

Ministry of Defence

Synopsis of Causation

Eye Infections

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Disclaimer

This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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1. Definition

- 1.1. Eye infections may be classified according to the infectious organism or the structure within the eye that is affected. A wide variety of bacteria, viruses, fungi, and parasites can be responsible. The different structures that can become infected are determined by the anatomy of the eye, as illustrated in Fig. 1. The frequency of these various conditions ranges from the common to the rare, whilst severity ranges from generally self-limiting conditions to those that threaten sight. **The synopsis aims to provide an overview of this range of conditions with a predominant focus on the aetiology and prognosis of serious eye infections that have the potential to engender an adverse visual outcome.**

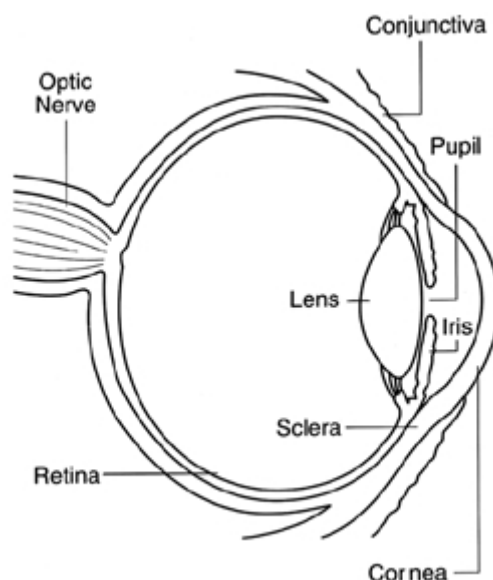


Fig. 1: Anatomy of the eye

Courtesy: National Eye Institute, National Institutes of Health

- 1.2. Based on a structural classification, the following eye infections may be recognised:¹
- 1.2.1. **Conjunctivitis** is a very common condition, and overall may account for around 60% of eye-related consultations in primary practice in the UK.² It most frequently arises as a result of a viral or bacterial infection of the [mucous membrane](#) of the eye (conjunctiva). However, noninfectious cases of conjunctivitis are also common, arising as a result of a seasonal or perennial allergic response. The condition may be acute or chronic, although cases due to either viral or bacterial infection are frequently self-limiting. However, serious consequences can develop in relation to infections due to certain organisms, particularly *Chlamydia trachomatis* and *Neisseria gonorrhoea*.
- 1.2.2. **Keratitis** denotes an inflammation of the cornea that may be may be ulcerative or nonulcerative, and is characterised by infiltrates or opacities in the cornea. **Keratoconjunctivitis** denotes an inflammation of both the cornea and

conjunctiva. Keratitis arises from a wide variety of causes, the origin of which may be infectious or, less frequently, noninfectious e.g. [collagen vascular diseases](#). Keratitis is a more serious, sight threatening condition than conjunctivitis, although severity varies widely. In **epithelial keratitis**, infection is confined to the superficial layer of the cornea. **Stromal keratitis**, in which deeper layers of the cornea are affected, is more serious as there is a greater likelihood of scarring. A **corneal ulcer** commences with an epithelial defect, which then leads to breakdown of the corneal stroma. Corneal ulcers always result in scarring of the cornea and may impair vision permanently or even lead to perforation of the eye.

- 1.2.3. **Episcleritis** involves inflammation of the episclera, the thin membrane that covers the sclera. Most cases are [idiopathic](#), but a proportion can be linked to a variety of systemic conditions, including some infectious diseases. Episcleritis is a common condition, which is usually mild and non-sight threatening, and only very rarely progresses to scleritis.
- 1.2.4. **Scleritis** poses a significant threat to vision. Most cases are immune-mediated although the condition can be triggered by infection. Typically, it is a severe, painful inflammatory condition centred in the sclera that may also involve the cornea, adjacent episclera, and underlying uvea. Scleritis may affect the anterior sclera, posterior sclera, or both. Anterior scleritis is the most common manifestation of the disease, and may be diffuse, nodular, or necrotising (the most severe form). Posterior scleritis may be diffuse or nodular, and may occur in isolation or in association with anterior scleritis.
- 1.2.5. **Uveitis**. The uvea consists collectively of the iris, ciliary body, and choroid. Inflammatory processes involving these structures may be infectious or noninfectious in origin. Inflammation of the iris (iritis) or ciliary body (cyclitis) constitutes **anterior uveitis**, which is also known as iridocyclitis. **Posterior uveitis** encompasses choroiditis, retinitis, and chorioretinitis (synonym retinochoroiditis). Anterior uveitis is the most common form of uveitis in most Western countries. **Panuveitis** and **diffuse uveitis** are terms used to describe the involvement of both the anterior and posterior segments.
- 1.2.6. **Endophthalmitis** involves inflammation of the internal ocular spaces (i.e. anterior chamber and vitreous cavity) and adjacent structures of the eye, exclusive of the sclera. **Panophthalmitis** refers to inflammation of all ocular tissue layers, including the sclera. Endophthalmitis is most commonly infectious in origin, although noninfectious cases may occur. Endophthalmitis is a true ophthalmic emergency as irreparable visual loss can occur within 24-48 hours.
- 1.2.7. Infections may also affect the **ocular adnexae**, such as the eyelids (preseptal cellulitis), orbital tissue (orbital cellulitis), lachrymal gland (dacryoadenitis), lachrymal drainage system ([dacryocystitis](#)), and periorbital tissues (cellulitis). Such infections are not considered in this Synopsis.

1.3. **Infectious organisms.** A selection of the more common and/or harmful organisms responsible for eye infections is included in the following list.

1.3.1. Bacteria

- *Staphylococcus* spp. especially *S. aureus* and coagulase-negative *Staphylococcus*
- *Streptococcus* spp. especially *S. pneumoniae*
- *Haemophilus* spp especially *H. influenzae*
- *Pseudomonas aeruginosa*, which causes very rapid ulceration
- *Serratia* spp. especially *Serratia marcescens*, which also has a propensity to cause severe disease
- *Nocardia* spp.
- *Neisseria gonorrhoeae*, which is a cause of infection both in neonates and in sexually active adults
- *Chlamydia trachomatis*, which is a cause of infection both in neonates and in sexually active adults, and is also the organism responsible for trachoma
- *Mycobacterium* spp.
- *Moraxella* spp.
- *Klebsiella* spp.

1.3.2. Viruses

- Adenovirus: certain strains, notably types 8, 19, and 37 cause epidemic keratoconjunctivitis (see section 2.2.2)
- Enteroviruses including coxsackievirus
- Herpes simplex virus (see section 4.1)
- Varicella zoster virus (see section 4.2)
- Cytomegalovirus (mainly arises in patients who are suffering from AIDS)
- Avian paramyxovirus serotype 1 (causes Newcastle disease, which may infect humans by spread from poultry)
- Rubella virus
- Mumps virus
- Epstein-Barr virus

1.3.3. Fungi

- *Fusarium* spp.
- *Aspergillus* spp.
- *Candida* spp.

