

## The eye in endocrine disease

Chun H Lau, Susan Lightman

### INTRODUCTION

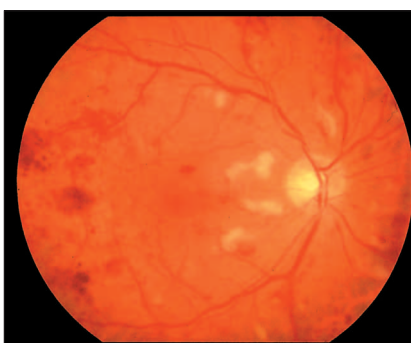
The eye and its adnexae can be involved in several different ways in endocrine disorders and the ocular manifestations vary. Ocular symptoms and signs may herald the diagnosis and patients may present with early or late signs of disease.

### ENDOCRINE DISEASES AND THE EYE

The eye can be affected by disorders of the pituitary gland, hypothalamus, thyroid gland and pancreas. This article describes the functional ocular impairment and associated symptoms and signs commonly encountered in endocrine diseases as well as their management. The ocular manifestations of these disorders can involve the adnexae, external eye, ocular surface, intraocular structures, orbit and intracranial pathways and centres related to ocular function.

Occasionally other endocrine diseases can also affect the eye. Thus

*Figure 1. Hypertensive retinopathy (grade III) with multiple peripapillary cotton wool spots and associated central retinal vein occlusion.*



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Cushing's syndrome can rarely induce central serous retinopathy whereas pheochromocytoma and hyperaldosteronism can induce hypertension with ocular consequences (Table 1, Figure 1). Darkening of skin including periorbital skin can be seen in both Addison's disease and Nelson's syndrome.

### DIABETES MELLITUS

Both type 1 and type 2 diabetes commonly affect the eyes. Given its high prevalence (about 2–5% of the population in developed countries), it represents a huge burden to health care worldwide. The high prevalence of diabetic retinopathy (Klein et al, 1984a,b), and in particular diabetic macular oedema (Klein et al, 1995), explains why it is the leading cause of blindness in developed countries. A significant cause of visual loss in type 1 diabetes is proliferative diabetic retinopathy whereas in type 2 diabetes macular oedema predominates (Table 2).

Diabetes induces microangiopathy, macroangiopathy and hyperlipidaemia which can cause cerebrovascular, cardiovascular and peripheral vascular diseases. These explain the high prevalence of diabetic retinopathy (Figures 2 and 3), nephropathy and neuropathy. Certain hormonal disorders (e.g. acromegaly, Cushing's syndrome, pheochromocytoma, hyperaldosteronism and thyrotoxicosis) are associated with or increase the risk of diabetes.

Management involves preventing or delaying the onset of diabetic eye diseases, especially retinopathy, by good control of the blood sugar and blood lipid levels, and the blood pressure (Stratton et al, 2001). Regular follow up by an ophthalmologist is required when retinopathy is detected. Laser treatment includes focal or grid-pattern for maculopathy, and panretinal photocoagulation for proliferative retinopathy (Diabetic Retinopathy Study Research Group, 1994). More severe complications such as retinal detachment or persistent vitreous haemorrhage may require surgery (Diabetic Retinopathy Vitrectomy Study Research Group, 1990).

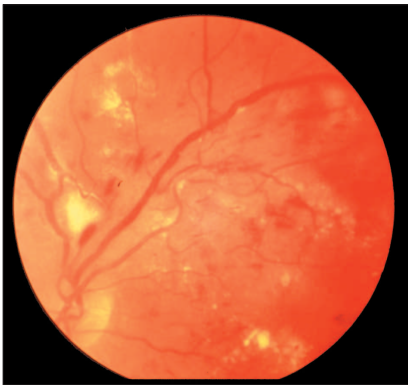
### THYROID DISEASE

Hyperthyroidism is a common disorder affecting about 2% of women (mainly aged between 20 and 40 years) and 0.2% of men. Causes include a hyperfunctioning thyroid nodule, excessive thyroid-stimulating hormone from the anterior pituitary, excessive thyroid hormone replacement therapy, increased thyroid hormone release in early thyroiditis and Grave's disease, which alone accounts for about 80% of all hyperthyroidism and is commonly associated with thyroid eye disease.

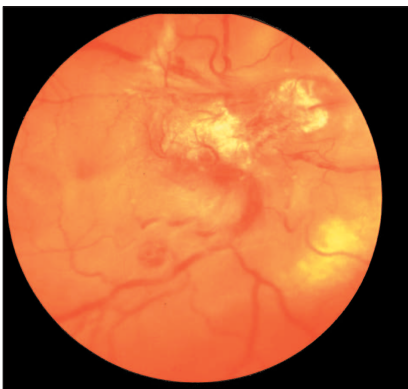
The ocular inflammatory process produces deposition of highly hydrophilic glycosaminoglycans in the extraocular muscles and orbit with cellular infiltration and subsequent fibro-

**TABLE 1.**  
Ocular manifestations of hypertension

Cranial nerve III, IV, VI palsies with ocular motility sequelae
Subconjunctival haemorrhage
Branch or central retinal artery or vein occlusion
Swollen disc from central or branch retinal vein occlusion and papilloedema
Hypertensive retinopathy: narrowed arterioles, arteriovenous crossing changes (nicking), cotton wool spots, retinal flame haemorrhages, hard exudates, macular star, papilloedema
Non-arteritic ischaemic optic neuropathy
Amaurosis fugax, visual loss, visual field defects, cortical blindness from stroke



**Figure 2.** Combined diabetic retinopathy and hypertensive retinopathy with hard exudates, cotton wool spots, irregular venous calibre, intraretinal microvascular abnormalities, macular oedema, and associated branch retinal vein occlusion with extensive flame-shaped haemorrhages.



