

The episclera, sclera and conjunctiva

An overview of relevant ocular anatomy

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Module 9 Part 2
Differential Diagnosis
of Ocular Disease

Course code: c-2688

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Whereas the last article in this module (OT 13/01/06) concentrated on the ocular adnexa, this article will highlight those ocular maladies pertaining to the episclera, sclera and conjunctiva. A sound knowledge of the ocular anatomy, and its relevance to ocular disease, is essential for diagnosing and providing an appropriate management plan for the patient.

Episclera and sclera

Anatomy

The sclera consists of two main layers – namely the lamina fusca, which lies adjacent to the supraciliary and suprachoroidal lamellae of the uveal tract, and the episcleral layer anteriorly. The latter, which lies between the superficial scleral stroma and Tenon's capsule, consists of dense vascular connective tissue.

Essentially, the vascular layers may be compartmentalised into the conjunctival vessels, the vessels within Tenon's capsule, and those confined to the deep vascular plexus. The most superficial vessels – the conjunctival vessels – can be easily manually moved over the underlying sclera, and consist of tortuous arteries and straight veins. The vessels within Tenon's capsule are entirely straight and adopt a radial configuration; these vessels can also be moved manually over the sclera. In episcleritis, it is these vessels which become engorged. In episcleritis, the episclera and Tenon's capsule become infiltrated with inflammatory cells. The sclera, however, is spared. The vessels confined to the deep vascular plexus, which are located in the superficial sclera, adopt maximum dilatation in scleritis.

From a practical standpoint, instillation of

topical phenylephrine blanches the conjunctival vessels, and some of the vessels confined to Tenon's capsule. By contrast, those associated with the deep vascular plexus remain unaltered. Furthermore, the same vasculature cannot be manually moved over the avascular scleral stroma.

Episcleritis

Episcleritis is a benign, self-limiting condition which typically presents with an acute onset of hyperaemia and mild pain, with some degree of lacrimation in one or both eyes. It is frequently recurrent and has a predilection for young adults. It is further classified into either diffuse (simple) (Figure 1) or nodular forms (Figure 2). With the former, which is the most common, the hyperaemia may be either sectorial or diffuse and usually resolves within seven to 10 days. Depending on the degree of co-existing lacrimation, the patient's vision is usually unaffected. The more aggressive nodular form is characterised by a localised, raised congested nodule. It is typically associated with more pain and adopts a longer time course. Following recurrent episodes, the superficial sclera may appear more translucent – a consequence of fibre rearrangement within the superficial sclera.

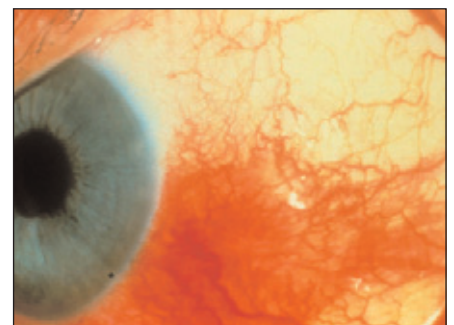
»» Figure 1

Diffuse episcleritis. Note dilated blood vessels with preservation of the normal radial pattern of the episcleral vessels

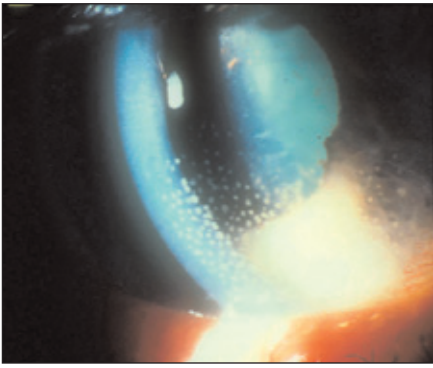


»» Figure 2

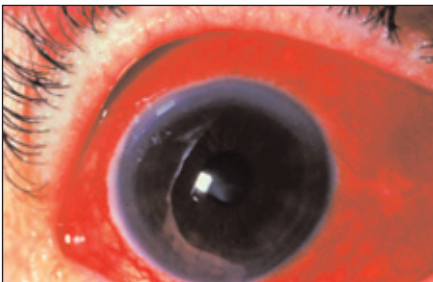
Nodular episcleritis. Note a white inflammatory nodule is present within the inflamed area while the rest of the episclera is uninvolved



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» **Figure 3**
Anterior uveitis – keratic precipitates seen on lower half of cornea



» **Figure 4**
Non-necrotising (diffuse) anterior scleritis. Note the vascular engorgement has a dark violaceous colour, with loss of the normal radial pattern of the episcleral vessels (pupil is dilated)



» **Figure 5**
Necrotising anterior scleritis. Note large area where the sclera is ulcerated and the overlying conjunctiva and episclera are missing

Although treatment is seldom instituted apart from topical unguents or artificial tears, the nodular form may require topical corticosteroids in order to ameliorate the patient's symptoms.