1.3.4. Parasites

- *Acanthamoeba* (see section 3.4)
- *Toxoplasma gondii* (see section 4.3)
- *Toxocara*

2. Clinical Features

- 2.1. A detailed discussion of the symptoms, signs and investigation of eye infections is outwith the scope of this synopsis. A brief outline only is provided. The features of herpes simplex ocular infection, herpes zoster ophthalmicus and ocular toxoplasmosis are described separately at section 4.
- 2.2. **Conjunctivitis and keratoconjunctivitis**
 - 2.2.1. **Viral conjunctivitis** typically produces a red, irritated eye with watery discharge, [tarsal](#) follicles, and preauricular [lymphadenopathy](#). Infection often spreads from one eye to the other over a period of a few days. The ocular symptoms and signs may be isolated or part of a systemic viral syndrome.
 - 2.2.2. **Epidemic keratoconjunctivitis (EKC)** is caused by certain strains of adenovirus, notably types 8, 19, and 37. EKC may be preceded by influenza-like symptoms, and ocular symptoms are mainly sudden onset of irritation, soreness, red eye, photophobia, foreign body sensation, and excessive [tearing](#). In more severe cases, patients can present with ocular pain and decreased visual acuity, and EKC can lead to persistent corneal opacities and blurred vision.
 - 2.2.3. **Bacterial conjunctivitis** presents similarly to viral conjunctivitis, but usually has a more abrupt onset and greater mucopurulent discharge. Infection typically spreads quickly to the other eye.
 - 2.2.4. **Hyperacute bacterial conjunctivitis** is caused by *Neisseria gonorrhoeae* (and more rarely *N. meningitidis*) infection of the eye. This condition has an abrupt onset, is rapidly progressive and can have sight-threatening repercussions. Signs include a copious [purulent](#) discharge, marked conjunctival [chemosis](#), and preauricular lymphadenopathy. When untreated, rapid and severe corneal involvement occurs, leading to ulceration and subsequent perforation, which may occur within 2 days. Neonates can be affected, whilst adult patients may demonstrate accompanying genitourinary symptoms such as discharge and [dysuria](#).
 - 2.2.5. **Chlamydial conjunctivitis** is an [inclusion conjunctivitis](#) caused by sexually transmitted *Chlamydia trachomatis* infection. The condition can be mild, but may progress to severe infection with [mucopurulent](#) discharge, preauricular lymphadenopathy, marked chemosis and [ptosis](#). Infection may be unilateral or bilateral, and chronic infection may also occur. Neonates can be affected, whilst adult patients may demonstrate accompanying genitourinary symptoms such as discharge and dysuria.
 - 2.2.6. **Trachoma** is a chronic bacterial keratoconjunctivitis and is the leading infectious cause of blindness in the developing world. Repeated infections of the eyes with the relevant strains of *Chlamydia trachomatis* result in a sequence of tarsal conjunctivitis, scarring, shortening of the upper lid (so that the eyelashes abrade the cornea), [trichiasis](#), and finally, corneal opacity. Although there has been a steady downward trend in trachoma rates, the disease remains endemic in 55 countries. The World Health Organization (WHO) reports that 55

million people are infected, and 3 million are visually impaired or blind because of trachoma. The WHO advocates a range of preventative measures with the aim of eliminating blinding trachoma globally by 2020.³

- 2.3. **Keratitis** is a potentially sight-threatening condition that may have an infectious or noninfectious aetiology. The worldwide incidence of ulcerative keratitis has been estimated at around 500,000 persons annually.⁴
 - 2.3.1. Keratitis presents acutely with a red eye but with much more pain and light sensitivity than is evident in conjunctivitis. Discharge may be thick and profuse and the eyelids may be swollen. Corneal ulcer is characterised by acute pain, foreign body sensation, [blepharospasm](#), [photophobia](#) and visual disturbance. The infected portion of the cornea will usually contain a focal area of stromal infiltrate with an overlying area of epithelial excavation. Severe cases of bacterial keratitis lead to profound anterior chamber reaction and [hypopyon](#).
 - 2.3.2. The host corneal inflammatory response may in some cases cause more damage than the infection itself. The condition is sight threatening if corneal scarring or perforation occurs. The severity of visual loss is dependent on the location of the lesion and tends to be linked to clinical severity. Corneal ulcers that are located centrally rather than peripherally pose a greater threat to vision.
- 2.4. **Episcleritis and scleritis**. Episcleritis is usually mild and self-limiting although it may be recurrent. The typical presentation involves a bright red eye often localised to a patch on one eye. It may be asymptomatic or be associated with a feeling of grittiness. In contrast in scleritis, severe pain is usually prominent, intensified by eye movement and accompanied by globe tenderness. Approximately 25% of patients have bilateral disease at presentation, rising ultimately to 50% of patients. Patients with scleritis may present with simultaneous peripheral ulcerative keratitis, although this latter condition may also present independently. Patients suffering from posterior scleritis may present with reduced vision with or without pain.⁵
- 2.5. **Anterior uveitis** may present suddenly with a red eye, deep aching pain, photophobia and on occasion, blurred vision. In children it can be asymptomatic. The pupil contracts (miosis) and tiny aggregates of cells may be seen on the inner surface of the cornea (keratic precipitates). In severe cases, a hypopyon may form and the iris may adhere to the anterior lens surface, causing posterior [synechiae](#). **Posterior uveitis** is characterised by floaters and visual changes without redness or significant pain. Blind spots or flashing lights may occur with retinal involvement.
- 2.6. **Endophthalmitis** generally presents with sudden onset of red eye with severe pain and progressively worsening vision, although there can be substantial variation in the presenting features. Many patients are misdiagnosed initially and the diagnosis should be suspected in anyone presenting with decreasing visual acuity and a painful, inflamed eye, especially if there is a history of eye surgery, penetrating ocular trauma, or immunosuppression. Features include conjunctival hyperaemia, chemosis, ocular discharge, corneal oedema, anterior chamber inflammation, and [vitreal](#) inflammation. A hypopyon may be present and intraocular pressure may be raised significantly. The diagnosis and treatment of endophthalmitis represents an ophthalmic emergency.⁶ Patients with endogenous endophthalmitis (see section 3.9.4) may present with systemic features of infection, most commonly fever and joint pain, and are often very ill and toxic. Specific symptoms associated with the primary infection may also be evident.

2.7. **Investigations.** Conjunctival swabs, corneal swabs and corneal scrapes are often taken in an effort to identify the causative organism. However, the yield from microbiological investigation may be low despite direct inoculation of a sample on the culture media.⁴ Depending on the clinical features, other examination techniques and investigations are utilised as appropriate, including slit lamp examination, fluorescein angiography, ultrasonography, orbital CT scan, orbital magnetic resonance imaging, biopsy, and blood tests.

3. Aetiology

Note: The features of herpes simplex ocular infection, herpes zoster ophthalmicus and ocular toxoplasmosis are described separately in section 4.

3.1. Conjunctivitis and keratoconjunctivitis

- 3.1.1. **Viral conjunctivitis** is the most common form of infectious conjunctivitis, with adenovirus being the most common causative viral pathogen. Modes of transmission include hand-eye contact, medical instruments, and swimming pool water. The sharing of personal items that come into contact with the eyes (e.g. towels) will encourage spread. The condition is very contagious, frequently associated with upper respiratory tract infections, and often transmitted among family members, in schools, workplaces, and in day care settings. Infected individuals may remain contagious for up to two weeks.
- 3.1.2. **Epidemic keratoconjunctivitis (EKC)** tends to occur in closed institutions, including schools, hospitals and military bases. The major mode of transmission involves person-to-person contact with eye secretions e.g. by touch, shared tissues or towels. Other possible methods of transmission are through airborne droplets and possibly swimming pools.
- 3.1.3. **Bacterial conjunctivitis** is less common than viral conjunctivitis, and can be associated with upper respiratory tract infections and [dacryocystitis](#).
- 3.1.4. **Gonococcal and chlamydial conjunctivitis** (caused by infection with *Neisseria gonorrhoeae* and *Chlamydia trachomatis* respectively) are sexually transmitted diseases that are associated with genital infections by these agents. It is thought that these infections are usually transmitted from genital secretions to the eye by way of the hands. In adults, co-infection with other sexually transmitted pathogens may be present. Gonococcal and chlamydial eye infections may also be transmitted to newborn infants during their passage down the birth canal. Chlamydial inclusion conjunctivitis is caused by serovars (biological subtypes) D-K of *C. trachomatis*. Around 1 in 300 of adult patients with chlamydial genital tract infection develops inclusion conjunctivitis, although this figure may be an underestimate.⁷
- 3.1.5. **Trachoma** is caused by four other serovars of *C. trachomatis* (A, B, Ba, and C). These serovars are rarely encountered in the UK, but trachoma is a leading cause of blindness in the developing world, occurring predominantly in populations that live in unsanitary conditions. The disease stems from recurrent infections and is thought to be mediated by an immune response to chlamydial antigens. The organism is transmitted by direct contact from eye to eye by hands or towels used on the face, whilst moisture-seeking flies may play a lesser role.

