Review Article

Clinical anatomy: cornea and ocular surface

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ABSTRACT

Background: The cornea and ocular surface serve as a vital barrier and the eye's primary refractive medium, requiring precise coordination to maintain transparency, structural integrity, and immune protection. Constantly exposed to environmental stressors, this interface relies on the stability of the tear film, epithelial architecture, mucin layers, and limbal stem cells to preserve function. Disruption in any component can impair vision and increase vulnerability to disease. Advances in imaging and molecular diagnostics have deepened our understanding of these structures, offering new avenues for early detection and personalized treatment strategies. A comprehensive review is needed to integrate recent findings and assess their clinical relevance.

Methods: A targeted literature search was conducted using PubMed/MEDLINE and Google Scholar to identify English-language publications from 1 January 2000 to 30 May 2025. Keywords included "anatomy," "histology," "cornea," "ocular surface," "epithelium," "Bowman's layer," "stroma," "Descemet's membrane," "endothelium," "conjunctiva," "lacrimal functional unit," and "eyelids." Studies were selected irrespective of design, and reference lists of included articles were manually screened for additional relevant sources.

Results: Eighty-six publications were reviewed. Findings highlight that the cornea and ocular surface constitute an integrated anatomical and physiological continuum essential for optical clarity, visual acuity, and ocular health. This dynamic unit comprises the cornea, conjunctiva, tear film (mucin, aqueous, and lipid layers), meibomian glands, goblet cells, and the limbal stem cell niche. Collectively, these elements provide lubrication, immune defense, epithelial homeostasis, and structural integrity. Disruption in any component—such as in dry eye disease, limbal stem cell deficiency, or meibomian gland dysfunction—can precipitate epithelial breakdown, neovascularization, or stromal scarring, ultimately compromising vision. Recognizing this interdependence has reframed ocular surface disease as a multifactorial condition rather than an isolated disorder. A comprehensive understanding of the structural and immunological dynamics of this system is therefore critical for refining surgical strategies and developing targeted therapies.

Conclusions: The cornea and ocular surface components function synergistically to maintain a transparent, stable refractive surface essential for vision. Their coordinated roles in protection, lubrication, immune defense, and tissue repair reveal the importance of anatomical understanding for developing targeted therapies and improving clinical outcomes. A comprehensive understanding of this anatomy is essential for clinicians and researchers aiming to develop more precise therapeutic strategies and surgical techniques to enhance patient outcomes and preserve visual function. Future research should focus on advancing regenerative strategies and personalized treatments to address complex ocular surface disorders more effectively.

KEYWORDS

corneas, anatomies, histology, anatomy, descemets membrane, corneal endothelium, corneal epithelium, limbal stem cell, corneal stromas

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INTRODUCTION

The cornea and ocular surface constitute a highly specialized and dynamic interface between the external environment and the internal ocular structures, playing a critical role in both protection and vision [1–5]. As a transparent, avascular tissue, the cornea functions simultaneously as a physical barrier and the principal refractive element of the eye, necessitating a delicate balance between structural integrity and optical clarity despite continuous environmental challenges [6–8]. This equilibrium is sustained through the coordinated interaction of epithelial cell architecture, tear film stability, mucin and glycocalyx layers, limbal stem cell function, and robust immunological defense mechanisms [9–12].

This narrative review aims to present a comprehensive examination of records concerning the anatomical, molecular, and immunological features of the cornea and ocular surface. In addition, it highlights recent advances in diagnostic technologies and explores their translational relevance for contemporary clinical practice.

METHODS

A targeted literature search was conducted using PubMed/MEDLINE and Google Scholar to identify relevant English-language publications. The search strategy incorporated combinations of the following keywords and terms: "anatomy," "histology," "cornea," "ocular surface," "epithelium," "Bowman's layer," "stroma," "Descemet's membrane," "endothelium," "conjunctiva," "lacrimal functional unit," and "eyelids." Studies published between 1 January 2000 and 30 May 2025 were included, without restrictions on study design. In addition, the reference lists of selected articles were manually screened to identify further pertinent literature for inclusion in this narrative review.

RESULTS

A total of 86 records were included in this review. The findings indicate that the cornea [1, 4, 7, 8] and ocular surface [5, 12–15] function as a unified anatomical and physiological entity, crucial to preserving the optical performance and overall health of the eye. This integrated system extends beyond the transparent cornea to encompass the conjunctiva, tear film (comprising mucin, aqueous, and lipid layers), meibomian glands, goblet cells, and the limbal stem cell niche [9, 12, 14–20]. Collectively, these components form a complex and interdependent ecosystem, where disruption in any single element can compromise the integrity of the entire ocular surface.

This intricate interrelationship has informed a shift in clinical perspective: ocular surface disease [1, 2, 18] is now recognized not as a singular, isolated pathology, but as a spectrum of multifactorial disorders involving various components of this anatomical unit. As such, maintaining corneal clarity [4, 10, 21–25] and function requires a holistic understanding of the ocular surface's structural and immunological balance [2, 4, 5, 12, 20, 26]. These insights carry important implications for clinical practice, particularly in the context of surgical planning [27, 28] and the formulation of targeted therapeutic strategies [2, 29–31]. A detailed synthesis and interpretation of these anatomical and clinical insights are provided in the Discussion section.