Despite the recurrent nature of this condition, a cause is seldom found. Occasionally, it may be associated with systemic disease such as rheumatoid arthritis or gout.

Differential diagnosis

The main differential diagnoses are scleritis (see later), conjunctivitis (see later) and anterior uveitis (**Figure 3**).

Unlike anterior uveitis, episcleritis is not associated with cells or flare in the anterior chamber, and the patient's vision is rarely affected. In addition, the degree of photo-

phobia experienced by the patient harbouring uveitis is far greater than those suffering from episcleritis.

Scleritis

Scleritis is associated with oedema and infiltration of the entire sclera and, if left untreated, its effects on the patient's vision are met with far more deleterious consequences than its benign counterpart, episcleritis. Typically, the patient experiences severe eye pain, which is deep and boring in nature and frequently radiates to the forehead, brow or jaw. It is noteworthy that the pain is not acute in the majority of cases, but gradual in onset.

In approximately 50% of cases, the aetiology may be ascribed to a systemic disease. The most common systemic progenitor is rheumatoid arthritis. Other systemic maladies associated with scleritis include Wegener's granulomatosis (a systemic condition that has a predilection for small and medium sized vessels), relapsing polychondritis (affecting cartilage) and polyarteritis nodosa (collagen vascular disease affecting small and medium sized vessels).

Scleritis may be secondary to a whole host of infectious agents ranging from bacterial organisms, such as *pseudomonas aeruginosa* and *staphylococcus aureus*, to viruses such as *varicella zoster*. That said, scleritis secondary to fungal agents is exceedingly rare.

Surgically induced scleritis is a well-documented complication, which characteristically affects females and occurs six months following the initial procedure. Thus, a full ocular history should be sought in at risk patients. Patients who have also received beta irradiation or mitomycin C following removal of a pterygium are also at risk.

Anatomically, scleritis may be subdivided anteriorly and posteriorly. The former is the most common mode of presentation, accounting for over 95% of cases. The anterior form may be further subdivided into either non-necrotising (**Figure 4**) and necrotising (**Figure 5**). Recognising the form is essential, as the gravity associated with the latter is such that high dose immunosuppressants are required in order to abrogate the signs and symptoms.

Anterior non-necrotising scleritis may be either diffuse or nodular. Although this form of scleritis is similar in appearance to episcleritis, it can be readily differentiated by the fact that the engorged vasculature cannot be entirely constricted with topical phenylephrine; the pain is typically more severe and the onset is more gradual than episcleritis. Moreover, the scleral nodule cannot be moved over the underlying tissue in the nodular form of the disease.

Necrotising scleritis with inflammation is characterised by avascular patches as a result of vascular occlusion. The surrounding vascular network is engorged. Left untreated, scleral necrosis ensues resulting in overlying conjunctival ulceration.

Extensive necrosis may result in the sclera adopting a blueish hue, due to the enhanced visualisation of the underlying uvea secondary to scleral thinning.

Further ocular sequelae associated with this form of scleritis include staphyloma formation and anterior uveitis, with concomitant spread into further uveal tissues. Thus, practitioners should be aware that while anterior uveitis may be one of the conditions that must be differentially diagnosed with scleritis, it may actually co-exist. The presence of a co-existing uveitis compounds the risk to the eye owing to attendant sequelae, namely cataract, glaucoma and macular oedema.

As mentioned earlier, management of the necrotising form requires far more potent therapy than its non-necrotising counterpart. Therapy ranges from oral corticosteroids alone to the use of other specialised immunosuppressive agents, such as cyclophosphamide or cyclosporin. For those patients in whom the degree of necrosis is extensive, an intravenous regimen may be required in order to salvage the eye.

Although unlikely to be encountered in everyday optometric practice, scleromalacia perforans (an anterior, necrotising scleritis without inflammation), which is associated with a painless extension of scleral thinning such that the whole sclera adopts a blue hue, is frequently bilateral and is associated with patients who suffer from rheumatoid arthritis. The prognosis is poor in these patients for two reasons: first, there is no effective ocular treatment; and second, the presence of scleromalacia perforans confers widespread vascular disease with a concomitant high mortality risk.

Owing to the gravity associated with this ocular malady, it remains incumbent on all practitioners to be cognisant with the signs and symptoms of this disease. It is imperative that patients suspected of suffering from scleritis are referred to a hospital eye department that same day, so that a treatment regimen can be started.

Conjunctiva

Anatomy

This mucous membrane may be subdivided into three compartments – the palpebral, forniceal and bulbar conjunctivae. Whilst the palpebral component is firmly adhered to the tarsal plate, the tarsal conjunctiva is rather loose in comparison. The bulbar conjunctiva envelopes the anterior sclera. Although it is tightly bound to the underlying Tenon's capsule at the limbus, its attachments to the structure elsewhere are looser.

