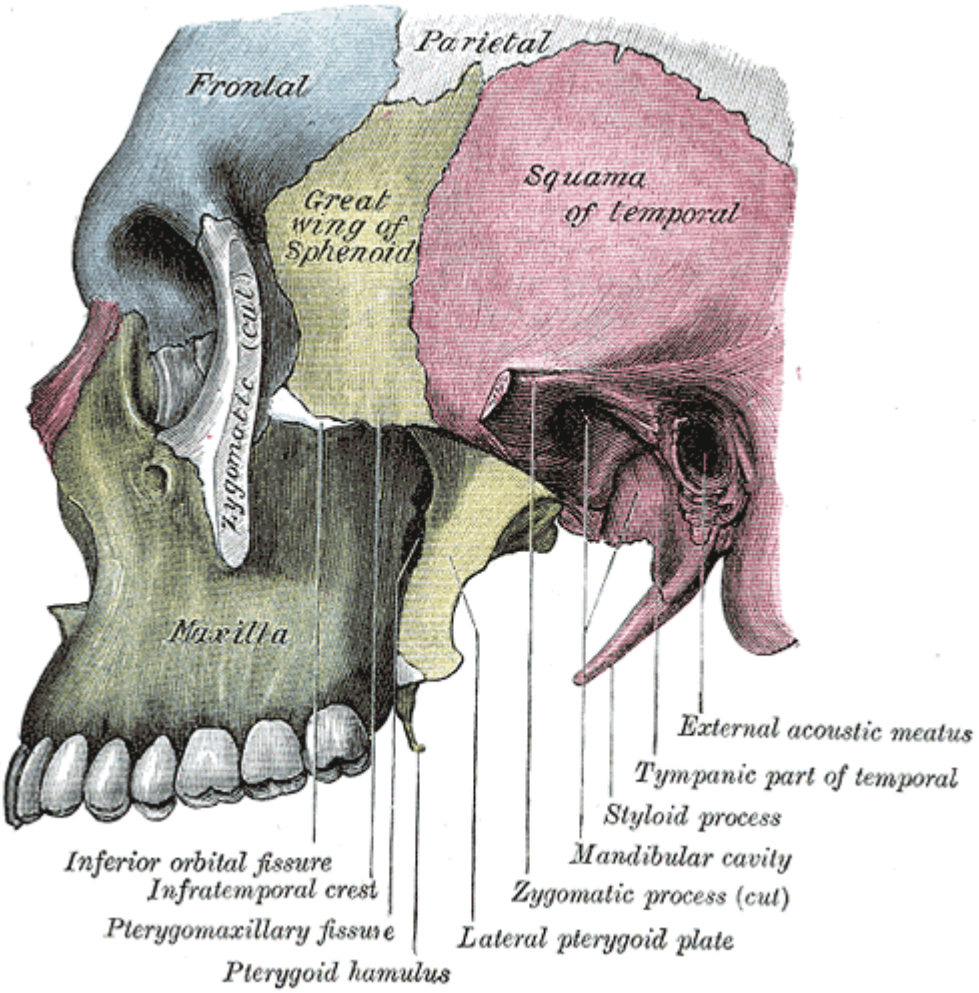
- Ear mites in animals.

Earwax

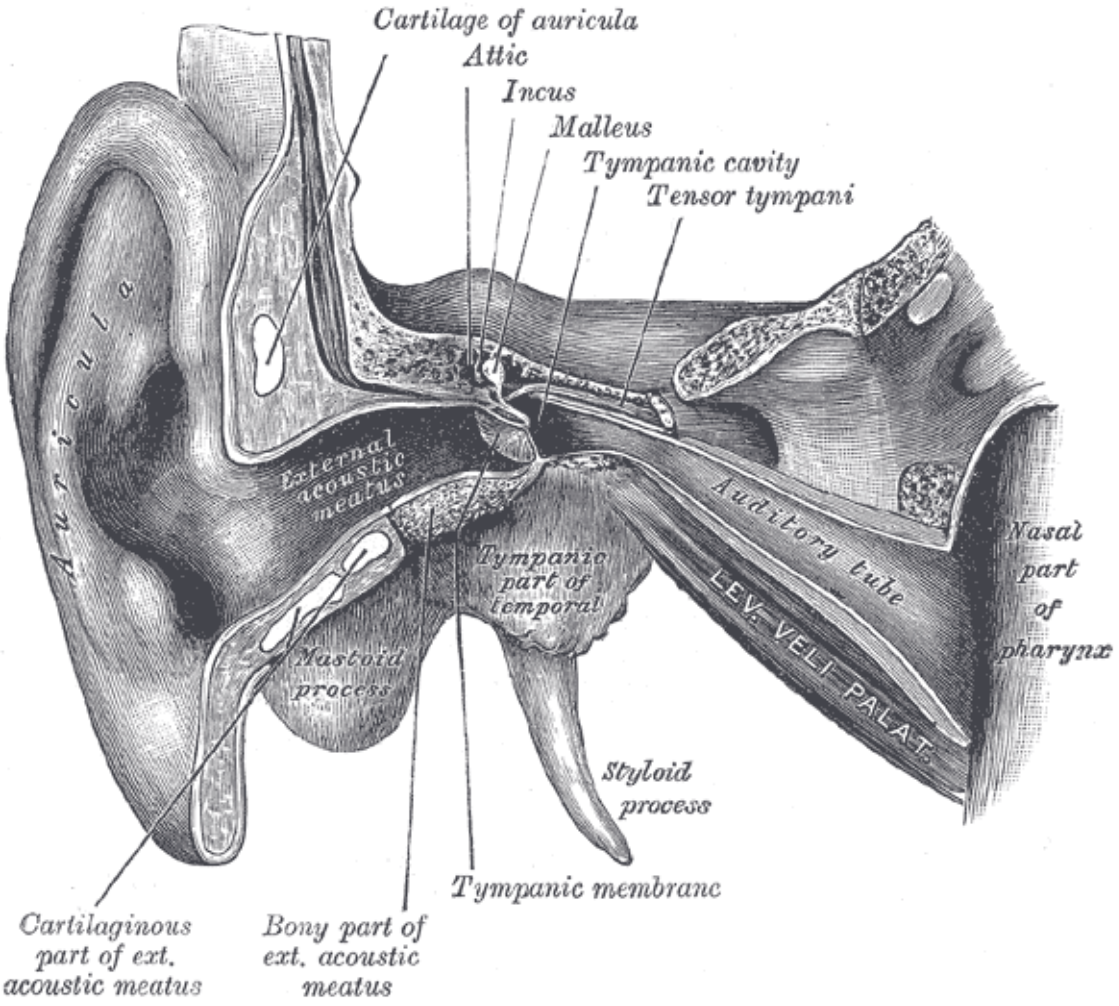
Earwax, also known as cerumen, is a yellowish, waxy substance secreted in the ear canals. It plays an important role in the human ear canal, assisting in cleaning and lubrication, and also provides some protection from bacteria, fungi, and insects. Excess or impacted cerumen can press against the eardrum and/or occlude the external auditory canal and impair hearing.



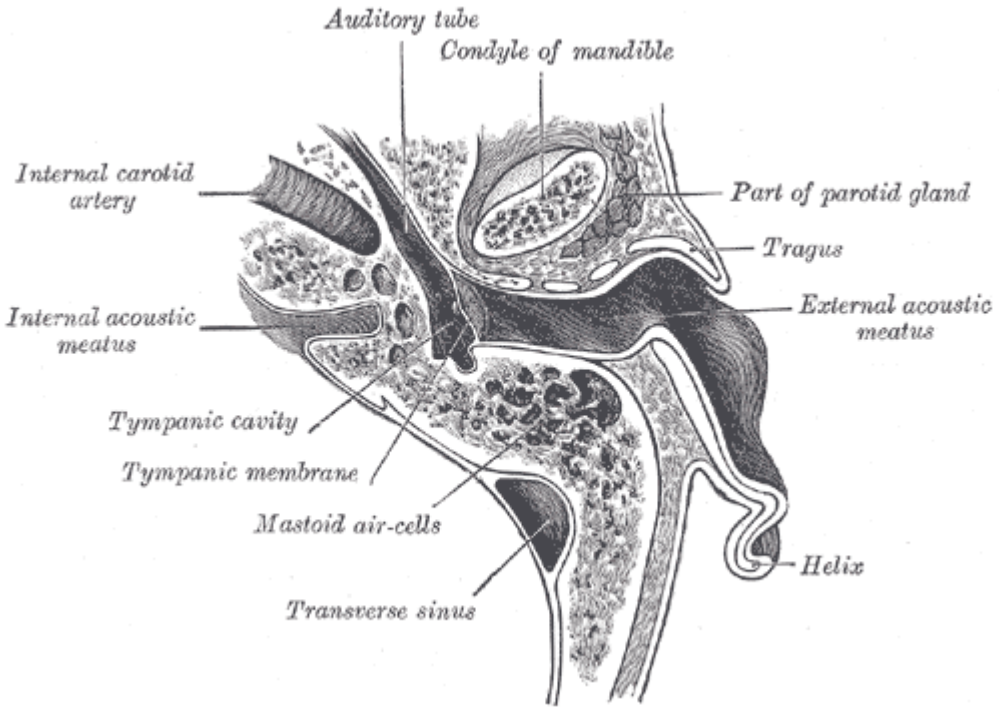
Base of skull. Inferior surface



Left infratemporal fossa



External and middle ear, opened from the front. Right side.



Horizontal section through left ear; upper half of section

Chapter 20

Earlobe and Endolymph

Earlobe

Earlobe

Latin *lobulus auriculae (singular), lobuli auricularum (plural)*

Gray's *subject #229 1034*

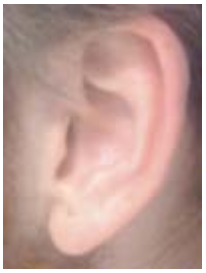
System Auditory system

The **earlobe** is composed of tough areolar and adipose (fatty) connective tissues, lacking the firmness and elasticity of the rest of the pinna. Since the earlobe does not contain cartilage it has a large blood supply and may help to warm the ears and maintain balance. However earlobes are not generally considered to have any major biological function.

Size and shape

Earlobes average about 2 cm long, and elongate slightly with age. Whether the earlobe is free or attached is a classic example of a simple genetic dominance relationship; freely hanging earlobes are the dominant allele and attached earlobes are recessive. Therefore, a person whose genes contain one allele for free earlobes and one for attached lobes will display the freely hanging lobe trait. It is a common misconception that this implies a precise 3-to-1 ratio between free and attached lobes in the human population. Such a ratio

would require that the allele frequency for free lobes were precisely 50%, which there is no reason to assume. The frequency of attached earlobes among Japanese subjects is 67.1%, and in Chinese it is 64.3%.



A free (not attached) earlobe

Earlobes are normally smooth, but occasionally exhibit creases. Creased earlobes are associated with genetic disorders, including Beckwith-Wiedemann syndrome. Earlobe creases are also associated with an increased risk of heart attack and coronary heart disease; however, since earlobes become more creased with age, and older people are more likely to experience heart disease than younger people, age may account for the findings linking heart attack to earlobe creases. however, this correlation proved to be untrue in persons of Asian descent (Chinese and Japanese) and Native American Indians.

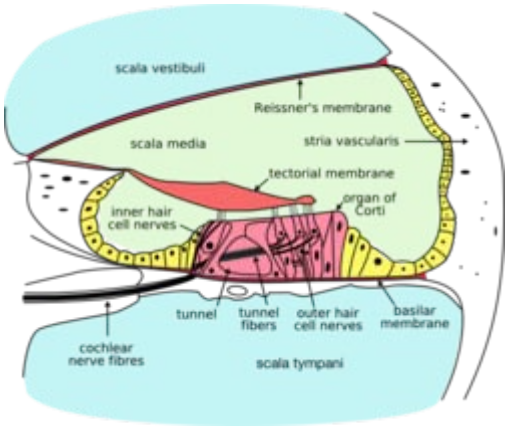
The earlobe contains many nerve endings, and for some people is an erogenous zone.

Earlobe piercing

Around the world and throughout human history, the earlobe is the most common location for a body piercing. It is common to tear the earlobe with the weight of very heavy earring, or a traumatic pull of an earring. Some cultures practice earlobe stretching, using piercing ornaments to stretch and enlarge the earlobes. Sailors used to believe that piercing one earlobe gave greater acuity in the opposite ear.

