PRIMEVIEW

CORNEAL DYSTROPHIES

nature reviews disease primers

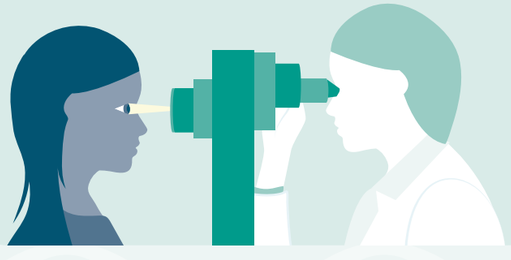
For the Primer, visit doi:10.1038/s41572-020-0178-9

Corneal dystrophies are inherited, usually progressive, bilateral disorders of the eye without inflammation or systemic effects. They often involve accumulation of material in one or more layers of the cornea, which may affect vision.

DIAGNOSIS

Corneal dystrophies are classified into four major types on the basis of the affected corneal layer and the underlying genetic cause. These types are epithelial and subepithelial dystrophies, epithelial–stromal *TGFBI* dystrophies, stromal dystrophies and endothelial dystrophies. Disease severity can range from asymptomatic to severe impairment of visual acuity. Most dystrophies present in adulthood and can be detected during routine ophthalmic assessment, but a few manifest at birth or early in life. Ophthalmic assessment includes examination of the cornea with different illumination and visualization techniques to determine the overall distribution of corneal deposits (for example, by broad-beam illumination) or to precisely pinpoint the location of deposits in the cornea (for example, by slit-beam illumination, in vivo specular or confocal microscopy, and anterior segment optical coherence tomography). Analysis of corneal thickness and sensation and measuring intraocular pressure are useful adjuvant tests.

The genes and/or mutations associated with some types of corneal dystrophy have been identified, whereas for others they remain to be mapped or identified

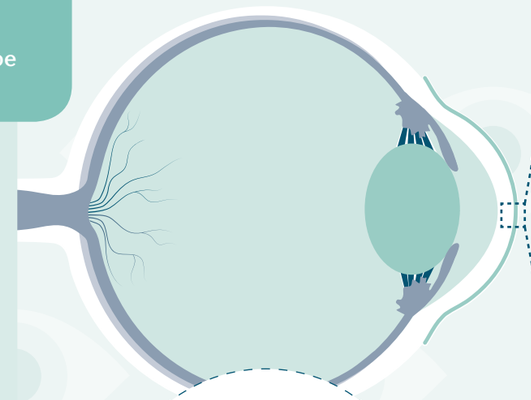


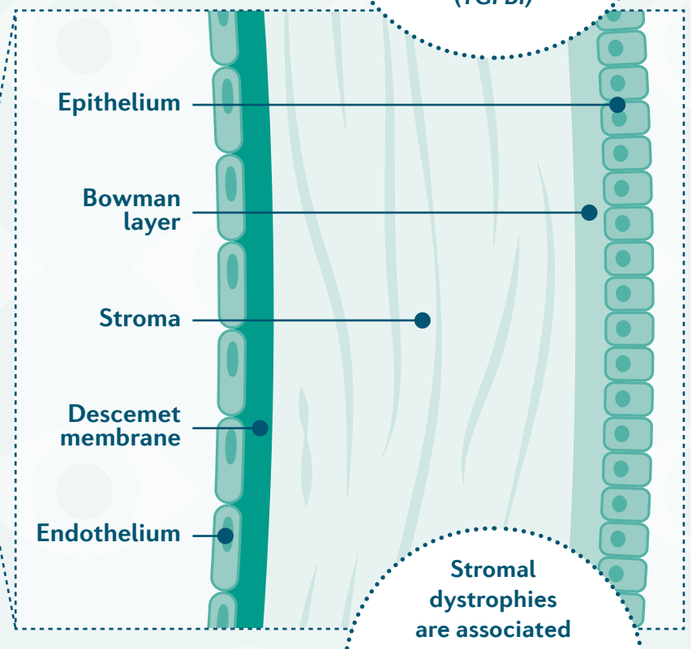
PATHOPHYSIOLOGY

Epithelial and subepithelial dystrophies are associated with mutations in various genes, including *TGFBI*, *TACSTD2*, *KRT3* and *KRT12*

The cornea comprises five layers — namely, the epithelium, the Bowman layer, the stroma, the Descemet membrane and the endothelium

Epithelial–stromal *TGFBI* dystrophies involve mutations in the cell adhesion modulator transforming growth factor β-induced (*TGFBI*)





Endothelial dystrophies are associated with mutations in various transcription factors, such as *TCF4*, *OVOL2*, *ZEB1* and *GRHL2*

Stromal dystrophies are associated with mutations in *CHST6*, *UBIAD1*, *DCN*, *PIKFYVE* and *STS*, amongst others

MANAGEMENT

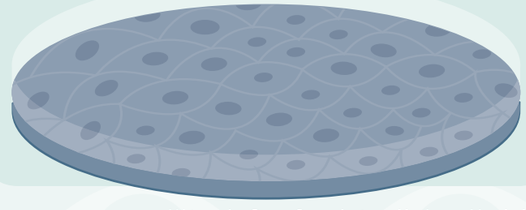
Management can be conservative (for example, optical lubricants or pharmacological agents) or involve laser surgery or corneal transplantation (keratoplasty) and depends on aspects of the disease, such as the type of dystrophy, its severity and the effect on visual function, and on patient factors, such as age, visual requirements and suitability for transplantation. Access to cadaveric donor tissue and availability of surgical and post-transplantation recovery expertise also influence treatment choice. Keratoplasty is typically required in cases of severe visual impairment and can involve replacing some or all layers of the cornea.

EPIDEMIOLOGY

Corneal dystrophies are rare disorders with variable prevalence, although most types probably have a prevalence of <1 case per 1 million individuals. Some corneal dystrophies show differences in prevalence based on ethnicity or sex, and higher prevalences have been reported in some populations as a result of founder effects (for example, in Iceland) or high rates of consanguinity (for example, in Saudi Arabia). Accurate estimates of the prevalence and incidence of corneal dystrophies are lacking owing to their rarity and variable recording or reporting of cases.

OUTLOOK

Novel strategies to improve the management of corneal dystrophies are being investigated, although most are only in early stages of clinical development. Genetic approaches include gene silencing with RNA interference methods to downregulate mutant allele expression or selective genome editing (for example, using CRISPR–Cas9) to repair mutations. Furthermore, a worldwide shortage of cadaveric donor tissue has encouraged research into alternatives, including regenerative therapy (stimulating regrowth of endogenous, non-diseased cells) and cell augmentation therapy (expanding donor tissue in vitro for distribution to multiple transplant recipients). Novel pharmacological treatments also hold promise, including drugs that protect cells from pathogenetic insults, such as oxidative stress, or those that boost cell survival after transplantation.



doi:10.1038/s41572-020-0186-9; Article citation ID: (2020) 6:47

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