Histologically, the conjunctiva consists of an epithelium and stroma. The rich vascular network is confined to the stromal layer and is separated from the epithelium via a basement membrane. The superficial region of the stroma contains adenoid tissue and is not present at birth. In fact, it takes three months to develop. The significance of this

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is that neonates and infants below this age are not able to elicit a follicular response in the presence of conjunctival inflammation.

The conjunctiva contains numerous glands consisting of mucin secretors, such as goblet cells, and the accessory lacrimal glands of Krause and Wolfring. In the context of conjunctival disease, it is important to appreciate that chronic inflammatory disorders may result in augmentation of the goblet cells, whereas destructive lesions, such as chemical burns, are associated with reduction of the same said secretors.

Signs and symptoms

Inflammation of the conjunctiva (conjunctivitis) may be due to a multitude of causes, including bacteria, viruses, allergens and chlamydia. Although the definitive diagnosis relies on positive laboratory identification of the contagion, such a methodological approach is seldom adopted in the clinical setting. Rather, recognition of co-existing signs and symptoms is utilised by the practitioner to determine the appropriate treatment regimen.

Conjunctivitis *per se* may be associated with non-specific symptoms irrespective of the causative agent. These include lacrimation, photophobia and generalised ocular irritation. However, a patient complaining of pain implies co-existing corneal involvement. Although itching may be associated with keratoconjunctivitis sicca, it is virtually pathognomonic of allergic eye disease.

Discharge, resulting from exudates from the dilated conjunctival vasculature, may vary in consistency depending on the causative agent. Whereas a purely mucoid discharge is typically seen in patients suffering from vernal conjunctivitis or keratoconjunctivitis sicca, a mucopurulent form is observed in chlamydial and mild bacterial cases. A thick purulent discharge is observed in severe bacterial infections. The discharge associated with viral and allergic eye disease, by contrast, is watery in nature.

Subconjunctival haemorrhages, when associated with generalised conjunctival inflammation, are frequently associated with viruses. That said, bacteria such as *streptococcus (strep.) pneumoniae* may also produce such a haemorrhagic reaction.

Conjunctival oedema, known as chemosis, is associated with allergic eye disease and severe inflammation of any cause and is due to exudation of protein rich fluid through the inflamed blood vessels.

Follicles, which consist of hyperplastic lymphoid tissue, characteristically appear as slightly elevated lesions encircled by blood vessels. They are typically seen in medicamentosa (reaction to topical agents) and viral or chlamydial conjunctivitis. Interestingly, folliculosis may occur especially in children despite a paucity of conjunctival inflammation.

Papillae consist of hyperplastic conjunctival tissue with central vessels that are replete with inflammatory cells, such as

polymorphonuclear leukocytes, eosinophils, plasma cells and lymphocytes. They are most commonly observed in the palpebral conjunctiva. Unlike follicles, the presence of papillae is far less effective diagnostically and is associated with a plethora of ophthalmic conditions such as allergic eye disease, bacterial conjunctivitis and, of course, contact lens wear.

Pseudomembranes, consisting of coagulated exudates adherent to the conjunctival epithelium, may be associated with severe adenoviral and gonococcal infections. True membranes, which infiltrate the superficial layers of the conjunctiva, are rarely encountered in practice as their presence is indicative of severe infections such as diphtheria. Pseudomembranes may be differentiated from their deeper counterpart clinically, since they can be peeled off with relative ease. Moreover, bleeding is not typical unlike the attempted removal of a true membrane.

As mentioned in the previous article, knowledge of the lymphatic drainage system is important. To reiterate, the upper lid and lateral canthus drain to the preauricular node, whilst the lower lid and medial canthus drain to the submandibular nodes. The presence of lymphadenopathy frequently co-exists with viral and chlamydial infections. A marked lymphadenopathy is also seen in a rare condition, known as Parinaud oculoglandular syndrome – a granulomatous conjunctivitis with very painful ipsilateral lymphadenopathy that is associated with numerous causes.

Investigation of conjunctivitis

Although laboratory investigations remain the diagnostic method par excellence in identifying the aetiology of conjunctivitis, they are seldom used in everyday practice. That said, the use of such techniques is recommended in the following cases: first, in patients suspected of harbouring chlamydial infections, owing to the fact that referral to a genitourinary clinic has to be made together with notification of sexual partners; second, in patients with fulminant purulent conjunctivitis in order that the most appropriate antibiotic may be prescribed; and third, in all cases of neonatal conjunctivitis.

Conjunctival manifestations

Since it is beyond the scope of this article to provide a definitive description of conjunctival pathology, various conditions of those likely to be encountered by optometrists will be described with their relevant differential diagnoses. The following should therefore act as a trustworthy reference for those conditions likely to be encountered in everyday practice. Notwithstanding the fact that conjunctival tumours are rare, the inclusion of some is necessary as they may easily become confused with their benign, common, degenerative counterparts such as pterygium and pingueculae.

