Common corneal conditions

A patient presenting with reduced vision and ocular pain or discomfort may have one of many common corneal conditions. Accurate and prompt diagnosis is needed to prevent permanent visual loss. Management should be tailored to the specific problem and its severity.

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The cornea is the transparent, tough and exquisitively sensitive watchglass of the eye. It retains a precise shape and is maintained as a clear and lubricated optical surface by the tears, eyelids and stem cells.

Knowledge of corneal anatomy and physiology is helpful in understanding corneal disorders and their pathophysiology. The normal cornea is composed of five layers (the epithelium, Bowman's layer, stroma, Descemet's membrane, and the endothelium) and richly innervated by sensory nerves from the trigeminal nerve. The limbal region separates the cornea from the conjunctiva and is thought to be the source of the stem cells whose progeny regenerate the corneal epithelium.

Patients with corneal conditions typically suffer from reduced vision and ocular pain or discomfort. The most prevalent eye disease – dry eye – may involve the cornea,[1-3] and ulcers, infection and contact lens disorders commonly afflict it. A careful history and examination will usually reveal the diagnosis; some useful tips for rural GPs are listed in the box on page 23. Treatment should be tailored to the condition diagnosed and its severity. Permanent visual loss from corneal scarring, infection, and/or melting can be avoided by prompt diagnosis and management.

Dry eye

Dry eye may affect up to one in five people, and is increasingly common in the elderly. It interrupts the daily activities of sufferers and predisposes the eye to infection.

In dry eye, damage to the ocular surface and symptoms are caused by tear deficiency or excess evaporation.[4] Up to 80% of patients with severe

IN SUMMARY

- **Corneal disorders are important causes of visual loss and ocular pain or discomfort. Dry eye is the most prevalent eye disorder.[1-3]**
- **Corneal ulceration is commonly due to trauma. In such cases, the upper eyelid should be everted during examination to exclude the presence of a hidden foreign body.**
- **Patients with labial cold sores, patients on topical corticosteroids and patients with atopic eye disease are at risk for herpes simplex keratitis.**
- **Microbial keratitis is an ophthalmological emergency. The diagnosis should always be considered in the contact lens wearer.**
- **Avoid topical corticosteroids for the undiagnosed red eye. Arrange review by an ophthalmologist for diagnosis and, if corticosteroids are used, to monitor for side effects.**
- **Contact lenses can produce a variety of corneal disorders. A history of contact lens wear should always be sought in a patient presenting with a corneal disorder.**

Tips for rural GPs

- When a slit lamp is not available, the direct ophthalmoscope can be used to provide illumination as well as blue and green light for corneal examination. The illuminated cornea can then be viewed with a pair of magnifying loupes or the naked eye.
- Paper strips impregnated with fluorescein (Fluorets) or single use fluorescein 2% (Minims) can be used instead of bottles of fluorescein drops, which usually require refrigeration, to stain the cornea.
- Remember that corneal trauma is a risk factor for microbial keratitis. Fungal keratitis should be considered in patients presenting with agricultural injury.

dry eye have Sjögren's syndrome, an autoimmune condition in which lymphocytic infiltration of the lacrimal and salivary glands leads to dry eyes and mouth.[5] Systemic medications, particularly beta blockers, may produce or exacerbate dry eye.[6]

Diagnosis

There is no single test for dry eye. The diagnosis depends on the identification of key features: symptoms, ocular surface damage and tear film abnormalities.[4,7]

Symptoms

Patients with dry eye may complain of a variety of symptoms. These include the common complaints of conjunctivitis, such as a foreign body sensation and burning, as well as less specific symptoms, such as 'tiring' (ocular fatigue), soreness, and pain in the eyes. Sand or gravel sensation and photophobia are common, and in some patients the photophobia is disabling. Symptoms are typically worse in the evening and are often relieved by closing the eye or using artificial tears.

Ocular surface damage

Damage to the ocular surface can be revealed using special stains on slit lamp examination or by using the direct ophthalmoscope with a magnifier or a pair of magnifying loupes. Staining typically

Dry eye

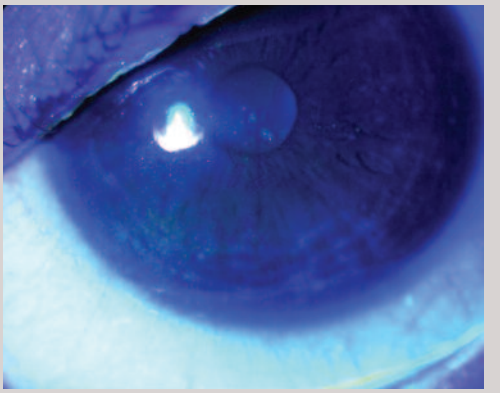

Figure 1. Punctate epithelial erosions on the lower two-thirds of the cornea in dry eye. The erosions have been stained with fluorescein and viewed with light passed through a cobalt blue filter.