Endolymph

Endolymph



Cross-section of cochlea. (Endolymph is located in the scala media - the light green region at the middle of the diagram.)

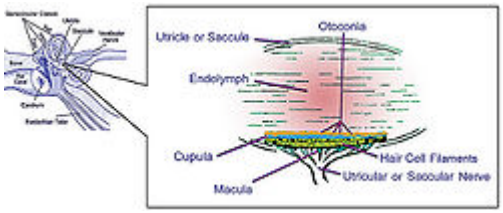


illustration of otolith organs showing detail of utricle, ococonia, endolymph, cupula, macula, hair cell filaments, and saccular nerve

Latin	*endolympha*
Gray's	*subject #232 1051*
MeSH	*Endolymph*

Endolymph is the fluid contained in the membranous labyrinth of the inner ear. It is also called *Scarpa's fluid*, after Antonio Scarpa.

Composition

The main cation of this unique extracellular fluid is potassium, which is secreted from the stria vascularis. The high potassium content of the endolymph means that potassium, not sodium, is carried as the depolarizing electrical current in the hair cells. This is known as the mechano-electric transduction (MET) current.

Endolymph has a high positive charge (from 80-120 mV in the cochlea), mainly due to the presence of positively-charged amino acids. It is mainly this electrical gradient that

allows potassium ions to flow into the negatively-charged hair cells during mechanical stimulation of the hair bundle. Because the hair cells are at a negative potential of about -50 mV, the electrical gradient from endolymph to hair cell is on the order of 150 mV, which is the largest electrical potential found in the body.

Contribution to Hearing

Fluid waves occur in the endolymph in the various parts of the membranous labyrinth in response to fluid waves in the perilymph.

- Cochlear duct: fluid waves in the endolymph of the cochlear duct stimulate the receptor cells, which in turn translate their movement into nerve impulses that the brain percceives as sound.
- Semicircular canals: angular acceleration of the endolymph in the semicircular canals stimulate the vestibular receptors of the endolymph. The semicircular canas of both inner ears act in concert to coordinate balance.

Pathology

Disruption of the endolymph due to jerky movements (like spinning around or driving over bumps while riding in a car) can cause motion sickness. A condition where the volume of the endolymph is greatly enlarged is called endolymphatic hydrops and has been linked to Ménière's disease.

Perilymph versus Endolymph

The inner ear has two parts: the bony labyrinth and the membranous labyrinth. The membranous labyrinth is contained within the bony labyrinth, and within the membranous labyrinth is a fluid called endolymph. Between the outer wall of the membranous labyrinth and the wall of the bony labyrinth is the location of perilymph.

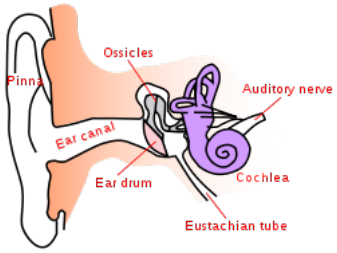
Perilymph and endolymph have unique ionic compositions suited to their functions in regulating electrochemical impulses of hair cells. The electric potential of endolymph is ~80-90 mV more positive than perilymph due to a higher concentration of K compared to Na.

Chapter 21

Eustachian Tube and Malleus

Eustachian tube

Eustachian Tube



Anatomy of the human ear.

Malleus

Tensor Tympani

Incus

Stapedius

Labyrinth

Stapes

Auditory Canal

Tympanic Membrane

(Ear Drum)

Eustachian Tube

Tympanic cavity

The middle ear

Latin	*tuba auditiva; tuba auditoria; tuba auditivea*
Gray's	*subject #230 1042*
Precursor	first branchial pouch
MeSH	*Eustachian+tube*

The **Eustachian tube** (or **auditory tube** or **pharyngotympanic tube**) is a tube that links the pharynx to the middle ear. It is a part of the middle ear. In adults the Eustachian tube is approximately 35 mm long. It is named after the sixteenth century anatomist Eustachius. Some modern medical books call this the **pharyngotympanic tube**.

Anatomy

The Eustachian tube extends from the anterior wall of the middle ear to the lateral wall of the nasopharynx, approximately at the level of the inferior nasal concha. A portion of the tube (~1/3) proximal to the middle ear is made of bone; the rest is composed of cartilage and raises a tubal elevation, the torus tubarius, in the nasopharynx where it opens.

In the equids (horses) and some rodent-like species such as the desert hyrax, an evagination of the eustachian tube is known as the guttural pouch and is divided into medial and lateral compartments by the stylohyoid bone of the hyoid apparatus. This is of great importance in equine medicine as the pouches are prone to infections, and due to their intimate relationship to the cranial nerves (VII, IX, X, XI) and the internal and external carotid artery, various syndromes may arise relating to which is damaged. Epistaxis (nosebleed) is a very common presentation to veterinary surgeons and this may often be fatal unless a balloon catheter can be placed in time to suppress bleeding.

Embryologic development

The Eustachian tube is derived from the first pharyngeal pouch, which during embryogenesis forms the tubotympanic recess. The distal part of the tubotympanic sulcus gives rise to the tympanic cavity, while the proximal tubular structure becomes the Eustachian tube.

Muscles

There are four muscles associated with the function of the Eustachian tube:

- Levator veli palatini (innervated by the vagus nerve)
- Salpingopharyngeus (innervated by the vagus nerve)
- Tensor tympani (innervated by the mandibular nerve of CN V)
- Tensor veli palatini (innervated by the mandibular nerve of CN V)

Functions

Pressure equalization

Normally the human Eustachian tube is closed, but it can open to let a small amount of air through to prevent damage by equalizing pressure between the middle ear and the atmosphere. Pressure differences cause temporary conductive hearing loss by decreased motion of the tympanic membrane and ossicles of the ear. Various methods of ear clearing such as yawning, swallowing, chewing gum, or performing the valsalva maneuver may be used intentionally to open the tube and equalize pressures. When this happens, humans hear a small popping sound, an event familiar to aircraft passengers, scuba divers or drivers in mountainous regions.

Mucus drainage

The Eustachian tube also drains mucus from the middle ear. Upper airway infections or allergies can cause the Eustachian tube to become swollen, trapping bacteria and causing ear infections. This swelling can be reduced through the use of pseudoephedrine. Earaches are more common in children because the tube is more horizontal, shorter and has a smaller floppier opening, making the movement of fluid more difficult.

Disorders

Otitis media, or inflammation of the middle ear, commonly affects the Eustachian tube. Children under 7 are more susceptible to this condition because the Eustachian tube is shorter and at more of a horizontal angle than in the adult ear.

Barotitis, a form of barotrauma, may occur when there is a substantial difference in air or water pressure between the outer inner and the inner ear, for example in a rapid ascent while scuba diving, or a sudden decompression of an aircraft at high altitude.

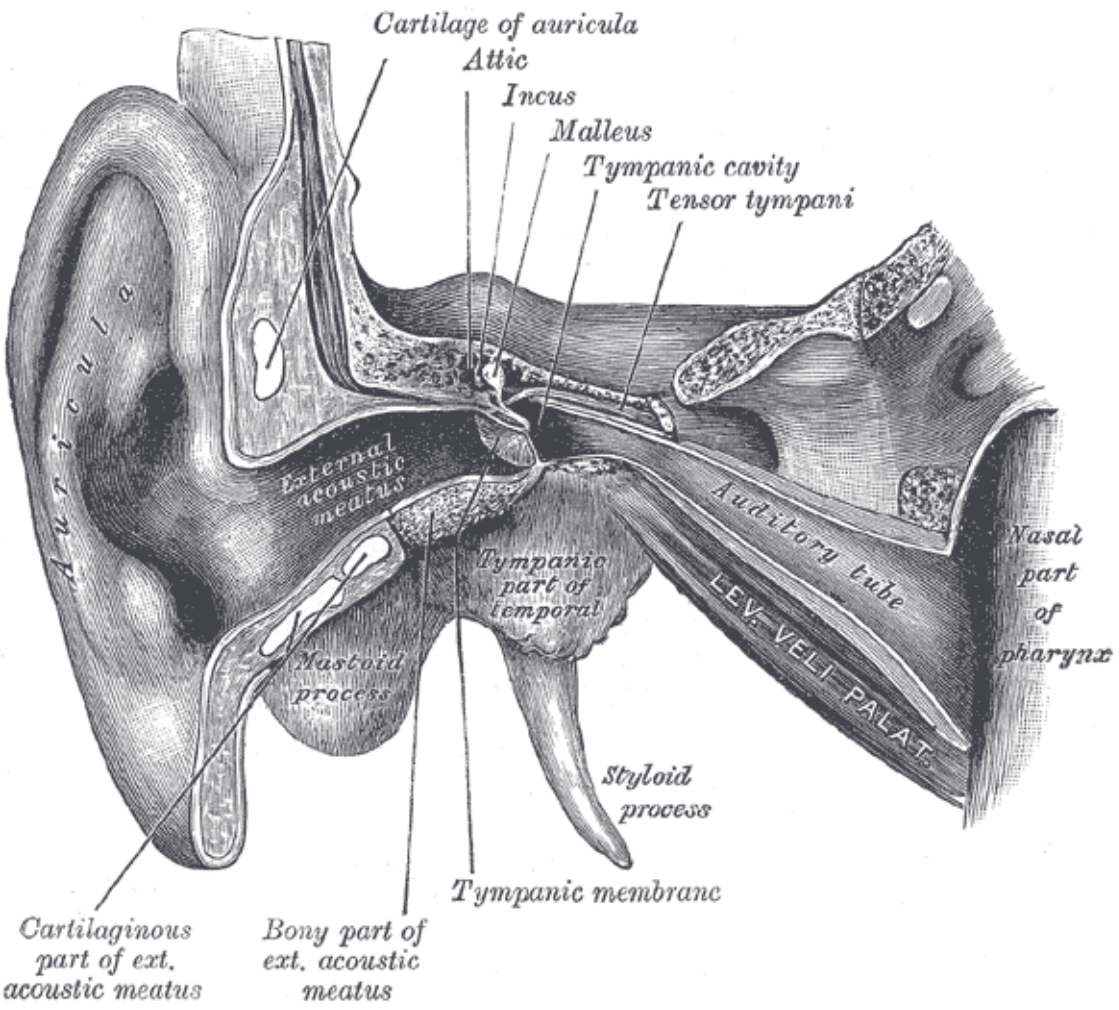
Some people are born with a dysfunctional Eustachian tube, which is much slimmer than the usual human Eustachian tube. This may be genetic, but it has also been suggested to be a condition in which the patient did not fully recover from the effects of pressure on the middle ear during birth (**retained birth compression**). This disorder may result in a large amount of mucus accumulating in the middle ear, often impairing hearing to a

degree. This condition is known as otitis media with effusion, and may result in the mucus becoming very thick and glue-like, a condition known as **glue ear**.

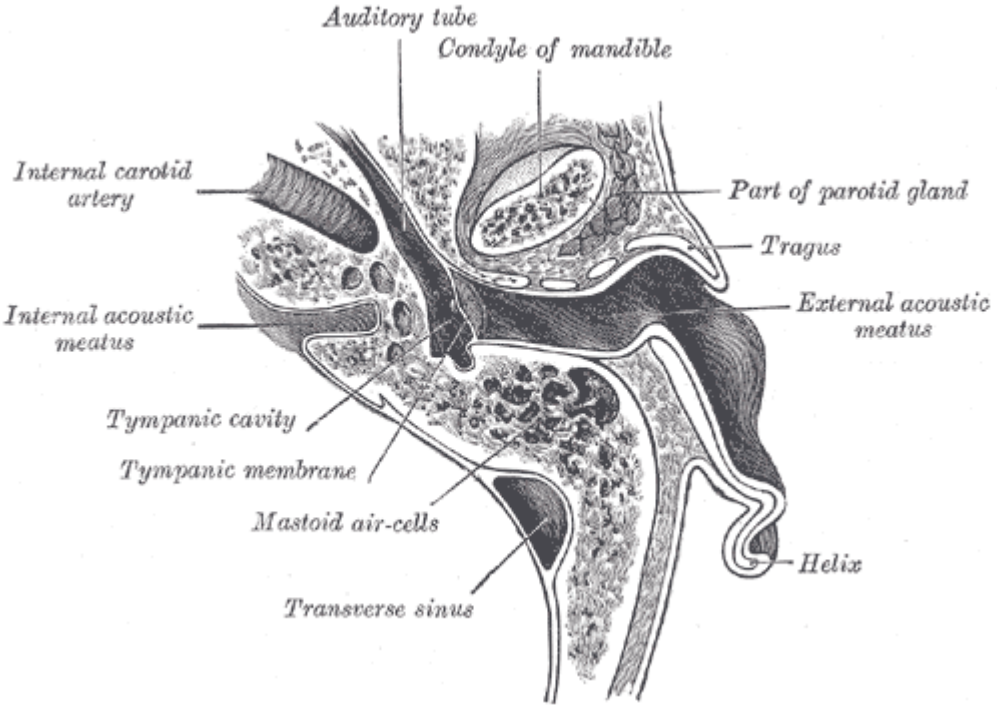
A patulous Eustachian tube is a rare condition, in which the Eustachian tube remains intermittently open, causing an echoing sound of the person's own heartbeat, breathing, and speech. This may be temporarily relieved by moving into a position where the head is upside down.