DISCUSSION

Cornea

The cornea, together with the sclera, forms the outermost layer of the eye, serving as a critical protective barrier for the intraocular structures [1, 4, 8]. As a transparent, avascular tissue, the cornea not only shields the eye from environmental insults and microbial invasion but also plays an essential role in visual function [4, 8]. In conjunction with the tear film, it provides the primary refractive interface of the eye [4, 8, 9, 19]. The refractive index of the cornea is 1.376. The cornea accounts for approximately two-thirds of the eye's total refractive power. When the refractive contributions at the interfaces between media—air to tear film (+44 diopters [D]), tear film to cornea (+5 D), and cornea to aqueous humor (−6 D)—are summed, the cornea's total refractive power is approximately +43 D, accounting for about 70% of overall refractive power of the eye [8].

The cornea is a convex, aspheric structure, characterized by a steeper curvature centrally and a flatter contour peripherally. This geometric configuration is accompanied by a gradual increase in thickness from the central to the peripheral cornea, primarily due to a higher concentration of collagen fibers in the peripheral stroma [1, 32]. Various assessment techniques show that the central corneal thickness in normal eyes ranges from 551–566 micrometers (μm), the peripheral thickness from 612–640 μm. This thickness tends to decrease with age [32].

In a newborn, the corneal diameter measures approximately 10 mm and reaches its adult size by the age of 6. The anterior corneal diameter ranges from 11–12 mm horizontally and 9–11 mm vertically, the posterior surface displays an average diameter of 11.7 mm. The mean (standard deviation [SD]) corneal diameter is 11.77 (0.37) mm in men and 11.64 (0.47) mm in women, with observed ranges of 11.04–12.50 mm and 10.7–12.58 mm, respectively [33]. The limbus is widest in the superior and inferior regions

of the cornea, while the central third constitutes the optic zone. The anterior radius of curvature ranges from 7.5–7.8 mm, the average posterior radius of curvature from 6.5–6.8 mm. Anterior stromal stiffness plays a critical role in maintaining corneal curvature, as the anterior corneal surface exhibits greater resistance to changes in stromal hydration compared to the posterior stroma [4].

The facial artery, a branch of the external carotid artery, and the terminal branches of the ophthalmic artery, derived from the internal carotid artery, anastomose at the limbus. This vascular network, together with the aqueous humor and tear film, provides nourishment to the cornea [4]. The central cornea is normally devoid of antigen-producing and antigen-presenting cells. However, in pathological conditions such as infection, immunologic rejection, and trauma, immune cells including Langerhans cells and T lymphocytes may infiltrate the cornea from the limbal periphery [12]. The cornea is also highly innervated. Approximately 70–80 branches of the long posterior ciliary nerves, originating from the ophthalmic division of the trigeminal nerve, enter the cornea through the sclera, episclera, and conjunctiva. These nerves lose their myelin sheaths 1–2 mm after crossing the limbus and subsequently form a network of plexuses beneath Bowman's layer, sending fine branches into the epithelium [1, 4].

Anatomy and Histology of Cornea

The cornea is composed of both cellular elements—keratocytes and endothelial cells—and non-cellular components, including collagen and glycosaminoglycans [1, 4, 34]. The epithelial cells originate from the epidermal ectoderm, whereas keratocytes and endothelial cells are derived from the neural crest. Structurally, the cornea is organized into five distinct layers: three cellular layers (epithelium, stroma, and endothelium) and two acellular interfaces (Bowman's membrane and Descemet's membrane) [1, 4, 34]. In recent years, the advancement of lamellar surgical techniques has led to the identification of an additional acellular layer—the pre-Descemet or Dua's layer—which lies between the stroma and Descemet's membrane [34]. Representative hematoxylin and eosin (H&E) image of a normal cornea is shown in Figure 1.

Corneal epithelium: The corneal epithelium is composed of non-keratinized, stratified squamous epithelial cells and has an approximate thickness of 50–90 μm. Centrally, it averages around 55 μm and becomes progressively thicker toward the periphery [1, 4]. It is derived from the surface ectoderm during the 5th to 6th weeks of gestation. The epithelium undergoes continuous self-renewal, with an average turnover cycle of approximately 7 to 10 days, involving processes of involution, apoptosis, and desquamation. Its primary roles are to function as a barrier against environmental pathogens and mechanical insults, and to maintain a smooth refractive surface [1, 4].

The corneal epithelium maintains a symbiotic relationship with the overlying tear film. The mucus layer of the tear film, secreted by conjunctival goblet cells, is in direct contact with the epithelial surface. It closely interacts with the epithelial cell glycocalyx, facilitating uniform spread of the tear film with each blink [1, 4, 9, 19]. Histologically, the epithelium consists of 5 to 6 cell layers, organized into 3 distinct cell types: superficial squamous cells, wing cells, and basal columnar epithelial cells [1, 4, 8].

Superficial cells occupy the outermost layer of the corneal epithelium and are arranged in two to three rows of flat, polygonal cells. These cells measure approximately 2–6 μm in thickness and 40–60 μm in diameter. Their apical surfaces are covered with microvilli and microplicae, which increase surface area and enhance mucin absorption, thereby contributing to tear film stability [1, 4]. The tear film, which overlies the epithelium, is approximately 7 μm thick and plays a critical optical role by smoothing minor surface irregularities [1, 4, 9, 19]. In addition to its optical function, the tear film contains antimicrobial components such as lysozyme and lactoferrin, and supplies essential nutrients to the corneal epithelium [1, 4, 9, 19]. Intercellular cohesion between superficial cells is maintained by desmosomes, while tight junction complexes create an impermeable barrier, preventing the paracellular passage of tears, toxins, and microorganisms [1, 4]. These cells undergo rapid self-renewal within a few days, and their regenerative capacity ensures that epithelial damage typically heals without scarring [35].