**Figure 3.** Proliferative diabetic retinopathy with neovascularization from the disc and associated tractional retinal detachment.

sis to the muscles. The consequences are orbital volume expansion producing proptosis (*Figure 4*) with exposure keratopathy, compressive optic neuropathy with visual loss, and diplopia caused by fibrosis and tethering limitation to the levator and extraocular muscles. Thyroid eye disease (*Table 3*) can occur before, during or after the thyroid disease has been diagnosed or treated (Tallstedt et al, 1992) and can therefore be associated with euthyroid, hyper- or hypothyroid status.

Ophthalmic management includes protecting the overexposed ocular surface by generous lubrication (artificial tear drops and ointments), relieving optic nerve compression when vision is threatened by decompression proce-

TABLE 2. Ocular manifestations of diabetes	
Manifestations	Lesions
Binocular diplopia	Cranial nerve III, IV or VI palsy
Dry eyes	Autonomic neuropathy
Corneal erosions	More common
Cataract	Onset on average 10 years earlier than non-diabetic, occasionally cataract can develop acutely
Reduced vision	Cataract, retinopathy, advanced diabetic eye diseases, optic neuropathy
Neovascular glaucoma	Iris, angle neovascularization impeding aqueous drainage
Diabetic retinopathy (background, preproliferative)	Subclassified into stages with increasing severity and risk of developing into proliferative stage. Signs include dot/blot haemorrhage, hard exudate, venous beading, cotton wool spot, oedema, intraretinal microvascular anomalies
Maculopathy	Macular oedema which may be non-ischaemic or ischaemic
Proliferative	Neovascularization at optic disc, elsewhere in retina, iris or angle
Advanced diabetic eye diseases	Neovascular glaucoma, vitreous haemorrhage, retinal detachment
Ischaemic optic neuropathy	Non-arteritic
Diabetic papillitis	Swollen disc (unilateral or bilateral)
Ocular manifestations related to hypertension	Hypertension mainly secondary to nephropathy
Increased prevalence of infection	Postoperative ocular infection, chalazia are more common, orbital mucormycosis is serious fungal infection extending from adjacent paranasal sinuses

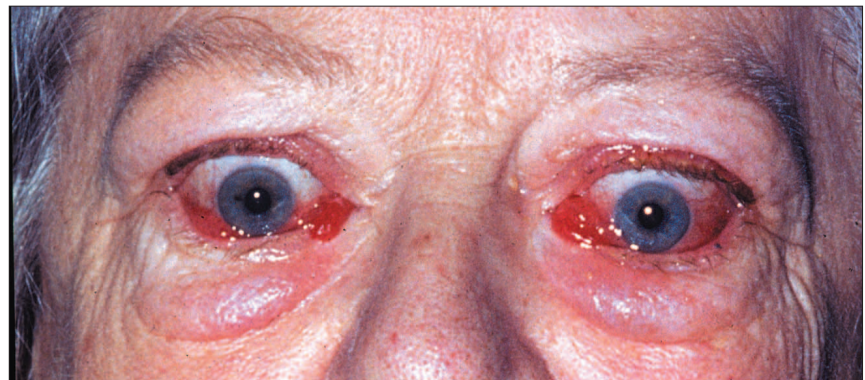
dures (medically with steroids, external beam radiotherapy or surgically by removal of orbital walls), restoring cosmesis by oculoplastic procedures (e.g. repositioning of lids), correction of diplopia and improvement of binocular single vision by extraocular muscle surgery.

### PITUITARY DISEASE

Pituitary disorders involve the eye in various ways. Hypersecretion of growth hormone (GH) from a pituitary

tumour causes acromegaly in adults. GH acts via the GH receptor as well as stimulation of hepatic and extrahepatic production of insulin-like growth factor-1 which promotes proliferation of bone, cartilage and soft tissues, resulting in increased size. In acromegaly there are prominent supraorbital ridges and ocular signs secondary to the associated diabetes and hypertension. Overproduction of thyroid-stimulating hormone resulted in hyperthyroidism with ocular consequences.

**Figure 4.** Thyroid eye disease with bilateral proptosis, congested episcleral vessels, conjunctival chemosis, lid oedema and retraction. There is no exposure keratopathy with frequent topical lubricant treatment.