Acute conjunctivitis

Hyperacute onset

A conjunctivitis which rapidly develops into a fulminant inflammatory state within a 12-hour period is usually referred to as hyperacute. The pathogen most likely to be responsible is the gram negative bacteria, *neisseria gonorrhoea*. Recognition of this condition is imperative as the organism is capable of penetrating an intact cornea. Therefore, failure to treat this condition may lead to corneal perforation and endophthalmitis.

Typically, the discharge is purulent in nature and there is marked chemosis, conjunctival papillae and preauricular lymphadenopathy. Owing to the dire consequences of this condition, patients are usually admitted to hospital and, once cultures of the eye have been taken, are administered antibiotics intravenously. Thus, any patient presenting to practice with a dense purulent discharge should be referred immediately to the hospital eye department.

Acute onset

Simple bacterial conjunctivitis

Simple bacterial conjunctivitis is frequently seen in children and arises from direct contact of infected secretions. Common pathogens include *strep. pneumoniae* and *staph. epidermidis*. Classically, the eyelids are stuck together in the morning as a result of overnight accumulation of exudates. Although the degree of hyperaemia is maximal in the fornices, the conjunctivae are diffusely hyperaemic. The discharge transforms from a watery consistency to a more viscous mucopurulent form several days later. The fact that the condition will resolve without any treatment, application of broad-spectrum antibiotics, in combination with a daily eyelid hygiene regimen serves to expedite resolution of the condition.

Viral conjunctivitis

The most common type of virus to affect the conjunctiva is adenovirus. Although there are numerous strains of the virus, six are notable with regard to conjunctival disease. Serotypes 3, 4, 5 and 7 are responsible for pharyngoconjunctival fever. Children are predisposed to this infection and frequently present with a co-existing upper respiratory tract infection. Serotypes 8 and 19 cause the more ominous epidemic keratoconjunctivitis. It is highly contagious and is spread easily by hand to eye contact, inadequate disinfection of instruments (e.g. applanation tonometer prisms) and solutions. Whilst systemic features are common and keratitis rare in pharyngoconjunctival fever, the keratitis associated with the epidemic form, by contrast, is common and severe.

The presentation consists of acute hyperaemia, photophobia and watery discharge.

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Owing to the contagious nature of this condition, the conjunctivitis is frequently bilateral. The eyelids are frequently oedematous and the discharge watery in nature. Conjunctival follicles are observed in the palpebral conjunctiva and fornices. Although not diagnostic, lymphadenopathy, which is frequently tender, may be present. In severe cases, pseudomembranes and subconjunctival haemorrhages may also occur. The keratitis associated with the condition develops approximately eight to 10 days following the onset of symptoms. Although the lesions are confined to the epithelium initially, they soon become subepithelial and then anterior stromal. It has been suggested that the deeper opacifications represent the immune response to the virus.

Unfortunately, the quest for an effective topical anti-adenoviral agent remains elusive. As such, treatment is usually merely supportive with topical lubricants. However, topical steroids and non-steroidal anti-inflammatories may be administered in patients with severe symptoms or poorly resolving keratitis.

Allergic conjunctivitis

Allergic rhinoconjunctivitis is the most common form of ocular and nasal allergy. It is essentially a type I hypersensitivity reaction involving the cross-linking of immunoglobulin E (IgE) bound to mast cells that results in the release of histamine and other pro-inflammatory mediators. It may be further classified into a seasonal form (also known as hay fever conjunctivitis) and a perennial form. Although the latter is invariably milder in nature, it is more persistent. Patients who suffer from the perennial form are usually allergic to fungal spores and the house dust mite. Although it is difficult to avoid fungal spores, abrogation of the house dust mite may be achieved through daily hoovering at home especially the bed sheets.

The conjunctiva may not appear tremendously hyperaemic due to the concomitant conjunctival oedema. The lids are also frequently oedematous, and small papillae are invariably present on the tarsal conjunctivae.

Fortunately, the condition is innocuous and is amenable to both conservative and topical treatment. Indeed, the optometrist is

well placed to deal with this form of allergic eye disease. Conservative measures include the frequent application of cold compresses, together with eye baths in order to dilute the allergen. The optometrist can manage this ocular malady with topical mast cell stabilisers, such as sodium cromoglycate and nedocromil sodium, topical antihistamines such as levocabastine or emedastine, or combination mast cell stabiliser and antihistamine agents, such as olopatadine.

Vernal and atopic conjunctivitis

Both conditions are the result of Type I and Type IV hypersensitivity reactions combined. In other words, their pathology incorporates both IgE and a cell mediated immune response involving T-lymphocytes.

