OT CET CONTINUING EDUCATION & TRAINING

1 FREE CET POINT

OT CET content supports Optometry Giving Sight

ACADEMY FOR EYECARE EXCELLENCE. CIBAVISION

Approved for: Optometrists ✔ Dispensing opticians ✔ CLPs ✔

Having trouble signing in to take an exam?
View CET FAQ Go to www.optometry.co.uk

Anterior eye complications in diabetes mellitus: Part 1

COURSE CODE C-16466 O/D/CL

Alan Hawrami BSc (Hons) PGDip

Diabetes mellitus (DM) is clinically divided into two major types; insulin-dependent (Type 1) and non-insulin dependent (Type 2). Both types can result in complications due to oxidative and osmotic stress from chronic hyperglycaemia. Although Type 1 DM pathogenesis differs from that of Type 2, it is thought that the pathophysiology of secondary DM complications at a cellular level is the same.[1] Aside from vascular changes to the retina, which are the most common effect of DM, the anterior structures of the eye can also become dysfunctional due to hyperglycaemia. It is vital for eye care professionals to recognise such changes so that early and rapid treatment can prevent irreversible damage. This article outlines the complications that occur in the anterior eye of people with DM.

Type 1 DM is the direct consequence of irreversible pancreatic beta-cell destruction in an autoimmune attack by the body,[2] leading to complete dependence on insulin created external from the patient.[3] A rise in blood glucose in the absence of insulin therapy will cause a tendency to develop ketoacidosis (diabetic coma).[4] Type 1 DM has a young age onset[5] and the prevalence varies between countries, as it is linked with ethnicity and race, with a particularly high incidence seen in Finland, Sweden and Norway.[6] The disease is also associated with genetic markers, particularly through genes in the HLA region,[7] and twin studies have shown that a genetic factor is present.[8] Type 1 idiopathic DM is a variant of Type 1 DM and may present with no known cause and no sign of autoimmune attack.[9] Common symptoms include acute polydipsia (excessive thirst), polyuria (increase in urine volume and frequency), polyphagia (excessive hunger), and weight loss.[10]

Type 2 DM is the most common form of DM and is insidious in onset.[11] The main causes of Type 2 DM are a reduction in insulin secretion, a resistance to insulin action or a combination of both.[12,13] It is suggested that insulin resistance occurs as a result of altered mitochondrial function through the electron transport chain.[14,15] Commonly, the age of onset for Type 2 DM occurs in the middle age group[16] and usually presents with obesity, but it can be asymptomatic.[17] Hyperglycaemia in Type 2 DM is milder than in Type 1, therefore it is controlled primarily by diet and oral hypoglycaemic agents,[18] although insulin may also be required when diet and tablet therapy fail to induce blood glucose homeostasis. Type 2 DM is associated with a strong genetic component, but personal diet and lifestyle also play a part,[19] as daily glucose levels depend on the patient's dietary intake.[11] Patients with a southern Asian or Middle Eastern background are at an increased risk of developing Type 2 DM, including people who have emigrated from these areas to other countries.[20]

Epidemiology

The number of people over the age of 20 years globally with DM was estimated to be 171 million during the year 2000, and is projected to rise by almost three-fold in the year 2030 due to population growth, increased life expectancy and altered diets and living.[21] India, China and USA have the highest estimated numbers.[21] In the UK, 1.4 million people are diagnosed with DM, of which 200,000 are Type 1 and 1.2 million are Type 2. The number of undiagnosed cases is estimated to be of a similar amount.[22]

Ocular complications

tear film and tearproduction

Dry Eye Syndrome (DES) is a common occurrence amongst patients with DM, with tear film stability and tear break up time (TBUT) being greatly decreased compared to healthy patients.[23-26] In one study, nearly 70% of patients with DM presented with a TBUT of less than ten seconds, while none of the control subjects had poor TBUT values.[23] A reduced TBUT seems to be unrelated to the duration of DM or to retinopathy status, but it is linked to poor metabolic control and peripheral neuropathy of lacrimal gland innervation.[23,25,27] The mucin layer of the tear film is produced by goblet cells residing in the conjunctiva and corneal epithelium, and it is a component of tears that is necessary for tear film spreading and wetting. The goblet cell density is significantly reduced in patients with DM, compared to healthy patients, which may give another explanation as to the reduced tear film stability and TBUT.[23,28]

Total and basal tear secretions are reduced in patients with DM, and this

is shown by significantly decreased Schirmer test values; as with TBUT, the reduced Schirmer value is linked to peripheral neuropathy and poor glycaemic control,[23,27] but it is also linked to an advanced stage of diabetic retinopathy. Furthermore, there is a reduction in reflex tearing, which may be due to a decrease in corneal sensitivity (see later).[23,24,26,27]