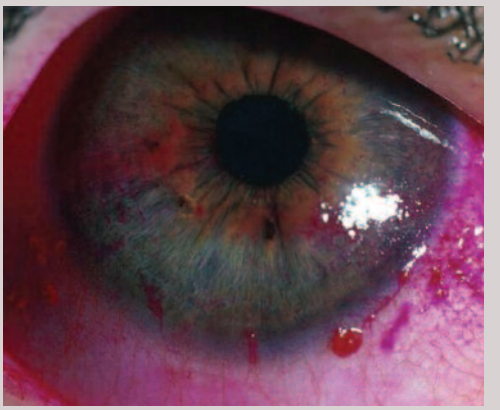

Figure 2. Rose bengal staining of the bulbar conjunctiva in severe dry eye.

occurs in the lower two-thirds of the cornea. Fluorescein reveals areas of epithelial cell loss and is best visualised using light passed through a cobalt blue filter (Figure 1). Typically, rose bengal staining occurs in a triangle (with base at the limbus) on the bulbar conjunctiva – this pattern is practically pathognomonic for dry eye (Figure 2). Rose bengal is found in the nuclei of the epithelial cells and stains dead or injured cells – such staining is best viewed on the slit lamp with a green light. Lissamine green stain may be used instead of rose bengal because it is less irritating, but it is not widely available.[8]

Tear film abnormalities

Schirmer's I test is the most common test used to measure tear secretion by the lacrimal gland. A Whatman #41 paper strip is placed, without anaesthetic, at the outer two-thirds of the lower

eyelid for five minutes and the patient asked to look forward and blink normally. Care should be taken to avoid touching the paper because oils from the skin can contaminate it. After five minutes, the length of the strip made wet by tears is measured. A value of less than 10 mm is considered abnormal; less than 5 mm indicates moderate to severe dry eye.

Tear film instability can be assessed by the tear break-up time, although such measurements may not be reproducible. This is done by instilling fluorescein in the eye and asking the patient to blink and move the eyes (to distribute the dye) and to then close the eyes. The time from re-opening the eyes to the appearance of the first dry spot is then measured. A value of less than 10 seconds may be abnormal.

Tear film hyperosmolarity can distinguish between tear deficient and evaporative states, but there is no simple test that is available for use in routine clinical practice.

Management

Treatment for dry eye should be tailored to the severity of the problem (Table 1). There is no 'single treatment' cure, and patients should be told that therapy is usually needed long term and that compliance will improve their comfort. Dry eye is often associated with blepharitis; in such cases, lid hygiene can improve tear quality and dry eye symptoms.[6]

Mild dry eye can be managed with preserved tear supplements unless they are required more than four times a day – in such cases, nonpreserved supplements should be prescribed to prevent damage to the ocular surface by excessive amounts of preservatives. Lubricating ointments may be beneficial, particularly at night. Increased oral water intake may help.

Moderate to severe dry eye can be difficult to manage, and many patients continue to suffer despite receiving maximal standard therapy. Well designed punctum plugs for tear conservation are available and can be considered if symptoms persist after tear deficiency is confirmed by Schirmer's I test. Disease modification has been tried with corticosteroids and cyclosporin A. Topical corticosteroids may be beneficial in some patients, but monitoring by an ophthalmologist is required for potential side effects (raised intraocular pressure, cataract and microbial keratitis). Recently, topical cyclosporin A has been found to be beneficial; it is available as a commercial preparation (Restasis) under the Special Access Scheme or can be manufactured in a hospital-based pharmacy. The potential for disease modification with oral corticosteroids and oral cyclosporin A (Cicloral, Cysporin, Neoral, Sandimmun) is still uncertain.