Smoking can also cause damage to the cilia that protect the Eustachian tube from mucus, which can result in the clogging of the tube and a buildup of bacteria in the ear, leading to a middle ear infection in some cases.

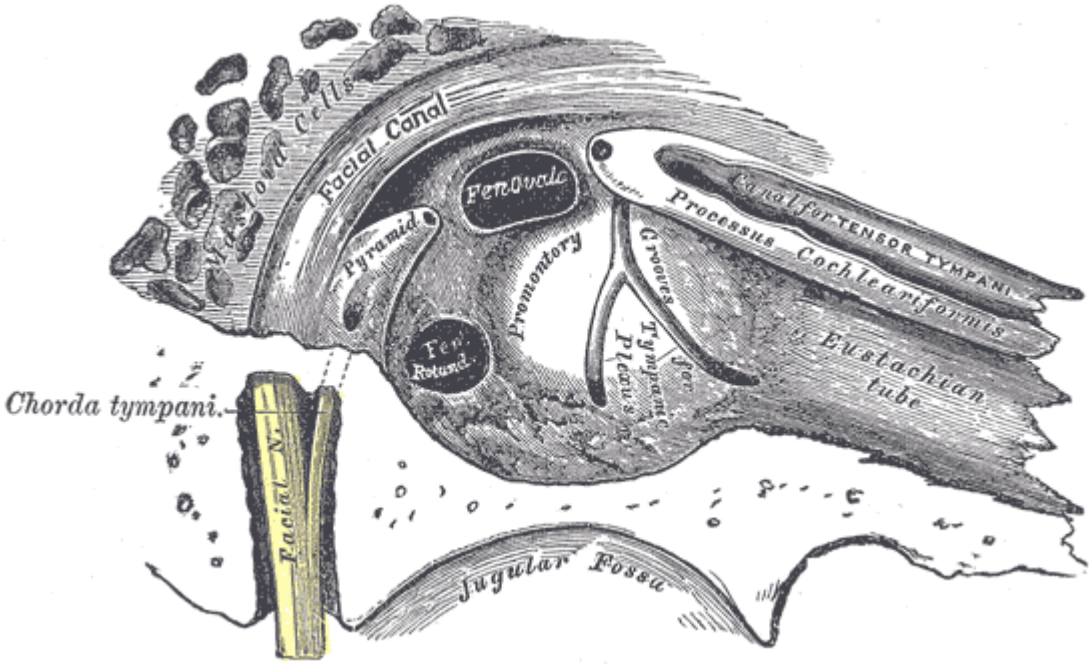
Eustachian tube dysfunction can be caused by recurring and chronic cases of sinus infection. This results from excessive mucus production which causes obstruction to the openings of the Eustachian tubes.



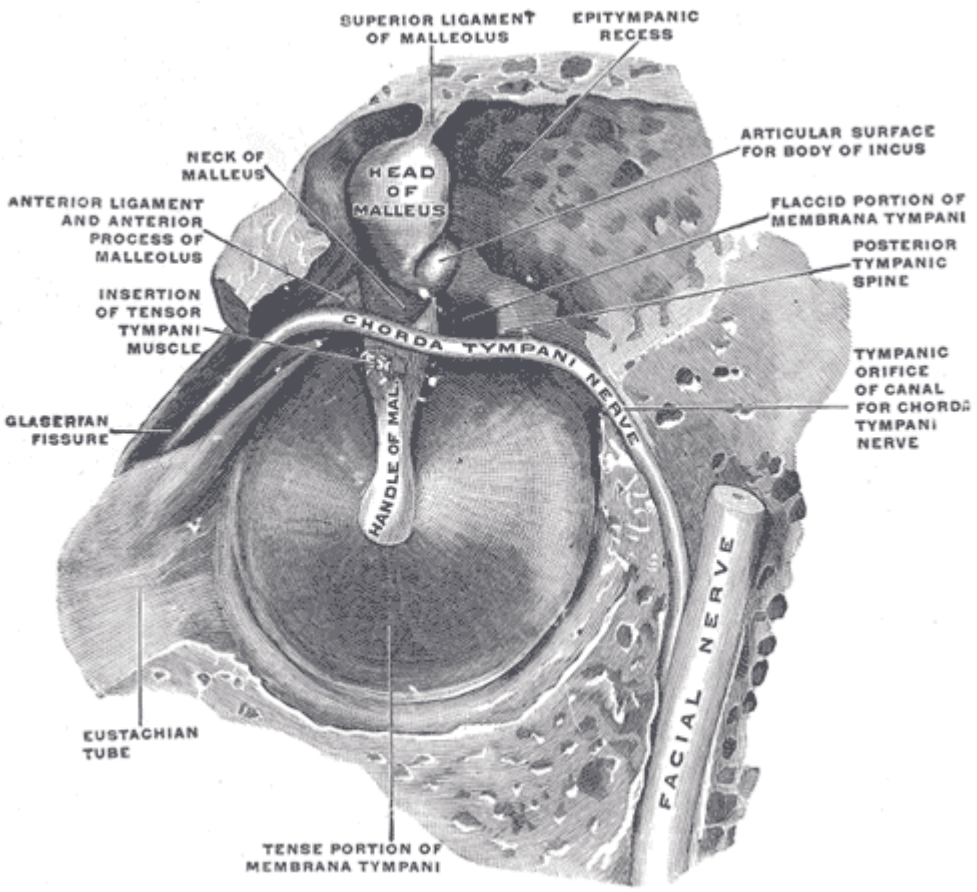
External and middle ear, opened from the front; right side



Horizontal section through left ear; upper half of section



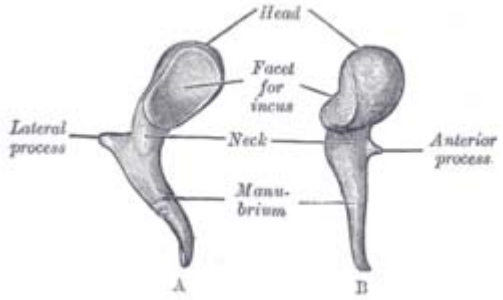
View of the inner wall of the tympanum



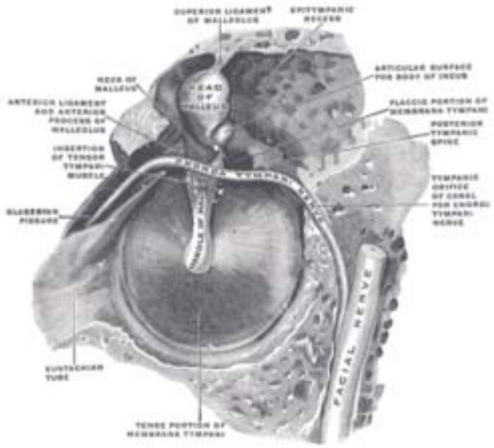
The right membrana tympani with the hammer and the chorda tympani, viewed from within, from behind, and from above

Malleus

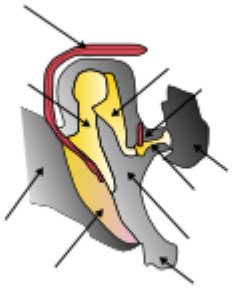
Bone: Malleus



Left malleus. A. From behind. B. From within.



The right membrana tympani with the hammer and the chorda tympani, viewed from within, from behind, and from above. (Malleus visible at center.)



Malleus
Tensor Tympani
Incus
Stapedius
Labyrinth
Stapes
Auditory Canal
Tympanic Membrane
(Ear Drum)
Eustachian Tube
Tympanic cavity

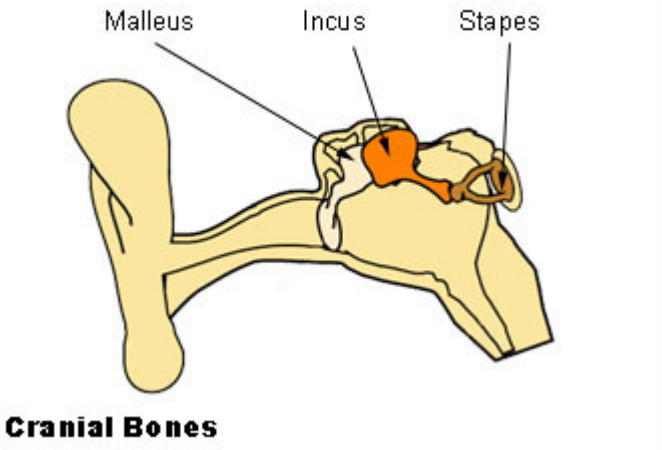
Bones and muscles in the tympanic cavity in the middle ear

Latin	*Malleus*
Gray's	*subject #231 1044*
Precursor	1st branchial arch
MeSH	*Malleus*

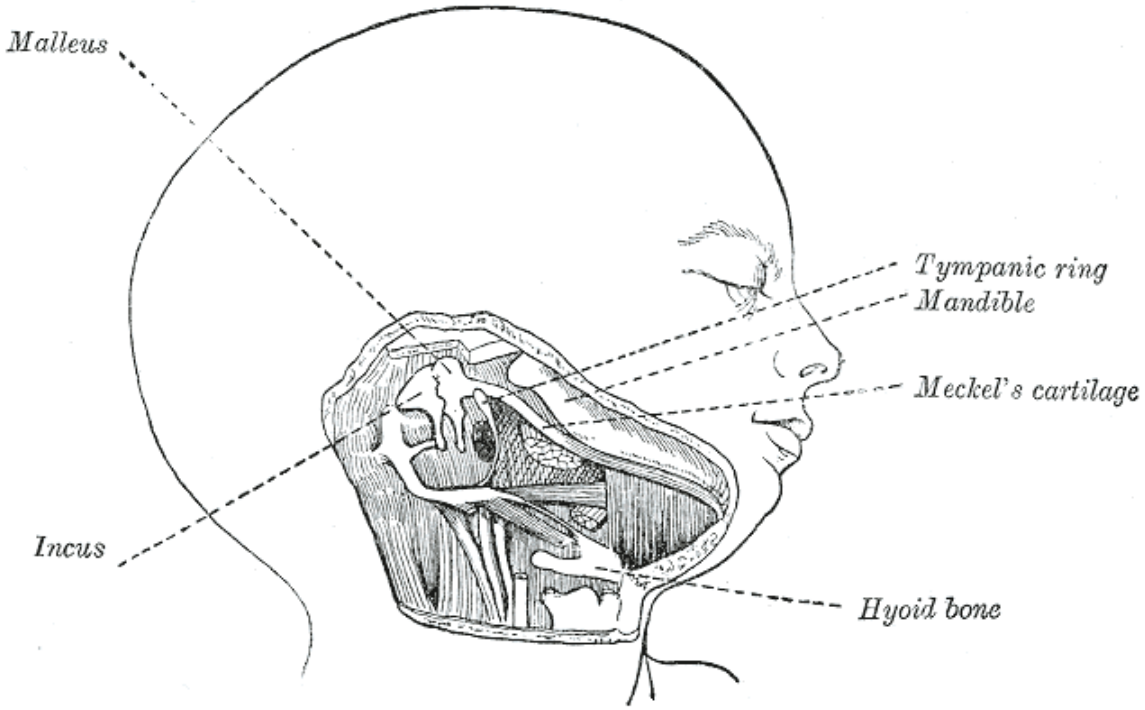
The **malleus** or **hammer** is a hammer-shaped small bone or ossicle of the middle ear which connects with the incus and is attached to the inner surface of the eardrum. The word is Latin for *hammer*.

