



## Review

## The autoimmune diseases of the eyes



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## ABSTRACT

The eye is divided anatomically in three layers: an outer or fibrous layer (cornea/sclera), middle or vascular layer (uvea – iris, ciliary body, and choroid) and an inner or sensorineural layer (retina). They compose the several anatomic and functional layers that enable the immune protection of the eye. The first layer involves an intact anatomic border with the blood–ocular barrier and immunosuppressive neuropeptides in the native aqueous humor. The second layer trusts on the capability of the eye to reestablish an immunosuppressive micro-environment by activating latent TGF- $\beta$  and reestablishing the anterior chamber-associated immune deviation. The third layer involves a mechanism that is not yet completely recognized, but that has the ability to overcome a predominantly Th1 intraocular immune response and to reestablish anterior chamber-associated immune deviation. Understanding the comprehensive mechanisms of these pathways, will lead to the development of new treatments strategies in order to prevent damage to the eye from persistent or exacerbated inflammation, directed at first to pathogens, but that may develop an autoimmune reaction.

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**1. Introduction**

**1.1. Eye anatomy**

The eye is divided anatomically in three distinguished layers: an outer or fibrous layer (cornea/sclera), middle or vascular layer (uvea, a continuous structure comprising iris, ciliary body, and choroid) and an inner or sensorineural layer (retina). The human eye maintains a pressure between 10 and 20 mm Hg, which is generated by the unidirectional flow of fluid (aqueous humor secreted by the ciliary body) from the posterior chamber into the anterior chamber, leaving the eye via the trabecular meshwork, to drain into the episcleral veins [1]. (See Table 1.)

**1.2. Fibrous layer**

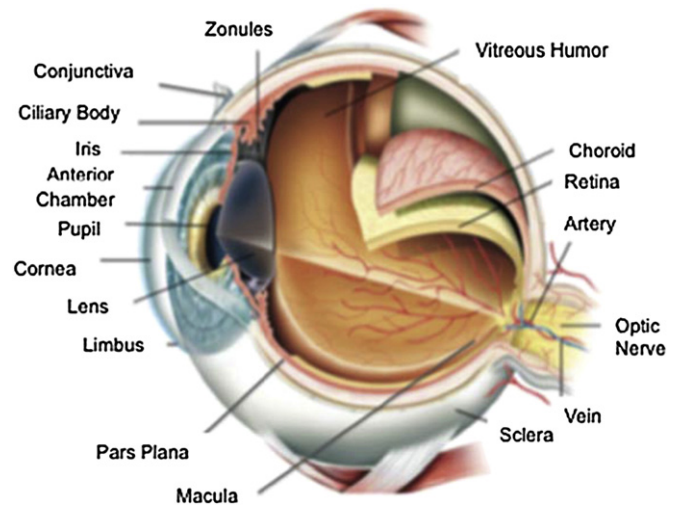
As seen in Fig. 1, the fibrous layer of eye is composed of three structures: cornea, sclera and limbus. This layer is a dense tissue, poorly vascularized, and homologous to the dura mater of the central nervous system (CNS). This layer is opaque in 5/6 of its length (sclera) and it is transparent in the anterior portion (cornea), for optical purposes [2].

**1.3. Cornea**

The cornea consists primarily of three layers: an outer layer containing an epithelium, a middle stromal layer consisting of a collagen-rich extracellular matrix interspersed with keratocytes and an inner layer of endothelial cells. The cornea is an avascular and transparent tissue; which ensures two-thirds of refractive power of the eye, being the steepest region of the fibrous tunic [3,4]. It has an elliptical shape with the long axis and the meniscus with a more pronounced curvature than the other parts [5,6]. The tear film covers the convex anterior surface and the concave posterior surface is circular and is in direct contact with the aqueous humor.

The cornea constitutes an anatomical and physiological protective barrier of the ocular internal structures and its strength comes from its own substance (stroma) [7]. The stroma represents 90% of the corneal structural thickness [8]. It is composed of collagen fibrils (types I, III, V, VI and XII, of which collagen type I is the predominant) that are arranged in crystalline structures as seen in Fig. 2, separated by proteoglycans, being renewed and synthesized by keratocytes that are organized in a network of interconnected cells [9–12].

The spatial organization of the collagen fibrils and their diameter uniformity avoid the diffraction the rays of light and allow the passage to the aqueous humor of the incident visible light [13,14]. The transmission of light, refraction and reflection are the optical properties of the



**Fig. 1.** Schematic view of a coronal session of a normal eye depicting the fibrous layer (cornea, limbus and sclera), the vascular layer (iris, ciliary body and choroid) and the sensorineural layer (retina).

cornea and these functions are dependable on the maintenance of its transparency, which means that its own substance is kept in a condition of relative dehydration [15].

**1.4. Limbus**

The limbus is a translucent area consisting of elements that are part of the cornea and the sclera. The contribution of each tissue to the formation of the limbus varies from its surface to its deepest part, as well as in various sectors around the circumference of the limb [16,17]. It is not only important as a translucent surgical landmark, but also due to the unusual cell composition and the presence of stem cells in the conjunctival and episcleral tissues strongly adhered above it.

A new corneal epithelium derives from this region and due to the high antigen concentration present in the cells of this tissue; it is of major importance in the immunological changes that occur in the sclera and the cornea during the inflammatory process [18].

The conjunctiva is a mucosal membrane lining that begins at the limbus and covers the anterior portion of the eye (Fig. 3). It allows independent movements of the eyelids and the eyeball, provides mucus for lubrication and contains lymphoid cells that participate in its

**Table 1**

Layers, structures and physiologic functions of the different parts of the eye.

Layers	Structures	Main components	Function	Related diseases
External or fibrous layer	Cornea	Collagen fibrils (type I)	Protective barrier	Mooren's ulcer, rheumatoid arthritis, juvenile idiopathic arthritis, relapsing polychondritis, scleritis, episcleritis
	Limbus	Stem cells	Optical properties	
	Sclera	Collagen lamellae	New corneal epithelium	Sjögren's syndrome
	Conjunctiva	Mucosal membrane	Immunological changes/inflammatory process	
Median or vascular layer (uvea)	Iris	Blood ocular barrier	Visual integrity of the eye	Spondyloarthritis, juvenile idiopathic arthritis, sarcoidosis, granulomatosis with polyangiitis, Behçet's, Blau's syndrome, intermediate uveitis, sympathetic ophthalmia
	Ciliary body	• Pigmented – epithelial cells	Lubrication, Immunologic protection	
	Choroid	• Highly vascularized	Controls light entering the eye.	Systemic lupus erythematosus, VKH, antiphospholipid syndrome, sarcoidosis, Behçet's, vitiligo, birdshot retinochoroidopathy, autoimmune neuropathies
		Collagen fibers, various cell types and melanocytes	Production of aqueous humor.	
Internal or sensorineural layer	Retina	Blood ocular barrier	Supply oxygen and temperature control of the retina	Collecting and carrying the light and images
	• Macula	• Pigmented-epithelial cells		
	• Optic nerve	• Vascular-endothelial cells		
	• Vitreous humor			

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