Patients with vernal conjunctivitis are frequently atopic, suffering from conditions such as asthma and eczema. The condition typically develops after five years of age and rarely persists after 25 years. Indeed, it frequently resolves around the age of puberty. Despite the condition adopting a perennial timescale, there are frequent exacerbations in the Spring and Summer months. Corneal ectatic conditions, such as keratoconus and pellucid margin degeneration, are more frequently encountered in those suffering from vernal conjunctivitis.

The hallmark sign of vernal conjunctivitis are giant cobblestone papillae on the upper eyelid. In time, although the papillae diminish in size and become more separated, they may remain indefinitely. The limbal form is characterised by raised, white, mucoid nodules, known as Trantas' dots. These nodules are composed of degenerative eosinophils. The keratopathy affiliated with this condition ranges from superficial punctuate erosions, which may progress to shield ulceration, and the formation of corneal plaques. The latter occurs when the base of the ulcer becomes coated with desiccated mucus, making it refractory to wetting and re-epithelialisation.

Although mast cell stabilisers may be employed prophylactically, their use during acute exacerbations is futile. Topical steroids or cyclosporin in steroid resistant cases are administered in order to quell the signs and

symptoms. Indeed, sub tarsal steroid injections are administered in recalcitrant cases. Owing to the potential severity of the condition, patients should be referred to an ophthalmologist during acute exacerbations.

Atopic conjunctivitis shares similarities to its vernal counterpart except that, unlike vernal conjunctivitis which resolves spontaneously, it may persist for many years. Owing to the chronic nature, the visual morbidity associated with this condition is high. The patient is typically male and suffers from atopic dermatitis. Other ocular manifestations of this dermatological condition include presenile anterior and posterior subcapsular cataracts, keratoconus and retinal detachment.

The lids are usually indurated and oedematous. The conjunctivitis has a predilection for the inferior fornices and tarsal conjunctivae. The tarsal conjunctivae may appear featureless due to the degree of infiltration. As the disease progresses, chemosis and papillae may ensue. In extreme cases, cicatrization occurs with the formation of symblepharon. It is not uncommon for these patients to possess bacterial eyelid margin disease and since the corneal complications are similar to those described for vernal disease, such patients are at risk of acquiring microbial keratitis.

The treatment regimen for atopic keratoconjunctivitis is similar to that recommended for vernal disease. Owing to the protracted timescale of the condition and the co-existing bacterial eyelid margin disease, treating these patients is an arduous task. They can, therefore, be most appropriately managed by an ophthalmologist with a special interest in external eye disease.

Chronic conjunctivitis

Chronic conjunctivitis is usually reserved for eyes with a discharge, hyperaemia and ocular irritation of four weeks duration or more. The aetiology may be due to toxicity to topical medications, eyelid conditions such as molluscum contagiosum or chlamydia. In view of the seriousness associated with the latter, further elaboration of this condition is merited.

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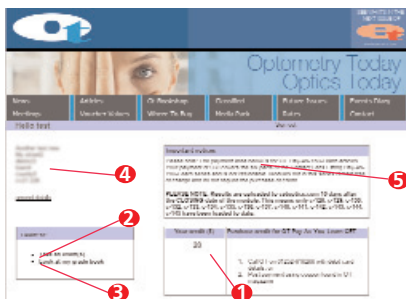
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Chlamydial inclusion conjunctivitis

Adult chlamydial conjunctivitis is a sexually transmitted disease due to chlamydial serotypes D-K (serotypes A-C cause trachoma). While female patients usually have a concomitant cervicitis, males have a urethritis. Despite the presence of active infection, the patient may be asymptomatic. Transmission of the organism is from autoinoculation from genital secretions.

The presentation is subacute and is associated with a stringy mucous discharge. The condition may be either unilateral or bilateral. The follicles tend to be prodigious and have a tendency to reside in the inferior forniceal conjunctiva. There may be palpebral oedema. Corneal infiltrates typically occur two to three weeks after the onset of the conjunctivitis. As mentioned previously, chlamydial disease is associated with tender lymphadenopathy.

Patients suspected of suffering from chlamydia should be referred to the hospital eye department, as they would require laboratory investigations and treatment at a genitourinary clinic together with contact tracing of partners. Treatment includes systemic oral antibiotic such as azithromycin as a single dose, together with topical tetracycline ointment for at least one month.

Subconjunctival haemorrhage

This is commonly encountered in optometric practice and usually develops acutely. It is painless and does not interfere with patients' vision. Most cases are idiopathic in origin. Valsalva manoeuvres are common progenitors and the history should incorporate questions about sneezing, vomiting, coughing or constipation. Other causes include trauma, systemic disease such as hypertension and the use of anticoagulant drugs such as warfarin. It may co-exist with conjunctivitis.

If a clear, benign cause can be established from the history then the patient should be reassured and advised that the blood staining will resolve over several weeks.