Abnormal tear film production and composition not only causes discomfort for the patient, but can also lead to potentially serious complications of the corneal epithelium.[24] Management is centred on treatment of the underlying cause of the dry eye, but for symptomatic patients, artificial tear substitutes such as cellulose ethers can give temporary relief.[29]

Conjunctiva

In patients with DM, vascular defects occur in the conjunctiva, including conjunctival aneurysms (Figure 1),[30] reduced blood flow, and macro-vessel dilation.[31] Increased tortuosity of the vessels in the conjunctiva can also be observed and it appears to mirror micro-vascular changes in the retina.[32]

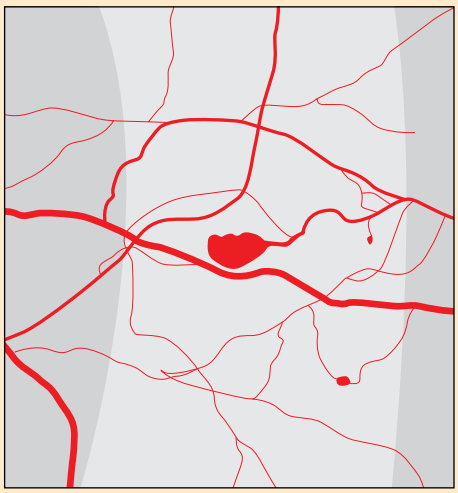

Figure 1
Conjunctival aneurysms in diabetes mellitus. Produced based on a picture in McCulloch & Pashby.[30]

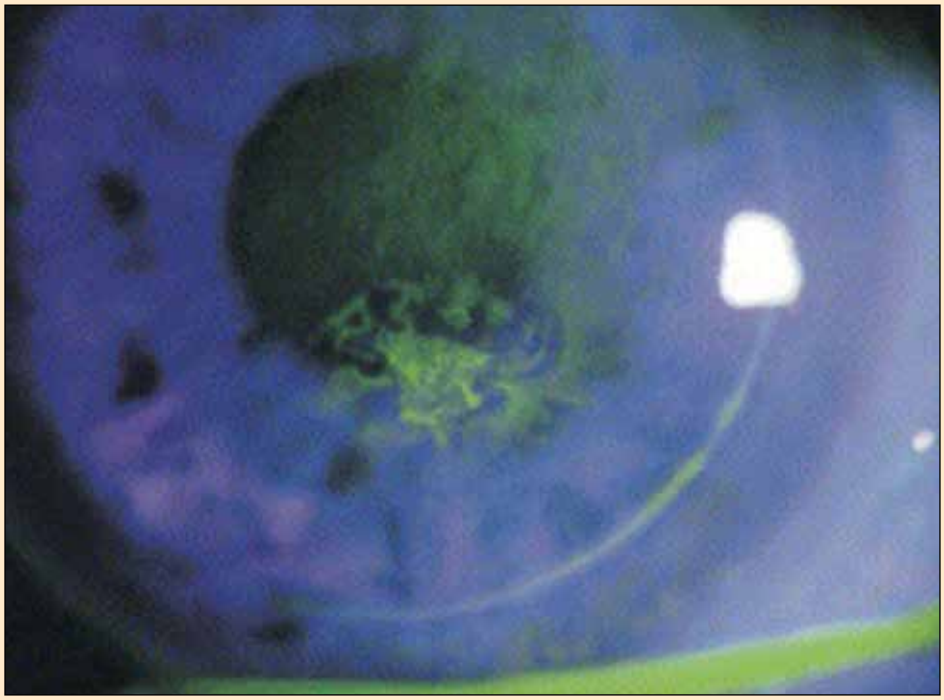

Figure 2
Recurrent corneal epithelial erosion. Positive fluorescein staining shows areas of epithelial defect. Reproduced with permission from Elsevier.[37]

There is also an increased risk of acquiring acute infectious conjunctivitis.[33] Altered structures in the conjunctiva can consist of thickened basement membrane along with the appearance of collagen-like fibrils.[34] These metabolic and structural changes naturally occur with age, however they are accelerated in patients with DM.[34] These patients also show more prominent signs of conjunctival metaplasia, which could be due to the abnormal reflex tearing, which induces chronic damage of the conjunctival surface.[35] Consequently, the compromised conjunctival structure results in increased risk of invasion by pathogens, causing infection.