Oral pilocarpine can be used for tear stimulation, and may help salivary secretion in Sjögren's syndrome, but systemic side effects may limit its use. Therapeutic contact lenses may favourably modify the ocular surface, but patients will require careful monitoring by the ophthalmologist because of the risks of microbial keratitis. Physiological tear substitutes such as autologous serum drops (which are prepared from a patient's own serum) are beneficial when other therapies have failed, but these are not widely available. Acetylcysteine drops are useful for excessive mucus – they can be prepared at a

Table 1. Management options for dry eye

Mild to moderate
- Preserved tear supplements
- Lubricating ointments
- Increased oral water intake
- Lid hygiene

Moderate to severe
- All management options listed above
- Nonpreserved tear supplements
- Punctal occlusion
- Topical corticosteroids
- Topical cyclosporin A
- Oral pilocarpine
- Autologous serum drops
- Therapeutic contact lens
- Acetylcysteine

Severe
- All management options listed above
- Systemic corticosteroids
- Systemic cyclosporin
- Moisture goggles

Common causes of corneal ulceration

Trauma
A common reason for presentations to eye casualty and general emergency departments.

Neurotrophic
Caused by interruption of the trigeminal nerve supply to the cornea (e.g. after neurosurgery).

Contact lens wear
Caused by trauma during lens handling or by trapped foreign bodies behind lens, deposits on lens or poor lens fitting.

Infection
An infiltrate typically accompanies the epithelial defect.

Recurrent corneal erosion
Spontaneous breakdown of the corneal epithelium, typically in the morning. There may be a history of preceding trauma or corneal dystrophy.

Immune-related
Rheumatoid arthritis is a common cause. Ulceration typically develops in the peripheral cornea.

Corneal ulcers

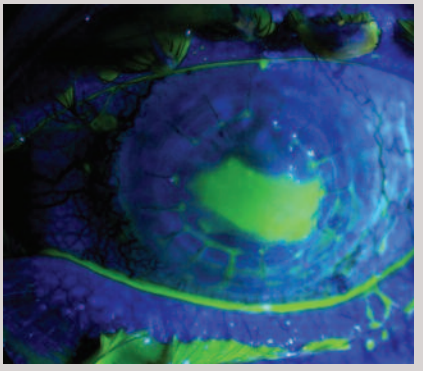

Figure 3. A corneal ulcer following a corneal graft. The ulcer has been stained with fluorescein and viewed with light passed through a cobalt blue filter.

Figure 4. In this case of traumatic corneal ulcer, a foreign body was found on eversion of the upper lid.

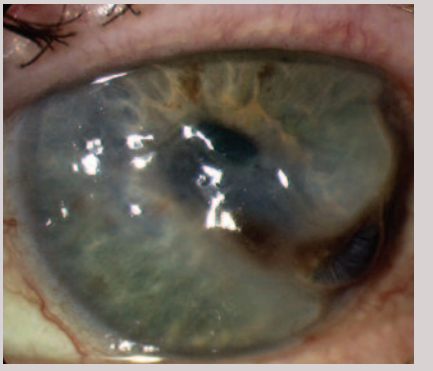

Figure 5. Rheumatoid corneal melting resulting in corneal perforation with iris prolapse.

concentration of 5 or 10% by a hospital-based pharmacy.

Corneal ulcers

A corneal ulcer is a defect in the epithelial cell layer of the cornea. It can be caused by a variety of insults (see the box on page 24).

Diagnosis

Patients with a corneal ulcer complain of reduced vision and ocular pain. The exception is the patient with a neurotrophic corneal ulcer, as these may be painless. The ulcer is best seen using topical fluorescein and a cobalt blue light on the slit lamp; alternatively, a cobalt blue filter on the direct ophthalmoscope can be used (Figure 3). In cases of trauma, the upper lid should be everted to exclude a foreign body (Figure 4).

Management

Unhealed ulcers compromise the integrity of the ocular surface and render the cornea liable to vision-threatening infection, scarring and melting. They should be managed by topical antibiotic ointment, such as chloramphenicol 1% (Chloromycetin, Chlorsig), with or without an eyepad, and frequent review. Topical cycloplegics such as homatropine 2% (Isopto, Minims), cyclopentolate 1% (Cyclogyl, Minims) or atropine 1% (Atropt, Minims) can relieve ciliary spasm and may be given to improve comfort. A therapeutic contact lens may be used, but requires close supervision by an ophthalmologist because of the risk of microbial keratitis. An eyepad should not be used in treatment of infectious ulcers.