It transmits the sound vibrations from the eardrum to the *incus*.

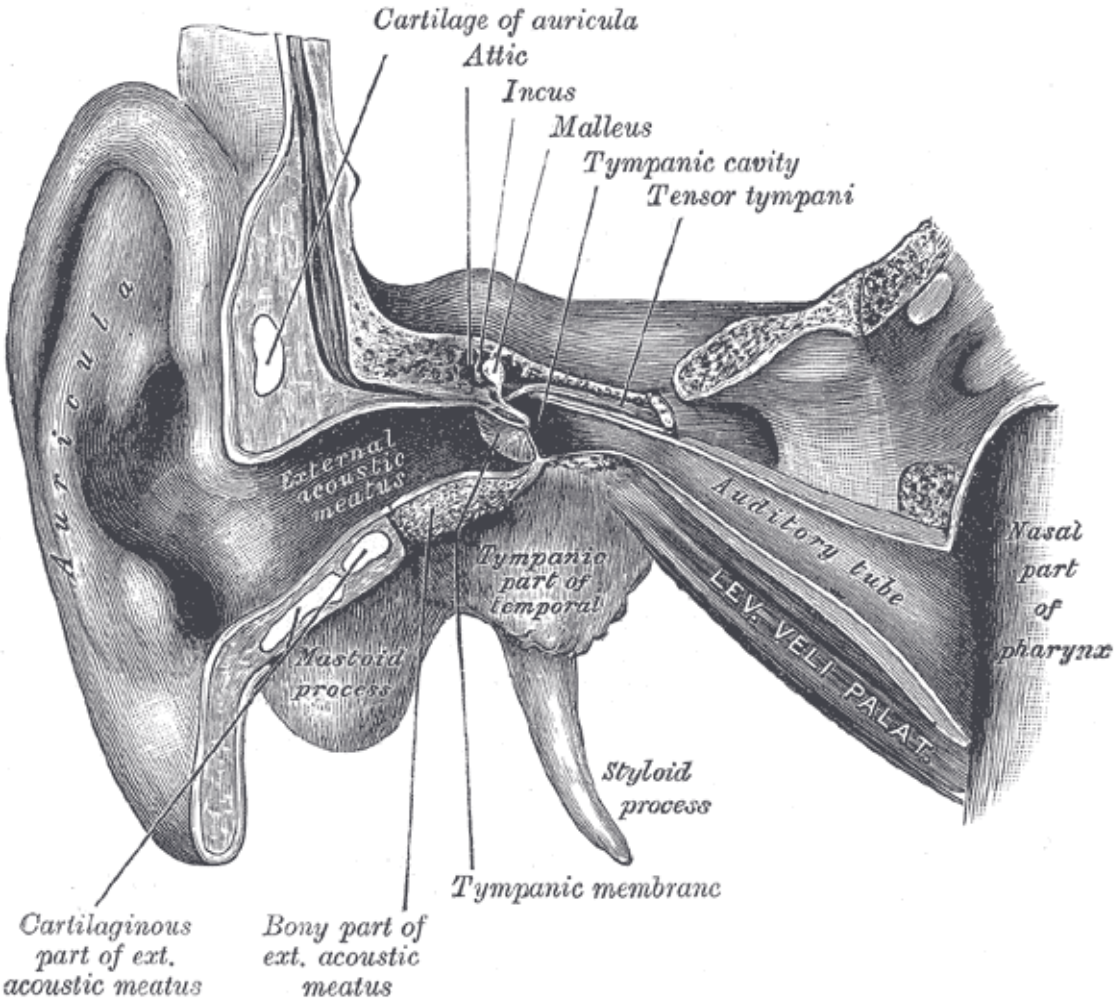
The malleus is unique to mammals, and evolved from a lower jaw bone in basal amniotes called the articular, which still forms part of the jaw joint in reptiles and birds. Embryologically it is derived from the first pharyngeal arch along with the rest of the bones of mastication, such as the maxilla and mandible.



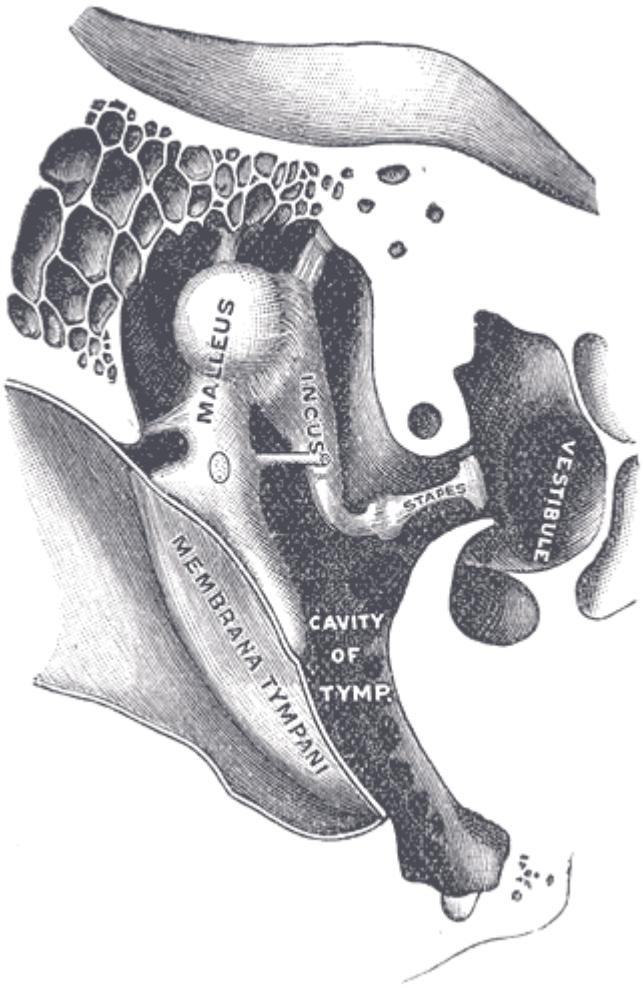
Ossicles



Head and neck of a human embryo eighteen weeks old, with Meckel's cartilage and hyoid bone exposed.



External and middle ear, opened from the front. Right side.



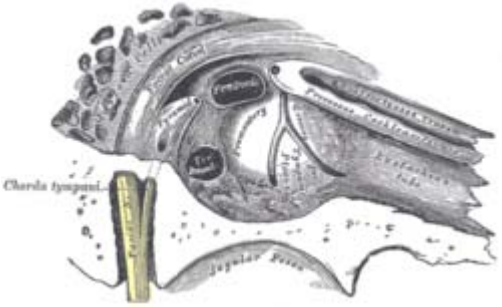
Chain of ossicles and their ligaments, seen from the front in a vertical, transverse section of the tympanum.

Chapter 22

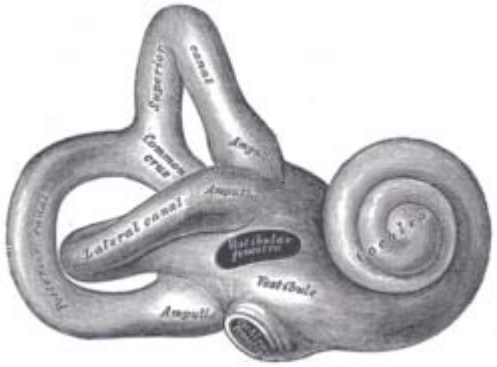
Oval Window and Round Window

Oval window

Oval window



View of the inner wall of the tympanum. (label is 'fen. oval.' - black circle near top.)



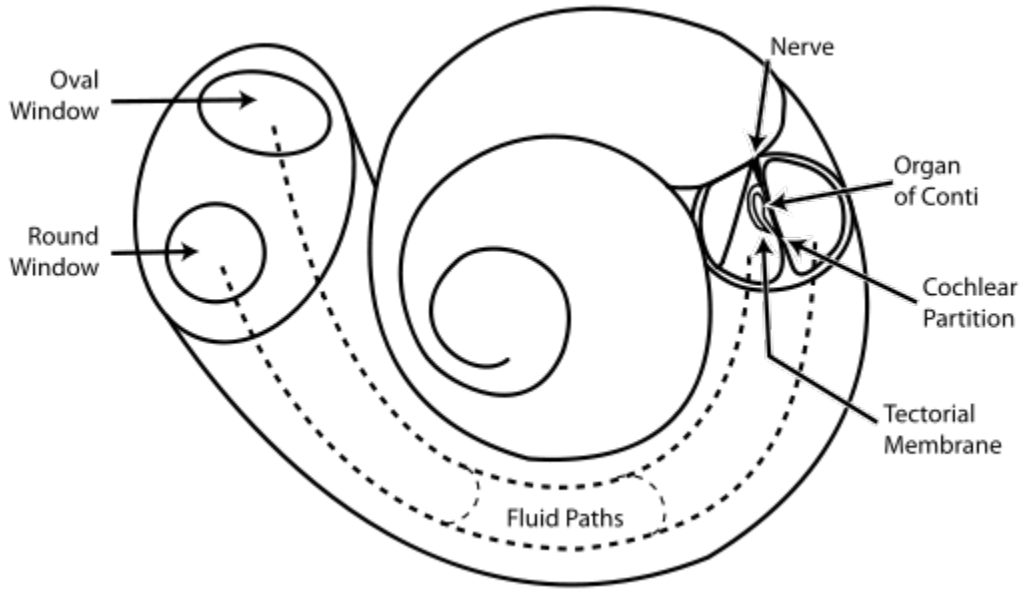
Right osseous labyrinth. Lateral view. (label is 'vestibular fenestra' - black circle near center.)

Latin	*fenestra vestibuli, fenestra ovalis*
Gray's	*subject #230 1040*
MeSH	*Oval+Window*
Dorlands/Elsevier	*Oval window*

The **oval window** (or **vestibular window**) is a membrane-covered opening which leads from the middle ear to the vestibule of the inner ear.

Vibrations that come into contact with the tympanic membrane travel through the three ossicles and into the inner ear. The oval window is the intersection of the middle ear with the inner ear, and is directly contacted by the stapes; by the time vibrations reach the oval window, they have been amplified over twenty times from what they were when they contacted the tympanic membrane, a testament to the amplifying power of the middle ear.

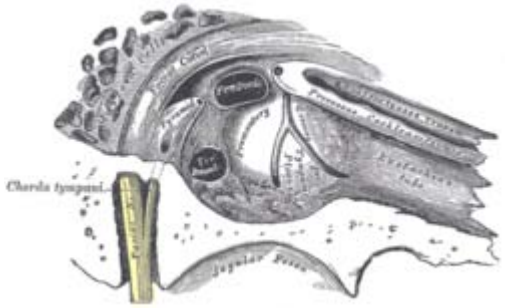
It is a reniform (kidney-shaped) opening leading from the tympanic cavity into the vestibule of the internal ear; its long diameter is horizontal, and its convex border is upward. In the recent state it is occupied by the base of the stapes, the circumference of which is fixed by the annular ligament to the margin of the foramen.



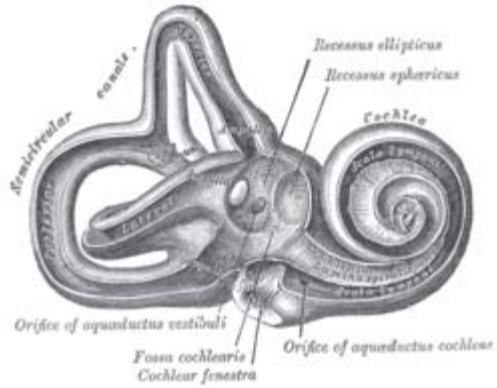
Cochlea

Round window

Round window



View of the inner wall of the tympanum. (label is 'fen. rotund.' - lower of two black circles.)



Interior of right osseous labyrinth. (label is 'cochlear fenestra', at bottom center.)

Latin	*fenestra cochleae, fenestra rotunda*
Gray's	*subject #232 1051*
MeSH	*Round+Window*

The **round window** is one of the two openings into the inner ear. It is closed off from the middle ear by the round window membrane, which vibrates with opposite phase to vibrations entering the inner ear through the oval window. It allows fluid in the cochlea to move, which in turn ensures that hair cells of the basilar membrane will be stimulated and that audition will occur.

Anatomy

The round window is situated below and a little behind the oval window, from which it is separated by a rounded elevation, the promontory.