Conjunctival degenerations and their differential diagnoses

Pingueculum

This common condition is slow growing and appears as a yellow-white, flat or slightly raised conjunctival lesion in the interpalpebral fissure adjacent to the limbus. The cornea is spared. Treatment is only initiated for those lesions, which are abnormally raised and, as such, are causing symptoms due to the resultant inability to wet the eye or for those patients who develop a pingueculitis. A short course of topical steroids can ameliorate the inflammation and assuage the patient's symptoms, whereas surgical excision is required to remove those that disrupt the tear film.

Although pingueculae are readily identi-

fied, several lesions may be confused with this innocuous lesion such as early pterygia, gouty tophi (crystallisation) and xanthelasma associated with Type IIa hypercholesterolaemia.

Pterygium

A pterygium is a triangular fibrovascular growth of conjunctival tissue that invades the cornea. The term 'pterygos' literally translates as 'wing'. The invading pterygium consists of: a cap at the apex of the lesion that penetrates Bowman's layer and as such remains firmly adherent to the cornea; a head which is firmly attached to both the cornea and limbus; and finally the body which is located on the conjunctiva. The true aetiology of this lesion has yet to be made, suffice to say that ultraviolet radiation is the primary insult. It is noteworthy that pterygia only occur at interpalpebral nasal or temporal limbus, more commonly at the former. This distribution has led to the conjecture that of pterygia may be the result of localised stem cell damage.

Complications associated with pterygia are relatively common and include ocular irritation secondary to disruption of the tear film, visual disturbance either secondary to involvement of the visual axis or from induced astigmatism and, finally, the pterygium itself may become inflamed.

Unfortunately, simple excision of these lesions leads to a high rate of recurrence. Numerous studies have shown the recurrence rate to be in the region of 90% after six months. This has led to the introduction of adjunctive agents such as beta radiation and mitomycin C. However, these agents are not without their own ocular complications. Other techniques employed include conjunctival autografts and amniotic membrane transplantation.

The differential diagnosis of pterygia include pseudopterygia, which are folds of conjunctiva adherent to a corneal lesion. The lesion may be an ulcer or area of peripheral thinning. However, unlike true pterygia where the conjunctiva is adherent to the whole cornea, their pseudo counterparts are only adherent to the corneal lesion in question.

Another important lesion that must be recognised in the differential diagnosis is conjunctival and corneal intraepithelial neoplasia (CCIN). Essentially, this is a dysplastic lesion with a low potential for malignant transformation. Histologically, there is dysplasia (abnormal cellular changes) of the epithelium, ranging from the basal third to its full thickness. Once the whole epithelium becomes dysplastic, it is known as carcinoma *in situ* as the basement membrane is not breached.

The appearance of CCIN may adopt various guises that include a raised gelatinous lesion, one that is papillomatous in appearance and a diffuse non-descript area of conjunctival thickening.

Patients suspected of acquiring CCIN

should be referred urgently as there still is a risk, albeit low, of the lesion transforming into a squamous cell carcinoma. Treatment usually involves excision with adjunctive cryotherapy or the use of topical anti-metabolites, such as mitomycin C or 5-fluorouracil. The lesion is usually slow growing and is rare in young patients (except patients suffering from AIDS). A history of ultraviolet exposure is common.

Other tumours that may be confused with either pterygia or CCIN include sessile papillomata and amelanotic melanoma.

Pigmented lesions

Pigmented lesions of the conjunctiva are common, especially in dark skinned individuals. 'Conjunctival epithelial melanosis' is the term used to describe the pigmentation observed in such patients. Although the pigmentation is bilateral, it is not uncommon for the degree to be asymmetrical. Since the pigmentation is confined to the epithelium, it will move freely over the globe when manually displaced. Sometimes the pigmentation may extend into the peripheral cornea.

Common pigmented lesions that may be confused with melanosis include axenfeld loops, which is an area of melanosis surrounding a intrascleral nerve, conjunctival freckles and adrenochrome deposits. The latter should be rarely encountered now, as it is representative of clumps of pigment associated with the use of adrenaline drugs (now seldom employed) in the treatment of glaucoma.

Primary acquired melanosis (PAM) is invariably a unilateral condition, which affects middle aged caucasian individuals. Unlike conjunctival epithelial melanosis, PAM may be a pre-malignant condition. Indeed, the risk of transformation into malignant melanoma may be as great as 50% in patients who demonstrate cellular atypia (atypical cells) on biopsy and immuno-histochemistry. Since PAM, with or without atypia, maybe indistinguishable clinically, an ophthalmological opinion should be sought for any melanotic lesion in a caucasian individual acquired later in life. Ominous signs include melanosis in the caruncle and the appearance of nodules. It is imperative that the optometrist everts both lids to exclude intraepithelial spread.

Conclusion

This article has outlined the various conjunctival, episcleral and scleral lesions, together with their aetiologies and differentials, which might present to the ophthalmic practitioner. A brief referral guide has been included where appropriate in order to highlight the most appropriate, management plan.