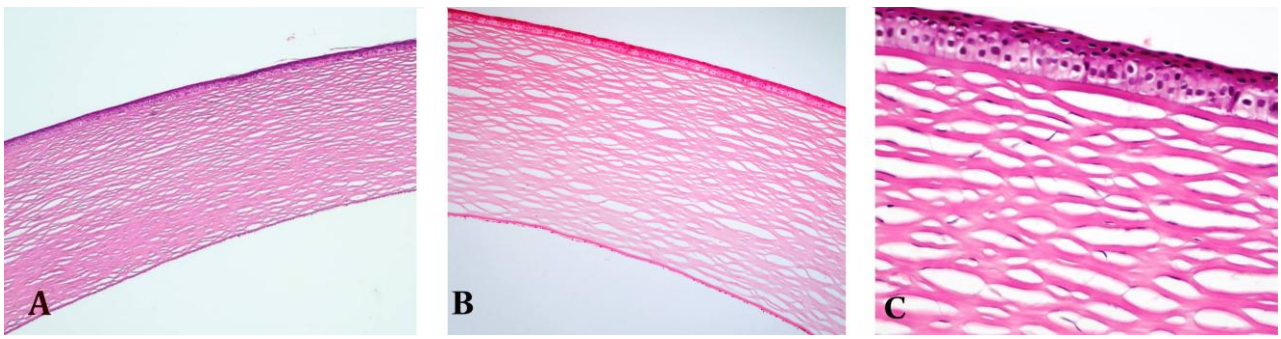

Figure 1. Representative hematoxylin and eosin (H&E)-stained sections of a normal cornea at different magnifications (A: 40×, B: 100×, C: 1000×), demonstrating the epithelium, Bowman's layer, stroma, Descemet's membrane, and endothelium (courtesy of Dr. Zohreh Nozarian).

Wing cells are arranged in two to three layers beneath the superficial epithelial cells. They are named for their distinctive lateral extensions, which resemble wings. Similarly to the superficial layer, wing cells are interconnected by tight junctions, contributing to the structural integrity and barrier function of the corneal epithelium [4].

Basal columnar epithelial cells form a single row of cylindrical germinal cells, approximately 20 μm in length, situated directly on the basement membrane [1, 4, 8]. This is the only epithelial layer where mitotic activity occurs, serving as the progenitor source for both wing and superficial cells [1, 4, 8]. Within the limbal region, the proliferative zone contains stem cells and transient amplifying cells, whereas the non-proliferative zone consists of postmitotic and terminally differentiated cells [8]. The Vogt palisades—undulating structures in the basement membrane—enhance vascular support, increase surface area for cellular attachment, and offer protection to resident stem cells. Perilimbal basal epithelial cells continuously proliferate and differentiate into superficial cells. During this maturation process they develop microvilli on their outermost surfaces and are ultimately shed into the tear film, completing the epithelial turnover cycle within 7–14 days [1].

In the central cornea, the epithelium comprises 5–7 layers, with basal cells appearing columnar. Melanocytes and Langerhans cells are absent in this region, and a flat basal cell layer containing keratan sulfate is present, along with an absence of lymphatic vessels [1]. In contrast, the peripheral corneal epithelium is thicker, consisting of 7–10 layers. Here the basal cells are cuboidal, and both melanocytes and Langerhans cells are present. Unlike the central cornea, the peripheral region lacks keratan sulfate and lymphatic vessels [1].

Beneath the epithelial cells lies the epithelial basement membrane, which plays a critical role in maintaining epithelial integrity and promoting wound healing. The epithelium adheres to this membrane through hemidesmosomes, which provide essential mechanical stability [36–38]. This attachment constitutes the primary structural interface between the epithelium and the underlying corneal layers. Tight junctions are restricted to the lateral walls of apical epithelial cells, forming a barrier to paracellular permeability, and adherens junctions are confined to the lateral membranes of these cells [39].

Electron microscopy studies in humans, rabbits, and various other species have demonstrated that the basement membrane consists of two distinct layers: the lamina lucida, positioned between the epithelial cells and the lamina densa, and the lamina densa itself [39]. This basement membrane is composed of an extracellular matrix secreted by the deeper epithelial cells. Under normal conditions, it measures approximately 40–60 nm in thickness and consists of Type IV collagen and laminin, both synthesized by basal epithelial cells [1]. Anchoring fibrils, composed of Type VII collagen, traverse the basement membrane and terminate as connective plaques formed of Type I collagen [1]. The basement membrane is firmly adherent to the underlying Bowman layer. Additionally, unmyelinated nerve fibers are frequently located within the epithelial layers, mainly in the basal cell layer [8].

Bowman's layer is an acellular, collagenous membrane formed by the condensation of the superficial stromal layer located directly beneath the epithelium. In essence, it represents a dense aggregation of collagen and proteoglycans. This 12-μm-thick layer is composed of type I and type V collagen, along with proteoglycans [1, 4]. The collagen fibrils are randomly oriented on the posterior surface, merging seamlessly with the anterior stroma to create a smooth anterior interface. Bowman's layer contributes to the mechanical stability of the cornea; however, it does not regenerate following injury, and its damage may lead to scarring [40]. While traditionally regarded as a purely structural component, emerging evidence suggests that Bowman's layer may also play a role in modulating anterior stromal fibrosis and scarring [40, 41].