Corneal epithelium

There is a greater risk of developing complications of the corneal epithelium in patients with DM, and these can be found in up to two-thirds of asymptomatic patients.[36] Keratopathy including recurrent corneal erosions (Figure 2),[37] punctate keratitis (Figure 3),[38,39] and regular corneal epithelial defects can be present.[40] The epithelial lesions are primarily found at the lower half of the cornea and can vary from very superficial to full thickness defects.[41] These complications are also present in patients with DM at a higher degree of severity compared to healthy patients.[26] A simple corneal abrasion can lead to deeper damage compared to a healthy patient's eye, even possibly leading to detachment of the basement membrane.

The epithelium barrier function is considerably weakened in the cornea of a person with DM, making it more susceptible to foreign bodies and organisms.[42] Studies have shown that fluorescein uptake is considerably increased in patients with DM compared to those without DM, and impaired barrier function in the corneal epithelium is more likely to occur with a higher level of HbA1c and the

Figure 3
Punctate keratitis as viewed with a slit lamp.[38] Reproduced with permission from Elsevier.

presence of diabetic retinopathy.[42,43]

The corneal epithelium in patients with DM heals at a slower rate than a healthy epithelium and therefore requires closer medical attention,[44,45] especially when contact lenses are involved. The corneal epithelium normally undergoes constant regeneration, with a full epithelium turnover of 4-7 days.[46] An abnormally slow rate of re-epithelisation of the cornea is present in patients with DM, which is thought to be due to abnormal corneal basement membrane adhesions.[40,47] Basement membrane thickening and irregular basement membrane attachment to the stroma are some of the mechanisms theorised behind the delay in healing, however it is not precisely understood.[48,49]

Structural microfolds in Bowman's layer can also be present.[50] However, Bowman's layer is believed to have no critical function.[51] Corneal hysteresis is increased in patients with DM, which would have an effect on the intraocular pressure (IOP) reading.[52] Newer tonometers, such as the ocular response analyser, have, however, been developed to compensate for corneal viscoelasticity into the IOP reading.[53]

Contact lenses

With all the corneal problems experienced by a patient with DM, it would be naturally assumed that contact lenses would be contraindicated in these patients. However, numerous studies have shown that in well-controlled patients and with no corneal epitheliopathy, there would be no reason to argue against the use of contact lenses, so long as appropriate advice and precaution is taken.[54-56]

Lid conditions such as blepharitis, styes and lid infections are more common in patients with DM,[55] which, if present, could irritate and cause problems for the patient. Rigid gas permeable (RGP) lenses seem to reduce the risk of infection,[57] while a soft lens would reduce the risk of any abrasions that would compromise the patient's cornea because of delayed healing.

Recent advances in contact lens technology have made it possible to have a micro-sized glucose sensor within the actual contact lens itself, which would make the monitoring of DM much more efficient.[58]

Corneal endothelium and central corneal thickness

The corneal endothelium of a patient with DM has been shown to exhibit polymegathism and pleomorphism[59-60] (Figure 4). However, the changes are more difficult to differentiate in patients with Type 2 DM, as these changes naturally occur with increasing age too.[59]

The main two functions of the corneal endothelium are to allow nutrients to pass to the outer layers of the cornea,