**TABLE 3.**  
**Ocular manifestations in thyroid eye disease**

Manifestations	Features
Globe displacement	Usually bilateral axial proptosis (may be asymmetric) from orbital volume expansion
Puffy lids	Swelling from periorbital oedema
Upper and lower lid retraction	Increased sympathetic tone secondary to presumed increase in tissue catecholamine receptors
Upper lid lag on downgaze	
Restrictive ocular movement	Restricted upgaze and lateral gaze with diplopia, hypotropia, esotropia
Injected conjunctiva	Episcleral venous tortuosity and conjunctival chemosis from orbital congestion
Exposure keratopathy	Corneal ulcer from dryness secondary to proptosis, retracted eyelids and incomplete lid closure
Raised intraocular pressure	On upgaze (Spierer and Eisenstein, 1991)
Compressive optic neuropathy	Reduced visual acuity and colour vision Relative or absolute afferent pupil defect Pale or swollen optic disc Visual field defects (central or cecentral scotoma, altitudinal, constriction)

The pituitary gland can be damaged in various ways (e.g. local pressure effect from pituitary adenoma or craniopharyngioma, post-irradiation) resulting in hypopituitarism. Features are generalized hair loss and thinning including the eyebrows and eyelashes, and pale and thin skin including periorbital skin. Pituitary tumours may extend to the suprasellar area with direct compression of the optic chiasm (Figures 5 and 6) and thus produce specific patterns of visual field defects (Budenz and Siatkowski, 1990). Typically the visual field defects begin as bitemporal supraquadrantopia because inferonasal fibres are first involved before becoming hemianopia. A pale disc or optic atrophy may fol-

low. Raised intracranial pressure can occur with associated papilloedema.

### MANAGEMENT

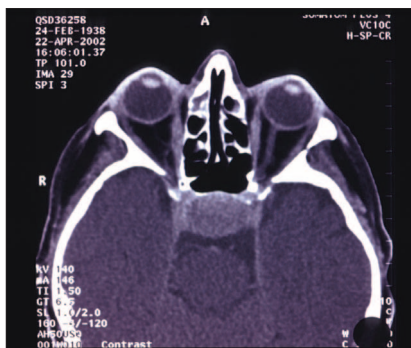
As mentioned above, ophthalmic management varies among the conditions. The principles of ocular management of eye conditions in relation to endocrine diseases are:

1. Early diagnosis by a complete medical history, physical examination including blood pressure measurement, neurological examination, eye examination with the help of appropriate imaging like ultrasound, X-ray, computed tomography and magnetic resonance imaging when needed

**Figure 6. Computed tomography scan of same patient as Figure 5 showing suprasellar extension of tumour and compression on optic chiasm.**



**Figure 5. Computed tomography scan showing pituitary tumour.**



2. Referral to endocrinologist and other experts for confirmation of suspected diagnosis and treatment of underlying endocrine disorder
3. Preservation of visual function
4. Restoration of cosmesis by reconstructive procedures. For these reasons, the management team is usually multidisciplinary and includes an ophthalmologist and an endocrinologist. Radiologists, surgeons, neurologists and neurosurgeons may be needed too.

### CONCLUSIONS

Prompt medical attention, early diagnosis and referral, and appropriate therapy are important for the best prognosis. Continuous follow-up care is essential. **HM**

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Budenz DL, Siatkowski RM (1990) Chiasmal visual field loss. In: Glaser JS, ed. *Neuro-ophthalmology*. 2nd edn. JB Lippincott, Philadelphia: 257-74

Diabetic Retinopathy Study Research Group (1994) Indications for photocoagulation treatment of diabetic retinopathy. Diabetic Retinopathy Study Report Number 14. *Invest Ophthalmol Clin* 27: 239-53

Diabetic Retinopathy Vitrectomy Study Research Group (1990) Early vitrectomy for severe vitreous hemorrhage in diabetic retinopathy: Four-year results of a randomized trial. Diabetic Retinopathy Vitrectomy Study Report Number 5. *Arch Ophthalmol* 108: 958-64

Klein R, Klein BE, Moss SE, Davis MD, DeMets DL (1984a) The Wisconsin Epidemiologic Study of Diabetic Retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol* 102: 520-6

Klein R, Klein BE, Moss SE, Davis MD, DeMets DL (1984b) The Wisconsin Epidemiologic Study of Diabetic Retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 years or greater. *Arch Ophthalmol* 102: 527-32

Klein R, Klein BE, Moss SE, Cruickshanks KJ (1995) The Wisconsin Epidemiologic Study of Diabetic Retinopathy. XV. The long-term incidence of macular edema. *Ophthalmology* 102: 7-16

Spierer A, Eisenstein Z (1991) The role of increased intraocular pressure on upgaze in the assessment of Graves' ophthalmopathy. *Ophthalmology* 98: 1491-4

Stratton IM, Kohner EM, Aldington SJ, Turner RC, Holman RR, Manley SE, Matthews DR (2001) UKPDS 50: risk factors for incidence and progression of retinopathy in Type II diabetes over 6 years from diagnosis. *Diabetologia* 44: 156-63

Tallstedt L, Lundell G, Torring O, Wallin G, Ljunggren JG, Blomgren H, Taube A (1992) Occurrence of ophthalmopathy after treatment for Grave's hyperthyroidism. The Thyroid Study Group. *N Engl J Med* 326: 1733-8