Stroma accounts for approximately 90% of the total corneal thickness and is composed predominantly of orthogonally arranged collagen fibrils (types I and V) embedded within a proteoglycan-rich matrix [42, 43]. The stroma contains 200–300 collagen lamellae that span the full diameter of the cornea, oriented obliquely in the anterior one-third and parallel in the posterior two-thirds. These lamellae are loosely interconnected and exhibit uniform length and thickness, with a regularly organized structure [42, 43]. This highly ordered lamellar arrangement and uniform fibril diameter are essential for preserving corneal transparency—a principle initially proposed by Maurice's lattice theory and subsequently validated through advanced imaging technologies [21]. Type I collagen is the principal component of the stroma, with additional contributions from types III, V, VI, and XII collagen [1, 44]. Keratocytes, the resident stromal cells, are responsible for maintaining the extracellular matrix and mediating responses to injury [22]. These cells are predominantly located in the anterior stroma [1]. In the event of stromal injury, keratocytes migrate to the affected area, differentiate into fibroblasts, and synthesize collagen, leading to scar formation [22, 43]. Figure 2 schematically illustrates corneal wound healing and the cascade of stromal opacity.

The space between collagen fibrils is filled with a matrix of glycosaminoglycans, primarily keratan sulfate, chondroitin sulfate, and dermatan sulfate. Keratocytes, along with approximately 300 regularly arranged collagen lamellae, are embedded within this matrix, with keratan sulfate being the predominant glycosaminoglycan. Hyaluronan is present during infancy [1].