- 3.2. **Keratitis.** The incidence of bacterial keratitis is increasing in developed countries. The relatively avascular cornea predisposes to infection, particularly when the epithelium is compromised. Microbial keratitis is rare in the absence of predisposing factors. Common risk factors for microbial keratitis and corneal ulcers include:⁴

- Contact lens wear, which is now the most commonly identified risk factor
- Ocular surface disorders, e.g. previous herpetic infection, dry eye syndrome, [trichiasis](#), use and abuse of topical medications, [neurotrophic keratopathy](#), and exposure keratopathy
- Certain other ocular diseases e.g. chronic [dacryocystitis](#), [blepharitis](#)
- History of ocular trauma, including corneal abrasion
- History of ocular or eyelid surgery
- Comatose patients on ventilators, who are at increased risk because of corneal exposure
- Any condition that causes incomplete closure of the eyelids, such as facial nerve (Bell's) palsy
- Any condition that causes corneal anaesthesia, such as fifth cranial nerve palsy
- Debilitating systemic diseases (e.g. diabetes mellitus) immunocompromised states, and chronic use of immunosuppressive drugs⁸

Although corneal ulcers most commonly result from infectious causes, the condition can also be caused by noninfectious aetiologies, including vitamin A deficiency, rosacea, and [collagen vascular diseases](#).⁹

- 3.2.1. There is a bimodal age distribution; the association with contact lens wear and corneal trauma is more apparent in younger patients, and that with predisposing ocular surface diseases and eyelid diseases in an older group.
- 3.2.2. **Microbiology.** Keratitis and corneal ulcers are caused by many of the same organisms responsible for conjunctivitis. Cultures of corneal scrapings are positive in around half to two-thirds of cases. Patients with negative cultures tend to have milder keratitis.¹⁰ Differences in keratitis profile have been reported between populations living in rural or city areas, and between Western and developing countries. For all causes of microbial keratitis, Gram positive bacterial species appear to be the organisms that are most commonly isolated in cultures taken from patients in temperate zones, whilst Gram negative species and fungi predominate in tropical climates.
- 3.2.3. Micro-organisms have been classified into [endogenous](#) and environmental groups. Endogenous organisms more commonly cause a peripheral lesion whilst environmental organisms are more likely to cause central disease. Endogenous Gram positive bacteria that are found in the normal ocular flora, such as *Staphylococci* and *Streptococci*, can be inoculated easily into damaged or abnormal corneal tissues, and it is these organisms that are most commonly implicated in cases of infectious keratitis. The environmental organisms that are involved include Gram negative bacteria, *Nocardia*, fungi, and *Acanthamoeba*. These environmental micro-organisms are more virulent, and may be associated with more severe keratitis and less favourable disease outcome in terms of rate of vision loss and duration of symptoms. For example, keratitis due to *Pseudomonas aeruginosa* can spread rapidly, invading the entire cornea in a matter of hours causing ulceration that may progress to perforation.¹¹
- 3.2.4. Infections with Gram negative organisms have been rising due to an association with contact lens wear. In particular a higher prevalence of Gram negative rods, such as *Pseudomonas aeruginosa* and *Serratia* spp, has been reported in patients who wear contact lens as compared to those who do not. Nevertheless,

infections caused by Gram positive cocci, such as *Staphylococcus aureus*, are responsible for approximately two-thirds of contact lens-related bacterial keratitis. Geographic and climatic factors are also relevant in this context. Contact lens wearers who live in or travel to the tropics are more likely to have disease caused by environmental organisms, with a consequent increase in severe contact lens-related microbial keratitis in warmer, humid regions. In contrast in temperate climates, there appears to be an increased association with Gram positive bacteria. Another notable consideration is that *P. aeruginosa* and *Serratia marcescens* are commonly resistant to contact lens disinfecting solutions.¹¹

- 3.2.5. **Fungal keratitis** accounts for 5-10% of all cases, although a higher proportion of fungal infection has been reported from various locations around the world including Florida, Nepal, and Bangladesh, and fungal keratitis is generally more common in tropical and subtropical regions than in temperate zones.¹² Trauma from vegetable matter is the most important risk factor. The most common fungal agents responsible for corneal infections are *Aspergillus* and *Fusarium*. Other species that may be responsible include *Candida* and *Curvularia*. Ocular and systemic defects and prior application of corticosteroids are other important risk factors for fungal infections.¹³
 - 3.2.6. **Ocular trauma** has generally been identified as the cause of microbial keratitis in 15-24% of cases. Trauma is frequently secondary to welding or grinding, and patients are predominantly male.¹⁴ Corneal injury with soil, sand or stone appears to carry a greater risk of developing bacterial keratitis than does corneal injury with other traumatising agents.¹⁵ In particular, although keratitis due to *Nocardia asteroides* is a rare entity, it has been reported that 90% of patients who develop this condition have a history of ocular injury with soil or sand.¹⁶
 - 3.2.7. **Other factors.** The use of a topical corticosteroid prior to the diagnosis of bacterial keratitis predisposes to ulcerative keratitis in eyes with preexisting corneal disease. Moreover, once microbial keratitis has occurred, prior corticosteroid use significantly increases the risk of antibiotic treatment failure or other infectious complications.¹⁷ Bacterial and fungal corneal ulcers have developed during treatment with the topical antibiotic gentamycin (used alone or in combination with corticosteroids).
- 3.3. **Contact lens** wear is a major cause of microbial keratitis and corneal ulcer, especially in young adults. Various studies have reported that around one-third to two-thirds of new cases of microbial keratitis are associated with contact lens wear. It must be emphasised that microbial keratitis is a rare complication of contact lens wear, affecting approximately 4-5 per 10,000 wearers per year overall. Of these cases, around 13% experience a permanent reduction in best-corrected visual acuity of ≥ 2 lines, representing an annualised incidence of vision loss of 0.6 per 10,000 wearers.¹⁸
 - 3.3.1. Nevertheless, over 7% of adults in the UK wear contact lenses. In view of this large at-risk population and the significant visual morbidity associated with microbial keratitis, these considerations carry considerable public health implications. It is important to note that microbial keratitis is the only sight-threatening complication of an otherwise safe method of vision correction, and current studies indicate that contact lenses can be worn with a substantially

lower risk of vision loss than laser refractive surgery procedures such as [LASIK](#).¹⁹

3.3.2. Around 90% of contact lens wearers use soft contact lenses. A summary of the main types of lens is provided in the following table:

Type of contact lens	Main characteristics
Rigid gas-permeable (RGP) daily wear lenses	Rigid lenses that must be removed and cleaned each night. Lenses are durable and can last for approximately one year.
Daily wear soft lenses	Soft lenses that must be removed and cleaned each night. Planned replacement programmes can be established to maintain a regular replacement schedule, most commonly fortnightly, monthly, or quarterly.
Extended wear soft lenses	Soft lenses worn continually for up to six days and then discarded, with no need for cleaning.
Daily disposable soft lenses	Worn for single day then discarded. Intended to reduce the risk of infection due to poor cleaning habits or over-wearing lenses.
Silicone hydrogel lenses	Highly oxygen-permeable lenses that are designed for continuous wear for extended periods of up to 30 nights.

3.3.3. The pathogenesis of corneal infection is multifactorial. The issues includes the propensity of bacteria to adhere to deposits on the contact lens, the changes in the corneal epithelium induced by contact lens wear, and the possibility of breakdown of the protective epithelial barrier with adherence of pathogenic bacteria.

3.3.4. The results of epidemiological studies of contact lens-related microbial keratitis have proved consistent across time and geographic location. The principal risk factor has remained overnight wear of contact lenses, and the magnitude of risk increases with exposure to longer continuous periods of overnight wear. Moreover, soft contact lenses are associated with a significantly higher risk than hard lenses. Thus, the annual incidence of microbial keratitis is lowest for users of rigid gas-permeable daily wear lenses, this being in the order of 1 in 10,000, followed by 3 to 4 in 10,000 for daily-wear soft contact lenses, and 10 to 20 per 10,000 for extended-wear soft contact lenses.^{19,20}

3.3.5. Two new types of contact lens have been introduced in the decade following the completion of the main epidemiologic studies from which the above estimates were derived. **Daily disposable soft lenses**, available since 1995, were designed to eliminate issues surrounding contact lens hygiene and storage, which have been shown to be a principal cause of microbial contamination. **Silicone hydrogel lenses** were introduced in 1999. These lenses are highly oxygen-

permeable and, by virtue of increasing oxygen transmission to the cornea through the lens, lead to a reduction in corneal hypoxia, which has been proposed as a major risk factor for corneal infection.

