Ophthalmology and Otolaryngology

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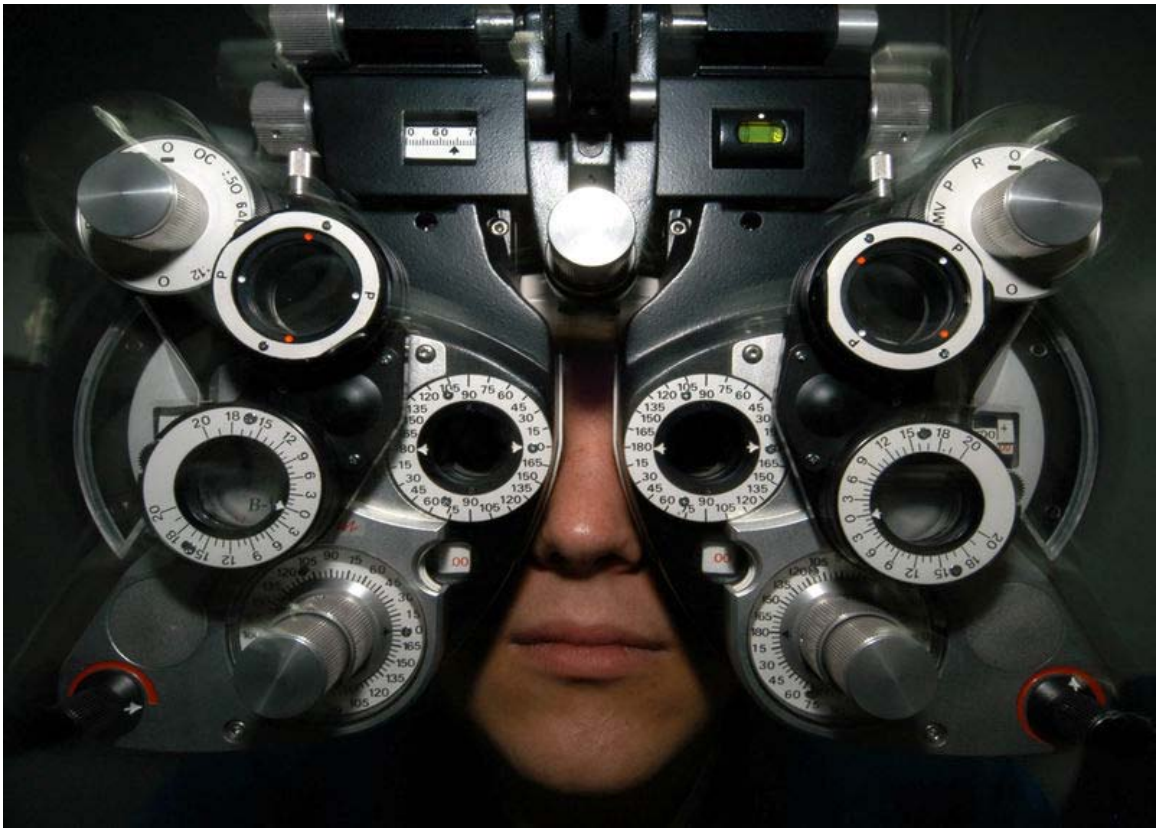
Ophthalmology

Slit lamp examination of eyes in an Ophthalmology Clinic



A phoropter in use

Ophthalmology is the branch of medicine which deals with the anatomy, physiology and diseases of the eye. The term **ophthalmologist** refers to a specialist in medical and surgical eye problems. Since ophthalmologists perform operations on eyes, they are considered to be both surgical and medical specialists.

The word *ophthalmology* comes from the Greek roots *ophthalmos* meaning *eye* and *logos* meaning *word*, *thought,* or *discourse*; ophthalmology literally means "the science of eyes". "Opthomology" is a common mis-hearing or mis-remembering of the term. As a discipline, it applies to animal eyes also, since the differences from human practice are surprisingly minor and are related mainly to differences in anatomy or prevalence, not differences in disease processes. However, veterinary medicine is regulated separately in many countries and states/provinces resulting in few ophthalmologists treating both humans and animals.

Early Developments

Sushruta

Sushruta wrote *Sushruta Samhita* in Sanskrit in about 800 BC He described 76 ocular diseases (of these 51 surgical) as well as several ophthalmological surgical instruments and techniques. His description of cataract surgery was more akin to extracapsular lens

extraction than to couching. The Indian surgeon Sushruta has been described as the first cataract surgeon.

Pre-Hippocrates

The pre-Hippocratics largely based their anatomical conceptions of the eye on speculation, rather than empiricism. They recognized the sclera and transparent cornea running flushly as the outer coating of the eye, with an inner layer with pupil, and a fluid at the centre. It was believed, by Alcamaeon and others, that this fluid was the medium of vision and flowed from the eye to the brain via a tube. Aristotle advanced such ideas with empiricism. He dissected the eyes of animals, and discovering three layers (not two), found that the fluid was of a constant consistency with the lens forming (or congealing) after death, and the surrounding layers were seen to be juxtaposed. He, and his contemporaries, further put forth the existence of three tubes leading from the eye, not one. One tube from each eye met within the skull.

Rufus

Rufus recognised a more modern eye, with conjunctiva, extending as a fourth epithelial layer over the eye. Rufus was the first to recognise a two chambered eye; with one chamber from cornea to lens (filled with water), the other from lens to retina (filled with an egg-white-like substance). Galen remedied some mistakes including the curvature of the cornea and lens, the nature of the optic nerve, and the existence of a posterior chamber. Though this model was roughly a correct but simplistic modern model of the eye, it contained errors. Yet it was not advanced upon again until after Vesalius. A ciliary body was then discovered and the sclera, retina, choroid and cornea were seen to meet at the same point. The two chambers were seen to hold the same fluid as well as the lens being attached to the choroid. Galen continued the notion of a central canal, though he dissected the optic nerve, and saw it was solid, He mistakenly counted seven optical muscles, one too many. He also knew of the tear ducts.

Middle Eastern ophthalmology

Medieval Islamic physicians are considered founders of ophthalmology as an independent discipline. One of the pioneers of ophthalmology was the Persian physician Rhazes. Innovations from this period include “injection syringe”, invented by the Iraqi physician Ammar ibn Ali of Mosul, which was used for the extraction by suction of soft cataracts. In cataract surgery, Ammar ibn Ali attempted the earliest extraction of cataracts using suction. He introduced a hollow metallic syringe hypodermic needle through the sclera and successfully extracted the cataracts through suction.

Ibn al-Haytham (Alhazen) wrote extensively on optics and the anatomy of the eye in his *Book of Optics* (1021). He was the first to hint at the retina being involved in the process of image formation.

Ibn al-Nafis, in *The Polished Book on Experimental Ophthalmology*, discovered that the muscle behind the eyeball does not support the ophthalmic nerve, and that the optic nerves transect but do not get in touch with each other. He also discovered new treatments for glaucoma and the weakness of vision in one eye when the other eye is affected by disease. Salah–ud-din bin Youssef al-Kalal bi Hama (i.e. the eye doctor of Hama) was a Syrian oculist who flourished in Hama in 1296. He wrote an elaborate treatise of ophthalmology entitled Nur al-Uyun wa Jami al-Funun (light of the eyes and collection of rules).

Seventeenth and eighteenth century

The seventeenth and eighteenth century saw the use of hand lenses (by Malpighi), microscopes (van Leeuwenhoek), preparations for fixing the eye for study (Ruysch) and later the freezing of the eye (Petit). This allowed for detailed study of the eye and an advanced model. Some mistakes persisted such as: why the pupil changed size (seen to be vessels of the iris filling with blood), the existence of the posterior chamber, and of course the nature of the retina. In 1722 Leeuwenhoek noted the existence of rods and cones though they were not properly discovered until Gottfried Reinhold Treviranus in 1834 by use of a microscope.

Ophthalmic surgery in Great Britain

The first ophthalmic surgeon in Great Britain was John Freke, appointed to the position by the Governors of St Bartholomew's Hospital in 1727, but the establishment of the first dedicated ophthalmic hospital in 1805; now called Moorfields Eye Hospital in London, England was a transforming event in modern ophthalmology. Clinical developments at Moorfields and the founding of the Institute of Ophthalmology (now part of the University College London) by Sir Stewart Duke Elder established the site as the largest eye hospital in the world and a nexus for ophthalmic research.

Professional requirements

Ophthalmologists are medical doctors (MD/MBBS or D.O., not OD or BOptom) who have completed a college degree, medical school, and residency in ophthalmology. In many countries, ophthalmologists also undergo additional specialized training in one of the many subspecialities. Ophthalmology was the first branch of medicine to offer board certification, now a standard practice among all specialties.

Australia and New Zealand

In Australia and New Zealand, the FRACO/FRANZCO is the equivalent postgraduate specialist qualification. It is a very competitive speciality to enter training and has a closely monitored and structured training system in place over the five years of postgraduate training. Overseas-trained Ophthalmologists are assessed using the pathway published on the RANZCO website. Those who have completed their formal training in the UK and have the CCST/CCT are usually deemed to be comparable.

Canada

In Canada, an Ophthalmology residency after medical school is undertaken. The residency lasts a minimum of five years after the MD degree although subspecialty training is undertaken by about 30% of fellows (FRCSC). There are about 30 vacancies per year for ophthalmology training in all of Canada.

Finland

In Finland, physicians willing to become Ophthalmologists must undergo a five year specialization which includes practical training and theoretical studies.

Germany

In Germany, physicians willing to become Ophthalmologists must undergo a five year specialization of practical training.

India

In India, after completing MBBS degree, post-graduation in Ophthalmology is required. The degrees are Doctor of Medicine (MD), Master of Surgery (MS), Diploma in Ophthalmic Medicine and Surgery (DOMS) or Diplomate of National Board (DNB). The concurrent training and work experience is in the form of a Junior Residency at a Medical College, Eye Hospital or Institution under the supervision of experienced faculty. Further work experience in form of fellowship, registrar or senior resident refines the skills of these eye surgeons. All India Ophthalmological Society (AIOS) and various state level Ophthalmological Societies (like DOS) hold regular conferences and actively promote continuing medical education. Royal colleges of the united kingdom, mainly Royal college of surgeons of Edinburgh (RCSEd), Royal College of ophthalmologists (RCOphth) and Royal college of physicians and Surgeons of Glasgow (RCPSG) have conducted their fellowship and membership examinations since the mid-1990s and awarding fellowships and memberships to the successful candidates.

Pakistan

In Pakistan, after MBBS, a 4 year full time residency programme leads to FCPS in Ophthalmology. Moreover, a two and a half years residency programme leads to MCPS while 2 years training of DOMS is also being offered. M.S.(Ophthalmology) is also one of the specialty programmes. In addition to programmes for Doctors, various diplomas and degrees for Opticians are also being offered to produce competent Optic technicians in this field. These programmes are being offered notably by Punjab Institute of Preventive Ophthalmology (PIPO) Lahore,Pakistan. Sub-specialty Fellowships are also being offered in the field of Pediatric Ophthalmology and Vitreo-Retinal Ophthalmology.

Philippines

Ophthalmology is a considered a medical specialty that uses medicine and surgery to treat diseases of the eye. To become a general ophthalmologist, a candidate must have completed a Doctor of Medicine degree or its equivalent (e.g. MBBS), have passed the physician licensure exam, completed an internship in medicine, and completed residency at any Philippine Academy of Ophthalmology (PAO) accredited program. Attainment of board certification in ophthalmology from PBO is optional, but is preferred and required to gain privileges in most major health institutions. Graduates of residency programs can receive further training in subspecialties of ophthalmology such as neuro-ophthalmology, etc. by completing a fellowship program which varies in length depending on each program's requirements. The leading professional organization in the country is the Philippine Academy of Ophthalmology which also regulates ophthalmology residency programs and board certification through its accrediting agency, the Philippine Board of Ophthalmology.

United Kingdom and Republic of Ireland

In the United Kingdom, there are three colleges that grant postgraduate degrees in ophthalmology. The Royal College of Ophthalmologists grants MRCOphth and FRCOphth (postgraduate exams), the Royal College of Edinburgh grants MRCSEd, the Royal College of Glasgow grants FRCS. In Ireland the Royal College of Ireland grants FRCSI. Work experience as a specialist registrar and one of these degrees is required for specialisation in eye diseases. There are only 2.3 ophthalmologists per 100,000 population in the UK -fewer pro rata than in any other nation in the European Union.

United States

In the United States, four years of residency training after medical school are required, with the first year being an internship in surgery, internal medicine, pediatrics, or a general transition year. Optional fellowships in advanced topics may be pursued for several years after residency. Most currently practicing ophthalmologists train in medical residency programs accredited by the Accreditation Council for Graduate Medical Education (ACGME) and are board certified by the American Board of Ophthalmology. Some physicians that train in osteopathic medical schools may hold a Doctor of Osteopathy ("DO") degree rather than an MD. The same residency and certification requirements for ophthalmology training must be fulfilled by osteopathic physicians. Completing the requirements of continuing medical education is mandatory for continuing licensure and re-certification. Professional bodies like the AAO and ASCRS organize conferences and help members through continuing medical education programs to maintain certification, in addition to political advocacy and peer support.

Sub-specialities

Ophthalmology includes sub-specialities which deal either with certain diseases or diseases of certain parts of the eye. Some of them are:

- Anterior segment surgery
- Cataract — not usually considered a subspecialty *per se*, since most general ophthalmologists perform cataract surgery
- Cornea, ocular surface, and external disease
- Glaucoma
- Medical retina, deals with treatment of retinal problems through non-surgical means.
- Neuro-ophthalmology
- Ocular oncology
- Oculoplastics & Orbit surgery
- Ophthalmic pathology
- Pediatric ophthalmology/Strabismus (mis-alignment of the eyes)
- Refractive surgery
- Uveitis/Immunology
- Veterinary Formal specialty training programs in veterinary ophthalmology now exist in some countries.
- Vitreo-retinal surgery, deals with surgical management of retinal and posterior segment diseases and disorders. Medical retina and vitreo-retinal surgery sometimes together called posterior segment subspecialisation.

Notable ophthalmologists

18th-19th century

- Sir William Adams (UK) Founder of Exeter's West of England Eye Infirmary.
- Carl Ferdinand von Arlt (1812–1887), the elder (Austrian) proved that myopia is largely due to an excessive axial length, published influential textbooks on eye disease, and ran annual eye clinics in needy areas long before the concept of volunteer eye camps became popular. His name is still attached to some disease signs, e.g., von Arlt's line in trachoma. His son Ferdinand Ritter von Arlt, the younger, was also an ophthalmologist.
- Jacques Daviel (France) claimed to be the 'father' of modern cataract surgery in that he performed extracapsular extraction instead of needling the cataract or pushing it back into the vitreous. It is said that he carried out the technique on 206 patients in 1752-3, out of which 182 were reported to be successful. These figures are not very credible, given the total lack of both anaesthesia and aseptic technique at that time.
- Frans Cornelis Donders (1818–1889) (Dutch) published pioneering analyses of ocular biomechanics, intraocular pressure, glaucoma, and physiological optics. Made possible the prescribing of combinations of spherical and cylindrical lenses to treat astigmatism.
- Albrecht von Graefe (1828–1870) (Germany) Along with Helmholtz and Donders, one of the 'founding fathers' of ophthalmology as a specialty. A brilliant clinician and charismatic teacher who had an international influence on the development of ophthalmology. A pioneer in mapping visual field defects and diagnosis and treatment of glaucoma. Introduced a cataract extraction technique

that remained the standard for over 100 years, and many other important surgical techniques such as iridectomy. Rationalised the use of many ophthalmically important drugs, including mydriatics & miotics. The founder of the one of the earliest ophthalmic societies (German Ophthalmological Society, 1857) and one of the earliest ophthalmic journals (Graefe's Archives of Ophthalmology). The most important ophthalmologist of the nineteenth century.

- Allvar Gullstrand (Sweden), Nobel Prize winner in 1911 for his research on the eye as a light-refracting apparatus. Described the *schematic eye* a mathematical model of the human eye based on his measurements known as the *optical constants* of the eye. His measurements are still used today.
- Hermann von Helmholtz, great German polymath, invented the ophthalmoscope (1851) and published important work on physiological optics, including colour vision (1850s).
- Hermann Snellen (Netherlands) introduced the Snellen chart to study visual acuity.
- Sir Arthur Conan Doyle (United Kingdom). English writer, primarily of the Sherlock Holmes stories. Trained in but apparently never practiced Ophthalmology.
- Jose Rizal (Philippines). The Philippines National Hero was an Ophtalmologist, One of his works was operation of his mother's eye for twice from cataract.

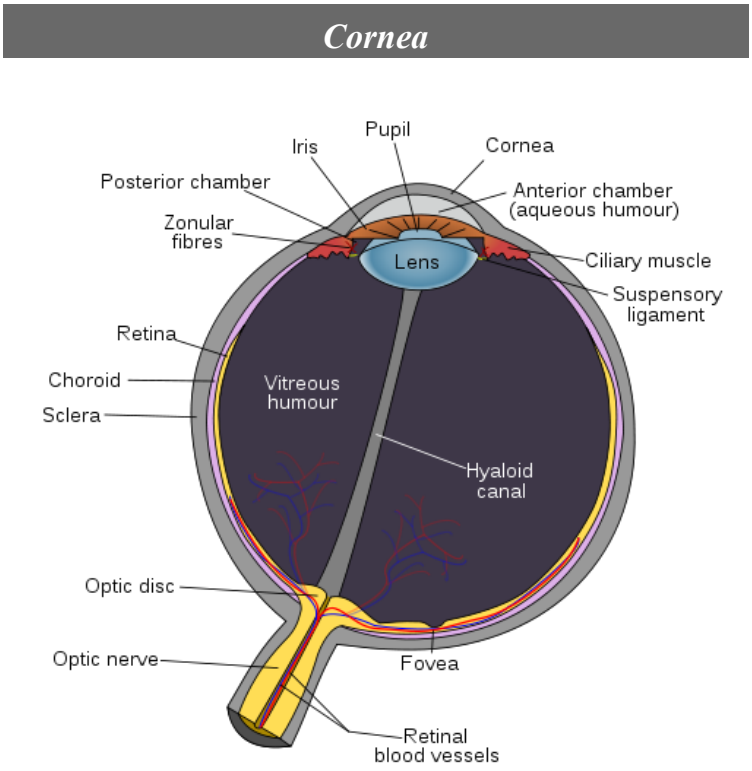
20th-21st century

- William Horatio Bates (1860–1931) (United States) Creator of the unorthodox Bates Method, credited for being the founder of the Natural Vision Improvement movement.
- Vladimir Petrovich Filatov (1875–1956) (Ukraine) His contributions to the medical world include the tube flap grafting method, corneal transplantation and preservation of grafts from cadaver eyes and tissue therapy. He founded The Filatov Institute of Eye Diseases & Tissue Therapy, Odessa, one of the leading eye care institutes in the world.
- Ignacio Barraquer (1884–1965) (Spain) In 1917, invented the first motorized vacuum instrument (erisophake) for intracapsular cataract extraction. Founded of the Barraquer Clinic in 1941 and the Barraquer Institute in 1947 in Barcelona, Spain.
- Tsutomu Sato (Japan) Pioneer in incisional refractive surgery, including techniques for astigmatism and the invention of radial keratotomy for myopia.
- Jules Gonin (1870–1935) (Switzerland) "Father of retinal detachment surgery".
- Sir Harold Ridley (United Kingdom) In 1949, may have been the first to successfully implant an artificial intraocular lens after observing that plastic fragments in the eyes of wartime pilots were well tolerated. He fought for decades against strong reactionary opinions to have the concept accepted as feasible and useful.
- Charles Schepens (Belgium) "Father of modern retinal surgery". Developer of the Schepens indirect binocular ophthalmoscope whilst at Moorfields Eye Hospital. Founder of the Schepens Eye Research Institute in Boston, Massachusetts. This

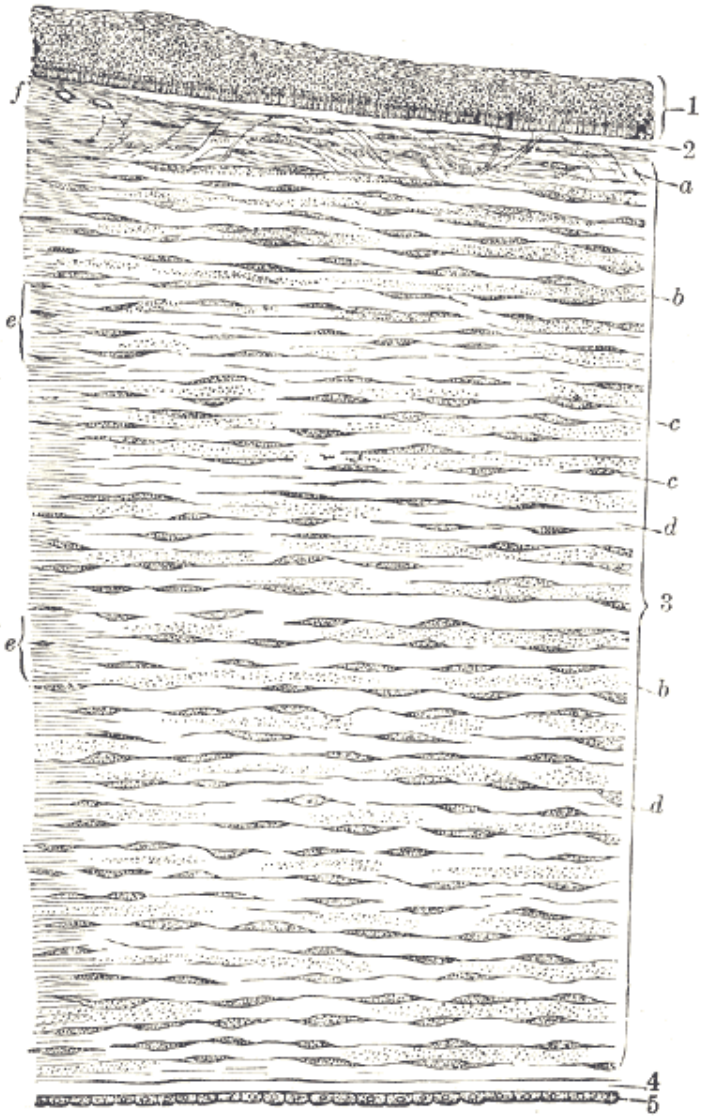
premier research institute is associated with Harvard Medical School and Massachusetts Eye & Ear Infirmary.
- Marshall M. Parks "Father of pediatric ophthalmology".
- José Ignacio Barraquer (1916–1998) (Spain) "Father of modern refractive surgery". In the 1960s, developed lamellar techniques including keratomileusis and keratophakia, as well as the first microkeratome and corneal microlathe.
- Tadeusz Krwawicz (Poland) In 1961, developed the first cryoprobe for intracapsular cataract extraction.
- Svyatoslav Fyodorov (Russia) Popularizer of radial keratotomy.
- Charles Kelman (United States) Developed the ultrasound and mechanized irrigation and aspiration system for phacoemulsification, first allowing cataract extraction through a small incision.
- Ioannis Pallikaris (Greece) Performed the first laser-assisted intrastromal keratomileusis or LASIK surgery.
- Fred Hollows (New Zealand/Australia) Pioneered programs in Nepal, Eritrea, and Vietnam, and among Australian aborigines, including the establishment of cheap laboratory production of intraocular lenses in Nepal and Eritrea.
- Ian Constable (Australia) Founded the Lions Eye Institute in Perth, Western Australia, the largest eye research institute in the southern hemisphere and home to ten ophthalmologists.
- Rand Paul (United States) is a current member of The United States Senate from Kentucky. His father is U.S. Representative Ron Paul.
- L. L. Zamenhof (Poland) Creator of the Esperanto language.
- Bashar al-Assad (Syria) The President of Syria. He did his ophthalmology residency in a hospital in London.
- Syed Modasser Ali (Bangladesh) An ophthalmic surgeon who used to be the Director-General of Health Services for the government of Bangladesh. He wrote the first book on community ophthalmology (public eye health).
- David Taylor Pediatric ophthalmologist and author.
- Wallace Foulds (United Kingdom) Founder president of the Royal College of Opthamologists, founder of the Scottish Ophthalmic Oncology Service, and provided support for the founding of the Singapore Eye Research Institute.

Chapter 2

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.

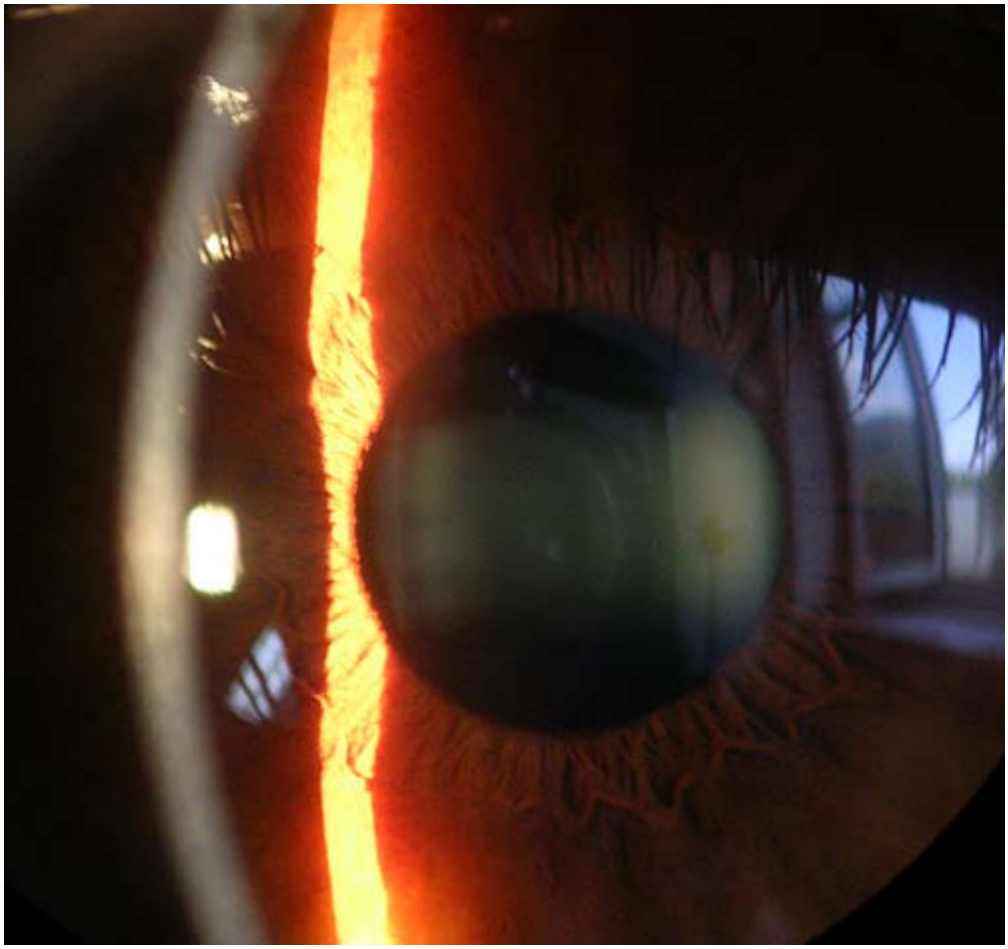
Corneal nerves of the subepithelial layer terminate near superficial epithelial layer of the cornea in a logarithmic spiral pattern.

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 3

Pediatric Ophthalmology and Orthoptics

Pediatric ophthalmology

Pediatric ophthalmology is a sub-speciality of ophthalmology concerned with eye diseases, visual development, and vision care in children.

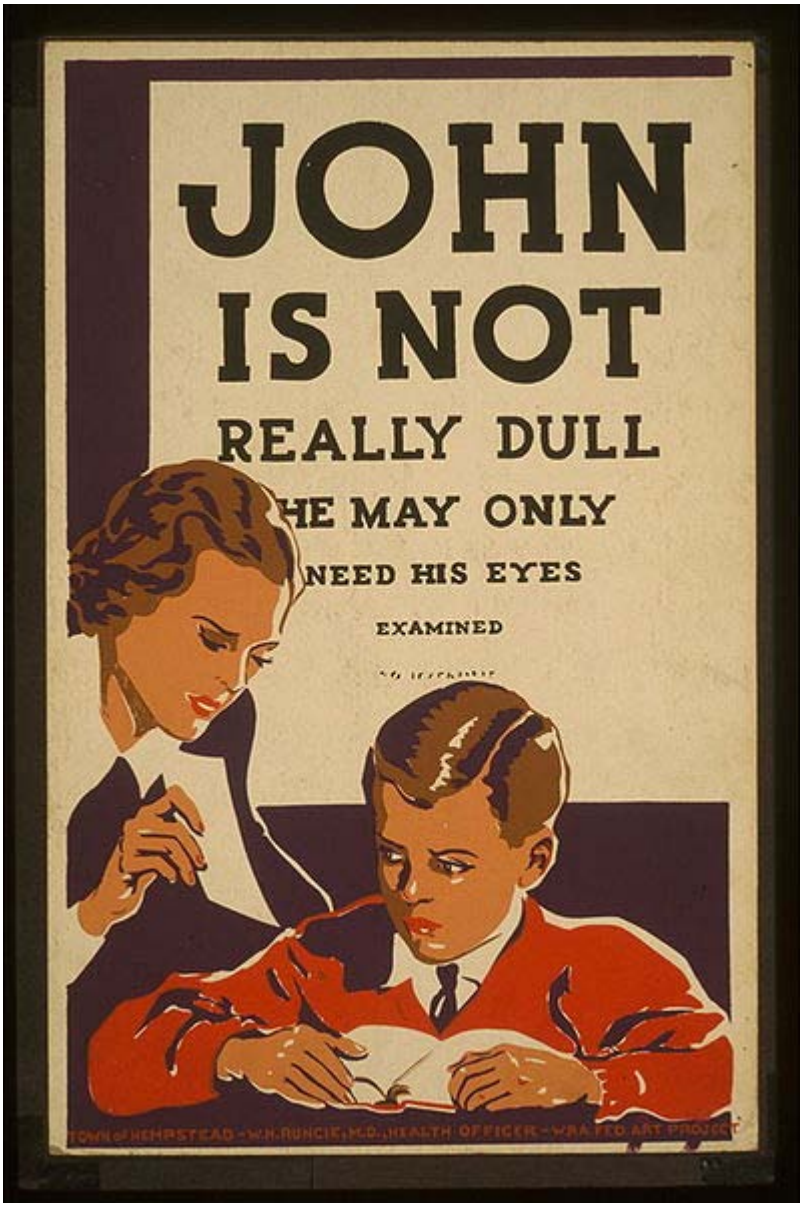
Training

In the United States, pediatric ophthalmologists are physicians who have completed medical school, a 1-year internship, 3-year residency in ophthalmology, and a 1-2 year fellowship in pediatric ophthalmology and strabismus. Pediatric ophthalmology fellowships in the United States are accredited by the American Association for Pediatric Ophthalmology and Strabismus.

Clinical expertise

Pediatric ophthalmologists focus on the development of the visual system and the various diseases that disrupt visual development in children. Pediatric ophthalmologists also have expertise in managing the various ocular diseases that affect children. Pediatric ophthalmologists are qualified to perform complex eye surgery as well as to manage children's eye problems using glasses and medications. Many ophthalmologists and other physicians refer pediatric patients to a pediatric ophthalmologist for examination and management of ocular problems due to children's unique needs. In addition to children with obvious vision problems, children with head turns, head tilts, squinting of the eyes, or preferred head postures (torticollis) are typically referred to a pediatric ophthalmologist for evaluation. Pediatric ophthalmologists typically also manage adults with eye movement disorders (strabismus) due to their familiarity with strabismus conditions.

Eye problems in children



Public education poster urging eye exams for children (Works Progress Administration, circa 1937)

Children experience a variety of eye problems, many quite distinct from adult eye diseases. Pediatric ophthalmologists are specially trained to manage the following disorders:

- Infections (conjunctivitis).
- Strabismus is a misalignment of the eyes that affects 2-4% of the population; it is often associated with amblyopia. The inward turning gaze commonly referred to as "crossed-eyes" is an example of strabismus. The term strabismus applies to

other types of misalignments, including an upward, downward, or outward turning eye.
- Amblyopia (aka lazy eye) occurs when the vision of one eye is significantly better than the other eye, and the brain begins to rely on the better eye and ignore the weaker one. Amblyopia affects 4% of the population and is clinically diagnosed when the refractive error of one eye is more than 1.5 diopters different than the other eye. The management of amblyopia involves correcting of significant refractive errors and using techniques that encourage the brain to pay attention to the weaker eye such as patching the stronger eye.
- Blocked tear ducts.
- Ptosis
- Retinopathy of prematurity
- Visual inattention
- Pediatric cataracts
- Pediatric glaucoma
- Abnormal vision development
- Genetic disorders often cause eye problems for affected children. Since approximately 30% of genetic syndromes affect the eyes, examination by a pediatric ophthalmologist can help with the diagnosis of genetic conditions. Many pediatric ophthalmologists participate with multi-disciplinary medical teams that treat children with genetic syndromes.
- Congenital malformations affecting vision or the tear drainage duct system can be evaluated and possibly surgically corrected by a pediatric ophthalmologist.
- Orbital tumours
- Refractive errors such as myopia (near-sightedness) and astigmatism can often be corrected with prescriptions for glasses or contacts.
- Accommodative insufficiency
- Convergence insufficiency and asthenopia
- Evaluation of visual issues in education, including dyslexia and attention deficit disorder.

Pediatric ophthalmologists often work in conjunction with orthoptists in the treatment of strabismus.

History

Frank D. Costenbader was an American physician frequently credited as the world's first pediatric ophthalmologist. Costenbader and Marshall M. Parks (his mentee who would later be known to many as "the father of pediatric ophthalmology") began the first ophthalmology fellowship trained program of any subspecialty at the Children's Hospital in Washington, D.C., now known as the Children's National Medical Center. Parks trained many pediatric ophthalmologists during his career and was instrumental in the establishment of the American Association for Pediatric Ophthalmology and Strabismus, a national organization dedicated to improving the quality and management of pediatric ocular disease. Over time, over 30 programs were developed for the training of pediatric ophthalmologists throughout the United States. The American Academy of Pediatric

Ophthalmology and Strabismus works with the American Academy of Pediatrics on issues related to pediatric eye disease and vision screening guidelines.

Orthoptics

Orthoptics (from the Greek words *ortho* meaning "straight", and *optikas* meaning "vision" is a discipline dealing with the diagnosis and treatment of defective eye movement and coordination (such as nystagmus), binocular vision, and amblyopia by eye care professionals. There are five areas of treatment for orthoptic problems:

- corrective lenses (spherical, cylindrical lens, prismatic and Fresnel lenses)
- strabismic-related orthoptics as an "eye exercise" is limited to the treatment of eye coordination problems by increasing the range of binocular fusion.
- eyepatching
- pharmaceuticals, such as cycloplegics
- surgery

However the term *orthoptics* is sometimes used to refer simply to eye exercises which are a component of strabismic-related vision therapy.

Orthoptists

Orthoptists are Eye care professionals who specialise in the diagnosis and management of binocular vision problems alongside Ophthalmologists. Orthoptists are represented worldwide by the International Orthoptic Association.

Orthoptics is usually studied as a primary or master's degree, or as a 2 to 4 years post graduate training course. Orthoptists usually work in close cooperation with Ophthalmologists, pediatricians, and sometimes neurologists. Continuing professional development and registration is required in most countries.

History

Orthoptists and ophthalmologists introduced a wide variety of techniques for the improvement of binocular function in the 1930s. The first pioneer was Mary Maddox, the daughter of an English ophthalmologist.

The orthoptic health care profession evolved and specialised as scientific development increased in the diagnosis, management and pre/post-surgical care of patients with strabismus, binocular vision abnormalities and specific pediatric disorders. Because of their lower prevalence and variational presentation, these were beyond the realm of a primary eyecare consultation at a spectacle shop (where most Optometrists work) and

beyond the Ophthalmologists' demanding surgical workload and practice. Hence, Orthoptists began to specialize in hospitals with these problems throughout more than 20 countries.

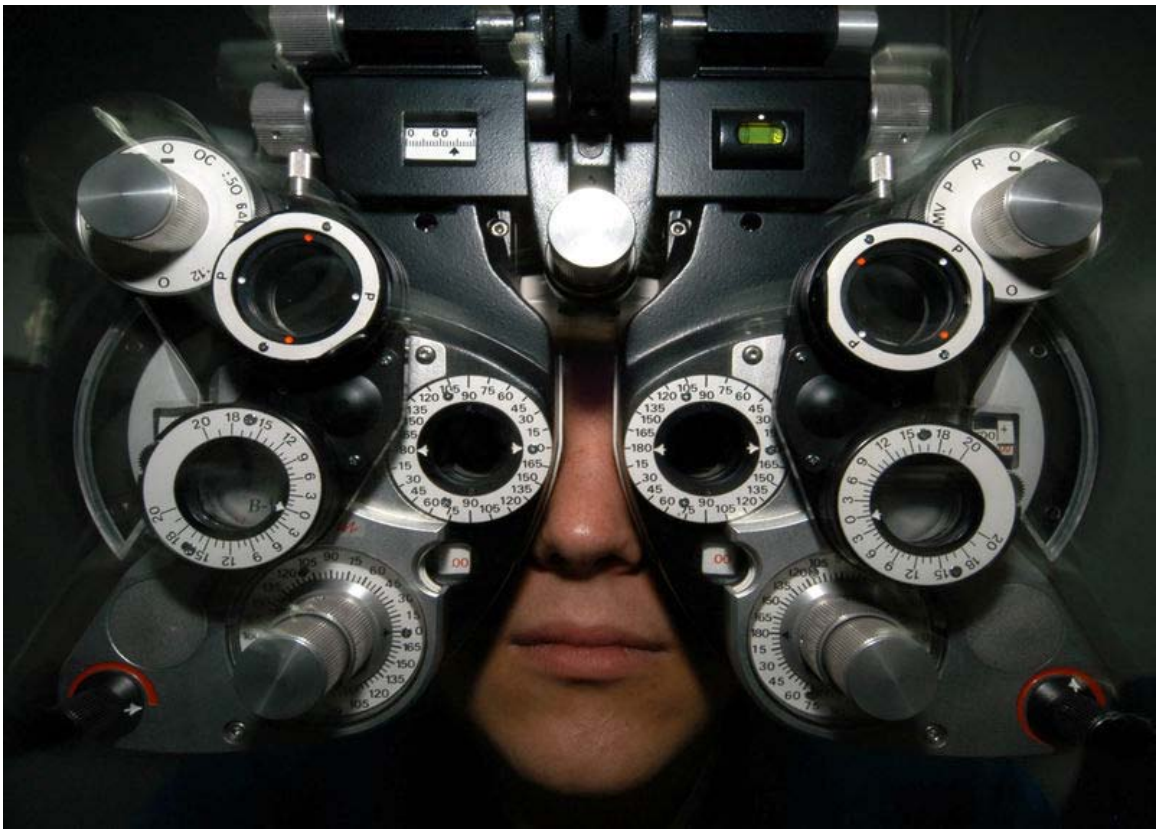
Current orthoptic practice

Orthoptists are mainly involved with diagnosing and managing patients with binocular vision disorders which relate to amblyopia, extraocular muscle balance such as with version, refractive errors, vergence, accommodation imbalances, (positive relative accommodation, negative relative accommodation) and pathological causes. They work closely with ophthalmologists to ensure that patients with eye muscle disorders are offered a full range of treatment options. According to the International Orthoptic Association, professional orthoptic practice involves the following:

- **Primary activities**
  - Ocular motility diagnosis & co-management
  - Vision screening
  - Assessment of special needs
  - Assessment and rehabilitation in neurological disorders
- **Secondary activities**
  - Low Vision assessment and management
  - Glaucoma assessment & stable glaucoma management
  - Biometry (includes sonography work)
  - Fundus photography & screening
  - Visual electrodiagnosis
  - Retinoscopy and refraction, such as using a phoropter to assess refractive errors
- **Further activities**
  - Specific outpatient waiting list initiatives to reduce the delay for children referred to the eye clinic (filter screening)
  - Joint multidisciplinary children’s vision screening clinics (orthoptics/optometry)
  - Organisation/prioritisation of the strabismus surgical admissions list according to agreed criteria
  - Assistance with surgical procedures

Chapter 4

Optometry



An optical refractor (phoropter) in use

Optometry is a health care profession concerned with eyes and related structures, as well as vision, visual systems, and vision information processing in humans. Optometrists are qualified to diagnose and treat eye diseases such as infections and glaucoma.

Like most professions, optometry education, certification, and practice is regulated in most countries. Optometrists and optometry-related organizations interact with governmental agencies, other health care professionals, and the community to deliver eye and vision care. Optometrists are one of three eye care professionals, the others being ophthalmologists (medical doctors), and opticians.

Background

The term "optometry" comes from the Greek words ὄψις (opsis), meaning *sight*, and μέτρον (metron), meaning *measurement.*

The eye, including its structure and mechanism, has fascinated scientists and the public in general since ancient times. Many of the expressions in the English language that mean to understand are equivalent vision terms. "I see," to mean I understand.

Many patients will be more concerned about diseases that affect vision than other, more lethal diseases when told that they may have an eye problem. Being deprived of sight can have a devastating effect on the psyche, as well as economic and social effects. Many blind individuals require significant assistance with activities of daily living and are often unable to continue gainful employment that might have previously been held while they could see. It is also well-known that serious diseases such as myasthenia gravis, diabetes, and atherosclerosis can show their first signs during an eye examination, well before a patient experiences any symptoms.

The maintenance of ocular health and correction of eye problems that decrease vision contribute greatly to the ability to appreciate the longer lifespan that all of medicine continues to allow. Given the importance of vision to quality of life, many optometrists consider their job to be rewarding, as they are often able to restore or improve a patient's sight.

Behavioral optometry is a related area of non-strabismus vision therapy that some optometrists practice. Generally ophthalmologists and orthoptists do not practice this. It generally involves intense therapy that requires at least a weekly visit with eye exercises at home. In some cases it can improve vision beyond that which eyeglasses alone can do.

In the United States, optometry is currently governed by state boards that determine their scope of practice. The scope of practice can vary dramatically from state to state. Optometrists have been successful in getting the right to use some types of medication, including pills, eye drops, and injections. In Oklahoma, optometrists are allowed by the state legislature to perform laser surgery.

History

Optometric history is tied to the development of

- vision science (related areas of medicine, microbiology, neurology, physiology, psychology, etc)
- optics, optical aids
- optical instruments, imaging techniques
- other eye care professions

The history of optometry can be traced back to the early studies on optics and image formation by the eye.

The origins of optometric science date back a few thousand years BC as evidence of the existence of lenses for decoration has been found. It is unknown when the first spectacles were made. According to research by David A. Goss, O.D., Ph.D., they originated in the late 13th century in Italy as stated in a manuscript from 1305 AD where a monk from Pisa named Rivalto stated “It is not yet 20 years since there was discovered the art of making eyeglasses”. Spectacles were manufactured in Italy, Germany, and the Netherlands by 1300 AD.

Benito Daza de Valdes published the third book on optometry in 1623, where he mentioned the use and fitting of eyeglasses. The term *optometrist* was coined by Edmund Landolt in 1886, referring to the "fitter of glasses". Prior to this, there was a distinction between "dispensing" and "refracting" opticians in the 19th century. The latter were later called optometrists.

In 1692, William Molyneux wrote a book on optics and lenses where he stated his ideas on myopia and problems related to close-up vision.

The scientists Claudius Ptolemy and Johannes Kepler also contributed to the creation of optometry. Kepler discovered how the retina in the eye creates vision.

From 1773 until around 1829, Thomas Young discovered the disability of astigmatism and it was George Biddell Airy who designed glasses to correct that problem that included spherocylindrical lens.

A pilgrim named Peter Brown is believed to be the first person to wear a pair of glasses in the US, however, eyeglasses were only made in Europe for a long period of time which made them both expensive and difficult to find. The first man to buy a pair of eyeglasses in the US was John McAllister Sr., from Philadelphia Pennsylvania, in 1783. McAllister, together with his son, John McAllister Jr. started making the first eyeglasses in the US in 1811. Their business continued until the 20th century. The family also taught refraction, and one of their students, James W. Queen also began his own business in 1853.

Benjamin Pike and James Prentice were two other early optometrists who studied in England and came to the US in 1847. They trained their sons, and James's son, Charles Prentice, had an important role in the development of optometry in the US.

The American Optometric Association was then formed on January 11, 1922 after Morris Steinfeld held a meeting with seven optometrists to discuss whether optometry should be a business or a profession. At the end of this meeting, they formed the American Academy of Optometry with the vision to transform the entire body optometric to a profession with a scientific base. The American Optometric Society was formed in August 2009. Doctors were concerned that policy decisions by the AOA leadership did

not represent the desires of the majority of the profession and were considered to not be in the best interest of the profession.

The first schools of optometry were established in 1850–1900 (in USA), and contact lenses were first used in 1940s

The first schools of optometry in the US began in the late 19th century, with the Illinois College of Optometry in 1872, and the New England College of Optometry in 1894. In 1914, a program in optometry began at The Ohio State University after Professor Charles Sheard gave a presentation to the Ohio State Optical Association who assisted him financially to open the program. It started as a two-year course that later became a four-year degree-granting program. Until 1937 the program was known as Applied Optics, when it then became known as Optometry.

Nowadays, there are many community and local resources to help those with financial difficulties to secure free or reduced cost eye care. Contact can be made to charities or non-profit organizations in the are to receive such help.

Licensing

Most countries have regulations concerning optometry education and practice. Optometrists like many other health care professionals are required to participate in ongoing continuing education courses to stay current on the latest standards of care.

Optometry is officially recognized:

- in North America (Canada and US)
- in Latin America and some Caribbean countries
- in most English speaking countries including UK, Republic of Ireland, Australia, New Zealand and South Africa
- in Europe including Spain, Germany and the English speaking European countries
- in Asia including China, Hong Kong, Malaysia, Philippines, Singapore, Taiwan and Thailand
- in the Middle East including Saudi Arabia, Iran and Israel

Argentina

In Argentina optometrists are required to register with the local Ministry of Public Information, but licensing is not required. Anyone holding a Bachelor's degree may register as an optometrist after completing a written exam. Fees for the exam are set by the provincial government and vary from province to province.

Australia

Australia currently has three recognised courses in Optometry. These are offered through the University of New South Wales: Bachelor of Optometry Bachelor of Science

(BOptom BSc), a 5 year course; Queensland Universtiy of Technology: Bachelor of Vision Science and Masters of Optometry, a 5 year course; and Melbourne University which is transitioning to a Doctor of Optometry course a 4 year postgraduate course. These courses are developments of prior course offerings at these institutions that have been expanded along with the increased scope of practice for Optometrists in Australia, specifically the ability to prescribe certain therapeautic agents.

New courses are being developed at Flinders University in South Australia, which accepted students in a science degree in 2010 and will begin the post graduate component of the course in 2013. A second new course is expected to be offered at Deakin University in Geelong, Vic at the beginning of 2012.

Canada

In Canada optometrists hold a Doctorate of Optometry degree and are licensed by the boards in the provinces they wish to practice. There are two schools of optometry, one at the University of Waterloo and the other at Universite de Montreal.

Colombia

In Colombia optometry education has been accredited by the Ministry of Health. The last official revision to the laws regarding health care standards in the country was issued in 1992 through the Law 30. Currently there are eight official universities that are entitled by ICFES to grant the Optometrist certification. The first optometrists arrived in the country from North America and Europe circa 1914. These professionals specialized in optics and refraction. In 1933, under Decrees 449 and 1291, the Colombian Government officially set the rules for the formation of professionals in the field of optometry. In 1966 La Salle University opened its first Faculty of Optometry after recommendation from a group of professionals. At the present time optometrists are encouraged to keep up with new technologies through congresses and scholarships granted by the government or the private sector (such as Bausch & Lomb).

Europe

Currently, optometry education and licensing varies throughout Europe. For example, in Germany, optometric tasks are performed by ophthalmologists and professionally trained and certified opticians. In France, there is no regulatory framework and optometrists are sometimes trained by completing an apprenticeship at an ophthalmologists' private office.

Since the formation of the European Union, "there exists a strong movement, headed by the Association of European Schools and Colleges of Optometry (AESCO), to unify the profession by creating a European-wide examination for optometry" and presumably also standardized practice and education guidelines within EU countries. The first examinations of the new European Diploma in Optometry were held in 1998 and this was a landmark event for optometry in continental Europe.

Ireland

The profession of Optometry has been represented for over a century by the Association of Optometrists, Ireland [AOI]. In Ireland an optometrist must first complete a four year degree in optometry at D.I.T. Kevin Street. Following successful completion of the a degree, an optometrist must then complete Professional Qualifying Examinations in order to be entered into the register of the Opticians Board [Bord na Radharcmhaistoiri]. Optometrists must be registered with the Board in order to practice in the Republic of Ireland.

The A.O.I. runs a comprehensive continuing education and professional development program on behalf of Irish optometrists. The legislation governing Optometry was drafted in 1956. Some feel that the legislation restricts optometrists from using their full range of skills, training and equipment for the benefit of the Irish public. The amendment to the Act in 2003 addressed one of the most significant restrictions - the use of cycloplegic drugs to examine children.

United Kingdom

In the United Kingdom, optometrists have to complete a 3 or 4 (Scotland) year undergraduate honours degree followed by a minimum of a one-year "pre-registration period" where they complete supervised practice under the supervision of an experienced qualified practitioner. During this year the pre-registration candidate is given a number of quarterly assessments and on successfully passing all of these assessments, a final one-day set of examinations (Examination details correct for candidates from 2006 onwards). Following successful completion of these assessments and having completed one year's supervised practice, the candidate is eligible to register as an optometrist with the General Optical Council (GOC) and, should they wish, are entitled to membership of The College of Optometrists. Registration with the GOC is mandatory to practice in the UK. Members of the College of Optometrists (incorporated by a Royal Charter) may use the suffix MCOptom. There are 9 universities which offer optometry in the UK.

Philippines

Optometry is regulated by the Professional Regulation Commission of the Philippines. To be eligible for licensing, each candidate must have satisfactorily completed a Doctor of Optometry course at an accredited institution and demonstrate good moral character with no previous record of professional misconduct. Professional organizations of optometry in the Philippines include Optometric Association of the Philippines and Integrated Philippine Association of Optometrists, Inc. (IPAO)

Russia

In Russia optometry education has been accredited by the Federal Agency of Health and Social Development. There are only two educational institutions that teach optometry in Russia: Saint Petersburg Medical Technical College, formerly known as St. Petersburg

College of Medical Electronics and Optics, and The Helmholz Research Institute for Eye Diseases. They both belong and are regulated by the Ministry of Health. The Optometry program is a 4 year program. It includes 1–2 science foundation years, 1 year focused on clinical and proficiency skills, and 1 year of clinical rotations in hospitals. Graduates take college/state examinations and then receive a specialist diploma. This diploma is valid for only 5 years and must be renewed every 5 years after receiving additional training at state accredited programs.

United States

The American Optometric Association (AOA) and the American Optometric Society (AOS) represent optometrists nationally in the USA. Prior to admittance into optometry school, optometrists typically complete four years of undergraduate study, culminating in a bachelor's degree. Required undergraduate coursework for pre-optometry students covers a variety of health, science and mathematics courses. These courses include: 4 semesters of chemistry to include organic and biochemistry, 2 semesters of physics and biology, as well as 1 semester of calculus, statistics, physiology, anatomy, microbiology, and psychology. Additional requirements are imposed by specific institutions. Once completing these courses in order to be admitted to an optometry doctorate program one must score well on the O.A.T., Optometry Admission Tests. There are currently 20 optometry schools in the United States, and admission into these schools are considered to be extremely competitive.

Optometrists are required to complete a four-year postgraduate degree program to earn their Doctor of Optometry (O.D.) titles. The four-year program includes classroom and clinical training in geometric, physical, physiological and ophthalmic optics, ocular anatomy, ocular disease, ocular pharmacology, neuroanatomy and neurophysiology of the vision system, binocular vision, color, form, space, movement and vision perception, design and modification of the visual environment, and vision performance and vision screening. In addition, an optometric education also includes a thorough study of human anatomy, general pharmacology, general pathology, sensory and perceptual psychology, biochemistry, statistics and epidemiology. There are three new colleges of optometry (Midwestern University Arizona College of Optometry, University of the Incarnate World School of Optometry, Western University of Health Sciences College of Optometry) that have received the pre-accreditation status of preliminary approval from the Accreditation Council on Optometric Education (ACOE). Programs with "Preliminary Approval" have shown that they are developing within the ACOE's standards. The programs have approval to begin recruiting and admitting students, and to begin offering the program.

Upon completion of an accredited program in optometry, graduates hold the Doctor of Optometry (O.D. - Oculis Doctor) degree. Optometrists must then pass a national examination administered by the National Board of Examiners in Optometry (NBEO). The three-part exam includes basic science, clinical science and patient care. (The structure and format of the NBEO exams are subject to change beginning in 2008.) Some optometrists go on to complete 1–2 year residencies with training in a specific sub-

specialty such as pediatric eyecare, geriatric eyecare, specialty contact lens, ocular disease or neuro-optometry. All optometrists are required to fulfill continuing education requirements to stay current regarding the latest standards of care.

Within the healthcare system, optometrists function as primary eye care providers that are especially experienced in fitting contact lenses and glasses prescriptions. Although they are not technically physicians, in that they do not hold an MD or DO degree, some states, such as Florida, refer to optometrists as "Optometric Physicians" in a legal sense. Optometrists also have the ability to treat a wide variety of eye diseases though the administration of topical, oral and injectable medicines (depending on the state) although their scope is limited to the eye. Optometrists may be trained in some surgical techniques, including those for foreign body removal, corneal injury, eyelid & lacrimal disease, and others. In Oklahoma, the state optometry board also allows state-certified optometrists to perform laser surgeries limited to the anterior segment of the eye. Additionally, Department of Veterans Affairs (VA) facilities permit optometrists who have been trained in these laser techniques and hold licensure in Oklahoma to perform laser surgeries in any VA facility in the country, not just Oklahoma VA hospitals.