It is placed at the bottom of a funnel-shaped depression (the round window niche) and, in the macerated bone, opens into the cochlea of the internal ear; in the fresh state it is closed by a membrane, the secondary tympanic membrane or round window membrane, which is a complex saddle point shape. The visible central portion is concave toward the tympanic cavity and convex toward the cochlea but towards the edges, where it is hidden in the round window niche, it curves the other way.

This membrane consists of three layers:

- an external, or mucous, derived from the mucous lining of the tympanic cavity;
- an internal, from the lining membrane of the cochlea;
- and an intermediate, or fibrous layer.

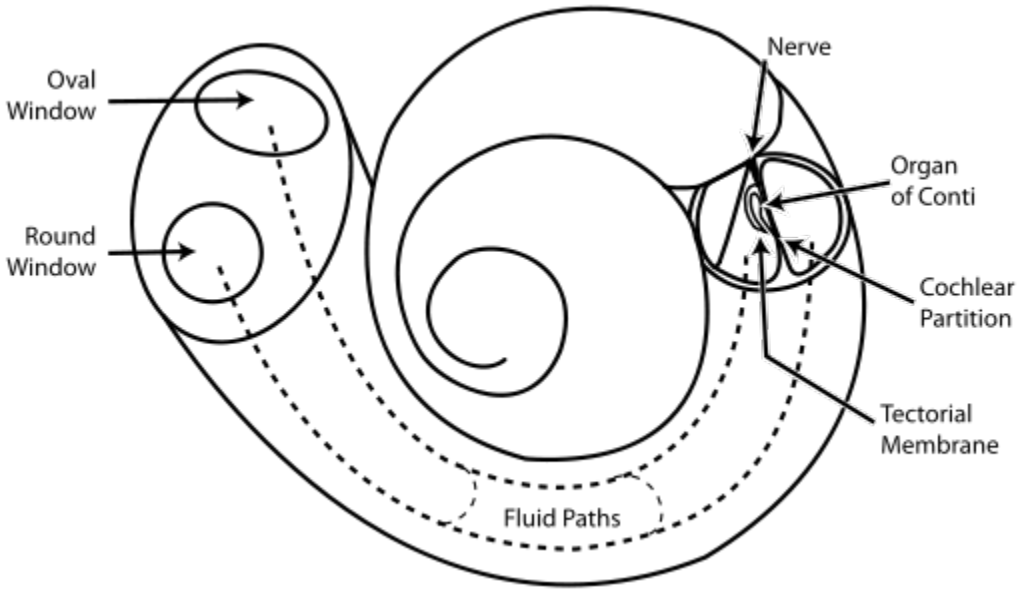
Both the oval and round windows are about the same size, approximately 2.5 mm^2. The entrance to the round window niche is often much smaller than this.

Function

The stapes bone transmits movement to the oval window. As the stapes footplate moves into the oval window, the round window membrane moves out, and this allows movement of the fluid within the cochlea, leading to movement of the cochlear inner hair cells and thus hearing. If the round window were to be absent or rigidly fixed (as can happen in some congenital abnormalities), the stapes footplate would be pushing incompressible fluid against the unyielding walls of the cochlea. It would therefore not move to any useful degree leading to a hearing loss of about 60dB. This is, unsurprisingly, the same as for conditions where the stapes itself is fixed, such as otosclerosis.

Medical implications

The round window sometimes fails to develop correctly and causes the hearing loss mentioned above. Unfortunately round window malformations are often associated with other ear malformations and the hearing loss can be much more severe. Some types of ear surgery (now generally abandoned) used to leave the round window open to the outside world and covered over the oval window. Sound pressure therefore hit the round window but was shielded from the oval window. It therefore travelled "backwards" around the cochlea but still gave useful hearing as the hair cells were still deflected in the same way. The round window is often used as an approach for cochlear implant surgery. It has also recently been used as a site to place middle ear implantable hearing aid transducers. This work has been publicised by Prof. Vittorio Colletti in Verona.


Oval
Window
Round
Window
Nerve
Organ
of Conti
Cochlear
Partition
Tectorial
Membrane
Fluid Paths

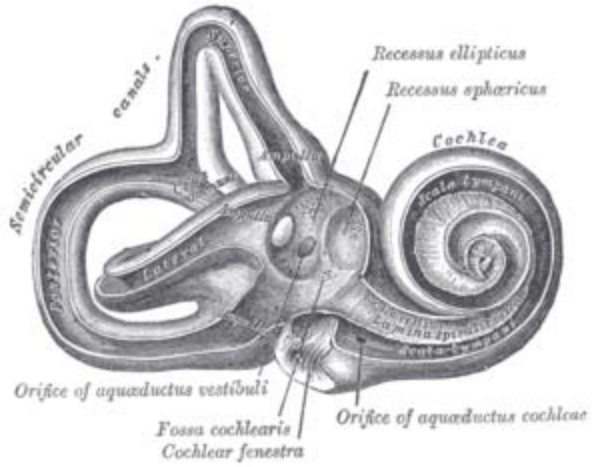
Cochlea

Chapter 23

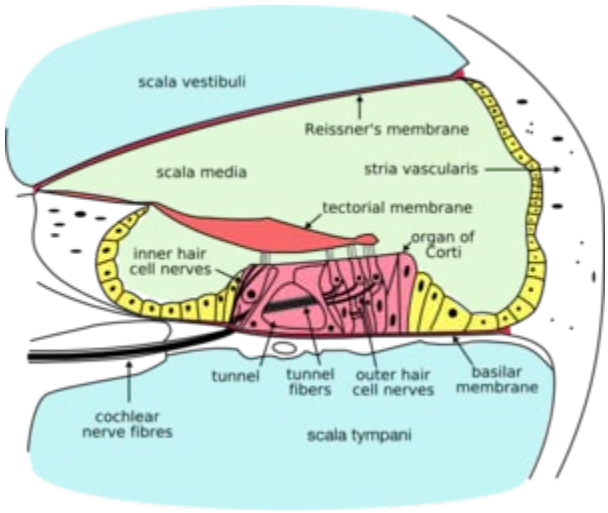
Scala Tympani and Tensor Tympani Muscle

Scala tympani

Scala tympani



Interior of right osseous labyrinth. (Scala tympani labeled at right, inside cochlea.



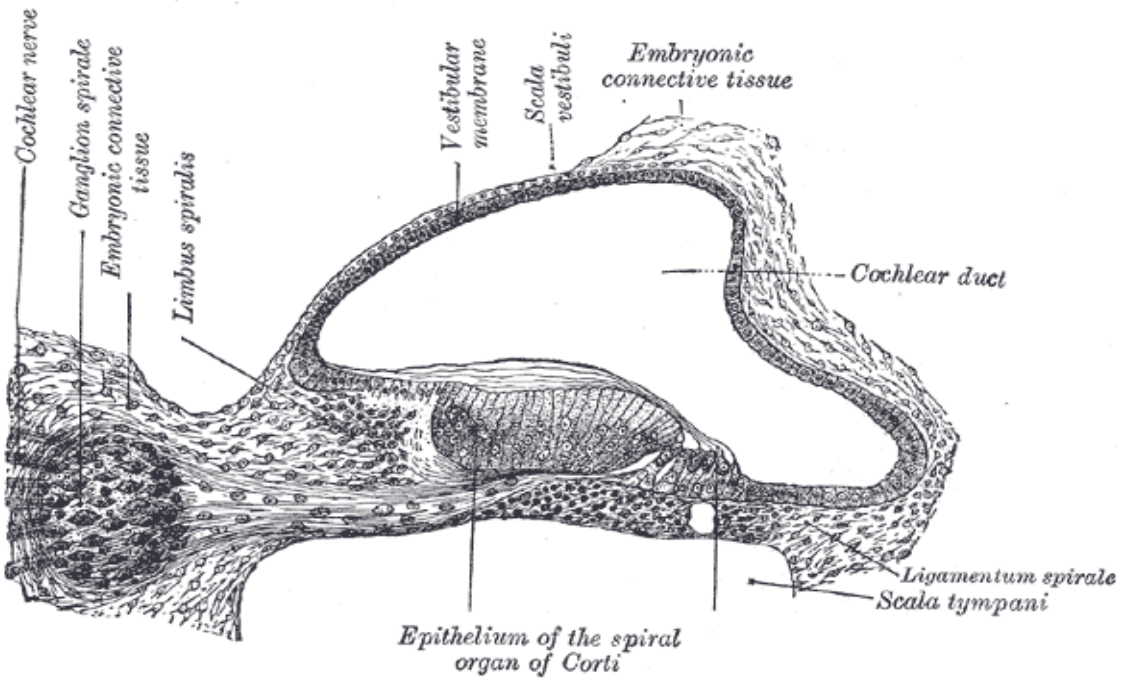
Cross section of the cochlea (scala tympani labeled at bottom)

Gray's *subject #232 1050*

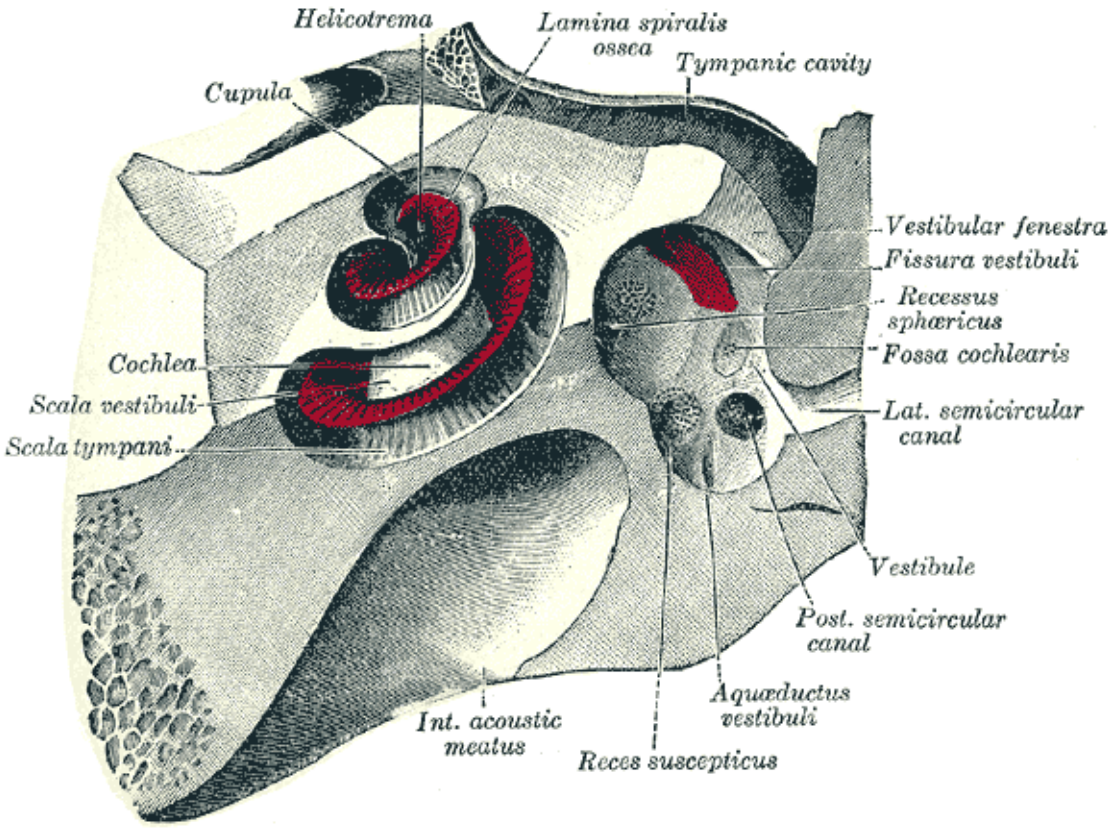
MeSH *Scala+Tympani*

Scala tympani is one of the perilymph-filled cavities in the cochlear labyrinth of the human ear. It is separated from the scala media by the basilar membrane, and it extends from the round window to the helicotrema, where it continues as scala vestibuli.