- 3.3.6. One study has reported that the risk of developing severe keratitis was reduced five-fold for extended silicone hydrogel lens wear as compared to conventional soft contact lens overnight use.²¹ However other studies, notably from Australia and from Moorfields Eye Hospital in London, have failed to demonstrate that either of these innovations has had the expected effect of reducing the risk of microbial keratitis. These studies found that for the majority of cases of microbial keratitis (i.e. those classified as moderate or mild), there was either a greater risk with daily disposable lenses as compared with planned replacement daily wear soft lenses (UK study) or no difference between the two types (Australian study). In contrast, the risk of developing severe microbial keratitis with sight loss, was found to be less for daily disposable soft lenses than for daily wear soft lenses.
- 3.3.7. Both studies found that silicone hydrogel lenses had no significant effect on the risk or severity of microbial keratitis. The Australian researchers reported an annual risk of 19.5 per 10,000 wearers in extended wear (overnight use) soft lenses and of 25.4 per 10,000 wearers for silicone hydrogel lenses. Of note is the longer continuous duration of overnight wear with silicone hydrogel contact lenses (up to 30 nights) compared with around 6 nights for extended wear soft lenses. The Moorfields Eye Hospital team reported that different brands of contact lens may be associated with significantly different risks of keratitis. These findings suggest that differences in contact lens design may be more important in the development of corneal infection than oxygen levels and contact lens case contamination.^{18,19}
- 3.3.8. Advances have been made in the chemical agents used as contact lens cleaners. New solutions are now available that reduce bacterial adherence to the lenses and are more effective in controlling bacterial and, potentially, amoebal contamination of the lenses.²²
- 3.3.9. The clear association between overnight wear of any type of contact lens with an increased risk of microbial keratitis has been documented in detail above. However, various studies have suggested **additional risk factors** for the development of infection in contact lens wearers. An increased risk of infection has been reported with younger users (age 15-24 years) as compared to older contact lens wearers. A further risk factor is unsupervised or uninstructed wear e.g. use of coloured cosmetic contact lenses. Other reported findings have included poor storage case hygiene including poor adherence to cleaning schedules and use of home-made saline solutions, poor hand hygiene, internet supply of lenses, <6 months wear experience, swimming whilst wearing lenses, hypermetropia, younger age, male gender, and smoking. It is possible that some of these characteristics may be surrogates for other factors, such as risk-taking behaviour or general health status.^{18,19,20,23}
- 3.3.10. Successful contact lens wear is dependent on appropriate education of the user in the proper handling and care of the lenses. Contact lens use must be discontinued during treatment for an eye infection.

- 3.3.11. *Acanthamoeba* is a microscopic, free-living protozoa that is relatively common in the environment. It has been isolated from water (including pools or hot tubs), drinking water systems, sewage systems, soil, and air (in association with cooling towers, heating, ventilation and air conditioner systems).
- 3.3.12. *Acanthamoeba* keratitis is an uncommon but serious condition that may progress to severe visual loss. The clinical picture is usually characterised by severe pain, sometimes disproportionate to the signs. Bilateral infection may occur occasionally, either concurrently or sequentially.²⁴ The condition may develop after corneal trauma, often minor in nature, especially if this occurs in a rural, dusty, or watery environment. However, around 93% of cases arise in association with contact lens wear, predominantly in those who use daily wear or extended wear soft contact lenses. Annual incidence in the United States has been estimated at around 2 per million contact lens wearers.²⁵
- 3.3.13. *Acanthamoeba* keratitis emerged as a public health problem in the early 1980s, arising mainly from inadvertent contamination of the contact lens storage case by waterborne microorganisms. Thus risk factors for *Acanthamoeba* infection revolve around inappropriate or ineffective lens maintenance including the failure to disinfect lenses as frequently as recommended, exposure to tap water, the use of chlorine-based disinfectants compared with other chemical systems, and use of home-made instead of commercially prepared saline solution. There have also been occasional reports of the condition in patients who have ignored instructions and reused daily disposable lenses. Some cases have involved exposure of the contact lenses to other sources of water e.g. swimming. Use of a dual or common-well storage case risks contamination of both lenses. In a military context, issues arise around the ability to maintain proper lens hygiene in a combat or field environment.^{26,27,28}
- 3.3.14. It has been estimated that over 90% of cases of *Acanthamoeba* keratitis arising in contact lens wearers could have been prevented by the avoidance of known risk factors.
- 3.4. **Episcleritis.** Although most cases are idiopathic, episcleritis may be associated with various systemic diseases, including the [collagen vascular diseases](#) and with infectious diseases such as tuberculosis, Lyme disease, syphilis, and herpes zoster.
- 3.5. **Scleritis.** The most common association is with a variety of [autoimmune](#) conditions e.g. rheumatoid arthritis and Wegener's granulomatosis. Although the condition may occur at any age, patients are predominantly middle-aged, and women are affected approximately twice as often as men. However the condition can also be triggered by infection, ocular surgery, tumours, trauma, or drugs. Approximately 5% to 10% of anterior scleritis is infectious in origin, although the mechanism of inflammation is often thought to be partly or wholly immune mediated. The agent involved may be viral, bacterial, fungal, or parasitic. The most common infectious cause of scleritis is herpes zoster ophthalmicus,²⁹ followed by *Treponema pallidum* (syphilitic) infection. Other causes include the following:³⁰
- Bacteria: Lyme disease, leprosy, tuberculosis, *Pseudomonas aeruginosa*, *Staphylococcus* spp. (following surgery or beta-irradiation), *Streptococcus* spp. (following beta-irradiation or streptococcal pharyngitis), *Haemophilus influenzae*, *Serratia* spp., and *Nocardia* spp. (usually associated with trauma)
 - Viruses: Herpes simplex virus, Epstein-Barr virus, Coxsackie B5

- Fungi: *Aspergillus*, which follows trauma or surgery and may remain undiagnosed for months
 - Parasites: *Acanthamoeba* (associated with keratitis)
- 3.5.1. Infectious scleritis is more likely to occur in the presence of infectious keratitis, or in tissue compromised by disease, accidental trauma, or ocular surgery, e.g. removal of [pterygium](#), cataract surgery, or repair of retinal detachment. A particular risk factor has been identified where pterygium surgery was accompanied by adjunctive treatment to the globe (beta irradiation or administration of the antimetabolite, mitomycin C) aimed at reducing the rate of recurrence. A patient may present with bacterial scleritis (most commonly due to *Pseudomonas aeruginosa*) months to years after pterygium surgery.³¹
- 3.5.2. The aetiology of peripheral ulcerative keratitis is similar to that of scleritis, being associated with a variety of systemic conditions, most commonly the collagen vascular diseases, and with a similar range of microbial pathogens.
- 3.6. **Anterior uveitis** is predominantly associated with the histocompatibility antigen [HLA B-27](#) and a variety of systemic diseases including ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease, and sarcoidosis. In contrast, systemic infection (e.g. syphilis, tuberculosis, leptospirosis, or Lyme disease) is an uncommon cause of anterior uveitis. The ocular manifestations of herpes simplex and herpes zoster may include anterior uveitis.
- 3.7. **Posterior uveitis** may be associated with systemic infections. Causes include:
- Syphilis can cause chorioretinitis, usually occurring in the secondary stage of the disease and therefore uncommon in areas where antibiotic treatment is available
 - Ocular tuberculosis is now uncommon but can manifest in various forms including chorioretinal involvement or a chronic panuveitis
 - West Nile virus is a cause of retinitis and retinal vasculitis
 - Cytomegalovirus can cause a severe and rapidly progressive posterior uveitis in immunocompromised individuals, particularly patients with AIDS. The incidence has declined since the introduction of highly active antiretroviral therapy for HIV infection
 - Herpes simplex and varicella zoster viruses can cause necrotising retinitis. The prognosis of herpetic retinitis remains poor, as it is associated with a high incidence of complications³²
 - Fungal species, including *Candida*, can cause chorioretinal lesions. Severely ill patients with indwelling catheters are susceptible to candidal infections, as are those who are immunocompromised or receiving long-term antibiotic therapy
 - *Histoplasma capsulatum*, a systemic infection acquired through incidental exposure in endemic areas, typically causes asymptomatic chorioretinal scars
 - *Toxocara canis* and *Toxocara cati* are parasitic infections involving the retina
 - Toxoplasmosis is the most common cause of posterior uveitis in immunocompetent subjects (see section 4.3)
- 3.8. **Endophthalmitis** may be either infectious or, less commonly, noninfectious in origin. Causes of the latter include noninfectious postoperative inflammation, toxic agents, intraocular blood, and necrosis of an intraocular tumour. **Infectious endophthalmitis** is classified as either [exogenous](#) or [endogenous](#). Infection is usually bacterial or fungal, but viral and parasitic infections may occur.

