Conditions of the anterior eye
Part 2: Band keratopathy and corneal dystrophies
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This article is the follow-up to the first part published in the January 2017 issue of Dispensing Optics. It will continue to look at a number of corneal conditions, which may be encountered in hospital or during community practice by optometrists, contact lens opticians or dispensing opticians.

BAND KERATOPATHY
Band keratopathy is a chronic degenerative disease typified by granular crystalline calcium phosphate mineral (calcium hydroxyapatite) deposition in the cornea (anterior stroma and Bowman’s layer). Initially, it occurs at the corneal periphery but tends to progress and coalesce towards the centre until a band of grey opaque plaques are formed (Figure 1). These are separated by clear corneal zones due to the presence of corneal nerve channels. Plaque development usually takes months or even years though sometimes progress can be rapid depending on the underlying cause.

SYMPTOMS
Symptoms can vary widely, ranging from patients being unaware of their condition to complaints of a reduction in vision, photophobia, haloes and glare as the condition progresses and the visual axis is affected. The patient’s visual acuity tends to deteriorate in tandem with condition progression and they may also be concerned about ocular cosmesis. If the integrity of the epithelium is compromised from below, disruption of the ocular surface also results. Individuals may report pain, irritation, lacrimation and discomfort coinciding with epithelial defects visible on slit lamp examination, which stain with fluorescein. Epithelial healing may also be compromised – so these patients are more at risk of developing corneal infections1.

CAUSES AND ASSOCIATED CONDITIONS
There are numerous documented causes of band keratopathy. It is usually unilateral
following various ocular disorders. One study found that the most common cause of band keratopathy was chronic corneal oedema, closely followed by idiopathic cases (unknown causes). Other associated ocular disorders include inflammatory conditions such as interstitial keratitis and chronic conjunctivitis, including that seen in children and adolescents as a result of idiopathic juvenile arthritis. In the latter, band keratopathy can be the presenting sign.

Other ocular conditions associated with band keratopathy include phthysis bulbi. This is the term used to describe an eye which produces insufficient aqueous, is shrunken due to hypotony (a very low intraocular pressure) and contains atrophic disorganised ocular structures. This ocular status can result from several different conditions, including non-infective uveitis, trauma, ocular inflammation and surgery.

Less commonly, it is the consequence of long-term retinal detachment, end-stage glaucoma (such as neovascular glaucoma) and orbital vasculitis (which can be observed in many different diseases with different vessel types and ocular structure being affected).

Band keratopathy has been reported to progress more rapidly in individuals with dry eye conditions. There is a higher rate of tear evaporation in keratoconjunctivitis sicca patients. This is a causative factor in the calcium salt precipitation that band keratopathy is characterised by.

Band keratopathy can also develop following emulsification of the silicone oil used in retinal surgery as a tamponade to hold the retina in the required position. Emulsification is the term used to describe the inability of small bubbles formed (from the initial oil droplet applied) to coalesce back together. The risk of emulsification increases with the length of time that the oil is left in the eye. It is usually left in the eye for several months following retinal detachment surgery. Contact of silicone oil with the corneal endothelium can have a number of structural effects including the development of band keratopathy.

When band keratopathy is associated with systemic disorders in which serum calcium or phosphate levels are elevated, it tends to occur bilaterally. An example is chronic renal failure in which phosphate levels are elevated. A matched cohort study in Taiwan found that patients with end-stage renal disease were approximately 12 times more likely to develop band keratopathy compared to age matched controls.

Hyperparathyroidism is a rare condition in which an excess of hyperparathyroid hormone is produced by hyperparathyroid glands. There are four of these structures situated behind the thyroid glands in the neck. Their function is to regulate the calcium, phosphate and vitamin D levels in the bones and blood. The majority of cases are due to the presence of a tumour (parathyroid adenoma). Hyperparathyroidism results in an increase in calcium and a drop in phosphate blood levels. Symptoms include nausea, fatigue, abdominal pain and the development of kidney stones as excess calcium is excreted in the urine in an attempt to bring calcium levels back to normal. Band keratopathy may consequently be observed in patients with this condition.