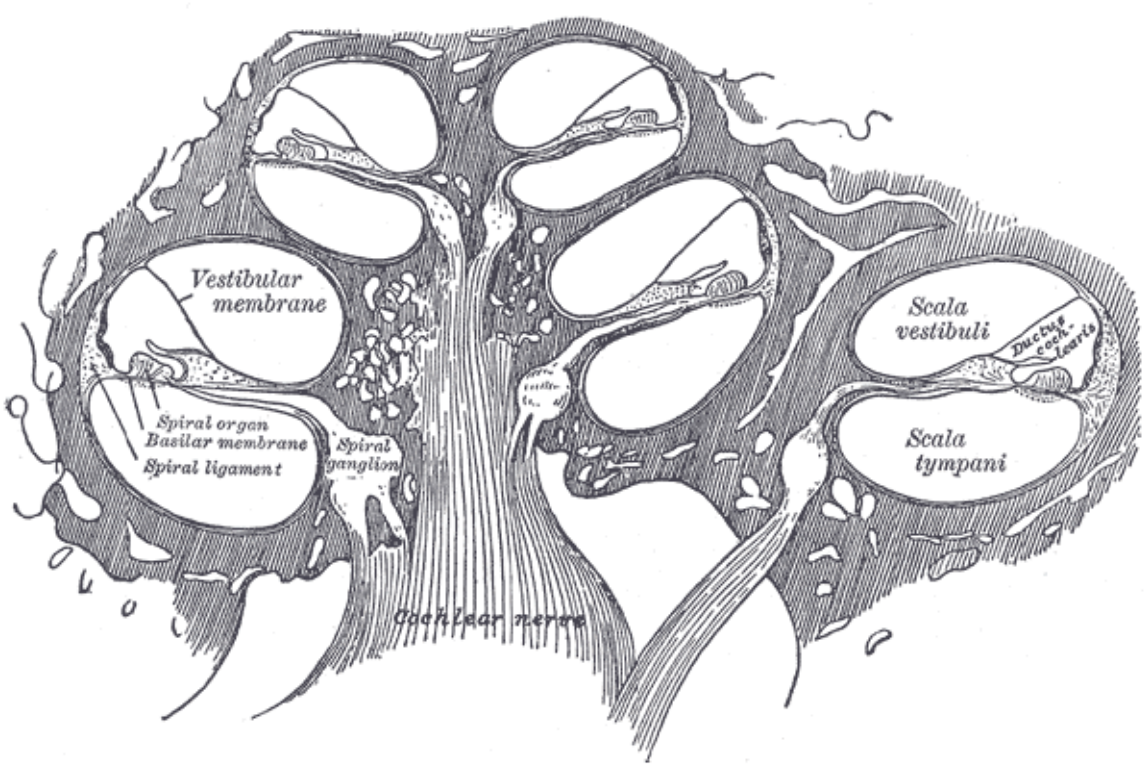
The purpose of the perilymph-filled scala tympani and scala vestibuli is to transduce the movement of air that causes the tympanic membrane and the ossicles to vibrate, to movement of liquid and the basilar membrane. This movement is conveyed to the organ of Corti inside the scala media, composed of hair cells attached to the basilar membrane and their stereocilia embedded in the tectorial membrane. The movement of the basilar membrane compared to the tectorial membrane causes the sterocilia to bend. They then depolarise and send impulses to the brain via the cochlear nerve. This produces the sensation of sound.



Transverse section of the cochlear duct of a fetal cat



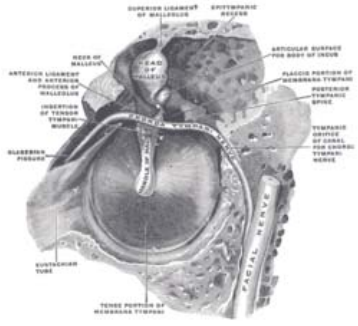
The cochlea and vestibule, viewed from above



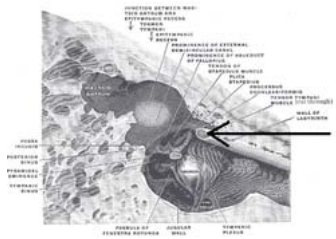
Diagrammatic longitudinal section of the cochlea

Tensor tympani muscle

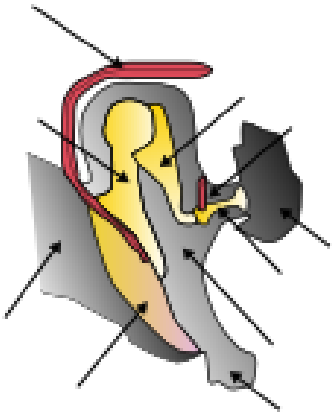
Tensor tympani muscle



The right membrana tympani with the hammer and the chorda tympani, viewed from within, from behind, and from above.



The medial wall and part of the posterior and anterior walls of the right tympanic cavity, lateral view. (Label for "Tensor tympani muscle" is at right, second from bottom.)



Malleus
Tensor Tympani
Incus
Stapedius
Labyrinth
Stapes
Auditory Canal
Tympanic Membrane
(Ear Drum)
Eustachian Tube
Tympanic cavity

Bones and muscles in the tympanic cavity in the middle ear

Latin	*musculus tensor tympani*
Gray's	*subject #231 1046*
Origin	auditory tube
Insertion	handle of the malleus
Artery	superior tympanic artery
Nerve	medial pterygoid nerve from the mandibular nerve (V3)

Actions tensing the tympanic membrane

The **tensor tympani**, the larger of the two muscles of the tympanic cavity, is contained in the bony canal above the osseous portion of the auditory tube. Its role is to dampen sounds, such as those produced from chewing.

Origin and insertion

It arises from the cartilaginous portion of the auditory tube and the adjoining part of the great wing of the sphenoid, as well as from the osseous canal in which it is contained.

Passing backward through the canal, it ends in a slender tendon which enters the tympanic cavity, makes a sharp bend around the extremity of the septum, known as the processus cochleariformis, and is inserted into the handle (manubrium) of the malleus, near its root.

Function

When tensed, the action of the muscle is to pull the malleus medially, tensing the tympanic membrane, damping vibration in the ear ossicles and thereby reducing the amplitude of sounds. This muscle is contracted primarily to dampen the noise produced by chewing. (Compare to the more general dampening function of the stapedius muscle.)

In many people with hyperacusis, an increased activity develops in the tensor tympani muscle in the middle ear as part of the startle response to some sounds. This lowered reflex threshold for tensor tympani contraction is activated by the perception/anticipation of loud sound, and is called tonic tensor tympani syndrome (TTTS). In some people with hyperacusis, the tensor tympani muscle can contract just by thinking about a loud sound. Following exposure to intolerable sounds, this contraction of the tensor tympani muscle tightens the ear drum, which can lead to the symptoms of ear pain/a fluttering sensation/a sensation of fullness in the ear (in the absence of any middle or inner ear pathology). A small percentage of the population can actually voluntarily contract this muscle, inducing a noticeable and (until explained) odd 'rumbling' sound to occur .

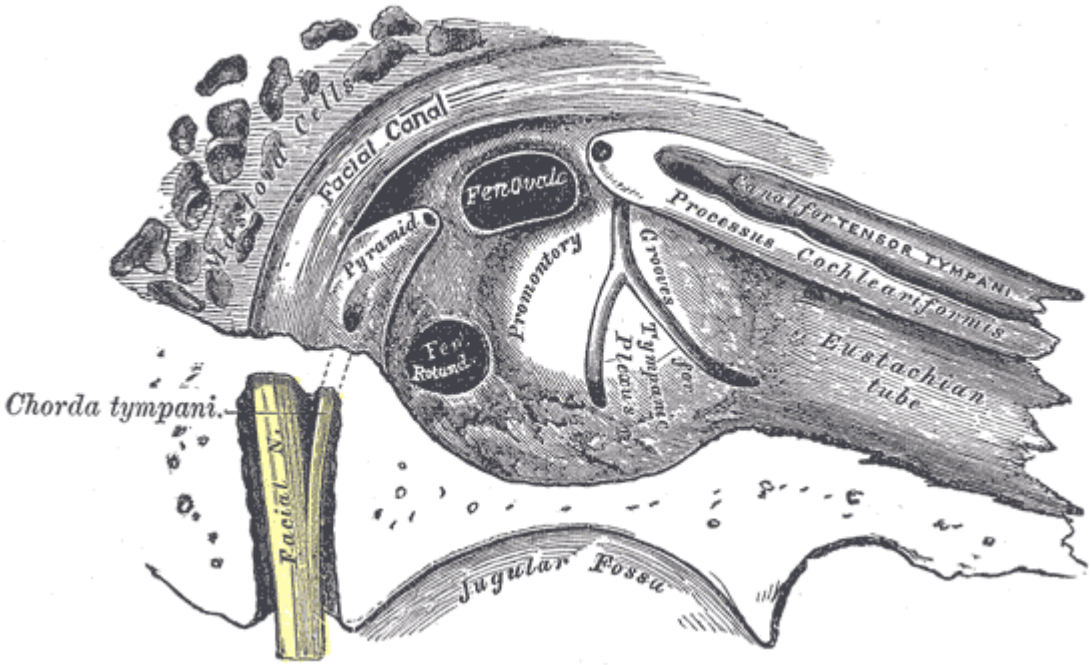
Innervation

Innervation of the tensor tympani is from the tensor tympani nerve, a branch of the mandibular division of the trigeminal nerve (cranial nerve V, specifically V3). As the tensor tympani is innervated by motor fibres of the trigeminal nerve, it does not receive fibres from the trigeminal ganglion, which has sensory fibres only.

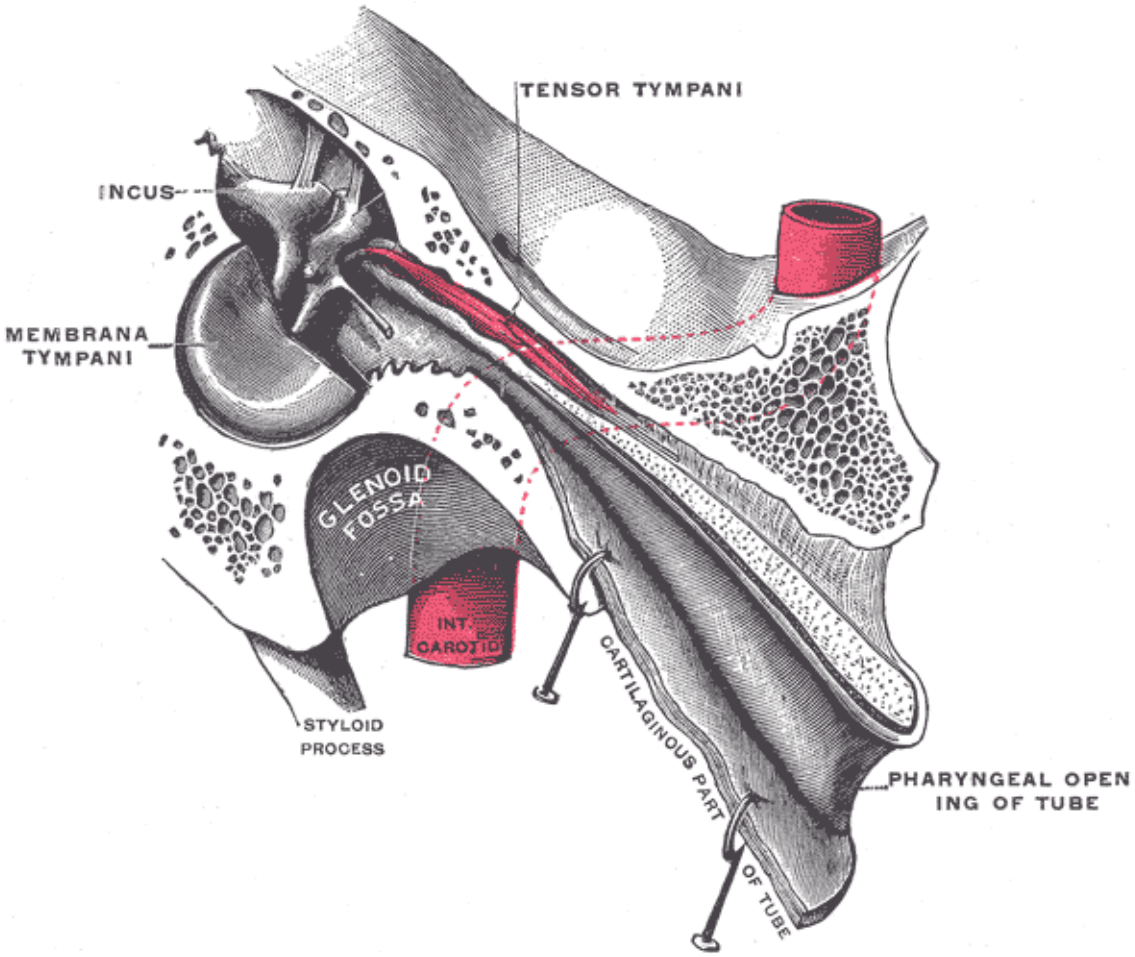
Voluntary control

Contracting muscles produce vibration and sound. Slow twitch fibers produce 10 to 30 contractions per second (equivalent to 10 to 30 Hz sound frequency). Fast twitch fibers

produce 30 to 70 contractions per second (equivalent to 30 to 70 Hz sound frequency). The vibration can be witnessed and felt by highly tensing one's muscles, as when making a firm fist. The sound can be heard by pressing a highly tensed muscle against the ear, again a firm fist is a good example. The sound is usually described as a rumbling sound. Some individuals can voluntarily produce this rumbling sound by contracting the **tensor tympani muscle** of the middle ear. The rumbling sound can also be heard when the neck or jaw muscles are highly tensed.