- 3.8.1. **Exogenous endophthalmitis** occurs when the external ocular barriers are breached by intraocular surgery, penetrating injury, corneal ulcer or periocular infection, thus allowing an infective agent direct access to the intraocular spaces.
- 3.8.2. Over 70% of cases of endophthalmitis occur following eye surgery, notably cataract extraction. The incidence following cataract surgery may be related to operative technique, and has been reported in various studies at around 1 in 400 to 1 in 1700 cases. Postoperative endophthalmitis is most often caused by the normal bacterial flora of the conjunctiva and eyelid margins, although almost any bacteria can cause opportunistic endophthalmitis. Although acute postoperative endophthalmitis usually presents within two weeks of ocular surgery, delayed-onset postoperative endophthalmitis may take weeks, or even months, before symptoms manifest themselves. Following filtering surgery for glaucoma, endophthalmitis associated with a conjunctival filtering bleb can occur at any time.
- 3.8.3. Post-traumatic cases generally present soon (i.e. days to weeks) after penetrating trauma. In these cases, endophthalmitis may also be caused by normal bacterial flora although, as compared with postoperative cases, there is a higher rate of environmental organisms. Penetrating trauma accounts for 7-30% of cases, the risk being further increased if there is an intraocular foreign body or lens disruption. The incidence of endophthalmitis following open globe injury is 3.3-16.5%. Fungal infections, which are exceedingly rare after surgery, are linked particularly to contamination of a penetrating injury with vegetable matter or soil.
- 3.8.4. **Endogenous endophthalmitis** occurs when organisms reach the eye via the bloodstream, enter the internal ocular spaces by crossing the blood-ocular barrier, resist host defences, and multiply within the eye. Endogenous infection is less common than exogenous endophthalmitis, and accounts for only 2-6% of all cases of endophthalmitis, with an annual incidence of around 0.5 cases per 100,000 population. The disease can occur at any age but peaks at about 50 years. Gram positive organisms are responsible for the majority of cases reported from North America and Europe, but Gram negative organisms are more common in East Asia.
- 3.8.5. Patients may develop endogenous endophthalmitis following development of conditions such as liver abscess, pneumonia, meningitis, endocarditis, or renal and urinary tract infection. There may be a history of recent invasive medical procedures such as urinary catheterisation, intravascular central line, haemodialysis, or dental procedures. Indwelling urinary catheters and intravenous lines increase risk.
- 3.8.6. Most patients with endogenous endophthalmitis have a predisposing risk factor in the form of a severe systemic illness or immunodeficiency. These predisposing factors include leukaemia, lymphoma, disseminated carcinoma, intravenous drug use, collagen vascular diseases and other autoimmune conditions, HIV infection and AIDS, asplenia, diabetes, and long-term use of corticosteroids. A finding of diabetes is particularly common in patients with endogenous endophthalmitis caused by *Klebsiella* spp.⁶

4. Herpes Simplex Ocular Disease, Herpes Zoster Ophthalmicus, and Ocular Toxoplasmosis

4.1. Herpes simplex virus (HSV)

- 4.1.1. HSV is the viral infection most commonly associated with serious corneal disease. The predominant strain responsible for herpes simplex ocular disease is herpes simplex virus type 1 (HSV-1), also known as human herpesvirus type 1 (HHV-1). Clinical ocular disease develops in less than 1% of the population infected with the virus. Ocular HSV infection is reported to be prevalent in approximately 0.15% of the population of developed countries.³³
- 4.1.2. Infection is usually spread by direct contact. Initially, eye infection may develop either from spread to the eye from a non-ocular site, principally the mouth, or from direct entry to the ocular surface by means of droplet spread. Latency is then established principally in the [trigeminal](#) nerve ganglion. Periodic reactivation initiates [anterograde axonal](#) spread to the cornea, causing recurrent **herpes simplex keratitis (HSK)**. Recent evidence suggests that latent HSV-1 in the cornea may also act as a source of recurrent disease. Moreover, recurrent disease may be due to either reactivation or reinfection with a new strain.³³ Thus episodes of HSV-1-related ocular surface disease can result from each of the following events:
 - primary disease (i.e. eye disease occurring in a subject with no previous exposure to HSV-1)
 - initial ocular disease (i.e. eye disease occurring for the first time in a host who has previously been infected with HSV-1 at another site)
 - recurrent herpes simplex keratitis
 - superinfection with a different strain of HSV-1
- 4.1.3. Different HSV-1 isolates have been associated with varying severity of disease, ranging from relatively asymptomatic to severe disease with corneal scarring. Primary infection with HSV, which often occurs in childhood, is frequently asymptomatic. The initial (not necessarily primary) manifestation of herpetic eye involvement may be mild, presenting as [blepharitis](#), conjunctivitis, or corneal epithelial keratitis. Keratitis occurs in 33-50% of primary infections, and usually appears 1 to 2 weeks after the appearance of skin lesions. Recurrent disease accounts for most cases of ocular HSV and presents classically with unilateral corneal defects, although the lid and conjunctiva may be involved as well. Recurrent attacks may lead to corneal scarring, decreased corneal sensation, and visual loss.⁹
- 4.1.4. In **herpetic epithelial keratitis**, the characteristic presentation comprises a dendritic ulcer, which demonstrates a linear branching pattern with terminal bulbs. Enlargement may occur, leading to a geographic ulcer. Although epithelial disease often resolves spontaneously, complications may ensue, such as corneal erosions or [neurotrophic keratopathy](#).

- 4.1.5. **Herpetic stromal keratitis** accounts for 2% of initial presentations and 20–48% of recurrent herpetic disease. Stromal keratitis can lead to significant visual morbidity through corneal scarring, thinning, perforation, and [neovascularisation](#). It is considered that stromal keratitis represents viral invasion of the stroma combined with a marked host immune response. The keratitis may be necrotising or non-necrotising. Severe iridocyclitis and raised intraocular pressure may occur. Retinitis may also develop.
- 4.1.6. Patients with herpetic eye infection are at risk of **recurrent eye disease** throughout their lives. A reasonable estimate of the recurrence rate of HSK after epithelial or stromal disease is approximately 10% per year. Corneal scarring occurs in 18–28% of patients with a corresponding reduction in visual acuity to <6/12 in 10-25% of cases and <6/30 in 3-12%. Although mainly unilateral, bilateral disease occurs in 1.3-12% of cases, principally in a younger age group. Bilateral disease tends to be associated with a higher incidence of atopy and immune abnormalities. In patients with bilateral disease, visual acuity is reduced to <6/12 in up to 42% of cases, and <6/60 in 17%.
- 4.1.7. Some of the evidence regarding **triggers** for reactivation has been conflicting. Experimental models have suggested that HSV-1 reactivation may be triggered by stressors such as UV light³⁴ and recent ocular surgery.³⁵ A multicentre study reported no association found between episodes of recurrence and a number of exposure variables i.e. psychological stress, systemic infection, sunlight exposure, menstrual period, contact lens wear, and eye injury.³⁶ The same research team found that age, gender, ethnicity, and nonocular herpes were also not linked to recurrences, nor were seasonal effects observed. Previous epithelial keratitis was not a risk factor for recurrent epithelial keratitis. However, previous episodes of stromal keratitis increased the probability of subsequent stromal keratitis and the risk was strongly correlated with the number of previous episodes.³⁷
- 4.1.8. Although HSV keratitis may resolve spontaneously, numerous studies have shown a benefit from treatment with topical antivirals. Most patients will have minimal change in visual acuity, but others will be left with significant visual impairment.⁹ Recurrent HSK is the principal cause of visual loss. There is some evidence that the recurrence rate for all forms of HSV eye disease is diminished with longer-term oral administration of the antiviral, acyclovir.³⁸
- 4.1.9. Once a visually disabling corneal scar develops, options for improving vision are limited to surgery, with [penetrating keratoplasty](#) as the treatment of choice. Complications of penetrating keratoplasty for HSK include recurrent disease in the new cornea and corneal transplant rejection. Recurrence rates of HSK as high as 27% have been reported in the first year following penetrating keratoplasty. The use of prophylactic topical and systemic antivirals for at least 1 year post-operatively has led to a significant reduction in post-transplant recurrence of HSK.³³
- 4.1.10. The development of HSK has also been recorded after penetrating keratoplasty undertaken for other reasons and without a clinical history of HSV in the host. This effect is particularly evident in the first 2 years after such surgery.³⁹ Experimental studies indicate that it is most likely that HSK post-transplantation arises from host HSV-1. However, a case study has been

