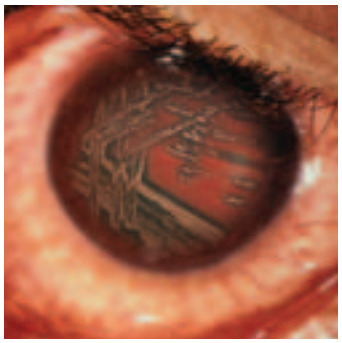
BUG EYED



R A Armstrong reveals the bugs responsible for bacterial eye infections together with their treatment

THE SURFACE OF THE EYE is rich in proteins, carbohydrates, lipids, and electrolytes and consequently, supports a rich commensal flora of microorganisms.

Species commonly present on the surface of the eye include diptheroids, *Moraxella*, *Staphylococcus*, and *Streptococcus*. The presence of a commensal flora, together with the physical action of the lids and the chemical effect of tears, normally prevent colonization by pathogenic bacteria. Nevertheless, infections of the external structures of the eye are common and result from either the acquisition of a particularly virulent microorganism or uncontrolled growth of an existing bacterium due to lowered host resistance. In addition, the globe of the eye is relatively impermeable to microorganisms, but if breached by trauma or surgery, the contents of the eye, such as the aqueous and vitreous, also provide an excellent medium for the growth of bacteria and subsequent infection. Furthermore, an infection within the eye may be 'endogenous', i.e., a consequence of a systemic disease transmitted to the eye via the blood stream or lymphatic system. This article is a brief introduction to the eye infections most commonly caused by bacteria (summarised in the Table on page 29) together with their treatment.

Eye infections caused by bacteria

The eyelids

Infection and subsequent inflammation of the eyelashes, termed blepharitis, and often caused by *Staphylococcus epidermidis*, is one of the most common infections seen by ophthalmologists, a significant proportion of cases being secondary to infection of the meibomian (fat) glands of the lids. Blepharitis can also lead to the development of a 'stye', a localised painful infection of the follicles, or a meibomian gland cyst characterised by inflammation of the lids and accompanied by a white discharge from the glands themselves. Blepharitis caused by *Staphylococcus* may also lead to a chronic inflammation of the outer membranes of the eye, *viz.*, conjunctivitis and keratitis affecting the conjunctiva and cornea respectively. In elderly people, or occasionally in immune depressed patients,

the skin of the lids may become involved in an acute infection called 'erysipelas' caused by species of *Streptococcus* toxic to blood cells.

The conjunctiva

The conjunctiva is the outer membrane of the eye and covers the white fibrous sclera. This membrane is continuous with that of the cornea and also extends on to the upper and lower lids. Infection of this membrane is often exogenous and due to the introduction of a virulent bacterium or the proliferation of an opportunistic species as a result of lowered host resistance. The result is an acute conjunctivitis (Fig 1). Many types of bacteria may be responsible for this condition, the most important being species of *Pneumococcus*, *Streptococcus*, *Staphylococcus*, *Meningococcus*, and *Gonococcus*. In addition, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, and *Chlamydia trachomatis* have been identified as pathogens causing conjunctivitis in early infancy ('*ophthalmia neonatorum*' Krohn *et al.*, 1993).

Studies have suggested that these bacteria are often transmitted to the eyes of the new born after birth and are not acquired from the birth canal of the mother. Uncomplicated bacterial conjunctivitis in adults can be treated with a variety of compounds including chloramphenicol and norfloxacin. Conjunctivitis caused by *Chlamydia* can be treated with tetracycline, erythromycin or quinoline derivatives. Generally, however, in the treatment of uncomplicated conjunctivitis, there is little difference in the effectiveness of the commonly used antibacterial agents (Leeming 1999).

The cornea

The cornea is the transparent region of the eye through which light is transmitted to the retina. *Staphylococcus aureus*, *Streptococcus pneumoniae* and Gram-negative coliform bacteria are the most important causes of inflammation of the cornea and of corneal ulceration. Tissue destruction results from a combination of secreted bacterial enzymes, toxins, and host immune reactions with patients using extended wear contact lenses being at particular risk of this type of infection (Fleiszig and Efron 1992). The organism most commonly associated with a corneal ulcer underneath a contact lens is *Pseudomonas aeruginosa* (Fig 2), the virulence of which may be attributable to the formation of a novel exoprotein protease IV (O'Callaghan *et al.*, 1996). Untreated, the cornea may be penetrated, and this can result in a permanent loss of vision in some cases. *Flavobacterium indologenes* (Lu and Chan 1997) and species of Serratia (Parment 1997) are also possible causes of keratitis. In addition, in *Mycobacterium tuberculosis* infection, characteristic nodules may form in the cornea with the development of new blood vessels in the superficial and deeper layers followed by corneal scarring. Bacterial keratitis due to Gram-positive cocci can also occur in children and predisposing factors for this condition include trauma, severe systemic illness, contact lens use, non-inflammatory disorders of the cornea, and previous ocular surgery. Keratitis caused by Gram-positive bacteria is treated with vancomycin and Gram-negative infections with gentamycin. In addition, ciprofloxacin, a broad-spectrum antibiotic, may be used in some circumstances.