View of the inner wall of the tympanum



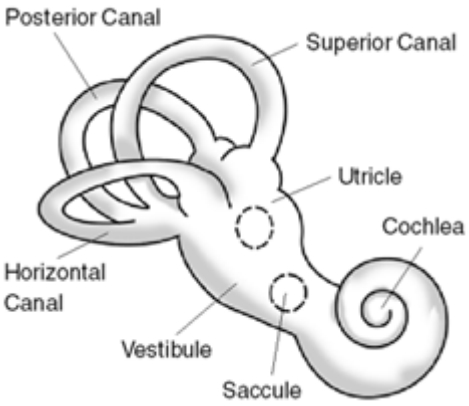
Auditory tube, laid open by a cut in its long axis

Chapter 24

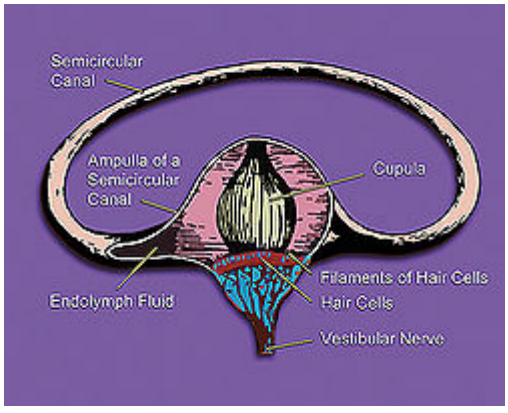
Semicircular Canal and Tragus (Ear)

Semicircular canal

Semicircular canal



Exterior of labyrinth.



Inner ear illustration showing semicircular canal, hair cells, ampulla, cupula, vestibular nerve, & fluid

Latin *canalis semicircularis*

Gray's *subject #232 1049*

Artery	stylomastoid artery
MeSH	*Semicircular+Canals*

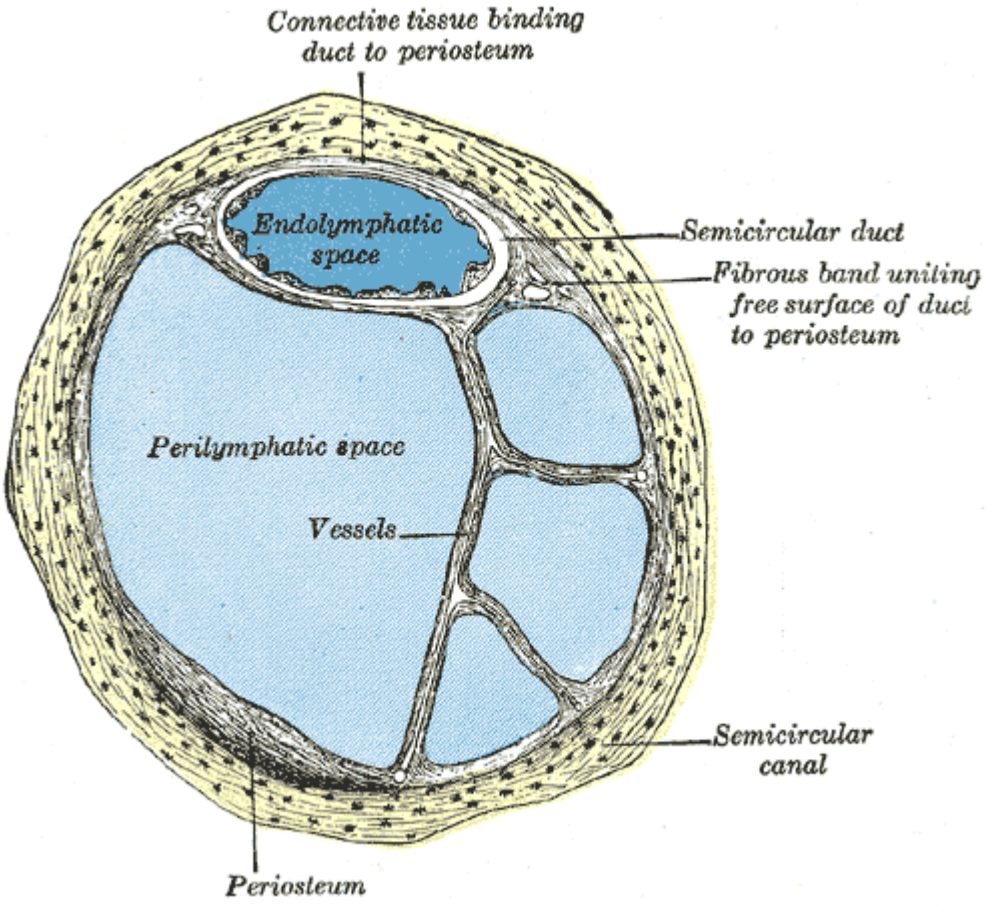
The **semicircular canals** are three half-circular, interconnected tubes located inside each ear. The three canals are the horizontal semicircular canal (also known as the lateral semicircular canal), superior semicircular canal (also known as the anterior semicircular canal), and the posterior semicircular canal.

The canals are aligned approximately orthogonally to one another. The horizontal canal is aligned roughly horizontally in the head. The superior and posterior canals are aligned roughly at a 45 degree angle to a vertical plane drawn from the nose to the back of the skull. Thus, the horizontal canal detects horizontal head movements (such as when doing a pirouette), while the superior and posterior canals detect vertical head movements.

Each canal is filled with a fluid called endolymph and contains a motion sensor with little hairs (cilia) whose ends are embedded in a gelatinous structure called the cupula. As the skull twists in any direction, the endolymph is thrown into different sections of the canals. The cilia detect when the endolymph rushes past, and a signal is then sent to the brain.

The semicircular canals are a component of the bony labyrinth.

Among species of mammals, the size of the semicircular canals is correlated with their type of locomotion. Specifically, species that are agile and have fast, jerky locomotion have larger canals relative to their body size than those that move more cautiously.



Transverse section of a human semicircular canal and duct

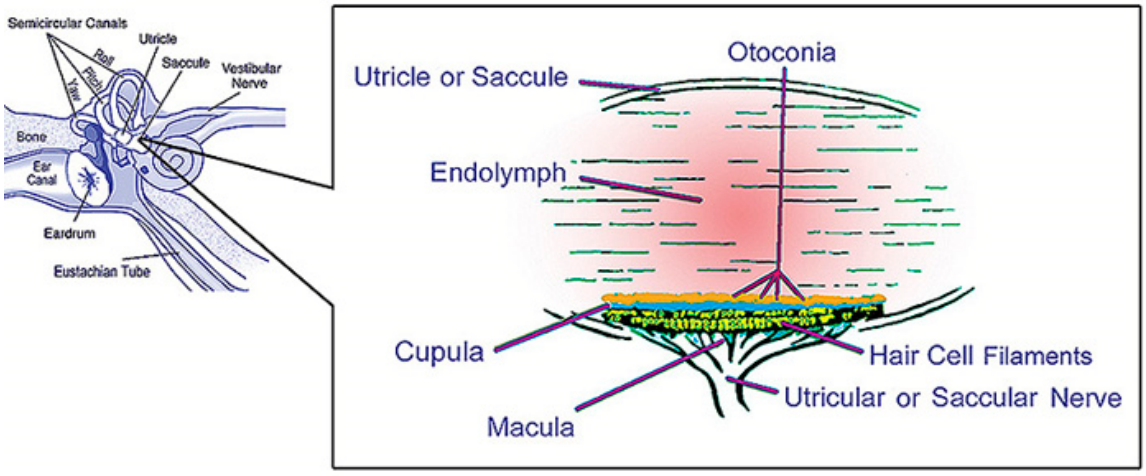
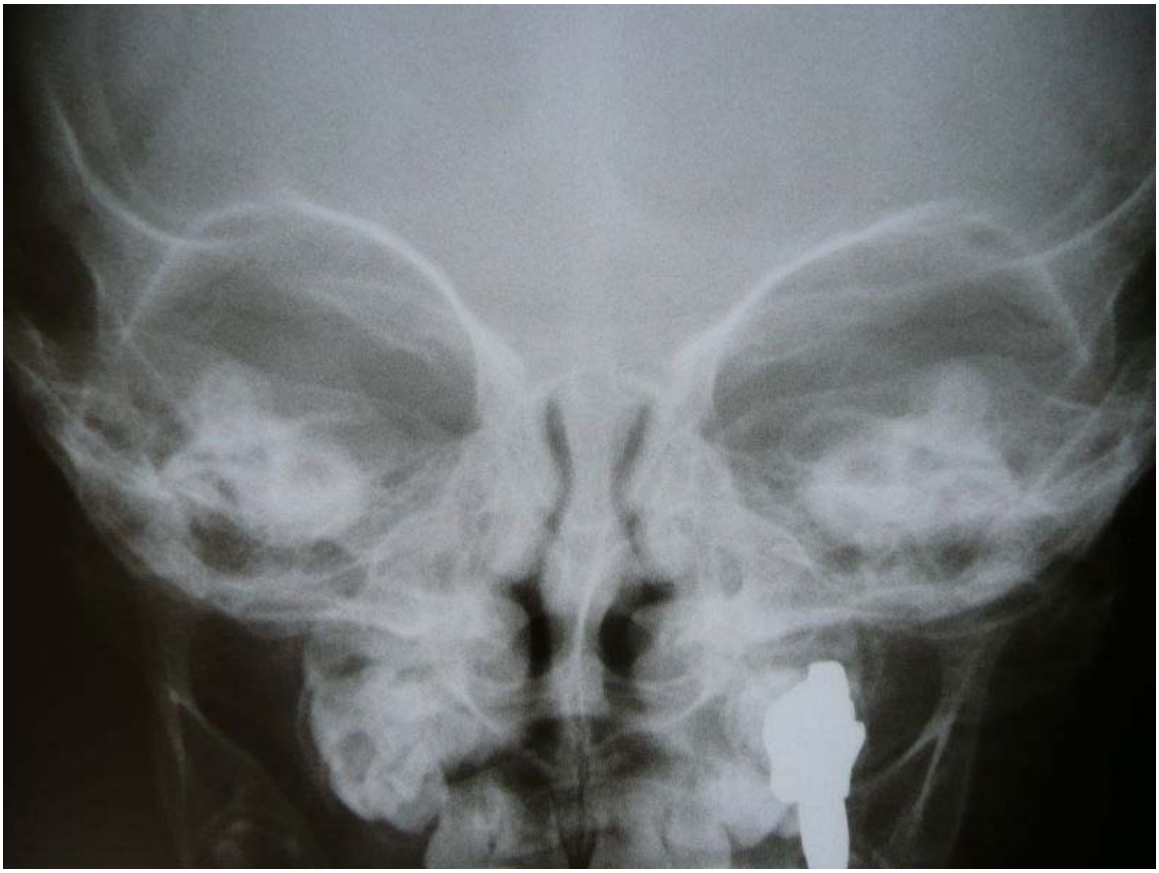