published documenting an apparently rare instance of donor-to-host transmission of HSV-1 by means of penetrating keratoplasty.⁴⁰

4.2. Herpes zoster ophthalmicus (HZO)

- 4.2.1. Varicella zoster virus (VZV) is distributed worldwide and is the cause of two distinct illnesses. Primary infection presents as varicella (chickenpox), usually during childhood. Herpes zoster (HZ) or shingles represents the second manifestation of VZV infection and results from reactivation of latent VZV within the sensory ganglia. Herpes zoster usually presents as unilateral pain in a [dermatomal](#) distribution accompanied by a characteristic [vesicular](#) rash. The affected area may be intensely painful. Whilst most immunocompetent patients experience spontaneous and complete recovery within a few weeks, the most frequent and debilitating complication of HZ regardless of dermatomal distribution is postherpetic neuralgia, a neuropathic pain syndrome that persists or develops after the rash has resolved.
- 4.2.2. Although HZ may occur at any age (including children), incidence and severity increase with advancing age, especially in those older than 60 years. Around one in four adults will experience an attack during their lifetime.⁴¹ Patients treated with immunosuppressive drugs and individuals with HIV have an increased risk for developing HZ. Asymptomatic periodic release of VZV from the ganglia, which occurs throughout an individual's lifetime, as well as periodic exposures to persons with varicella, boost the cell-mediated immune response to VZV, which in turn delays the occurrence of HZ for decades. Studies have suggested that adults who live with children or who come into contact with them through their work have a lower risk of developing HZ than those adults who have infrequent contact with children.⁴²
- 4.2.3. Herpes zoster ophthalmicus (HZO) is defined as HZ involvement of the ophthalmic division of the fifth cranial ([trigeminal](#)) nerve, and typically presents with a vesicular skin rash within this distribution. Rarely, patients may develop the ophthalmic symptoms of HZO without an accompanying skin rash. HZO accounts for approximately 10-20% of all cases of HZ. Without antiviral treatment such as acyclovir, about half of patients with HZO would develop ocular involvement but this proportion is reduced to 20-30% for patients who receive early antiviral drug treatment (within 72 hours of rash onset). Involvement of the cornea becomes particularly likely when the herpetic rash involves the tip of the nose (Hutchinson's sign), as both areas are supplied by the nasociliary branch of the first division of the trigeminal nerve. However, the risk of ophthalmic complications is not related to age or severity of the skin rash.⁴³ The range of ophthalmic involvement and complications includes conjunctivitis, epithelial or stromal keratitis, episcleritis, scleritis, uveitis, optic neuritis, retinitis, ocular motor palsies, and [neurotrophic keratopathy](#). Some complications may develop months or years after the acute phase. If serious complications are not diagnosed and treated adequately, the patient's sight may be affected permanently. Some studies have proposed a greater risk of chronic postherpetic pain in patients with HZO as compared to HZ elsewhere, but this association has not been demonstrated consistently.

4.3. Toxoplasmosis

- 4.3.1. **Toxoplasmosis** is an infection caused by *Toxoplasma gondii*, a protozoan parasite. The condition is considered in the Synopsis *Biological Diseases of Protozoal Origin*. Members of the cat family act as the definitive hosts. The course of disease in immunocompetent adults is usually asymptomatic and self-limiting. However, eye involvement, which is termed **ocular toxoplasmosis (OT)**, can result in permanent visual impairment and blindness. *Toxoplasma gondii* occurs worldwide but prevalence of infection varies with the population group and geographic location. The organism is estimated to infect at least 10% of adults in northern temperate countries and more than half of adults in Mediterranean and tropical countries. The lifetime risk of symptoms resulting from OT is very much lower, having been estimated to range from 18 in 100,000 in people born in the United Kingdom to 382 in 100,000 in people born in West Africa.
- 4.3.2. OT may be unilateral or bilateral and predominantly involves acute chorioretinitis, characterised by severe inflammation and necrosis. The condition may keep recurring, thus increasing the chances of permanent damage. Toxoplasmosis constitutes the most common cause of posterior uveitis in immunocompetent subjects. Bilateral disease is found in around 22-40% of patients.⁴⁴
- 4.3.3. OT may be [congenital](#) or acquired postnatally i.e. at any time after birth. The birth prevalence of congenital toxoplasmosis ranges from one to ten per 10,000 live births. Maternal infection acquired before gestation poses little or no risk to the foetus. However, primary infection acquired during pregnancy, especially in the first or second trimester, may cause severe congenital damage and can result in death of the foetus. By contrast, maternal infection in the last trimester, where rates of transmission are more than 60%, usually results in a normal appearing newborn. Here infection may initially go unnoticed but, if untreated, the child can develop chorioretinitis later.⁴⁵ The risk of chorioretinitis for congenital toxoplasmosis has been estimated at approximately 20% up to 6 years of age, but lesions can occur for the first time in adolescence. Given that congenital toxoplasmosis is approximately 1000 times less common than postnatally acquired infection, it follows that most cases of toxoplasmic chorioretinitis are the result of postnatal disease.⁴⁶
- 4.3.4. Primary postnatally acquired infection is usually subclinical but cervical [lymphadenopathy](#) or ocular disease may be present in some patients. More commonly, OT manifests during the chronic phase of the disease. Clinically, active OT appears as solitary or multiple creamy-white focal retinal lesions, overlain with an intense [vitreal](#) inflammatory reaction. In the case of recurrent disease, old pigmented chorioretinal scars are present in either eye, and the active lesions are often recorded at the borders of these scars. Anterior uveitis is also a common finding. Symptoms, which include sudden onset of discomfort or pain in the eye, floaters, visual loss, and photophobia, mainly resolve spontaneously within six to eight weeks.⁴⁷ Although the diagnosis is based predominantly on clinical findings, this may be supported by the laboratory detection of antibodies and *T. gondii* DNA.