Ophthalmologists differ from optometrists in that ophthalmologists are physicians who are licensed to perform all eye surgeries, can treat systemic diseases, and who have completed 4 years of medical school and a residency in ophthalmology. In many cases optometrists and ophthalmologists work together in the treatment and management of patients with various eye conditions. Opticians generally dispense corrective eye wear, and in some cases will also construct the corrective eye wear. The scope of practice in optometry varies as it is regulated by each state.

Chapter 5

Eye Disease

The World Health Organization publishes a classification of known diseases and injuries called the International Statistical Classification of Diseases and Related Health Problems or ICD-10. This list uses that classification.

H00-H06 Disorders of eyelid, lacrimal system and orbit

- (H00.0) Hordeolum ("stye" or "sty") — a bacterial infection of sebaceous glands of eyelashes.
- (H00.1) Chalazion — a cyst in the eyelid (usually upper eyelid)
- (H01.0) Blepharitis — inflammation of eyelids and eyelashes; characterized by white flaky skin near the eyelashes
- (H02.0) Entropion and trichiasis
- (H02.1) Ectropion
- (H02.2) Lagophthalmos
- (H02.3) Blepharochalasis
- (H02.4) Ptosis
- (H02.6) Xanthelasma of eyelid
- (H03.0*) Parasitic infestation of eyelid in diseases classified elsewhere
    - Dermatitis of eyelid due to Demodex species (B88.0+)
    - Parasitic infestation of eyelid in:
        - leishmaniasis (B55.-+)
        - loiasis (B74.3+)
        - onchocerciasis (B73+)
        - phthiriasis (B85.3+)
- (H03.1*) Involvement of eyelid in other infectious diseases classified elsewhere
    - Involvement of eyelid in:
        - herpesviral (herpes simplex) infection (B00.5+)
        - leprosy (A30.-+)
        - molluscum contagiosum (B08.1+)
        - tuberculosis (A18.4+)
        - yaws (A66.-+)
        - zoster (B02.3+)
- (H03.8*) Involvement of eyelid in other diseases classified elsewhere
    - Involvement of eyelid in impetigo (L01.0+)
- (H04.0) Dacryoadenitis

- (H04.2) Epiphora
- (H06.2*) Dysthyroid exophthalmos it is shown that if your eye comes out that it will shrink because the optic fluids drain out

H10-H13 Disorders of conjunctiva

- (H10) Conjunctivitis — inflammation of the conjunctiva
- (H11.0) Pterygium — benign growth of the conjunctiva
- (H11.3) Subconjunctival hemorrhage — burst blood vessels on conjunctiva
- (H13.1*) Conjunctivitis in infectious and parasitic diseases classified elsewhere
    - Conjunctivitis (due to):
        - Acanthamoeba (B60.1+)
        - adenoviral follicular (acute) (B30.1+)
        - chlamydial (A74.0+)
        - diphtheritic (A36.8+)
        - gonococcal (A54.3+)
        - haemorrhagic (acute)(epidemic) (B30.3+)
        - herpesviral [herpes simplex] (B00.5+)
        - meningococcal (A39.8+)
        - Newcastle (B30.8+)
        - zoster (B02.3+)

H15-H22 Disorders of sclera, cornea, iris and ciliary body

- (H15.0) Scleritis — a painful inflammation of the sclera
- (H16) Keratitis — inflammation of the cornea
- (H16.0) Corneal ulcer / Corneal abrasion — loss of the surface epithelial layer of the eye's cornea
- (H16.1) Snow blindness / Arc eye — a painful condition caused by exposure of unprotected eyes to bright light
- (H16.1) Thygeson's superficial punctate keratopathy
- (H16.4) Corneal neovascularization
- (H18.5) Fuchs' dystrophy — cloudy morning vision
- (H18.6) Keratoconus — the cornea thins and changes shape to be more like a cone than a parabole
- (H19.3) Keratoconjunctivitis sicca — dry eyes
- (H20.0) Iritis — inflammation of the iris
- (H20.0, H44.1) Uveitis — inflammatory process involving the interior of the eye; Sympathetic ophthalmia is a subset.

H25-H28 Disorders of lens

- (H25-H26) Cataract — the lens becomes opaque

H30-H36 Disorders of choroid and retina

H30 Chorioretinal inflammation

(H30) Chorioretinal inflammation

- (H30.0) Focal chorioretinal inflammation
    - Focal:
        - chorioretinitis
        - choroiditis
        - retinitis
        - retinochoroiditis
- (H30.1) Disseminated chorioretinal inflammation
    - Disseminated:
        - chorioretinitis
        - choroiditis
        - retinitis
        - retinochoroiditis

    - Excludes: exudative retinopathy (H35.0)

- (H30.2) Posterior cyclitis
    - Pars planitis
- (H30.8) Other chorioretinal inflammations
    - Harada's disease
- (H30.9) Chorioretinal inflammation, unspecified
    - Chorioretinitis
    - Choroiditis
    - Retinitis

    - Retinochoroiditis

H31 Other disorders of choroid

(H31) Other disorders of choroid

- (H31.0) Chorioretinal scars
    - Macula scars of posterior pole (postinflammatory) (post-traumatic)
    - Solar retinopathy
- (H31.1) Choroidal degeneration
    - Atrophy
    - Sclerosis
        - Excludes: angioid streaks (H35.3)
- (H31.2) Hereditary choroidal dystrophy
    - Choroideremia
    - Dystrophy, choroidal (central areolar) (generalized) (peripapillary)

    - Gyrate atrophy, choroid
        - Excludes: ornithinaemia (E72.4)
- (H31.3) Choroidal haemorrhage and rupture
    - Choroidal haemorrhage:
        - NOS (Not Otherwise Specified)
        - expulsive
- (H31.4) Choroidal detachment
- (H31.8) Other specified disorders of choroid
- (H31.9) Disorder of choroid, unspecified

H32 Chorioretinal disorders in diseaseas classified elsewhere

(H32) Chorioretinal disorders in diseases classified elsewhere

- (H32.0) Chorioretinal inflammation in infectious and parasitic diseases classified elsewhere
    - Chorioretinitis:
        - syphilitic, late (A52.7+)
        - toxoplasma (B58.0+)
        - tuberculous (A18.5+)
- (H32.8) Other chorioretinal disorders in diseases classified elsewhere

H33 Retinal detachments and breaks

- (H33) Retinal detachment — the retina detaches from the choroid, leading to blurred and distorted vision
- (H33.1) Retinoschisis — the retina separates into several layers and may detach

H35 Other retinal disorders

- (H35.0) Hypertensive retinopathy — burst blood vessels, due to long-term high blood pressure
    - (H35.0/E10-E14) Diabetic retinopathy — damage to the retina caused by complications of diabetes mellitus, which could eventually lead to blindness
- (H35.0-H35.2) Retinopathy — general term referring to non-inflammatory damage to the retina
- (H35.1) Retinopathy of prematurity — scarring and retinal detachment in premature babies
- (H35.3) Age-related macular degeneration — the photosensitive cells in the macula malfunction and over time cease to work
- (H35.3) Macular degeneration — loss of central vision, due to macular degeneration
- (H35.3) Epiretinal membrane — a transparent layer forms and tightens over the retina
- (H35.4) Peripheral retinal degeneration

- (H35.5) Hereditary retinal dystrophy
- (H35.5) Retinitis pigmentosa — genetic disorder; tunnel vision preceded by night-blindness
- (H35.6) Retinal haemorrhage
- (H35.7) Separation of retinal layers
- (H35.8) Other specified retinal disorders
- (H35.81) Macular edema — distorted central vision, due to a swollen macula
- (H35.9) Retinal disorder, unspecified

H40-H42 Glaucoma

- (H40-H42) Glaucoma — optic neuropathy

H43-H45 Disorders of vitreous body and globe

- (H43.9) Floaters — shadow-like shapes which appear singly or together with several others in the field of vision

H46-H48 Disorders of optic nerve and visual pathways

- (H47.2) Leber's hereditary optic neuropathy — genetic disorder; loss of central vision
- (H47.3) Optic disc drusen — globules progressively calcify in the optic disc, compressing the vasculature and optic nerve fibers

H49-H52 Disorders of ocular muscles, binocular movement, accommodation and refraction

- (H49-H50) Strabismus (Crossed eye/Wandering eye/Walleye) — the eyes do not point in the same direction
    - (H49.3-4) Ophthalmoparesis — the partial or total paralysis of the eye muscles
    - (H49.4) Progressive external ophthalmoplegia — weakness of the external eye muscles
    - (H50.0, H50.3) Esotropia — the tendency for eyes to become cross-eyed
    - (H50.1, H50.3) Exotropia — the tendency for eyes to look outward
- H52 Disorders of refraction and accommodation
    - (H52.0) Hypermetropia (Farsightedness) — the inability to focus on near objects (and in extreme cases, any objects)
    - (H52.1) Myopia (Nearsightedness) — distant objects appear blurred
    - (H52.2) Astigmatism — the cornea or the lens of the eye is not perfectly spherical, resulting in different focal points in different planes
    - (H52.3) Anisometropia — the lenses of the two eyes have different focal lengths
    - (H52.4) Presbyopia — a condition that occurs with growing age and results in the inability to focus on close objects

    - (H52.5) Disorders of accommodation
        - Internal ophthalmoplegia

H53-H54.9 Visual disturbances and blindness

- (H53.0) Amblyopia (lazy eye) — poor or blurry vision due to either no transmission or poor transmission of the visual image to the brain
- (H53.0) Leber's congenital amaurosis — genetic disorder; appears at birth, characterised by sluggish or no pupillary responses
- (H53.1, H53.4) Scotoma (blind spot) — an area impairment of vision surrounded by a field of relatively well-preserved vision
- (H53.5) Color blindness — the inability to perceive differences between some or all colors that other people can distinguish
    - (H53.5) Achromatopsia / Maskun — a low cone count or lack of function in cone cells
- (H53.6) Nyctalopia (Nightblindness) — a condition making it difficult or impossible to see in the dark
- (H54) Blindness — the brain does not receive optical information, through various causes
    - (H54/B73) River blindness — blindness caused by long-term infection by a parasitic worm (rare in western societies)
    - (H54.9) micro-opthalmia/coloboma — a disconnection between the optic nerve and the brain and/or spinal cord

H55-H59 Other disorders of eye and adnexa

- (H57.9) Red eye — conjunctiva appears red typically due to illness or injury
- (H58.0) Argyll Robertson pupil — small, unequal, irregularly shaped pupils

Other codes

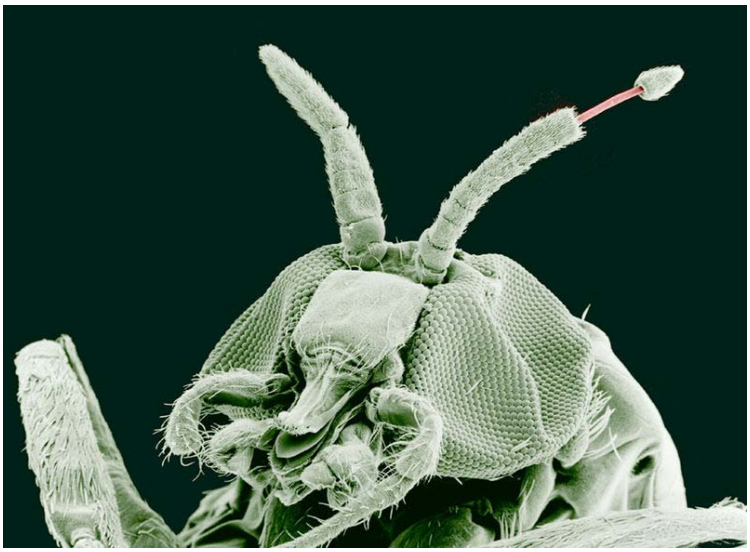
The following are not classified as diseases of the eye and adnexa (H00-H59) by the World Health Organization:

- (B36.1) Keratomycosis — fungal infection of the cornea
- (E50.6-E50.7) Xerophthalmia — dry eyes, caused by vitamin A deficiency
- (Q13.1) Aniridia — a rare congenital eye condition leading to underdevelopment or even absence of the iris of the eye

Chapter 6

Onchocerciasis

Onchocerciasis



Adult Black Fly (*Simulium yahense*) with parasite (*Onchocerca volvulus*) emerging from the insect's antenna. Magnified 100x.

ICD-10	B73.
ICD-9	125.3
DiseasesDB	9218
eMedicine	med/1667 oph/709
MeSH	D009855

Onchocerciasis also known as **river blindness** and **Robles' Disease**, is a parasitic disease caused by infection by *Onchocerca volvulus*, a nematode (roundworm). Onchocerciasis is the world's second-leading infectious cause of blindness. It is not the nematode but its endosymbiont, *Wolbachia pipientis*, that causes the severe inflammatory response that leaves many blind. The parasite is transmitted to humans through the bite of a blackfly of the genus *Simulium*. The larval nematodes spread throughout the body.

When the worms die their Wolbachia symbionts are released, triggering a host immune system response that causes intense itching and can destroy nearby tissue, such as the eye.

The vast majority of infections occur in sub-Saharan Africa, although cases have also been reported in Yemen and isolated areas of Central and South America. An estimated 18 million people suffer from onchocerciasis, with approximately 270,000 cases of blindness related to the infection.

In 1915, Dr. Rodolfo Robles Valverde's study on patients with river blindness in Guatemala led to the discovery that the disease is caused by filaria volvulus and sheds light on the life cycle and transmission of the parasite. Using case studies of coffee plantation workers in Guatemala, Robles hypothesized that the vector of the disease is a day-biting insect, and more specifically two anthrophilic species of Simulium flies found in the endemic areas. He publishes his findings on a “new disease” from Guatemala associated with subcutaneous nodules, anterior ocular lesions, dermatitis, and microfilariae in 1917.

Treatment may involve the use of the drug ivermectin. For best effect, entire communities are treated at the same time. A single dose may kill first-stage larvae (microfilariae) in infected people and prevents transmission for many months in the remaining population. Other drugs are also available including the tetracycline-class antibiotic doxycycline, which kills the Wolbachia and renders the female nematodes sterile. The removal of the palpable nodules is popular in Guatemala, Ecuador, and Mexico.

Classification

Onchocerciasis may be divided into the following phases or types:

Erisipela de la costa
: An acute phase characterized by swelling of the face with erythema and itching. Onchocerciasis causes different kinds of skin changes and these changes vary in different geographic regions. This skin change, erisípela de la costa, of acute onchocerciasis is most commonly seen among victims in Central and South America.

Mal morando
: A cutaneous condition characterized by inflammation that is accompanied by hyperpigmentation.

Sowda
: A cutaneous condition, a localized type of onchocerciasis.

Additionally, the various skin changes associated with onchocerciasis may be described as follows:

Leopard skin
: A term referring to the spotted depigmentation of the skin that may occur with onchocerciasis.

Elephant skin
: A term used to describe the thickening of human skin that may be associated with onchocerciasis.

Lizard skin
: A term used to describe the thickened, wrinkled skin changes that may result with onchocerciasis.

Life cycle of onchocerca volvulus

The life of the O. Volvulus parasite can be traced through the black fly and the human hosts in the following steps:

1. A Simulium female black fly takes a blood meal on an infected human host ingesting microfilaria.
2. The microfilaria enter the gut and thoracic flight muscles of the black fly progressing into the first larval stage (J1.).
3. The larvae mature into the second larval stage (J2.) and moves to the proboscis and into the saliva in its third larval stage (J3.). Mature in about 7 days.
4. The black fly takes another blood meal passing the larvae into the next human host's blood.
5. The larvae migrate to the subcutaneous tissue and undergo two more molts. They form nodules as they mature into adult worms over six to twelve months.
6. After maturing, adult male worms mate with female worms in the subcutaneous tissue to produce between 700 and 1,500 microfilaria per day.
7. The microfilaria migrate to the skin during the day and the black flies only feed in the day, so the parasite is in a prime position for the female fly to ingest it. Black flies take blood meals to ingest these microfilaria to restart the cycle.

Signs and symptoms

Adult worms remain in subcutaneous nodules, limiting access to the host's immune system. Microfilariae, in contrast, are able to induce intense inflammatory responses, especially upon their death. Dying microfilariae have been recently discovered to release *Wolbachia Surface Protein* that activates TLR2 and TLR4, triggering innate immune responses and producing the inflammation and its associated morbidity. Wolbachia species have been found to be endosymbionts of *O. volvulus* adults and microfilariae, and are thought to be the driving force behind most of *O. volvulus* morbidity. The severity of illness is directly proportional to the number of infected microfilariae and the power of the resultant inflammatory response.

Skin involvement typically consists of intense itching, swelling, and inflammation. A grading system has developed to categorize the degree of skin involvement:

- Acute papular onchodermatitis - scattered pruritic papules;
- Chronic papular onchodermatitis - larger papule, resulting in hyperpigmentation;
- Lichenified onchodermatitis - hyperpigmented papules and plaques, with edema, lymphadenopathy, pruritus and common secondary bacterial infections;
- Skin atrophy - loss of elasticity, skin resembles tissue paper, 'lizard skin' appearance;
- Depigmentation - 'leopard skin' appearance, usually on anterior lower leg.

Ocular involvement provides the common name associated with onchocerciasis, river blindness and may involve any part of the eye from conjunctiva and cornea to uvea and posterior segment including retina and optic nerve. The microfilariae migrate to the surface of the cornea. Punctate keratitis occurs in the infected area. This clears up as the inflammation subsides. However, if the infection is chronic, sclerosing keratitis can occur, making the affected area become opaque. Over time the entire cornea may become opaque, thus leading to blindness. There is some evidence to suggest that the effect on the cornea is caused by an immune response to bacteria present in the worms.

The Mazzotti reaction, first described in 1948, is a symptom complex seen in patients after undergoing treatment of onchocerciasis with the medication diethylcarbamazine (DEC). Mazzotti reactions can be life-threatening and are characterized by fever, urticaria, swollen and tender lymph nodes, tachycardia, hypotension, arthralgias, oedema, and abdominal pain that occur within seven days of treatment of microfilariasis. The phenomenon is so common when DEC is used for the treatment of onchocerciasis that this drug is the basis of a skin patch test used to confirm that diagnosis. The drug patch is placed on the skin, and if the patient is infected with the microfilaria of Onchocerca volvulus, localized pruritus and urticaria are seen at the application site.

Prevention

There are various control programs that aim to stop onchocerciasis from being a public health problem. The first was the Onchocerciasis Control Programme (OCP), which was launched in 1974 and at its peak covered 30 million people in eleven countries. Through the use of larvicide spraying of fast flowing rivers to control black fly populations and, from 1988 onwards, the use of ivermectin to treat infected people, the OCP eliminated onchocerciasis as a public health problem. The OCP, a joint effort of the World Health Organisation, the World Bank, the United Nations Development Programme and the UN Food and Agriculture Organization, was considered to be a success and came to an end in 2002. Continued monitoring ensures that onchocerciasis cannot reinvade the area of the OCP.

In 1992 the Onchocerciasis Elimination Programme for the Americas (OEPA) was launched. The OEPA also relies on ivermectin.

In 1995 the African Programme for Onchocerciasis Control (APOC) began covering another nineteen countries and mainly relying upon the use of ivermectin. Its goal is to

set up a community-directed supply of ivermectin for those who are infected. In these ways, transmission has declined.

Treatment

The burden of onchocerciasis: children leading blind adults in Africa.

In mass drug administration (MDA) programmes, the treatment for onchocerciasis is ivermectin (trade name: Mectizan); infected people can be treated with two doses of ivermectin, six months apart, repeated every three years. The drug paralyses and kills the microfilariae, causing fever, itching, and possibly oedema, arthritis and lymphadenopathy. Intense skin itching is eventually relieved and progression towards blindness halted. In addition, while the drug does not kill the adult worm, it does prevent them from producing additional offspring. The drug therefore prevents both morbidity and transmission.

Ivermectin treatment is particularly effective because it only needs to be taken once or twice a year, needs no refrigeration, and has a wide margin of safety, with the result that it has been widely given by minimally trained community health workers.

Antibiotics

For the treatment of individuals, doxycycline is used to kill the Wolbachia bacteria that lives in adult worms. This adjunct therapy has been shown to significantly lower microfilarial loads in the host, and may have activity against the adult worms, due to the symbiotic relationship between Wolbachia and the worm. In four separate trials over ten years with various dosing regimes of doxycycline for individualized treatment, doxycycline was found to be effective in sterilizing the female worms and reducing their numbers over a period of four to six weeks. Research on other antibiotics such as rifampicin has shown it to been effective in animal models at reducing Wolbachia both as an alternative and as an adjunct to doxycycline. However, doxycycline treatment requires daily dosing for at least four to six weeks, making it more difficult to administer in the affected areas.

Ivermectin

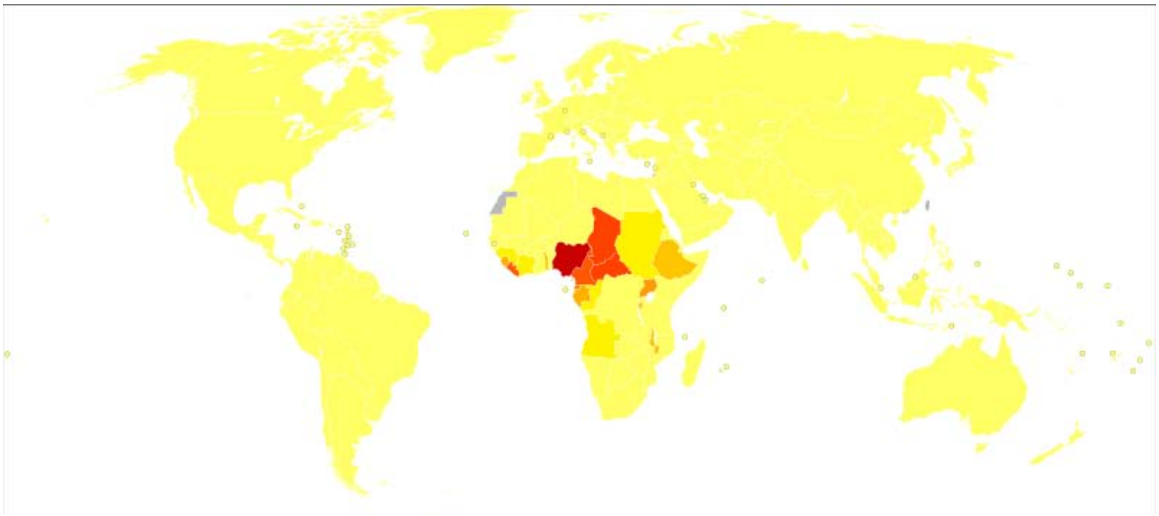
Ivermectin kills the parasite by interfering with the nervous system and muscle function, in particular, by enhancing inhibitory neurotransmission. The drug binds to and activates glutamate-gated chloride channels (GluCls). These channels, present in neurons and myocytes, are not invertebrate-specific, but are protected in vertebrates from the action of ivermectin by the blood-brain barrier. Ivermectin is thought to irreversibly activate these channel receptors in the worm, eventually causing an inhibitory postsynaptic potential (IPSP). The chance of a future action potential occurring in synapses between neurons decreases and the nematodes experience flaccid paralysis followed by death.

Ivermectin is directly effective against the larval stage microfilariae *Onchocerca volvulus*, which it paralyzes so that they can be killed by eosinophils and macrophages. Ivermectin does not kill adult females (macrofilariae) but causes them to cease releasing microfilariae, perhaps by paralyzing the reproductive tract.

Since 1988, ivermectin has been provided free of charge for use in humans by Merck through the Mectizan donation program (MDP). The MDP works together with ministries of health and non-governmental development organisations such as the World Health Organization to provide free ivermectin to those who need it in endemic areas.

A study of 2501 people in Ghana showed that the prevalence rate doubled between 2000 and 2005 despite treatment, suggesting that the parasite is developing resistance to the drug. A clinical trial of another antiparasitic agent, moxidectin (manufactured by Wyeth), began on July 1, 2009 (NCT00790998).

Epidemiology



Disability-adjusted life year for onchocerciasis per 100,000 inhabitants.
- no data
- less than 10
- 10-50
- 50-60
- 60-70
- 70-80
- 80-90
- 90-100
- 100-150
- 150-200
- 200-300
- 300-400
- more than 400

99% of onchocerciasis cases occur in Africa. As of 2008 about 18 million people were infected with this parasite; approximately 300,000 had been permanently blinded. Onchocerciasis is currently endemic in 30 African countries, Yemen, and isolated regions of South America. Travelers who do not stay long in those areas have little risk of developing the disease as it requires prolonged exposure to the fly bites and parasite introduction.

Onchocerciasis is endemic in 36 countries across Africa, Latin America and Yemen. Over 85 million people live in endemic areas and half of these reside in Nigeria. Another 120 million people are at risk for contracting the disease. Due to the vector's breeding habitat, the disease is more severe along the major rivers in the northern and central areas of the continent, and severity declines in villages farther from rivers.

According to a 2002 WHO report, Onchocerciasis has not caused a single death, but its global burden is 987,000 disability adjusted life years (DALYs). The severe pruritis alone

accounts for 60% of the DALYs. Infection reduces the host's immunity and resistance to other diseases. This results in an estimated reduction in life expectancy of 13 years.

Research

Animal models for the disease are somewhat limited, as the parasite only lives in primates, but there are close parallels. *Litomosoides sigmodontis*, which will naturally infect cotton rats, has been found to fully develop in BALB/c mice. *Onchocerca ochengi*, the closest relative of *O. volvulus*, lives in intradermal cavities in cattle and is also spread by blackflies. Both systems are useful but not exact animal models.

Chapter 7

Conjunctivitis

Conjunctivitis

An eye with viral conjunctivitis.

ICD-10	H10.
ICD-9	372.0
DiseasesDB	3067
MedlinePlus	001010
eMedicine	emerg/110
MeSH	D003231

Conjunctivitis (also called **pink eye** or **madras eye**) refers to inflammation of the conjunctiva (the outermost layer of the eye and the inner surface of the eyelids). It is most commonly due to an infection (usually viral, but sometimes bacterial) or an allergic reaction.

Classification

Classification can be either by cause or by extent of the inflamed area.

By cause

- Allergic conjunctivitis
- Bacterial conjunctivitis
- Viral conjunctivitis
- Chemical conjunctivitis
- Neonatal conjunctivitis is often defined separately due to different organisms

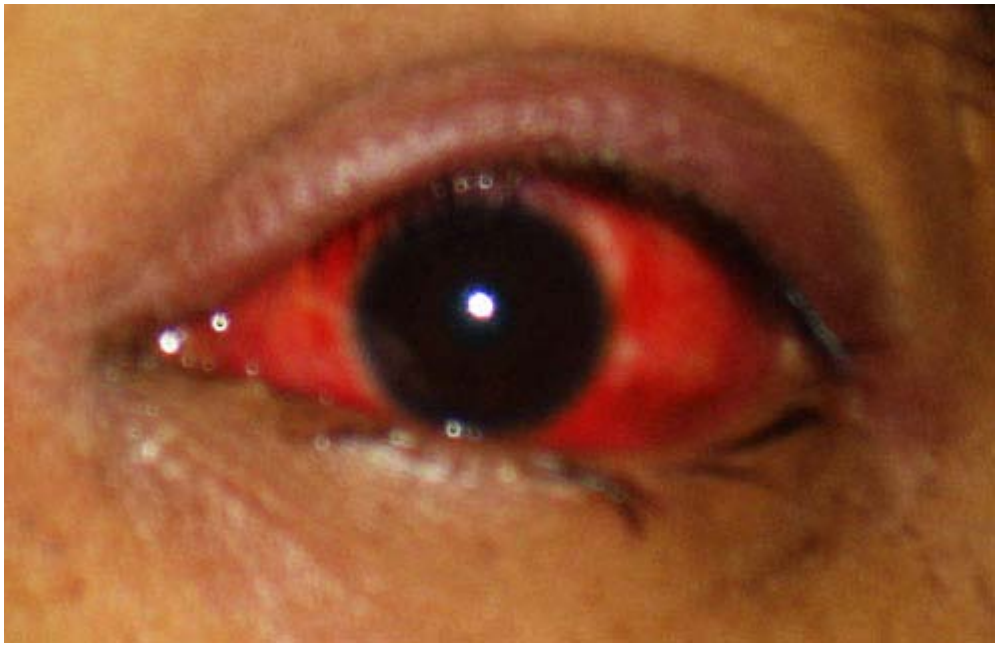
By extent of involvement

Blepharoconjunctivitis is the dual combination of conjunctivitis with blepharitis (inflammation of the eyelids).

Keratoconjunctivitis is the combination of conjunctivitis and keratitis (corneal inflammation).

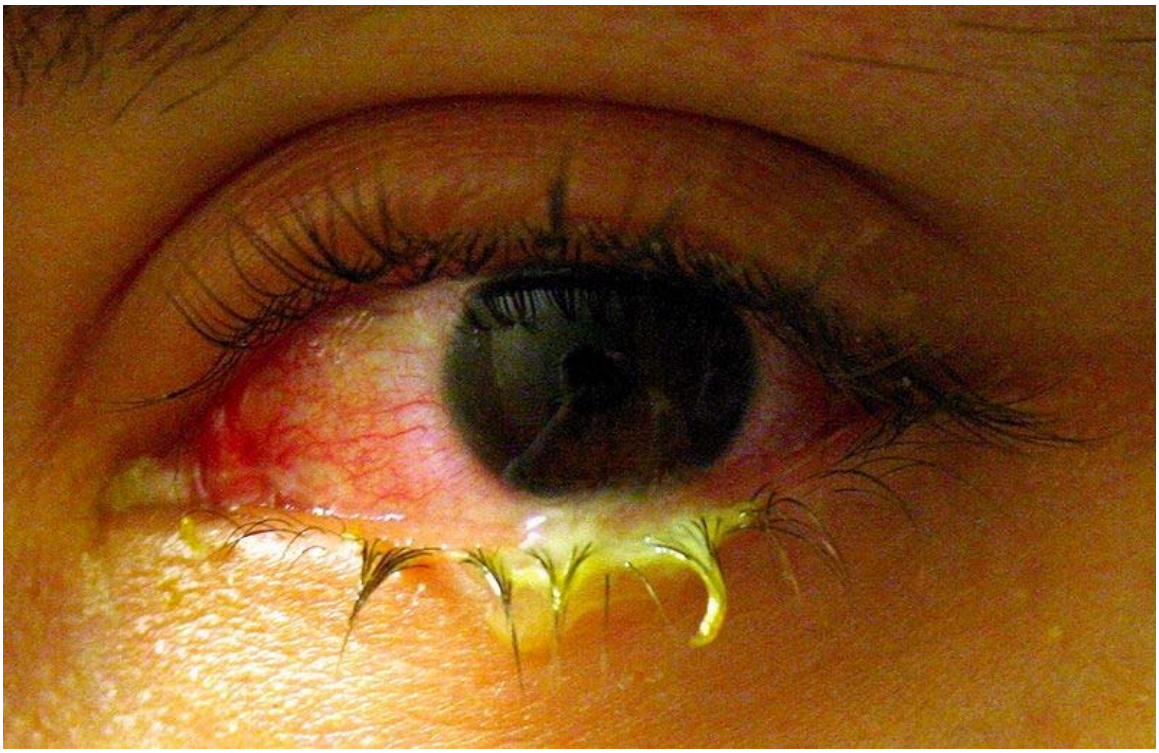
Episcleritis is an inflammatory condition that produces a similar appearance to conjunctivitis, but without discharge or tearing.

Signs and symptoms



An eye, red due to acute conjunctivitis

Eyes with conjunctivitis



An eye with bacterial conjunctivitis

Red eye (hyperaemia), irritation (chemosis) and watering (epiphora) of the eyes are symptoms common to all forms of conjunctivitis. However the pupils should be normally reactive and the visual acuity normal.

Viral

Viral conjunctivitis is often associated with an infection of the upper respiratory tract, a common cold, and/or a sore throat. Its symptoms include watery discharge and variable itch. The infection usually begins with one eye, but may spread easily to the other.

Viral conjunctivitis, commonly known as "pink eye" shows a fine diffuse pinkness of the conjunctiva which is easily mistaken for the 'ciliary injection' of iritis, but there are

usually corroborative signs on microscopy, particularly numerous lymphoid follicles on the tarsal conjunctiva, and sometimes a punctate keratitis.

Bacterial

Bacterial conjunctivitis due to the common pyogenic (pus-producing) bacteria causes marked grittiness/irritation and a stringy, opaque, greyish or yellowish mucopurulent discharge that may cause the lids to stick together, especially after sleep. Another symptom that could be caused by bacterial conjunctivitis is severe crusting of the infected eye and the surrounding skin. However discharge is not essential to the diagnosis, contrary to popular belief. Bacteria such as *Chlamydia trachomatis* or *Moraxella* can cause a non-exudative but persistent conjunctivitis without much redness. The gritty and/or scratchy feeling is sometimes localized enough for patients to insist they must have a foreign body in the eye. The more acute pyogenic infections can be painful. Like viral conjunctivitis, it usually affects only one eye but may spread easily to the other eye. However, it is dormant in the eye for three days before the patient shows signs of symptoms.

Chemical

Chemical eye injury is due to either an acidic or alkali substance getting in the eye. Alkalis are typically worse than acidic burns. Mild burns will produce conjunctivitis while more severe burns may cause the cornea to turn white. Litmus paper is an easy way to rule out the diagnosis by verifying that the pH is within the normal range of 7.0—7.2. Large volumes of irrigation is the treatment of choice and should continue until the pH is 6—8. Local anaesthetic eye drops can be used to decrease the pain.

Irritant or toxic conjunctivitis show primarily marked redness. If due to splash injury, it is often present only in the lower conjunctival sac. With some chemicals, above all, with caustic alkalis such as sodium hydroxide—there may be necrosis of the conjunctiva with a deceptively white eye due to vascular closure, followed by sloughing of the dead epithelium. This is likely to be associated with slit-lamp evidence of anterior uveitis.

Other

Inclusion conjunctivitis of the newborn (ICN) is a conjunctivitis that may be caused by the bacteria *Chlamydia trachomatis*, and may lead to acute, purulent conjunctivitis. However, it is usually self-healing.

Conjunctivitis is identified by irritation and redness of the conjunctiva. Except in obvious pyogenic or toxic/chemical conjunctivitis, a slit lamp (biomicroscope) is needed to have any confidence in the diagnosis. Examination of the tarsal conjunctiva is usually more diagnostic than the bulbar conjunctiva.

Causes

Conjunctivitis is most commonly caused by viral infection, but bacterial infections, allergies, other irritants and dryness are also common etiologies for its occurrence. Both bacterial and viral infections are contagious. Commonly, conjunctival infections are passed from person-to-person, but can also spread through contaminated objects or water.

The most common cause of viral conjunctivitis is adenoviruses. Herpetic keratoconjunctivitis (caused by herpes simplex viruses) can be serious and requires treatment with acyclovir. Acute hemorrhagic conjunctivitis is a highly contagious disease caused by one of two enteroviruses, Enterovirus 70 and Coxsackievirus A24. These were first identified in an outbreak in Ghana in 1969 and have spread worldwide since then, causing several epidemics.

Differential diagnosis

Conjunctivitis is a relatively non-specific symptom. Even after bio microscopy, laboratory tests are often necessary if proof of etiology is needed.

A purulent discharge (a whitish-yellow, yellow or yellow-brown substance more commonly known as pus) strongly suggests a cause from fecal matter, unless there is known exposure to toxins. It can also be caused by bacteria from feces, pet hair, or by smoke or other fumes. Infection with *Neisseria gonorrhoeae* should be suspected if the discharge is particularly thick and copious.

Itching (rubbing eyes) is the hallmark symptom of allergic conjunctivitis. Other symptoms include past history of eczema, or asthma.

A diffuse, less "injected" conjunctivitis (looking pink rather than red) suggests a viral cause, especially if numerous follicles are present on the lower tarsal conjunctiva on bio microscopy.

Scarring of the tarsal conjunctiva suggests trachoma, especially if seen in endemic areas, if the scarring is linear (von Arlt's line), or if there is also corneal vascularisation.

Clinical tests for lagophthalmos, dry eye (Schirmer test) and unstable tear film may help distinguish the various types of conjunctivitis.

Other symptoms including pain, blurring of vision and photophobia should not be prominent in conjunctivitis. Fluctuating blurring is common, due to tearing and mucoid discharge. Mild photophobia is common. However, if any of these symptoms are prominent, it is important to exclude other diseases such as glaucoma, uveitis, keratitis and even meningitis or caroticocavernous fistula.

Many people who have conjunctivitis have trouble opening their eyes in the morning because of the dried mucus on their eyelids. There is often excess mucus over the eye after sleeping for an extended period.

Diagnosis

These are done infrequently because most cases of conjunctivitis are treated empirically and (eventually) successfully, but often only after running the gamut of the common possibilities.

Swabs for bacterial culture are necessary if the history and signs suggest bacterial conjunctivitis, but there is no response to topical antibiotics. Research studies indicate that many bacteria implicated in low-grade conjunctivitis are not detected by the usual culture methods of medical microbiology labs, so false negative results are common. Viral culture may be appropriate in epidemic case clusters. Conjunctival scrapes for cytology can be useful in detecting chlamydial and fungal infections, allergy and dysplasia, but are rarely done because of the cost and the general lack of laboratory staff experienced in handling ocular specimens. Conjunctival incisional biopsy is occasionally done when granulomatous diseases (e.g., sarcoidosis) or dysplasia are suspected.

Management

Conjunctivitis resolves in 65% of cases without treatment, within 2 – 5 days. The prescribing of antibiotics to most cases is not necessary.

Allergic

For the allergic type, cool water poured over the face with the head inclined downward constricts capillaries, and artificial tears sometimes relieve discomfort in mild cases. In more severe cases, non-steroidal anti-inflammatory medications and antihistamines may be prescribed. Persistent allergic conjunctivitis may also require topical steroid drops.

Bacterial

Bacterial conjunctivitis usually resolves without treatment. Antibiotics, eye drops, or ointment are thus only needed if no improvement is observed after 3 days. In patients receiving no antibiotics recovery was in 4.8 days, immediate antibiotics 3.3 days, delayed antibiotics 3.9 days. No serious effects were noted either with or without treatment.

Viral

Although there is no specific treatment for viral conjunctivitis, symptomatic relief may be achieved with cold compresses and artificial tears. People are often advised to avoid touching their eyes or sharing towels and washcloths.

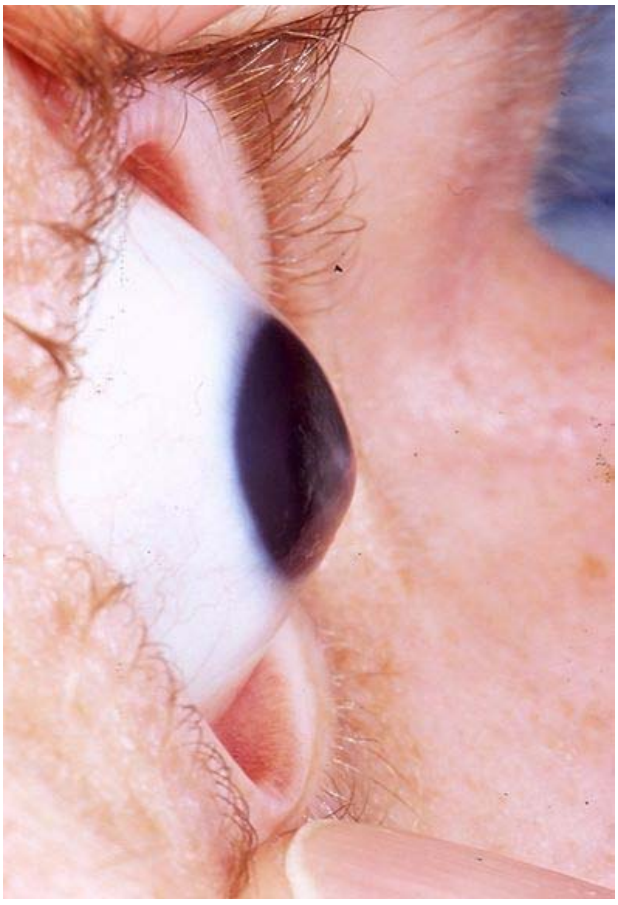
Chemical

Conjunctivitis due to chemicals is treated via irrigation with Ringer's lactate or saline solution. Chemical injuries (particularly alkali burns) are medical emergencies as they can lead to severe scarring, and intraocular damage.Do not touch your eyes. Even if you washed your hands still no touching. This may cause it to spread on to another eye.

Chapter 8

Keratoconus

Keratoconus



The "conical cornea" that is characteristic of keratoconus

ICD-10	H18.6
ICD-9	371.6
OMIM	148300
DiseasesDB	7158

MedlinePlus	001013
eMedicine	oph/104

Keratoconus (from Greek: *kerato-* horn, cornea; and *konos* cone), is a degenerative disorder of the eye in which structural changes within the cornea cause it to thin and change to a more conical shape than its normal gradual curve.

Keratoconus can cause substantial distortion of vision, with multiple images, streaking and sensitivity to light all often reported by the patient. It is typically diagnosed in the patient's adolescent years and attains its most severe state in the twenties and thirties. If afflicting both eyes, the deterioration in vision can affect the patient's ability to drive a car or read normal print. In most cases, corrective lenses are effective enough to allow the patient to continue to drive legally and likewise function normally. Further progression of the disease may require surgery including intrastromal corneal ring segments, corneal collagen cross-linking, or corneal transplantation. However, despite the disease's unpredictable course, keratoconus can often be successfully managed with little or no impairment to the patient's quality of life.

Keratoconus affects around one person in a thousand. It seems to occur in populations throughout the world, although it occurs more frequently in certain ethnic groups such as South Asians. The exact cause of keratoconus is uncertain, but has been associated with detrimental enzyme activity within the cornea. A genetic link seems likely, as the incidence rate is greater if a family member has been diagnosed. The progression of keratoconus is rapid in patients having Down syndrome.

Signs and symptoms

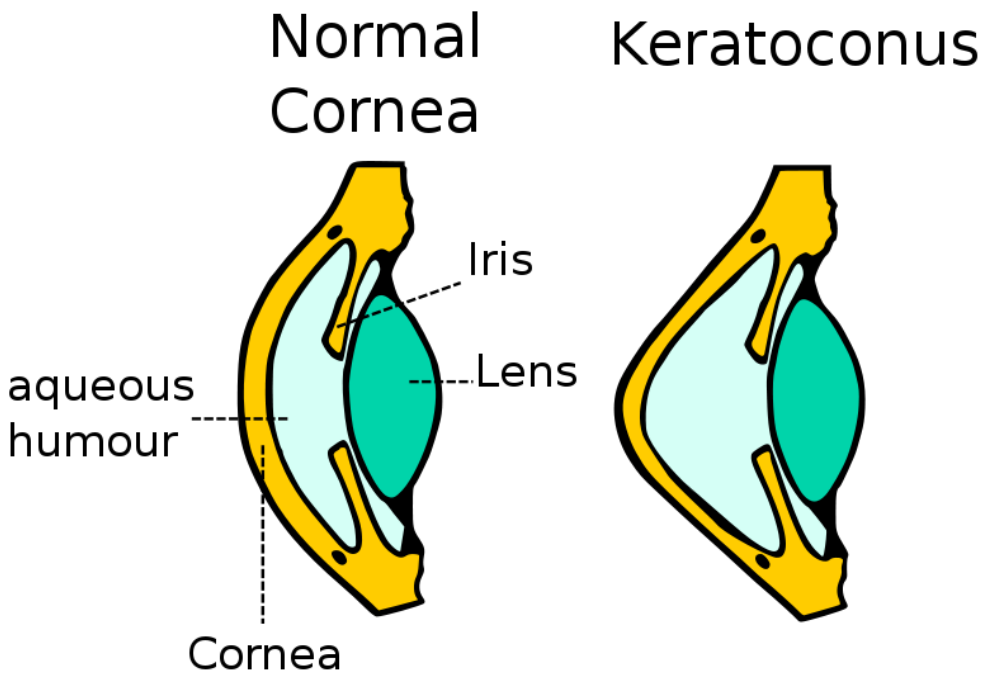
multiple images seen by a person with keratoconus.
"... a candle, when looked at, appears like a number of lights, confusedly running into one another" — Nottingham

People with early keratoconus typically notice a minor blurring of their vision and come to their clinician seeking corrective lenses for reading or driving. At early stages, the symptoms of keratoconus may be no different from those of any other refractive defect of the eye. As the disease progresses, vision deteriorates, sometimes rapidly. Visual acuity becomes impaired at all distances, and night vision is often quite poor. Some individuals have vision in one eye that is markedly worse than that in the other eye. The disease is often bilateral, though asymmetrical in many patients. Some develop photophobia (sensitivity to bright light), eye strain from squinting in order to read, or itching in the eye, but there is normally little or no sensation of pain.

The classic symptom of keratoconus is the perception of multiple 'ghost' images, known as monocular polyopia. This effect is most clearly seen with a high contrast field, such as a point of light on a dark background. Instead of seeing just one point, a person with keratoconus sees many images of the point, spread out in a chaotic pattern. This pattern does not typically change from day to day, but over time it often takes on new forms. Patients also commonly notice streaking and flaring distortion around light sources. Some even notice the images moving relative to one another in time with their heart beat.

The predominant optical aberration of the eye as an optical system in keratoconus is the so-called coma.

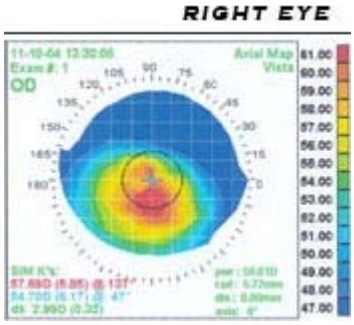
Diagnosis



A schematic digram showing change in cornea

Prior to any physical examination, the diagnosis of keratoconus frequently begins with an ophthalmologist's or optometrist's assessment of the patient's medical history, particularly the chief complaint and other visual symptoms, the presence of any history of ocular disease or injury which might affect vision, and the presence of any family history of ocular disease. An eye chart, such as a standard Snellen chart of progressively smaller letters, is then used to determine the patient's visual acuity. The eye examination may proceed to measurement of the localised curvature of the cornea with a manual keratometer, with detection of irregular astigmatism suggesting a possibility of keratoconus. Severe cases can exceed the instrument's measuring ability. A further indication can be provided by retinoscopy, in which a light beam is focused on the patient's retina and the reflection, or *reflex*, observed as the examiner tilts the light source back and forth. Keratoconus is amongst the ophthalmic conditions that exhibit a *scissor reflex* action of two bands moving toward and away from each other like the blades of a pair of scissors.

If keratoconus is suspected, the ophthalmologist or optometrist will search for other characteristic findings of the disease by means of slit lamp examination of the cornea. An advanced case is usually readily apparent to the examiner, and can provide for an unambiguous diagnosis prior to more specialised testing. Under close examination, a ring of yellow-brown to olive-green pigmentation known as a Fleischer ring can be observed in around half of keratoconic eyes. The Fleischer ring, caused by deposition of the iron oxide hemosiderin within the corneal epithelium, is subtle and may not be readily detectable in all cases, but becomes more evident when viewed under a cobalt blue filter. Similarly, around 50% of subjects exhibit Vogt's striae, fine stress lines within the cornea caused by stretching and thinning. The striae temporarily disappear while slight pressure is applied to the eyeball. A highly pronounced cone can create a V-shaped indentation in the lower eyelid when the patient's gaze is directed downwards, known as Munson's sign. Other clinical signs of keratoconus will normally have presented themselves long before Munson's sign becomes apparent, and so this finding, though a classic sign of the disease, tends not to be of primary diagnostic importance.



Corneal topogram of a keratoconic eye

A handheld keratoscope, sometimes known as *Placido's disk*, can provide a simple non-invasive visualization of the surface of the cornea by projecting a series of concentric rings of light onto the cornea. A more definitive diagnosis can be obtained using corneal

topography, in which an automated instrument projects the illuminated pattern onto the cornea and determines its topology from analysis of the digital image. The topographical map indicates any distortions or scarring in the cornea, with keratoconus revealed by a characteristic steepening of curvature which is usually below the centreline of the eye. The technique can record a snapshot of the degree and extent of the deformation as a benchmark for assessing its rate of progression. It is of particular value in detecting the disorder in its early stages when other signs have not yet presented.

Once keratoconus has been diagnosed, its degree may be classified by several metrics:

- The steepness of greatest curvature from *mild* (< 45 D), *advanced* (up to 52 D) or *severe* (> 52 D);
- The morphology of the cone: *nipple* (small: 5 mm and near-central), *oval* (larger, below-center and often sagging), or *globus* (more than 75% of cornea affected);
- The corneal thickness from mild (> 506 μm) to advanced (< 446 μm).

Increasing use of corneal topography has led to a decline in use of these terms.

Cause

A specimen of keratoconic cornea taken out six years after diagnosis: thin stroma, wrinkled posterior surface.

Despite considerable research, the etiology of keratoconus remains somewhat of a mystery. A number of sources suggest that keratoconus likely arises from a number of different factors: genetic, environmental or cellular, any of which may form the trigger for the onset of the disease.

A genetic predisposition to keratoconus has been observed, with the disease running in certain families, and incidences reported of concordance in identical twins. The frequency of occurrence in close family members is not clearly defined, though it is known to be considerably higher than that in the general population, and studies have obtained estimates ranging between 6% and 19%. A responsible gene has not been identified: two studies involving isolated, largely homogenetic communities have contrarily mapped putative gene locations to chromosomes 16q and 20q. However, most genetic studies agree on an autosomal dominant model of inheritance. Keratoconus is also diagnosed more often in people with Down syndrome, though the reasons for this link have not yet been determined. Keratoconus has been associated with atopic diseases, which include asthma, allergies, and eczema, and it is not uncommon for several or all of these diseases to affect one person. A number of studies suggest that vigorous eye rubbing contributes to the progression of keratoconus, and that patients should be discouraged from the practice.

Iatrogenic keratoconus has also been observed following LASIK surgery, caused by removal of excessive stromal bed tissue.

Pathophysiology

Once initiated, the disease normally develops by progressive dissolution of Bowman's layer, which lies between the corneal epithelium and stroma. As the two come into contact, cellular and structural changes in the cornea adversely affect its integrity and lead to the bulging and scarring that are characteristic of the disorder. Within any individual keratoconic cornea, there may be found regions of degenerative thinning coexisting with regions undergoing wound healing.

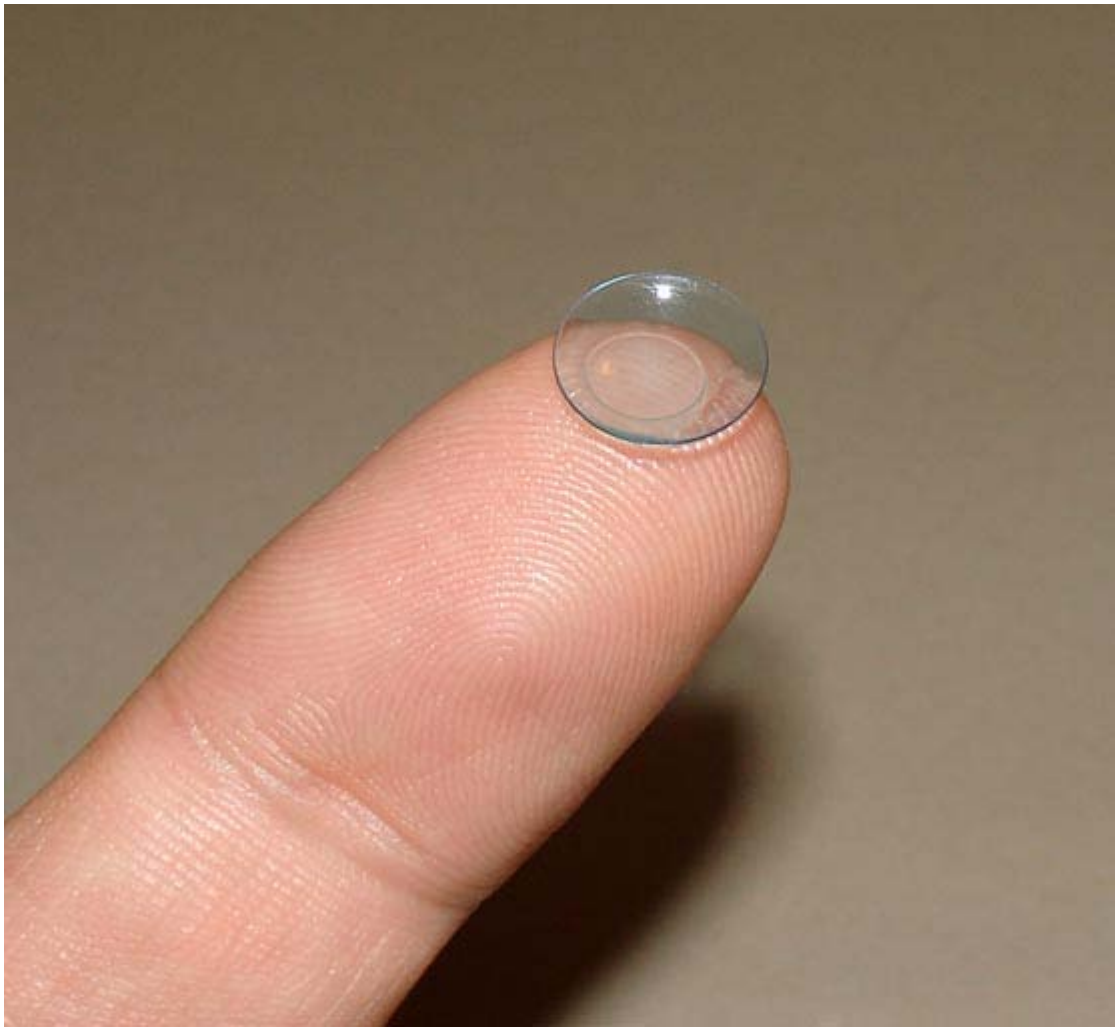
The visual distortion experienced by the patient comes from two sources, one being the irregular deformation of the surface of the cornea; the other being scarring that occurs on its exposed highpoints. These factors act to form regions on the cornea that map an image to different locations on the retina and give rise to the symptom of monocular polyopia. The effect can worsen in low light conditions as the dark-adapted pupil dilates to expose more of the irregular surface of the cornea. Scarring appears to be an aspect of the corneal degradation; however, a recent, large, multi-center study suggests that abrasion by contact lenses may increase the likelihood of this finding by a factor of over two. A number of patients complain of chronic eye rubbing and also think it as a possible cause to the disease but it is not so; however, it has been observed that keratoconus progresses faster due to eye-rubbing.

