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NOW YOU SEE ME, NOW YOU DON'T: PATHOPHYSIOLOGY, DIAGNOSIS AND THERAPY OF CORNEAL DISEASE

Introduction

Critically important functions of the cornea are the transmission and refraction of light, for which the preservation of corneal transparency, curvature and surface smoothness are absolutely essential. As the outer protective shell of the eye, the cornea is exposed to environmental hazards and many disorders can lead to opacification of the cornea and subsequent vision loss. As ophthalmologists it is our job to optimize the medical and surgical treatment of corneal diseases in ways that help preserve both the structural integrity and transparency, and thus the main functions, of the cornea.

Anatomy and physiology

The cornea consists of four distinct layers: the anterior epithelium covered by the precorneal tear film, the stroma, Descemet's membrane and the endothelium. Each of these layers (apart from Descemet's membrane) has its own highly specialized cell type, which is crucial to normal function and maintenance of the cornea.

Tear film

The tear film is an exceedingly complex structure, consisting of 3 main layers. The precorneal tear film is approximately 7 µm thick. The meibomian gland-derived lipid layer is partitioned on the surface of the aqueous layer produced by the main and accessory tear glands. The aqueous layer is intermixed with soluble mucins, which connect with membrane bound mucins on the corneal epithelial surface. The tear film provides lubricating qualities and a smooth optical air/tear film interface. It also protects the epithelium from airborne contaminants, provides natural immunity to infectious agents through secretory immunoglobulin molecules and has an important role in cleansing the corneal surface.

Epithelium

The anterior corneal epithelium is a several cell layers thick, stratified, squamous, non-keratinized epithelium that forms a smooth, transparent optical surface together with the precorneal tear film and provides physical and molecular barriers to injury and the diffusion of compounds, including drugs.

Stroma

The stroma makes up most of the corneal thickness and is responsible for the tectonic strength and protective functions of the cornea. It consists of approximately 200 lamellae composed of fine diameter (approximately 35 nm) collagen fibres that are of uniform dimension and are evenly spaced at about 42 to 44 nm apart. The small, consistent diameter of the fibrils and the tight interfibrillar spacing have been implicated as the basis for corneal transparency.

Descemet's membrane

Descemet's membrane is the elastic basal lamina of the endothelium.

Endothelium

The corneal endothelium is one cell layer thick. Normal leakage of aqueous humor from the anterior chamber into the corneal stroma occurs around the endothelial cells. This leakage is important since the stroma derives most of its nutrition from the aqueous humor. Active and passive transport processes across the endothelial cell membranes in the direction of the anterior chamber counterbalance this leakage and maintain the relatively dehydrated status and clarity of the corneal stroma.

Non-ulcerative keratitis

Non-ulcerative keratitides are usually caused by chronic ocular surface irritation as a result of immune mediated diseases, tear film disorders or chronic exposure. These diseases are characterized by one or more of the following basic responses of the cornea to irritation: vascularization, edema, corneal fibrosis, pigmentation and epithelial keratinization. Non-ulcerative keratitis is accompanied by variable amounts and qualities of ocular discharge and blepharospasm. In severe cases vision can deteriorate due to loss of corneal transparency.

The most important non-ulcerative keratitides that will be discussed include keratoconjunctivitis sicca (KCS), chronic superficial keratitis (pannus, shepherd keratitis), brachycephalic syndrome and eosinophilic keratitis.

Ulcerative keratitis

Ulcerative keratitis is a common diagnosis in domestic animals. As a result of the surface defect present ulcers are always accompanied by pain (blepharospasm, epiphora) and conjunctival hyperemia.

The most important questions to answer during the diagnostic process are:

1) is the lesion superficial or deep? Here it is important to distinguish between lesions that involve the epithelium only and lesions in which a loss of corneal stroma has occurred. Fluorescein staining and proper use of a slit-lamp are required to make the distinction.
2) is the lesion infected or not? The presence of cellular (neutrophil) infiltrates, loss of corneal stroma and active corneal 'melting' suggest an infectious etiology
3) can a cause be identified? Mechanical causes (eyelid malposition, distichiasis, ectopic cilia, trichiasis, conjunctival foreign bodies) and exposure related disease (tear film abnormalities, brachycephalic composition) need to be identified/excluded.

The most important ulcerative keratitides that will be discussed include superficial, non-infected ulcerative diseases such as simple superficial erosive keratitis and spontaneous chronic corneal epithelial defects (SCCEDs, indolent ulcers, boxer ulcers). Infectious diseases of the cornea that will be discussed include herpes keratitis, deep and melting corneal ulcers and corneal lacerations/perforations.