- 4.3.5. The prognosis of OT is generally favourable in immunocompetent individuals.⁴⁸ Nonetheless, there is a risk of loss of vision, primarily associated with episodes of recurrent disease. Permanent visual impairment occurs when lesions affect the vision-critical structures at centre of the retina, including the [macula](#) and optic disk, if there is damage to the eye from inflammation, or if there are complications such as retinal detachment or [neovascularisation](#). Peripheral scars may cause field loss but do not impair central visual acuity.⁴⁶
- 4.3.6. Humans generally acquire the infection by ingestion of food or water that is contaminated with oocysts that have been shed by cats, or by eating undercooked or raw meat that contains tissue cysts. Following ingestion, the organism is disseminated via the bloodstream and infects many tissues, including the eye, central nervous system, skeletal and heart muscle, and placenta.⁴⁷ The risk of ocular involvement has been estimated to be 0.3-0.7% after one year for postnatally acquired infection, but may be as high as 3%.⁴⁶ The only risk factor to be identified as yet for the development of ocular involvement in the wake of postnatally acquired infection is immunosuppression, e.g. people with AIDS or those receiving immunosuppressive treatment.
- 4.3.7. *T. gondii* may also be transmitted by organ transplantation e.g. heart, heart-lung, kidney, liver, and liver-pancreas transplants. Rarely, infection is transmitted by transfusion of blood products. Infections in laboratory personnel have arisen accidentally by contact with contaminated needles and glassware or with infected animals.⁴⁵
- 4.3.8. Initial presentation occurs between the ages of 15-35 years in around 60% of patients. For most patients, their exact age on contracting OT remains unknown, because old subclinical chorioretinal scars are usually detected at the time of first clinical presentation with active disease. Furthermore, for presentations during the chronic phase, it can be impossible to distinguish congenital from postnatal infection, as the appearance of toxoplasmic chorioretinitis is similar in both instances.⁴⁵ Moreover, laboratory methods cannot differentiate between congenital and postnatal infection. In one study, recurrences were reported in 79% of patients followed for more than 5 years, occurring predominantly in a previously affected eye (with old scars) and only rarely in a previously healthy contralateral eye.⁴⁴
- 4.3.9. Following the initial infection, the parasite forms latent cysts that remain within the retina. Recurrent toxoplasmic chorioretinitis arises when these tissue cysts release live organisms that invade and destroy retinal cells, stimulating an inflammatory reaction and resulting in the formation of new, clinically apparent chorioretinal lesions. The factors responsible for the reactivation of disease in otherwise healthy individuals remain unknown. It has been proposed that tissue cysts periodically rupture spontaneously, possibly from senescent changes.⁴⁹
- 4.3.10. No specific associations that herald the onset of recurrences have been identified.⁴⁴ The timing of recurrences cannot be predicted, although they tend to occur in clusters over time. The recurrence risk appears to be highest immediately after an episode, and then reduces with the increasing passage of time from the last episode of active disease. Nonetheless, a risk of recurrence remains and, as this risk rises again after each recurrence, a patient can develop

a cluster after a prolonged disease-free interval.⁵⁰

- 4.3.11. In one study, complications developed in nearly half (44%) of patients. These complications included cataracts, retinal detachment, anterior uveitis, ischaemic retinal areas, [cystoid macular oedema](#), optic nerve atrophy, and posterior [synechiae](#). Legal blindness (defined as the best-corrected visual acuity of the affected eye $\leq 6/60$) in one or both eyes occurred in 24% of patients. Risk factors for visual loss included congenital infection, OT manifesting during the acute phase of systemic infection, central location and/or extensive retinal lesions, and the erroneous treatment with corticosteroids without a covering shield of antiparasitic drugs.⁴⁴
- 4.3.12. Episodes of OT infection in immunocompetent patients are ultimately self-limiting. Antibiotic treatment, with or without the addition of corticosteroids, is frequently prescribed to patients with acute toxoplasma chorioretinitis, especially those with a severe inflammatory response or proximity of retinal lesions to the [macula](#) or optic disk. However, there is no strong evidence available that antibiotics in the short or long-term prevent vision loss in most patients with toxoplasmic chorioretinitis, although there is weak evidence that long-term treatment may reduce the rate of recurrence.^{47,49}

5. Prognosis

- 5.1. Topical ophthalmic preparations with appropriate antimicrobial activity are the mainstay of treatment for most eye infections. Depending on the site and severity of the infection, the agent may be administered as drops, ointment, subconjunctival injection, or intraocular injection. Supportive measures and other therapeutic interventions including topical corticosteroids are introduced when indicated. Surgical intervention and systemic drugs, such as oral corticosteroids and immunosuppressive agents, are used in some circumstances. Any contact lens wearer who experiences pain or redness of the eye should remove the lens immediately. More detailed discussion of the treatment of the various forms of acute eye infection is outwith the scope of this Synopsis.
- 5.2. **Conjunctivitis.** Most cases of viral or bacterial conjunctivitis are either self-limiting or respond readily to treatment. Even for patients with serious conjunctival infection (i.e. chlamydial conjunctivitis, hyperacute bacterial conjunctivitis), the prognosis is very good as long as they are referred quickly for specialist treatment.
 - 5.2.1. **Epidemic keratoconjunctivitis** is generally self-limiting and tends to resolve spontaneously within 1-3 weeks. In some cases, corneal opacities can persist for a few weeks to months (rarely up to 2 years). This phenomenon can significantly decrease visual acuity and cause glare symptoms. In rare instances, conjunctival scarring and [symblepharon](#) can occur.
- 5.3. **Keratitis and corneal ulcers** cause scarring of the cornea, which if in the visual axis, will decrease visual acuity. The severity of microbial keratitis ranges from a condition that resolves quickly with intensive antibiotic therapy to one that requires long periods of hospitalisation and surgery for restoration of vision.
 - 5.3.1. The majority of cases of bacterial keratitis respond to empirical broad-spectrum antibiotics, generally administered topically. It is usually possible to avoid serious visual impairment with prompt treatment, including adjunctive surgery in some cases. Antibiotic therapy should not be delayed for any reason, as sight-threatening complications can occur rapidly. The result of any subsequent positive culture will guide the choice of appropriate antibiotic therapy. Controversy remains regarding the use of topical corticosteroids in addition to antimicrobial therapy as a means of combating host corneal inflammatory responses.⁴ Corneal transplant ([penetrating or lamellar keratoplasty](#)) may be required in cases of severe infectious keratitis that do not respond to medical treatment, often where the infection is caused by *Acanthamoeba* or fungi.
 - 5.3.2. Loss of vision of 2 or more lines of best corrected visual acuity is relatively infrequent in contact lens-related microbial keratitis, reported in 11-13% of cases. The prognosis tends to be worse in cases that develop in the absence of contact lens wear.²⁶ Disease outcome may also be influenced considerably by modifiable factors such as delays in receiving appropriate therapy, especially if greater than 12-24 hours, and by initial inappropriate therapy.⁵¹
 - 5.3.3. The outcome in microbial keratitis is related to the severity of the presenting signs e.g. depth of the infiltrate, presence of corneal [neovascularisation](#), and presence of anterior chamber inflammation.⁸ The causative organism is a

dominant factor in determining disease severity in contact lens-related microbial keratitis. Those cases with an environmental causative organism, i.e. Gram-negative bacteria, *Nocardia*, amoebic or fungal organisms, are more likely to result in vision loss. In particular, *Acanthamoeba* keratitis and fungal keratitis can be subject to delayed diagnosis leading to ineffective treatment before the correct diagnosis is made. Most patients with *Acanthamoeba* keratitis are misdiagnosed initially as having herpes simplex keratitis. Prevention based on education remains the most effective approach to contact lens-related microbial keratitis, focusing on the optimal care of contact lenses, periodic cleansing and replacement of lens storage cases, and avoidance of exposure to tap water or other environmental sources of water during contact lens wear.

5.3.4. Corneal ulcers may thin the cornea sufficiently to cause perforation of the eye and endophthalmitis. Severe corneal scarring or thinning may require a corneal transplant to restore vision. Administration of ophthalmic antibiotic preparations is now practised routinely as a prophylactic measure following many surgical procedures e.g. cataract extraction.

5.4. **Episcleritis and scleritis.** The ocular complications of episcleritis tend to be mild (mainly mild anterior uveitis) and not associated with a loss of visual acuity. In contrast, ocular complications occur in around 50-60% of patients with scleritis. These complications include keratitis, uveitis, cataract, angle-closure or open-angle glaucoma, [cystoid macular oedema](#) and exudative retinal detachment. Loss of 2 or more lines of visual acuity has been reported in 16-37% of patients with scleritis. Visual loss is generally greater in patients with an underlying systemic disease, whilst necrotising scleritis results in greater visual loss than the non-necrotising form. In addition, loss of vision is more common in posterior scleritis than in anterior scleritis.^{29,30,52}

5.4.1. Infectious scleritis is often difficult to treat because penetration of antimicrobials into the avascular necrotic sclera is poor. However, improved success has been achieved with surgical intervention in addition to antimicrobial therapy, or by using a combination of parenteral antimicrobials.³⁰

5.5. **Anterior uveitis.** Prompt treatment is needed to prevent serious complications such as cataracts. [Synechiae](#) may form, and these can produce an irregularly shaped pupil and subsequently lead to angle-closure glaucoma.