A number of studies have indicated that keratoconic corneas show signs of increased activity by proteases, a class of enzymes that break some of the collagen cross-linkages in

the stroma, with a simultaneous reduced expression of protease inhibitors. Other studies have suggested that reduced activity by the enzyme aldehyde dehydrogenase may be responsible for a build-up of free radicals and oxidising species in the cornea. It seems likely that, whatever the pathogenetical process, the damage caused by activity within the cornea results in a reduction in its thickness and biomechanical strength. While keratoconus is considered a non-inflammatory disorder, one study shows that rigid contact lens wear by patients leads to overexpression of pro-inflammatory cytokines, such as IL-6, TNF-alpha, ICAM-1, and VCAM-1 in the tear fluid.

Treatment

Contact lenses



Rigid gas permeable lens for keratoconus

In early stages of keratoconus, spectacles or soft contact lenses can suffice to correct for the mild astigmatism. As the condition progresses, these may no longer provide the patient with a satisfactory degree of visual acuity, and most clinical practitioners will

move to managing the condition with rigid contact lenses, known as rigid gas-permeables, or RGPs. RGP lenses provide a good level of visual correction, but do not arrest progression of the condition.

In keratoconic patients, rigid contact lenses improve vision by means of tear fluid filling the gap between the irregular corneal surface and the smooth regular inner surface of the lens, thereby creating the effect of a smoother cornea. Many specialized types of contact lenses have been developed for keratoconus, and affected people may seek out both doctors specialized in conditions of the cornea, and contact lens fitters who have experience managing patients with keratoconus. The irregular cone presents a challenge and the fitter will endeavour to produce a lens with the optimal contact, stability and steepness. Some trial-and-error fitting may prove necessary.

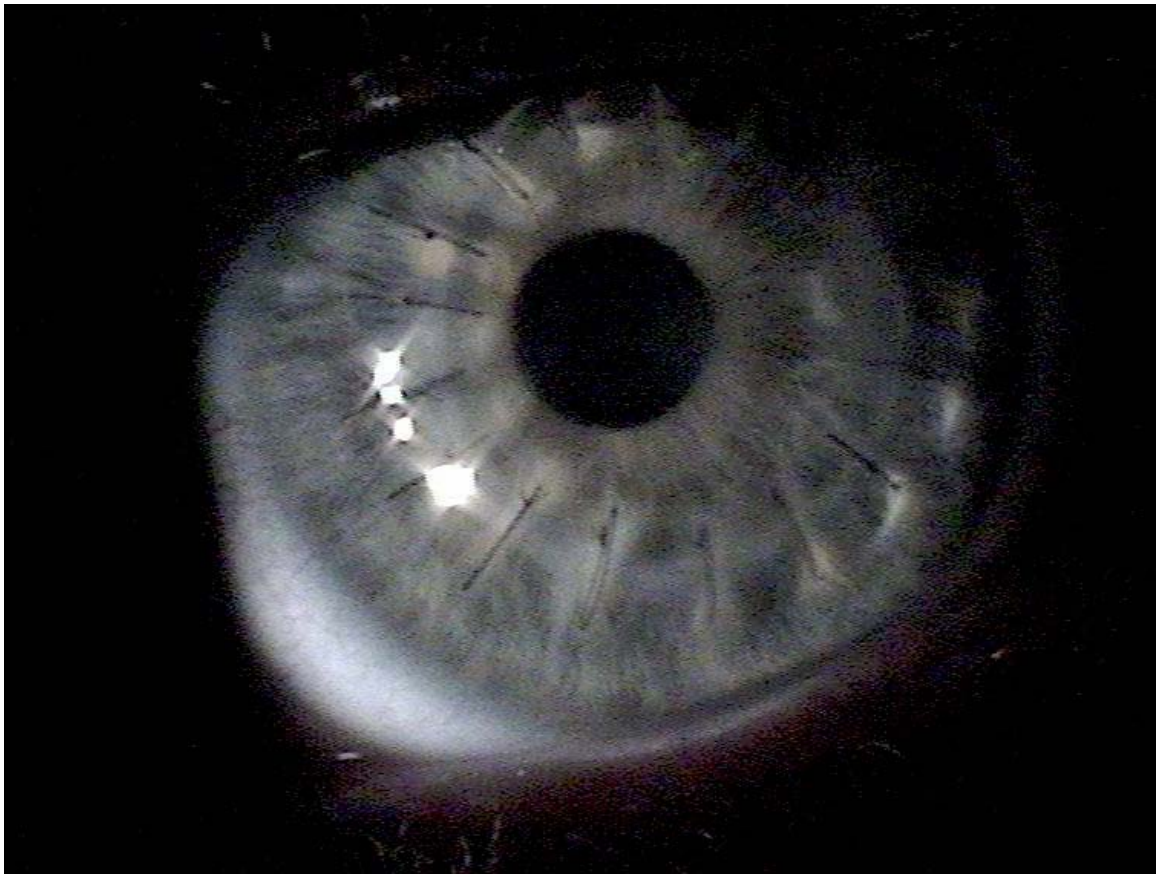
Traditionally, contact lenses for keratoconus have been the 'hard' or rigid gas-permeable variety, although manufacturers have also produced specialized 'soft' or hydrophilic lenses and, most recently, silicone hydrogel lenses. A soft lens has a tendency to conform to the conical shape of the cornea, thus diminishing its effect. To counter this, hybrid lenses have been developed which are hard in the centre and encompassed by a soft skirt. However, soft or earlier generation hybrid lenses did not prove effective for every patient. Early generation lenses like SoftPerm have been discontinued. The fourth generation of hybrid lens technology has improved significantly, giving more patients an option that combines the comfort of a soft lens with the visual acuity of an RGP lens. The new generation of technology fixes the issues that were prevalent in earlier generations and allows contact lenses to be fit for the majority of patients.

Some patients also find good vision correction and comfort with a "piggyback" lens combination, in which gas-permeable rigid lenses are worn over soft lenses, both providing a degree of vision correction. One form of piggyback lens makes use of a soft lens with a countersunk central area to accept the rigid lens. Fitting a piggyback lens combination requires experience on the part of the lens fitter, and tolerance on the part of the keratoconic patient.

Scleral lenses are sometimes prescribed for cases of advanced or very irregular keratoconus; these lenses cover a greater proportion of the surface of the eye and hence can offer improved stability. The larger size of the lenses may make them unappealing or uncomfortable to some; however, their easier handling can find favour with patients with reduced dexterity, such as the elderly.

Surgical options

Corneal transplant



Corneal transplant for keratoconus, approximately one week after surgery. Multiple light reflections indicate folds in the cornea which later resolved.

Between 10% and 25% of cases of keratoconus will progress to a point where vision correction is no longer possible, thinning of the cornea becomes excessive, or scarring as a result of contact lens wear causes problems of its own, and a corneal transplantation or *penetrating keratoplasty* becomes required. Keratoconus is the most common grounds for conducting a penetrating keratoplasty, generally accounting for around a quarter of such procedures. The corneal transplant surgeon trephines a lenticule of corneal tissue and then grafts the donor cornea to the existing eye tissue, usually using a combination of running and individual sutures. The cornea does not have a direct blood supply, and so donor tissue is not required to be blood type matched. Eye banks check the donor corneas for any disease or cellular irregularities.

Spanish-born eye surgeon Ramon Castroviejo successfully performed keratoplasty as early as 1936

The acute recovery period can take four to six weeks and full post-operative vision stabilization often takes a year or more but most transplants are very stable in the long term. The National Keratoconus Foundation reports that penetrating keratoplasty has the most successful outcome of all transplant procedures, and when performed for keratoconus in an otherwise healthy eye, its success rate can be 95% or greater. The sutures used usually dissolve over a period of three to five years but individual sutures can be removed during the healing process if they are causing irritation to the patient.

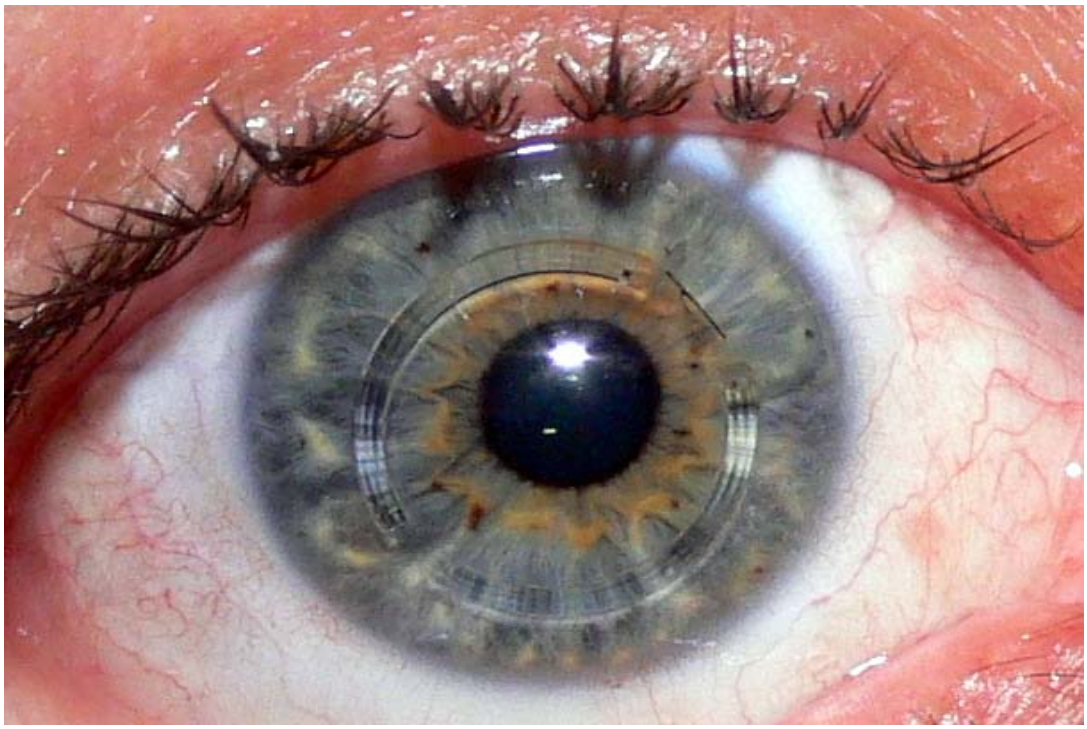
In the USA, corneal transplants (also known as corneal grafts) for keratoconus are usually performed under sedation as outpatient surgery. In other countries, such as Australia and the UK, the operation is commonly performed with the patient undergoing a general anaesthetic. All cases require a careful follow-up with an eye surgeon (ophthalmologist) for a number of years. Frequently, vision is greatly improved after the surgery, but even if the actual visual acuity does not improve, because the cornea is a more normal shape after the healing is completed, patients can more easily be fitted with corrective lenses. Complications of corneal transplants are mostly related to vascularization of the corneal tissue and rejection of the donor cornea. Vision loss is very rare, though difficult-to-correct vision is possible. When rejection is severe, repeat transplants are often attempted, and are frequently successful. Keratoconus will not normally reoccur in the

transplanted cornea; incidences of this have been observed, but are usually attributed to incomplete excision of the original cornea or inadequate screening of the donor tissue. The long-term outlook for corneal transplants performed for keratoconus is usually favorable once the initial healing period is completed and a few years have elapsed without problems.

Corneal ring segment inserts

A recent surgical alternative to corneal transplant is the insertion of intrastromal corneal ring segments. A small incision is made in the periphery of the cornea and two thin arcs of polymethyl methacrylate are slid between the layers of the stroma on either side of the pupil before the incision is closed. The segments push out against the curvature of the cornea, flattening the peak of the cone and returning it to a more natural shape. The procedure, carried out on an outpatient basis under local anaesthesia, offers the benefit of being reversible and even potentially exchangeable as it involves no removal of eye tissue.

The principal intrastromal ring available is known by the trade name of *Intacs*. Internationally, *Ferrara Rings* are also available. Intacs are a patented technology and are placed outside the optical zone versus the smaller prismatic Ferrara rings that are placed just inside the 5 mm optical zone. Intacs are the only corneal implants that have gone through the FDA Phase I, II and III clinical trials and were first approved by the Food and Drug Administration (FDA) in the United States in 1999 for myopia; this was extended to the treatment of keratoconus in July 2004.

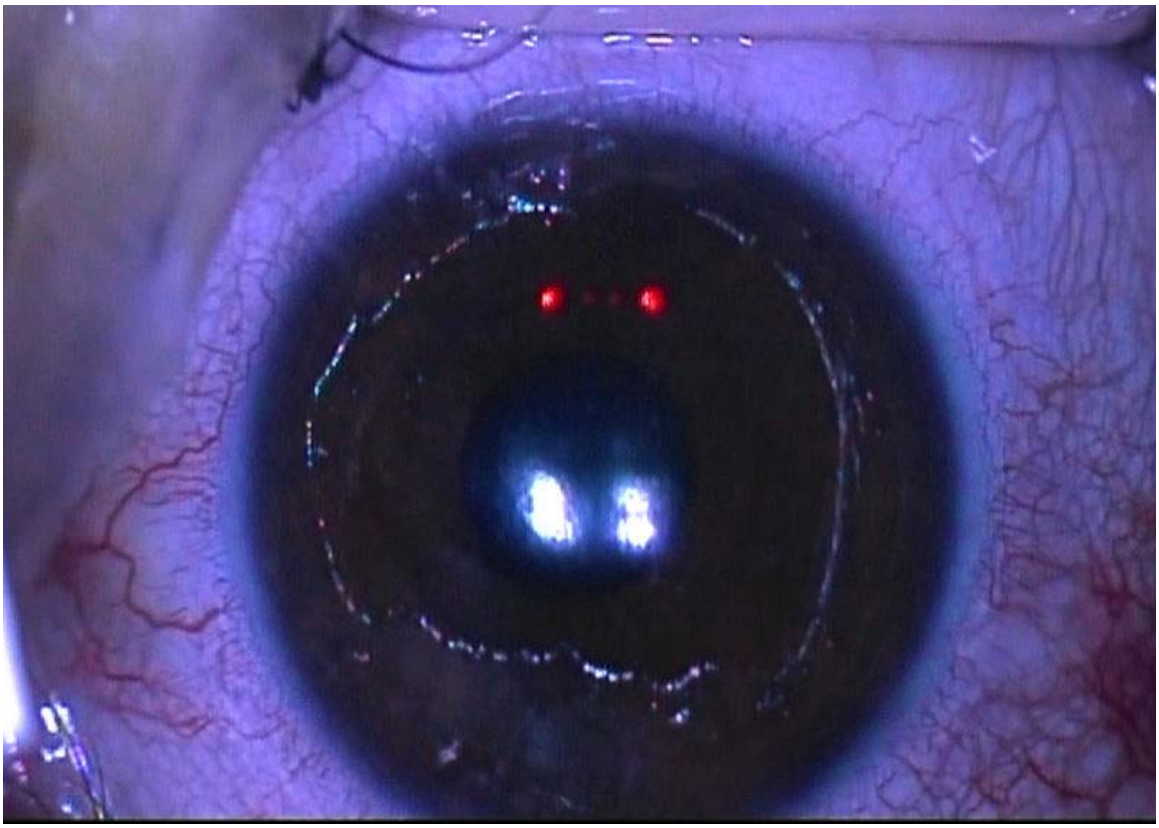


A pair of *Intacs* after insertion into the cornea

Clinical studies on the effectiveness of intrastromal rings on keratoconus are in their early stages, and results have so far been generally encouraging, though they have yet to enter into wide acceptance with the refractive surgery community. In common with penetrating keratoplasty, the requirement for some vision correction in the form of spectacles or hydrophilic contact lenses may remain subsequent to the operation. Potential complications of intrastromal rings include accidental penetration through to the anterior chamber when forming the channel, post-operative infection of the cornea, and migration or extrusion of the segments. The rings offer a good chance of vision improvement even in otherwise hard to manage eyes, but results are not guaranteed and in a few cases may worsen.

Early studies on intrastromal corneal rings involved use of two segments to cause global flattening of the cornea. A later study reported that better results could be obtained for those cones located more to the periphery of the cornea by using a single Intacs segment. This leads to preferential flattening of the cone below, but also to steepening the over-flat upper part of the cornea.

Corneal collagen crosslinking with riboflavin



Removed corneal epithelium during CCR operation on an eye with post-LASIK complication

A treatment developed at the Technische Universität Dresden, and which has shown early success is Corneal Collagen Crosslinking with Riboflavin, also known as CXL, CCR, CCL and KXL. A one-time application of riboflavin solution is administered to the eye and is activated by illumination with UV-A light for approximately 30 minutes. The riboflavin causes new bonds to form across adjacent collagen strands in the stromal layer of the cornea, which recovers and preserves some of the cornea's mechanical strength. The corneal epithelial layer is generally removed in order to increase penetration of the riboflavin into the stroma.

Clinical trials are ongoing, but crosslinking is seeing increasing adoption by the ophthalmological community, and has shown success in treating early cases of the disease. And early results from an Australian study are very promising in reporting stabilization in all treated eyes, and a slight correction in visual acuity in most patients. The procedure, with epithelium removed, is approved for use throughout Europe, and commenced clinical trials in the USA in 2008. Over 300 patients have now been treated in the United States in those trials, which are composed of two randomized, controlled, multi-site clinical trials for the treatment of progressive keratoconus and post LASIK ectasia. Avedro, Inc., the trial's sponsor, is closing the follow-up phase of the study and completing the necessary steps to file the results with the FDA.

In some cases, crosslinking may also be successfully combined with other treatment methods such as corneal ring segment inserts and Keraflex, a new refractive correction procedure, which recently received CE Mark in Europe. Corrective lenses may still be required after these treatments but with more normal prescriptions possible now, and these newer methods may have an important role in limiting deterioration of vision, increasing unaided/uncorrected vision and reducing the case for corneal transplantation.

Radial keratotomy

Radial keratotomy is a refractive surgery procedure where the surgeon makes a spoke-like pattern of incisions into the cornea to modify its shape. This early surgical option for myopia has been largely superseded by LASIK and other similar procedures. LASIK itself is absolutely contraindicated in keratoconus and other corneal thinning conditions as removal of corneal stromal tissue will further damage an already thin and weak cornea.

For similar reasons, radial keratotomy has also generally not been used for keratoconic patients. However, an Italian clinic has reported some success with a modified asymmetric radial keratotomy procedure, in which the incisions are confined to one sector of the eye. The corneal thickness is first measured using a pachymeter, then the surgeon makes cuts to a depth of 70–80% of the measured thickness. The patient may initially experience photophobia and fluctuation of vision, in common with other forms of refractive surgery. This technique has yet to go through the official experimentation and follow-up period which is generally required by the Italian National Health Service to accept a new surgery technique before it can be offered to patients.

DALK transplants

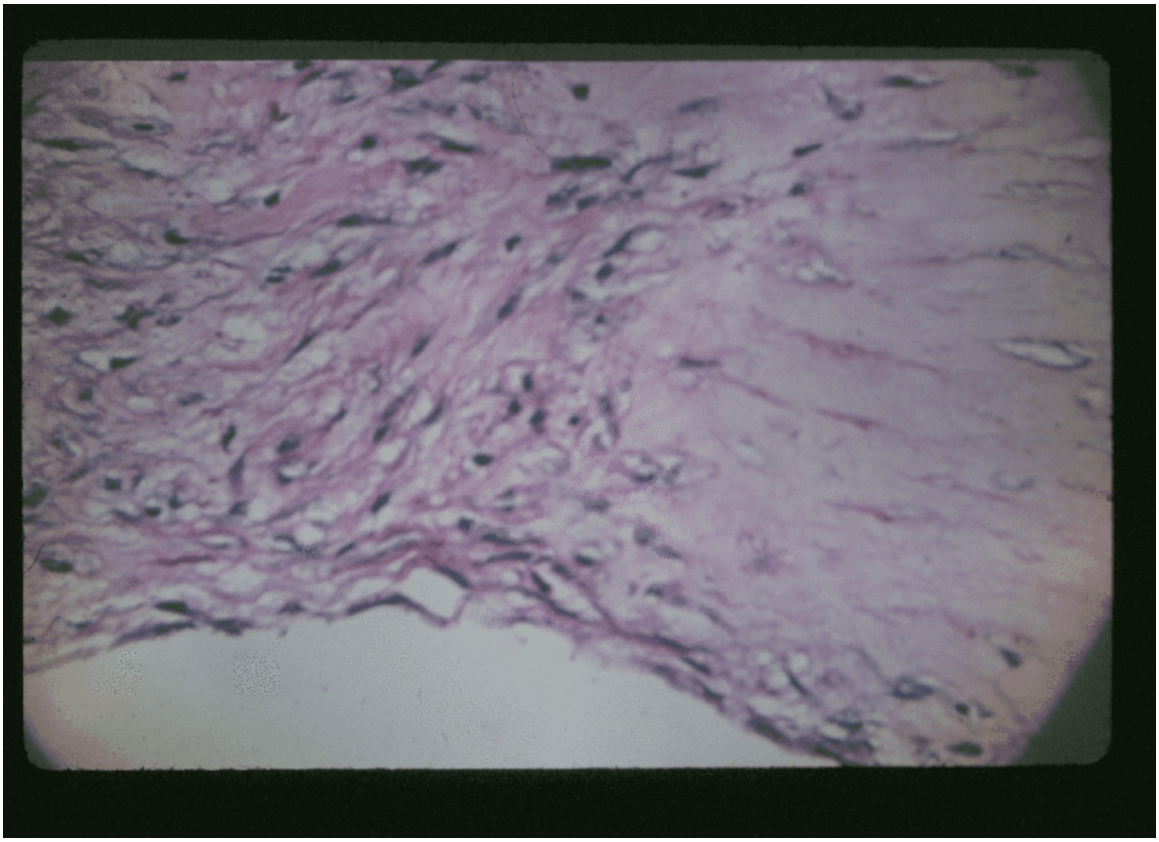
One way of reducing the risk of rejection is to use a newer technique called a *Deep Anterior Lamellar Keratoplasty*, referred to as *DALK*. In a DALK graft, only the outermost epithelium and the main bulk of the cornea, the stroma, are replaced; the patient's rearmost endothelium layer and the Descemet's membrane are left, giving some additional structural integrity to the post-graft cornea. Because a graft rejection usually begins in the endothelium, the chance of a rejection episode is greatly reduced. Furthermore, it is possible to transplant tissue from a donor which has been freeze-dried. The freeze-drying process ensures that this tissue is dead, so there is no chance of a rejection.

Some surgeons prefer to remove the donor epithelium, others leave the donor's cells in place. Removing it can cause a slight improvement in overall vision, but a corresponding increase in visual recovery time.

Epikeratophakia

Rarely, a non-penetrating keratoplasty known as an *epikeratophakia* (or *epikeratoplasty*) may be performed in cases of keratoconus. The corneal epithelium is removed and a lenticule of donor cornea grafted on top of it. The procedure requires a greater level of skill on the part of the surgeon, and is less frequently performed than a penetrating keratoplasty as the outcome is generally less favorable. However, it may be seen as an option in a number of cases, particularly for young patients.

Prognosis



A small rupture of Descemet's membrane (magnified view)

Patients with keratoconus typically present initially with mild astigmatism, commonly at the onset of puberty, and are diagnosed as having the disease by the late teenage years or early 20s. In rare cases keratoconus can occur in children or is not present until later adulthood. A diagnosis of the disease at an early age may indicate a greater risk of severity in later life. Patients' vision will seem to fluctuate over a period of months, driving them to change lens prescriptions frequently, but as the condition worsens, contact lenses are required in the majority of cases. The course of the disorder can be quite variable, with some patients remaining stable for years or indefinitely, while others progress rapidly or experience occasional exacerbations over a long and otherwise steady course. Most commonly, keratoconus progresses for a period of ten to twenty years before the course of the disease generally ceases.

leads to *corneal hydrops*

In advanced cases, bulging of the cornea can result in a localized rupture of Descemet's membrane, an inner layer of the cornea. Aqueous humor from the eye's anterior chamber seeps into the cornea before Descemet's membrane reseals. The patient experiences pain and a sudden severe clouding of vision, with the cornea taking on a translucent milky-white appearance known as a *corneal hydrops*. Although disconcerting to the patient, the effect is normally temporary and after a period of six to eight weeks the cornea usually returns to its former transparency. The recovery can be aided non-surgically by bandaging with an osmotic saline solution. Although a hydrops usually causes increased scarring of the cornea, occasionally it will benefit a patient by creating a flatter cone, aiding the fitting of contact lenses. Occasionally, in extreme cases, the cornea thins to the point that a partial rupture occurs, resulting in a small, bead-like swelling on the cornea that has been filled with fluid. When this occurs, a corneal transplant can become urgently necessary to avoid complete rupture and resulting loss of the eye.

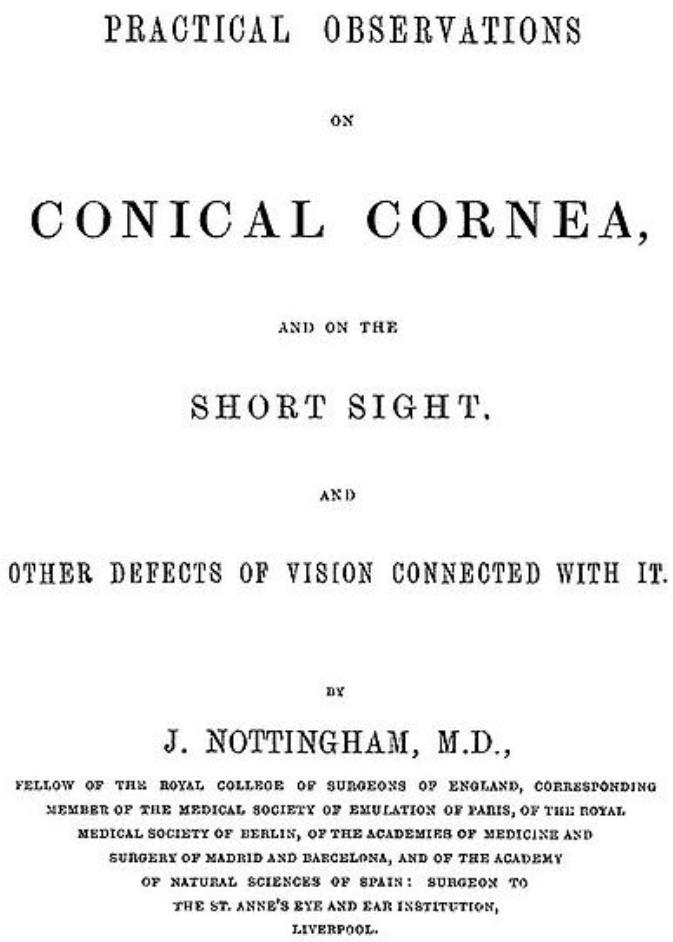
Epidemiology

The National Eye Institute reports that keratoconus is the most common corneal dystrophy in the United States, affecting approximately 1 in 2,000 Americans, but some reports place the figure as high as 1 in 500. The inconsistency may be due to variations in diagnostic criteria, with some cases of severe astigmatism interpreted as those of keratoconus, and vice versa. A long-term study found a mean incidence rate of 2.0 new cases per 100,000 population per year. It is suggested that males and females, and all

ethnicities appear equally susceptible, though some recent studies have cast doubt upon this, suggesting a higher prevalence amongst females; the literature, however, varying as to its extent. Also, a study carried out in the UK suggests that people of a South Asian heritage are 4.4 times as likely to suffer from keratoconus as Caucasians, and are also more likely to be affected with the condition earlier.

Keratoconus is normally bilateral (affecting both eyes) although the distortion is usually asymmetric and is rarely completely identical in both corneas. Unilateral cases tend to be uncommon, and may in fact be very rare if a very mild condition in the better eye is simply below the limit of clinical detection. It is common for keratoconus to be diagnosed first in one eye and not until later in the other. As the condition then progresses in both eyes, the vision in the earlier-diagnosed eye will often persist to be poorer than that in its fellow.

History



PRACTICAL OBSERVATIONS

ON

CONICAL CORNEA,

AND ON THE

SHORT SIGHT,

AND

OTHER DEFECTS OF VISION CONNECTED WITH IT.

BY

J. NOTTINGHAM, M.D.,

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Practical observations on conical cornea, Nottingham's ground-breaking text on keratoconus, 1854

In a 1748 doctoral dissertation, the German oculist Burchard Mauchart provided an early description of a case of keratoconus, which he called *staphyloma diaphanum*. However, it was not until 1854 that British physician John Nottingham clearly described keratoconus and distinguished it from other ectasias of the cornea. Nottingham reported the cases of "conical cornea" that had come to his attention, and described several classic features of the disease, including polyopia, weakness of the cornea, and difficulty matching corrective lenses to the patient's vision. In 1859 British surgeon William Bowman used an ophthalmoscope (recently invented by Hermann von Helmholtz) to diagnose keratoconus, and described how to angle the instrument's mirror so as to best see the conical shape of the cornea. Bowman also attempted to restore the vision by pulling on the iris with a fine hook inserted through the cornea and stretching the pupil into a vertical slit, like that of a cat. He reported that he had had a measure of success with the technique, restoring vision to an 18-year old woman who had previously been unable to count fingers at a distance of 8 inches (20 cm). By 1869, when the pioneering Swiss ophthalmologist Johann Horner wrote a thesis entitled *On the treatment of keratoconus*, the disorder had acquired its current name. The treatment at that time, endorsed by the leading German ophthalmologist Albrecht von Graefe, was an attempt to physically reshape the cornea by chemical cauterization with a silver nitrate solution and application of a miosis-causing agent with a pressure dressing. In 1888 the treatment of keratoconus became one of the first practical applications of the then newly invented contact lens, when the French physician Eugène Kalt manufactured a glass scleral shell which improved vision by compressing the cornea into a more regular shape. Since the start of the twentieth century, research on keratoconus has both improved understanding of the disease and greatly expanded the range of treatment options. The first successful transplantation of cornea to treat keratoconus was done in 1936 by Ramon Castroviejo.

Related disorders

Several other non-inflammatory eye disorders, generally rarer than keratoconus, also cause thinning of the cornea:

Keratoglobus
: Keratoglobus is a very rare condition that causes corneal thinning primarily at the margins, resulting in a spherical, slightly enlarged eye. It may be genetically related to keratoconus.

Pellucid Marginal Degeneration
: Pellucid marginal degeneration causes thinning of a narrow (1–2 mm) band of the cornea, usually along the inferior corneal margin. It causes irregular astigmatism that can often be corrected by spectacles. Differential diagnosis may be made by slit-lamp examination.

Posterior keratoconus
: Keratoconus and posterior keratoconus are distinct disorders, despite their similar names. Posterior keratoconus is a rare abnormality, usually congenital, which causes a non-progressive thinning of the inner surface of the cornea, while the curvature of the anterior surface remains normal. Normally only a single eye is affected.

Chapter 9

Keratoconjunctivitis Sicca

Keratoconjunctivitis sicca	
ICD-10	H19.3, M35.0 (ILDS M35.010)
ICD-9	370.33, 710.2
DiseasesDB	12155
eMedicine	article/1196733 article/1210417
MeSH	D007638

Keratoconjunctivitis sicca (KCS), also called **keratitis sicca**, **xerophthalmia**, **dry eye syndrome** (**DES**), or simply **dry eyes**, is an eye disease caused by decreased tear production or increased tear film evaporation commonly found in humans and some animals. The phrase "keratoconjunctivitis sicca" is Latin, and its literal translation is "dryness of the cornea and conjunctiva".

Symptoms

Typical symptoms of keratoconjunctivitis are dryness, burning and a sandy-gritty eye irritation that gets worse as the day goes on. Symptoms may also be described as itchy, scratchy, stingy or tired eyes. Other symptoms are pain, redness, a pulling sensation, and pressure behind the eye. There may be a feeling that something, such as a speck of dirt, is in the eye. The resultant damage to the eye surface increases discomfort and sensitivity to bright light. Both eyes usually are affected.

There may also be a stringy discharge from the eyes. Although it may seem strange, dry eye can cause the eyes to water. This can happen because the eyes are irritated. One may experience excessive tearing in the same way as one would if something got into the eye. These reflex tears will not necessarily make the eyes feel better. This is because they are the watery type that are produced in response to injury, irritation, or emotion. They do not have the lubricating qualities necessary to prevent dry eye.

Because blinking coats the eye with tears, symptoms are worsened by activities in which the rate of blinking is reduced due to prolonged use of the eyes. These activities include

prolonged reading, computer usage, driving, or watching television. Symptoms increase in windy, dusty or smoky (including cigarette smoke) areas, in dry environments, high altitudes including airplanes, on days with low humidity, and in areas where an air conditioner (especially in a car), fan, heater, or even a hair dryer is being used. Symptoms reduce during cool, rainy, or foggy weather and in humid places, such as in the shower.

Most people who have dry eyes experience mild irritation with no long-term effects. However, if the condition is left untreated or becomes severe, it can produce complications that can cause eye damage, resulting in impaired vision or (rarely) in the loss of vision.

Symptom assessment is a key component of dry eye diagnosis - to the extent that many believe dry eye syndrome to be a symptom-based disease. Several questionnaires have been developed to determine a score that would allow for dry eye diagnosis. The McMonnies & Ho dry eye questionnaire is often used in clinical studies of dry eyes. It has 14 questions, resulting in a score from 0 to 45. Scores above 14.5 are consistent with dry eyes.

Pathophysiology

Having dry eyes for a while can lead to tiny abrasions on the surface of the eyes. In advanced cases, the epithelium undergoes pathologic changes, namely squamous metaplasia and loss of goblet cells. Some severe cases result in thickening of the corneal surface, corneal erosion, punctate keratopathy, epithelial defects, corneal ulceration (sterile and infected), corneal neovascularization, corneal scarring, corneal thinning, and even corneal perforation.

Causes

Any abnormality of any one of the three layers of tears produces an unstable tear film, resulting in symptoms of keratitis sicca.

Deficient tear production

Keratoconjunctivitis sicca is usually due to inadequate tear production. The aqueous tear layer is affected, resulting in **aqueous tear deficiency** (**ATD**) or **lacrimal hyposecretion**. The lacrimal gland does not produce sufficient tears to keep the entire conjunctiva and cornea covered by a complete layer. This usually occurs in people who are otherwise healthy. Increased age is associated with decreased tearing. This is the most common type found in postmenopausal women.

Causes include idiopathic, congenital alacrima, xerophthalmia, lacrimal gland ablation, and sensory denervation. In rare cases, it may be a symptom of collagen vascular diseases, including rheumatoid arthritis, Wegener's granulomatosis, and systemic lupus erythematosus. Sjögren's syndrome and autoimmune diseases associated with Sjögren's syndrome are also conditions associated with aqueous tear deficiency. Drugs such as

isotretinoin, sedatives, diuretics, tricyclic antidepressants, antihypertensives, oral contraceptives, antihistamines, nasal decongestants, beta-blockers, phenothiazines, atropine, and pain relieving opiates such as morphine can cause or worsen this condition. Infiltration of the lacrimal glands by sarcoidosis or tumors, or postradiation fibrosis of the lacrimal glands can also cause this condition.

Abnormal tear composition

Keratoconjunctivitis sicca can also be caused by abnormal tear composition resulting in rapid evaporation or premature destruction of the tears. When caused by rapid evaporation, it is termed **evaporative dry eyes**. In this, although the tear gland produces a sufficient amount of tears, the rate of evaporation of the tears is too rapid. There is a loss of water from the tears that results in tears that are too "salty" or hypertonic. As a result, the entire conjunctiva and cornea cannot be kept covered with a complete layer of tears during certain activities or in certain environments.

Additional causes

Aging is one of the most common causes of dry eyes. This is because tear production decreases with age. It may be caused by thermal or chemical burns, or (in epidemic cases) by adenoviruses. A number of studies have found that diabetics are at increased risk for the disease.

About half of all people who wear contact lenses complain of dry eyes. There are two potential connections between contact usage and dry eye. Traditionally, it was believed that soft contact lenses, which float on the tear film that covers the cornea, absorb the tears in the eyes. However, it is also now known that contact usage damages corneal nerve sensitivity, which subsequently may lead to decreased lacrimal gland tear production and dry eye. The effect of contact on corneal nerve sensitivity is well established for hard contacts as well as soft and rigid gas permeable. The connection between this loss in nerve sensitivity and tear production is the subject of current research.

Dry eyes also occurs or gets worse after LASIK and other refractive surgeries, in which the corneal nerves are cut during the creation of a corneal flap. The corneal nerves stimulate tear secretion. Dry eyes caused by these procedures usually resolves after several months. Persons who are thinking about refractive surgery should consider this.

An eye injury or other problem with the eyes or eyelids, such as bulging eyes or a drooping eyelid can cause keratoconjunctivitis sicca. Disorders of the eyelid can impair the complex blinking motion required to spread tears.

Abnormalities of the lipid tear layer caused by blepharitis and rosacea, and abnormalities of the mucin tear layer caused by vitamin A deficiency, trachoma, diphtheric keratoconjunctivitis, mucocutaneous disorders and certain topical medications are causes of keratoconjunctivitis sicca.

Persons with keratoconjunctivitis sicca have elevated levels of tear nerve growth factor (NGF). It is possible that this ocular surface NGF plays an important role in ocular surface inflammation associated with dry eyes.

Diagnosis

Dry eyes can usually be diagnosed by the symptoms alone. Tests can determine both the quantity and the quality of the tears. A slit lamp examination can be performed to diagnose dry eyes and to document any damage to the eye.

A Schirmer's test can measure the amount of moisture bathing the eye. This test is useful for determining the severity of the condition. A five-minute Schirmer's test with and without anesthesia using a Whatman #41 filter paper 5 mm wide by 35 mm long is performed. For this test, wetting under 5 mm with or without anesthesia is considered diagnostic for dry eyes.

If the results for the Schirmer's test are abnormal, a Schirmer II test can be performed to measure reflex secretion. In this test, the nasal mucosa is irritated with a cotton-tipped applicator, after which tear production is measured with a Whatman #41 filter paper. For this test, wetting under 15 mm after five minutes is considered abnormal.

A tear breakup time (TBUT) test measures the time it takes for tears to break up in the eye. The tear breakup time can be determined after placing a drop of fluorescein in the cul-de-sac.

A tear protein analysis test measures the lysozyme contained within tears. In tears, lysozyme accounts for approximately 20 to 40 percent of total protein content.

A lactoferrin analysis test provides good correlation with other tests.

The presence of the recently described molecule Ap4A, naturally occurring in tears, is abnormally high in different states of ocular dryness. This molecule can be quantified biochemically simply by taking a tear sample with a plain Schirmer test. Utilizing this technique it is possible to determine the concentrations of Ap4A in the tears of patients and in such way diagnose objectively if the samples are indicative of dry eye.

Treatment

A variety of approaches can be taken to treatment. These can be summarised as: avoidance of exacerbating factors, tear stimulation and supplementation, increasing tear retention, and eyelid cleansing and treatment of eye inflammation.

General measures

Dry eyes can be exacerbated by smokey environments, dust and air conditioning and by our natural tendency to reduce our blink rate when concentrating. Purposefully blinking,

especially during computer use and resting tired eyes are basic steps that can be taken to minimise discomfort. Rubbing one's eyes can irritate them further, so should be avoided. Conditions such as blepharitis can often co-exist and paying particular attention to cleaning the eyelids morning and night with mild shampoos and warm compresses can improve both conditions.

Environmental control

Dry, drafty environments and those with smoke and dust should be avoided. This includes avoiding hair dryers, heaters, air conditioners or fans, especially when these devices are directed toward the eyes. Wearing glasses or directing gaze downward, for example, by lowering computer screens can be helpful to protect the eyes when aggravating environmental factors cannot be avoided. Using a humidifier, especially in the winter, can help by adding moisture to the dry indoor air.

Rehydration

For mild and moderate cases, supplemental lubrication is the most important part of treatment.

Artificial tears

Application of artificial tears every few hours can provide temporary relief.

Autologous serum eye drops

None of the commercially available artificial tear preparations include essential tear components such as epidermal growth factor, hepatocyte growth factor, fibronectin, neurotrophic growth factor, and vitamin A-all of which have been shown to play important roles in the maintenance of a healthy ocular surface epithelial milieu. Autologous serum eye drops contain these essential factors. However, there is some controversy regarding the efficacy of this treatment. At least one study (PubMed) has demonstrated that this modality is more effective than artificial tears in a randomized control study.

Additional options

Lubricating tear ointments can be used during the day, but they generally are used at bedtime due to poor vision after application. They contain white petrolatum, mineral oil, and similar lubricants. They serve as a lubricant and an emollient. Application requires pulling down the eyelid and applying a small amount (0.25 in) inside. Depending on the severity of the condition, it may be applied from every hour to just at bedtime. It should not be used with contact lenses. Specially designed glasses that form a moisture chamber around the eye may be used to create additional humidity.

Medication

Inflammation occurring in response to tears film hypertonicity can be suppressed by mild topical steroids or with topical immunosuppressants such as ciclosporin. Elevated levels of tear NGF can be decreased with 0.1% prednisolone.

Fish consumption and omega-3 fatty acids

Consumption of dark fleshed fish containing dietary omega-3 fatty acids is associated with a decreased incidence of dry eyes syndrome in women. This finding is consistent with postulated biological mechanisms. Early experimental work on omega-3 has shown promising results when used in a topical application or given orally.

Restasis

Topical ciclosporin (topical cyclosporin A, tCSA) 0.05% ophthalmic emulsion is an immunosuppressant, marketed in the United States by Allergan under the trade name Restasis. Approved as a prescription product by the U.S. Food and Drug Administration in 2002, the drug decreases surface inflammation. It is thought to work through inhibition of transcription factors required for cytokine production and T-lymphocyte maturation. In a trial involving 1200 people, Restasis increased tear production in 15% of people, compared to 5% with placebo.

Usually, 1 gtt (drop) of Restasis is instilled in each eye twice a day, 12 hours apart. It should not be used while wearing contact lenses, during eye infections or in people with a history of herpes virus infections. Side effects include burning sensation (common), redness, discharge, watery eyes, eye pain, foreign body sensation, itching, stinging, and blurred vision. Long term use of ciclosporin at high doses is associated with an increased risk of cancer.

Generic alternatives

Cheaper generic alternatives to Restasis are available in some countries. In India, it is marketed as Cyclomune by Sun Pharma.

Conserving tears

There are methods that allow both natural and artificial tears to stay longer.

Blocking tear drainage

In each eye, there are two puncta — little openings that drain tears into the tear ducts. There are methods to partially or completely close the tear ducts. This blocks the flow of tears into the nose, and thus more tears are available to the eyes.

Punctal plugs

Punctal plugs are inserted into the puncta to block tear drainage. For people who have not found dry eye relief with drugs, punctal plugs may help. They are reserved for people with moderate or severe dry eye when other medical treatment has not been adequate.

Cauterization

If punctal plugs are effective, thermal or electric cauterization of puncti can be performed.

In thermal cauterization, a local anesthetic is used, and then a hot wire is applied. This shrinks the drainage area tissues and causes scarring, which closes the tear duct.

Customized contact lenses

Persons with severe dry eyes may benefit from the Boston Scleral Lens which is a customized contact lens. Resting on the sclera, it creates a fluid filled layer over the cornea, thus preventing it from drying.

Surgery

In severe cases of keratoconjunctivitis sicca, tarsorrhaphy may be performed where the eyelids are partially sewn together. This reduces the palpebral fissure (eyelid separation), ideally leading to a reduction in tear evaporation.

Prognosis

Keratoconjunctivitis sicca usually is a chronic problem. Its prognosis shows considerable variance, depending upon the severity of the condition. Most patients have mild-to-moderate cases, and can be treated symptomatically with lubricants. This provides an adequate relief of symptoms.

When dry eyes symptoms are severe, they can interfere with quality of life. People sometimes feel their vision blurs with use, or severe irritation to the point that they have trouble keeping their eyes open or they may not be able to work or drive.

Prevention

There is no way to prevent keratoconjunctivitis sicca. Complications can be prevented by use of wetting and lubricating drops and ointments.

Epidemiology

Keratoconjunctivitis sicca is relatively common within the United States, especially so in older patients. Specifically, the persons most likely to be affected by dry eyes are those aged 40 or older.

While persons with autoimmune diseases have a high likelihood of having dry eyes, most persons with dry eyes do not have an autoimmune disease. Instances of Sjögren syndrome and keratoconjunctivitis sicca associated with it are present much more commonly in women, with a ratio of 9:1. In addition, milder forms of keratoconjunctivitis sicca also are more common in women. This is partly because hormonal changes, such as those that occur in pregnancy, menstruation, and menopause, can decrease tear production.

In areas of the world where malnutrition is common, vitamin A deficiency is a common cause. This is rare in the United States.

Racial predilections do not exist for this disease.

Occurrence in animals

Among animals, keratoconjunctivitis sicca occurs in dogs, cats, and horses.

Dogs

Keratoconjunctivitis sicca is common in dogs. Most cases are caused by a genetic predisposition, but chronic conjunctivitis, canine distemper, and drugs such as sulfasalazine and trimethoprim-sulfonamide also cause the disease. Symptoms include eye redness, a yellow or greenish discharge, ulceration of the cornea, pigmented cornea, and blood vessels on the cornea. Diagnosis is made by measuring tear production with a Schirmer tear test. Less than 15 millimeters of tears produced in a minute is abnormal.

Tear replacers are a mainstay of treatment, preferably containing methylcellulose or carboxymethyl cellulose. Ciclosporin stimulates tear production and acts as a suppressant on the immune-mediated processes that cause the disease. Topical antibiotics and corticosteroids are sometimes used to treat secondary infections and inflammation. A surgery known as parotid duct transposition is used in some extreme cases where medical treatment has not helped. This redirects the duct from the parotid salivary gland to the eye. Saliva replaces the tears. Dogs suffering from cherry eye should have the condition corrected to help prevent this disease.

Commonly affected breeds include:

- Cavalier King Charles Spaniel
- Bulldog
- Chinese Shar-Pei

- Lhasa Apso
- Shih Tzu
- West Highland White Terrier
- Pug
- Bloodhound
- Cocker Spaniel
- Pekingese
- Boston Terrier
- Miniature Schnauzer
- Samoyed

Cats

Keratoconjunctivitis sicca is uncommon in cats. Most cases seem to be caused by chronic conjunctivitis, especially secondary to feline herpesvirus. Diagnosis, symptoms, and treatment are similar to those for dogs.

Chapter 10

Glaucoma

Glaucoma

Acute angle closure glaucoma of the right eye. Note the mid sized pupil, which was non-reactive to light, and injection of the conjunctiva.

ICD-10	H40.-H42.
ICD-9	365
DiseasesDB	5226
eMedicine	oph/578
MeSH	D005901

Glaucoma is an eye disorder in which the optic nerve suffers damage, permanently impacting vision in the affected eye(s) and progressing to complete blindness if untreated. It is often, but not always, associated with increased pressure of the fluid in the eye (aqueous humour).

The nerve damage involves loss of retinal ganglion cells in a characteristic pattern. There are many different sub-types of glaucoma but they can all be considered a type of optic neuropathy. Raised intraocular pressure is a significant risk factor for developing glaucoma (above 21 mmHg or 2.8 kPa). One person may develop nerve damage at a relatively low pressure, while another person may have high eye pressure for years and yet never develop damage. Untreated glaucoma leads to permanent damage of the optic nerve and resultant visual field loss, which can progress to blindness.

Glaucoma can be divided roughly into two main categories, "open angle" and "closed angle" glaucoma. Closed angle glaucoma can appear suddenly and is often painful; visual loss can progress quickly but the discomfort often leads patients to seek medical attention before permanent damage occurs. Open angle, chronic glaucoma tends to progress at a slower rate and the patient may not notice that they have lost vision until the disease has progressed significantly.

Glaucoma has been nicknamed the "silent thief of sight" because the loss of vision normally occurs gradually over a long period of time and is often only recognized when the disease is quite advanced. Once lost, this damaged visual field cannot be recovered. Worldwide, it is the second leading cause of blindness. It is also the leading cause of blindness among African Americans. Glaucoma affects 1 in 200 people aged fifty and younger, and 1 in 10 over the age of eighty. If the condition is detected early enough it is possible to arrest the development or slow the progression with medical and surgical means.

The word *glaucoma* comes from the Greek γλαύκωμα, "opacity of the crystalline lens".

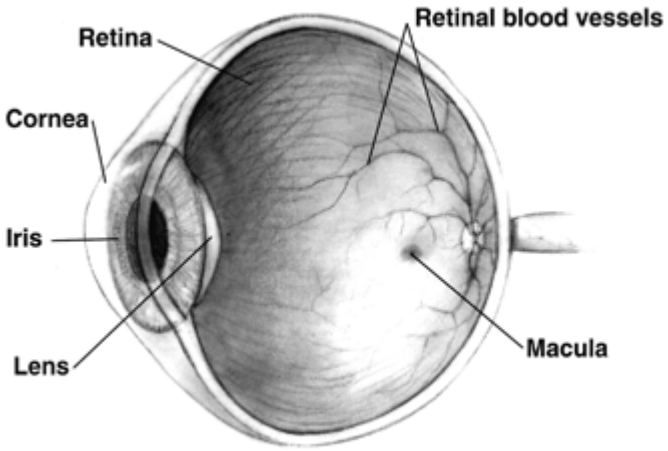
Signs and symptoms

There are two main types of glaucoma: **open-angle glaucoma** and **closed-angle glaucoma.**

Open-angle glaucoma accounts for 90% of glaucoma cases in the United States. It is painless and does not have acute attacks. The only signs are gradually progressive visual field loss, and optic nerve changes (increased cup-to-disc ratio on fundoscopic examination).

Closed-angle glaucoma accounts for less than 10% of glaucoma cases in the United States, but as much as half of glaucoma cases in other nations (particularly Asian countries). About 10% of patients with closed angles present with acute angle closure crises characterized by sudden ocular pain, seeing halos around lights, red eye, very high intraocular pressure (>30 mmHg), nausea and vomiting, sudden decreased vision, and a fixed, mid-dilated pupil. Acute angle closure is an ocular emergency.

Pathophysiology



Human eye cross-sectional view

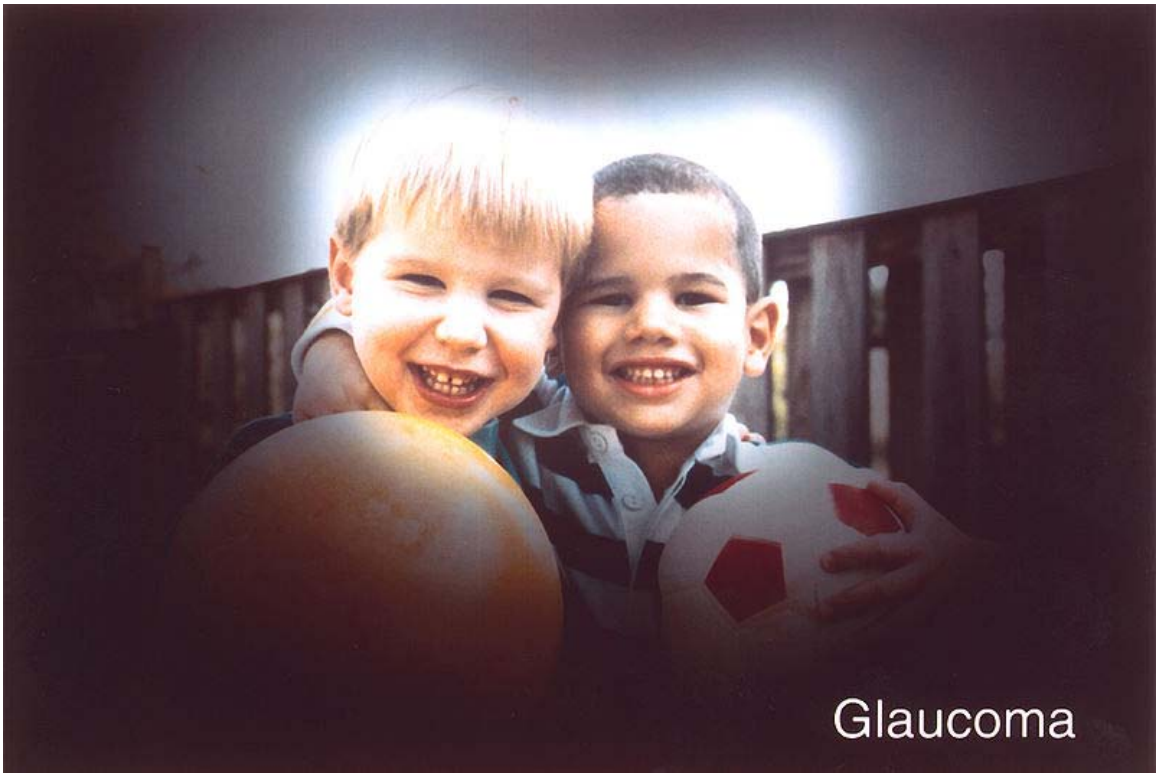
The major risk factor for most glaucomas and focus of treatment is increased intraocular pressure. Intraocular pressure is a function of production of liquid aqueous humor by the ciliary processes of the eye and its drainage through the trabecular meshwork. Aqueous humor flows from the ciliary processes into the posterior chamber, bounded posteriorly by the lens and the zonules of Zinn and anteriorly by the iris. It then flows through the pupil of the iris into the anterior chamber, bounded posteriorly by the iris and anteriorly by the cornea. From here the trabecular meshwork drains aqueous humor via Schlemm's canal into scleral plexuses and general blood circulation. In open angle glaucoma there is reduced flow through the trabecular meshwork; in angle closure glaucoma, the iris is apposed to the lens resulting in the inability of the aqueous fluid to flow from the posterior to the anterior chamber and then out of the trebecular network.