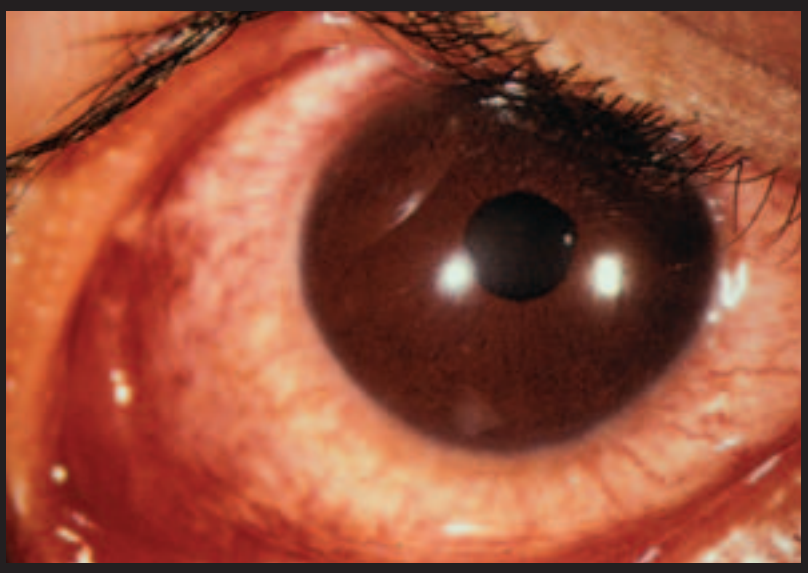


Fig 1. *An acute conjunctivitis caused by bacterial infection. The conjunctiva on the surface of the eye and of the lids is swollen and the eye is red. (Reprinted with permission from Mandell G.L. and Bleck T.P. 1995)*

Anterior segment of the eye

The commonest causes of bacterial infection within the eye are intraocular surgery, penetrating injury, or spread from the blood stream. The anterior segment of the eye contains the aqueous, a substance rich in carbohydrates, sugars, proteins, and inorganic nutrients. Inflammation may affect individual structures within the eye, e.g., iritis (inflammation of the iris), but the reaction rarely remains confined to a single region and often results in a more general inflammation (often termed 'endophthalmitis' if the infection remains contained within the eye). The inflammatory process progresses rapidly and without treatment, a total loss of vision may be the result. In addition, the ocular surface contributes significantly to the transmission of microbes during cataract surgery; the most frequently recovered organisms being *Staphylococcus epidermides* and *Propionibacterium acnes* (Fig 3). Delayed-onset postoperative endophthalmitis can also be caused by species of Actinomyces (Roussel *et al.*, 1991) and *Corynebacterium* (Salvanet-Bouccara *et al.*, 1992). Current therapies for the treatment of intraocular infection are often unsuccessful. Topical antibiotics, given before an operation, may be ineffective at eradicating microbes in the anterior chamber. Hence, whether or not a patient develops an inflammatory disorder after eye surgery may

depend, in part, on the degree of host resistance. Intravitreal vancomycin can be used to treat *Propionobacterium acnes* endophthalmitis. The sensitivity of *Corynebacterium* endophthalmitis to antibiotics, however, varies greatly (Salvanet-Bouccara *et al.*, 1992).

The vitreous body

The vitreous body is the gel-like connective tissue that occupies the posterior segment of the eye. Inflammatory reactions within the vitreous (vitritis) result in liquefaction, opacification, shrinkage, and tissue necrosis. Bacterial infections of the vitreous may progress very rapidly and often result in an abscess. Initially, the vitreous is invaded by neutrophils and eosinophils but later lymphocytes and phagocytes appear and there may be proliferation of fibroblasts encysting the developing abscess. Vitritis may also be a primary manifestation of ocular syphilis in patients who are HIV positive (Kuo *et al.*, 1998).

The optic disc and nerve

The optic nerve leaves the eye at the optic disc ('blind spot') and conveys visual information from the eye to the visual cortex of the brain. The optic nerve can be affected by infections spreading from the eye, orbit, or brain resulting in inflammation of the optic disc (papillitis). Tissue damage elsewhere in the eye results in the release of toxins that diffuse into the optic nerve head causing swelling of the disc and accumulation of lymphocytes around blood vessels. Bacteria such as *Staphylococcus*, *Pneumococcus*, *Meningococcus*, and *Mycobacterium* are often associated with this condition.