Corneal ulcers may be resistant to healing with standard therapy, particularly if the patient has other eye disease (e.g. dry eye). Autologous serum drops, ptosis induced by botulinum toxin type A (Botox, Dysport) or surgery to reduce the size of the palpebral fissure (e.g. tarsorrhaphy) may then be required. Immune-related corneal ulceration may require systemic immunosuppression (Figure 5).

Herpes simplex keratitis

Herpes simplex may cause epithelial (dendritic ulceration), stromal and endothelial disease. The most common cause of dendritic (branching) corneal ulceration is herpes simplex keratitis (Figure 6).

Diagnosis

The patient with herpes simplex type 1 ocular infection typically presents with an acutely painful red eye. A history of similar episodes that typically occur during times of stress and are less severe than the original episode is common. Risk factors include a history of labial herpes (cold sores), topical corticosteroid use and atopic eye disease.

Slit lamp biomicroscopy or illumination with the direct ophthalmoscope can be used in epithelial disease to reveal the presence of a dendritic ulcer staining with rose bengal and/or fluorescein. In stromal or endothelial disease, corneal opacity with or without an epithelial lesion is seen. Corneal vascularisation typically occurs with chronic disease (Figure 7).

Management

Epithelial disease

Treatment for epithelial herpes simplex keratitis involves topical aciclovir 3%

Herpes simplex keratitis

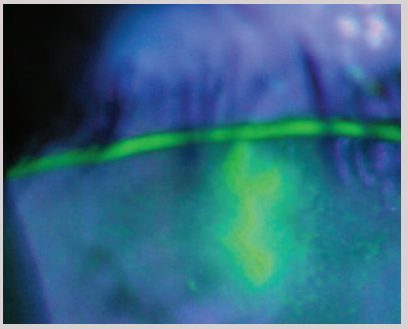

Figure 6. Herpes simplex keratitis staining with fluorescein and viewed with light passed through a cobalt blue filter. Note the branching pattern of the ulcer.

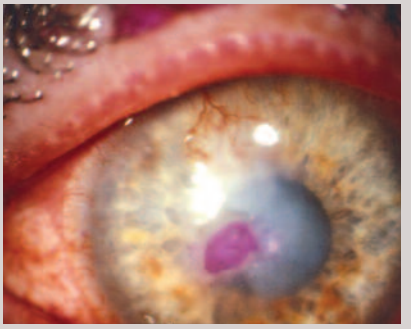

Figure 7. Corneal scarring and vascularisation from recurrent herpes simplex keratitis. Note the corneal ulcer stained with rose bengal.

(Zovirax Ophthalmic Ointment), applied five times a day and continued for at least three days after healing. Ideally, a sample should be taken to confirm the diagnosis by viral culture – this procedure will also debride the lesion and speed resolution. Topical corticosteroids should be avoided because they can cause rapid progression of a dendritic ulcer to a large geographic ulcer.[9,10]

Stromal or endothelial disease

Treatment for stromal or endothelial disease involves an oral antiviral agent, such as aciclovir, 200 mg four to five times daily, or its prodrug, valaciclovir (Valtrex), 500 mg twice daily.

Topical corticosteroids are only given with antiviral therapy, and in this case patients require close supervision by an ophthalmologist.[9]

Recurrent disease

Repeated episodes of herpes simplex keratitis can lead to corneal scarring and reduced vision (Figure 7). Long term treatment with oral antiviral agents at reduced dosage may be prescribed to prevent frequent recurrence.

For patients with reduced vision from a herpetic scar (inactive disease), penetrating keratoplasty may be performed and has a 62% chance of graft survival at 15 years; if a graft is performed for active disease, the chance of survival is halved.[11] Deep lamellar keratoplasty with oral antiviral cover may provide an alternative to penetrating keratoplasty and has a lower risk of rejection.[12] This involves placing a full thickness corneal stroma and epithelial button into a host bed that contains little or no stromal tissue, on top of Descemet's membrane such that patients retain their own endothelium. However, long term data are not available for this technique in herpes simplex keratitis.

Patients with recurrent disease should be counselled that early presentation and good compliance with treatment may help reduce the long term sequelae of herpes simplex keratitis.