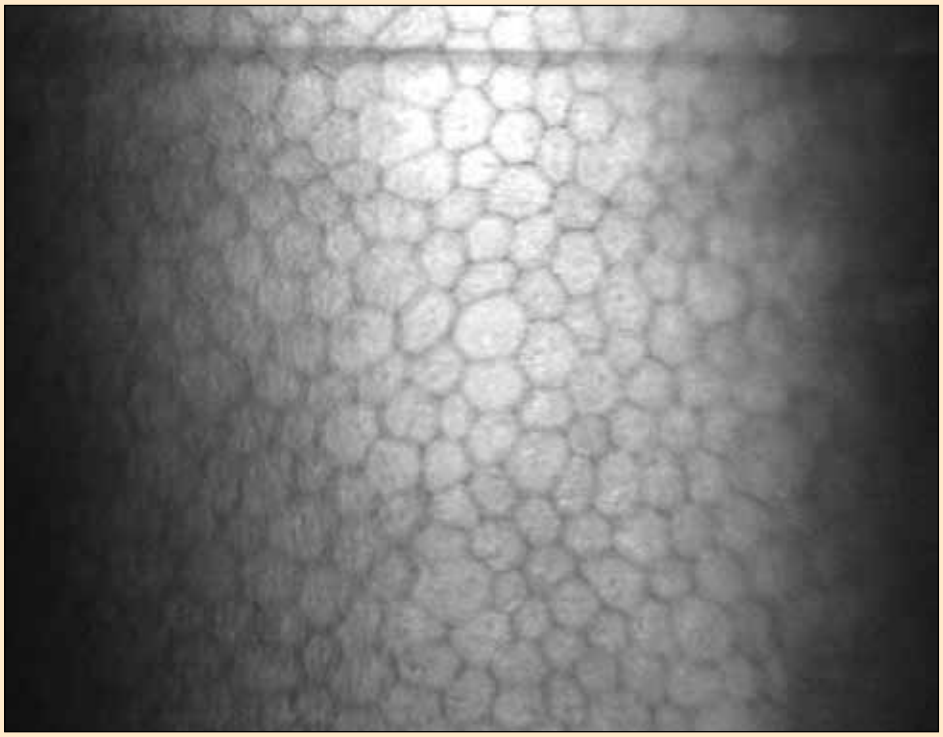

Figure 4
Early corneal polymegathism and pleomorphism, as indicated by differing sizes and shapes of cells.

and to prevent the stroma from being overloaded with water by pumping it from the stroma into the aqueous. Corneal endothelial function is decreased in patients with DM, more markedly in eyes presenting with retinopathy and/or with abnormal glucose levels.[61] These changes are also responsible for an increase in central corneal thickness (CCT). However, there are numerous conflicting studies regarding the effects of DM on corneal thickness, in both types of the disease, with some suggesting an increase in both types of DM, including diabetic retinopathy,[62,63] whilst others have shown that it doesn't increase in either Type 1[64] or Type 2 DM.[59,60] Larsson et al.[59] suggested that these endothelial changes naturally occur with increasing age and are therefore not specific to DM.

Folds in Descemet's membrane are characteristic of corneal oedema, as the cornea can only swell posteriorly, thus reducing the posterior corneal surface area, which therefore suggests that an increase in CCT may be due to higher water content within the cornea.[62] An increase in CCT occurs at the early stages of DM, and may possibly be one of the first noticeable changes in the diabetic eye.[49,62] Busted et al.[62] also asserted that the link between CCT and retinopathy could perhaps be an indication of upcoming retinal complications.

An increased CCT has implications for IOP measurement, since a thicker cornea will result in an increased IOP reading; the increase averages 0.46mmHg with non-contact tonometry (NCT), and 0.28mmHg with Goldmann applanation tonometry (GAT), for every 10µm increase in CCT.[65]

Corneal sensitivity

Reduced corneal sensitivity is a well-documented phenomenon in patients with DM,[23,24,27,49,66] representing the neurological effects of the systemic disease. The cornea is innervated by a network of nerve endings located primarily in the anterior stroma, and is supplied by long ciliary nerves originating from the trigeminal nerve.[67] Neuropathy of the ophthalmic division of the trigeminal nerve results in neurotrophic keratopathy, which results in a loss of sensory innervation to the cornea.[68] Neurotrophic keratopathy was not orginally associated with DM,[69] however, a more recent report on the condition acknowledges it as a manifestation of DM.[70] Neurotrophic keratopathy can present in three different stages.[70] Stage 1 consists of epithelial irregularity, punctate epitheliopathy and hyperplasia, with possible superficial neovascularisation. Stage 2 is characterised by persistent epitheliopathy (Figure 5),[71] poor epithelial healing, folds in Descemet's membrane and stromal swelling. Stage 3 is characterised by a corneal ulcer that can advance to perforation or stromal melting (dissolving of the stroma).