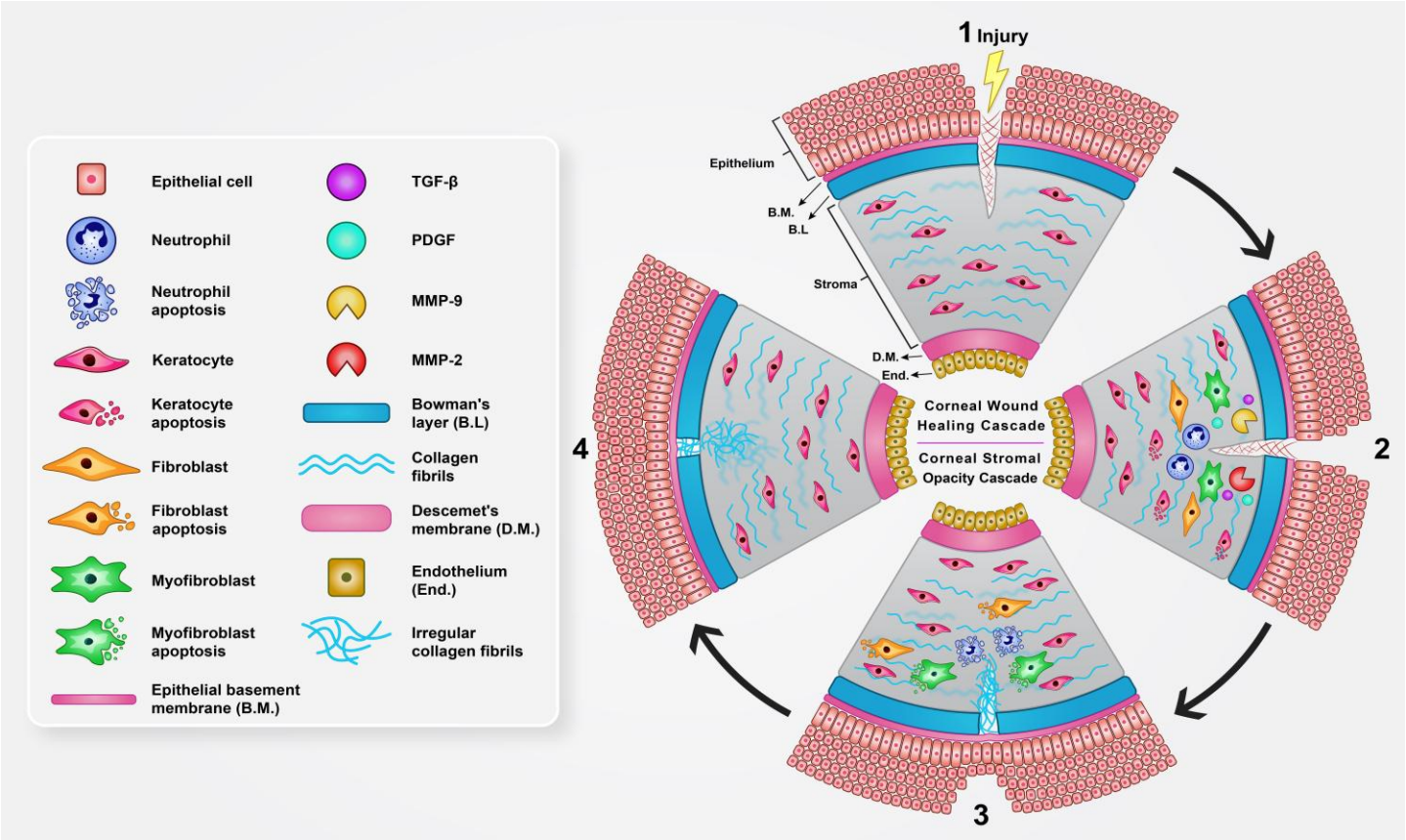

Figure 2. Diagram of corneal wound healing and stromal opacity pathways. After epithelial injury (1), keratocyte apoptosis and necrosis are triggered, initiating early epithelial repair (2). Subsequent processes involve keratocyte proliferation and migration, differentiation into myofibroblasts, and infiltration of inflammatory cells (2). This is followed by stromal remodeling, re-epithelialization of the surface, and eventual clearance of myofibroblasts and inflammatory cells through apoptosis or necrosis (3), allowing keratocytes to revert to a quiescent state (4). Corneal opacity develops when transforming growth factor-β (TGF-β) and platelet-derived growth factor (PDGF) drive keratocyte differentiation into myofibroblasts, accompanied by deposition of a provisional extracellular matrix (ECM). Degradation of the epithelial basement membrane (EBM) by matrix metalloproteinases MMP-2 and MMP-9 facilitates continued stromal penetration of TGF-β and PDGF (2), sustaining myofibroblast activation (2, 3). Prolonged myofibroblast survival results in excessive, disorganized ECM accumulation, leading to stromal scarring and opacity (4). This figure has been reused with the permission of *Medical hypothesis, discovery & innovation in optometry* [45].

These glycosaminoglycans create an anionic environment by binding water and cations. In stromal edema, increased water content expands the interfibrillar space, resulting in increased corneal thickness. Keratan sulfate and chondroitin sulfate are the main glycosaminoglycans contributing to the stroma's hydrophilic properties [1, 4]. Proteoglycans help maintain proper spacing between collagen fibrils, thereby minimizing light scattering and preserving corneal transparency [8].

Descemet's membrane is a specialized basement membrane secreted by the corneal endothelium. It thickens progressively with age, transitioning from an embryologically banded layer to a postnatal, non-banded amorphous structure [46, 47]. Formation begins during the eighth week of gestation [1]. At birth, the membrane measures approximately 3 μm in thickness. Endothelial cells continue to secrete Descemet's membrane through life. The prenatally secreted portion exhibits a distinct banded morphology, whereas the postnatally produced membrane is unbanded and amorphous in texture [1]. With advancing age and sustained endothelial function, the membrane thickens to approximately 10 μm in adults. Functionally, it serves as the basement membrane of the endothelial layer. Its elastic nature causes it to recoil or fold when dissected. At the corneal periphery, Descemet's membrane terminates by forming the Schwalbe line [1]. This fusion zone, known as Schwalbe's line, serves as a gonioscopic landmark delineating the end of Descemet's membrane and the beginning of the trabecular meshwork [1, 4]. Recent proteomic studies have identified a range of unique matrix proteins within Descemet's membrane, contributing to its structural resilience and regenerative potential [48–50].

Dua layer: the sixth corneal layer, situated between the stroma and Descemet's membrane, and first described by Dua in 2013 [34]. Known as the Pre-Descemet or Dua layer, it is collagen-rich and has an average thickness of 15 μm. A thorough understanding of this layer is critical in the context of corneal surgical anatomy, particularly in procedures such as lamellar

keratoplasty and the management of posterior corneal pathologies [27, 28, 51–54].

Endothelium: a vital layer responsible for maintaining corneal deturgescence—the mechanism that preserves relative stromal hydration—through ionic pumps and tight intercellular junctions. It consists of a single layer of hexagonal cells and is approximately 5 μm thick [1, 4, 23]. Appearing as a honeycomb mosaic, the endothelium originates from the neural crest and initially comprises regularly arranged cuboidal cells during early embryogenesis, which gradually flatten over time. While its thickness is about 10 μm at birth, it stabilizes at approximately 4–5 μm in adulthood [1, 4].

The endothelial cell density in young adults is approximately 3000 cells/mm². Unlike epithelial cells, endothelial cells possess limited proliferative capacity. At birth, the density is around 3500 cells/mm² [1, 4]. As these cells do not regenerate with age, the density declines by roughly 0.6% annually. Neighboring cells expand to compensate for lost cells, leading to increased polymegathism (variation in cell size) and pleomorphism (diversity in cell shape and a reduction in hexagonality) [1, 4] (Figure 3). Over time, cell density drops from 3000–4000 cells/mm² to approximately 2600 cells/mm², with the proportion of hexagonal cells declining from about 75% to 60%. Corneal edema typically develops when cell density falls to around 500 cells/mm². Loss or dysfunction of these cells results in corneal edema and vision impairment, as seen in conditions like Fuchs endothelial corneal dystrophy [55–58].

Endothelial cells are metabolically active and regulate corneal hydration via an endothelial pump mechanism. Two key ion transport pathways contribute to this function: the membrane-bound Na^+/K^+ ATPase on the basolateral membrane and the intracellular carbonic anhydrase pathway. Both facilitate net ion flux from the stroma to the aqueous humor, a process critical for maintaining corneal transparency [1, 4, 23]. The numerous hemidesmosomes contained in the basal surface of the endothelium secure its attachment to Descemet's membrane [1, 4].

Clinical and Surgical Relevance to the Cornea's Anatomy

Corneal transparency is primarily maintained through the precise arrangement of stromal collagen fibrils, the regulation of stromal hydration, and the integrity of endothelial pump function [23–25]. The stroma, comprising approximately 300 lamellae of collagen fibers, is mainly responsible for this transparency. These collagen fibrils, ranging in diameter from 22.5 to 35 nm with a mean (SD) of 41.4 (0.5) nm, are spaced at intervals smaller than half the wavelength of visible light. This regular, lattice-like configuration—particularly of type I and V collagen—minimizes light scattering and facilitates optimal light transmission [1, 4, 7, 21, 22, 24, 25].