Microbial keratitis

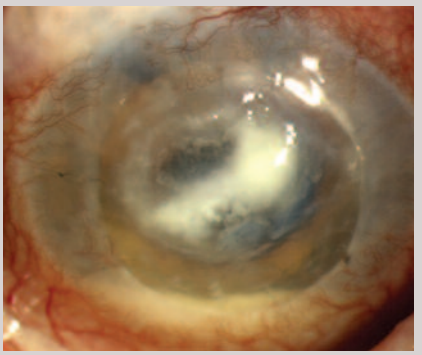

Figure 8. Bacterial keratitis in a corneal graft. Note the corneal infiltrate, conjunctival injection and hypopyon.

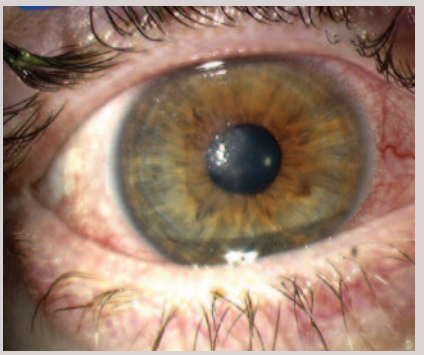

Figure 9a. A case of early *Acanthamoeba* keratitis. The corneal epithelium is irregular and opaque.

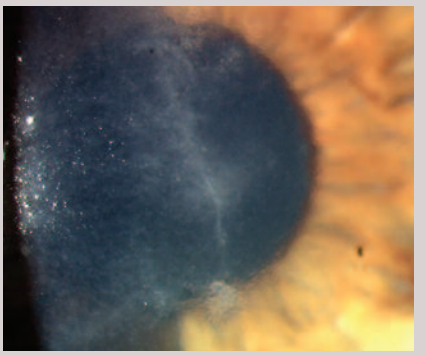

Figure 9b. Perineural infiltrates are pathognomonic of *Acanthamoeba* keratitis.

Microbial keratitis

Microbial keratitis is responsible for at least 1.5 million new cases of unilateral blindness every year in the developing world. Although it is not a common cause of blindness in developed countries, it has significant associated morbidity. The risk factors for microbial keratitis include:

- contact lens wear
- corneal trauma
- corneal surgery
- postherpetic corneal disease
- corneal anaesthesia
- corneal exposure
- dry eye
- ocular surface disease.[13,14]

In this country, contact lens wear is the greatest risk factor for bacterial and amoebic keratitis. Corneal trauma – particularly agricultural injury – is the most common risk factor in the developing world and is also common in rural settings in Australia.

Diagnosis

An acutely red and painful eye along with blurred vision and photophobia is the typical presentation for patients with microbial keratitis. In *Acanthamoeba* keratitis, the pain can be severe.

On examination, a corneal ulcer with underlying infiltrate is seen, along with perilimbal injection, conjunctival erythema, a variable anterior chamber reaction and stromal thinning (Figure 8). Fungal keratitis typically has an indolent course, and presents with a deep central corneal lesion with ill defined borders and finger-like extensions into the stroma, satellite lesions, hypopyon and an endothelial plaque. In *Acanthamoeba* keratitis, perineural infiltrates may occur and they are said to be a pathognomonic finding (Figures 9a and b). Slit lamp examination provides the best means of diagnosis, but the direct ophthalmoscope and a pair of loupes can be used as an alternative.

Pseudomonas aeruginosa is the most common causative organism in contact lens wearers. Fungal infections are rare – they occur more commonly after trauma, particularly in rural settings, and with corticosteroid use. Amoebic keratitis is not common but has a preference for contact lens wearers and, compared with bacterial keratitis, inadequate hygiene has a greater role in its development.[13] Lack of disinfection, chlorine disinfection systems and swimming while wearing contact lenses are significant risk factors for *Acanthamoeba* keratitis. Tank-stored tap water can harbour *Acanthamoeba*. Over 30 species of acanthamoebae have now been identified and at least eight have been

reported to cause keratitis: *A. castellani, A. polyphagia, A. hatchetii, A. culbertsoni, A. rhysodes, A. lugdenesis, A. quina* and *A. griffini*.[15]

Patients who are taking topical corticosteroids for ocular surface disease may develop microbial keratitis in which the inflammatory signs are minimal but in whom destructive keratitis can still occur.[10] Organisms such as alpha-haemolytic streptococci and *Candida* are of low virulence and are common in such patients.