The orbit

Acute inflammation of the orbit ('orbital cellulitis') is usually derived from a source of infection in the paranasal sinus, the eye, teeth, or middle ear. A major cause in adults is *Staphylococcus aureus* infection originating in an adjacent sinus. In children, however, the condition may be caused by *Haemophilus influenzae* but the incidence of this bacterium has decreased over the last decade with species of *Streptococcus* now predominating (Donahue and Schwartz 1998). Preorbital cellulitis caused by *Staphylococcus aureus* can be treated with ampicillin.

Conclusions

There have been significant changes in the micro-organisms associated with the eye over the last 20 years, e.g., the incidence of *Staphylococcus aureus* has declined (Huberspitzy *et al.*, 1992) but there has been a resurgence of ocular tuberculosis and syphilis. In addition, contact lens wear has encouraged the development of *Pseudomonas*, *Serratia*, and *Acanthamoeba* infections. Bacteria, not normally associated with the ocular flora, e.g., *Flavobacterium indologenes*, have also been isolated from the eye (Lu and Chan 1997). Hence, continuous monitoring of the ocular flora is an essential part of predicting future eye infections.

Interactions between different microorganisms at the eye surface may be important in determining whether a patient develops a particular infection. For example, a layer of the bacterium *Pseudomonas* in a biofilm on a contact lens may enhance the adsorption of the protozoan *Acanthamoeba* and increase the risk of inflammation of the cornea (Simmons *et al.*, 1998). Hence, basic research into the interactions of microbes at the ocular surface is needed to understand the risk factors that may encourage a particular ocular infection.

A major concern is that bacteria that cause eye infection are acquiring resistance to current antimicrobial therapies. Approximately 75% of ocular *Staphylococcus* species are now resistant to tetracycline; one of the most commonly used preparations. In addition, considerable resistance to antibiotics has been reported in recent years in bacteria causing keratitis. In bacterial isolates from corneal ulcers, 50% of bacteria were resistant to all the common antibiotics with the exception of the fluoroquinolines (Satpathay and Vishalakshi 1995). In addition, *Flavobacterium indologenes* has developed resistance to most antibiotics (Lu and Chan 1997) while *Streptococcus pneumoniae* and some strains of *Pneumococcus* are resistant

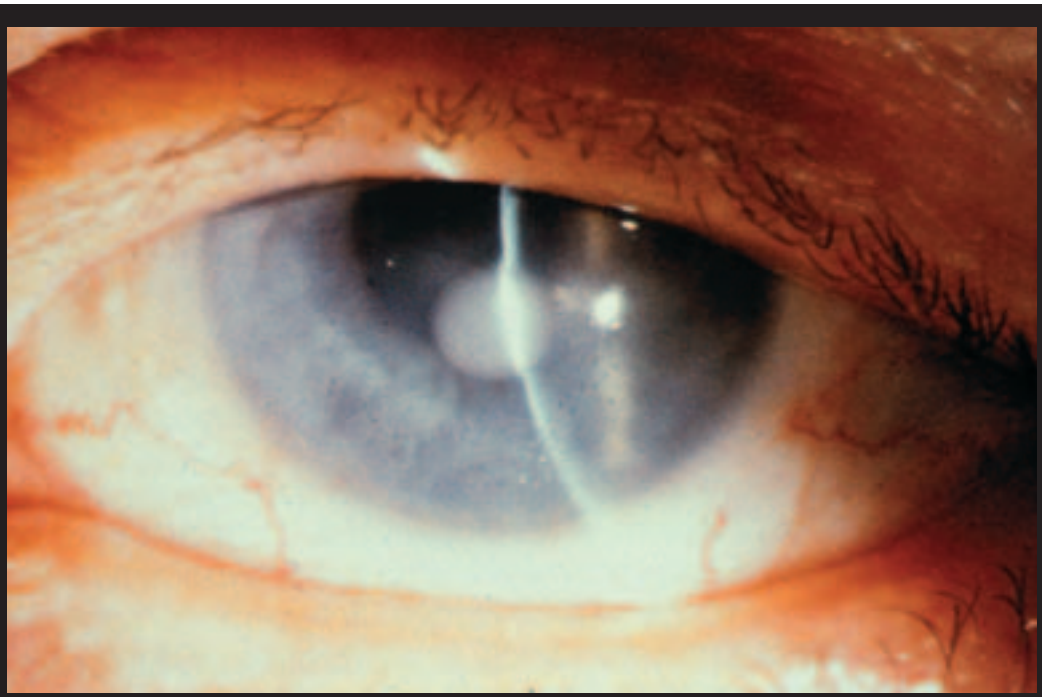


Fig 2. *A bacterial corneal ulcer under a contact lens. The most common organism associated with this condition is Pseudomonas (Reprinted with permission from Mandell G.L. and Bleck T.P. 1995)*