The inconsistent relationship of glaucomatous optic neuropathy with ocular hypertension has provoked hypotheses and studies on anatomic structure, eye development, nerve compression trauma, optic nerve blood flow, excitatory neurotransmitter, trophic factor, retinal ganglion cell/axon degeneration, glial support cell, immune, and aging mechanisms of neuron loss.

The major types of glaucoma are discussed below.

Causes and risk factors

A normal range of vision



The same view with advanced vision loss from glaucoma

There are several causes for glaucoma. *Those at risk are advised to have a dilated eye examination at least once a year.*

Ocular hypertension (increased pressure within the eye) is the largest risk factor in most glaucomas, but in some populations only 50% of patients with primary open angle glaucoma actually have elevated ocular pressure.

Those of African descent are three times more likely to develop primary open angle glaucoma.

Elderly people have thinner corneal thickness and often suffer from hypermetropia. They are also at higher risk for primary open angle glaucoma.

People with a family history of glaucoma have about six percent chance of developing glaucoma.

Many East Asian groups are prone to developing angle closure glaucoma due to their shallower anterior chamber depth, with the majority of cases of glaucoma in this population consisting of some form of angle closure. Inuit also have a twenty to forty times higher risk than Caucasians of developing primary angle closure glaucoma. Women are three times more likely than men to develop acute angle-closure glaucoma due to their shallower anterior chambers.

Other factors can cause glaucoma, known as "secondary glaucomas," including prolonged use of steroids (steroid-induced glaucoma); conditions that severely restrict blood flow to the eye, such as severe diabetic retinopathy and central retinal vein occlusion (neovascular glaucoma); ocular trauma (angle recession glaucoma); and uveitis (uveitic glaucoma).

Primary open angle glaucoma (POAG) has been found to be associated with mutations in genes at several loci. Normal tension glaucoma, which comprises one third of POAG, is associated with genetic mutations.

There is increasing evidence that ocular blood flow is involved in the pathogenesis of glaucoma. Current data indicate that fluctuations in blood flow are more harmful in glaucomatous optic neuropathy than steady reductions. Unstable blood pressure and dips are linked to optic nerve head damage and correlate with visual field deterioration.

A number of studies also suggest a possible correlation between hypertension and the development of glaucoma. In normal tension glaucoma, nocturnal hypotension may play a significant role.

There is no clear evidence that vitamin deficiencies cause glaucoma in humans. It follows then that oral vitamin supplementation is not a recommended treatment for glaucoma.

Various rare congenital/genetic eye malformations are associated with glaucoma. Occasionally, failure of the normal third trimester gestational atrophy of the hyaloid canal and the tunica vasculosa lentis is associated with other anomalies. Angle closure induced ocular hypertension and glaucomatous optic neuropathy may also occur with these anomalies and modelled in mice.

Diagnosis

Screening for glaucoma is usually performed as part of a standard eye examination performed by ophthalmologists, orthoptists and optometrists. Testing for glaucoma should include measurements of the intraocular pressure via tonometry, changes in size or shape of the eye, anterior chamber angle examination or gonioscopy, and examination of the optic nerve to look for any visible damage to it, or change in the cup-to-disc ratio and also rim appearance and vascular change. A formal visual field test should be performed. The retinal nerve fiber layer can be assessed with imaging techniques such as optical coherence tomography (OCT), scanning laser polarimetry (GDx), and/or scanning laser ophthalmoscopy also known as Heidelberg Retina Tomography (HRT3). Owing to the sensitivity of all methods of tonometry to corneal thickness, methods such as Goldmann tonometry should be augmented with pachymetry to measure central corneal thickness (CCT). A thicker-than-average cornea can result in a pressure reading higher than the 'true' pressure, whereas a thinner-than-average cornea can produce a pressure reading lower than the 'true' pressure. Because pressure measurement error can be caused by more than just CCT (i.e., corneal hydration, elastic properties, etc.), it is impossible to 'adjust' pressure measurements based only on CCT measurements. The Frequency

Doubling Illusion can also be used to detect glaucoma with the use of a Frequency Doubling Technology (FDT) perimeter. Examination for glaucoma also could be assessed with more attention given to sex, race, history of drug use, refraction, inheritance and family history.

Management

The modern goals of glaucoma management are to avoid glaucomatous damage, nerve damage, preserve visual field and total quality of life for patients with minimal side effects. This requires appropriate diagnostic techniques and follow up examinations and judicious selection of treatments for the individual patient. Although intraocular pressure is only one of the major risk factors for glaucoma, lowering it via various pharmaceuticals and/or surgical techniques is currently the mainstay of glaucoma treatment. Vascular flow and neurodegenerative theories of glaucomatous optic neuropathy have prompted studies on various neuroprotective therapeutic strategies including nutritional compounds some of which may be regarded by clinicians as safe for use now, while others are on trial.

Medication

Intraocular pressure can be lowered with medication, usually eye drops. There are several different classes of medications to treat glaucoma with several different medications in each class.

Each of these medicines may have local and systemic side effects. Adherence to medication protocol can be confusing and expensive; if side effects occur, the patient must be willing either to tolerate these, or to communicate with the treating physician to improve the drug regimen. Initially, glaucoma drops may reasonably be started in either one or in both eyes.

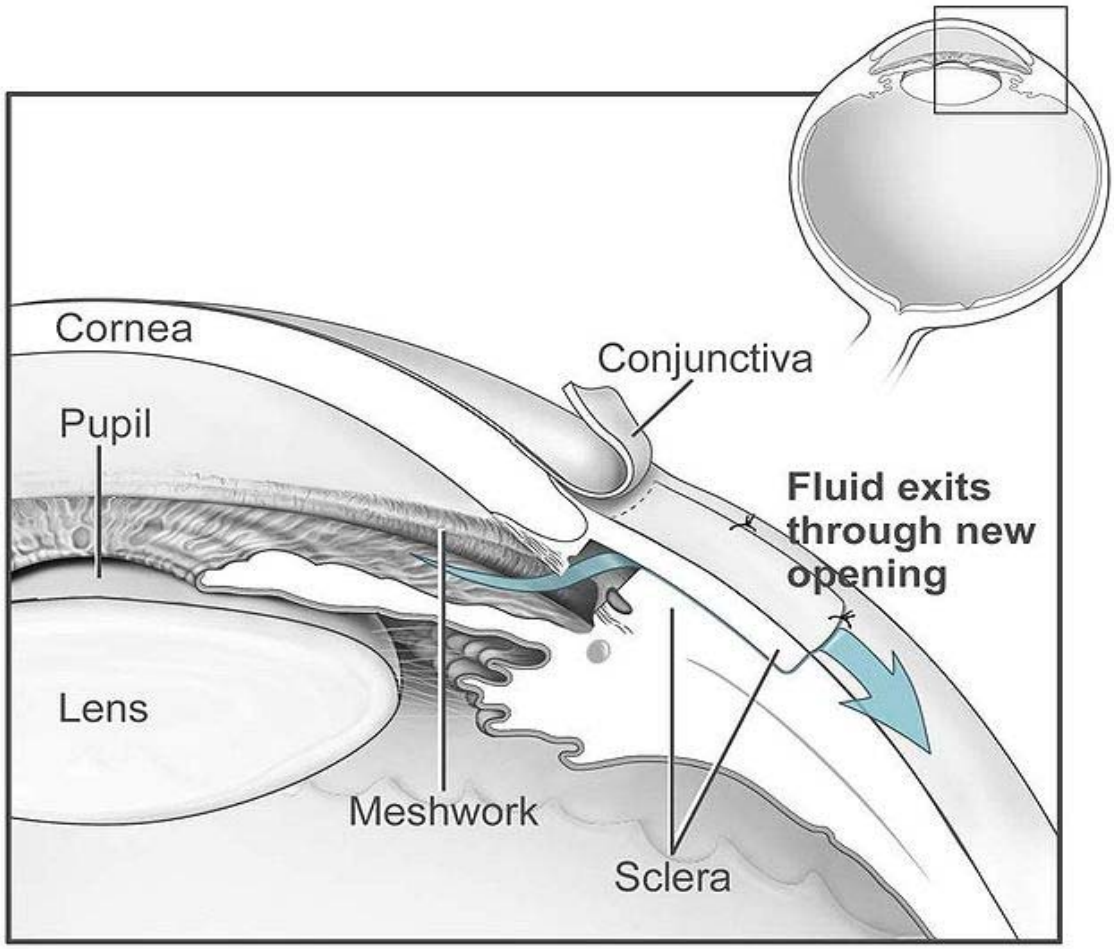
Poor compliance with medications and follow-up visits is a major reason for vision loss in glaucoma patients. A 2003 study of patients in an HMO found that half failed to fill their prescription the first time and one in four failed to refill their prescriptions a second time. Patient education and communication must be ongoing to sustain successful treatment plans for this lifelong disease with no early symptoms.

The possible neuroprotective effects of various topical and systemic medications are also being investigated.

- Prostaglandin analogs like latanoprost (Xalatan), bimatoprost (Lumigan) and travoprost (Travatan) increase uveoscleral outflow of aqueous humor. Bimatoprost also increases trabecular outflow
- Topical beta-adrenergic receptor antagonists such as timolol, levobunolol (Betagan), and betaxolol decrease aqueous humor production by the ciliary body.

- Alpha2-adrenergic agonists such as brimonidine (Alphagan) work by a dual mechanism, decreasing aqueous humor production and increasing trabecular outflow.
- Less-selective sympathomimetics such as epinephrine decrease aqueous humor production through vasoconstriction of ciliary body blood vessels.
- Miotic agents (parasympathomimetics) like pilocarpine work by contraction of the ciliary muscle, tightening the trabecular meshwork and allowing increased outflow of the aqueous humour. Ecothiopate is used in chronic glaucoma.
- Carbonic anhydrase inhibitors like dorzolamide (Trusopt), brinzolamide (Azopt), acetazolamide (Diamox) lower secretion of aqueous humor by inhibiting carbonic anhydrase in the ciliary body.
- Physostigmine is also used to treat glaucoma and delayed gastric emptying.

Surgery



Conventional surgery to treat glaucoma makes a new opening in the meshwork. This new opening helps fluid to leave the eye and lowers intraocular pressure.

Both laser surgeries and conventional surgeries are performed to treat glaucoma.

Surgery is the primary therapy for those with congenital glaucoma.

Generally, these operations are a temporary solution, as there is not yet a cure for glaucoma.

Canaloplasty

Canaloplasty is a nonpenetrating procedure utilizing microcatheter technology. To perform a canaloplasty, an incision is made into the eye to gain access to Schlemm's canal in a similar fashion to a viscocanalostomy. A microcatheter will circumnavigate the canal around the iris, enlarging the main drainage channel and its smaller collector channels through the injection of a sterile, gel-like material called viscoelastic. The catheter is then removed and a suture is placed within the canal and tightened. By opening the canal, the pressure inside the eye may be relieved, although the reason is unclear since the canal (of Schlemm) does not have any significant fluid resistance in glaucoma or healthy eyes. Long-term results are not available.

Laser surgery

Laser trabeculoplasty may be used to treat open angle glaucoma. It is a temporary solution, not a cure. A 50 μm argon laser spot is aimed at the trabecular meshwork to stimulate opening of the mesh to allow more outflow of aqueous fluid. Usually, half of the angle is treated at a time. Traditional laser trabeculoplasty utilizes a thermal argon laser. The procedure is called Argon Laser Trabeculoplasty or ALT. A newer type of laser trabeculoplasty exists that uses a "cold" (non-thermal) laser to stimulate drainage in the trabecular meshwork. This newer procedure which uses a 532 nm frequency-doubled, Q-switched Nd:YAG laser which selectively targets melanin pigment in the trabecular meshwork cells, called Selective Laser Trabeculoplasty or SLT. Studies show that SLT is as effective as ALT at lowering eye pressure. In addition, SLT may be repeated three to four times, whereas ALT can usually be repeated only once.

Nd:YAG laser peripheral iridotomy (LPI) may be used in patients susceptible to or affected by angle closure glaucoma or pigment dispersion syndrome. During laser iridotomy, laser energy is used to make a small full-thickness opening in the iris. This opening equalizes the pressure between the front and back of the iris correcting any abnormal bulging of the iris. In people with narrow angles, this can uncover the trabecular meshwork. In some cases of intermittent or short-term angle closure this may lower the eye pressure. Laser iridotomy reduces the risk of developing an attack of acute angle closure. In most cases it also reduces the risk of developing chronic angle closure or of adhesions of the iris to the trabecular meshwork.

Diode laser cycloablation lowers IOP by reducing aqueous secretion by destroying secretory ciliary epithelium.

Trabeculectomy

The most common conventional surgery performed for glaucoma is the trabeculectomy. Here, a partial thickness flap is made in the scleral wall of the eye, and a window opening made under the flap to remove a portion of the trabecular meshwork. The scleral flap is then sutured loosely back in place. This allows fluid to flow out of the eye through this opening, resulting in lowered intraocular pressure and the formation of a bleb or fluid bubble on the surface of the eye. Scarring can occur around or over the flap opening, causing it to become less effective or lose effectiveness altogether.

Glaucoma drainage implants

There are also several different glaucoma drainage implants. These include the original Molteno implant (1966), the Baerveldt tube shunt, or the valved implants, such as the Ahmed glaucoma valve implant or the ExPress Mini Shunt and the later generation pressure ridge Molteno implants. These are indicated for glaucoma patients not responding to maximal medical therapy, with previous failed guarded filtering surgery (trabeculectomy). The flow tube is inserted into the anterior chamber of the eye and the plate is implanted underneath the conjunctiva to allow flow of aqueous fluid out of the eye into a chamber called a bleb.

- The first-generation Molteno and other non-valved implants sometimes require the ligation of the tube until the bleb formed is mildly fibrosed and water-tight This is done to reduce postoperative hypotony—sudden drops in postoperative intraocular pressure (IOP).
- Valved implants such as the Ahmed glaucoma valve attempt to control postoperative hypotony by using a mechanical valve.

The ongoing scarring over the conjunctival dissipation segment of the shunt may become too thick for the aqueous humor to filter through. This may require preventive measures using anti-fibrotic medication like 5-fluorouracil (5-FU) or mitomycin-C (during the procedure), or additional surgery. And for Glaucomatous painful Blind Eye and some cases of Glaucoma, Cyclocryotherapy for ciliary body ablation could be considered to be performed.

Veterinary implant

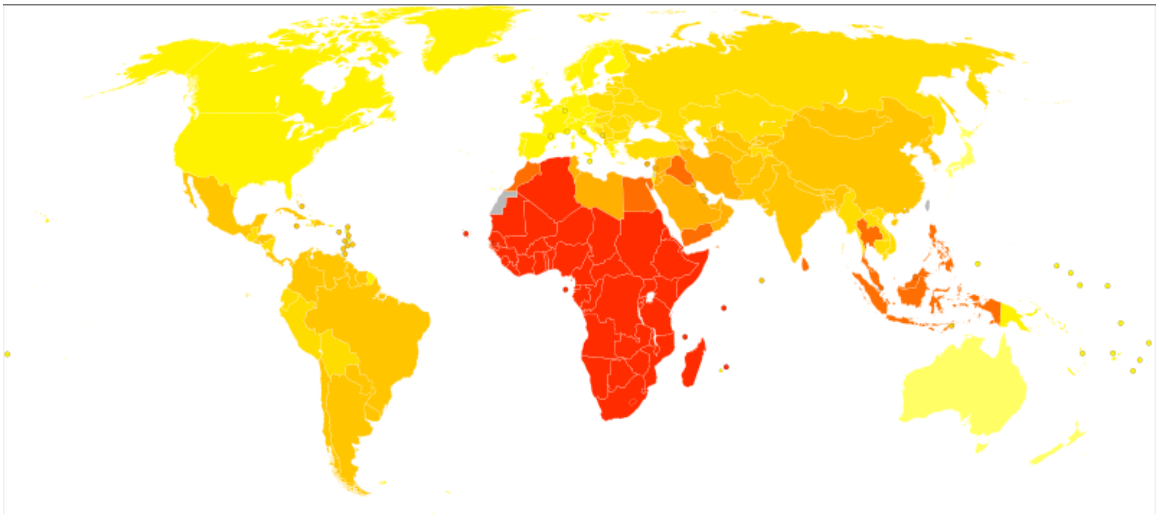
TR BioSurgical has commercialized a new implant specifically for veterinary medicine, called TR-ClarifEYE. The implant consists of a new biomaterial, the STAR BioMaterial, which consists of silicone with a very precise homogenous pore size, a property which reduces fibrosis and improves tissue integration. The implant contains no valves and is placed completely within the eye without sutures. To date, it has demonstrated long term success (> 1yr) in a pilot study in medically refractory dogs with advanced glaucoma

Laser assisted non-penetrating deep sclerectomy

The most common surgical approach currently used for the treatment of glaucoma, is trabeculectomy, in which the sclera is punctured to alleviate intraocular pressure (IOP), the pressure inside the eye. Non-penetrating deep sclerectomy (NPDS) surgery is a similar but modified procedure, in which instead of puncturing the scleral wall, a patch of the sclera is skimmed to a level, upon which, percolation of liquid from the inner eye is achieved and thus alleviating IOP, without penetrating the eye. NPDS is demonstrated to cause a significantly less side effects than trabeculectomy. However, NPDS is performed manually and requires great skill to achieve a lengthy learning curve.

Laser assisted NPDS is the performance of NPDS with the use of a CO_2 laser system. The laser-based system is self-terminating once the required scleral thickness and adequate drainage of the intra ocular fluid have been achieved. This self-regulation effect is achieved as the CO_2 laser essentially stops ablating as soon as it comes in contact with the intra-ocular percolated liquid, which occurs as soon as the laser reaches the optimal residual intact layer thickness.

Epidemiology



Disability-adjusted life year for glaucoma per 100,000 inhabitants in 2004.

- no data
- fewer than 20
- 20-43
- 43-66
- 66-89
- 89-112
- 112-135
- 135-158
- 158-181
- 181-204
- 204-227

227-250
more than 250

Research

- Advanced Glaucoma Intervention Study (AGIS) - large American National Eye Institute (NEI) sponsored study designed "to assess the long-range outcomes of sequences of interventions involving trabeculectomy and argon laser trabeculoplasty in eyes that have failed initial medical treatment for glaucoma." It recommends different treatments based on race.
- Early Manifest Glaucoma Trial (EMGT) -Another NEI study found that immediately treating people who have early stage glaucoma can delay progression of the disease.
- Ocular Hypertension Treatment Study (OHTS) -NEI study findings: "...Topical ocular hypotensive medication was effective in delaying or preventing onset of Primary Open Angle Glaucoma (POAG) in individuals with elevated Intraocular Pressure (IOP). Although this does not imply that all patients with borderline or elevated IOP should receive medication, clinicians should consider initiating treatment for individuals with ocular hypertension who are at moderate or high risk for developing POAG."
- Blue Mountains Eye Study "The Blue Mountains Eye Study was the first large population-based assessment of visual impairment and common eye diseases of a representative older Australian community sample." Risk factors for glaucoma and other eye disease were determined.

Compounds in research

Natural compounds of research interest in glaucoma prevention or treatment include: fish oil and omega 3 fatty acids, bilberries, vitamin E, cannabinoids, carnitine, coenzyme Q10, curcurmin, Salvia miltiorrhiza, dark chocolate, erythropoietin, folic acid, Ginkgo biloba, Ginseng, L-glutathione, grape seed extract, green tea, magnesium, melatonin, methylcobalamin, N-acetyl-L cysteine, pycnogenols, resveratrol, quercetin and salt. Magnesium, ginkgo, salt and fludrocortisone, are already used by some physicians.

Cannabis

Studies in the 1970s showed that marijuana, when smoked, effectively lowers intraocular pressure. In an effort to determine whether marijuana, or drugs derived from marijuana, might be effective as a glaucoma treatment, the US National Eye Institute supported research studies from 1978 to 1984. These studies demonstrated that some derivatives of marijuana lowered intraocular pressure when administered orally, intravenously, or by smoking, but not when topically applied to the eye.

In 2003 the American Academy of Ophthalmology released a position statement which said that "studies demonstrated that some derivatives of marijuana did result in lowering of IOP when administered orally, intravenously, or by smoking, but not when topically

applied to the eye. The duration of the pressure-lowering effect is reported to be in the range of 3 to 4 hours".

However, the position paper qualified that by stating that marijuana was not more effective than prescription medications, stating that "no scientific evidence has been found that demonstrates increased benefits and/or diminished risks of marijuana use to treat glaucoma compared with the wide variety of pharmaceutical agents now available."

The first patient in the United States federal government's Compassionate Investigational New Drug program, Robert Randall, was afflicted with glaucoma and had successfully fought charges of marijuana cultivation because it was deemed a medical necessity (*U.S. v. Randall*) in 1976.

5-HT_{2A} agonists

Peripherally selective 5-HT_{2A} agonists such as the indazole derivative AL-34662 are currently under development and show significant promise in the treatment of glaucoma.

Classification

Glaucoma has been classified into specific types:

Primary glaucoma and its variants (H40.1-H40.2)

- Primary glaucoma
    - Primary angle-closure glaucoma, also known as primary closed-angle glaucoma, narrow-angle glaucoma, pupil-block glaucoma, acute congestive glaucoma
    - Acute angle-closure glaucoma
    - Chronic angle-closure glaucoma
    - Intermittent angle-closure glaucoma
    - Superimposed on chronic open-angle closure glaucoma ("combined mechanism" - uncommon)
    - Primary open-angle glaucoma, also known as chronic open-angle glaucoma, chronic simple glaucoma, glaucoma simplex
    - High-tension glaucoma
    - Low-tension glaucoma
- Variants of primary glaucoma
    - Pigmentary glaucoma

- Exfoliation glaucoma, also known as pseudoexfoliative glaucoma or glaucoma capsulare

Primary angle-closure glaucoma – This is caused by contact between the iris and trabecular meshwork, which in turn obstructs outflow of the aqueous humor from the eye. This contact between iris and trabecular meshwork (TM) may gradually damage the function of the meshwork until it fails to keep pace with aqueous production, and the pressure rises. In over half of all cases, prolonged contact between iris and TM causes the formation of synechiae (effectively "scars"). These cause permanent obstruction of aqueous outflow. In some cases, pressure may rapidly build up in the eye causing pain and redness (symptomatic, or so called "acute" angle-closure). In this situation the vision may become blurred, and halos may be seen around bright lights. Accompanying symptoms may include headache and vomiting. Diagnosis is made from physical signs and symptoms: pupils mid-dilated and unresponsive to light, cornea edematous (cloudy), reduced vision, redness, pain. However, the majority of cases are asymptomatic. Prior to very severe loss of vision, these cases can only be identified by examination, generally by an eye care professional. Once any symptoms have been controlled, the first line (and often definitive) treatment is laser iridotomy. This may be performed using either Nd:YAG or argon lasers, or in some cases by conventional incisional surgery. The goal of treatment is to reverse, and prevent, contact between iris and trabecular meshwork. In early to moderately advanced cases, iridotomy is successful in opening the angle in around 75% of cases. In the other 25% laser iridoplasty, medication (pilocarpine) or incisional surgery may be required.

Primary open-angle glaucoma – Optic nerve damage resulting in progressive visual field loss. This is associated with increased pressure in the eye. Not all people with primary open-angle glaucoma have eye pressure that is elevated beyond normal, but decreasing the eye pressure further has been shown to stop progression even in these cases. The increased pressure is caused by trabecular blockage which is where the aqueous humor in the eye drains out. Because the microscopic passage ways are blocked, the pressure builds up in the eye and causes imperceptible very gradual vision loss. Peripheral vision is affected first but eventually the entire vision will be lost if not treated. Diagnosis is made by looking for cupping of the optic nerve. Prostaglandin agonists work by opening uveoscleral passageways. Beta blockers such as timolol, work by decreasing aqueous formation. Carbonic anhydrase inhibitors decrease bicarbonate formation from ciliary processes in the eye, thus decreasing formation of Aqueous humor. Parasympathetic analogs are drugs that work on the trabecular outflow by opening up the passageway and constricting the pupil. Alpha 2 agonists (brimonidine, apraclonidine) both decrease fluid production (via. inhibition of AC) and increase drainage.

Developmental glaucoma (Q15.0)

- Developmental glaucoma
    - Primary congenital glaucoma
    - Infantile glaucoma

- Glaucoma associated with hereditary of familial diseases

Secondary glaucoma (H40.3-H40.6)

- Secondary glaucoma
    - Inflammatory glaucoma
    - Uveitis of all types
    - Fuchs heterochromic iridocyclitis
    - Phacogenic glaucoma
    - Angle-closure glaucoma with mature cataract
    - Phacoanaphylactic glaucoma secondary to rupture of lens capsule
    - Phacolytic glaucoma due to phacotoxic meshwork blockage
    - Subluxation of lens
    - Glaucoma secondary to intraocular hemorrhage
    - Hyphema
    - Hemolytic glaucoma, also known as erythroclastic glaucoma
    - Traumatic glaucoma
    - Angle recession glaucoma: Traumatic recession on anterior chamber angle
    - Postsurgical glaucoma
    - Aphakic pupillary block
    - Ciliary block glaucoma
    - Neovascular glaucoma
    - Drug-induced glaucoma
    - Corticosteroid induced glaucoma
    - Alpha-chymotrypsin glaucoma. Postoperative ocular hypertension from use of alpha chymotrypsin.
    - Glaucoma of miscellaneous origin
    - Associated with intraocular tumors
    - Associated with retinal detachments
    - Secondary to severe chemical burns of the eye
    - Associated with essential iris atrophy
    - Toxic Glaucoma

Neovascular glaucoma is an uncommon type of glaucoma that is difficult or nearly impossible to treat. This condition is often caused by proliferative diabetic retinopathy (PDR) or central retinal vein occlusion (CRVO). It may also be triggered by other conditions that result in ischemia of the retina or ciliary body. Individuals with poor blood flow to the eye are highly at risk for this condition.

Neovascular glaucoma results when new, abnormal vessels begin developing in the angle of the eye that begin blocking the drainage. Patients with such condition begin to rapidly lose their eyesight. Sometimes, the disease appears very rapidly, specially after cataract surgery procedure. A new treatment for this disease, as first reported by Kahook and colleagues, involves use of a novel group of medications known as Anti-VEGF agents. These injectable medications can lead to a dramatic decrease in new vessel formation and, if injected early enough in the disease process, may lead to normalization of intraocular pressure.

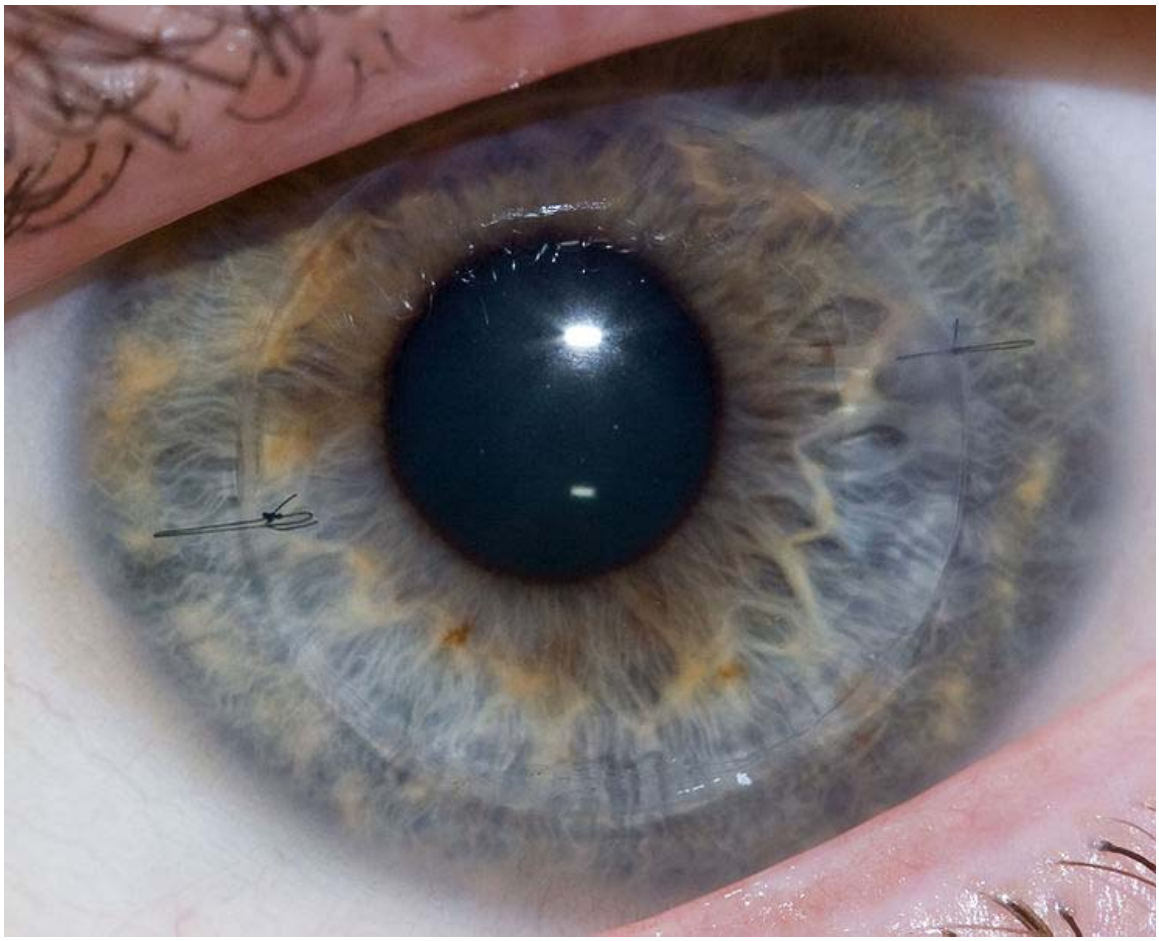
Toxic glaucoma is open angle glaucoma with an unexplained significant rise of intraocular pressure following unknown pathogenesis. Intraocular pressure can sometimes reach 80 mmHg (11 kPa). It characteristically manifests as ciliary body inflammation and massive trabecular oedema that sometimes extends to Schlemm's Canal. This condition is differentiated from malignant glaucoma by the presence of a deep and clear anterior chamber and a lack of aqueous misdirection. Also, the corneal appearance is not as hazy. A reduction in visual acuity can occur followed neuroretinal breakdown. Associated factors include inflammation, drugs, trauma and intraocular surgery, including cataract surgery and vitrectomy procedures. Gede Pardianto (2005) reports on four patients who had toxic glaucoma. One of them underwent phaecoemulsification with small particle nucleus drops. Some cases can be resolved with some medication, vitrectomy procedures or trabeculectomy. Valving procedures can give some relief but further research is required.

Absolute glaucoma (H44.5)

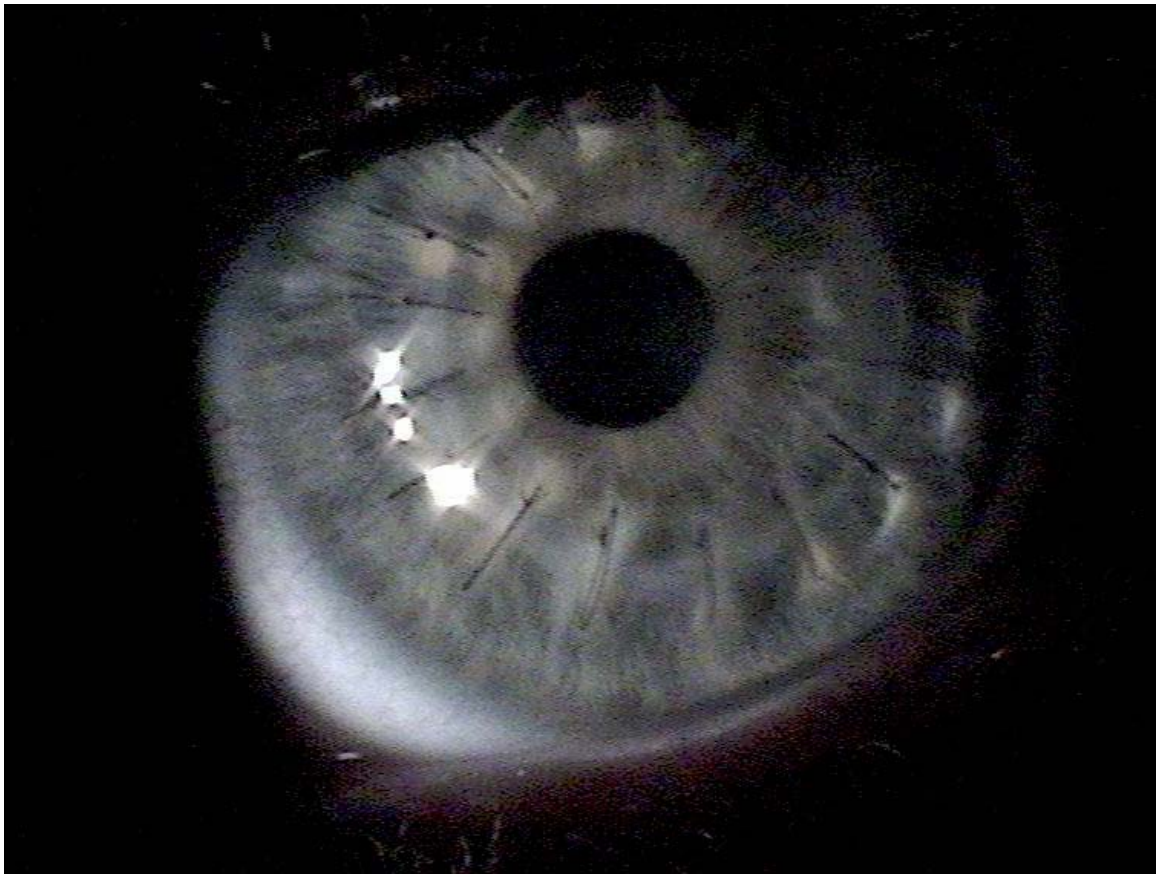
- Absolute glaucoma is the end stage of all types of glaucoma. The eye has no vision, absence of PL and PR, and has a stony appearance. Severe pain is present in the eye. The treatment of absolute glaucoma is a destructive procedure like cyclocryo application, cyclophotocoagulation, or injection of 100% alcohol.

Chapter 11

Corneal Transplantation



Cornea transplant after one year of healing, two stitches are visible



Cornea transplant approximately one week after surgery. Multiple light reflections indicate folds in the cornea, which later resolved.

Corneal transplantation, also known as **corneal grafting**, is a surgical procedure where a damaged or diseased cornea is replaced by donated corneal tissue (the graft) in its entirety (penetrating keratoplasty) or in part (lamellar keratoplasty). The graft has been removed from a recently deceased individual with no known diseases or other factors that may affect the viability of the donated tissue or the health of the recipient. The cornea is the transparent front part of the eye that covers the iris, pupil and anterior chamber. The surgical procedure is performed by ophthalmologists, medical doctors who specialize in eyes, and is often done on an outpatient basis.

Indications

Indications for corneal transplantation include the following:

- Optical: To improve visual acuity by replacing the opaque or distorted host tissue by clear healthy donor tissue. The most common indication in this category is pseudophakic bullous keratopathy, followed by keratoconus, corneal degeneration, keratoglobus and dystrophy, as well as scarring due to keratitis and trauma.

- Tectonic/reconstructive: To preserve corneal anatomy and integrity in patients with stromal thinning and descemetoceles, or to reconstruct the anatomy of the eye, e.g. after corneal perforation.
- Therapeutic: To remove inflamed corneal tissue unresponsive to treatment by antibiotics or anti-virals.
- Cosmetic: To improve the appearance of patients with corneal scars that have given a whitish or opaque hue to the cornea.

Pre-operative examination

In most instances, the patient will meet with their ophthalmologist for an examination in the weeks or months preceding the surgery. During the exam, the ophthalmologist will examine the eye and diagnose the condition. The doctor will then discuss the condition with the patient, including the different treatment options available. The doctor will also discuss the risks and benefits of the various options. If the patient elects to proceed with the surgery, the doctor will have the patient sign an informed consent form. The doctor might also perform a physical examination and order lab tests, such as blood work, X-rays, or an EKG.

The surgery date and time will also be set, and the patient will be told where the surgery will take place. The surgery only takes place when the best corresponding donor tissue is found. This can take weeks and months.

Procedure

On the day of the surgery, the patient arrives to either a hospital or an outpatient surgery center, where the procedure will be performed. The patient is given a brief physical examination by the surgical team and is taken to the operating room. In the OR, the patient lies down on an operating table and is either given general anesthesia, or local anesthesia and a sedative.

With anesthesia induced, the surgical team prepares the eye to be operated on and drapes the face around the eye. An eyelid speculum is placed to keep the lids open, and some lubrication is placed on the eye to prevent drying. In children, a metal ring is stitched to the sclera which will provide support of the sclera during the procedure.

Penetrating keratoplasty

A trephine (a circular cutting device) is then placed over the cornea and is used by the surgeon to cut the host cornea, which removes a circular disc of the patient cornea. The trephine is then removed and the surgeon cuts a circular graft (a "button") from the donor cornea. Once this is done, the surgeon returns to the patient's eye and removes the host cornea.

The donor cornea is then brought into the surgical field and maneuvered into place with forceps. Once in place, the surgeon will fasten the cornea to the eye with a running stitch

(as used in the upper image above) or a multiple interrupted stitches (as in the lower image). The surgeon then reforming the anterior chamber with a sterile solution injected by a cannula, then testing that it's watertight by placing a dye on the wound exterior.

Antibiotic eyedrops placed, the eye is patched, and the patient is taken to a recovery area while the effects of the anesthesia wear off. The patient typically goes home following this and sees the doctor the following day for the first post operative appointment.

Lamellar keratoplasty

This procedure consists in leaving just the patient's own Descemet membrane and endothelium, while transplanting approximately 95% of the cornea. The great advantage of this technique is the virtually "no rejection" post-op. The main disadvantage is that the visual acuity is not as sharp as it is with the full cornea transplantation penetrating keratoplasty). The final visual acuity is usually around 20/40.

Risks

While the cornea is avascular, there is still a potential for some blood loss, usually from suturing the metal ring to the sclera. Any blood loss is typically less than 2 ml (0.07 imp fl oz; 0.07 US fl oz).

There is also a risk of infection. Since the cornea has no blood vessels (it takes its nutrients from the aqueous humor) it heals much more slowly than a cut on the skin. While the wound is healing, it is possible that it might become infected by various microorganisms. This risk is minimized by antibiotic prophylaxis (using antibiotic eyedrops, even when no infection exists).

Graft failure can occur at any time after the cornea has been transplanted, even years or decades later. The causes can vary, though it is usually due to new injury or illness. Treatment can be either medical or surgical, depending on the individual case. An early, technical cause of failure, may be an excessively tight stitch cheesewiring through the sclera.

Prognosis

When the primary purpose of a cornea transplant is to improve visual acuity, the prognosis is dependent upon whether the rest of the eye is healthy. If it is, then it should be possible to recover normal vision.

History

The first cornea transplant was performed in 1905 by Eduard Zirm, making it one of the first types of transplant surgery successfully performed. Another pioneer of the operation was Ramon Castroviejo. Russian eye surgeon Vladimir Filatov's attempts at tranplanting cornea started with the first try in 1912 and were continued, gradually improving until at

6 May 1931 he successfully grafted a patient using corneal tissue from a deceased person. He widely reported of another transplant in 1936, disclosing his technique in full detail. In 1936, Castroviejo did a first transplantation in an advanced case of keratoconus, achieving significant improvement in patient's vision.

Advances in operating microscopes enabled surgeons to have a more magnified view of the surgical field, while advances in materials science enabled them to use sutures finer than a human hair.

Instrumental in the success of cornea transplants were the establishment of eye banks. These are organizations located throughout the world to coordinate the distribution of donated corneas to surgeons, as well as providing eyes for research. Some eye banks also distribute other anatomical gifts.

Synthetic corneas

Boston keratoprosthesis

The Boston keratoprosthesis is the most widely used synthetic cornea to date with over 900 procedures performed worldwide in 2008. The Boston KPro was developed at the Massachusetts Eye and Ear Infirmary under the leadership of Claes Dohlman, MD, PhD.

AlphaCor

In cases where there have been several graft failures or the risk for keratoplasty is high, synthetic corneas can substitute successfully for donor corneas. Such a device contains a peripheral skirt and a transparent central region. These two parts are connected on a molecular level by an interpenetrating polymer network, made from poly-2-hydroxyethyl methacrylate (pHEMA). AlphaCor is an FDA-approved type of synthetic cornea measuring 7.0 mm in diameter and 0.5 mm in thickness. The main advantages of synthetic corneas are that they are biocompatible, and the network between the parts and the device prevents complications that could arise at their interface. The probability of retention in one large study was estimated at 62% at 2 years follow-up. AlphaCor carry lesser risk of diseases that could be transmitted through donor tissue. However, they also cost $10,000.

AlphaCor surgery is reserved for patients who have had traditional cornea transplants either: 1) fail repeatedly, 2) reject due to autoimmune process, or 3) have a highly vascularized cornea that makes traditional cornea transplantation unsuitable.

Use of AlphaCor involved a two part procedure. First the AlphaCor disc is implanted under the tissue. Second, after healing many months later the membrane covering the lens of the disc is removed allowing that eye to see. Glasses will still be needed to optimize vision afterwards.

Osteo-Odonto-Keratoprosthesis

In a very rare and complex multi-step surgical procedure, employed to help the most disabled patients, a lamina of the patient's tooth is grafted into the eye, with an artificial lens installed in the transplanted piece.

Alternatives

Phototherapeutic keratectomy (PTK)

Diseases that only affect the surface of the cornea can be treated with an operation called phototherapeutic keratectomy. With the precision of an excimer laser and a modulating agent coating the eye, irregularities on the surface can be removed. However, in most of the cases where corneal transplantation is recommended, PTK would not be effective.

Intrastromal corneal ring segments

The implants manufactured under the trade name Intacs are the only patented intrastromal corneal implant that has US FDA approval and European CE Mark for both Myopia and Keratoconus. There are over one-hundred clinical articles at for clinical reference (search for Intacs and they all are arranged in chronological order) and are a well documented clinical solution for treating keratoconus. Another version of intrastromal cornea ring segments is manufactured under the trade name KeraRing and is available in South America and Europe.

With this procedure, the implants are placed in the stroma to reshape the cornea into a more natural shape. In mild myopia, this corrects a patients vision. In keratoconus, the goal is to reshape the cornea to where contact lens intolerant patients are able to achieve functional vision with contact lenses or glasses. Although, surgical procedure don't carry a guarantee, one clinically proven benefit of Intacs is that they can be safely removed and the cornea returns to its pre-operative state. Future treatment options are not affected.

Contact lenses

In the early stages and up to the more advanced stages of keratoconus, contact lenses are often used to improve vision. Contact lenses improve visual acuity of the majority of the keratoconus patients. The majority of the patients need to use hard contact lenses. Only 10 to 20% will need cornea tranplantion during their lifetimes due to progression of the disease.

New technology

High speed lasers

Blades are being replaced by high speed lasers in order to make surgical incisions more precise. These improved incisions allow the cornea to heal more quickly and the sutures

to be removed sooner. The cornea heals more strongly than with standard blade operations. Not only does this dramatically improve visual recovery and healing, it also allows the possibility for improvement in visual outcomes.

Since 2004, Amnitrans Eyebank in Rotterdam, The Netherlands, provides donor corneas pre-cut for advanced keratoplasty procedures, such as DSEK, DSAEK, FS-DSEK and DMEK. In 2007, Seattle-based SightLife, one of the leading corneal tissue banks in the world, introduced a process for the preparation of donated corneal tissue using a Femtosecond Laser. This process is known as Custom Corneal Tissue.

DSEK/DSAEK/DMEK

Endothelial keratoplasty (EK) has been introduced by Melles et al. in 1998. Today there are three forms of EK. Deep Lamellar Endothelial Keratoplasty (DLEK) in which the posterior part of the recipient cornea is replaced by donor tissue. Descemet's Stripping (Automated) Endothelial Keratoplasty (DSEK/DSAEK) in which the diseased Descemet's membrane is removed and replaced by a healthy donor posterior transplant. The transplant tissue can be prepared by a surgeon's hand or ordered already prepared for surgery. Ocular Systems Inc. was the first organization to deliver prepared grafts for surgery in 2005. DSEK/DSAEK uses only a small incision that is either self-sealing or may be closed with a few sutures. The small incision offers several benefits over traditional methods of corneal transplant such as Penetrating Keratoplasty. Because the procedure is less invasive, DSAEK leaves the eye much stronger and less prone to injury than full-thickness transplants. New medical devices such as the EndoSaver (patent pending) are designed to ease process of inserting endothelial tissue into the cornea. Additionally, DSAEK has a more rapid rate of visual recovery. Vision is typically restored in one to six months rather than one to two years. Descemet Membrane Endothelial Keratoplasty (DMEK)] is the most recent EK technique in which an isolated Descemet membrane is transplanted. The DMEK procedure combines the anatomical benefits of DSEK/DSAEK with visual rehabilitation to 20/40 or better in 90% of cases and 20/25 or better in 60% of cases within the first three months. In the UK (2010) the omly surgeon offering DMEK procedure under the auspices of the National Health Service is Mr. Ewan Craig of the Royal Shrewsbury Hospital.

Not all patients with diseased corneas are candidates for endothelial keratoplasty. These procedures correct corneal endothelial failure, but are not able to correct corneal scarring, thinning, or surface irregularity. There is currently very little data on long-term survival of DMEK grafts.

Stem cells

There is a bioengineering technique that uses stem cells to create corneas or part of corneas that can be transplanted into the eyes. Corneal stem cells are removed from a healthy cornea. They are collected and, through laboratory procedures, made into five to ten layers of cells that can be stitched into a patient’s eye. The stem cells are placed into the area where the damaged cornea tissue has been removed. This is a good alternative

for those that cannot gain vision through regular cornea transplants. A new development, announced by the University of Cincinnati Medical School in May 2007, would use bone marrow stem cells to regrow the cornea and its cells. This technique, which proved successful in mouse trials, would be of use to those suffering from inherited genetic degenerative conditions of the cornea, especially if other means like a transplant aren't feasible. It works better than a transplant because these stem cells keep their ability to differentiate and replicate, and so keep the disease from recurring, longer and better.

Biosynthetic corneas

On 25 August 2010 investigators from Canada and Sweden reported results from the first 10 people in the world treated with the biosynthetic corneas. Two years after having the corneas implanted, six of the 10 patients had improved vision. Nine of the 10 experienced cell and nerve regeneration, meaning that corneal cells and nerves grew into the implant. To make the material, the researchers placed a human gene that regulates the natural production of collagen into specially programmed yeast cells. They then molded the resulting material into the shape of a cornea. This research shows the potential for these bioengineered corneas but the outcomes in this study were not nearly as good as those achieved with human donor corneas. This may become an excellent technique, but right now it is still in the prototype stage and not ready for clinical use. The results were published in the journal Science Translational Medicine.

Epidemiology and economics

Corneal transplant is one of the most common transplant procedures. Although approximately 100,000 procedures are performed worldwide each year, some estimates report that 10,000,000 people are affected by various disorders that would benefit from corneal transplantation.

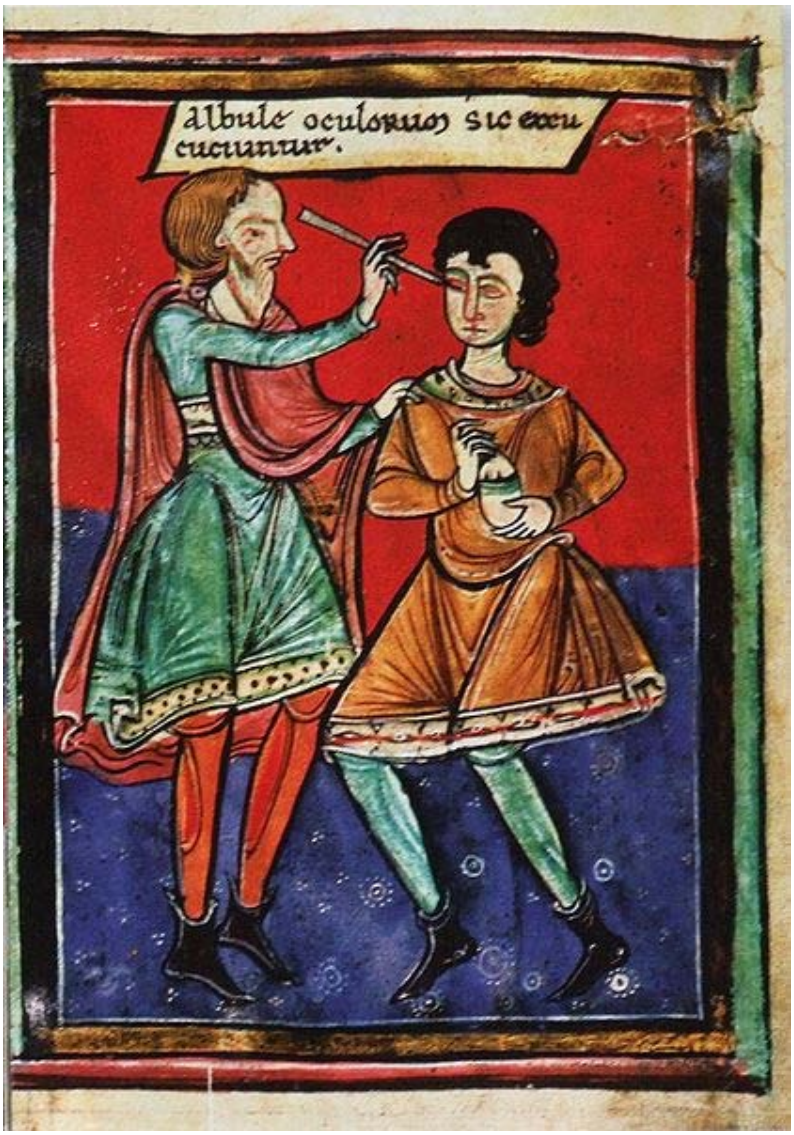
In Australia, approximately 1,500 grafts are performed each year. According to the NHS Blood and Transplant, over 2,300 corneal transplant procedures are performed each year in the United Kingdom. Between April 1, 2005 and March 31, 2006, 2,503 people received corneal transplants in the UK.

In the United States, the cost is usually covered in part by Medicare and health insurers. Reimbursement depends on your personal healthcare provider. Usually 80% of the cost will be covered by your agency. Those on Medicare will be reimbursed up to $1,200 while the remainder is left up to the patient. The average cost of the procedure ranges from $7,500 to $11,000.

In 2005, there were about 32,840 corneal transplant recipients. The estimated first year billed charges per patient, including medications, was $19,100. There were a larger number of transplants for patients over 65 than under, 18,000 compared to 14,840. There were 41,652 corneal transplants performed in the United States in 2008.

Chapter 12

Eye Surgery



Eye surgery in the Middle Ages

Eye surgery, also known as **orogolomistician surgery** or **ocular surgery**, is surgery performed on the eye or its adnexa, typically by an ophthalmologist.

Preparation and precautions

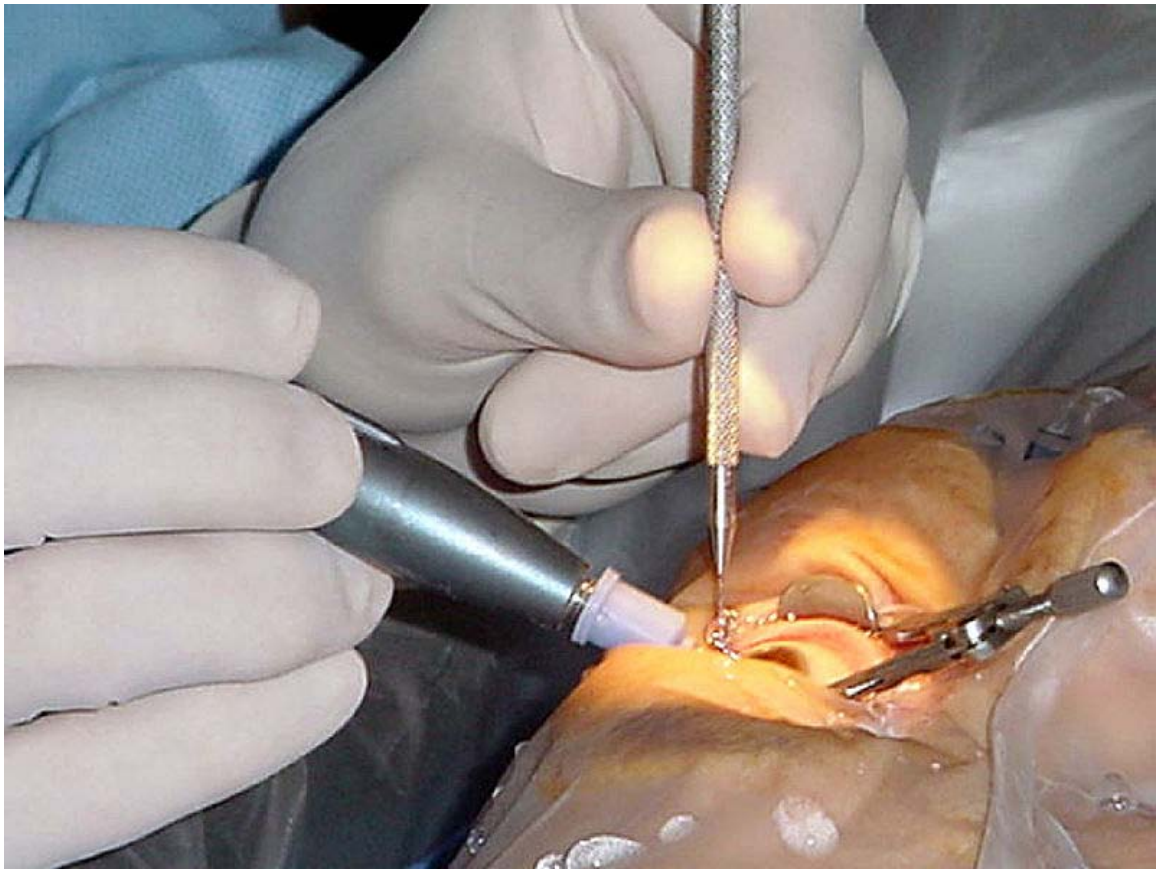
The eye is a fragile organ, requiring extreme care before, during and after a surgical procedure. An expert eye surgeon must identify the need for specific procedure and be responsible for conducting the procedure safely. Many university programmes allow patients to specify if they want to be operated upon by the consultant or the resident / fellow.