Gout is an inflammatory disease which is becoming more prevalent. The risk of developing gout is greater in men and increases with age. Gout results from increased uric acid levels in the blood caused by overproduction or a reduction in excretion rates. It is thought to be multifactorial in that both genetic and environmental factors are responsible. The latter may include obesity, hyperlipidaemia, diabetes (type 2), hypertension and kidney disease.

There is also a link between gout and certain medications, which increase uric acid levels or reduce the efficiency of urate excretion from the kidneys such as aspirin and thiazide diuretics (used in the treatment of hypertension) respectively. A meat rich diet and alcohol consumption (particularly beer) has also been found to be a risk factor for gout development.

Untreated gout may result in uric acid crystalline deposition in the joint spaces resulting in arthritis as well as the formation of renal stones. In the eye, the presence of uric acid can result in ocular inflammation such as scleritis and episcleritis due to pockets of urate crystal build up (tophi). This can also occur in the conjunctiva and periorcular tissue. Band keratopathy can develop in untreated gout but as it is caused by uric acid rather than calcium accumulation it is yellower in appearance.

Band keratopathy can also be inherited. Congenital band keratopathy is extremely rare and tends to recur following treatment.

Any ocular and/or systemic co-existing condition needs to be assessed, diagnosed and treated first. If conditions are well controlled, this can lead to a reduction of corneal deposition (such as following the treatment of arthritis resulting from gout by the first line treatment of non-steroidal anti-inflammatories). Conversely, recurrence is more likely to occur despite surgical treatment of band keratopathy if there is an underlying cause and that associated condition is unstable.

There is also a link between various medications and calcific band keratopathy. Excessive ingestion of antacids such as calcium carbonate (milk-alkali syndrome) has been associated with the development of band keratopathy. Band keratopathy is also linked to excessive use of calcium supplements (such as calcium carbonate used to treat bone loss associated with osteoporosis) or vitamin D supplements. The latter has a role in calcium level regulation and levels higher than the therapeutic index (vitamin D toxicity) may lead to hypercalcemia.

It is also thought that band keratopathy can develop in patients using phosphate containing eye drops, such as artificial tears and topical corticosteroids. Phosphates are usually present as a buffer or occasionally as part of the active substance and can bind to the calcium deposits. However, this is rare (less than one case per 10,000 bottles) and the risk for patients without pre-existing corneal damage is not clinically significant.

TREATMENT OPTIONS
Mild symptoms of ocular irritation may be addressed with topical ocular lubricants including eye drops, gels and ointments depending on the severity. Band keratopathy can be treated surgically where necessary, for example, if the patient’s vision is compromised or they are severely symptomatic. One treatment option involves phototherapeutic keratectomy (PTK) laser treatment. This remodels the cornea, smoothing out irregularities. It aims to increase corneal transparency and reduce the presence of calcium deposition.

However, PTK can alter the refractive power of the cornea so spectacles or contact lenses may be required following healing. This may also be a safe form of treatment for band keratopathy in children in whom prevention of amblyopia is also a consideration. However, the prognosis also depends on the presence of other factors, such as chronic inflammatory disease.

An alternative treatment option involves the application of a chelating agent such as disodium ethylenediaminetetraacetic acid (EDTA) after removal of the epithelium. This agent dissolves the calcium build-up. After a few minutes, the corneal surface may be gently rubbed with a sponge to enhance the chelation process until the cornea becomes clear. Following either procedure, a temporary bandage contact
lens is inserted. This promotes corneal recovery by preventing disruption of the corneal epithelium by blinking. The patient is also usually prescribed a short course of topical non-steroidal anti-inflammatory (NSAID) eyedrops and oral analgesic to use whilst the epithelium is healing.