Corneal hydration, essential to transparency, is tightly controlled by a balance of epithelial and endothelial barriers, alongside the active transport mechanisms of the endothelium. The stroma contains approximately 78% water, a hydration equilibrium that is primarily maintained by endothelial metabolic pumps that prevent fluid overload and stromal edema, thereby preserving

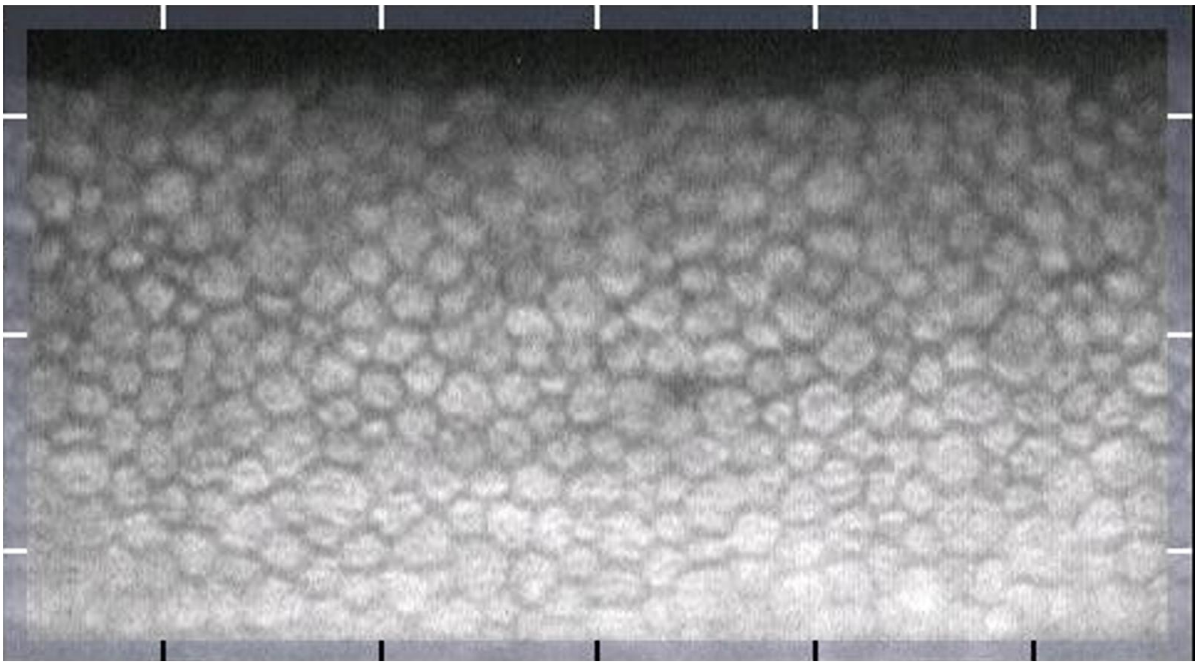

Figure 3. Specular microscopy of corneal endothelium: 261 cells analyzed; cell density 2600 cells/mm²; mean cell area 385 ± 139 μm² (coefficient of variation [CV] 36%); range 144–901 μm² (courtesy of Dr. Alejandro Rodriguez Garcia).

optical clarity [1, 7, 4, 21–25]. These pumps rely on temperature-sensitive Na^+/K^+-ATPase activity. Additionally, negatively charged glycosaminoglycans in the stroma repel each other, generating swelling pressure. The net suction pressure within the corneal stroma is defined by the balance between this swelling pressure and the opposing intraocular pressure [1, 4, 7, 21–25, 59].

A thorough understanding of corneal anatomy and the mechanisms that preserve its transparency [4, 7, 21, 22, 24, 25] is pivotal for preventing and managing visual impairment. Accurate preoperative evaluation is equally vital for procedures such as phacoemulsification and for anticipating potential intraoperative risks [60].

In clinical practice, comprehensive anatomical knowledge underpins the diagnosis and treatment of corneal pathologies and informs surgical approaches such as refractive surgery, keratoplasty, and corneal cross-linking [23, 61, 62]. Advances in imaging technologies, including anterior segment optical coherence tomography and in vivo confocal microscopy, have further refined our understanding of corneal microarchitecture [63–66]. Among anterior segment imaging modalities, specular microscopy stands out as a non-invasive and widely used tool to assess both the morphology and density of the corneal endothelium [67–69].

Pivotal Recent Discoveries About the Cornea

Recent anatomical insights have identified a distinct, thin, tough, and acellular layer located between the stroma and Descemet's membrane, known as the pre-Descemet or Dua's layer [27, 34, 52]. While its precise physiological role continues to be explored, its discovery has significant implications for deep anterior lamellar keratoplasty (DALK), a preferred alternative to penetrating keratoplasty (PK) in cases where the endothelium remains unaffected [27, 52, 70].

This layer, also referred to as the pre-Descemet layer, Dua-thin layer, or pre-posterior limiting lamina, is primarily composed of type I and type VI collagen, along with a rich concentration of elastin [52]. This elastin imparts exceptional tensile strength (with a bursting pressure of up to 700 mmHg), air impermeability, and structural integrity, despite the layer being virtually acellular. Its recognition has led to the development of novel surgical procedures, including pre-Descemet endothelial keratoplasty, suture techniques for acute hydrops, DALK-triple, and Fogla's mini-DALK procedure [52]. Ongoing investigations continue to elucidate the role of elastin within Dua's layer [28, 70].