Anesthesia is essential for any eye surgery. Local anesthesia is most commonly used. Retrobulbar and peribulbar techniques for infiltrating the local area surrounding the eye muscle cone are used to immobilize the extraocular muscles and eliminate pain sensation. Topical anesthesia using lidocaine topical gel is preferred for quick procedures. In topical anesthesia, patient cooperation is a must for a smooth procedure. General anesthesia is recommended for children, traumatic eye injuries, major orbitotomies and for apprehensive patients. Cardiovascular monitoring is preferable in local anesthesia and is mandatory in general anesthesia. Proper sterile precautions are taken to prepare the area for surgery, including use of antiseptics like povidone-iodine. Sterile drapes, gowns and gloves are a must. A plastic sheet with a receptacle helps collect the fluids during phacoemulsification. An eye speculum is inserted to keep the eyes wide open.

Laser eye surgery

Although the terms laser eye surgery and refractive surgery are commonly used as if they were interchangeable, this is not the case. Lasers may be used to treat nonrefractive conditions (e.g. to seal a retinal tear), while radial keratotomy is an example of refractive surgery without the use of a laser.

Cataract surgery



Cataract surgery, using a temporal approach phacoemulsification probe (in right hand) and "chopper"(in left hand) being done under operating microscope at a Navy medical center

A cataract is an opacification or cloudiness of the eye's crystalline lens due to aging, disease, or trauma that typically prevents light from forming a clear image on the retina. If visual loss is significant, surgical removal of the lens may be warranted, with lost optical power usually replaced with a plastic intraocular lens (IOL). Owing to the high prevalence of cataracts, cataract extraction is the most common eye surgery. Rest after surgery is recommended.

Glaucoma surgery

Glaucoma is a group of diseases affecting the optic nerve that results in vision loss and is frequently characterized by raised intraocular pressure (IOP). There are many types of glaucoma surgery, and variations or combinations of those types, that facilitate the escape of excess aqueous humor from the eye to lower intraocular pressure, and a few that lower IOP by decreasing the production of aqueous humor.

Canaloplasty

Canaloplasty is an advanced, nonpenetrating procedure designed to enhance drainage through the eye's natural drainage system to provide sustained reduction of IOP. Canaloplasty utilizes microcatheter technology in a simple and minimally invasive procedure. To perform a canaloplasty, an Ophthalmologist creates a tiny incision to gain access to a canal in the eye. A microcatheter circumnavigates the canal around the iris, enlarging the main drainage channel and its smaller collector channels through the injection of a sterile, gel-like material called viscoelastic. The catheter is then removed and a suture is placed within the canal and tightened. By opening up the canal, the pressure inside the eye can be reduced. Long-term results are available, published in the *Journal of Cataract and Refractive Surgery*.

Refractive surgery

Refractive surgery aims to correct errors of refraction in the eye, reducing or eliminating the need for corrective lenses

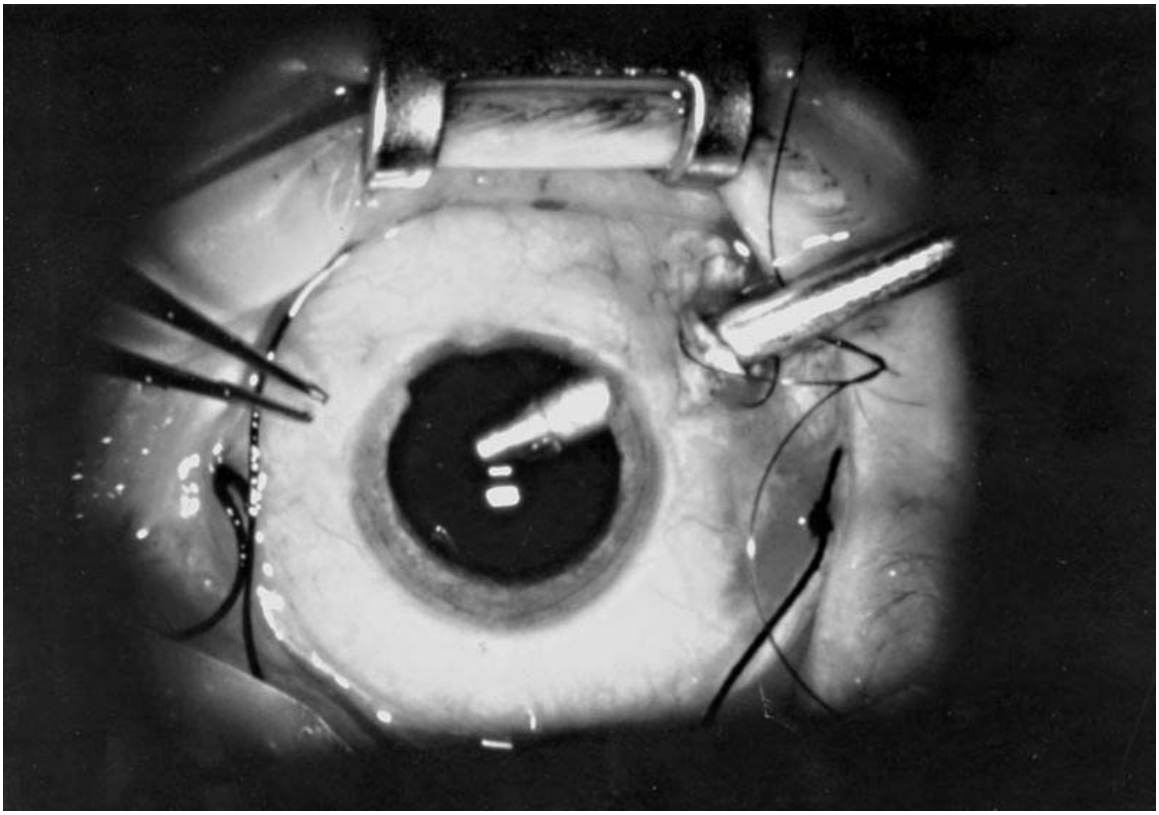
- **Keratomilleusis** is method of reshaping the cornea surface to change its optical power. A disc of cornea is shaved off, quickly frozen, lathe-ground, then returned to its original power.
- **Automated lamellar keratoplasty** (ALK)
- **Laser assisted in-situ keratomileusis** (LASIK)
    - **IntraLASIK**
- **Laser assisted sub-epithelial keratomileusis** (LASEK), aka Epi-LASIK
- **Photorefractive keratectomy** (PRK)
- **Laser thermal keratoplasty** (LTK)
- **Conductive keratoplasty** (CK) uses radio frequency waves to shrink corneal collagen. It is used to treat mild to moderate hyperopia.
- Limbal relaxing incisions (LRI) to correct minor astigmatism
- **Astigmatic keratotomy** (AK), aka Arcuate keratotomy or Transverse keratotomy
- **Radial keratotomy** (RK)
- **Hexagonal keratotomy** (HK)
- **Epikeratophakia** is the removal of the corneal epithelium and replacement with a lathe cut corneal button.
- **Intracorneal rings** (ICRs), or corneal ring segments (*Intacs*)
- Implantable contact lenses
- Presbyopia reversal
- Anterior ciliary sclerotomy (ACS)
- Laser reversal of presbyopia (LRP)
- Scleral expansion bands

Corneal surgery

Corneal surgery includes most refractive surgery as well as the following:

- **Corneal transplant surgery**, is used to remove a cloudy/diseased cornea and replace it with a clear donor cornea.
- **Penetrating keratoplasty** (PK)
- **Keratoprosthesis**(KPro)
- **Phototherapeutic keratectomy** (PTK)
- Pterygium excision
- Corneal tattooing
- Osteo-Odonto-Keratoprosthesis (OOKP), in which support for an artificial cornea is created from a tooth and its surrounding jawbone. This is a still-experimental procedure used for patients with severely damaged eyes, generally from burns.

Vitreo-retinal surgery



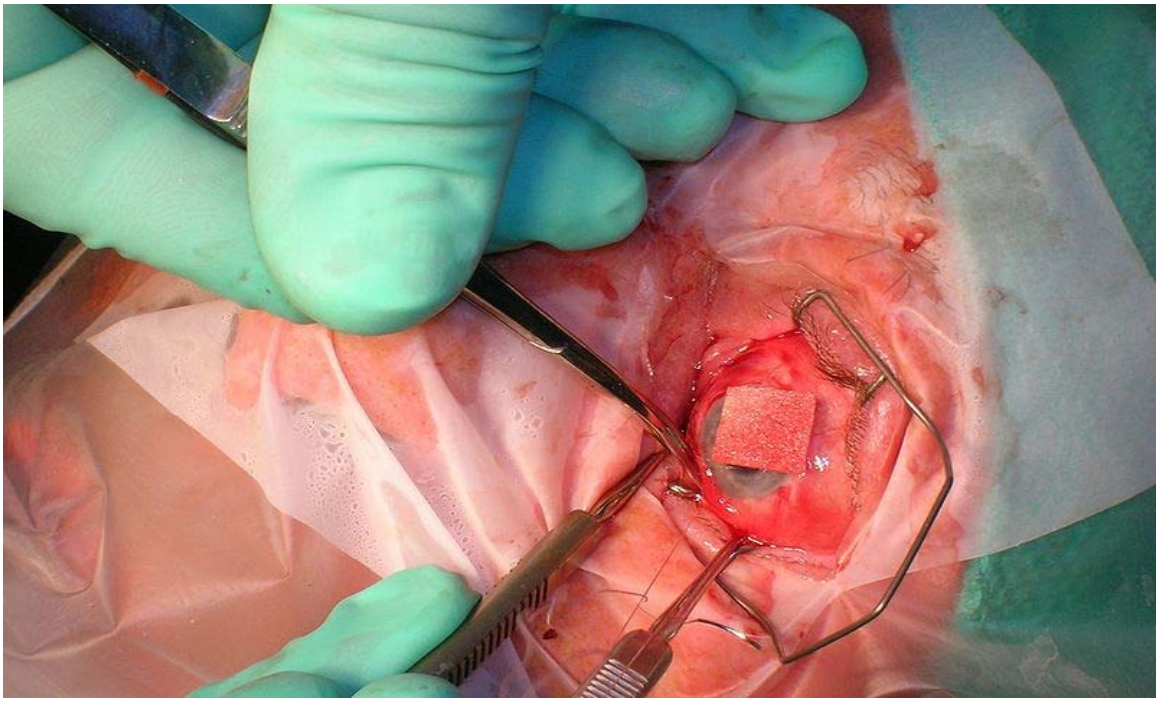
Vitrectomy

Vitreo-retinal surgery includes the following

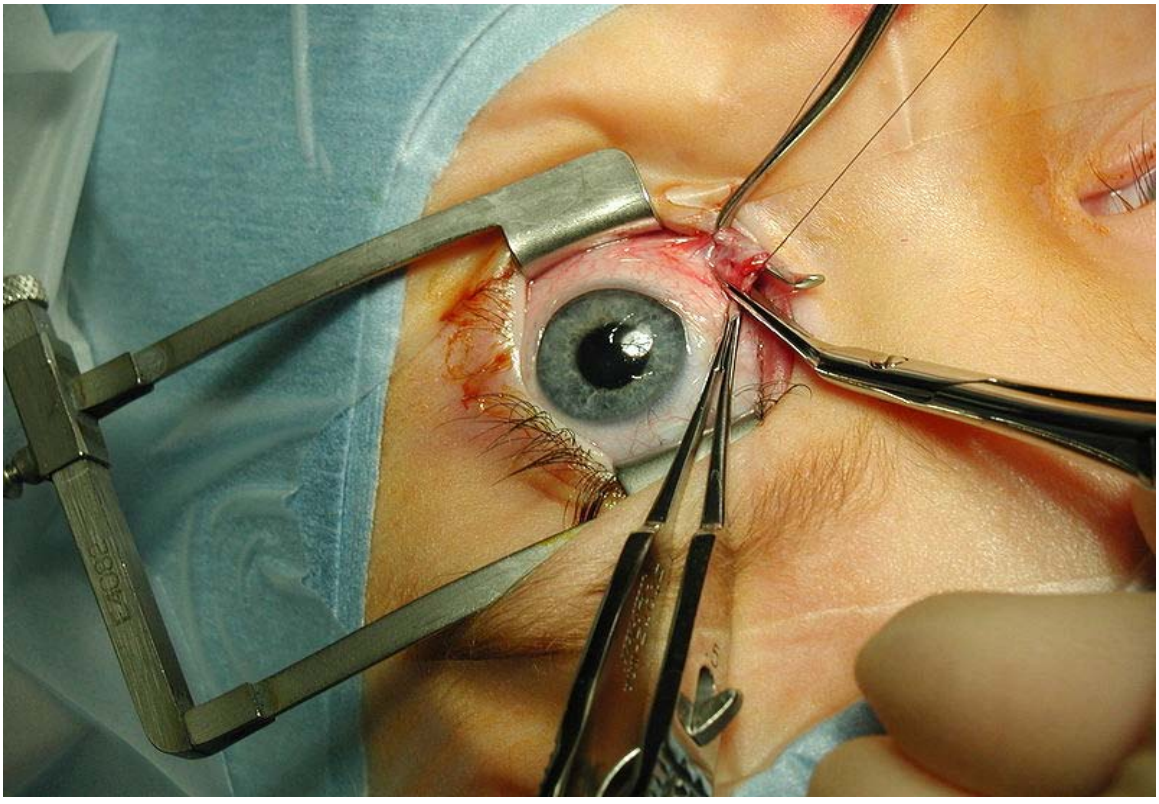
- **Vitrectomy**
  - **Anterior vitrectomy** is the removal of the front portion of vitreous tissue. It is used for preventing or treating vitreous loss during cataract or corneal

surgery, or to remove misplaced vitreous in conditions such as aphakia pupillary block glaucoma.
    - **Pars plana vitrectomy** (PPV), or trans pars plana vitrectomy (TPPV), is a procedure to remove vitreous opacities and membranes through a pars plana incision. It is frequently combined with other intraocular procedures for the treatment of giant retinal tears, tractional retinal detachments, and posterior vitreous detachments.
- **Pan retinal photocoagulation** (PRP) is a type of photocoagulation therapy used in the treatment of diabetic retinopathy.
- Retinal detachment repair
    - **Ignipuncture** is an obsolete procedure that involves cauterization of the retina with a very hot pointed instrument.
    - A scleral buckle is used in the repair of a retinal detachment to indent or "buckle" the sclera inward, usually by sewing a piece of preserved sclera or silicone rubber to its surface.
    - Laser photocoagulation, or photocoagulation therapy, is the use of a laser to seal a retinal tear.
    - **Pneumatic retinopexy**
    - **Retinal cryopexy**, or **retinal cryotherapy**, is a procedure that uses intense cold to induce a chorioretinal scar and to destroy retinal or choroidal tissue.
- Macular hole repair
- **Partial lamellar sclerouvectomy**
- **Partial lamellar sclerocyclochoroidectomy**
- **Partial lamellar sclerochoroidectomy**
- **Posterior sclerotomy** is an opening made into the vitreous through the sclera, as for detached retina or the removal of a foreign body.
- **Radial optic neurotomy**
- macular translocation surgery
    - through 360 degree retinotomy
    - through scleral imbrication technique

Eye muscle surgery



Isolating the inferior rectus muscle



Disinserting the medial rectus muscle, after pre-placing vicryl suture

With approximately 1.2 million procedures each year, extraocular muscle surgery is the third most common eye surgery in the United States.

- Eye muscle surgery typically corrects strabismus and includes the following :
    - Loosening / weakening procedures
        - Recession involves moving the insertion of a muscle posteriorly towards its origin.
        - Myectomy
        - Myotomy
        - Tenectomy
        - Tenotomy
    - Tightening / strengthening procedures
        - Resection
        - Tucking
        - Advancement is the movement of an eye muscle from its original place of attachment on the eyeball to a more forward position.
    - Transposition / repositioning procedures
    - Adjustable suture surgery is a method of reattaching an extraocular muscle by means of a stitch that can be shortened or lengthened within the first post-operative day, to obtain better ocular alignment.

Oculoplastic surgery

Oculoplastic surgery, or oculoplastics, is the subspecialty of ophthalmology that deals with the reconstruction of the eye and associated structures. Oculoplastic surgeons perform procedures such as the repair of droopy eyelids (blepharoplasty), repair of tear duct obstructions, orbital fracture repairs, removal of tumors in and around the eyes, and facial rejuvenation procedures including laser skin resurfacing, eye lifts, brow lifts, and even facelifts. Common procedures are:

Eyelid surgery

- Blepharoplasty (Eyelift)
    - **Blepharoplasty** is plastic surgery of the eyelids to remove excessive skin or subcutaneous fat.
        - **Asian blepharoplasty**
- Ptosis repair for droopy eyelid
    - Ectropion repair
- Entropion repair
- Canthal resection
    - A **canthectomy** is the surgical removal of tissue at the junction of the upper and lower eyelids.
    - **Cantholysis** is the surgical division of the canthus.
    - **Canthopexy**
    - A **canthoplasty** is plastic surgery at the canthus.

    - A **canthorrhaphy** is suturing of the outer canthus to shorten the palpebral fissure.
    - A **canthotomy** is the surgical division of the canthus, usually the outer canthus.
        - A **lateral canthotomy** is the surgical division of the outer canthus.
- **Epicanthoplasty**
- **Tarsorrhaphy** is a procedure in which the eyelids are partially sewn together to narrow the opening (i.e. palpebral fissure).

Orbital surgery

- Orbital reconstruction / Ocular prosthetics (False Eyes)
- Orbital decompression for Grave's Disease. Grave's Disease is a condition (often associated with over-active thyroid problems) in which the eye muscles swell. Because the eye socket is bone, there is nowhere for the swelling to be accommodated and as a result the eye is pushed forward into a protruded position. In some patients this is very pronounced. Orbitial decompression involves removing some bone from the eye socket to open up one or more sinuses and so make space for the swollen tissue and allowing the eye to move back into normal position.

Other oculoplastic surgery

- Botox injections
- Ultrapeel Microdermabrasion
- Endoscopic forehead and browlift
- Face lift (Rhytidectomy)
- Liposuction of the face and neck
- **Browplasty**

Surgery involving the lacrimal apparatus

- A **dacryocystorhinostomy** (DCR) or **dacryocystorhinotomy** is a procedure to restore the flow of tears into the nose from the lacrimal sac when the nasolacrimal duct does not function.
- **Canaliculodacryocystostomy** is a surgical correction for a congenitally blocked tear duct in which the closed segment is excised and the open end is joined to the lacrimal sac.
- **Canaliculotomy** involves slitting of the lacrimal punctum and canaliculus for the relief of epiphora
- A **dacryoadenectomy** is the surgical removal of a lacrimal gland.
- A **dacryocystectomy** is the surgical removal of a part of the lacrimal sac.
- A **dacryocystostomy** is an incision into the lacrimal sac, usually to promote drainage.
- A **dacryocystotomy** is an incision into the lacrimal sac.

Eye removal

- An **enucleation** is the removal of the eye leaving the eye muscles and remaining orbital contents intact.
- An **evisceration** is the removal of the eye's contents, leaving the scleral shell intact. Usually performed to reduce pain in a blind eye.
- An **exenteration** is the removal of the entire orbital contents, including the eye, extraocular muscles, fat, and connective tissues; usually for malignant orbital tumors.

Other surgery

Many of these described procedures are historical and are not recommended due to a risk of complications. Particularly, these include operations done on ciliary body in an attempt to control glaucoma, since highly safer surgeries for glaucoma, including lasers, non-penetrating surgery, guarded filtration surgery and seton valve implants have been invented.

- A **ciliarotomy** is a surgical division of the ciliary zone in the treatment of glaucoma.
- A **ciliectomy** is 1) the surgical removal of part of the ciliary body, or 2) the surgical removal of part of a margin of an eyelid containing the roots of the eyelashes.
- A **ciliotomy** is a surgical section of the ciliary nerves.
- A **conjunctivoanstrostomy** is an opening made form the inferior conjuctival cul-de-sac into the maxillary sinus for the treatment of epiphora.
- **Conjuctivoplasty** is plastic surgery of the conjunctiva.
- A **conjunctivorhinostomy** is a surgical correction of the total obstruction of a lacrimal canaliculus by which the conjuctiva is anastomosed with the nasal cavity to improve tear flow.
- A **corectomedialysis**, or **coretomedialysis**, is an excision of a small portion of the iris at its junction with the ciliary body to form an artificial pupil.
- A **corectomy**, or **coretomy**, is any surgical cutting operation on the iris at the pupil.
- A **corelysis** is a surgical detachment of adhesions of the iris to the capsule of the crystalline lens or cornea.
- A **coremorphosis** is the surgical formation of an artificial pupil.
- A **coreplasty**, or **coreoplasty**, is plastic surgery of the iris, usually for the formation of an artificial pupil.
- A **coreoplasy**, or **laser pupillomydriasis**, is any procedure that changes the size or shape of the pupil.
- A **cyclectomy** is an excision of portion of the ciliary body.
- A **cyclotomy**, or **cyclicotomy**, is a surgical incision of the ciliary body, usually for the relief of glaucoma.
- A **cycloanemization** is a surgical obliteration of the long ciliary arteries in the treatment of glaucoma.

- An **iridectomesodialsys** is the formation of an artificial pupil by detaching and excising a portion of the iris at its periphery.
- An **iridodialysis**, sometimes known as a **coredialysis**, is a localized separation or tearing away of the iris from its attachment to the ciliary body.
- An **iridencleisis**, or **corenclisis**, is a surgical procedure for glaucoma in which a portion of the iris is incised and incarcerated in a limbal incision. (Subdivided into **basal iridencleisis** and **total iridencleisis**.)
- An **iridesis** is a surgical procedure in which a portion of the iris is brought through and incarcerated in a corneal incision in order to reposition the pupil.
- An **iridocorneosclerectomy** is the surgical removal of a portion of the iris, the cornea, and the sclera.
- An **iridocyclectomy** is the surgical removal of the iris and the ciliary body.
- An **iridocystectomy** is the surgical removal of a portion of the iris to form an artificial pupil.
- An **iridosclerectomy** is the surgical removal of a portion of the sclera and a portion of the iris in the region of the limbus for the treatment of glaucoma.
- An **iridosclerotomy** is the surgical puncture of the sclera and the margin of the iris for the treatment of glaucoma.
- A **rhinommectomy** is the surgical removal of a portion of the internal canthus.
- A **trepanotrabeculectomy** is used in the treatment of chronic open and chronic closed angle glaucoma.

Chapter 13

Glaucoma Surgery and Keratoprosthesis

Glaucoma surgery

Glaucoma is a group of diseases affecting the optic nerve that results in vision loss and is frequently characterized by raised intraocular pressure (IOP). There are many glaucoma surgeries, and variations or combinations of those surgeries, that facilitate the escape of excess aqueous humor from the eye to lower intraocular pressure, and a few that lower IOP by decreasing the production of aqueous.

Procedures that facilitate outflow of aqueous humor

Laser trabeculoplasty

A **trabeculoplasty** is a modification of the trabecular meshwork. **Laser trabeculoplasty** (LTP) is the application of a laser beam to burn areas of the trabecular meshwork, located near the base of the iris, to increase fluid outflow. LTP is used in the treatment of various open-angle glaucomas. The two types of laser trabeculoplasty are **argon laser trabeculoplasty** (ALT) and **selective laser trabeculoplasty** (SLT). As its name suggests, argon laser trabeculoplasty uses an argon laser to create tiny burns on the trabecular meshwork. Selective laser trabeculoplasty is newer technology that uses a Nd:YAG laser to target specific cells within the trabecular meshwork and create less thermal damage than ALT. SLT shows promise as a long term treatment. In SLT a laser is used to selectively target the melanocytes in the trabecular meshwork. Though the mechanism by which SLT functions is not well understood, it has been shown in trials to be as effective as the older Argon Laser Trabeculoplasty. However, because SLT is performed using a much lower power laser, it does not appear to affect the structure of the trabecular meshwork (based on electron microscopy) to the same extent, so retreatment may be possible if the effects from the original treatment should begin wear off, although this has not been proven in clinical studies. ALT is repeatable to some extent with measurable results possible.

Iridotomy

An **iridotomy** involves making puncture-like openings through the iris without the removal of iris tissue. Performed either with standard surgical instruments or a laser, it is

typically used to decrease intraocular pressure in patients with angle-closure glaucoma. A **laser peripheral iridotomy** (LPI) is the application of a laser beam to selectively burn a hole through the iris near its base. LPI may be performed with either an argon laser or Nd:YAG laser.

Iridectomy

An **iridectomy**, also known as a **corectomy** or **surgical iridectomy**, involves the removal of a portion of iris tissue. A basal iridectomy is the removal of iris tissue from the far periphery, near the iris root; a peripheral iridectomy is the removal of iris tissue at the periphery; and a sector iridectomy is the removal of a wedge-shaped section of iris that extends from the pupil margin to the iris root, leaving a keyhole-shaped pupil.

Filtering procedures: penetrating vs. non-penetrating

Filtering surgeries are the mainstay of surgical treatment to control intraocular pressure. An **anterior sclerotomy** or **sclerostomy** is used to gain access to the inner layers of the eye in order to create a drainage channel from the anterior chamber to the external surface of the eye under the conjunctiva, allowing aqueous to seep into a bleb from which it is slowly absorbed. Filtering procedures are typically divided into either penetrating or non-penetrating types depending upon whether an intraoperative entry into the anterior chamber occurs.

Penetrating filtering surgeries are further subdivided into guarded filtering procedures, also known as protected, subscleral, or partial thickness filtering procedures (in which the surgeon sutures a scleral flap over the sclerostomy site), and full thickness procedures. **Trabeculectomy** is a guarded filtering procedure that removes of part of the trabecular meshwork. Full thickness procedures include sclerectomy, posterior lip sclerectomy (in which the surgeon completely excises the sclera on the area of the sclerostomy), trephination, thermal sclerostomy (Scheie procedure), iridenclesis, and sclerostomy (including conventional sclerostomy and enzymatic sclerostomy).

Non-penetrating filtering surgeries do not penetrate or enter the eye's anterior chamber. There are two types of non-penetrating surgeris: Bleb-forming and viscocanalostomy. Bleb forming procedures include ab externo trabeculectomy and deep sclerectomy. Ab externo trabeculectomy (AET) involves cutting from outside the eye inward to reach Schlemm's canal, the trabecular meshwork, and the anterior chamber. Also known as non-penetrating trabeculectomy (NPT), it is an ab externo (from the outside), major ocular procedure in which Schlemm's canal is surgically exposed by making a large and very deep scleral flap. The inner wall of Schlemm's canal is stripped off after surgically exposing the canal. Deep sclerectomy, also known as nonpenetrating deep sclerectomy (PDS) or nonpenetrating trabeculectomy is a filtering surgery where the internal wall of Schlemm's canal is excised, allowing subconjunctival filtration without actually entering the anterior chamber; it is commonly performed with the Aquaflow collagen wick. **Viscocanalostomy** is also an ab externo, major ocular procedure in which Schlemm's canal is surgically exposed by making a large and very deep scleral flap. In the VC

procedure, Schlemm's canal is cannulated and viscoelastic substance injected (which dilates Schlemm's canal and the aqueous collector channels).

Other surgical procedures

Goniotomy and **trabeculotomy** are similar simple and directed techniques of microsurgical dissection with mechanical disruption of the trabecular meshwork. Gonotomy procedures include surgical goniotomy and laser goniotomy. A surgical goniotomy involves cutting the fibers of the trabecular meshwork to allow aqueous fluid to flow more freely from the eye. Laser goniotomy is also known as goniophotoablation and laser trabecular ablation. In many patients suffering from congenital glaucoma, the cornea is not clear enough to visualize the anterior chamber angle. Although an endoscopic goniotomy, which employs an endoscope to view the anterior chamber angle, may be performed, a trabeculotomy which accesses the angle from the exterior surface of the eye, thereby eliminating the need for a clear cornea, is usually preferred in these instances. A specially designed probe is used to tear through the trabecular meshwork to open it and allow fluid flow.

Tube-shunt surgery or **drainage implant surgery** involves the placement of a tube or glaucoma valves to facilitate aqueous outflow from the anterior chamber. Trabeculopuncture uses a Q switched Nd:YAG laser to punch small holes in the trabecular meshwork with. **Goniocurretage** is an "ab interno" (from the inside) procedure that used an instrument "to scrape pathologically altered trabecular meshwork off the scleral sulcus". A surgical **cyclodialysis** is a rarely used procedure that aims to separate the ciliary body from the sclera to form a communication between the suprachoroidal space and the anterior chamber. A **cyclogoniotomy** is a surgical procedure for producing a cyclodialysis, in which the ciliary body is cut from its attachment at the scleral spur under gonioscopic control.

A **ciliarotomy** is a surgical division of the ciliary zone in the treatment of glaucoma.

Canaloplasty

Canaloplasty is a nonpenetrating procedure utilizing microcatheter technology. To perform a canaloplasty, an incision is made into the eye to gain access to Schlemm's canal in a similar fashion to a viscocanalostomy. A microcatheter will circumnavigate the canal around the iris, enlarging the main drainage channel and its smaller collector channels through the injection of a sterile, gel-like material called viscoelastic. The catheter is then removed and a suture is placed within the canal and tightened. By opening the canal, the pressure inside the eye can then be relieved. Long-term results are available, published in May 2009 in the *Journal of Cataract and Refractive Surgery.*

Procedures that decrease production of aqueous humor

Certain cells within the eye's ciliary body produce aqueous humor. A ciliary destructive or cyclodestructive procedure is one that aims to destroy those cells in order to reduce intraocular pressure.

Cyclocryotherapy, or cyclocryopexy, uses a freezing probe. Cyclophotocoagulation, also known as transscleral cyclophotocoagulation, ciliary body ablation, cyclophotoablation, and cyclophototherapy, uses a laser. **Cyclodiathermy** uses heat generated from a high frequency alternating electric current passed through the tissue, while **cycloelectrolysis** uses the chemical action caused by a low frequency direct current.

Keratoprosthesis

Keratoprosthesis is a surgical procedure where a severely damaged or diseased cornea is replaced with an artificial cornea. While conventional cornea transplant uses donor tissue for transplant, an artificial cornea is used in the Keratoprosthesis procedure. The surgery is performed to restore vision in patients suffering from severely damaged cornea due to congenital birth defects, infections, injuries and burns.

Keratoprotheses are made of clear plastic with excellent tissue tolerance and optical properties. They vary in design, size and even the implantation techniques may differ across different treatment centers. The procedure is done by ophthalmologists, often on an outpatient basis.

The idea of an artificial cornea is not new. It was first proposed in 1789 by French ophthalmologist Guillaume Pellier de Quengsy.

Types

Although many keratoprostheses have been developed only three are used commonly including the Boston keratoprosthesis, Osteo-Odonto-Keratoprosthesis (OOKP) and AlphaCor.

Indications

Indications of keratoprotheses include the following:

- Treatment of patients whose vision is less than 20/400 in the affected eye.
- Patients with failed corneal transplant using donor cornea and have little or no vision left.

- Patients with non-autoimmune diseases, congenital birth defects and other ocular problems.

Pre-operative examination

In most cases, the patient meets the ophthalmologist for eye examination and other tests weeks or months preceding surgery. During the meeting, the ophthalmologist will examine the eye and diagnose its condition. The doctor will also record the history of the patient's health and other previous eye treatments, if any. The doctor will discuss the risks and benefits of the surgery. If the patient elects for the surgery, the doctor will have the patient sign an informed consent form. The doctor may also perform physical and lab examinations, such as an X-ray, an EKG, a slit lamp test, an ultrasound B-scan, or an A-scan.

The surgery date and time is also set, and the patient will also be told where the surgery will take place. The patient can also make any other queries regarding the procedure.

Patient selection

- Vision should not be better than 20/400.
- Blink and tear mechanisms should be reasonably intact.
- Retina should be in place and there should not be extreme optic nerve cupping.
- Opposite eye has reduced vision.
- Intact nasal light projection.
- Consider shunt if patient is suffering from advanced stage of glaucoma.

Procedure

On the day of the procedure, the patient will arrive to the hospital where the surgery is to be performed. After a brief physical examination, he/she will be taken to the operating room. General anesthesia or local anesthesia is given before the surgery begins.

An eyelid speculum is used to keep the eye open throughout the surgery. Some lubrication may be used to prevent the eye from drying. An incision is made at the junction of the cornea and sclera. An intralamellar pocket is created within the cornea. The artificial cornea is then inserted into the intralamellar pocket. The flap is then repositioned and the incision is closed.

Typically, there is a follow up session few days after surgery, when patients' complaints are addressed and modifications are made, if needed.

Since Keratoprosthesis is a fairly rare surgical procedure, constant attempts are being made to improve the outcome of the surgery. Also, the material and design used in the artificial cornea may vary and as a result of this, there can be minor variations in surgical procedure as well.

The surgery is done on an outpatient basis with the patient returning home the same day.

Risks

Though the rate of success with Keratoprosthesis is high, in rare cases, certain serious complications could occur.

- Glaucoma and extrusion of the implant are serious complications that could occur.
- Sudden vitritis can cause a drastic reduction in vision. However, it is possible to treat this condition through antibiotics or by a minor laser surgery.
- Inflammation of the eye tissue could occur. This condition is also treatable.

Prognosis

The primary purpose of Keratoprosthesis is to improve vision in patients with complex ocular diseases who are at high risk for donor graft failure. After an impressive success record with Keratoprosthesis in adults, the procedure is used to treat young patients with severe ocular deformities.

Economics of the surgery

Keratoprosthesis is continuously evolving with newer generation materials that seek to improve treatment outcomes. However, the cost of surgery is on the expensive side and can typically run up to $35,000 in the US. In order to obtain surgical treatment at a lower cost, many patients choose to get the treatment done form popular medical tourism destinations like India and Singapore where the cost of treatment may be as little as one fourth the cost as in the US or UK.

Chapter 14

Refractive Surgery

Refractive eye surgery is any eye surgery used to improve the refractive state of the eye and decrease or eliminate dependency on glasses or contact lenses. This can include various methods of surgical remodeling of the cornea or cataract surgery. The most common methods today use excimer lasers to reshape curvature of the cornea. Successful refractive eye surgery can reduce or cure common vision disorders such as myopia, hyperopia and astigmatism.

According to surveys of members of the American Society of Cataract and Refractive Surgery, approximately 948,266 refractive surgery procedures were performed in the United States during 2004 and 928,737 in 2005.

History

The first experimental studies about refractive surgery were published in 1896 by Lendeer Jans Lans, an ophthalmology teacher in Holland, where he developed a theoretical work proposing penetrating corneal cuts to correct astigmatism. In 1930 the Japanese ophthalmologist Tsutomu Sato made the first practical attempt to perform such surgery in military pilots. He practiced radial cuts in the cornea to correct effects by up to 6 diopters, but this procedure was soon rejected by the medical community because of the high rate of corneal degeneration.

In 1963, in the Barraquer ophthalmologic clinic (Bogotá, Colombia) Ignacio Barraquer developed the first proficient refractive surgery technique called keratomileusis, meaning corneal reshaping (from Greek *κέρας* (kéras: horn) and *σμίλευσις* (smileusis: carving)). Keratomileusis allowed correction of not only myopia but also hyperopia. These early surgeries removed a corneal layer, froze it so it could be manually sculpted in the required shape, and finally reimplanted the layer (Keratomileusis with freezing). While this form of surgery was later improved by Dr. Swinger in 1986 (keratomileusis without freezing), it was still a relatively imprecise technique.

Meanwhile, experiments in 1970 using a xenon dimer and in 1975 using noble gas halides resulted in the invention of a type of laser called an excimer laser. While excimer lasers were initially used for industrial purposes, in 1980, R. Srinivasan, a scientist of IBM who was using an excimer laser to make microscopic circuits in microchips for informatics equipment, discovered that the excimer could also be used to cut organic

tissues with high accuracy without significant thermal damage. The discovery of an effective biological cutting laser, along with the development of computers to control it, allowed new refractive techniques which were previously unavailable. In 1983, scientist Stephen Trokel of Columbia University in collaboration with Srinivasan performed the first Photorefractive Keratectomy (PRK) or keratomileusis in situ (without separation of corneal layer) in Germany. The first patent for LASIK was granted by the US Patent Office to Gholam A. Peyman, MD on June 20, 1989, US Patent #4,840,175, "METHOD FOR MODIFYING CORNEAL CURVATURE", describing the surgical procedure in which a flap is cut in the cornea and pulled back to expose the corneal bed. This exposed surface is then ablated to the desired shape with an excimer laser, following which the flap is replaced. In 1991 Creta University and the Vardinoyannion Eye coined the name "LASIK".

Techniques

Flap procedures

Excimer laser ablation is done under a partial-thickness lamellar corneal flap.

- Automated lamellar keratoplasty (ALK): The surgeon uses an instrument called a microkeratome to cut a thin flap of the corneal tissue. The flap is lifted like a hinged door, targeted tissue is removed from the corneal stroma, again with the microkeratome, and then the flap is replaced.
- Laser Assisted In-Situ Keratomileusis (LASIK): The surgeon uses a microkeratome or femtosecond laser to cut a flap of the corneal tissue (usually with a thickness of 100-180 micrometres). The flap is lifted like a hinged door, but in contrast to ALK, the targeted tissue is removed from the corneal stroma with an excimer laser. The flap is subsequently replaced. Another method of creating this flap is by using a procedure called IntraLase, in which a femtosecond laser is used to create the flap. Proponents of this method assert its superiority over "traditional" LASIK, but there have been no conclusive independent studies to prove that this is a true statement.

Surface procedures

The excimer laser is used to ablate the most anterior portion of the corneal stroma. These procedures do not require a partial thickness cut into the stroma. Surface ablation methods differ only in the way the epithelial layer is handled.

- Photorefractive keratectomy (PRK) is an outpatient procedure generally performed with local anesthetic eye drops (as with LASIK/LASEK). It is a type of refractive surgery which reshapes the cornea by removing microscopic amounts of tissue from the corneal stroma, using a computer-controlled beam of light (excimer laser). The difference from LASIK is that the top layer of the epithelium is removed (and a bandage contact lens is used), so no flap is created. Recovery time is longer with PRK than with LASIK, though the final outcome (after 3

months) is about the same (very good). More recently, customized ablation has been performed with LASIK, LASEK, and PRK.

- Laser Assisted Sub-Epithelium Keratomileusis (LASEK) is a procedure that also changes the shape of the cornea using an excimer laser to ablate the tissue from the corneal stroma, under the corneal epithelium, which is kept mostly intact to act as a natural bandage. The surgeon uses an alcohol solution to loosen then lift a thin layer of the epithelium with a trephine blade (usually with a thickness of 50 micrometres). During the weeks following LASEK, the epithelium heals, leaving no permanent flap in the cornea. This healing process can involve discomfort comparable to that with PRK.
- EPI-LASIK is a new technique similar to LASEK that uses an epi-keratome (rather than a trephine blade and alcohol), to remove the top layer of the epithelium (usually with thickness of 50 micrometres), which is subsequently replaced. For some people it can provide better results than regular LASEK in that it avoids the possibility of negative effects from the alcohol, and recovery may involve less discomfort.
- C-Ten (Customized TransEpithelial Non-contact ablation) is a refinement of Lasek, EPI-Lasik, and PRK. It is the newest and the fastest Laser treatment. “C” for Customized refers to the individualization of the treatment for each patient, conforming to each individual’s requirements determined by the shape of the cornea and the topography of its surface, the extent of the correction, pupillary size and reaction, and the patient’s lifestyle requirements. “TEN” (Trans Epithelial, Non-Contact) means that the ablation of the epithelial layer, the regenerative surface of the eye, is accomplished with the laser alone, with no direct contact with the eye. C-Ten is the only treatment technique done without actual contact with the eye. Prior to the start of the procedure each eye is examined and measurements are made using two instruments specially designed for the laser treatments. The “Precisio” measures the corneal topography, both its shape and thickness. The "Pupillometer” measures the size of the pupil under various light relationships. These measurements ensure that the area undergoing treatment is neither too small (with the danger of ensuing halos or blinding) nor too large (which could cause ablation of excessive tissue). After the Laser treatment the epithelium regenerates within a few days, all the while being protected by a contact lens. The technique, in comparison to other superficial laser treatments, causes the least post-operative discomfort. Over 80% of patients report almost no pain. In contrast to other laser treatments, C-Ten has a very low incidence of dry eye. Another advantage of C-Ten is the absence of flap associated complications that can occur after Lasik or Femto-Lasik and changes in corneal stability are minimal. This is in contrast to Lasik, after which there is an unmistakable decrease in. C-Ten is especially suited to the treatment of myopia and irregular astigmatism. Up 12 diopters of myopia and over 6 diopters of corneal distortions can be corrected. Surface treatments are less suited for correction of hyperopia.

M. G. La Tegola, G. Alessio, C. Sborgia: Topographic customized photorefractive keratectomy for regular and irregular astigmatism after penetrating keratoplasty using the

LIGI CIPTA/LaserSight platform. In: J. Refrst. Surg. 7, September 2007, S. 681–693. ↑ E. Pedrotti, A. Sbabo, G. Marchini: Customized transepithelial photorefractive keratectomy for iatrogenic ametropia after penetrating or deep lamellar keratoplasty. In: J. Refract. Surg. 32 Nr. 8, August 2006 S. 1288–1291.

Corneal incision procedures

- Radial keratotomy (RK) uses spoke-shaped incisions (usually made with a diamond knife) to alter the shape of the cornea and reduce myopia or astigmatism; this technique has now been largely replaced by the other methods (that use excimer laser).

- Arcuate keratotomy (AK) is similar to radial keratotomy, but the incisions on the cornea are done at the periphery of the cornea. Arcuate keratotomy is used to correct astigmatism. Although most incisional procedures are replaced nowadays by Lasik, AK is still used in some special cases (correction of residual astigmatism after a keratoplasty procedure or during cataract surgery).

- Limbal relaxing incisions (LRI) are incisions near the outer edge of the iris, used to correct minor astigmatism (typically less than 2 diopters). This is often performed in conjunction with an Intraocular Lens implantation.

Other procedures

- Thermal keratoplasty is used to correct hyperopia by putting a ring of 8 or 16 small burns surrounding the pupil, and steepen the cornea with a ring of collagen constriction. It can also be used to treat selected types of astigmatism.
- Laser thermal keratoplasty (LTK) is a non-touch thermal keratoplasty performed with a Holmium laser, while conductive keratoplasty (CK) is thermal keratoplasty performed with a high-frequency electric probe. Thermal keratoplasty can also be used to improve presbyopia or reading vision after age 40.
- Intrastromal corneal ring segments (Intacs) are approved by FDA for treatment of low degrees of myopia.
- Lens implantation inside the eye can also be used to change refractive errors.
- Generally refractive surgery can be broadly divided into : corneal surgery, scleral surgery, lens related surgery(including phakic IOL implantation, clear lens extraction, photophacoreduction and photophacomodulation for correction of pesbyopia)
- For presbyopia correction, a corneal inlay consisting of a porous black ring surrounding a small clear aperture was originally developed by D. Miller and a group at Acufocus. The inlay is placed under a lasik flap or in a stromal pocket.

Christie,B, et al: Optical performance of a corneal inlay for presbyopia. Invest Ophth Vis Sci. Abstract 695, 2005

Silvestrini, TA, et al: Analysis of glucose diffusion across Acufocus inlay. Invest Ophth Vis Sci, abstract 2195, 2005

Expectations

Research conducted by the Magill Research Center for Vision Correction, Medical University of South Carolina, showed that the overall patient satisfaction rate after primary LASIK surgery was 95.4%. They further differentiated between myopic LASIK (95.3%) and hyperopic LASIK (96.3%). They concluded that that vast majority (95.4%) of patients were satisfied with their outcome after LASIK surgery.

Risks

While refractive surgery is becoming more affordable and safe, it may not be recommended for everybody. Patients that have medical conditions such as glaucoma or diabetes, uncontrolled vascular disease, autoimmune disease, pregnant women or people with certain eye diseases involving the cornea or retina, are not good candidates for refractive surgery. Keratoconus, a progressive thinning of the cornea, is a common corneal disorder. Keratoconus occurring after refractive surgery is called Corneal Ectasia. It is believed that additional thinning of the cornea via refractive surgery may contribute to advancement of the disease, that may lead to the need for a corneal transplant. Therefore, keratoconus is a contraindication to refractive surgery. Corneal topography, pachymetry and, more recently, Pentacam exams are used to screen for abnormal corneas. Furthermore, some people's eye shape may not permit effective refractive surgery without removing excessive amounts of corneal tissue. Those considering laser eye surgery should have a full eye examination.

Although the risk of complications is decreasing compared to the early days of refractive surgery, there is still a small chance for serious problems. These include vision problems such as ghosting, halos, starbursts, double-vision, and dry-eye syndrome. With procedures that create a permanent flap in the cornea (such as LASIK), there is also the possibility of accidental traumatic flap displacement years after the surgery, with potentially disastrous results if not given prompt medical attention.

Chapter 15

Otolaryngology

Otolaryngologist performing an endoscopic sinus surgical procedure

Otolaryngology or **ENT** (**ear, nose, and throat**) is the branch of medicine and surgery that specializes in the diagnosis and treatment of ear, nose, throat, and head and neck disorders. The full name of the specialty is **otolaryngology–head and neck surgery.** Practitioners are called **otolaryngologists–head and neck surgeons**, or sometimes **otorhinolaryngologists** (ORL).

The term comes from the Classical Greek roots *ὠτ- - ot-* (root of οὖς) "ear", *λαρυγγ- - laryng-* (root of λάρυγξ) "larynx/throat", and the suffix *-logy* "study", and it literally means "the study of ear and throat".

The full term otorhinolaryngology (neoclassical Greek and modern Greek: ὠτο(ρ)ρινολαρυγγολογία), also includes *ῥίνο- - rhino-* (root of ῥίς) "nose".

Explanation

Otolaryngologists are medical doctors (MD, DO, MBBS, MBChB, etc.) who, in the United States, complete at least five years of surgical residency training. This is composed of one year in general surgical training and four years in otolaryngology–head and neck surgery; in the past it varied between two and three years of each.

Following residency training some otolaryngologists elect to complete advanced subspeciality fellowship training which can be 1–2 years in duration (pediatric otolaryngology, neuro-otology, laryngology, facial plastic and reconstructive surgery, rhinology, or head and neck oncology).

Subspecialties

Head and neck	Facial plastics	Otology	Neuro-otology*	Rhinology/ sinus	Laryngology	Pediatrics*
Surgical oncology	Facial cosmetic surgery	Ear	Middle and inner ear	Sinusitis	Voice therapy	Velopalatine insufficiency
Reconstruction	Maxillofacial	Hearing	Temporal bone	Allergy	Phono-surgery	Cleft lip and palate
Endocrine surgery	Trauma		Skull base	Anterior skull base		Airway
			Dizziness	Apnea and snoring		Vascular malformations
						Cochlear implant/BAHA

(* Currently recognized by American Board of Medical Subspecialties)

Topics in otolaryngology, head and neck surgery

Head and neck surgery

- Squamous cell carcinoma of the oral cavity, pharynx and larynx
- Oral cancer
- Thyroid cancer
- Endocrine surgery of the head and neck (thyroidectomy, parathyroidectomy)

- Microvascular free flap reconstruction
- Skull base surgery

Otology/neuro-otology

- Dizziness
    - BPPV – benign paroxysmal positional vertigo
    - labyrinthitis/vestibular neuronitis
    - Ménière's disease/endolymphatic hydrops
    - Perilymphatic fistula
    - acoustic neuroma

- Hearing loss
- Mastoiditis
- Otitis externa – outer ear or ear canal inflammation
- Otitis media – middle ear inflammation
- Otitis interna – inner ear inflammation
- Perforated eardrum (hole in the eardrum due to infection, trauma, explosion or loud noise)
- Ear surgery

Rhinology

Rhinology pertains to sinus diseases and the anterior skull base.

- Environmental allergies
- Sinusitis – acute, chronic
- Rhinitis
- Empty nose syndrome

Pediatrics

- Adenoidectomy
- Caustic ingestion
- Cricotracheal resection
- Decannulation
- laryngomalacia
- Laryngotracheal reconstruction
- Myringotomy and tubes
- Obstructive sleep apnea – pediatric
- Tonsillectomy

Laryngology

- Dysphonia/hoarseness
    - Laryngitis

    - Reinke's edema
    - Vocal cord nodules and polyps

- Spasmodic dysphonia
- Tracheostomy
- Cancer of the larynx
- Vocology – science and practice of voice habilitation

Facial plastic and reconstructive surgery

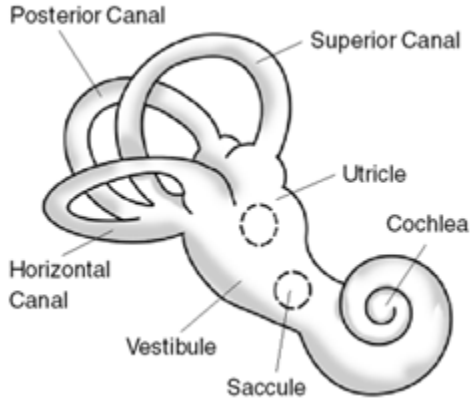
Facial plastic and reconstructive surgery is a one-year fellowship open to otolaryngologists and plastic surgeons who wish to specialize in the aesthetic and reconstructive surgery of the head, face, and neck.

- Rhinoplasty and septoplasty
- Facelift (rhytidectomy)
- Browlift
- Blepharoplasty
- Otoplasty
- Genioplasty
- Injectable cosmetic treatments
- Trauma to the face
    - Nasal bone fracture
    - Mandible fracture
    - Orbital fracture
    - Frontal sinus fracture
    - Complex lacerations and soft tissue damage

Chapter 16

Benign Paroxysmal Positional Vertigo

Benign paroxysmal positional vertigo



Exterior of labyrinth.

ICD-10	H81.1
ICD-9	386.11
OMIM	193007
DiseasesDB	1344
eMedicine	ent/761 emerg/57 neuro/411
MeSH	D014717

Benign paroxysmal positional vertigo (**BPPV**) is a disorder caused by problems in the inner ear. Its symptoms are repeated episodes of positional vertigo, that is, of a spinning sensation caused by changes in the position of the head.

Classification

Vertigo, a distinct process some people confuse with dizziness, accounts for about 6 million clinic visits in the U.S. every year, and 17–42% of these patients eventually are diagnosed with BPPV. Other causes of vertigo include:

- Motion sickness/ Motion Intolerance: a disjunction between visual stimulation, vestibular stimulation, and/or proprioception
- Visual exposure to nearby moving objects (examples of optokinetic stimuli: passing cars, falling snow)
- Other diseases: (labyrinthitis, Ménière's disease, migraine. etc.)

Signs and symptoms

- Symptoms
    - Vertigo: Spinning dizziness, which must have a rotational component.
    - Short duration (Paroxysmal): Lasts only seconds to minutes
    - Positional in onset: Can only be induced by a change in position.
    - Nausea is often associated
    - Visual disturbance: It may be difficult to read or see during an attack due to the associated nystagmus.
    - Pre-Syncope (feeling faint) or Syncope (fainting) is unusual.
    - Emesis (Vomiting) is uncommon but possible.

- Signs
    - Rotatory (torsional) nystagmus, where the top of the eye rotates towards the affected ear in a beating or twitching fashion, which has a latency and can be fatigued (if you repeatedly continue placing yourself in the position to cause vertigo the symptoms should lessen each time).

    -
    - Nystagmus should only last for 30 seconds to a minute.

Patients do not experience other neurological deficits such as numbness or weakness, and if these symptoms are present, a more serious etiology such as posterior circulation stroke, must be considered.

Cause

Within the labyrinth of the inner ear lie collections of calcium crystals known as otoconia. In patients with BPPV, the otoconia are dislodged from their usual position within the utricle and they migrate over time into one of the semicircular canals (the posterior canal is most commonly affected due to its anatomical position). When the head is reoriented relative to gravity, the gravity-dependent movement of the heavier otoconial debris (colloquially "**ear rocks**") within the affected semicircular canal causes abnormal (pathological) fluid endolymph displacement and a resultant sensation of vertigo. This more common condition is known as **canalithiasis**.

In rare cases, the crystals themselves can adhere to a semicircular canal cupula rendering it heavier than the surrounding endolymph. Upon reorientation of the head relative to gravity, the cupula is weighted down by the dense particles thereby inducing an

immediate and maintained excitation of semicircular canal afferent nerves. This condition is termed **cupulolithiasis**.

There is evidence in the dental literature that malleting of an osteotome during closed sinus floor elevation, otherwise known as *osteotome sinus elevation* or *lift*, transmits enough percussive and vibratory forces capable of detaching otoliths from their normal location and leading to the symptoms of BPPV.

It can be triggered by any action which stimulates the posterior semi-circular canal which may be:

- Tilting the head
- Rolling over in bed
- Looking up or under
- Sudden head motion
- Post head injury

BPPV may be made worse by any number of modifiers which may vary between individuals:

- Changes in barometric pressure - patients often feel symptoms approximately two days before rain or snow
- Lack of sleep (required amount of sleep may vary widely)
- Stress

BPPV is one of the most common vestibular disorders in patients presenting with dizziness and migraine is implicated in idiopathic cases. Proposed mechanisms linking the two are genetic factors and vascular damage to the labyrinth.

Diagnosis

The condition is diagnosed from patient history (feeling of vertigo with sudden changes in positions); and by performing the Dix-Hallpike maneuver which is diagnostic for the condition. The test involves a reorientation of the head to align the posterior canal (at its entrance to the ampulla) with the direction of gravity. This test stimulus is effective in provoking the symptoms in subjects suffering from archetypal BPPV. These symptoms are typically a short lived vertigo, and observed nystagmus. In some patients, though rarely, the vertigo can persist for years. Assessment of BPPV is best done by a health professional skilled in management of dizziness disorders, commonly a physiotherapist, audiologist or other medical physician.