**CORNEAL DYSTROPHIES**

There are numerous corneal dystrophies. Corneal dystrophies are hereditary conditions which cause corneal changes in the absence of inflammation, infection or other associated eye disease. They are usually slowly progressive and cause reduction in corneal clarity. A few of the more common forms will be described here.

**EPITHELIAL BASEMENT MEMBRANE DYSTROPHY**

Epithelial basement membrane dystrophy (EBMD) is the most commonly occurring type of corneal dystrophy. Broadly, it is due to changes in epithelial cell morphology and poor adhesion between these cells and the underlying basement membrane across the cornea. EBMD increases in prevalence with age with 76 per cent of individuals over 50 being affected. There are a variety of symptoms, ranging from none reported to ocular dryness, fluctuating vision and fingerprint-like epithelial lines and photophobia and grittiness.

A small proportion of cases are associated with recurrent corneal erosion (RCE) and patients may report waking with sharp ocular pain, photophobia and watering. A history of previous multiple episodes of RCE is highly suggestive of EBMD, especially if it occurs in more than one location which vary between episodes as well as in both eyes. This condition is a contraindication for certain types of refractive surgery (LASIK).

Slit lamp examination may show dot and fingerprint-like epithelial lines and intraepithelial microcysts often situated on the inferior cornea. The latter often correspond to regions of negative staining with sodium fluorescein. In severe cases, an epithelial defect may be present in conjunction with an area of loose epithelium.

Treatment modalities depend on the severity of the condition and are similar to those for band keratopathy. Topical lubricants, ointments or hyperosmotics may be prescribed. The latter removes fluid from corneal epithelial cells and promotes their adhesion to the underlying basement membrane. A bandage contact lens may also be inserted to promote healing by preventing disruption of the epithelial cells by the lid.

The College of Optometrists’ Clinical Guidelines recommend that patients with RCE are reviewed at monthly intervals for three months. If there are significant epithelial loss symptoms associated with pupillary spasm, optometrists with an independent prescribing qualification can also prescribe a short course of cycloplegic as well as a prophylactic antibiotic ointment to reduce the risk of corneal infection.

In patients who do not respond to these more conservative measures, PTK may be performed. Alternative forms of treatment include corneal epithelial debridement and corneal anterior stromal micropuncture. These treatments promote corneal healing in RCE patients and aim to achieve better epithelial-basement membrane adhesion with the new tissue. They have been approved by the National Institute for Health and Care Excellence (NICE) to treat band keratopathy, epithelial basement membrane dystrophies and a number of other corneal pathologies.

**FUCHS’ ENDOTHELIAL DYSTROPHY**

Fuchs’ endothelial dystrophy is another common corneal dystrophy with a prevalence of five per cent of the population in the USA. However, globally the proportion of corneal transplants (penetrating keratoplasty) performed as a result of Fuchs’ endothelial dystrophy varies greatly with a much lower proportion observed in India and Saudia Arabia compared to parts of the USA, Denmark and the UK.

Fuchs’ endothelial dystrophy is a progressive corneal condition that occurs more frequently in women than men, with women being up to three times more likely to be affected. Although there are rarer inherited forms which tend to have an earlier age of onset, it is usually observed in individuals over 50 years of age.

There is thought to be an association between Fuchs’ endothelial dystrophy and smoking. A study found that individuals who had smoked 20 cigarettes a day for more than 20 years had more than a two-fold chance of developing corneal guttata. Corneal guttata result from focal accumulation of collagen basement membrane material on the posterior surface of Descemet’s membrane.

Patients with Fuchs’ endothelial dystrophy may complain of a number of symptoms including blurred vision, particularly first thing in the morning, which tends to improve as the day progresses. They may also experience pain or irritation due to a foreign body sensation and glare. This disease tends to be bilateral but can often present asymetrically. Corneal guttata may be visible during slit lamp examination and can be observed in conjunction with pigment. Guttata appear as small dark areas against the dull gold appearance of the corneal endothelium when viewed monocularly with specular reflection under high magnification.