Major eye infections caused by bacteria

Region	Eye Infections
Lids, Lacrimal apparatus	*Staphylococcus blepharitis*, esp. *S. epidermidis*. May develop into a stye or meibomian gland cyst. Syphilis *(Treponema).* Erysipelas caused by haemolytic *Streptococcus*.
Conjuctiva	Acute conjunctivitis caused by *Pneumococcus, Streptococcus, Staphylococcus*, or *Gonoccocus*. Granulomatous inflammation associated with tuberculosis and syphilis. Conjunctivitis in infants caused by *Haemophilus influenzae, Streptococcus pneumoniae, Klebsiella pneumoniae, Neisseria,* or *Chlamydia.*
Cornea	Keratitis and corneal ulceration caused by *Staphylococcus aureus, Streptococcus pneumoniae, Pseudomonas, Mycobacterium, Flavobacterium indologenes,* or *Serratia.*
Uvea	Endophthalmitis caused by *Propionibacterium acnes, Staphylococcus epidermides, Actinomyces* and *Corynebacterium.* Purulent uveitis caused by *Staphylococcus.* Endogenous granulomatous uveitis associated with leprosy and tuberculosis.
Vitreous Retina	Inflammation and abscess formation. Acute septic retinitis. Chronic bacterial retinitis associated with tuberculosis, leprosy, or syphilis.
Optic disc/nerve	Papillitis and optic neuritis caused by *Staphylococcus, Pneumococcus, Meningococcus*, or *Mycobacterium.*
Orbit	Orbital cellulitis caused by *Staphylococcus aureus, Haemophilus influenzae,* or *Streptococcus. Actinomyces* infection.

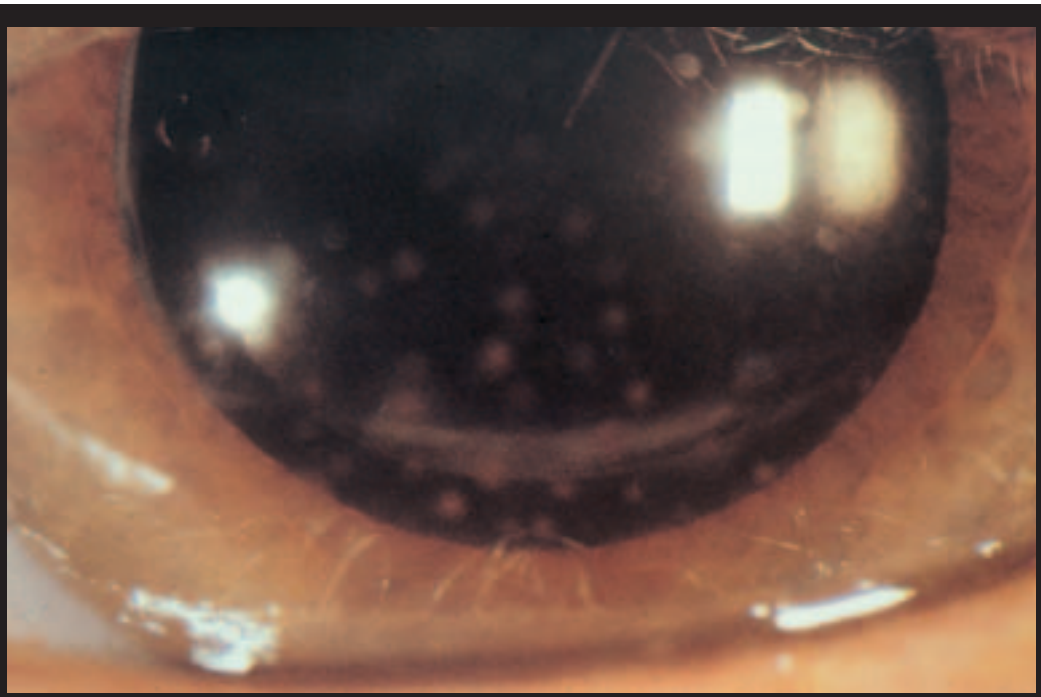


Fig 3. *Inflammation of the anterior segment of the eye associated with cataract surgery and caused by Propionibacterium acnes. The image shows inflammatory deposits on the inner surface of the cornea and a white plaque-like infiltrate associated with the lens implant. (Reprinted with permission from Mandell G.L. and Bleck T.P. 1995)*

to penicillin. Furthermore, approximately one third of *Staphylococcus* strains are resistant to gentamycin. Hence, new antibiotics will be required in future to combat many of the commonest pathogenic agents that cause ocular disease.

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Additional references are available on request. Please contact the Editor.