Further reading

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- Kanski JJ and Nischal KK (1999) Ophthalmology. Clinical Signs and Differential Diagnosis. Mosby, Philadelphia.
- Parrish II RK (2000) Atlas of Ophthalmology. Butterworth Heinemann, Oxford.

Acknowledgements

Figures 1-5 by courtesy of Professor Susan Lightman.

Module questions

Course code: c-2688

Please note, there is only one correct answer. Enter online or by using the form provided.

- Which one of the following statements regarding scleral anatomy is incorrect?
 - Episclera contains vascular connective tissue
 - The deep vascular plexus can be easily manually moved over the overlying structure
 - Conjunctival vessels blanch with topical vasoconstrictors
 - The lamina fusca lies adjacent to the uveal layers
- Which one of the following statements regarding episcleritis is correct?
 - The condition primarily affects the elderly
 - Pain typically radiates to the jaw
 - Urgent referral is mandatory
 - The condition is benign
- Which one of the following statements regarding scleritis is correct?
 - It is always associated with acute pain
 - Relapsing polychondritis is the most common cause
 - Ocular surgery is a risk factor
 - Vision is always spared
- Which one of the following statements regarding scleritis is incorrect?
 - Necrotising scleritis is characterised by avascular patches
 - It is usually treated with topical steroids
 - It may co-exist with anterior uveitis
 - Staphyloma is a known complication
- Which one of the following statements regarding the conjunctiva is incorrect?
 - The bulbar portion covers the anterior sclera
 - It consists of epithelial and stromal tissue
 - The goblet cells secrete mucin
 - The epithelium is highly vascularised
- Which one of the following statements regarding signs and symptoms of conjunctival disease is incorrect?
 - Subconjunctival haemorrhages may be observed in adenoviral infections
 - Follicles indicate the presence of severe episcleritis
 - Chemosis may be seen in severe inflammation
 - Papillae are present in allergic eye disease
- Which one of the following statements is correct?
 - Vernal keratoconjunctivitis can be managed entirely by the optometrist
 - Atopic keratoconjunctivitis normally resolves by puberty
 - The most common virus to affect the conjunctiva is herpes simplex
 - Chlamydial conjunctivitis may be unilateral
- Which one of the following statements is incorrect?
 - A purulent discharge suggests severe bacterial infection
 - A watery discharge is observed in viral conjunctivitis
 - Tender lymphadenopathy is characteristic of allergic conjunctivitis
 - Keratitis often co-exists with adenoviral serotype 8 conjunctivitis
- Which one of the following requires urgent referral to an ophthalmologist?
 - Adenoviral conjunctivitis
 - gonococcal conjunctivitis
 - Episcleritis
 - Simple bacterial conjunctivitis
- Which one of the following is not an example of conjunctival pigmentation?
 - Conjunctival epithelial melanosis
 - Primary acquired melanosis
 - Amelanotic melanoma
 - Axenfeld loops
- Which one of the following statements regarding pterygia is incorrect?
 - It is a fibrovascular overgrowth of the conjunctiva
 - It is most commonly found encroaching the temporal limbus
 - Surgery requires adjunctive therapy to reduce recurrence
 - It is a known cause of induced astigmatism
- Which one of the following statements is correct?
 - Primary acquired melanosis is common in dark skinned races
 - Pingueculae are pre-malignant lesions
 - Pseudopterygia are adherent to the whole cornea
 - Conjunctival and corneal intraepithelial neoplasia (CCIN) has malignant potential

An answer return form is included in this issue. It should be completed and returned to: CET initiatives (c-2688), OT, Victoria House, 178-180 Fleet Road, Fleet, Hampshire, GU51 4DA by March 8, 2006. Under no circumstances will forms received after this date be marked – the answers to the module will have been published in our March 10, 2006 issue.

Differential Diagnosis of Ocular Disease Module 9 Part 2

CET answers

Here are the correct answers to Module 9 Part 1 of Differential Diagnosis of Ocular Disease – The eyelids and the orbit – key signs for differential diagnosis and management Course code c-2686 which appeared in our January 13, 2006 issue.

1. Which one of the following statements is correct regarding orbital anatomy?

- The palatine bone forms part of the floor
- The zygomatic bone forms part of the medial wall
- The ethmoid bone forms part of the roof
- The lacrimal bone forms part of the lateral wall

a is correct

The orbit can be compartmentalised into five structures – namely the roof (lesser wing of sphenoid and orbital plate of the frontal bone), the floor (zygomatic, maxillary and palatine bones), the lateral (greater wing of sphenoid and zygomatic bones) and medial (maxillary, lacrimal, ethmoid and sphenoid bones) walls and, finally, the superior orbital fissure.