As the condition progresses, the number of guttata tends to increase and the...
endothelium has a beaten metal appearance when observed with retroillumination (with light reflected back from the iris retina) (Figure 3). Guttata eventually merge together becoming confluent and the overall area of affected cornea increases.

Fuchs’ endothelial dystrophy occurs as a consequence of insufficient endothelial function. The presence of guttata (focal deposition of collagen on the posterior face of Descemet’s membrane) is due to the corresponding loss of endothelial cells. Over time, a cumulative reduction in endothelial cell density results in the remaining endothelial pump mechanisms present being insufficient to maintain normal stromal hydration. The resultant influx of aqueous leads to stroma oedema. Stromal swelling causes the development of folds in the underlying Descemet’s membrane.

Progression also results in fluid containing cysts within the epithelium (epithelial oedema) with a characteristic ground glass appearance. These cysts are known as bullae. Severe cases of endothelial keratopathy are characterised by rupturing of these bullae causing intense pain and compromised vision. End-stage Fuchs’ endothelial dystrophy is typified by avascular subepithelial and stromal corneal scarring. The patient’s visual acuity is now severely affected and may be limited to perception of hand movements.

In the early stages, patients may be asymptomatic or may mention that their vision tends to be blurred in the morning (which is due to decreased tear evaporation during lid closure at night). Treatment of mild symptomatic cases includes instillation of topical hyperosmotic solutions (five per cent sodium chloride) to dehydrate the cornea. The dosage and duration of usage depending on the severity of the condition. This may be combined with the use of the ointment form at night. Gentle use of a hairdryer held at arm’s length in the mornings may also be recommended to increase evaporation of the tear film and help dehydrate the cornea.

Patients with bullous keratopathy may be fitted with a bandage contact lens to promote corneal healing and to mask irregular astigmatism associated with bullae. A short course of NSAIDs may be prescribed by the ophthalmologist as an analgesic to reduce pain. However, previous reports suggested an association between topical NSAIDs and the development of corneal melts. Although this appears to be rare, and an article concluded that the variability of treatment regimens indicated that there were other causative factors rather than drug toxicity alone, caution and close monitoring of patients prescribed these eye drops is recommended.

In severe cases of Fuchs’ endothelial dystrophy, corneal decompensation may result and surgical treatment involving a corneal graft is necessary. Previously, this involved a penetrating keratoplasty, which involves a long recovery period and carries a significant risk of graft failure (often as a result of endothelial rejection) as well as uncorrectable post-operative astigmatism.

Endothelial keratoplasty in the form of Descemet stripping endothelial keratoplasty (DSEK) and Descemet membrane endothelial keratoplasty (DMEK) are now alternative options for most patients. This technique specifically targets diseased tissue and involves removal and replacement with transplanted donor Descemet membrane and endothelium. The small incision required means that this is often a sutureless procedure. This results in faster recovery time, less likelihood of inflammation and infection and a reduced risk of rejection at one year post surgery (one per cent compared to 14 per cent in PK patients).

However, if the patient’s Fuchs’ endothelial dystrophy has reached a severe stage with bullous keratopathy, stromal scarring may result which may require a penetrating keratoplasty to achieve corneal clarity. To achieve a better prognosis, patients should be referred for ophthalmological assessment prior to this level of disease.

Patients with Fuchs’ endothelial dystrophy requiring cataract surgery need to be carefully evaluated as surgery can put stress on the cornea resulting in further endothelial cell loss, causing the condition to worsen. Specular microscopy can be used pre-operatively to perform an endothelial cell count. Although loss of endothelial cells is observed in normal individuals, this is more critical in those with Fuchs’ endothelial dystrophy. In cases needing cataract surgery where an endothelial keratoplasty is required, the two procedures may be performed simultaneously.

This article has followed on from the previous part of this series and has discussed further corneal conditions that may be encountered by the eyecare clinician in more depth.

A full set of references can be downloaded from the ABDO website.
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REFERENCES