5.6. **Retinitis or chorioretinitis,** because they affect the photoreceptors, decrease visual acuity if they involve the [macula](#), or may cause visual field defects if the peripheral retina is involved. Visual impairment may also result from other complications including cystoid macular oedema, retinal detachment, and neovascularisation.

5.7. If not treated immediately and aggressively, **endophthalmitis** usually results in complete loss of vision in the affected eye. [Vitreotomy](#) is undertaken in some cases. Even so, approximately 50% of patients suffer total loss of vision in the affected eye.⁵³ The visual prognosis is generally worse for Gram negative and fungal infections than for Gram positive infections, and worse for endogenous than exogenous endophthalmitis. The final visual outcome tends to relate to the severity of the initial loss. Enucleation may be required in the case of a blind and painful eye. The associated mortality rate in endogenous endophthalmitis is around 5% due to extraocular infection. Prophylactic antibiotic administration is advocated in relevant situations to reduce the risk of postoperative and post-traumatic endophthalmitis.⁶

6. Summary

- 6.1. A wide variety of bacteria, viruses, fungi, and parasites can cause eye infections, and various different structures within the eye can become affected. The frequency of these various conditions ranges from the common to the rare, whilst severity ranges from generally self-limiting conditions to those that threaten sight. Cases of infectious keratitis, scleritis, uveitis and endophthalmitis fall into the latter category.
- 6.2. Microbial keratitis is a leading cause of vision loss but is rare in the absence of predisposing factors. The main associations are with contact lens wear, ocular trauma, and ocular surface disease. Around one-third to two-thirds of new cases of microbial keratitis are associated with contact lens wear. The main risk factor is overnight wear, and soft contact lenses are associated with a significantly higher risk than hard lenses. Those cases with an environmental causative organism, i.e. Gram-negative bacteria, *Nocardia*, amoebic or fungal organisms, are more likely to result in vision loss.
- 6.3. Herpes simplex virus (HSV) is the viral infection that is most commonly associated with serious corneal disease. Nevertheless, clinical ocular disease develops in less than 1% of the population infected with the virus. Patients with herpetic eye infection are at risk of recurrent eye disease throughout their lives, and recurrent attacks of keratitis may lead to scarring, decreased corneal sensation, and vision loss. There is some evidence that recurrences could be triggered by UV light and by recent ocular surgery, but no other exposure variables have been conclusively linked to recurrences.
- 6.4. Herpes zoster ophthalmicus, which accounts for approximately 10-20% of all cases of herpes zoster, occurs when the ophthalmic division of the fifth cranial (trigeminal) nerve is involved. Various structures within the eye can be affected and postherpetic neuralgia may ensue. The incidence of herpes zoster increases with advancing age and with immunosuppression.
- 6.5. The most common association in scleritis is with a variety of autoimmune conditions although the condition can also be triggered by certain infections.
- 6.6. Toxoplasmosis constitutes the most common cause of posterior uveitis in immunocompetent subjects. The infection is generally acquired by ingestion of food or water that is contaminated with oocysts shed by cats, or by eating undercooked or raw meat that contains tissue cysts. Only a small proportion of patients goes on to develop ocular toxoplasmosis. For them, there is a risk of loss of vision, primarily associated with episodes of recurrent disease. The factors responsible for the reactivation of ocular disease in otherwise healthy individuals remain unknown.
- 6.7. Endophthalmitis constitutes an ophthalmic emergency. Infection may be endogenous or exogenous, with postoperative and post-traumatic cases being the most common. Vision may be lost totally, even with aggressive treatment.

7. Related Synopses

Biological Diseases of Protozoal Origin

Cataract

Eye injuries

Glaucoma

8. Glossary

adnexae	Appendages.
anterograde	Moving or extending forwards.
autoimmune disease	Illness that occurs when the tissues are attacked by the body's own immune system.
axonal	Pertaining to an axon, the long process found in each nerve that carries outgoing signals from the cell body.
blepharitis	Inflammation of the eyelid.
blepharospasm	Twitching of the eyelid.
chemosis	Fluid accumulation (oedema) of the conjunctiva, forming a swelling around the coloured portion of the eye (iris).
collagen vascular diseases	A group of generalised autoimmune diseases (q.v.) affecting connective tissue, including rheumatoid arthritis, systemic lupus erythematosus, scleroderma, dermatomyositis, and polyarteritis nodosa.
congenital	Pertaining to conditions present at birth.
cystoid macular oedema	Swelling of the macula (q.v.) due to leakage of fluid from the capillary blood vessels of the retina.
dacryocystitis	Inflammation of the lachrymal (tear secreting) gland.
dermatomal	Referring to the area of skin that is innervated by a single sensory nerve.
dysuria	Painful or difficult urination.
endogenous	Developed or originating within the organism, or arising from causes within the organism.
exogenous	Developed or originating outside the organism.
human leukocyte antigen B-27 (HLA B-27)	An antigen found on the surface of white blood cells in some people. Those individuals who have this protein exhibit an increased risk of developing certain autoimmune diseases (q.v.), including uveitis, Reiter's syndrome and ankylosing spondylitis.
hypopyon	An accumulation of pus cells in the anterior chamber of the eye, sometimes visible without the aid of magnification.
idiopathic	Of unknown causation.

inclusion conjunctivitis	A form of conjunctivitis that occurs with <i>Chlamydia trachomatis</i> infection and is characterised by follicles (small sacs) on the conjunctiva lining the eyelids.
LASIK surgery	Acronym for laser in situ keratomileusis, a form of eye surgery that utilises a laser to reshape the cornea in order to correct refractive errors including myopia (nearsightedness), hyperopia (farsightedness) and astigmatism.
lymphadenopathy	Abnormal enlargement of the lymph nodes.
macula	A small, highly sensitive area towards the centre of the retina, responsible for the detailed central vision that is required for activities such as reading.
mucopurulent	Containing both mucus and pus.
mucous membrane	A membrane that lines a body cavity and is covered in mucus, a smooth, slimy fluid composed of secretions, white blood cells, desquamated cells, and various salts.
neovascularisation	The formation of new blood vessels, especially in tissues where circulation has been impaired by trauma or disease.
neurotrophic keratopathy	A degenerative disease caused by conditions (including herpetic infection) that decrease corneal sensitivity. As a result, the cornea becomes more susceptible to injury.
penetrating keratoplasty	Corneal transplant with replacement of all layers of the cornea but retaining the peripheral cornea (cf. lamellar keratoplasty in which only the anterior layer of the cornea is used).
photophobia	Abnormal sensitivity to light.
pterygium	A superficial growth of vascular tissue radiating from the cornea over the surface of the eye.
ptosis	Drooping of the upper eyelid.
purulent	Consisting of or containing pus.
symblepharon	Adhesion of one or both eyelids to the eyeball.
synechia (-ae)	Adhesion of the iris to either the cornea or the capsule of the lens.
tarsal	Pertaining to the tarsus, a plate of dense connective tissue or cartilage in the eyelid.

tearing	A condition in which tears accumulate in the eye and trickle over the cheek.
trichiasis	An eye condition in which the eyelashes are turned in on the eyeball and thus produce constant irritation by the motion of the lids.
trigeminal	Relating to the 5 th pair of cranial nerves; the trigeminal nerves divide into three main branches, serving the orbits, jaws and parts of the mouth respectively.
vesicular	Made up of vesicles - small elevated lesions filled with clear fluid.
vitreal	Pertaining to the vitreous humour, the transparent gel-like substance that fills inner portion of the eyeball between the lens and retina.
vitrectomy	Removal of all or part of the vitreous. A procedure used in the treatment of some cases of endophthalmitis as well as some other ophthalmic conditions.

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