The nystagmus associated with BPPV has several important characteristics which differentiate it from other types of nystagmus.

- Positional: the nystagmus occurs only in certain positions
- Latency of onsent: there is a 5-10 second delay prior to onset of nystagmus

- Nystagmus lasts for 5–120 seconds
- Visual fixation does not suppress nystagmus due to BPPV
- Rotatory/Torsional component is present or (in the case of lateral canal involvement)the nystagmus beats in either a geotropic (towards the ground)or ageotropic (away from the ground) fashion
- Repeated stimulation, including via Dix-Hallpike maneuvers, cause the nystagmus to fatigue or disappear temporarily.

Treatment

Two treatments have been found effective for relieving symptoms of posterior canal BPPV: the canalith repositioning procedure (CRP) or Epley maneuver, and the liberatory or Semont maneuver. The CRP employs gravity to move the calcium build-up that causes the condition. The particle repositioning maneuver can be performed during a clinic visit by health professionals or taught to patients to practice at home. In the Semont maneuver, patients themselves are able to achieve canalith repositioning. Only limited data are available comparing the two treatments, and it is not known which is more effective.

The Epley maneuver (particle repositioning) does not address the actual presence of the particles (otoconia), rather it changes their location. The maneuver aims to move these particles from areas in the inner ear which cause symptoms, such as vertigo, and repositions them to where they do not cause these problems.

Medical treatment with anti-vertigo medications may be considered in acute, severe exacerbation of BPPV, but in most cases are not indicated. These primarily include drugs of the anti-histamine and anti-cholinergic class, such as meclozine and scopolamine respectively. These offer symptomatic treatment, and do not affect the disease process or resolution rate. Medications may be used to suppress symptoms during the positioning manoeuvres if the patient has severe symptoms and may be unable to tolerate them.

Surgical treatments, such as a semi-circular canal occlusion, do exist for BPPV but carry the same risk as any neurosurgical procedure. Surgery is reserved as a last resort option for severe and persistent cases which fail vestibular rehabilitation (including particle repositioning and habituation therapy).

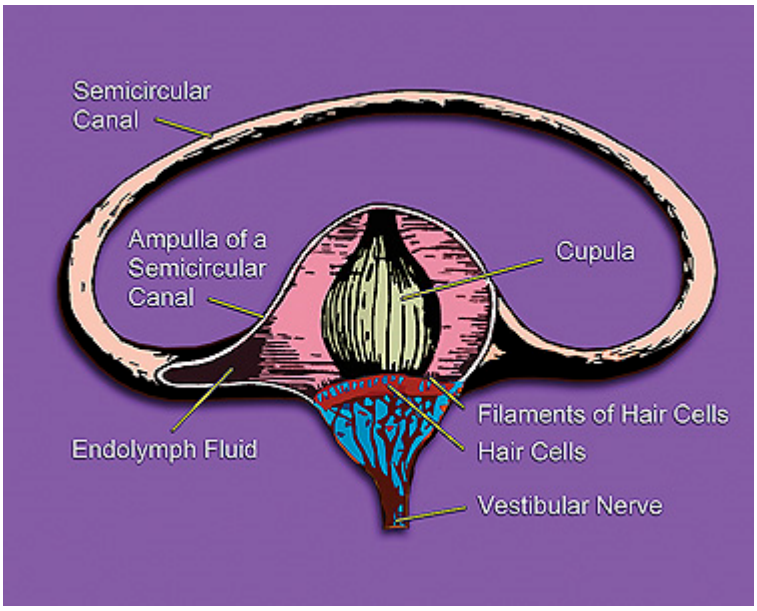
Devices such as a head over heels "rotational chair" are available at some tertiary care centers Home devices, like the DizzyFIX, are also available for the treatment of BPPV and vertigo.

Famous sufferers

- Richard Herring
- Roy Williams
- Zane Reynolds
- Elizabeth Yellin Morley

Chapter 17

Ménière's Disease

Ménière's disease


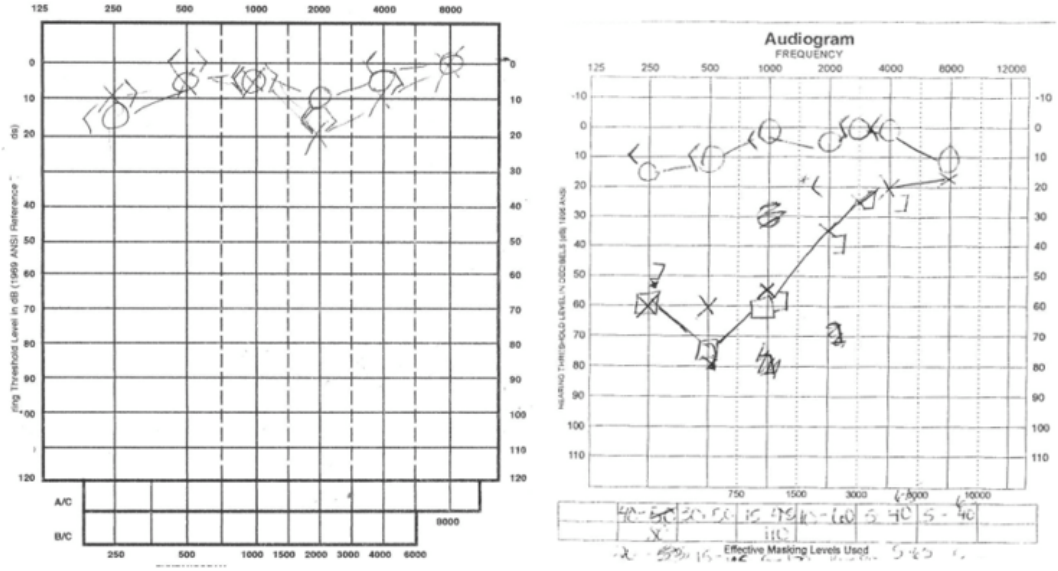
Inner ear

ICD-10	H81.0
ICD-9	386.0
OMIM	156000
DiseasesDB	8003
MedlinePlus	000702
eMedicine	emerg/308
MeSH	D008575

Ménière's disease is a disorder of the inner ear that can affect hearing and balance to a varying degree. It is characterized by episodes of vertigo and tinnitus and progressive hearing loss, usually in one ear. It is named after the French physician Prosper Ménière,

who, in an article published in 1861, first reported that vertigo was caused by inner ear disorders. The condition affects people differently; it can range in intensity from being a mild annoyance to a chronic, lifelong disability.

Signs and symptoms



An audiogram illustrating low pitch hearing loss

The symptoms of Ménière's are variable; not all sufferers experience the same symptoms. However, so-called "classic Ménière's" is considered to have the following four symptoms:

- Periodic episodes of rotary vertigo or dizziness.
- Fluctuating, progressive, unilateral (in one ear) or bilateral (in both ears) hearing loss, usually in lower frequencies.
- Unilateral or bilateral tinnitus.
- A sensation of fullness or pressure in one or both ears.

Ménière's often begins with one symptom, and gradually progresses. However, not all symptoms must be present for a doctor to make a diagnosis of the disease. Several symptoms at once is more conclusive than different symptoms at separate times.

Attacks of rotational vertigo can be severe, incapacitating, and unpredictable and can last anywhere from minutes to hours, but no longer than 24 hours. This combines with an increase in volume of tinnitus and temporary, albeit significant, hearing loss. Hearing may improve after an attack, but often becomes progressively worse. Nausea, vomiting,

and sweating sometimes accompany vertigo, but are symptoms of vertigo, and not of Ménière's.

Some sufferers experience what are informally known as "drop attacks"—a sudden, severe attack of dizziness or vertigo that causes the sufferer, if not seated, to fall without warning. Drop attacks are likely to occur later in the disease, but can occur at any time. Patients may also experience the feeling of being pushed or pulled. Some patients may find it impossible to get up for some time, until the attack passes or medication takes effect.

In addition to hearing loss, sounds can appear tinny or distorted, and patients can experience unusual sensitivity to noises.

Some sufferers also experience nystagmus, or uncontrollable rhythmical and jerky eye movements, usually in the horizontal plane, reflecting the essential role of non-visual balance in coordinating eye movements.

Migraine

There is an increased prevalence of migraine in patients with Ménière's disease. As well, migraine leads to a greater susceptibility of developing Ménière's disease. The distinction between migraine-associated vertigo and Ménière's is that migraine-associated vertigo may last for more than 24 hours.

Cause

Ménière's disease is idiopathic, but it is believed to be related to *endolymphatic hydrops* or excess fluid in the inner ear. It is thought that endolymphatic fluid bursts from its normal channels in the ear and flows into other areas, causing damage. This is called "hydrops". The membranous labyrinth, a system of membranes in the ear, contains a fluid called endolymph. The membranes can become dilated like a balloon when pressure increases and drainage is blocked. This may be related to swelling of the endolymphatic sac or other tissues in the vestibular system of the inner ear, which is responsible for the body's sense of balance. In some cases, the endolymphatic duct may be obstructed by scar tissue, or may be narrow from birth. In some cases there may be too much fluid secreted by the stria vascularis. The symptoms may occur in the presence of a middle ear infection, head trauma, or an upper respiratory tract infection, or by using aspirin, smoking cigarettes, or drinking alcohol. They may be further exacerbated by excessive consumption of salt in some patients.

It has also been proposed that Ménière's symptoms in many patients are caused by the deleterious effects of a herpes virus. Herpesviridae are present in a majority of the population in a dormant state. It is suggested that the virus is reactivated when the immune system is depressed due to a stressor such as trauma, infection or surgery (under general anesthesia). Symptoms then develop as the virus degrades the structure of the inner ear.

Ménière's symptoms can begin at any age, but typically begin between the ages of 30 and 60, and affects men slightly more than women. Hearing loss can affect both ears either simultaneously or with a variable interval between the first and the second ear.

Other possible conditions that may lead to Ménière's symptoms include syphilis, Cogan's syndrome, autoimmune disease of the inner ear, dysautonomia, perilymph fistula, multiple sclerosis, acoustic neuroma, and both hypo- and hyperthyroidism.

Diagnosis

Doctors establish a diagnosis with complaints and medical history. However, a detailed otolaryngological examination, audiometry and head MRI scan should be performed to exclude a tumour of the eighth cranial nerve or superior canal dehiscence which would cause similar symptoms. There is no definitive test for Ménière's, it is only diagnosed when all other causes have been ruled out. If any cause had been discovered, this would eliminate Ménière's disease, as by its very definition, as an exclusively idiopathic disease, it has no known causes.

History

Ménière's disease had been recognized as early as 1860s, but it was still relatively vague and broad at the time. The American Academy of Otolaryngology-Head and Neck Surgery Committee on Hearing and Equilibrium (AAO HNS CHE) set criteria for diagnosing Ménière's, as well as defining two sub categories of Ménière's: cochlear (without vertigo) and vestibular (without deafness).

In 1972, the academy defined criteria for diagnosing Ménière's disease as:

1. Fluctuating, progressive, sensorineural deafness.
2. Episodic, characteristic definitive spells of vertigo lasting 20 minutes to 24 hours with no unconsciousness, vestibular nystagmus always present.
3. Usually tinnitus.
4. Attacks are characterized by periods of remission and exacerbation.

In 1985, this list changed to alter wording, such as changing "deafness" to "hearing loss associated with tinnitus, characteristically of low frequencies" and requiring more than one attack of vertigo to diagnose. Finally in 1995, the list was again altered to allow for degrees of the disease:

1. Certain - Definite disease with histopathological confirmation
2. Definite - Requires two or more definitive episodes of vertigo with hearing loss plus tinnitus and/or aural fullness
3. Probable - Only one definitive episode of vertigo and the other symptoms and signs
4. Possible - Definitive vertigo with no associated hearing loss

Prevention

Several environmental and dietary changes are thought to reduce the frequency or severity of symptom outbreaks. Most patients are advised to adopt a low-sodium diet, typically one to two grams per day. Patients are advised to avoid alcohol, caffeine, and tobacco, all of which can aggravate symptoms of Ménière's. Patients are often prescribed a mild diuretic (sometimes vitamin B_6). Many patients will have allergy testing done to see if they are candidates for allergy desensitization, as allergies have been shown to aggravate Ménière's symptoms.

Treatments aimed at lowering the pressure within the inner ear include antihistamines, anticholinergics, steroids, and diuretics. Devices that provide transtympanic micropressure pulses are now showing some promise and are becoming more widely used as treatments for Ménière's.

The antiherpes virus drug acyclovir has also been used with some success to treat Ménière's Disease. The likelihood of the effectiveness of the treatment was found to decrease with increasing duration of the disease, probably because viral suppression does not reverse damage. Morphological changes to the inner ear of Ménière's sufferers have also been found in which it was considered likely to have resulted from attack by a herpes simplex virus. It was considered possible that long term treatment with acyclovir (greater than six months) would be required to produce an appreciable effect on symptoms. Herpes viruses have the ability to remain dormant in nerve cells by a process known as HHV Latency Associated Transcript. Continued administration of the drug should prevent reactivation of the virus and allow for the possibility of an improvement of symptoms. Another consideration is that different strains of a herpes virus can have different characteristics which may result in differences in the precise effects of the virus. Further confirmation that acyclovir can have a positive effect on Ménière's symptoms has been reported.

Treatment

Because Ménière's cannot be cured, treatments focus more on addressing symptoms.

Symptoms

Typical remedies to improve symptoms may include:

- Antihistamines considered antiemetics such as meclozine and dimenhydrinate
- Antiemetic drugs such as trimethobenzamide.
- Antivertigo/antianxiety drugs such as betahistine and diazepam.
- Herbal remedies such as ginger root.

Coping

Sufferers tend to have high stress and anxiety due to the unpredictable nature of the disease. Healthy ways to combat this stress can include aromatherapy, yoga, T'ai chi., and meditation.

Surgery

If symptoms do not improve with typical treatment, more permanent surgery is considered. Unfortunately, because the inner ear deals with both balance and hearing, few surgeries guarantee no hearing loss.

Nondestructive

Nondestructive surgeries include those which do not actively remove any functionality, but rather aim to improve the way the ear works.

Intratympanic steroid treatments involve injecting steroids (commonly dexamethasone) into the middle ear in order to reduce inflammation and alter inner ear circulation.

Surgery to decompress the endolymphatic sac has shown to be effective for temporary relief from symptoms. Most patients see a decrease in vertigo occurrence, while their hearing may be unaffected. This treatment, however, does not address the long-term course of vertigo in Ménière's disease. Danish studies even link this surgery to a very strong placebo effect, and that very little difference occurred in a 9-year followup, but could not deny the efficacy of the treatment.

Destructive

Destructive surgeries are irreversible, and involve removing entire functionality of most, if not all, of the affected ear.

The inner ear itself can be surgically removed via labyrinthectomy. Hearing is always completely lost in the affected ear with this operation. Alternatively, a chemical labyrinthectomy, in which a drug (such as gentamicin) that "kills" the vestibular apparatus is injected into the middle ear can accomplish the same results while retaining hearing.

Alternatively, surgeons can cut the nerve to the balance portion of the inner ear in a vestibular neurectomy. Hearing is often mostly preserved, however the surgery involves cutting open into the lining of the brain, and a hospital stay of a few days for monitoring would be required.

Vertigo (and the associated nausea and vomiting) typically accompany the recovery from destructive surgeries as the brain learns to compensate.

Prognosis

Ménière's disease usually starts confined to one ear, but it often extends to involve both ears over time. The number of patients who end up with bilaterial Ménière's is debated, with ranges spanning from 17% to 75%.

Some Ménière's disease sufferers, in severe cases, may end up losing their jobs, and will be on disability until the disease burns out. However, a majority (60-80%) of sufferers will not need permanent disability and will recover with or without medical help.

Hearing loss usually fluctuates in the beginning stages and becomes more permanent in later stages, although hearing aids and cochlear implants can help remedy damage. Tinnitus can be unpredictable, but patients usually get used to it over time.

Ménière's disease, being unpredictable, has a variable prognosis. Attacks could come more frequently and more severely, less frequently and less severely, and anywhere in between. However, Ménière's is known to "burn out" when vestibular function has been destroyed to a stage where vertigo attacks cease.

Studies done on both right and left ear sufferers show that patients with their right ear affected tend to do significantly worse in cognitive performance. General intelligence was not hindered, and it was concluded that declining performance was related to how long the patient had been suffering from the disease.

Notable cases

In history

- Alan B. Shepard, the first American astronaut, was diagnosed with Ménière's disease in 1964, grounding him after only one brief spaceflight. Several years later, an endolymphatic shunt surgery (which was then at the experimental stage) was performed, allowing Shepard to fly to the Moon on Apollo 14.
- Su Yu, PLA General who achieved many victories for the communists during the Chinese Civil War was hospitalized in 1949 and that prevented him from taking command in the Korean War, and Mao selected Peng Dehuai instead.

Possible cases

- Marilyn Monroe, American actress and cultural icon was known to experience the vertigo and compromised hearing associated with Ménière's.
- Charles Darwin may have suffered from Ménière's disease. This idea is based on a common list of symptoms which were present in Darwin's case, such as tinnitus, vertigo, dizziness, motion sickness, vomiting, continual malaise and tiredness. The absence of hearing loss and 'fullness' of the ear (as far as known) excludes, however, a diagnosis of typical Ménière's disease. Darwin himself had the opinion that most of his health problems had an origin in his 4-year bout with sea

sickness. Later, he could not stand traveling by carriage, and only horse riding would not affect his health. One of the diagnoses that he received from his physicians at the time was that of "suppressed gout". The source of Darwin's illness is not known for certain.
- Martin Luther wrote in letters about the distresses of vertigo, and suspected Satan was the cause.
- Julius Caesar was known to have suffered from the "falling sickness" as noted in Plutarch's *Parallel Lives*, and has been cited by Shakespeare, noting that Caesar was unable to hear fully in his left ear.
- It has been suggested that Vincent Van Gogh, the Dutch Post-Impressionist, may have suffered from Ménière's, though this is now considered conjectural.

Modern

- According to his blog, author and entrepreneur Guy Kawasaki has the illness.
- Contemporary artist and graphic designer Doc Hammer, of *The Venture Bros.* fame, has Ménière's syndrome according to his May 16, 2005 journal entry.
- Paddy McAloon, the singer and songwriter for the British pop group Prefab Sprout, was diagnosed with Ménière's in 2004.
- Basketball player Steve Francis suffers from Ménière's.
- The Cardinals singer Ryan Adams made it known he suffered from Ménière's disease when he announced his departure from the band.
- Dawn Miceli, podcaster, discovered she may have Ménière's disease while reading an article in *Redbook*.
- Shawnae Jebbia, Miss USA 1998, was diagnosed with Ménière's disease while fulfilling her duties as Miss USA for the following year. Previously, she had a successful run as a fitness model/instructor on ESPN2, but this forced Jebbia into retiring from the entertainment business.
- Singer and actress Kristin Chenoweth has performed on stage while suffering from severe symptoms of Ménière's disease. She wrote about her experience with Ménière's in her 2009 autobiography and talked about it on "Fresh Air with Terry Gross" in April 2009.
- Author Evelyn Dove Coleman was diagnosed with Ménière's disease in November 1997 and soon after took disability status.
- NHL forward Mattias Ritola was diagnosed with the disease in 2010 while playing with the Tampa Bay Lightning.
- Calvin Chen of boy band Fahrenheit was diagnosed on December 14, 2009 after being rushed to the hospital.
- 8 days later, another Fahrenheit member Aaron Yan was also diagnosed. Coincidentally, this disease was the same illness that his character in Mysterious Incredible Terminator (霹雳MIT) had, a role he took on the year before.

Chapter 18

Rhinitis and Empty Nose Syndrome

Rhinitis

Rhinitis	
ICD-10	J00., J30., J31.0
ICD-9	472.0, 477
OMIM	607154
DiseasesDB	26380
MedlinePlus	000813
eMedicine	ent/194 med/104, ped/2560
MeSH	D012220

Rhinitis commonly known as a **stuffy nose**, is the medical term describing irritation and inflammation of some internal areas of the nose. The primary symptom of rhinitis is nasal dripping. It is caused by chronic or acute inflammation of the mucous membrane of the nose due to viruses, bacteria or irritants. The inflammation results in the generating of excessive amounts of mucus, commonly producing the aforementioned runny nose, as well as nasal congestion and post-nasal drip. According to recent studies completed in the United States, more than 50 million Americans are current sufferers. Rhinitis has also been found to adversely affect more than just the nose, throat, and eyes. It has been associated with sleeping problems, ear conditions, and even learning problems. Rhinitis is caused by an increase in histamine, which is most often triggered by airborne allergens. These allergens may affect an individual's nose, throat, or eyes and cause an increase in fluid production within these areas.

Types

Rhinitis is categorized into three types: (i) infective rhinitis includes acute and chronic bacterial infections; (ii) nonallergic (vasomotor) rhinitis includes autonomic, hormonal,

drug-induced, atrophic, and gustatory rhinitis, as well as rhinitis medicamentosa; (iii) allergic rhinitis, the mic reaction triggered by pollen, mold, animal dander, dust and other similar inhaled allergens.

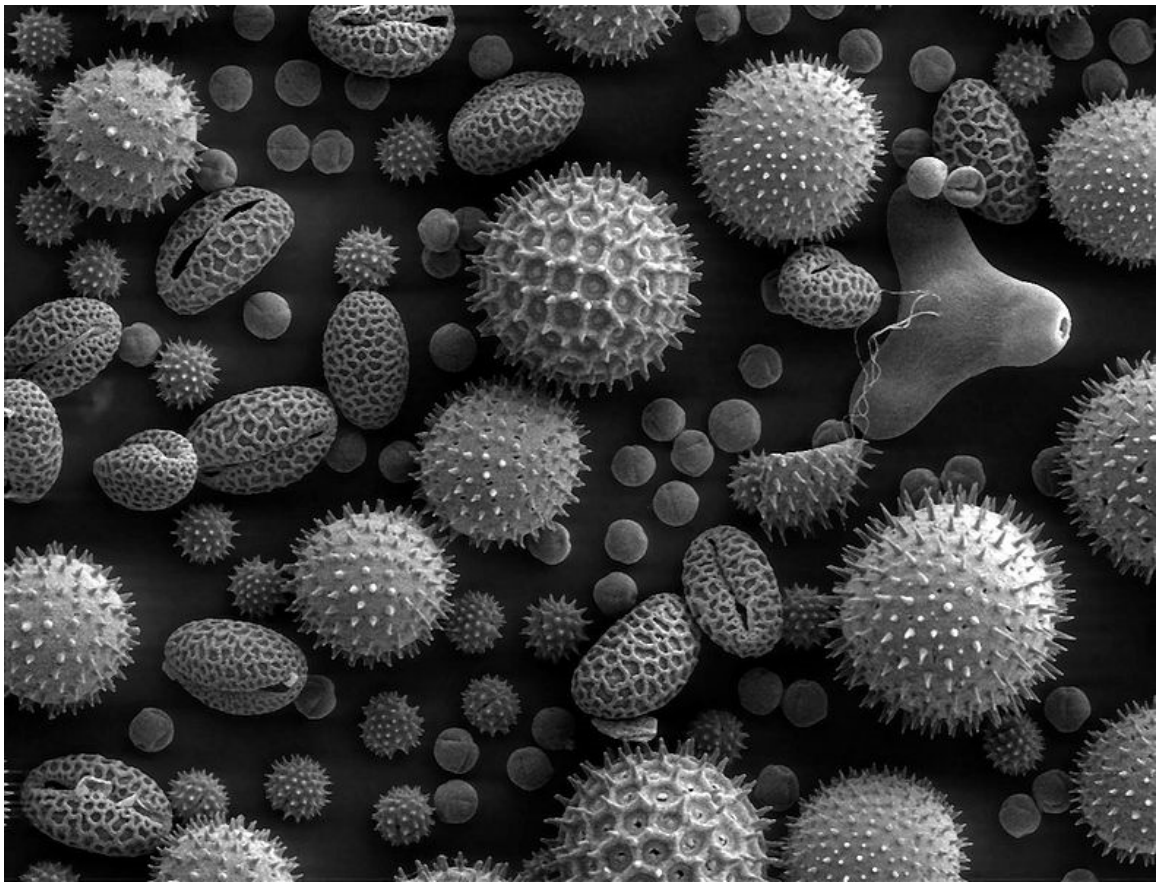
Infectious

Rhinitis is commonly caused by a viral or bacterial infection, including the common cold, which is caused by Rhinoviruses and Coronaviruses, or bacterial sinusitis. Symptoms of the common cold include rhinorrhea, sore throat (pharyngitis), cough, congestion, and slight headache.

Vasomotor rhinitis

Non-allergic rhinitis refers to runny nose that is not due to allergy. Non-allergic rhinitis can be classified as either non-inflammatory or inflammatory rhinitis. One very common type of non-inflammatory, non-allergic rhinitis that is sometimes confused with allergy is called vasomotor rhinitis, in which certain non-allergic triggers such as smells, fumes, smoke, dusts, and temperature changes, cause rhinitis. There is still much to be learned about this entity, but it is thought that these non-allergic triggers cause dilation of the blood vessels in the lining of the nose, which results in swelling, and drainage. Vasomotor rhinitis can coexist with allergic rhinitis, and this is called "mixed rhinitis." (Middleton's Allergy Principles and Practice, seventh edition.) The pathology of vasomotor rhinitis appears to involve neurogenic inflammation PMID 18651116 and is as yet not very well understood. More research is needed. Vasomotor rhinitis appears to be significantly more common in women than men, leading some researchers to believe that hormones play a role. In general, age of onset occurs after 20 years of age, in contrast to allergic rhinitis which can be developed at any age. Individuals suffering from vasomotor rhinitis typically experience symptoms year-round, though symptoms may exacerbate in the spring and autumn when rapid weather changes are more common. An estimated 17 million United States citizens have vasomotor rhinitis. The antihistamine azelastine has been shown to be effective for allergic, mixed, and vasomotor rhinitis. Fluticasone propionate in nostril spray form may also be used for symptomatic treatment.

Allergic



Pollen grains from a variety of common plants can cause *hay fever*.

Allergic rhinitis or hay fever is when an allergen such as pollen or dust is inhaled by an individual with a sensitized immune system, it triggers antibody production. These antibodies mostly bind to mast cells, which contain histamine. When the mast cells are stimulated by pollen and dust, histamine (and other chemicals) are released. This causes itching, swelling, and mucus production. Symptoms vary in severity between individuals. Very sensitive individuals can experience hives or other rashes. Particulate matter in polluted air and chemicals such as chlorine and detergents, which can normally be tolerated, can greatly aggravate the condition.

Characteristic physical findings in individuals who have allergic rhinitis include conjunctival swelling and erythema, eyelid swelling, lower eyelid venous stasis, lateral crease on the nose, swollen nasal turbinates, and middle ear effusion.

Rhinitis medicamentosa

It is a condition of rebound nasal congestion brought on by extended use of topical decongestants (*e.g.*, oxymetazoline, phenylephrine, xylometazoline, and naphazoline nasal sprays) that work by constricting blood vessels in the lining of the nose.

Chronic atrophic rhinitis

Chronic rhinitis in form of atrophy of the mucous membrane and glands.

Rhinitis sicca

Chronic form of dryness of the mucous membranes

Hypertrophic rhinitis

Chronic rhinitis with permanent thickening of the mucous membrane.

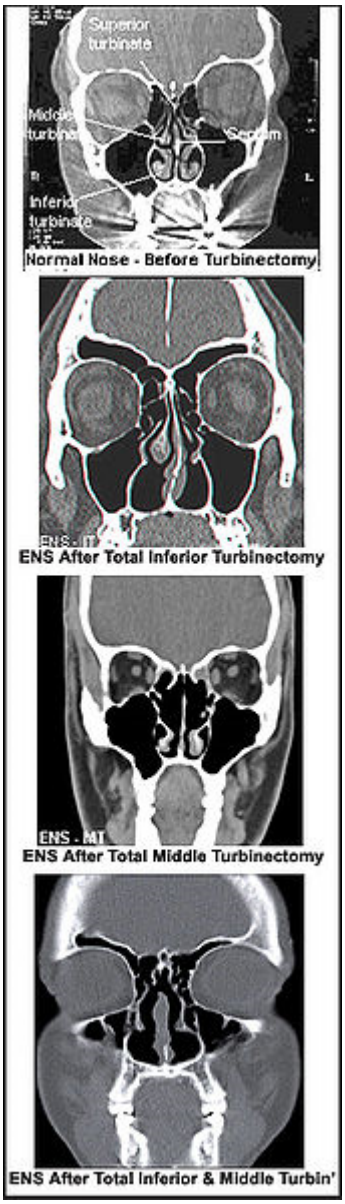
Polypous rhinitis

Chronic rhinitis associated with polyps in the nasal cavity.

Management

The management of rhinitis depends on the underlying cause.

Empty nose syndrome



CT pictures depicting different types of abnormal nasal anatomy following turbinectomies that result in ENS.

Empty nose syndrome (**ENS**) is a term that is used in otolaryngology to describe a nose that has been physiologically crippled by excessive surgical resection/reduction of turbinates in the nose (mainly the inferior turbinates) in a surgical procedure known as 'turbinectomy' or 'conchotomy'. It is therefore an iatrogenic condition that can and should be avoided.

Main symptoms

The 2 main physical symptoms are:

1.Chronic nasal dryness. Often leads to pain and repeated nasal infections. Repeated infections can cause areas of the mucosa to atrophy and this is why some studies refer to this condition as 'secondary atrophic rhinitis'. At least one large study concluded that it can take 7.1 years, on average, for atrophic rhinitis like symptoms to appear and urges the examining physician to look out for early signs and to try to counter them with self administered daily nasal irrigations and moisturization by the patient.

2.'Paradoxical obstruction' (difficulty inhaling through the nose despite not feeling any physical obstruction) leading to grogginess and dizziness.

The chronic nature of the physical symptoms have a significant impact on the patient's quality of life and sense of well-being, causing difficulty concentrating (appears in the medical literature as 'aprosexia nasalis'), pre-occupation with symptoms, anxieties, and often clinical depression.

Prognosis

There has been very little research conducted on this condition and hardly any long term follow ups. For many years this condition was over looked or mistaken because of secondary problems that usually occur after radical nasal trubinectomies. For instance - the remaining mucosal structures (the septum and the remaining turbinates) often hypertrophy causing actual physical obstruction on top of the already existing paradoxical obstruction.

The lack of long term follow ups of patients with this condition makes it difficult to estimate what percentage of patients, if any, will enjoy a spontaneous recovery or at least a significant enough improvement in their symptoms. But, given that the main cause of the systems is the gross loss of normal inner nasal anatomy, it is most likely that this condition will not cure itself.

The patients can replace some of the lost moisture to reduce the risks of mucosal atrophy by coating their nasal lining with protective gels and using saline mist sprays and irrigations, but it seems that unless the turbinates are functionally reconstructed there is little hope to fully recover from this condition.

In recent years there have been several reports of attempts to reconstruct the inferior turbinates of nose through submucusal implantation of various implant materials, in an attempt to restore normal nasal aerodynamics and physiology. The sample of patients reported on was very small and the follow up was relatively short, but the results show some promise.

There is hope among patients that with recent advances made in regenerative medicine otolaryngologists will begin to explore ways to use stem cells and tissue engineering technology to fully reconstruct the inferior turbinates of the nose and restore it back to normal.

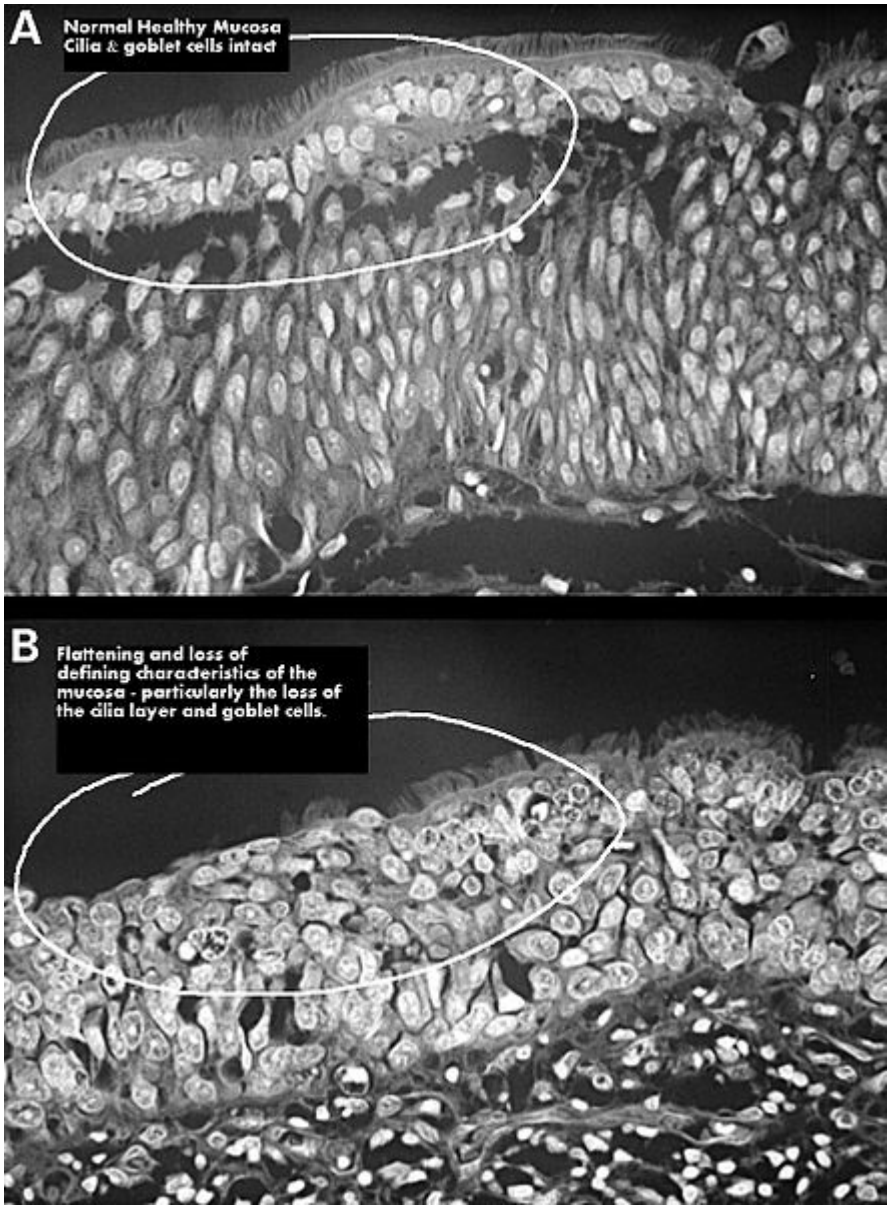
Diagnosis

The clinician should suspect ENS when the following findings are present: The patient complains of poor nasal breathing and often a sensation of suffocation or shortness of breath despite having a patent (typically over-patent) nasal airway. The patients typically complain of nasal and pharyngeal dryness too. These symptoms appeared only after the patient underwent a turbinate reductive procedure. Sometimes, many years later.

On examination the nasal cavity should look abnormally spacious, lacking (part of) one or both turbinates (the inferior and/or middle turbinates). Mucosal pathology varies greatly. In some patients, the mucosa is dry and pale because of metaplasia; in others, it is red because of chronic infection. Crusting may range from absent to severe. The symptoms and findings are believed to be caused by abnormal aerodynamics, chronic inflammation and dryness leading to loss of airflow sensation that feels like dyspnea.

The diagnosis is often complicated because it is common to find that the remaining tissues are hypertrophied (in response to the dryness and constant aggravation of over-turbulent air currents).

Etiology



Squamous metaplasia of nasal respiratory epithelium

The turbinates are known as the main humidifying, heat exchanging, air-filtering, airflow controlling and airflow sensing structures of the nose. They control, heat, humidify and filter the airflow by streamlining it around them as it progresses through the nose, thus significantly increasing the mucosal surface that comes into contact with the airflow. Their integrity and function is crucial for maintaining nasal and sinus health and physiology. Built aerodynamically from anterior to posterior they are designed to not over obstruct breathing while processing the airflow. The two main symptoms that effect every ENS sufferer are - mucosal dryness and paradoxical obstruction (the troubling feeling of needing more nasal resistance to inhale).

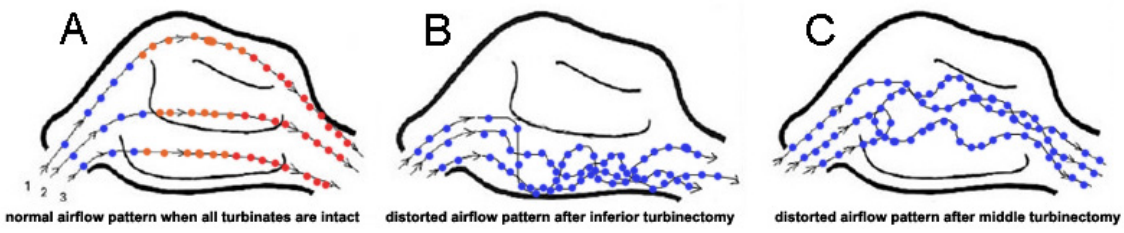
Mucosal Dryness

The dryness in ENS is caused by the loss of too much turbinate tissue (especially from the inferior turbinates at the front and lower part of the nasal airway) which robs the remaining mucosa from the protection of the turbinates (physical protection and physiological protection of the actual heat and moisture created by the turbinates themselves). This causes metaplasia, endertitis and chronic dryness of the remaining mucosa that may lead to areas of mucosal atrophy and sometimes to even full blown atrophic rhinitis and ozena.

Paradoxical Obstruction

Paradoxical nasal obstruction can be caused by two separate causes:

a) When the inferior turbinates are resected, especially when the heads of those turbinates are resected, the nose does not lose only its normal aerodynamical ability to streamline the airflow correctly, but also its ability to pressurize the air to flow fast enough through the nose. This forward motion is achieved in a normal nose by natural narrowness of the air passage at the nasal valve region which is made of the cartilages of the external nose on both sides of the septum, just past the nasal vestibules, and also by the heads of the inferior turbinates behind them. In fact the heads of the inferior turbinates are the dynamic part of this valve, as they congest and decongest in response to the body's ever changing needs, thus acting like a thumb on the tip of a water hose - to control the strength of the projection of the air jet through the nose. When the cross section of this valve is over enlarged, like due to an inferior turbinectomy, a troubling sensation of needing more nasal resistance to breath is generated and the patient needs to work much harder to inhale adequate amounts of air.



Distorted airflow patterns in the nose after middle or inferior turbinectomies

b) A second problem that contributes to paradoxical obstruction is the loss/reduction in airflow sensation - caused by loss of neural feedback (of the trigeminal cranial nerve that innervates most of the nose), either because of the receptors being imbedded in chronically dry and inflamed nasal mucosa, or by actual atrophy of nerve endings (neurotmesis). In addition - the turbinates themselves are known to be a major site of airflow sensation too.

Terminology

Turbinectomies have been performed for over 100 years. However, ENT specialists (otolaryngologists) were traditionally taught to respect the turbinates as a vital part of the nasal anatomy and physiology - to reduce them judiciously (when irreversibly hypertrophied) and to never fully resect them. Only in the late 20th century did they begin breaking from this tradition and treating the turbinates as structures that can be radically and even totally resected, thinking it will not cause serious consequence to nasal physiology. This was proven to be wrong and caused a dramatic surge in the number of patients who developed an identical sequella of symptoms. The term "empty nose syndrome" (ENS) was coined by Dr. Eugene Kern in 1994, after a remark made by a visiting colleague from Sweden (Dr. Stenqvist) who while examining the CT scans of these patients said that their nasal cavities seemed "empty".

These days the pendulum is shifting again as the vast majority of studies about turbinectomies published in the last decade call for as much preservation as possible of the turbinates, underlining their irreplaceable importance to nasal health and physiology.

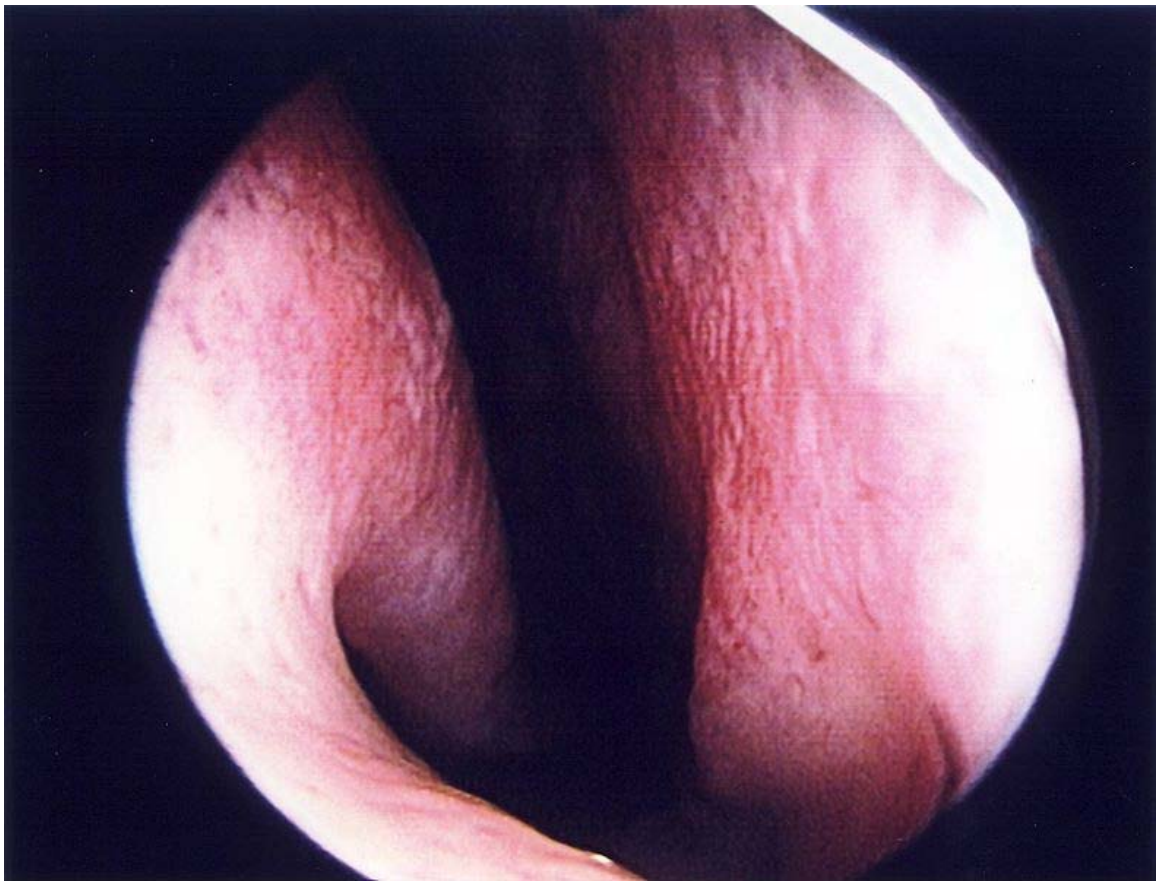
Currently available treatment options

Non-surgical treatment

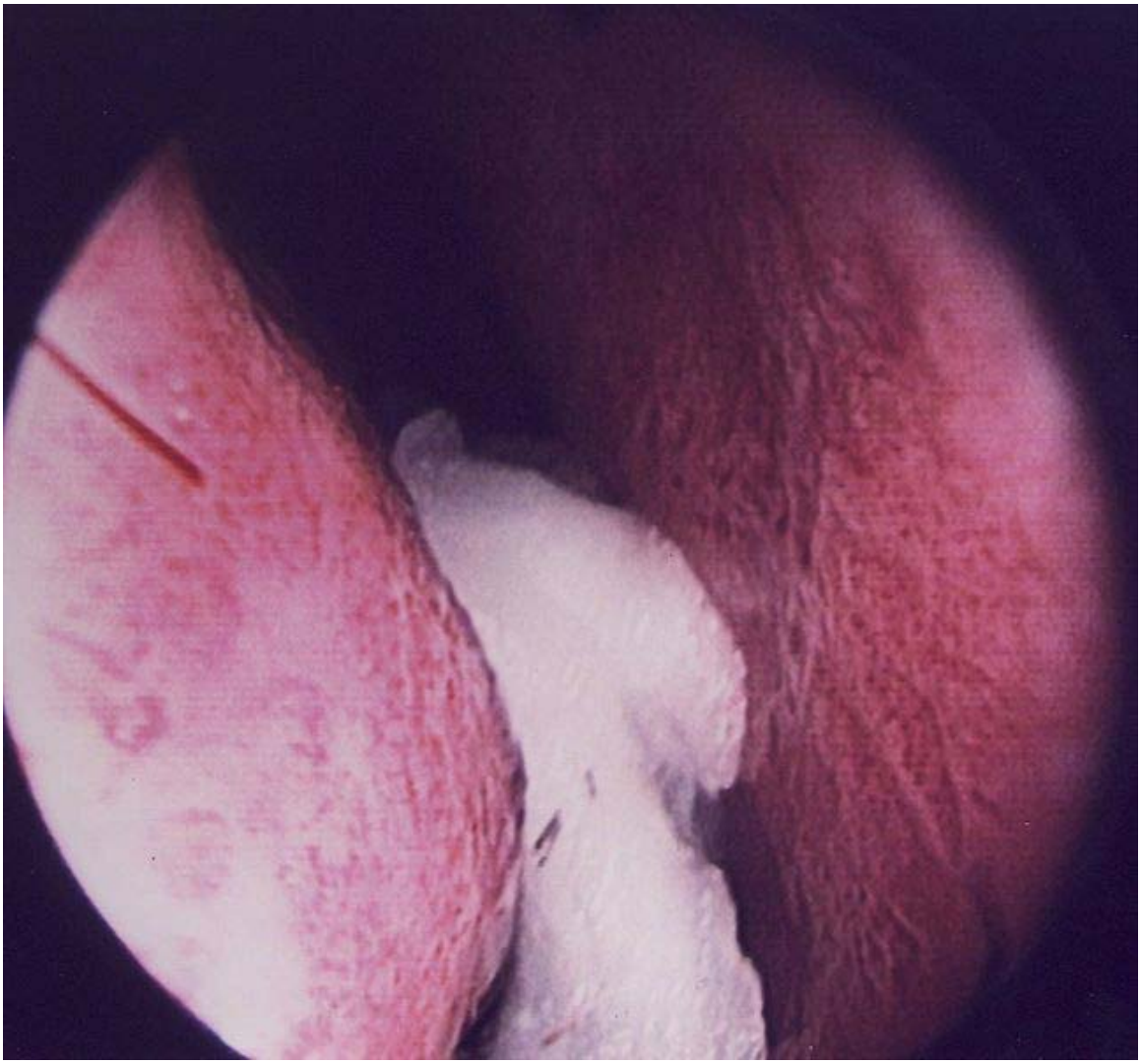
Non-surgical treatment options are meant to maintain and improve the health of the remaining nasal mucosa in the ENS nose by keeping it moist and free of infection and irritation and by maintaining a good blood supply:

- Keeping the nasal passages moist with saline based mist sprays or gels.
- Nasal irrigations of regular saline (Many patients prefer to use Ringer's Lactate solution with added xylitol instead, as they find it soothes the mucosa more than regular saline, and there are some empirical studies that back up that claim).
- Irrigations of saline with 80 mg of gentimycin if ozeana occurs.
- Systemic medication as indicated for pain and or depression which is common (about 50%) in patients with this syndrome.
- Sleeping with a cool mist humidifier.
- complimentary medicinal treatments such as Acupuncture, shiatsu and cranio-sacral therapy meant to improve nasal blood supply and nerve function and to reduce swelling.
- Regular daily physical exercise and maintaining good general health to reduce the risk of deterioration of symptoms.

Surgical treatment



Right partially reduced inferior turbinate before cotton test to verify ENS symptoms



Cotton apllied to simulate the resistance that an implant will add to the over-reduced inferior turbinate

Surgical treatment involves narrowing back the over enlarged nasal cavity—either by bulking up the partially resected turbinates with biological implant material (in cases where at least 50% of the inferior turbinate remain from anterior to posterior) or by creating neo-turbinates through submucosal implantation between the submucosa and bone in key locations in the nasal cavity. Of course, in some cases a combined approach is the best choice. The main difficulty with implant surgery is to achieve a long lasting bulk that will not get absorbed over time. Sometimes a procedure has to be repeated several times to get a sustainable result. The most physiological location for an implant is the lateral wall of the nasal cavity, where the inferior turbinate used to project from. An easier location to implant is the septum, but it is less favorable as it is not the natural location of the turbinates and may over obstruct the airflow.

The underlying rationale of surgery is to restore the natural inner nasal geometrical contours of the nasal passages of air (the inferior, middle, and superior meatuses), as much as possible, to mitigate the airflow just enough to restore normal rates of inner nasal humidity and temperature that will allow the mucosa to recuperate and sense the airflow well enough. It is paramount to do so while trying to restore the normal aerodynamics of the airflow in the nose, otherwise nasal obstruction will occur.

Pre-surgical planning has a tremendous impact on the success of the procedure. The surgeon is advised to perform a cotton test prior to the implantation: the surgeon places saline soaked chunks of cotton wool at the pre-planned site of implantation to simulate the implant. By doing so, he restricts and normalizes the nasal airflow patterns. This restores nasal aerodynamics. By trying different locations in accordance to the patient's feedbacks regarding the quality of his breathing and other ENS symptoms, it is possible to pinpoint the exact placement for the implants and their estimated shape and size.

Turbinate tissue is unique and there are no potential donor sites in the body from which to harvest similar tissue. However, in the nose, form equals function. It is therefore possible to restore some function by restoring the natural contours and proportions of the nasal passages: It is possible to create an artificial look-alike structure of a turbinate in the nasal cavities, and thus to regain some of the nose's capabilities to adequately resist, streamline, heat, humidify, filter, and sense the airflow.

- A video demonstrating lateral wall implantation to create a bulk of tissue that will simulate the shape and function of the resected inferior turbinate.

Implant materials

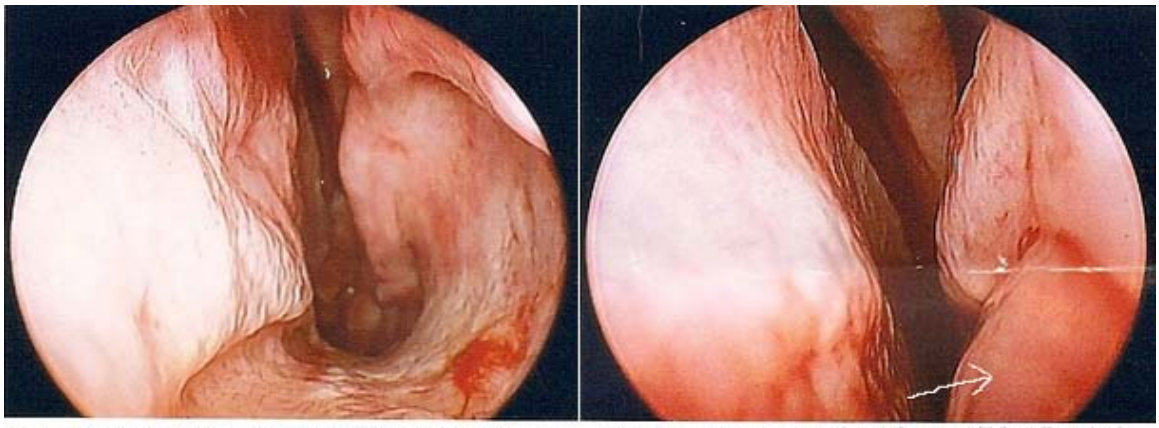
The bulking up of the sub-mucosa and mucosa to create a neo-turbinate structure can be achieved through implanting some supporting material between the bone/cartilage and also into the submucosal layer. Many materials have been tried over the past 100 years. In most cases this operation was used to restore heat and humidity to atrophic noses.

Generally speaking, the implant materials can be divided into 3 groups:

- autografts: bone, cartilage, fat, etc. from one site to another in the same patient. The problems here are relative shortage of tissue, and long term studies have shown high absorption rates in the nose. A Chinese study reported long-term success using illiac bone autografts.
- foreign materials: such as fibrin glue, Teflon, Gore-Tex, and plastipore, which solve the problem of shortage of autografts, are easy to shape and do not tend to get absorbed. However they have a high extrusion rate, and sometimes cause infection. A case study of good retention of hydroxyapetite cement in one patient has been reported in 2000, but the follow up was only 1 year long.
- allografts: In the last two decades scientists have been able to harvest and remove away genetic markers of some basic human tissues (like skin dermis) from donors, and thus supplying a human natural implant material which does not

stimulate the immune system to reject it. A good example for such material is acellular dermis (brand named "Alloderm"). It does not get rejected and in most areas retains most of its volume over long periods.

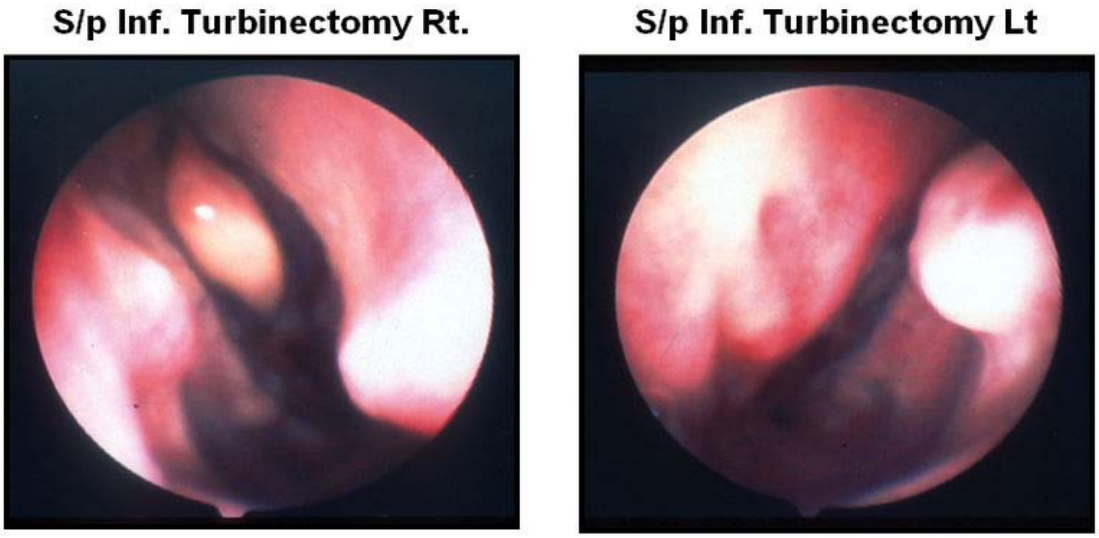
The ideal implant material, other than real original turbinate tissue should be something with low extrusion and rejection rates, minimal infection risk, and—very importantly—that will provide a strong and endurable enough structure and at the same time allow good permeability for blood vessel incorporation, which seems to be the key against long term absorption.