A major advancement in DALK surgery has been the introduction of the big bubble technique (BBT), which significantly improves procedural efficiency and has increased surgeon adoption of the procedure [27]. In BBT, air is injected into the stroma to induce separation between corneal layers, enabling the removal of diseased or scarred stroma while preserving the healthy endothelium. This technique has achieved clinical outcomes comparable to PK and permits the formation of a high-quality graft–host interface [27]. A detailed understanding of the anatomy and biomechanics underlying big bubble formation, centered on the properties of the Dua layer, is critical for optimizing surgical safety and reproducibility [27].

The identification of the Dua layer has also influenced the management of conditions such as Descemet's membrane detachment, acute corneal hydrops in keratoconus, and descemetocele [28]. The Dua layer has been implicated in the pathophysiology and clinical presentations of corneal infections and certain corneal dystrophies. Preliminary evidence suggests a potential role in keratoconus development, potentially linked to its elastin composition [53, 54]. The role of elastin tissue in glaucoma pathogenesis, particularly through its contribution to corneal biomechanics, is also an active area of ongoing research [29, 51, 52].

The cornea functions as a dynamic and highly specialized interface between the external environment and intraocular structures. In this context, the ocular surface and associated anatomical units are inextricably interconnected, each critically contributing to the cornea's functional integrity [1, 4, 5, 7–9, 12–20].

Ocular Surface

The ocular surface used to be simply defined as the integration of all mucosal components of the conjunctival sac and the corneal epithelium. With evolving understanding, additional structures have been incorporated into this system, culminating in the inclusion of the lacrimal functional unit (LFU) [5, 12–15]. The system, comprising the cornea, conjunctiva, lacrimal glands, and eyelids, is now recognized to function as an integrated unit [5, 13].

As anatomically defined by Gibson, the ocular surface includes the mucosa covering the bulbar and palpebral surfaces, the corneoscleral limbus, the corneal epithelium, and the tear film [5, 13]. The ocular surface thus encompasses the cornea, conjunctiva, limbus, tear film, and associated glands, including the lacrimal and meibomian glands. These components operate synergistically to maintain optical clarity, provide protection against environmental insults, and support immune surveillance [5, 13–16]. Being avascular, the cornea relies on the tear film and aqueous humor for nutrient supply and waste removal. The conjunctiva serves as a mucosal barrier and houses immune cells vital for ocular defense. The limbus contains limbal epithelial stem cells, which are essential for corneal epithelial regeneration and the maintenance of transparency [1, 4, 14, 15]. The sclera, by contrast, features more randomly oriented and irregular collagen fibrils than the cornea [1].

The ocular surface is equipped with both innate and adaptive immune mechanisms. Goblet cells secrete immunomodulatory factors such as TGF-β and retinoic acid, contributing to immune tolerance. The tear film contains antimicrobial factors including secretory IgA, lactoferrin, and lysozyme, offering frontline antimicrobial defense [1, 4, 9, 16, 19]. Additionally, corneal nerves—originating from the trigeminal nerve—not only mediate sensory input but also release neuropeptides that regulate inflammation and facilitate healing processes [1, 4, 17, 42].

Conjunctiva

The conjunctiva is a thin, transparent mucous membrane that lines the posterior surface of the eyelids (palpebral conjunctiva) and extends to cover the anterior sclera up to the limbus (bulbar conjunctiva) [1]. Medially, a crescent-shaped fold of the conjunctiva with thickened stroma is known as the plica semilunaris. The caruncle, located medial to the plica, marks the most medial aspect of the interpalpebral fissure. The bulbar conjunctiva is loosely attached to the underlying anterior Tenon capsule [1]. This structure plays essential roles in maintaining ocular surface homeostasis, contributing to immune surveillance, tear film stability, and epithelial regeneration [1].

Histologically, the conjunctiva is composed of a non-keratinized stratified epithelium supported by a highly vascularized substantia propria. The stratified squamous epithelium contains goblet cells—most densely distributed in the inferonasal fornix—that secrete MUC5AC, a key component of the tear film mucin layer [5]. Subepithelial immune cells, particularly antigen-presenting dendritic cells and lymphocytes, form part of the conjunctiva-associated lymphoid tissue, enabling the mucosa to function as an effective immunological barrier [5].

Recent metagenomic studies have demonstrated that the conjunctival surface harbors a distinct, low-biomass yet stable microbiome, comprising species such as Corynebacterium, Staphylococcus, and Cutibacterium. Dysbiosis of this microbiome has been linked to conditions including allergic conjunctivitis, dry eye disease, and ocular rosacea [3, 71–73]. Furthermore, single-cell RNA sequencing of the human conjunctiva reveals distinct epithelial and immune cell populations [74–76], offering deeper insights into tissue-specific responses in inflammatory and fibrotic disorders such as Stevens-Johnson syndrome [76].

Lacrimal Functional Unit

The LFU is an integrated system comprising the main and accessory lacrimal glands, the ocular surface (cornea and conjunctiva), meibomian glands, goblet cells, and the neural network connecting these components [5, 13]. This unit maintains tear film homeostasis and ocular surface integrity via a feedback mechanism involving sensory, motor, and autonomic pathways [5, 13].