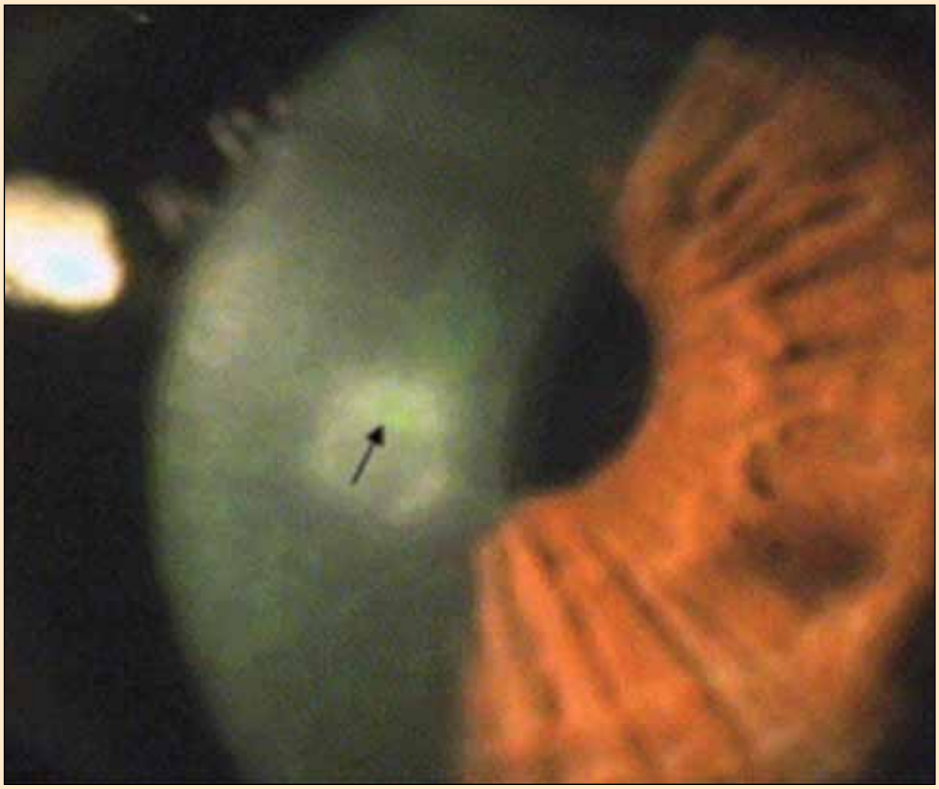

Figure 5
Neurotrophic keratopathy with a persistent epithelial defect.[71] Reproduced with permission from Elsevier.

Corneal sensitivity reduces with DM duration and is inversely related with the level of neuropathy.[49,72] However, Dogru et al.[23] discovered that reduced corneal sensitivity is directly linked to patients with poor metabolic control. The study also found that all of their patients presenting with peripheral neuropathy and corneal lesions had reduced corneal sensitivity, suggesting that corneal neuropathy and keratopathy may be manifestations of the distal peripheral neuropathy of DM.

Conclusion

This article has discussed some of the anterior eye complications that can arise from diabetes mellitus (DM), which eye care practitioners need to be aware of and be able to detect due to the risk of further clinical complications. The majority of these changes relate to poor

1 FREE CET POINT

OT CET content supports Optometry Giving Sight

ACADEMY FOR EYECARE EXCELLENCE. CIBA VISION

Approved for: Optometrists ✔ Dispensing opticians ✔ CLPs ✔

Having trouble signing in to take an exam?
View CET FAQ Go to www.optometry.co.uk

systemic glycaemic control and therefore such signs can be a useful indicator of the early stages of undiagnosed DM, in addition to any retinal vascular changes that may be present.

This article has concentrated on changes that can occur in the tear film, conjunctiva and cornea, whilst the next article in this series will delve deeper into the anterior eye segment structures, looking at changes that can occur in the aqueous humour, the iris, the pupil, the lens, and accommodation/refraction, due to DM.

About the author

Alan Hawrami obtained his optometry degree at City University and has completed a post-graduate degree at Aston University.

References

See http://www.optometry.co.uk clinical/index. Click on the article title and then download "references".

Module questions

Course code: C-16466 O/D/CL

1. Type 1 diabetes mellitus occurs as a result of:
a) Autoimmune pancreatic beta-cell destruction
b) Hyperglycaemia
c) An increase in the levels of insulin
d) Obesity

2. Which one of the following statements about diabetes mellitus is TRUE?
a) Conjunctival goblet cell density is increased
b) The mucin layer of the tear film is decreased
c) There is an increase in tear stability
d) Dry eye never occurs

3. Vascular defects of the conjunctiva in a patient with diabetes mellitus can include which of the following?
a) Conjunctival aneurysms
b) Vessel tortuosity
c) Blood flow reduction
d) All of the above

4. Which of the following statements about corneal keratopathy is FALSE?
a) It can include recurrent epithelial erosions
b) It takes longer to heal in patients with diabetes mellitus
c) It is not a contraindication for contact lens wear
d) It can be found in asymptomatic patients

5. Increased central corneal thickness in a patient with diabetes mellitus is due to:
a) Abnormal endothelial function
b) Increased IOP
c) Delayed re-epithelisation
d) Corneal epitheliopathy

6. Which of the following statements about corneal sensitivity in a patient with diabetes mellitus is TRUE?
a) It does not respond to increased or decreased metabolic control
b) It is abnormal due to impaired trigeminal nerve function
c) It is not acknowledged as a manifestation of diabetes mellitus when it is impaired
d) It is reduced because of corneal keratopathy

PLEASE NOTE There is only one correct answer. All CET is now FREE. Enter online. Please complete online by midnight on August 19 2011 - You will be unable to submit exams after this date – answers to the module will be published on www.optometry.co.uk. CET points for these exams will be uploaded to Vantage on August 29 2011.