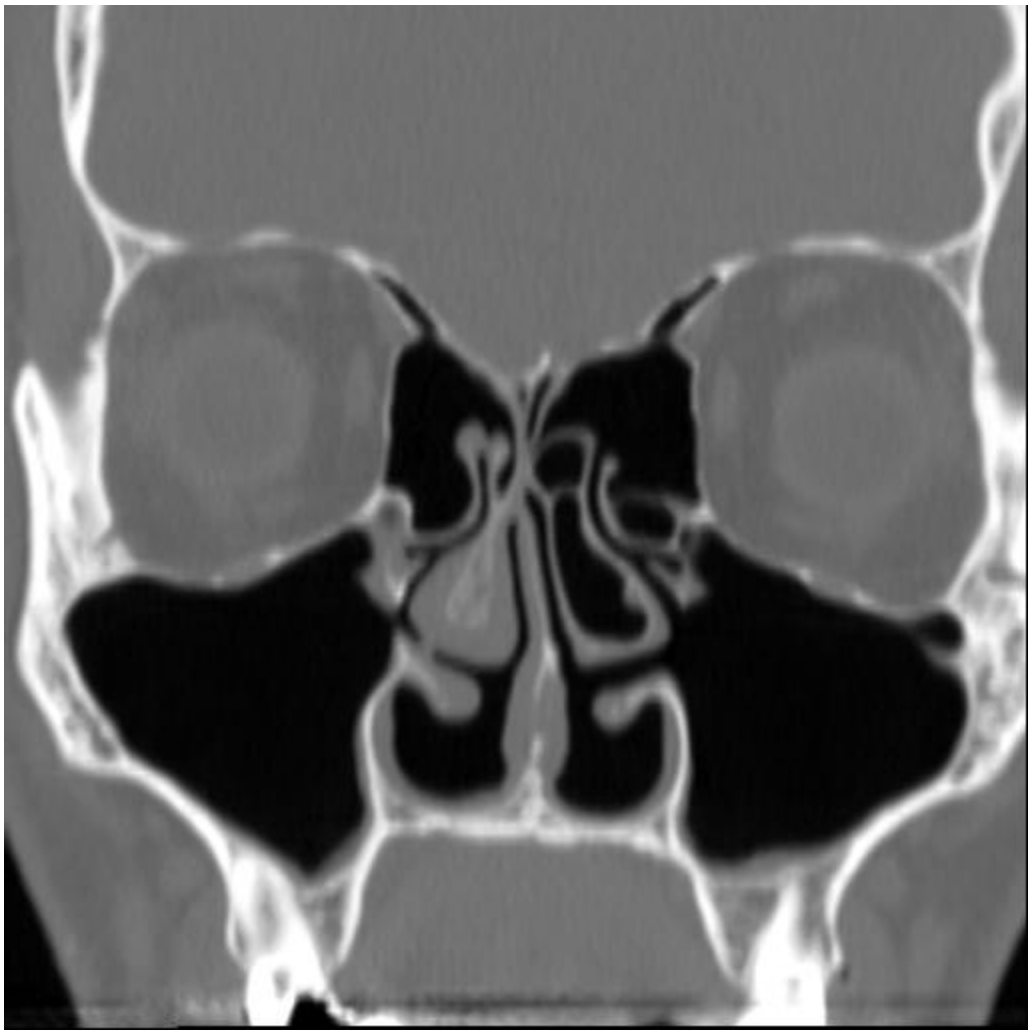
Left lateral wall after sub-total inferior turbinectomy After implant - Implant directs the airflow upwards

Before and after implantation of the lateral wall with Alloderm to simulate the function of the missing inferior turbinate

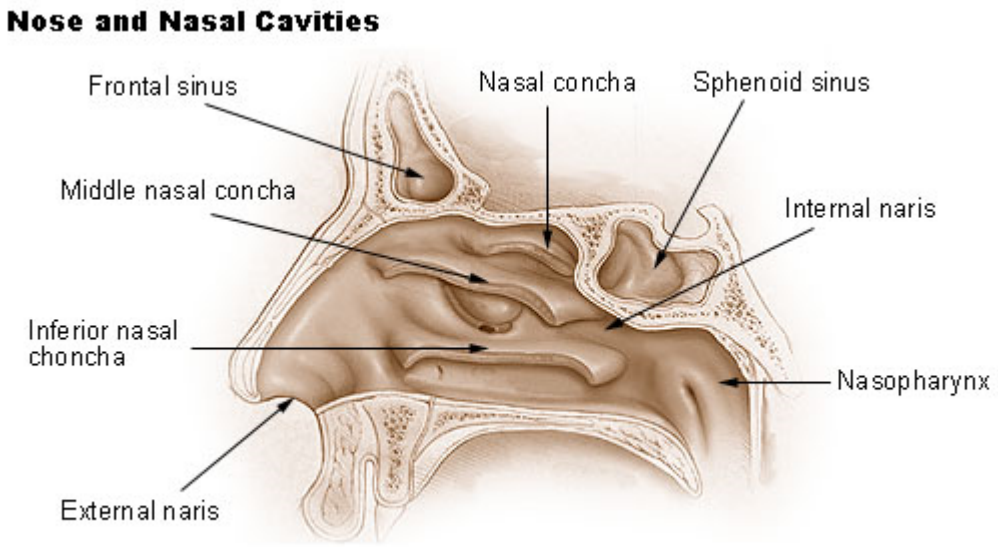
Additional images



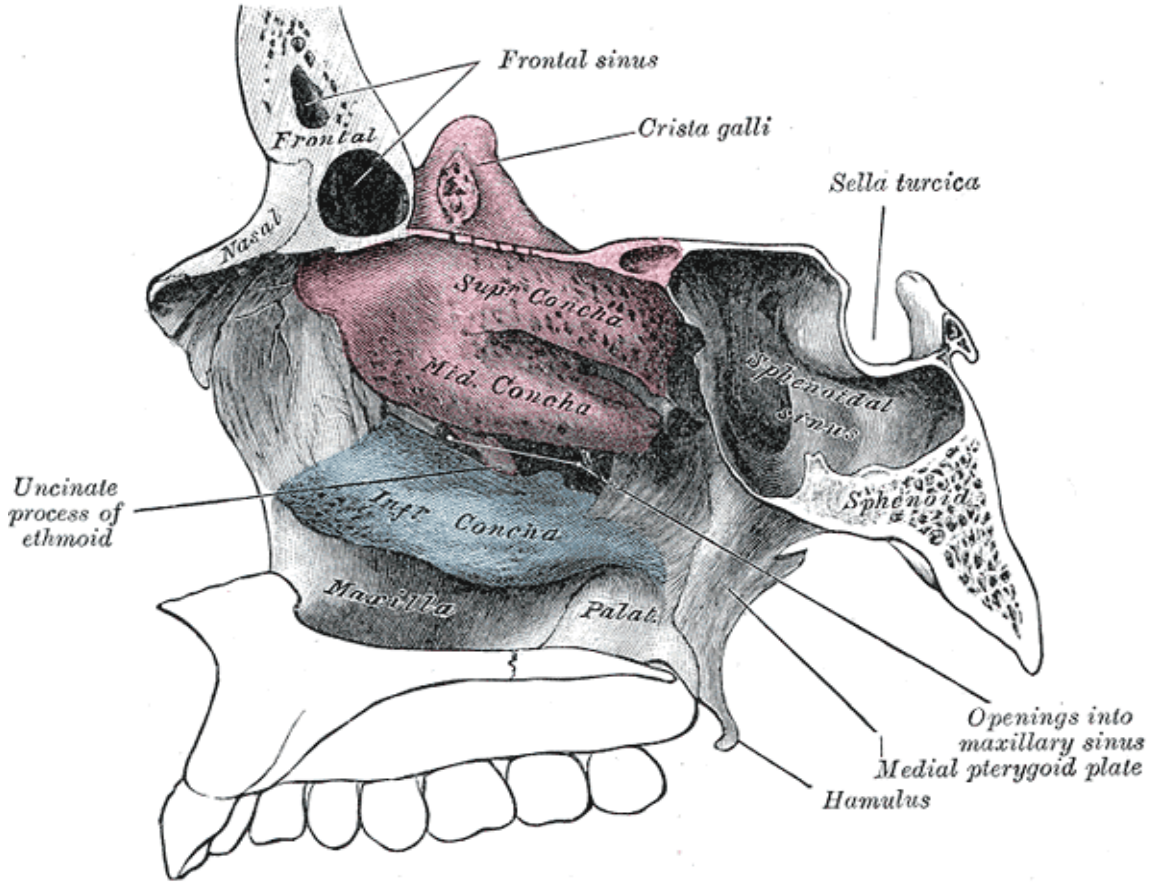
Internal view of the front inferior part of the nasal airways, after total inferior turbinectomy



Empty Nose Syndrome after subtotal inferior turbinectomy



All turbinates removed - Right lateral wall view

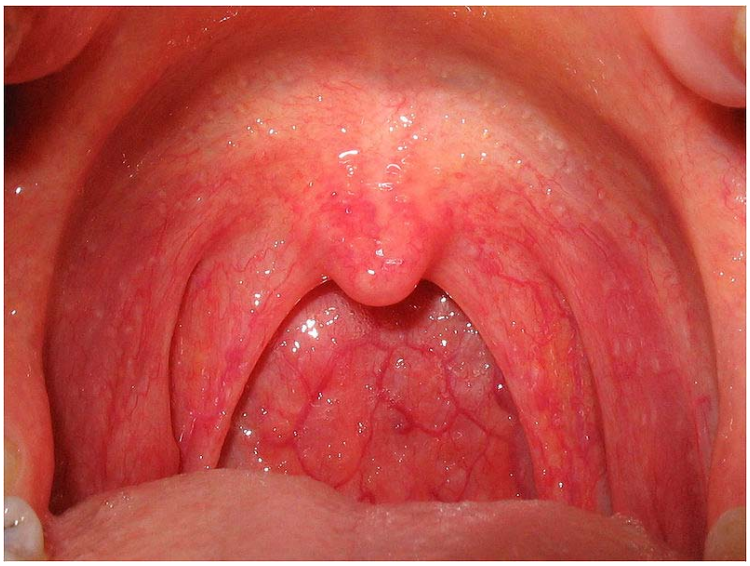


Anatomy of the nasal cavity

Chapter 19

Pharyngitis

Pharyngitis



Viral pharyngitis.

The oropharynx is swollen and red.

ICD-10	J02., J31.2
ICD-9	462, 472.1
DiseasesDB	24580
MedlinePlus	000655
eMedicine	emerg/419
MeSH	D010612

Pharyngitis is an inflammation of the throat or pharynx. In most cases it is painful and the initial infection can extend for a lengthy time period. It is the most common cause of a sore throat.

Like many types of inflammation, pharyngitis can be acute – characterized by a rapid onset and typically a relatively short course – or chronic. Pharyngitis can result in very large tonsils which cause trouble swallowing and breathing. Pharyngitis can be accompanied by a cough or fever, for example, if caused by an upper respiratory tract infection.

Most acute cases are caused by viral infections (40–80%), with the remainder caused by bacterial infections, fungal infections, or irritants such as pollutants or chemical substances. Treatment of viral causes are mainly symptomatic while bacterial or fungal causes may be amenable to antibiotics and anti-fungal respectively.

Classification

Pharyngitis is a type of upper respiratory tract infection that involves inflammation of the pharynx. It may include tonsillitis in which case it is known as pharyngotonsillitis. Another sub classification is nasopharyngitis (the common cold).

Cause

The majority of cases are due to an infectious organism acquired from close contact with an infected individual.

Viral

A throat infection which tested negative for streptococcus, thus presumably of viral origin. Note the white exudate on the tonsils which frequently also occurs with a viral infection.

These comprise about 40–80% of all infectious cases and can be a feature of many different types of viral infections.

- Adenovirus – the most common of the viral causes. Typically the degree of neck lymph node enlargement is modest and the throat often does not appear red, although it is very painful.
- Orthomyxoviridae which cause influenza – present with rapid onset high temperature, headache and generalised ache. A sore throat may be associated.
- Infectious mononucleosis ("glandular fever") caused by the Epstein-Barr virus. This may cause significant lymph gland swelling and an exudative tonsillitis with marked redness and swelling of the throat. The heterophile test can be used if this is suspected.
- Herpes simplex virus can cause multiple mouth ulcers.

- Measles
- Common cold: rhinovirus, coronavirus, respiratory syncytial virus, parainfluenza virus can cause infection of the throat, ear, and lungs causing standard cold-like symptoms and often extreme pain.

Bacterial

A number of different bacteria can infect the human throat. The most common is Group A streptococcus, however others include *Corynebacterium diphtheriae*, *Neisseria gonorrhoeae*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*.

Streptococcal pharyngitis

Streptococcal pharyngitis or strep throat is caused by group A beta-hemolytic streptococcus (GAS). It is the most common bacterial cause of cases of pharyngitis (15–30%). Common symptoms include fever, sore throat, and large lymph nodes. It is a contagious infection, spread by close contact with an infected individual. A definitive diagnosis is made based on the results of a throat culture. Antibiotics are useful to both prevent complications and speed recovery.

Fusobacterium necrophorum

Fusobacterium necrophorum are normal inhabitants of the oropharyngeal flora. Occasionally however it can create a peritonsillar abscess. In 1 out of 400 untreated cases Lemierre's syndrome occurs.

Diphtheria

Diphtheria is a potentially life threatening upper respiratory infection caused by *Corynebacterium diphtheriae* which has been largely eradicated in developed nations since the introduction of childhood vaccination programs, but is still reported in the Third World and increasingly in some areas in Eastern Europe. Antibiotics are effective in the early stages, but recovery is generally slow.

Others

A few other causes are rare, but possibly fatal, and include parapharyngeal space infections: peritonsillar abscess ("quinsy"), submandibular space infection (Ludwig's angina), and epiglottitis. Some medications may produce pharyngitis such as pramipexole and antipsychotics.

Other causes

Some cases of pharyngitis are caused by fungal infection such as *Candida albicans* causing oral thrush.

Diagnostic approach

It is hard to differentiate a viral and a bacterial cause of a sore throat based on symptoms alone. Thus often a throat swab is done to rule out a bacterial cause.

Management

The majority of time treatment is symptomatic. Specific treatments are effective for bacterial, fungal, and herpes simplex infections.

Medications

- Analgesics such as NSAIDs and acetaminophen can help reduce the pain associated with a sore throat.
- Steroids (such as dexamethasone) have been found to be useful for severe pharyngitis.
- Viscous lidocaine relieves pain by numbing the mucus membranes.
- Antibiotics are useful if group A streptococcus is the cause of the sore throat. For viral infections, antibiotics have no effect.

Alternative

Alternative medicines are promoted and used for the treatment of sore throats. They are however poorly supported by evidence, and UpToDate, an evidence-based peer-reviewed resource, recommends that they not be used to treat pharyngitis.

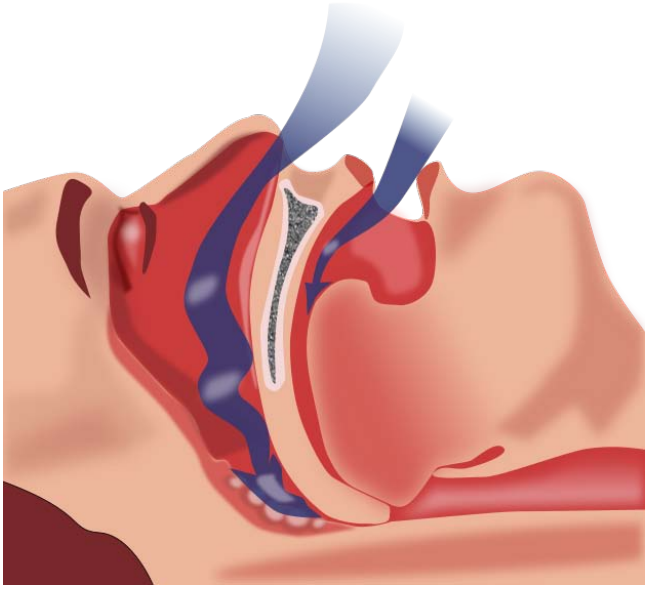
Epidemiology

Acute pharyngitis is the most common cause of a sore throat and is diagnosed in more than 1.9 million people a year in the United States.

Chapter 20

Sleep Apnea

Sleep apnea



Obstructive sleep apnea

ICD-10	G47.3
ICD-9	327.23, 780.57
eMedicine	ped/2114
MeSH	D012891

Sleep apnea (or **sleep apnoea** in British English) is a sleep disorder characterized by abnormal pauses in breathing or instances of abnormally low breathing, during sleep. Each pause in breathing, called an apnea, can last from a few seconds to minutes, and may occur 5 to 30 times or more an hour. Similarly, each abnormally low breathing event is called a hypopnea. Sleep apnea is diagnosed with an overnight sleep test called a polysomnogram, or "sleep study".

There are three forms of sleep apnea: central (CSA), obstructive (OSA), and complex or mixed sleep apnea (i.e., a combination of central and obstructive) constituting 0.4%, 84% and 15% of cases respectively. In CSA, breathing is interrupted by a lack of respiratory effort; in OSA, breathing is interrupted by a physical block to airflow despite respiratory effort, and snoring is common.

Regardless of type, an individual with sleep apnea is rarely aware of having difficulty breathing, even upon awakening. Sleep apnea is recognized as a problem by others witnessing the individual during episodes or is suspected because of its effects on the body (*sequelae*). Symptoms may be present for years (or even decades) without identification, during which time the sufferer may become conditioned to the daytime sleepiness and fatigue associated with significant levels of sleep disturbance.

Diagnosis

The diagnosis of Sleep Apnea is based on the conjoint evaluation of clinical symptoms (e.g. excessive daytime sleepiness and fatigue) and of the results of a formal sleep study (polysomnography, or reduced channels home based test). The latter aims at establishing an "objective" diagnosis indicator linked to the quantity of apneic events per hour of sleep (Apnea Hypnea Index(AHI), or Respiratory Disturbance Index (RDI)), associated to a formal threshold, above which a patient is considered as suffering from Sleep Apnea, and the severity of his sleep apnea can be then quantified. Nevertheless, due to the number and variability in the actual symptoms and nature of apneic events (hypopnea vs apnea, central vs. obstructive...), the variability of patients physiology, the intrinsic imperfections of the experimental setups and methods, this field is opened to debate. Within this context, the definition of an apneic event depends of several factors (e.g. patient's age) and account for this variability through a multi-criteria decision rule described in several, sometimes conflicting, guidelines. One example of a commonly adopted definition of an apnea (for an adult) includes a minimum 10 second interval between breaths, with either a neurological arousal (a 3-second or greater shift in EEG frequency, measured at C3, C4, O1, or O2) or a blood oxygen desaturation of 3–4% or greater, or both arousal and desaturation.

Classification

Obstructive sleep apnea

Obstructive sleep apnea (OSA) is the most common category of sleep-disordered breathing. The muscle tone of the body ordinarily relaxes during sleep, and at the level of the throat the human airway is composed of collapsible walls of soft tissue which can obstruct breathing during sleep. Mild occasional sleep apnea, such as many people experience during an upper respiratory infection, may not be important, but chronic severe obstructive sleep apnea requires treatment to prevent low blood oxygen (hypoxemia), sleep deprivation, and other complication.

Individuals with low muscle tone and soft tissue around the airway (e.g., because of obesity) and structural features that give rise to a narrowed airway are at high risk for obstructive sleep apnea. The elderly are more likely to have OSA than young people. Men are more likely to suffer sleep apnea than women and children are, though it is not uncommon in the latter two population groups.

The risk of OSA rises with increasing body weight, active smoking and age. In addition, patients with diabetes or "borderline" diabetes have up to three times the risk of having OSA.

Common symptoms include loud snoring, restless sleep, and sleepiness during the daytime. Diagnostic tests include home oximetry or polysomnography in a sleep clinic.

Some treatments involve lifestyle changes, such as avoiding alcohol or muscle relaxants, losing weight, and quitting smoking. Many people benefit from sleeping at a 30-degree elevation of the upper body or higher, as if in a recliner. Doing so helps prevent the gravitational collapse of the airway. Lateral positions (sleeping on a side), as opposed to supine positions (sleeping on the back), are also recommended as a treatment for sleep apnea, largely because the gravitational component is smaller in the lateral position. Some people benefit from various kinds of oral appliances to keep the airway open during sleep. Continuous positive airway pressure (CPAP) is the treatment of choice. There are also surgical procedures to remove and tighten tissue and widen the airway.

As already mentioned, snoring is a common finding in people with this syndrome. Snoring is the turbulent sound of air moving through the back of the mouth, nose, and throat. Although not everyone who snores is experiencing difficulty breathing, snoring in combination with other conditions such as overweight and obesity has been found to be highly predictive of OSA risk. The loudness of the snoring is not indicative of the severity of obstruction, however. If the upper airways are tremendously obstructed, there may not be enough air movement to make much sound. Even the loudest snoring does not mean that an individual has sleep apnea syndrome. The sign that is most suggestive of sleep apneas occurs when snoring *stops*.

Other indicators include (but are not limited to): hypersomnolence, obesity BMI >30, large neck circumference (16 in (410 mm) in women, 17 in (430 mm) in men), enlarged tonsils and large tongue volume, micrognathia, morning headaches, irritability/mood-swings/depression, learning and/or memory difficulties, and sexual dysfunction.

The term "sleep-disordered breathing" is commonly used in the U.S. to describe the full range of breathing problems during sleep in which not enough air reaches the lungs (hypopnea and apnea). Sleep-disordered breathing is associated with an increased risk of cardiovascular disease, stroke, high blood pressure, arrhythmias, diabetes, and sleep deprived driving accidents. When high blood pressure is caused by OSA, it is distinctive in that, unlike most cases of high blood pressure (so-called essential hypertension), the readings do *not* drop significantly when the individual is sleeping. Stroke is associated with obstructive sleep apnea.

In the June 27, 2008, edition of the journal *Neuroscience Letters*, researchers revealed that people with OSA show tissue loss in brain regions that help store memory, thus linking OSA with memory loss. Using magnetic resonance imaging (MRI), the scientists discovered that sleep apnea patients' mammillary bodies were nearly 20 percent smaller, particularly on the left side. One of the key investigators hypothesized that repeated drops in oxygen lead to the brain injury.

Central sleep apnea

In pure central sleep apnea or Cheyne-Stokes respiration, the brain's respiratory control centers are imbalanced during sleep. Blood levels of carbon dioxide, and the neurological feedback mechanism that monitors them, do not react quickly enough to maintain an even respiratory rate, with the entire system cycling between apnea and hyperpnea, even during wakefulness. The sleeper stops breathing and then starts again. There is no effort made to breathe during the pause in breathing: there are no chest movements and no struggling. After the episode of apnea, breathing may be faster (hyperpnea) for a period of time, a compensatory mechanism to blow off retained waste gases and absorb more oxygen.

While sleeping, a normal individual is "at rest" as far as cardiovascular workload is concerned. Breathing is regular in a healthy person during sleep, and oxygen levels and carbon dioxide levels in the bloodstream stay fairly constant. The respiratory drive is so strong that even conscious efforts to hold one's breath do not overcome it. Any sudden drop in oxygen or excess of carbon dioxide (even if tiny) strongly stimulates the brain's respiratory centers to breathe.

In central sleep apnea, the basic neurological controls for breathing rate malfunction and fail to give the signal to inhale, causing the individual to miss one or more cycles of breathing. If the pause in breathing is long enough, the percentage of oxygen in the circulation will drop to a lower than normal level (hypoxaemia) and the concentration of carbon dioxide will build to a higher than normal level (hypercapnia). In turn, these conditions of hypoxia and hypercapnia will trigger *additional* effects on the body. Brain cells need constant oxygen to live, and if the level of blood oxygen goes low enough for long enough, the consequences of brain damage and even death will occur. Fortunately, central sleep apnea is more often a chronic condition that causes much milder effects than sudden death. The exact effects of the condition will depend on how severe the apnea is and on the individual characteristics of the person having the apnea. Several examples are discussed below, and more about the nature of the condition is presented in the section on Clinical Details.

In any person, hypoxia and hypercapnia have certain common effects on the body. The heart rate will increase, unless there are such severe co-existing problems with the heart muscle itself or the autonomic nervous system that makes this compensatory increase impossible. The more translucent areas of the body will show a bluish or dusky cast from cyanosis, which is the change in hue that occurs owing to lack of oxygen in the blood ("turning blue"). Overdoses of drugs that are respiratory depressants (such as heroin, and

other opiates) kill by damping the activity of the brain's respiratory control centers. In central sleep apnea, the effects of sleep *alone* can remove the brain's mandate for the body to breathe.

- Normal Respiratory Drive: After exhalation, the blood level of oxygen decreases and that of carbon dioxide increases. Exchange of gases with a lungful of fresh air is necessary to replenish oxygen and rid the bloodstream of built-up carbon dioxide. Oxygen and carbon dioxide receptors in the blood stream (called chemoreceptors) send nerve impulses to the brain, which then signals reflex opening of the larynx (so that the opening between the vocal cords enlarges) and movements of the rib cage muscles and diaphragm. These muscles expand the thorax (chest cavity) so that a partial vacuum is made within the lungs and air rushes in to fill it.
- Physiologic effects of central apnea: During central apneas, the central respiratory drive is absent, and the brain does *not* respond to changing blood levels of the respiratory gases. No breath is taken despite the normal signals to inhale. The immediate effects of central sleep apnea on the body depend on how long the failure to breathe endures. At worst, central sleep apnea may cause sudden death. Short of death, drops in blood oxygen may trigger seizures, even in the absence of epilepsy. In people *with* epilepsy, the hypoxia caused by apnea may trigger seizures that had previously been well controlled by medications. In other words, a seizure disorder may become unstable in the presence of sleep apnea. In adults with coronary artery disease, a severe drop in blood oxygen level can cause angina, arrhythmias, or heart attacks (myocardial infarction). Longstanding recurrent episodes of apnea, over months and years, may cause an increase in carbon dioxide levels that can change the pH of the blood enough to cause a metabolic acidosis.

Mixed apnea and complex sleep apnea

Some people with sleep apnea have a combination of both types. When obstructive sleep apnea syndrome is severe and longstanding, episodes of central apnea sometimes develop. The exact mechanism of the loss of central respiratory drive during sleep in OSA is unknown but is most commonly related to acid-base and CO_2 feedback malfunctions stemming from heart failure. There is a constellation of diseases and symptoms relating to body mass, cardiovascular, respiratory, and occasionally, neurological dysfunction that have a synergistic effect in sleep-disordered breathing. In some cases, a side effect from the lack of sleep is a mild case of Excessive Daytime Sleepiness (EDS) where the subject has had minimal sleep and this extreme fatigue over time takes its toll on the subject. The presence of central sleep apnea without an obstructive component is a common result of chronic opiate use (or abuse) owing to the characteristic respiratory depression caused by large doses of narcotics.

Complex sleep apnea has recently been described by researchers as a novel presentation of sleep apnea. Patients with complex sleep apnea exhibit OSA, but upon application of positive airway pressure the patient exhibits persistent central sleep apnea. This central

apnea is most commonly noted while on CPAP therapy after the obstructive component has been eliminated. This has long been seen in sleep laboratories and has historically been managed either by CPAP or BiLevel therapy. Adaptive servo-ventilation (ASV) modes of therapy have been introduced to attempt to manage this complex sleep apnea. Studies have demonstrated marginally superior performance of the adaptive servo ventilators in treating Cheyne-Stokes breathing; however, no longitudinal studies have yet been published, nor have any results been generated that suggest any differential outcomes versus standard CPAP therapy. At the AARC 2006 in Las Vegas, NV, researchers reported successful treatment of hundreds of patients on ASV therapy; however, these results have not been reported in peer-reviewed publications as of July 2007.

An important finding by Dernaika et al. suggests that transient central apnea produced during CPAP titration (the so-called "complex sleep apnea") is "…transient and self-limited." The central apneas may in fact be secondary to sleep fragmentation during the titration process. As of July 2007, there has been no alternate convincing evidence produced that these central sleep apnea events associated with CPAP therapy for obstructive sleep apnea are of any significant pathophysiologic importance.

Research is ongoing, however, at the Harvard Medical School, including adding dead space to positive airway pressure for treatment of complex sleep-disordered breathing.

Treatment

For mild cases of sleep apnea, a treatment which is a lifestyle change is sleeping on one's side, which can prevent the tongue and palate from falling backwards in the throat and blocking the airway. Another is avoiding alcohol and sleeping pills, which can relax throat muscles, contributing to the collapse of the airway at night.

For moderate to severe sleep apnea, the most common treatment is the use of a continuous positive airway pressure (CPAP) device, which 'splints' the patient's airway open during sleep by means of a flow of pressurized air into the throat. The patient typically wears a plastic facial mask, which is connected by a flexible tube to a small bedside CPAP machine. The CPAP machine generates the required air pressure to keep the patient's airways open during sleep. Advanced models may warm or humidify the air and monitor the patient's breathing to ensure proper treatment. Although CPAP therapy is extremely effective in reducing apneas and less expensive than other treatments, some patients find it extremely uncomfortable. Many patients refuse to continue the therapy or fail to use their CPAP machines on a nightly basis.

In addition to CPAP, dentists specializing in sleep disorders can prescribe Oral Appliance Therapy (OAT). The oral appliance is a custom-made mouthpiece that shifts the lower jaw forward, opening up the airway. OAT is usually successful in patients with mild to moderate obstructive sleep apnea. OAT is a relatively new treatment option for sleep apnea in the United States, but it is much more common in Canada and Europe.

Several levels of obstruction may be addressed in physical treatment, including the nasal passage, throat (pharynx), base of tongue, and facial skeleton. Surgical treatment for obstructive sleep apnea needs to be individualized in order to address all anatomical areas of obstruction. Often, correction of the nasal passages needs to be performed in addition to correction of the oropharynx passage. Septoplasty and turbinate surgery may improve the nasal airway. Tonsillectomy and uvulopalatopharyngoplasty (UPPP or UP3) are available to address pharyngeal obstruction. Base-of-tongue advancement by means of advancing the genial tubercle of the mandible may help with the lower pharynx. A myriad of other techniques are available, including hyoid bone myotomy and suspension and various radiofrequency technologies.

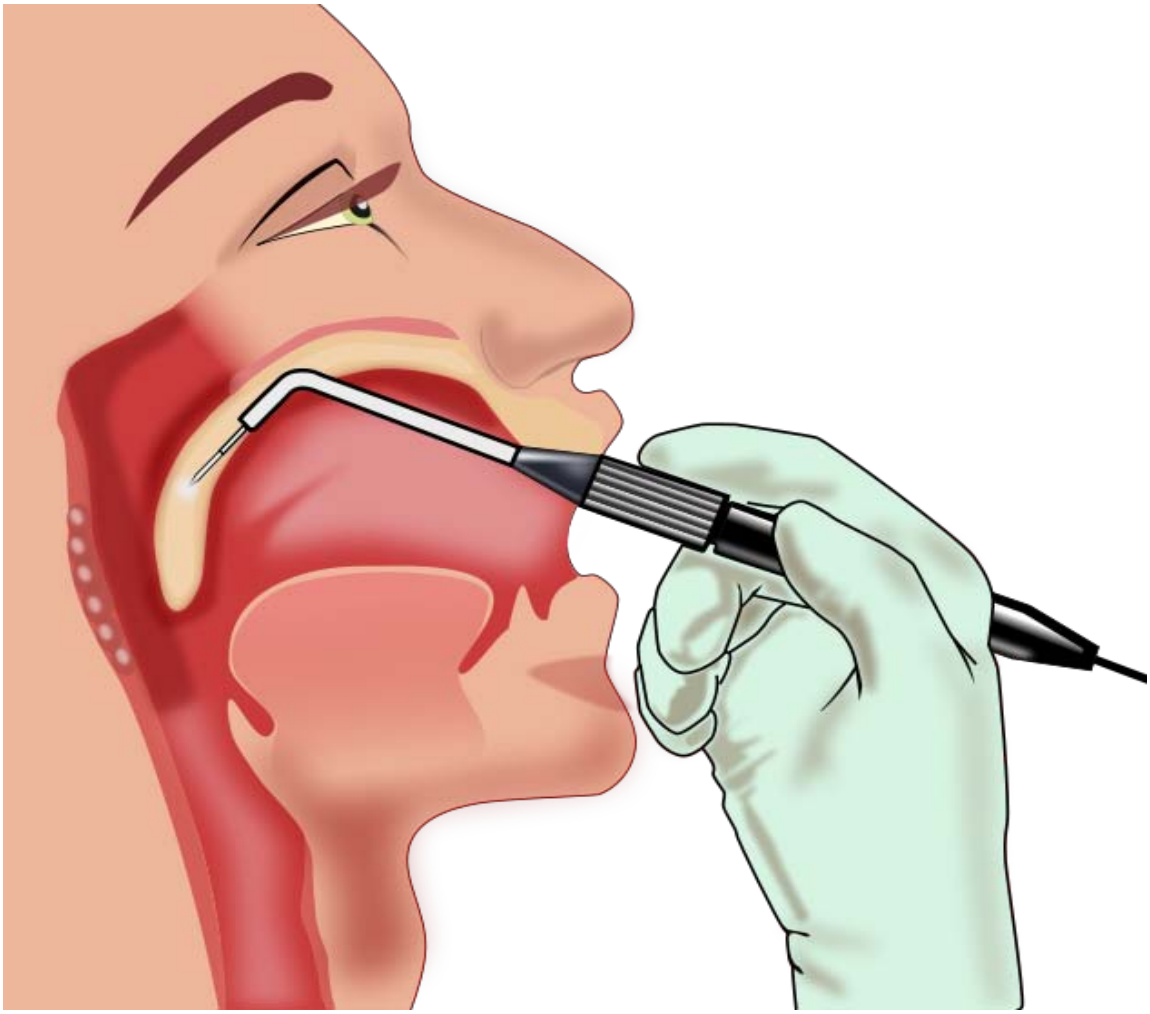


Illustration of surgery on the mouth and throat

Other surgery options may attempt to shrink or stiffen excess tissue in the mouth or throat, procedures done at either a doctor's office or a hospital. Small shots or other treatments, sometimes in a series, are used for shrinkage, while the insertion of a small piece of stiff plastic is used in the case of surgery whose goal is to stiffen tissues.

Possibly owing to changes in pulmonary oxygen stores, sleeping on one's side (as opposed to on one's back) has been found to be helpful for central sleep apnea with Cheyne-Stokes respiration (CSA-CSR).

Medications like Acetazolamide lower blood pH and encourage respiration. Low doses of oxygen are also used as a treatment for hypoxia but are discouraged due to side effects.

Surgery

CPAP is the most consistently safe and effective treatment for obstructive sleep apnea but it is not a cure, and people are less likely to use it in the long term. The Stanford Center for Excellence in Sleep Disorders Medicine achieved a 95% cure rate of sleep apnea patients by surgery. Maxillomandibular advancement (MMA) is considered the most effective surgery for sleep apnea patients, because it increases the posterior airway space (PAS). The main benefit of the operation is that the oxygen saturation in the arterial blood increases. In a study published in 2008, 93.3.% of surgery patients achieved an adequate quality of life based on the Functional Outcomes of Sleep Questionnaire (FOSQ). Surgery led to a significant increase in general productivity, social outcome, activity level, vigilance, intimacy and sex, and the total score postoperatively was P = .0002. Overall risks of MMA surgery are low: The Stanford University Sleep Disorders Center found 4 failures in a series of 177 patients, or about one out of 44 patients.

Several inpatient and outpatient procedures use sedation. Many drugs and agents used during surgery to relieve pain and to depress consciousness remain in the body at low amounts for hours or even days afterwards. In an individual with either central, obstructive or mixed sleep apnea, these low doses may be enough to cause life-threatening irregularities in breathing or collapses in a patient’s airways. Use of analgesics and sedatives in these patients postoperatively should therefore be minimized or avoided.

Surgery on the mouth and throat, as well as dental surgery and procedures, can result in postoperative swelling of the lining of the mouth and other areas that affect the airway. Even when the surgical procedure is designed to improve the airway, such as tonsillectomy and adenoidectomy or tongue reduction, swelling may negate some of the effects in the immediate postoperative period. Once the swelling resolves and the palate becomes tightened by postoperative scarring, however, the full benefit of the surgery may be noticed.

Sleep apnea patients undergoing any medical treatment must make sure his or her doctor and/or anesthetist are informed about their condition. Alternate and emergency procedures may be necessary to maintain the airway of sleep apnea patients. If an individual suspects he or she may have sleep apnea, communication with their doctor about possible preprocedure screening may be in order.

Alternative treatments

A 2005 study in the British Medical Journal found that learning and practicing the didgeridoo helped reduce snoring and sleep apnea as well as daytime sleepiness. This appears to work by strengthening muscles in the upper airway, thus reducing their tendency to collapse during sleep.

A 2009 study published in the American Journal of Respiratory and Clinical Care Medicine found that "oropharyngeal exercises derived from speech therapy may be an effective treatment option for patients with moderate" obstructive sleep apnea.

Epidemiology

The Wisconsin Sleep Cohort Study estimated in 1993 that roughly one in every 15 Americans were affected by at least moderate sleep apnea. It also estimated that in middle-age as many as nine percent of women and 24 percent of men were affected, undiagnosed and untreated.

The costs of untreated sleep apnea reach further than just health issues. It is estimated that in the U.S. the average untreated sleep apnea patient's annual health care costs $1,336 more than an individual without sleep apnea. This may cause $3.4 billion/year in additional medical costs. Whether medical cost savings occur with treatment of sleep apnea remains to be determined.

History

The clinical picture of this condition has long been recognized as a character trait, without an understanding of the disease process. The term "Pickwickian syndrome" that is sometimes used for the syndrome was coined by the famous early 20th century physician, William Osler, who must have been a reader of Charles Dickens. The description of Joe, "the fat boy" in Dickens's novel *The Pickwick Papers*, is an accurate clinical picture of an adult with obstructive sleep apnea syndrome.

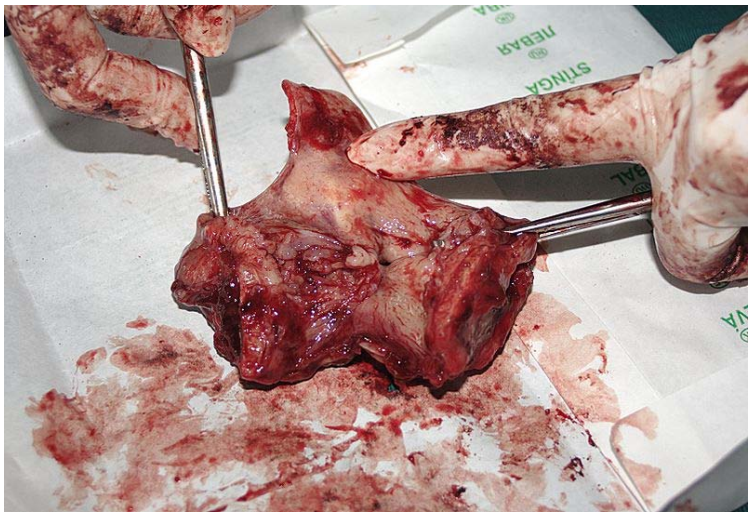
The early reports of obstructive sleep apnea in the medical literature described individuals who were very severely affected, often presenting with severe hypoxemia, hypercapnia and congestive heart failure.

The management of obstructive sleep apnea was revolutionized with the introduction of continuous positive airway pressure (CPAP), first described in 1981 by Colin Sullivan and associates in Sydney, Australia. The first models were bulky and noisy, but the design was rapidly improved and by the late 1980s CPAP was widely adopted. The availability of an effective treatment stimulated an aggressive search for affected individuals and led to the establishment of hundreds of specialized clinics dedicated to the diagnosis and treatment of sleep disorders. Though many types of sleep problems are recognized, the vast majority of patients attending these centers have sleep-disordered breathing.

Chapter 21

Laryngeal Cancer

Laryngeal cancer



Larynx cancer.

ICD-10 C32.

ICD-9 161

MeSH D007822

Laryngeal cancer may also be called **cancer of the larynx** or **laryngeal carcinoma**. Most laryngeal cancers are squamous cell carcinomas, reflecting their origin from the squamous cells which form the majority of the laryngeal epithelium. Cancer can develop in any part of the larynx, but the cure rate is affected by the location of the tumor. For the purposes of tumour staging, the larynx is divided into three anatomical regions: the glottis (true vocal cords, anterior and posterior commissures); the supraglottis (epiglottis, arytenoids and aryepiglottic folds, and false cords); and the subglottis.

Most laryngeal cancers originate in the glottis. Supraglottic cancers are less common, and subglottic tumours are least frequent.

Laryngeal cancer may spread by direct extension to adjacent structures, by metastasis to regional cervical lymph nodes, or more distantly, through the blood stream. Distant metastates to the lung are most common.

Risk factors

Larynx cancer - endoscopic view

Smoking is the most important risk factor for laryngeal cancer. Death from laryngeal cancer is 20 times more likely for heaviest smokers than for nonsmokers. Heavy chronic consumption of alcohol, particularly alcoholic spirits, is also significant. When combined, these two factors appear to have a synergistic effect. Some other quoted risk factors are likely, in part, to be related to prolonged alcohol and tobacco consumption. These include low socioeconomic status, male sex, and age greater than 55 years.

People with a history of head and neck cancer are known to be at higher risk (about 25%) of developing a second cancer of the head, neck, or lung. This is mainly because in a significant proportion of these patients, the aerodigestive tract and lung epithelium have been exposed chronically to the carcinogenic effects of alcohol and tobacco. In this situation, a field change effect may occur, where the epithelial tissues start to become diffusely dysplastic with a reduced threshold for malignant change. This risk may be reduced by quitting alcohol and tobacco.

Symptoms

The symptoms of laryngeal cancer depend on the size and location of the tumor. Symptoms may include the following:

- Hoarseness or other voice changes
- A lump in the neck
- A sore throat or feeling that something is stuck in the throat
- Persistent cough
- Stridor
- Bad breath
- Ear ache ("*referred*")

Incidence

Two in 20,000 (12,500 new cases per year) in USA. The American Cancer Society estimates that 9,510 men and women (7,700 men and 1,810 women) will be diagnosed with and 3,740 men and women will die of laryngeal cancer in 2006.

Laryngeal cancer is listed as a "rare disease" by the Office of Rare Diseases (ORD) of the National Institutes of Health (NIH). This means that laryngeal cancer affects fewer than 200,000 people in the U.S.

Each year, about 2,200 people in the U.K. are diagnosed with laryngeal cancer.

Diagnosis

Diagnosis is made by the doctor on the basis of a medical history, physical examination, and special investigations which may include a chest x-ray, CT or MRI scans, and tissue biopsy. The examination of the larynx requires some expertise, which may require specialist referral.

The physical exam includes a systematic examination of the whole patient to assess general health and to look for signs of associated conditions and metastatic disease. The neck and supraclavicular fossa are palpated to feel for cervical adenopathy, other masses, and laryngeal crepitus. The oral cavity and oropharynx are examined under direct vision. The larynx may be examined by indirect laryngoscopy using a small angled mirror with a long handle (akin to a dentist's mirror) and a strong light. Indirect laryngoscopy can be highly effective, but requires skill and practice for consistent results. For this reason, many specialist clinics now use fibre-optic nasal endoscopy where a thin and flexible endoscope, inserted through the nostril, is used to clearly visualise the entire pharynx and larynx. Nasal endoscopy is a quick and easy procedure performed in clinic. Local anaesthetic spray may be used.

If there is a suspicion of cancer, biopsy is performed, usually under general anaesthetic. This provides histological proof of cancer type and grade. If the lesion appears to be small and well localised, the surgeon may undertake excision biopsy, where an attempt is made to completely remove the tumour at the time of first biopsy. In this situation, the pathologist will not only be able to confirm the diagnosis, but can also comment on the completeness of excision, i.e., whether the tumour has been completely removed. A full endoscopic examination of the larynx, trachea, and esophagus is often performed at the time of biopsy.

For small glottic tumours further imaging may be unnecessary. In most cases, tumour staging is completed by scanning the head and neck region to assess the local extent of the tumour and any pathologically enlarged cervical lymph nodes.

The final management plan will depend on the site, stage (tumour size, nodal spread, distant metastasis), and histological type. The overall health and wishes of the patient must also be taken into account.

Treatment

Specific treatment depends on the location, type, and stage of the tumour. Treatment may involve surgery, radiotherapy, or chemotherapy, alone or in combination. This is a specialised area which requires the coordinated expertise of ear, nose and throat (ENT) surgeons (otolaryngologists) and oncologists.

Chapter 22

Spasmodic Dysphonia

Spasmodic dysphonia (or **laryngeal dystonia**) is a voice disorder characterized by involuntary movements of one or more muscles of the larynx (vocal folds or voice box) during speech.

Types of spasmodic dysphonia

The three types of spasmodic dysphonia (SD) are adductor spasmodic dysphonia, abductor spasmodic dysphonia and mixed spasmodic dysphonia.

Adductor spasmodic dysphonia

In adductor spasmodic dysphonia, sudden involuntary muscle movements or spasms cause the vocal folds (or vocal cords) to slam together and stiffen. These spasms make it difficult for the vocal folds to vibrate and produce voice. Words are often cut off or difficult to start because of the muscle spasms. Therefore, speech may be choppy and sound similar to stuttering. The voice of an individual with adductor spasmodic dysphonia is commonly described as strained or strangled and full of effort. Surprisingly, the spasms are usually absent while laughing, speaking at a high pitch, speaking while breathing and singing, but singers can experience a loss of range or the inability to produce certain notes of a scale or with projection. Stress, however, often makes the muscle spasms more severe.

Abductor spasmodic dysphonia

In abductor spasmodic dysphonia, sudden involuntary muscle movements or spasms cause the vocal folds to open. The vocal folds can not vibrate when they are open. The open position of the vocal folds also allows air to escape from the lungs during speech. As a result, the voices of these individuals often sound weak, quiet and breathy or whispery. As with adductor spasmodic dysphonia, the spasms are often absent during activities such as laughing or singing but singers can experience a loss of range or the inability to produce certain notes of a scale or with projection.

Mixed spasmodic dysphonia

Mixed spasmodic dysphonia involves muscles that open the vocal folds as well as muscles that close the vocal folds and therefore has features of both adductor and abductor spasmodic dysphonia.

Origins

The exact cause of spasmodic dysphonia (SD) is unknown. According to the National Institute on Deafness and Other Communication Disorders "research has revealed increasing evidence that most cases of spasmodic dysphonia are in fact neurogenic or having to do with the nervous system (brain and nerves)."

SD is a neurological disorder rather than a disorder of the larynx, and as in other forms of dystonia, interventions at the end organ (i.e., larynx) have not offered a definitive cure, only symptomatic relief. The pathophysiology underlying dystonia is becoming better understood as a result of discoveries in genetically based forms of the disorder, and this approach is the most promising avenue to a long-term solution.

The National Institute of Neurological Disorders and Stroke (NINDS) and the American Academy of Neurology (AAN) classify SD as a neurological disorder. However, because the voice can sound normal or near normal at times, some practitioners believe it to be psychogenic, that is, originating in the affected person's mind rather than from a physical cause. No medical organizations or groups take this position. A comparison of SD patients compared with vocal fold paralysis (VFP) patients found that 41.7% of the SD patients met the DSM-IV criteria for psychiatric comorbidity compared with 19.5% of the VFP group. However, another study found the opposite, with SD patients having significantly less psychiatric comorbidity compared to VFP patients: "The prevalence of major psychiatric cases varied considerably among the groups, from a low of seven percent (1/14) for spasmodic dysphonia, to 29.4 percent (5/17) for functional dysphonia, to a high of 63.6 percent (7/11) for vocal cord paralysis." A review in the journal Swiss Medicine Weekly states that "Psychogenic causes, a 'psychological disequilibrium', and an increased tension of the laryngeal muscles are presumed to be one end of the spectrum of possible factors leading to the development of the disorder". Alternatively, many investigators into the condition feel that the psychiatric comorbidity associated with voice disorders is a result of the social isolation and anxiety that patients with these conditions feel as a consequence of their difficulty with speech, as opposed to the cause of their dysfluency. The opinion that SD is psychogenic is not upheld by experts in the scientific community.

Evidence for a neurological basis

SD is formally classified as a movement disorder, one of the focal dystonias, and is also known as laryngeal dystonia. Supporting evidence that SD is a neurological disorder includes:

- SD may co-occur with other neurological movement disorders such as blepharospasm (excessive eye blinking and involuntary forced eye closure), tardive dyskinesia (involuntary and repetitious movement of muscles of the face, tongue, body, arms and legs), oromandibular dystonia (involuntary movements of the jaw muscles, lips and tongue), torticollis (involuntary movements of the neck muscles), or tremor (rhythmic, quivering muscle movements).
- Spasmodic dysphonia runs in some families and is thought to be inherited. Research has identified a possible gene on chromosome 9 that may contribute to the spasmodic dysphonia that is common to certain families.
- Histological examination of the nerve to the vocal cords in patients with SD demonstrates that the percentage of abnormally thin nerve fibers was higher than in normal controls
- Functional MRI signal is reduced in sensorimotor cortices associated with movement of the affected body part in laryngeal dystonia, supporting a dystonic basis for this voice disorder.

Diagnosis

Unfortunately, diagnosis of spasmodic dysphonia is often delayed due to lack of recognition of its symptoms by screening physicians. Most patients who are correctly diagnosed are evaluated by a team that usually includes an otolaryngologist, a speech-language pathologist and a neurologist. The otolaryngologist examines the vocal folds to look for other possible causes for the voice disorder. Fiberoptic laryngoscopy, a method whereby a small lighted flexible tube is passed through the nose and into the throat, is a helpful tool that allows the otolaryngologist to evaluate vocal cord movement during speech. Additional diagnostic testing may include stroboscopy, which allows the physician to view the vibrations of the vocal cords in slow motion. The speech-language pathologist evaluates the patient's voice and voice quality. The neurologist evaluates the patient for signs of other movement disorders.

Treatment

There is no known cure for spasmodic dysphonia.

The most effective treatment for reducing the symptoms of spasmodic dysphonia is injections of very small amounts of botulinum toxin (sold commercially under the brand names Botox, Dysport, and Myobloc) directly into the affected muscles of the larynx. The toxin weakens muscles by blocking the nerve impulse to the muscle. The botulinum toxin injections generally improve the voice for a period of three to four months after which the voice symptoms gradually return. This treatment requires continual injections to maintain a good speaking voice.

SD is sometimes confused with other hyperfunctional voice disorders that may respond to voice therapy, however voice therapy is not effective in treating SD.

An operation that cuts one of the nerves of the vocal folds (the recurrent laryngeal nerve) has improved the voice of many for several months to several years but the improvement is often temporary.

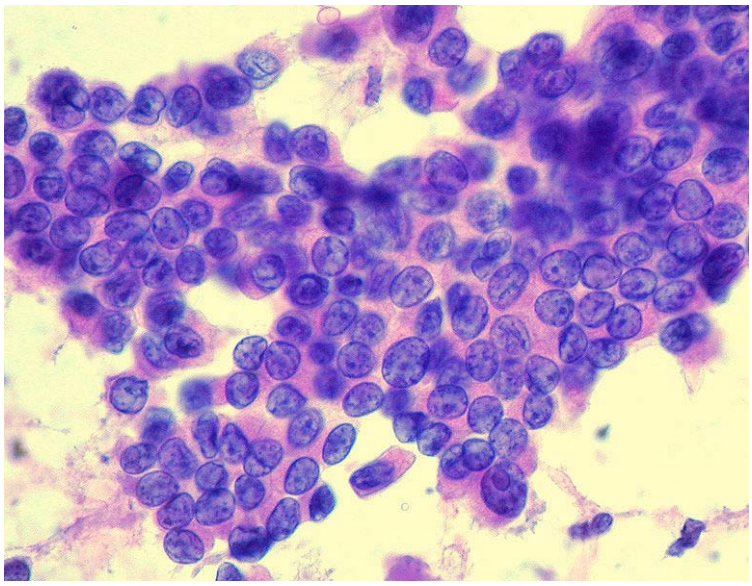
Notable people with spasmodic dysphonia

- Scott Adams, the creator of the comic strip *Dilbert*.
- Frank Allison, musician, leader of Frank Allison and the Odd Sox
- Johnny Bush, country & western musician and songwriter
- Keath Fraser, Canadian author who has documented the challenges and treatment of his condition in the book *The Voice Gallery: Travels With a Glass Throat* (2002).
- Sjors Fröhlich, former Dutch radio presenter, who had to give up his job as a presenter due to this disease.
- Robert F. Kennedy, Jr., son of United States Senator and presidential candidate Robert F. Kennedy, political and environmental activist
- Fred Lavery, a music producer, writer, musician, and recording studio co-owner from Cape Breton, Nova Scotia. Was lead singer of recording group Road and was later a solo artist, but developed the condition in the 1980s, and was forced to quit singing. Receives injections to keep voice fairly normal.
- Mary Lou Lord
- Andy MacWilliams, former radio broadcaster for the Cincinnati Stingers, Chicago Blackhawks and Cincinnati Cyclones.
- Darryl McDaniels of the rap group Run DMC
- Diane Rehm, host of the The Diane Rehm Show on National Public Radio (NPR).
- Mark Stuart, American rock musician (Audio Adrenaline)
- Linda Thompson, British folk-rock musician.