Management

Urgent referral to an ophthalmologist is needed for a patient with microbial keratitis because progression can occur within hours and *Pseudomonas* can produce rapid corneal perforation. A prompt corneal scrape is needed to obtain material for a Gram stain and culture, debulk necrotic material, and improve antibiotic penetration. Confocal microscopy and amplification of microbial DNA by polymerase chain reaction (PCR) may be available in some centres for a rapid diagnosis.

Antibiotic therapy for microbial keratitis

Bacterial keratitis. Following recent randomised controlled trials, broad spectrum monotherapy using ciprofloxacin 0.3% (Ciloxan, Ciloquin) or ofloxacin 0.3% (Ocuflox) is now the treatment of choice for bacterial keratitis.[13,16-18] Resistance to fluoroquinolones is emerging in India and the USA, but has not yet proved to be a problem in Australia or the UK.[19] Antibiotics prepared in the hospital pharmacy are required if there is resistance or hypersensitivity.

Fungal keratitis. Antifungal therapy should be based on local epidemiological data. Econazole 1% (Dermazole, Pevaryl Topicals) can be used for filamentary fungal keratitis, whereas amphotericin B 0.15% to 0.3% is the drug of choice for the treatment of *Candida albicans* keratitis.

Acanthamoeba keratitis. Polyhexamethyl biguanide 0.02% (prepared in a hospital pharmacy) or chlorhexidine 0.06% (Bausch & Lomb Conditioning Solution) alone or propamidine 0.1% (Brolene) are used for the treatment of *Acanthamoeba* keratitis.[15]

Topical broad spectrum antibiotics are given hourly for five days and overnight for the first two days of this period (see the box on page 29). For small ulcers, less intense treatment can be given. Topical antibiotics are selected on the basis of the clinical impression and Gram stain result – these have good penetration, particularly with an epithelial defect and frequent dosing. Systemic therapy, usually with quinolones, is only prescribed for deep corneal, limbal disease or scleritis.

The patient with microbial keratitis should be reviewed daily. Results of microbiological investigations are usually available after 48 hours, and therapy is adjusted if results suggest that the current choice of antibiotic is inappropriate. If the organisms are sensitive to the antibiotic being used in treatment, bacterial ulcers will usually be sterile by five days. For corneal ulcers containing fungi or *Acanthamoeba*, sterilisation usually takes longer.

The frequency of therapy is reduced as the ulcer enters the healing phase. Topical antibiotics may then be given as prophylaxis against reinfection while epithelialisation occurs. If there is deterioration, compliance failure should be excluded and the microbiology reassessed.

The patient should be advised that visual rehabilitation may take time. Corneal scarring can remodel, but to a limited degree. Options for problematic reduced vision include contact lens wear, excimer laser for superficial scarring or corneal grafting (deep lamellar or penetrating keratoplasty) for patients with deep scarring.

Contact lens disorders

Contact lenses are biomaterials that have both short and long term effects on the cornea. These include reduced sensation, decreased oxygen uptake, endothelial cell polymegethism, corneal warpage and, less frequently, limbal failure. A variety of corneal disorders may result (Table 2).[20]

Patients with contact lens disorders may be asymptomatic or they may complain of blurred vision, a red eye, and mild to severe ocular pain or discomfort. The lens should be inspected and then removed; if infection is suspected then it must be sent for culture. Examination, including fluorescein staining, will usually reveal the diagnosis. Some conditions, such as toxic keratopathy or overwear syndrome, resolve with removal of the contact lens. Follow up with an ophthalmologist or optometrist will then be needed to prevent recurrence. Microbial keratitis requires urgent referral to an ophthalmologist.

Final comments

Corneal conditions may produce visual loss and pain or discomfort. Dry eye is the most prevalent eye disease, and corneal ulcers, infection and contact lens disorders occur commonly. Prompt assessment, diagnosis and management is needed to ensure ocular comfort and, in some cases, to prevent loss of vision. MT

Table 2. Contact lens disorders[20]

Metabolic (hypoxia, hypercapnia)
Acute epithelial necrosis (overwear syndrome)
Microcystic epitheliopathy
Superior epithelial arcuate lesions
Stromal oedema, opacity and vascularisation
Endothelial polymegethism and pleomorphism
Mechanical or traumatic
Corneal abrasion or ulcer
Toxic or allergic
Toxic keratopathy
Contact lens associated papillary conjunctivitis (giant papillary conjunctivitis)
Suppurative keratitis
Sterile keratitis
Microbial keratitis
Tear resurfacing abnormalities
3 and 9 o'clock stain
Inferior corneal stain

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