2. Which one of the following statements regarding proptosis is correct?

- Dystopia always occurs in conjunction with proptosis
- Axial proptosis is never caused by tumours
- Ipsilateral enophthalmos is a cause of pseudoproptosis
- The degree of proptosis can be measured with a rule

d is correct

Dystopia may co-exist with proptosis or its recessive counterpart. Proptotic eyes that are axial in nature are usually associated with lesions confined to the muscle cone, such as optic nerve tumours. Causes of pseudoproptosis include an enlarged ipsilateral eye (for example, high myopia), ipsilateral eyelid retraction or contralateral enophthalmos. Proptosis may be quantified by measuring from the lateral orbital ridge to the corneal apex with a transparent rule.

3. Which one of the following is not a cause of pseudoproptosis?

- Nanophthalmos
- High myopia
- Ipsilateral eyelid retraction
- Contralateral enophthalmos

a is correct

Nanophthalmos is not a cause of pseudoproptosis. Causes of pseudoproptosis include an enlarged ipsilateral eye (for example, high myopia), ipsilateral eyelid retraction or contralateral enophthalmos.

4. Which one of the following is a myogenic cause of ptosis?

- Oculomotor nerve palsy
- Marcus Gunn jaw winking syndrome
- Horner's syndrome
- Myasthenia gravis

d is correct

Oculomotor nerve palsy, Marcus Gunn jaw

winking syndrome and Horner's syndrome are all neurogenic causes of ptosis. Myasthenia gravis is a myogenic cause of ptosis.

5. Which one of the following statements is incorrect regarding thyroid eye disease?

- Patients are typically hyperthyroid
- Eyelid retraction is a manifestation
- Treatment of the thyroid dysfunction always corrects the ophthalmic signs
- Corneal ulceration is a complication

c is correct

Thyroid eye disease or ophthalmic Grave's disease is most commonly associated with hyperthyroidism. Eyelid retraction and corneal ulceration are signs of thyroid eye disease.

6. Which one of the following is suggestive of orbital rather than preseptal cellulitis?

- Hyperaemic lid
- Ophthalmoplegia
- Tenderness
- Previous history of infection

b is correct

A hyperaemic lid, tenderness and a previous history of infection are all signs suggestive of preseptal cellulitis.

7. Which one of the following statements regarding eyelid anatomy is correct?

- Müller's muscle is innervated by the parasympathetic system
- The levator is innervated by the abducens nerve
- The glands of Zeiss are sweat glands
- The meibomian glands on the upper lid outnumber those on the lower

d is correct

Müller's muscle is innervated by the sympathetic nervous system. The levator muscle is innervated by the oculomotor nerve. The glands of Zeiss are modified sebaceous glands. The meibomian glands are more numerous in the upper tarsal plate, with approximately 25 in this region compared to approximately 20 in the lower.

8. Which one of the following signs are suggestive of malignancy?

- Normal lid architecture
- No documented growth
- Normally directed lashes
- Bleeding

d is correct

Lesions that have grown over a relatively short period of time, or have undergone morphological changes such as spontaneous or prolonged bleeding, should arouse suspicion of malignancy.

9. Which one of the following is not a differential diagnosis of ptosis?

- Contralateral hypotropia
- Contralateral eyelid retraction
- Dermatochalasis
- Brow ptosis

a is correct

Contralateral eyelid retraction, dermatochalasis and brow ptosis should all be considered in the differential diagnosis of ptosis.

10. Which one of the following is not a cause of ectropion?

- Dermatitis
- Lower lid mass
- Cicatrising lesion of the palpebral conjunctiva
- Horizontal lid laxity

c is correct

Dermatitis, a lower lid mass and horizontal lid laxity are all causes of ectropion.

11. Which one of the following is not a cause of madarosis?

- Anterior eyelid margin disease
- Psoriasis
- Hyperthyroidism
- Malignant lesions

c is correct

Anterior eyelid margin disease, psoriasis and hypothyroidism are the most frequent primary causes of madarosis to be encountered by the optometrist. In addition, malignant processes may cause madarosis.

12. Which one of the following statements is correct?

- Distichiasis is always congenital
- Choroidal folds are always symptomatic
- Optic neuropathy secondary to orbital disease is only associated with tumours
- Thyroid eye disease is the most common cause of unilateral proptosis

d is correct

Although distichiasis may be congenital, acquired cases are usually secondary to cicatrising lesions such as Stevens-Johnson syndrome and cicatrising pemphigoid. Although choroidal folds are contemporaneous with the onset of severe proptosis, their presence may, in certain circumstances, pre-date the onset of orbital signs. Thyroid eye disease is the most common cause of both unilateral and bilateral proptosis and as it may co-exist with optic neuropathy, formal tests to assess the health of the nerve should be performed on all patients. In addition, since the cause of optic neuropathy is compression secondary to the enlarged recti muscles, optic nerve dysfunction may not correlate with the degree of proptosis.