Chapter 23

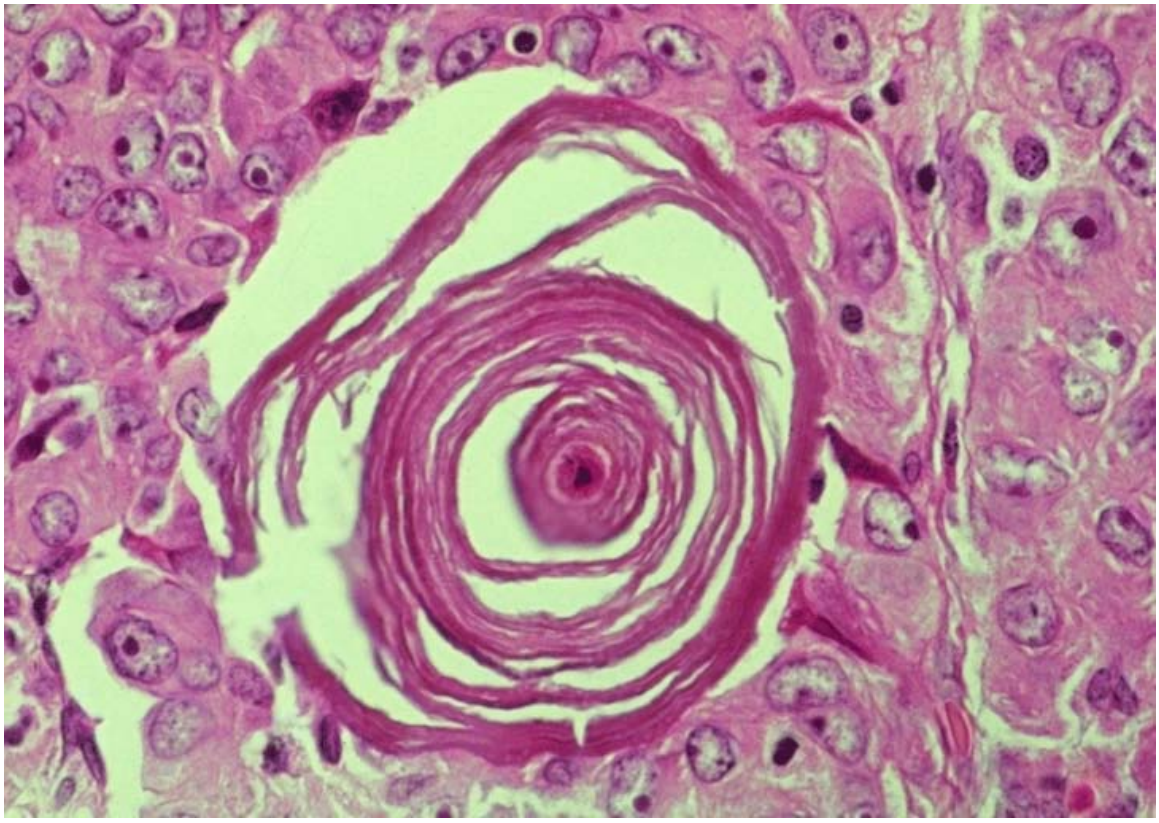
Papillary Thyroid Cancer

Papillary thyroid cancer



Papillary thyroid carcinoma.

ICD-10	C73.
ICD-9	193
OMIM	603744
eMedicine	med/2464
MeSH	D013964



A psammoma body in papillary carcinoma of the thyroid

Papillary thyroid cancer or **papillary thyroid carcinoma** is the most common type of thyroid cancer, representing 75% to 85% of all thyroid cancer cases. It occurs more frequently in women and presents in the 30-40 year age group. It is also the predominant cancer type in children with thyroid cancer, and in patients with thyroid cancer who have had previous radiation to the head and neck.

Markers

Thyroglobulin can be used as a tumor marker for well-differentiated papillary thyroid cancer. HBME-1 staining may be useful for differentiating papillary carcinomas from follicular carcinomas; in papillary lesions it tends to be positive.

Pathology

- Characteristic Orphan Annie eye nuclear inclusions (nuclei with uniform staining, which appear empty) and psammoma bodies on light microscopy. The former is useful in identifying the follicular variant of papillary thyroid carcinomas.

- Lymphatic spread is more common than hematogenous spread
- Multifocality is common

- The so-called Lateral Aberrant Thyroid is actually a lymph node metastasis from papillary thyroid carcinoma.
- Papillary microcarcinoma is a subset of papillary thyroid cancer defined as measuring less than or equal to 1 cm. The highest incidence of papillary thyroid microcarcinoma in autopsy series was reported by Harach et al. in 1985, who found 36 of 101 consecutive autopsies were found to have an incidental microcarcinoma. Michael Pakdaman et al. report the highest incidence in a retrospective surgical series at 49.9% of 860 cases. Management strategies for incidental papillary microcarcinoma on ultrasound (and confirmed on FNAB) range from total thyroidectomy with radioactive iodine ablation to observation alone. Harach et al. suggest using the term "occult papillary tumor" to avoid giving patients distress over having cancer.It was Woolner et al. who first arbitrarily coined the term "occult papillary carcinoma" in 1960, to describe papillary carcinomas ≤ 1.5 cm in diameter.

Although papillary carcinoma has a propensity to invade lymphatics, it is less likely to invade blood vessels. This kind of tumors are most commonly unencapsulated, and they have a high tendency to metastasize locally to lymph nodes, which may produce cystic structures near the thyroid that are difficult to diagnose because of the paucity of malignant tissue. Furthermore, papillary tumors may metastasize to the lungs and produce a few nodules or the lung fields may exhibit a snowflake appearance throughout.

Other characteristics of the papillary carcinoma is that E.M. shows increased mitochondria, increased RER, as well as increased apical microvilli. Moreover, papillary carcinomas have an indolent growth, and 40% of cases spread out of the capsule.

Associated mutations

Mutations associated with papillary thyroid cancer are mainly two forms of chromosomal translocation and one form of point mutation. These alterations lead to activation of a common carcinogenic pathway - the MAPK/ERK pathway.

Chromosomal translocations involving the RET proto-oncogene (encoding a tyrosine kinase receptor that plays essential roles in the development of neuroendocrine cells) located on chromosome 10q11 occur in approximately a fifth of papillary thyroid cancers. The fusion oncoproteins generated are termed RET/PTC proteins (ret/papillary thyroid carcinoma), and constitutively activate RET and the downstream MAPK/ERK pathway. The frequency of ret/PTC translocations is significantly higher in papillary cancers arising in children and after radiation exposure. The gene NTRK1 (encoding the TrkA receptor), located on chromosome 1q, is similarly translocated in approximately 5% to 10% of papillary thyroid cancers.

Approximately a third to a half of papillary thyroid carcinomas harbor point mutations in the BRAF oncogene, also activating the MAPK/ERK pathway. In those cases the BRAF mutations found were V600E mutation. After performing a multivariate analysis, it was found that the absence of tumor capsule was the only parameter associated (P=0.0005)

with BRAF V600E mutation. According to recent studies, papillary cancers carrying the common V600E mutation tend to have a more aggressive long term course. BRAF mutations are frequent in papillary carcinoma and in undifferentiated cancers that have developed from papillary tumors.

Diagnosis

Papillary thyroid carcinoma is usually discovered on routine examination as an asymptomatic thyroid nodule that appears as a neck mass. In some instances, the mass may have produced local symptoms. This mass is normally referred to a fine needle aspiration biopsy (FNA) for investigation. FNA accuracy is very high and it is a process widely used in these cases. Other investigation methods include ultrasound imaging and nuclear scan. The ultrasound is a useful test to distinguish solid from cystic lesions and to identify calcifications. The thyroid ultrasound is also very effective to discover microcarcinomas, which refer to very small carcinomas (<1 cm). A significant number of such carcinomas are malignant.

Papillary thyroid carcinomas are also discovered when a hard nodule is found in multinodular goiter, when enlarged cervical lymph nodes are detected, or when there are unidentified metastatic lesions elsewhere in the body. Expanding lesions found in the thyroid gland, especially if they are painful, should be examined as they may indicate the presence of papillary thyroid carcinoma. Other clinical signs that could indicate papillary thyroid are: fixation to the trachea, stony hardness, damage to recurrent laryngeal or cervical sympathetic nerves. Seventy five percent of the population will have these thyroid nodules, and the majority will always be benign.

Chest x rays are not commonly performed. In cases of metastasis, some other tests are run to obtain sufficient information before a surgery. Such tests include the ultrasound and MRI of the neck as well as the CAT scanning. Other options that have shown good results in identifying tumors or related outcomes are the use of Thallium201 chloride, which helps identify metastatic tumor; Gallium, which is helpful to visualize lymphomas; I-meatiodobenzylguanidine, which has proven useful in imaging MTC; Tc-MIBI, which has been effective in detecting deposits of metastatic thyroid cancer; PET scans, which are also helpful for the imaging of metastatic disease. Chia *et al.* report that TSHR mRNA measured with FNA enhances the preoperative detection of cancer in patients with thyroid nodules, reducing unnecessary surgeries, and immediate postoperative levels can predict residual/metastatic disease.

Prognosis

Depending on source, the overall 5-year survival rate for papillary thyroid cancer is 96% or 97%, with a 10-year survival rate of 93%.

For a more specific prognosis for individual cases, there are at minimum 13 known scoring systems for prognosis; among the more often used are:

- AGES - Age, Grade, Extent of disease, Size
- AMES - Age, Metastasis, Extent of disease, Size
- MACIS - Metastasis, Age at presentation, Completeness of surgical resection, Invasion (extrathyroidal), Size (this is a modification of the AGES system). It is probably the most reliable staging method available.
- TNM staging - Tumor, node, metastasis. Remarkable about the TNM staging for (differentiated) thyroid carcinoma is that the scoring is different according to age.

MAICS

The MAICS system of estimating the prognosis of papillary thyroid cancer was developed by the Mayo Clinic, and was based on careful evaluation of a large group of patients. It is probably the most reliable staging method available.

It assigns scores to the main factors involved, and uses the sum of this score to calculate the prognosis:

Factors		Score
Distant **M**etastasis: spread of the cancer to areas outside the neck	Yes	3
	No	0
Age at the time the tumor was discovered	Less than 39 years	3.1
	Over 40 years	0.08 x age
Invasion into surrounding areas of the neck as seen by the naked eye	Yes	1
	No	0
Completeness of surgical resection (or removal) of the tumor	Incomplete	1
	Complete	0
Size of the tumor		0.3 x size in cm

Sum of MAICS Score	20 yr Survival
< 6.0	99%
6.0 - 6.99	89%
7.0 - 7.99	56%
> 8.0	24%

Most patients fall into the low risk category (MAICS score less than 6.0) and are cured of the cancer at the time of surgery.

Overall stage

By overall cancer staging into stages I to IV, papillary thyroid cancer has a 5-year survival rate of 100% for stages I and II, 93% for stage III and 51% for stage IV.

Treatment

Surgical treatment:

- Minimal disease (diameter up to 1.0 centimeters) - hemithyroidectomy (or unilateral lobectomy) and isthmectomy may be sufficient. There is some discussion whether this is still preferable over total thyroidectomy for this group of patients.
- Gross disease (diameter over 1.0 centimeters) - total thyroidectomy, and central compartment lymph node removal is the therapy of choice. Additional lateral neck nodes can be removed at the same time if an ultrasound guided FNA and thyrobulin TG cancer washing was positive on the pre-operative neck node ultrasound evaluation.

Arguments for total thyroidectomy are:

- Reduced risk of recurrence, if central compartment nodes are removed at the original surgery.
- Papillary carcinoma is a multifocal disease (hemithyroidectomy may leave disease in the other lobe)
- Ease of monitoring with thyroglobulin (sensitivity for picking up recurrence is increased in presence of total thyroidectomy, and ablation of remnant normal thyroid by low dose radioiodine 131 after following a low iodine diet (LID).
- Ease of detection of metastatic disease by thyroid and neck node ultrasound.

Thyroid total body scans are less reliable at finding recurrence than TG and ultrasound.

Papillary tumors tend to be more aggressive in patients over age 45. In such cases it might be required to perform a more extensive resection including portions of the trachea. Also, the sternocleidomastoid muscle, jugular vein, and accessory nerve are to be removed if such procedure allows apparently complete tumor resection. If a significant amount of residual tumor is left in the neck, external radiotherapy has been indicated and has proven useful especially in those cases when residual tumor does not take up radioiodine.

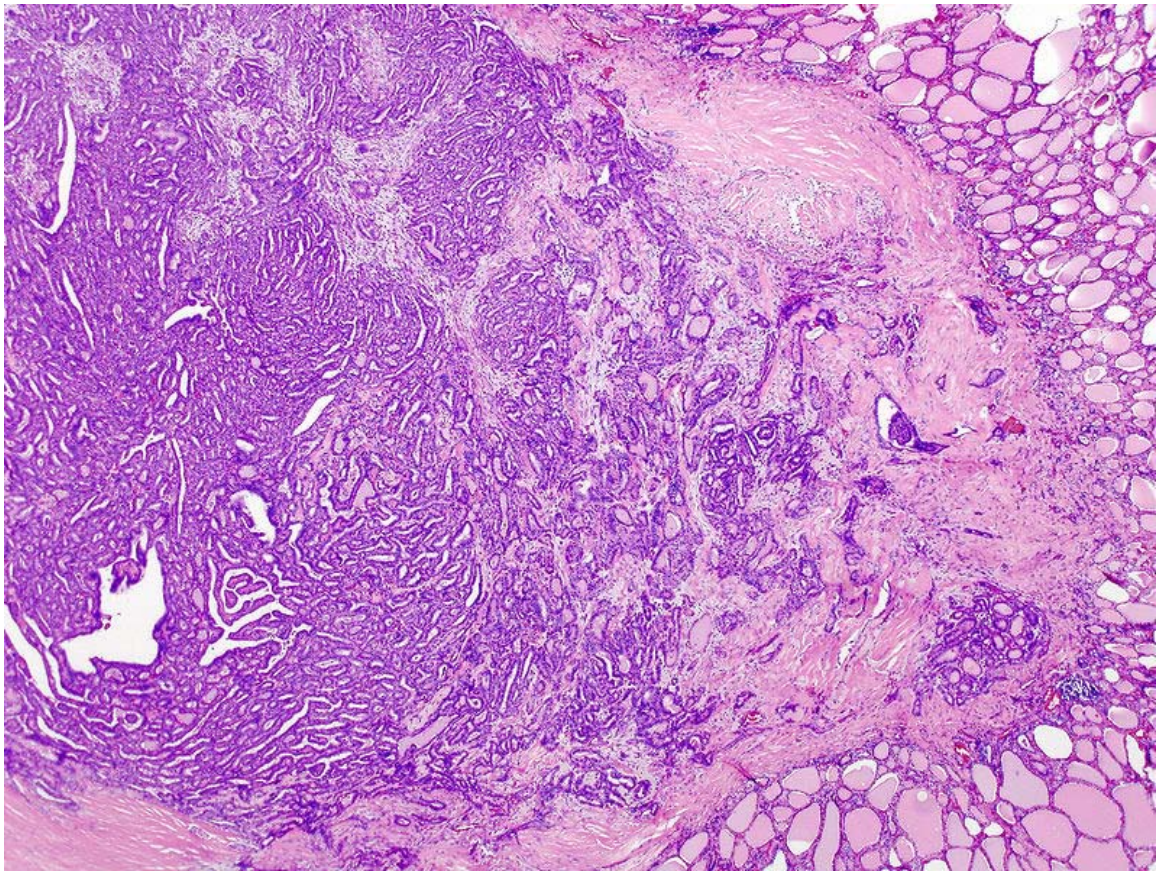
After surgical thyroid removal, the patient waits around 4–6 weeks to then have radioiodine therapy. This therapy is intended to both detect and destroy any metastasis and residual tissue in the thyroid. The treatment may be repeated 6–12 months after initial treatment of metastatic disease where disease recurs or has not fully responded.

Patients are administered hormone replacement levothyroxine for life after surgery, especially after total thyroidectomy. Chemotherapy with cisplatin or doxorubicin has proven limited efficacy, however, it could be helpful for patients with bone metastases to improve their quality of life. Patients are also prescribed levothyroxine and radioiodine after surgery. Levothyroxine influences growth and maturation of tissues and it is involved in normal growth, metabolism, and development. In case of metastases, patients

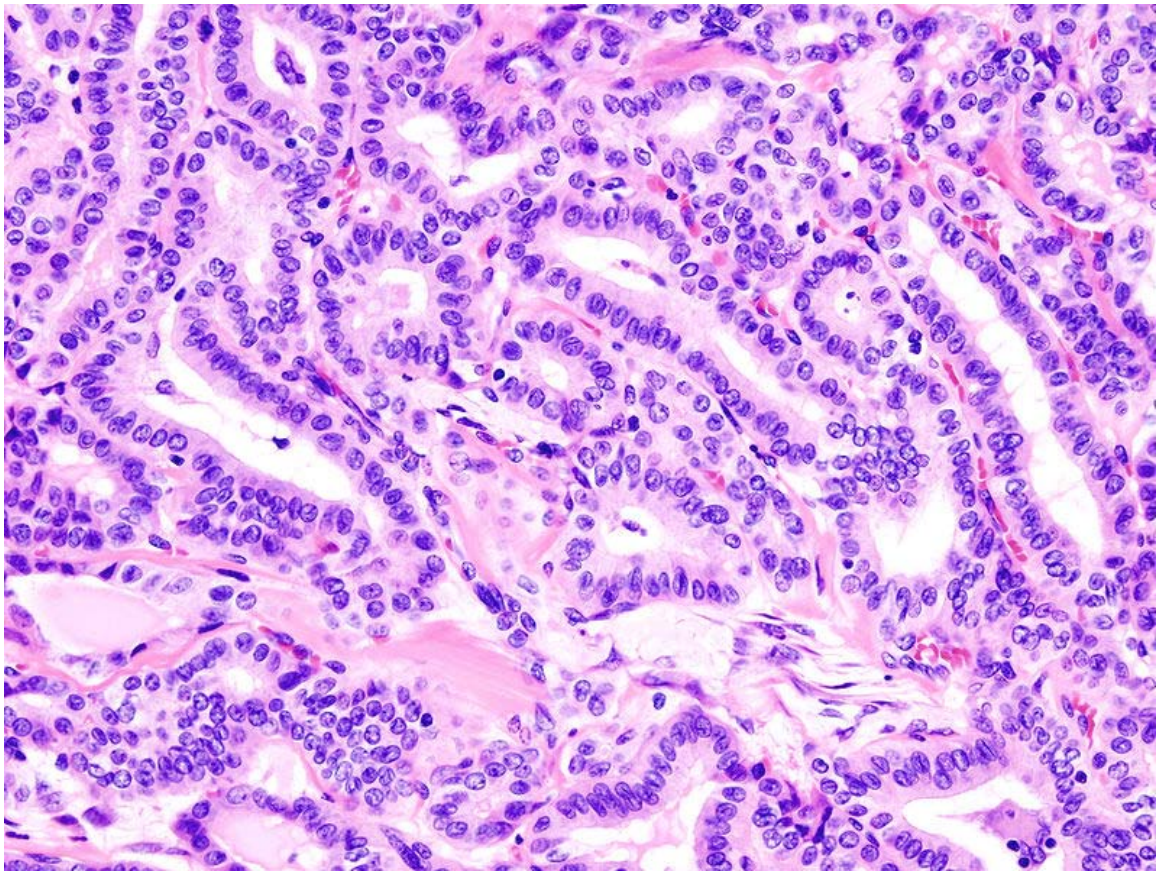
are prescribed antineoplastic agents which inhibit cell growth and proliferation and help in palliating symptoms in progressive disease.

After successful treatment, 35% of the patients may experience recurrence within a 40-year span. Also, patients may experience a high incidence of nodule metastasis, with 35% cases of cervical node metastases. Approximately 20% patients will develop multiple tumors within the thyroid gland.

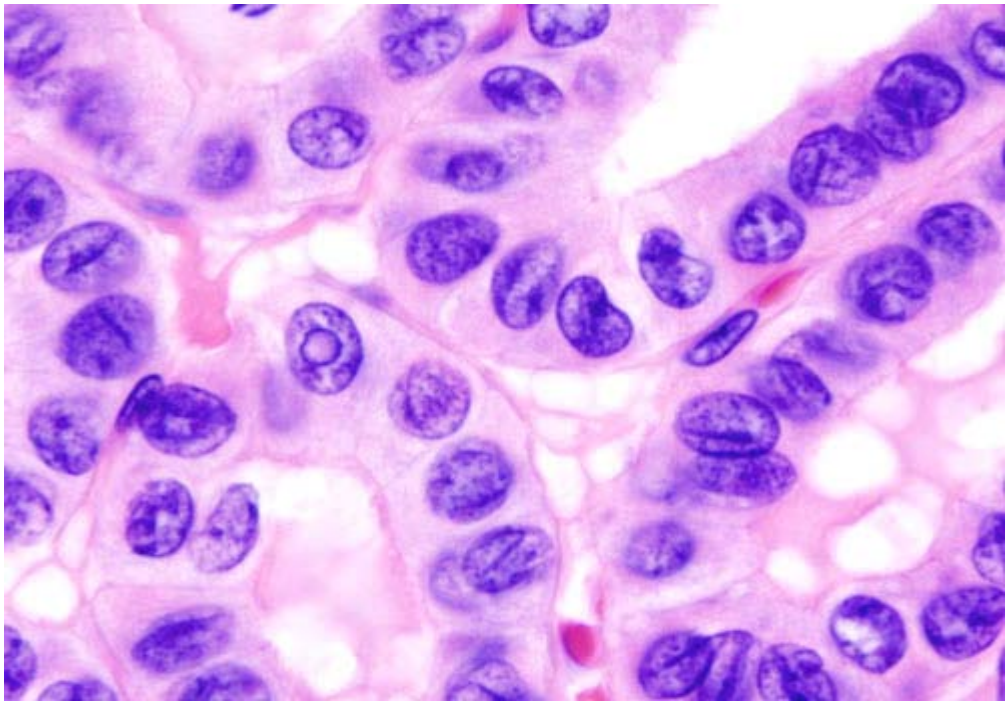
Additional images



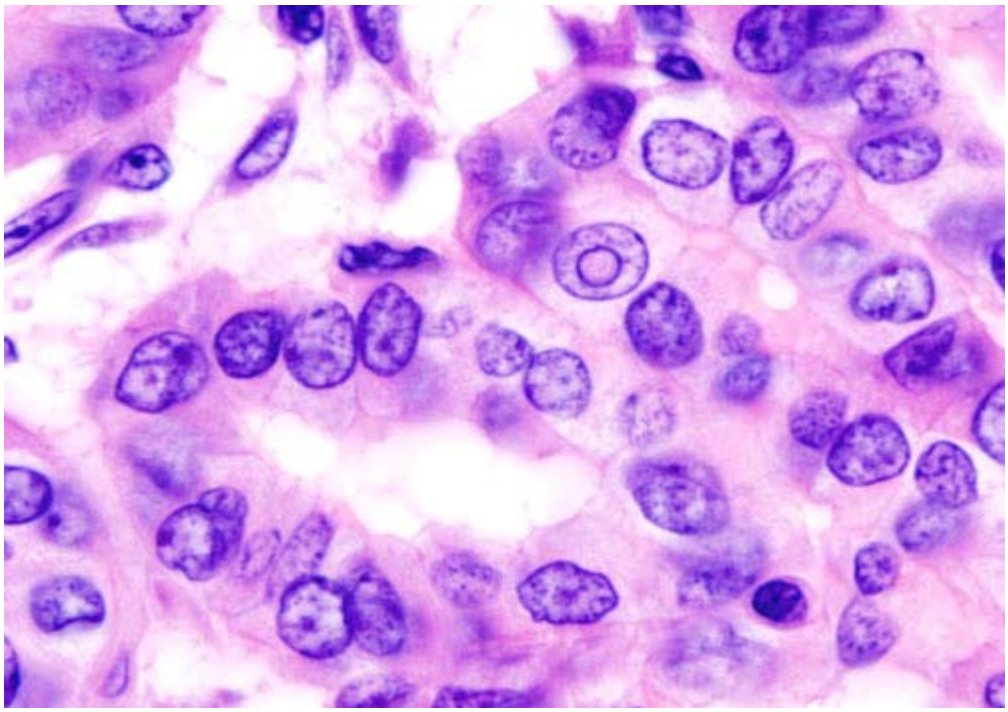
Micrograph of papillary thyroid carcinoma demonstrating prominent papillae with fibrovascular cores. H&E stain.



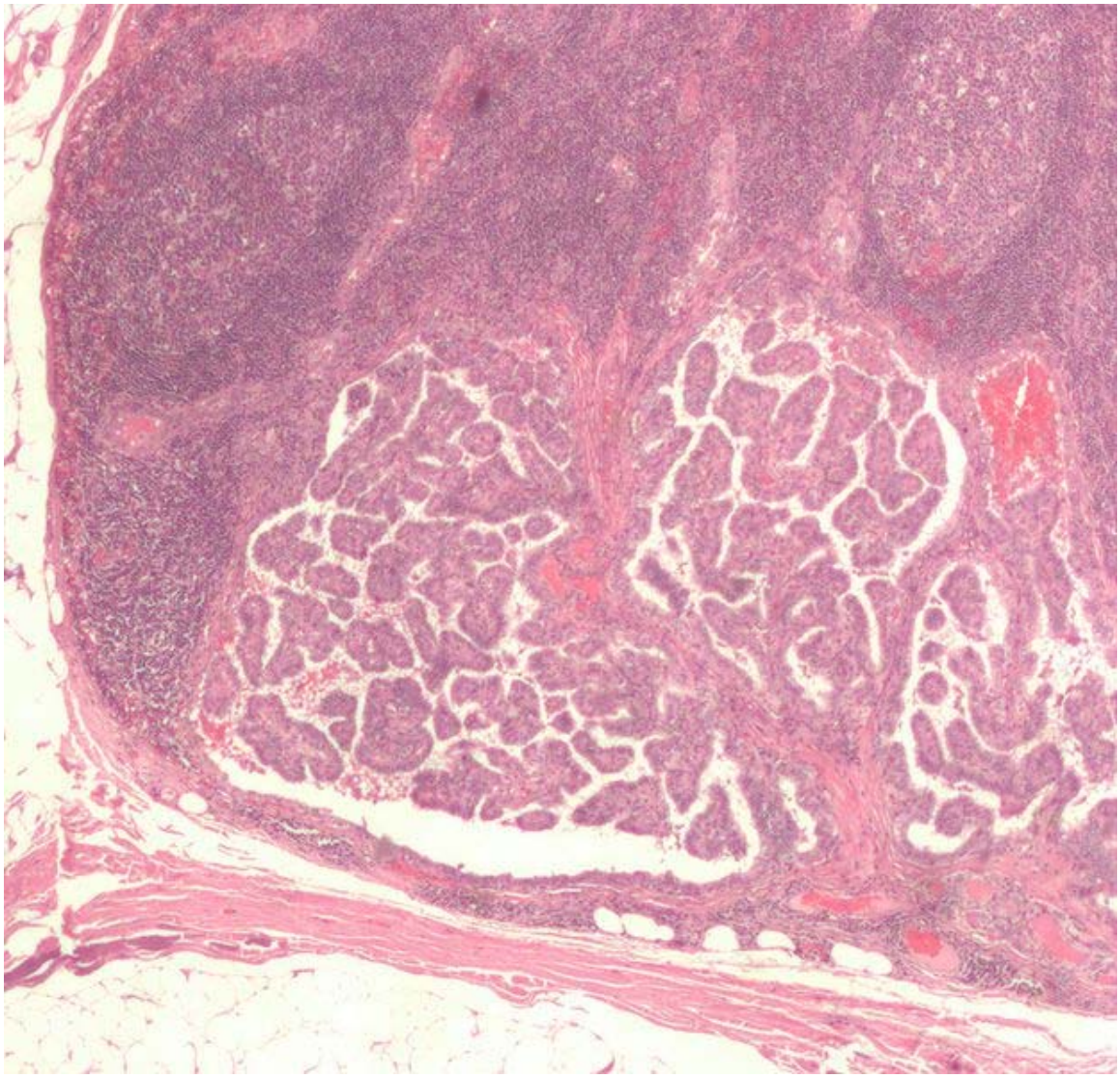
Micrograph showing that the papillae in papillary thyroid carcinoma are composed of cuboidal cells. H&E stain.



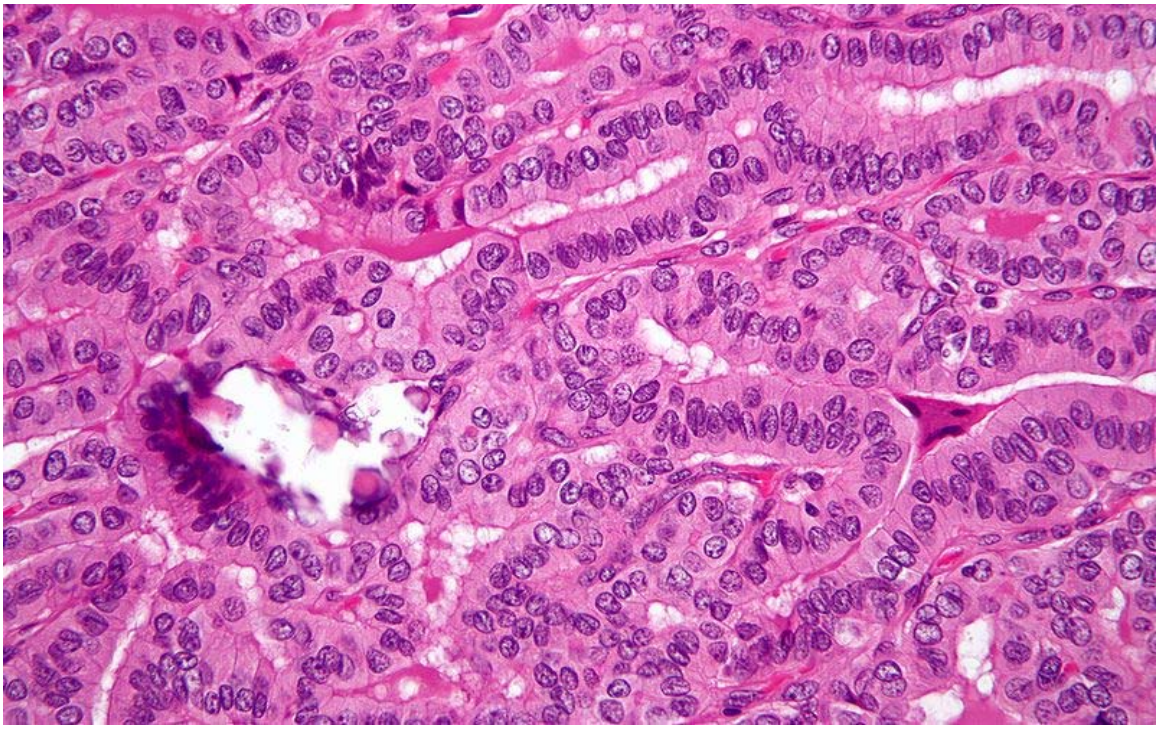
Micrograph (high power view) showing nuclear changes in papillary thyroid carcinoma (PTC), which include groove formation, optical clearing, eosinophilic inclusions and overlapping of nuclei. H&E stain.



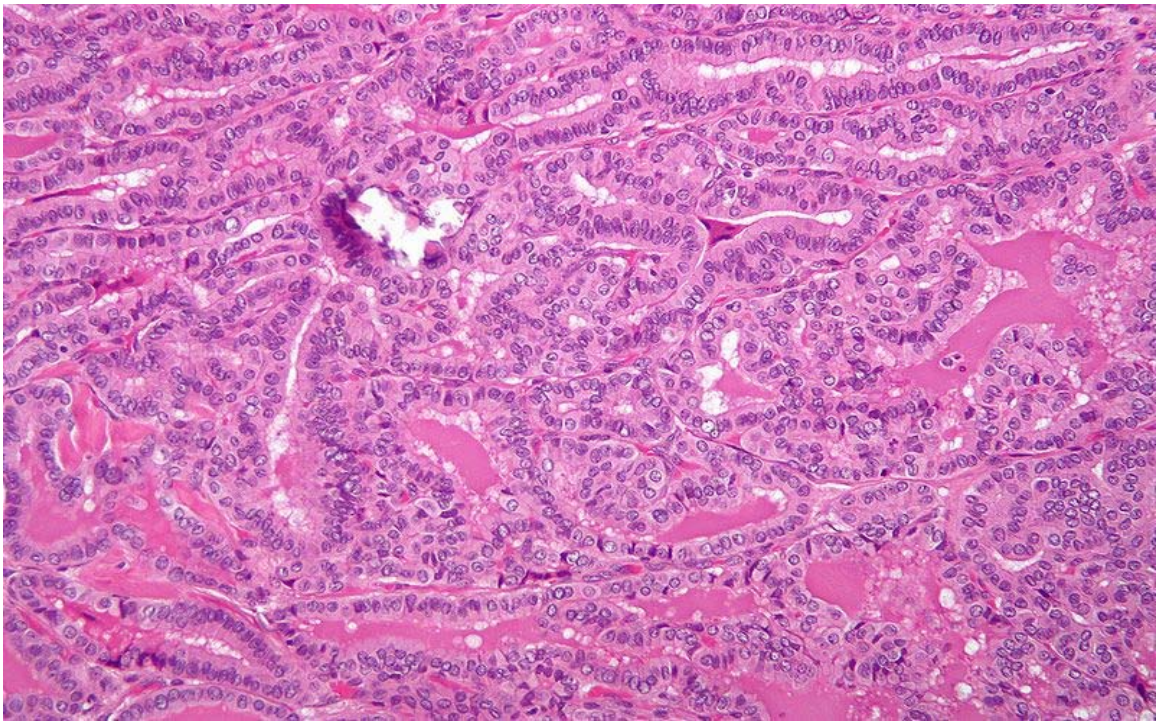
Micrograph (high power view) of PTC demonstrating nuclear clearing and overlapping nuclei. H&E stain.



Micrograph of metastatic papillary thyroid carcinoma to a lymph node. H&E stain.



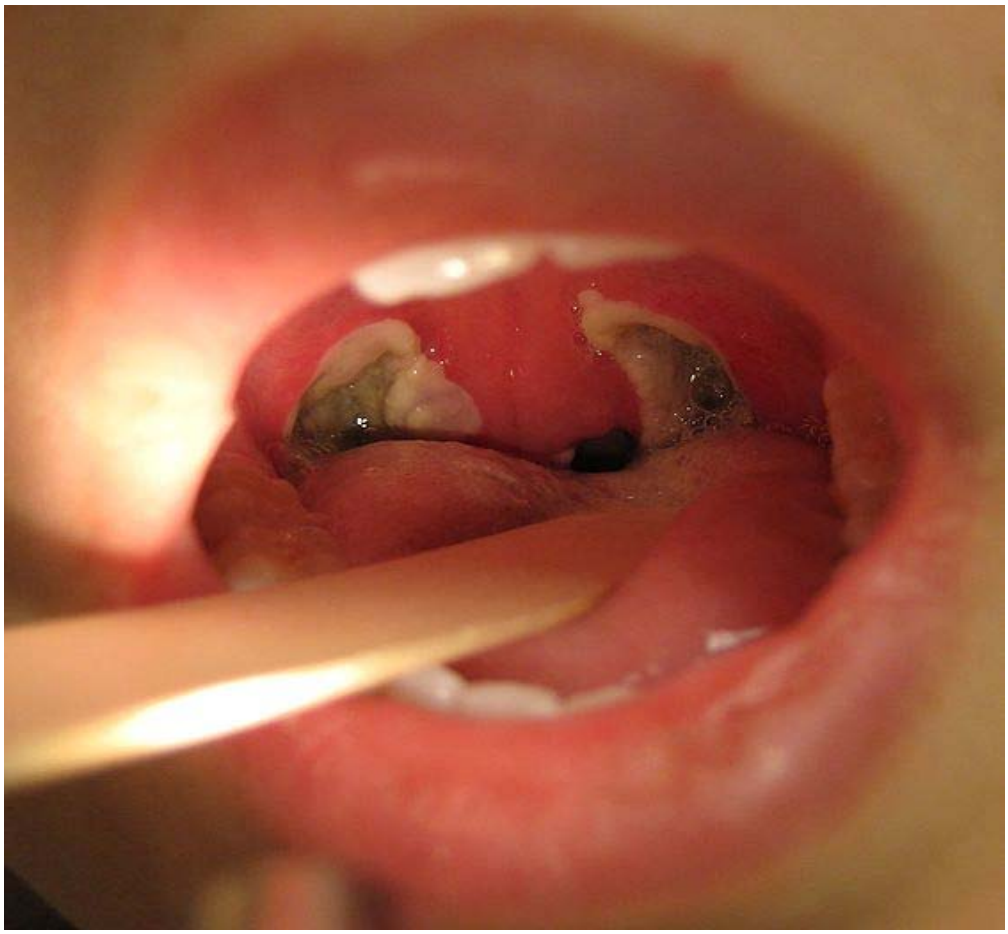
Micrograph of **papillary thyroid carcinoma, tall cell variant** - high magnification. H&E stain.



Micrograph of **papillary thyroid carcinoma, tall cell variant** - intermediate magnification. H&E stain.

Chapter 24

Tonsillectomy



Typical appearance of the back of the throat three days post tonsillectomy

A **tonsillectomy** is a 3,000-year-old surgical procedure in which the tonsils are removed from either side of the throat. The procedure is performed in response to cases of repeated occurrence of acute tonsillitis or adenoiditis, obstructive sleep apnea, nasal airway obstruction, snoring, or peritonsillar abscess. Sometimes the adenoids are removed at the same time, a procedure called adenoidectomy. Although tonsillectomy is being performed less frequently than in the 1950s, it remains one of the most common surgical procedures in children in the United States.

Indications

Tonsillectomy may be indicated when the patient:

- Experiences recurrent infections of acute tonsillitis. The number requiring tonsillectomy varies with the severity of the episodes. One case, even severe, is generally not enough for most surgeons to decide tonsillectomy is necessary. Paradise in 1983 defined recurrent tonsillitis warranting surgery by the attack frequency standard as *"Seven or more in a year, five or more per year for two years, or three or more per year for three years."* However according to the current guidelines (2000) of the American Academy of Otolaryngology & Head and Neck Surgery (AAO-HNS), tonsillectomy is indicated if a patient contracts *"Three or more attacks of sore throat per year despite adequate medical therapy."*
- Has chronic tonsillitis, consisting of persistent, moderate-to-severe throat pain.
- Has multiple bouts of peritonsillar abscess.
- Has sleep apnea (stopping or obstructing breathing at night due to enlarged tonsils or adenoids)
- Has difficulty eating or swallowing due to enlarged tonsils (very unusual reason for tonsillectomy)
- Produces tonsilloliths (tonsil stones) in the back of their mouth.
- Has abnormally large tonsils with crypts (Craters or impacts in the tonsils)

Controversy over indications

The American Academy of Otolaryngology & Head and Neck Surgery (AAO-HNS) stated that "In many cases, tonsillectomy may be a more effective treatment, and less costly, than prolonged or repeated treatments for an infected throat...For the past several years, the Academy has been developing clinical guidelines based on evidence and outcomes research, including ‘Quality of Life after Tonsillectomy,’ a January 2008 supplement to the journal Otolaryngology—Head and Neck Surgery."

Morbidity and mortality

The morbidity rate associated with tonsillectomy is 2% to 4% due to post-operative bleeding; the mortality rate is 1 in 15,000, due to bleeding, airway obstruction, or anesthesia.

Effectiveness

The effectiveness of the tonsillectomy has been questioned in a 2009 systematic review of 7765 papers, published in the journal Otolaryngology—Head and Neck Surgery. The review found that it was most likely not effective all the time, but rather was modestly effective, and that "not a single paper reported that tonsillectomy is invariably effective in eliminating sore throats". Another systematic review of cases involving children found that there was only a short-term benefit - "A child who meets these strict criteria will probably suffer from 6 throat infections in the next two years. A child who has surgery

now will probably suffer from 3 throat infections. In two years there will probably be no difference."

Post-operative care

A sore throat will persist for around two weeks after the operation. Most patients do not feel like swallowing anything during the first few days after surgery. Patients should try to get as much fluid down as possible, as it will help speed recovery. Very cold drinks will help bring down swelling. Ice cream, frozen yogurt and other dairy products are not recommended because they leave a film in the mouth that is difficult to swallow. Sorbet and popsicles, on the other hand, are recommended. Additionally, Slushies are particularly helpful for sore throats, especially when sugar-free.

Pain following the procedure is significant and may include a hospital stay. Recovery can take from 10 up to 20 days, during which narcotic analgesics are typically prescribed. Patients are encouraged to maintain diet of liquid and very soft foods for several days following surgery. Rough textured, acidic or spicy foods may be irritating and should be avoided. Proper hydration is very important during this time, since dehydration can increase throat pain, leading to a vicious circle of poor fluid intake.

At some point, most commonly 7–11 days after the surgery (but occasionally as long as two weeks (14 days) after), bleeding can occur when scabs begin sloughing off from the surgical sites. The overall risk of bleeding is approximately 1%–2% higher in adults. Approximately 3% of adult patients develop significant bleeding at this time. The bleeding might naturally stop quickly or else mild intervention (e.g., gargling cold water) could be needed (but ask the doctor before gargling because it might bruise the area of the skin that has been cauterized). Otherwise, a surgeon must repair the bleeding immediately by cauterization, which presents all the risks associated with emergency surgery (primarily the administration of anesthesia particularly on a patient whose stomach may not be empty).

Generally speaking, tonsils will be removed if a patient needs antibiotics to be prescribed six times a year for tonsilitis, and the general practitioner's recommendation is based on how the quality of life will be improved after the operation. Tonsillectomies can be performed while the patient is actually suffering from tonsillitis, however this increases the risk of bleeding.

Common causes, demographics

Infections requiring tonsillectomy are often a result of *Streptococcus ("strep throat"),* particularly *Streptococcus pyogenes*; some may be due to other bacteria, such as *Streptococcus viridans*, *Staphylococcus aureus*, and *Haemophilus influenzae*. However, the etiology of the condition is largely irrelevant in determining whether tonsillectomy is required.

Most tonsillectomies are performed on children, although many are also performed on teenagers and adults; in the United States, it is the most common major surgical procedure performed on children. The number of tonsillectomies in the United States has dropped significantly from over a million cases per year in the 1950s to approximately 600,000 in the late 1990s. This has been due in part to more stringent guidelines for tonsillectomy and adenoidectomy. Still, debate about the usefulness of tonsillectomies continues. Enlarged tonsils are removed more often among adults and children for sleep apnea (airway obstruction while sleeping), snoring, and upper airway obstruction. Children who have sleep apnea can do poorly in school, are tired during the day, may be bedwetters beyond what is normal, and have some links to ADHD.

Tonsillectomy in adults is more painful than in children, although each patient will have a different experience. Various procedures are available to remove tonsils, each with different advantages and disadvantages. Children and teenagers sometimes exhibit a noticeable change in voice after the operation.

Surgical procedure

The generally accepted procedure for tonsillectomy involves separating and removing the tonsils from the *subcapsular plane* – a fascia of tissue that surrounds the tonsils. Removal is typically achieved using a scalpel and blunt dissection or with electrocautery, although harmonic scalpels or lasers have also been used. Bleeding is stopped with electrocautery, ligation of sutures, and the topical use of thrombin, a protein that induces blood clotting.

The procedure is carried out with the patient lying flat on their backs, with the shoulders elevated on a small pillow so that the neck is hyperextended – the so-called 'Rose' position. A mouth gag is used to prop the mouth open; if an adenoidectomy is also being performed, the adenoids are first removed with a curette; the nasopharynx is then packed with sterile gauze. A tonsil is removed by holding it by the upper part, pulling it slightly medially, and making a cut over the anterior faucial pillar. After the tonsil is removed from its position, a snare can be used to make a small cut on the lower portion prior to removal of the tonsil. The use of electrocautery minimizes the blood loss.

Other methods

The scalpel is the preferred surgical instrument of many ear, nose, and throat specialists. However, there are other procedures available – the choice may be dictated by the extent of the procedure (complete tonsil removal versus partial tonsillectomy) and other considerations such as pain and post-operative bleeding. A quick review of each procedure follows:

- **Dissection and snare method**: Removal of the tonsils by use of a forceps and scissors with a wire loop called a 'snare' was formerly the most common method practiced by otolaryngologists, but has been largely replaced in favor of other techniques. The procedure requires the patient to undergo general anesthesia; the

tonsils are completely removed and the skin is cauterized. The patient will leave with minimal post-operative bleeding.

- **Electrocautery**: Electrocautery uses electrical energy to separate the tonsillar tissue and assists in reducing blood loss through cauterization. Research has shown that the heat of electrocautery (400°C) may result in thermal injury to surrounding tissue. This may result in more discomfort during the postoperative period.
- **Harmonic scalpel**: This medical device uses ultrasonic energy to vibrate its blade at 55kHz. Invisible to the naked eye, the vibration transfers energy to the tissue, providing simultaneous cutting and coagulation. The temperature of the surrounding tissue reaches 80°C. Proponents of this procedure assert that the end result is precise cutting with minimal thermal damage.
- **Radiofrequency ablation**: Monopolar radiofrequency thermal ablation transfers radiofrequency energy to the tonsil tissue through probes inserted in the tonsil. The procedure can be performed in an office (outpatient) setting under light sedation or local anesthesia. After the treatment is performed, scarring occurs within the tonsil causing it to decrease in size over a period of several weeks. The treatment can be performed several times. The advantages of this technique are minimal discomfort, ease of operations, and immediate return to work or school. Tonsillar tissue remains after the procedure but is less prominent. This procedure is recommended for treating enlarged tonsils and not chronic or recurrent tonsillitis.
- **Thermal Welding**: A new technology which uses pure thermal energy to seal and divide the tissue. The absence of thermal spread means that the temperature of surrounding tissue is only 2-3 °C higher than normal body temperature. Clinical papers show patients with minimal post-operative pain (no requirement for narcotic pain-killers), zero edema (swelling) plus almost no incidence of bleeding. Hospitals in the US are advertising this procedure as "Painless Tonsillectomy". Also known as Tissue Welding.
- **Carbon dioxide laser**: Laser tonsil ablation (LTA) finds the otolaryngologist employing a hand-held CO2 or KTP laser to vaporize and remove tonsil tissue. This technique reduces tonsil volume and eliminates recesses in the tonsils that collect chronic and recurrent infections. This procedure is recommended for chronic recurrent tonsillitis, chronic sore throats, severe halitosis, or airway obstruction caused by enlarged tonsils. The LTA is performed in 15 to 20 minutes in an office setting under local anesthesia. The patient leaves the office with minimal discomfort and returns to school or work the next day. Post-tonsillectomy bleeding may occur in 2-5% of patients. Previous research studies state that laser technology provides significantly less pain during the post-operative recovery of children, resulting in less sleep disturbance, decreased morbidity, and less need for medications. On the other hand, some believe that children are adverse to outpatient procedures without sedation.

- **Microdebrider**: The microdebrider is a powered rotary shaving device with continuous suction often used during sinus surgery. It is made up of a cannula or tube, connected to a hand piece, which in turn is connected to a motor with foot

control and a suction device. The endoscopic microdebrider is used in performing a partial tonsillectomy, by partially shaving the tonsils. This procedure entails eliminating the obstructive portion of the tonsil while preserving the tonsillar capsule. A natural biologic dressing is left in place over the pharyngeal muscles, preventing injury, inflammation, and infection. The procedure results in less post-operative pain, a more rapid recovery, and perhaps fewer delayed complications. However, the partial tonsillectomy is suggested for enlarged tonsils – not those that incur repeated infections.

- **Bipolar Radiofrequency Ablation**: This procedure produces an ionized saline layer that disrupts molecular bonds without using heat. As the energy is transferred to the tissue, ionic dissociation occurs. This mechanism can be used to remove all or only part of the tonsil. It is done under general anesthesia in the operating room and can be used for enlarged tonsils and chronic or recurrent infections. This causes removal of tissue with a thermal effect of 45-85 °C. It has been claimed that this technique results in less pain, faster healing, and less post operative care. However, review of 21 studies gives conflicting results about levels of pain, and its comparative safety has yet to be confirmed. This technique has been criticized for a higher than expected rate of bleeding presumably due to the low temperature which may be insufficient to seal the divided blood vessels.

History

The tonsillectomy has been practiced for 3,000 years, with varying popularity over the centuries. The procedure is first mentioned in "Hindu medicine" about 1000 BC; roughly a millennium later the Roman aristocrat Celcus (25 AD – 50 AD) described a procedure whereby using the finger (or a blunt hook if necessary), the tonsil was separated from the neighboring tissue prior to being cut out. Galen (121 – 200 AD) was the first to advocate the use of the surgical instrument known as the snare, a practice that was to become common until Aetius (490 AD) recommended partial removal of the tonsil, writing "Those who extirpate the entire tonsil remove, at the same time, structures that are perfectly healthy, and, in this way, give rise to serious Hæmorrhage". In the 7th century Paulus Aegineta (625 – 690) described a detailed procedure for tonsillectomy, including dealing with the inevitable post-operative bleeding. 1,200 years pass before the procedure is described again with such precision and detail.

The Middle Ages saw tonsillectomy fall into disfavor; Ambroise Pare (1509) wrote it to be "*a bad operation*" and suggested a procedure that involved gradual strangulation with a ligature. This method was not popular with the patients, however, due to the immense pain it caused, and the infection that usually followed. Scottish physician Peter Lowe in 1600 summarized the three methods in use at the time, including the *snare*, the *ligature*, and the *excision*. At the time, the function of the tonsils was thought to be to absorb secretions from the nose; it was assumed that removal of large amounts of tonsillar tissue would interfere with the ability to remove these secretions, causing them to accumulate in the larynx, resulting in hoarseness. For this reasons physicians like Dionis (1672) and Lorenz Heister censured the procedure.

Tonsil guillotine

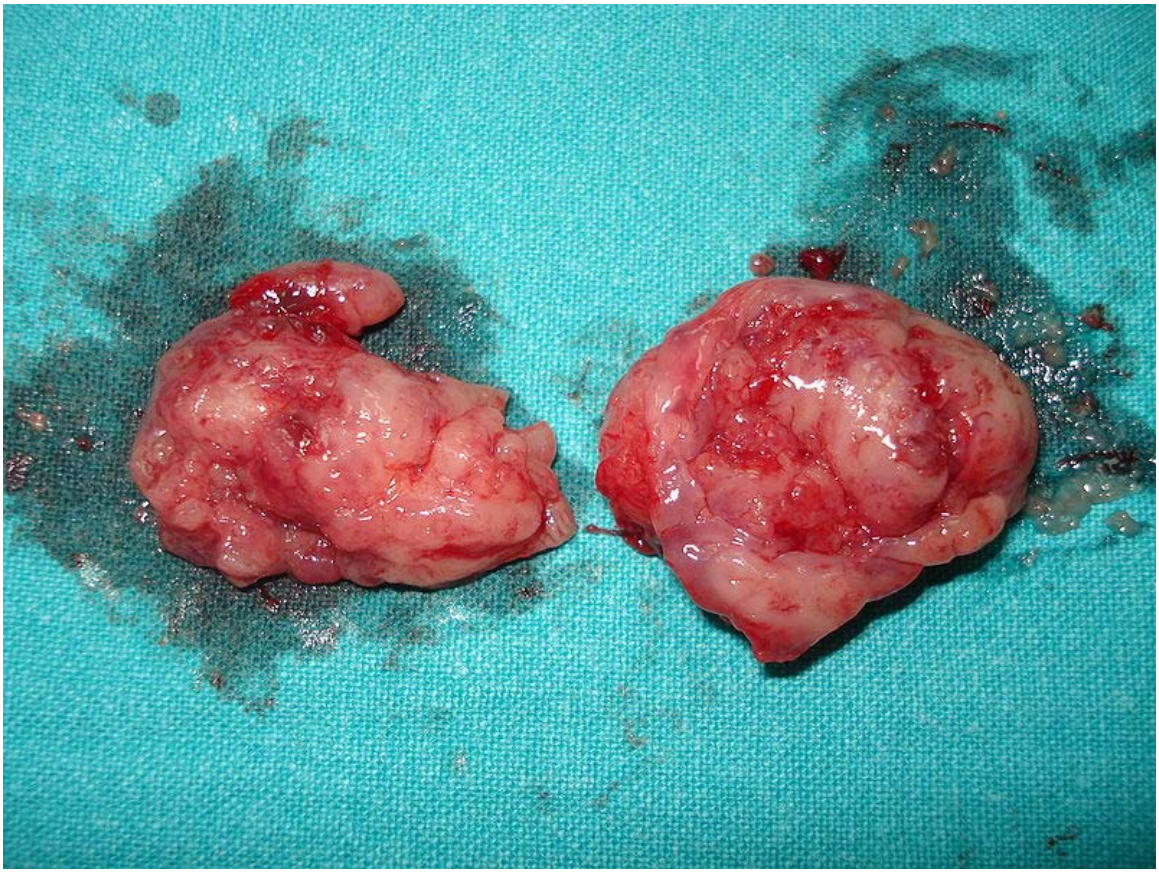
In 1828, physician Philip Syng Physick modified an existing instrument originally designed by Benjamin Bell for removing the uvula; the instrument, known as the tonsil guillotine (and later as a tonsillotome), became the standard instrument for tonsil removal for over 80 years. By 1897, it became more common to perform complete rather than partial removal of the tonsil after American physician Ballenger noted that partial removal failed to completely alleviate symptoms in a majority of cases. His results using a technique involving removal of the tonsil with a scalpel and forceps were much better than partial removal; tonsillectomy using the guillotine fell out of favor in America.

Tonsillectomy and weight gain in children

A recent study states that tonsillectomy increases the risk of being overweight or obese in the years following surgery by as much as 61% in cases where tonsillectomy without adenoidectomy is performed, and up to 136% in cases of where tonsillectomy with adenoidectomy was performed.

Additional Image

Throat with tonsillitis



Two removed tonsils

Throat 1 day after a tonsillectomy

Throat some days after a tonsillectomy