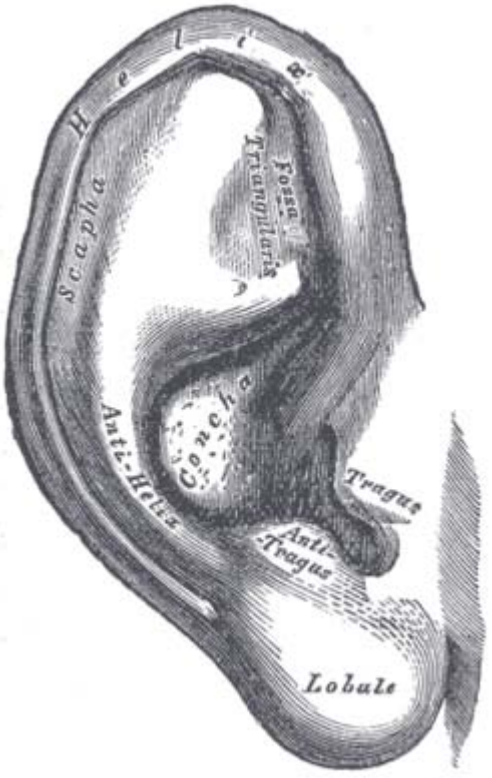
Illustration of otolith organs



Semicircular canals on skull X-ray

Tragus (ear)

Tragus



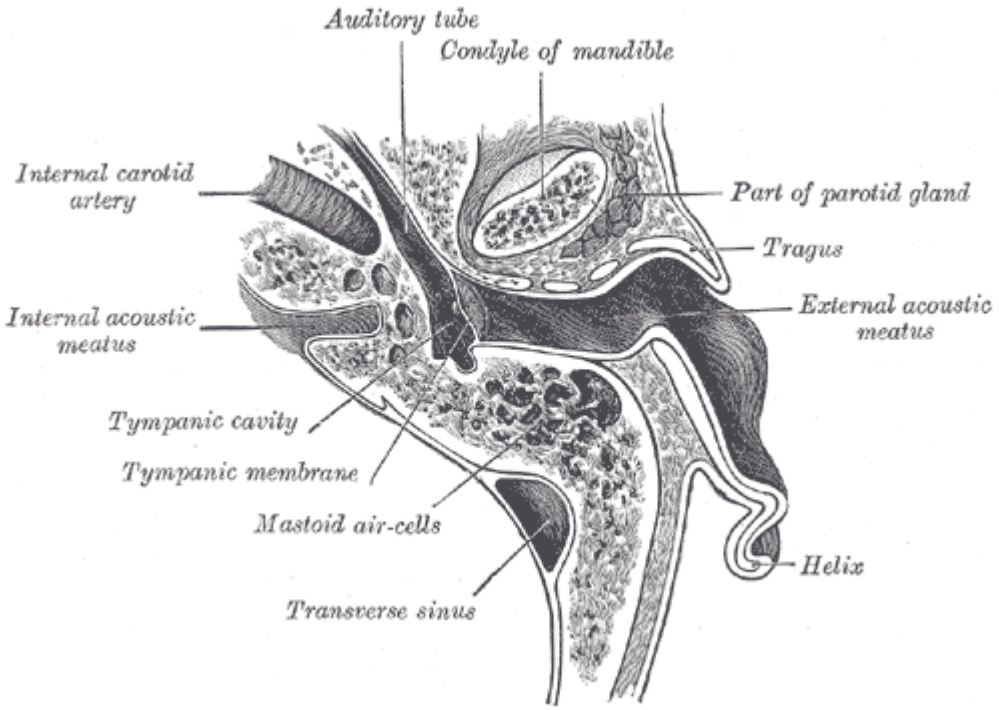
The auricula. Lateral surface.

Gray's *subject #229 1034*

The **tragus** is a small pointed eminence of the external ear, situated in front of the concha, and projecting backward over the meatus. Its name comes from the Greek: *tragos*, goat, and is descriptive of its general covering on its under surface with a tuft of hair, resembling a goat's beard.

Related facts

- Because the tragus face rearwards, it aids in collecting sounds from behind. These sounds are delayed more than sounds arriving from the front, assisting the brain to sense front vs. rear sound sources.
- Earbuds (a type of earphone) are held against the concha by the tragus.
- Some people prefer to push their tragus over the entrance of the auditory canal rather than putting their index finger in it or placing their palm over the entire ear when blocking out sound.
- In Tragus piercing often a ring or barbell is inserted. The antitragus (opposite the tragus) is also sometimes pierced.



Horizontal section through left ear; upper half of section

Chapter 25

Utricle (Ear)

Utricle (ear)

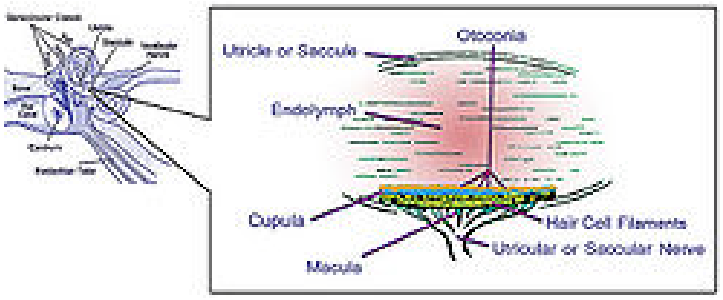


illustration of otolith organs showing detail of utricle, otoconia, endolymph, cupula, macula, hair cell filaments, and saccular nerve

Posterior Canal

Superior Canal

Utricle

Horizontal

Canal

Vestibule

Cochlea

Saccule

Components of the inner ear including the utricle

Latin	*utriculus*
Gray's	*subject #232 1051*
MeSH	*Saccule+and+Utricle*

The **utricle**, or utriculus, along with the saccule is one of the two otolith organs located in the vertebrate inner ear. These use small stones and a viscous fluid to stimulate hair cells to detect motion and orientation.

Anatomy

The utricle is larger than the saccule and is of an oblong form, compressed transversely, and occupies the upper and back part of the vestibule, lying in contact with the recessus ellipticus and the part below it.

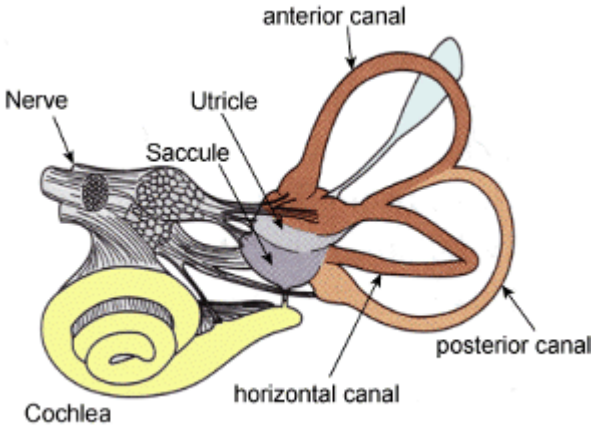
The utricle contains mechanoreceptors called hair cells that distinguish between degrees of tilting of the head, thanks to their apical cilia set-up. These are covered by otolith which, due to gravity, pull on the cilia and tilt them. Depending on whether the tilt is in the direction of the kinocilium or not, the resulting hair cell polarisation is excitatory (depolarising) or inhibitory (hyperpolarisation), respectively. Any orientation of the head causes a combination of stimulation to the utricles and saccules of the two ears. The brain interprets head orientation by comparing these inputs to each other and to other input from the eyes and stretch receptors in the neck, thereby detecting whether only the head is tilted of the entire body is tipping. The inertia of the otolithic membranes is especially important in detecting linear acceleration. Suppose you are sitting in a car at a stoplight and then begin to move. The otolithic membrane of the macula utriculi briefly lags behind the rest of the tissues, bends the stereocilia backwards, and stimulates the cells. This signal to the vestibular nerve (which takes it to the brainstem) does not adapt with time. The effect of this is that, for example, an individual lying down to sleep will continue to detect that they are lying down hours later when they awaken.

Labyrinthine activity responsible for the nystagmus induced by off-vertical axis rotation arises in the otolith organs and couples to the oculomotor system through the velocity storage mechanism.

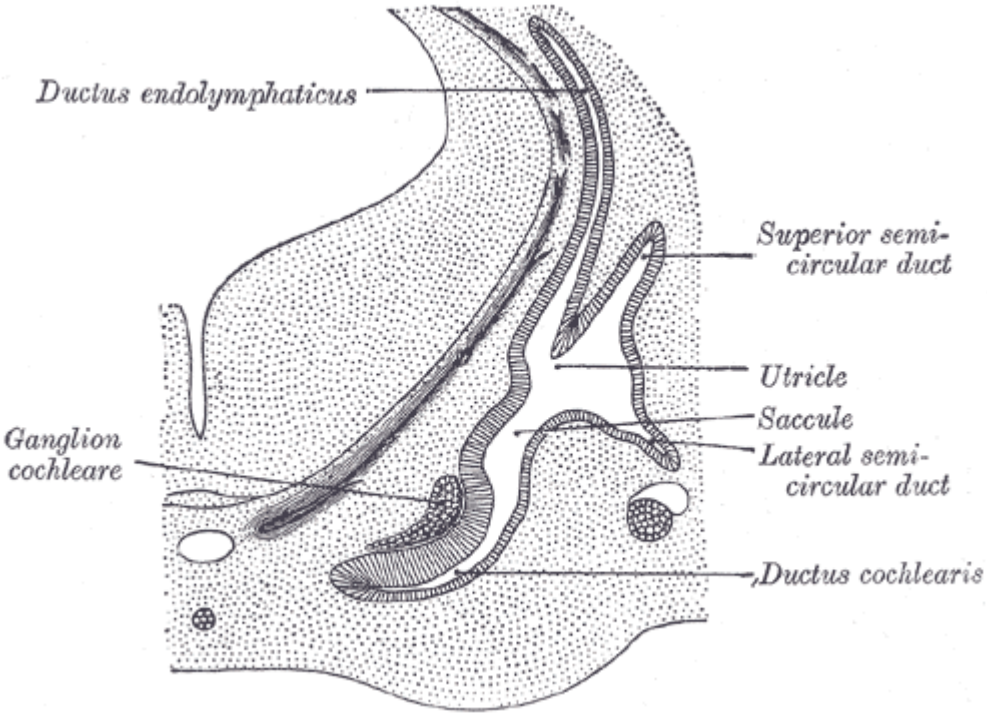
That portion which is lodged in the recess forms a pouch or cul-de-sac, the floor and anterior wall of which are thickened and form the **macula acustica utriculi**, which receives the utricular filaments of the acoustic nerve.

The cavity of the utricle communicates behind with the semicircular ducts by five orifices.

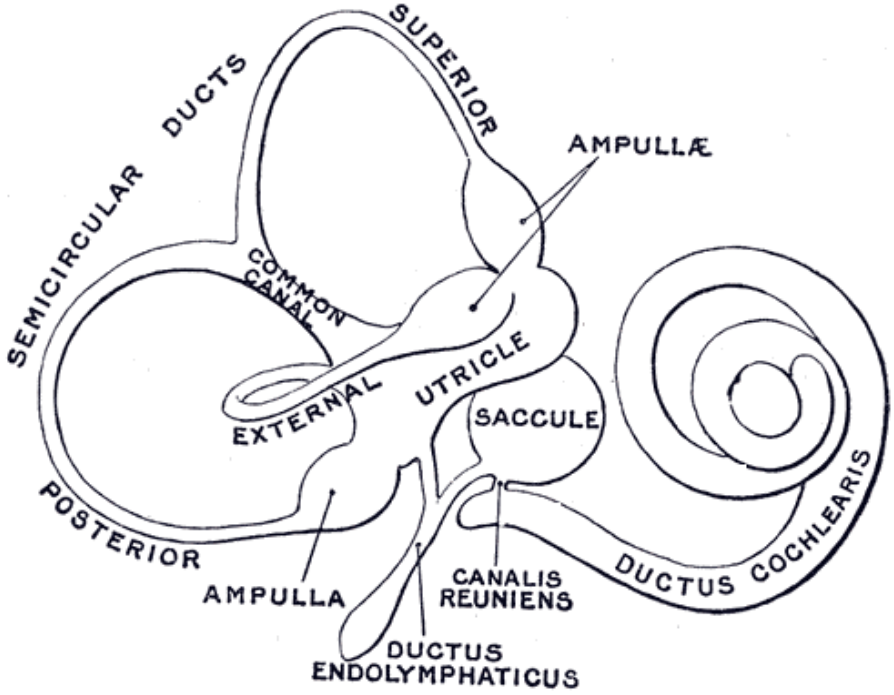
The **ductus utriculosaccularis** comes off of the anterior wall of the utricle and opens into the ductus endolymphaticus.



Vestibular system



Transverse section through head of fetal sheep, in the region of the labyrinth. X 30.



The membranous labyrinth