The tear film is composed of three distinct layers: an inner mucin layer produced by conjunctival goblet cells, a middle aqueous layer secreted by the lacrimal glands, and an outer lipid layer derived from the meibomian glands. This trilaminar structure provides ocular surface lubrication, nutrient delivery, and protection against environmental insults [9, 18, 19]. The lipid layer minimizes evaporation and ensures a smooth optical interface. The aqueous layer comprises water, electrolytes, proteins, and antimicrobial peptides, supplying essential nutrients and immune defense. The mucin layer facilitates tear film adherence to the ocular surface and entraps particulate matter [9, 18, 19]. Neural regulation of the LFU involves afferent sensory fibers from the trigeminal nerve and efferent autonomic fibers, orchestrating tear secretion in response to stimuli [5, 13, 19].

Tear fluid contains a complex mixture of proteins, lipids, electrolytes, and enzymes. Among the key proteins are lactoferrin, lysozyme, and secretory immunoglobulin A, which contribute to antimicrobial defense and immune modulation [9, 18, 19]. Recent proteomic analyses have identified over one thousand enzymes in human tears, highlighting the involvement of diverse metabolic pathways in preserving ocular surface homeostasis. The LFU also synthesizes lacritin, a glycoprotein that promotes basal tear secretion and epithelial cell proliferation. The role of lacritin in maintaining ocular surface integrity and its therapeutic potential continues to be investigated [20, 26, 77].

Clinical Evaluation and Diagnostic Approaches

Evaluation of LFU function involves both subjective symptom assessment and objective clinical testing. Schirmer's test quantifies aqueous tear production, while tear break-up time evaluates tear film stability [18, 19]. Advanced imaging techniques such as meibography and in vivo confocal microscopy enable detailed visualization of meibomian gland morphology and ocular surface alterations. Tear fluid biomarker analysis, including levels of lactoferrin and matrix metalloproteinase-9, provides further diagnostic insights into ocular surface inflammation and glandular function [26, 78–80].

Therapeutic Strategies and Future Directions

Management of LFU dysfunction focuses on restoring tear film homeostasis and mitigating inflammation. Therapeutic options include artificial tears, anti-inflammatory agents such as cyclosporine A and lifitegrast, and punctal occlusion using plugs. Innovative approaches are currently under investigation, including stem cell-based therapies and tissue engineering strategies

aimed at regenerating lacrimal gland function [30, 81]. Recent progress in lacrimal gland organoid models and mesenchymal stem cell therapies holds promise for restoring tear secretion and enhancing ocular surface health [31].

Eyelids

The eyelids (palpebrae) are critical anatomical and functional components of the ocular adnexa, playing an essential role in preserving the health and integrity of the ocular surface. Their specialized structure ensures mechanical protection, tear film distribution, and immune defense. Disorders affecting the eyelids can significantly compromise visual function and ocular surface homeostasis [1, 82, 83]. An important link to the LFU are the meibomian glands, located along the tarsal margin; they secrete lipids that constitute the superficial layer of the tear film. Each eyelash follicle is associated with the sebaceous glands of Zeis and the apocrine glands of Moll [1]. Anatomically, the eyelid comprises several distinct layers arranged from anterior to posterior: skin and subcutaneous tissue, orbicularis oculi muscle, orbital septum and tarsal plate, levator palpebrae superioris and Müller's muscle, and conjunctiva [1, 82, 83].

The eyelids protect the globe from environmental hazards and excessive light. Blinking ensures redistribution of the tear film, supporting corneal hydration and removal of debris [1]. The lipid layer of the tear film, synthesized by the meibomian glands in the tarsal plate, plays a crucial role in minimizing evaporation. The palpebral conjunctiva also contributes to ocular immune defense through its population of immune cells and lymphoid follicles [5, 14–16, 19].

Recent imaging advancements, including meibography and in vivo confocal microscopy, have enabled precise visualization of meibomian gland architecture and eyelid margin pathology [78–80]. Botulinum toxin injections have now become a mainstay in treating eyelid spastic disorders such as blepharospasm, while minimally invasive techniques like radiofrequency and laser-assisted blepharoplasty have enhanced the field of oculoplastic surgery [84–86].

This narrative review offers a concise synthesis of current knowledge on corneal anatomy and the components of the ocular surface, grounded in contemporary literature. One of the primary challenges encountered was the sheer breadth of existing research, which, although extensively explored, presents difficulties in cohesive integration and synthesis. Despite careful selection of relevant sources, several limitations warrant acknowledgment. Chief among them is the inherently subjective nature of narrative reviews, which may result in the inadvertent exclusion of pertinent studies due to the absence of a systematic search strategy. Additionally, the findings discussed are inherently shaped by the methodologies and technological constraints of the original studies reviewed, which may limit the generalizability of some conclusions and lead to underrepresentation of the most recent advancements. To address these limitations, future research should adopt more rigorous, systematic methodologies aimed at closing the identified knowledge gaps. In particular, further investigation into emerging surgical techniques and their implications for corneal microanatomy and ocular surface health is vital for advancing both clinical practice and foundational understanding.

CONCLUSIONS

These structures function in a finely coordinated manner to maintain a stable and transparent refractive surface, which is vital for optimal vision. The cornea, characterized by its avascularity and dense innervation, requires continuous protection and lubrication to preserve its transparency and biomechanical integrity. The conjunctiva contributes to immunological defense through its resident lymphoid tissue, plus supports epithelial repair. The tear film, composed of lipid, aqueous, and mucin layers, is continuously replenished to hydrate the ocular surface, remove debris, and deliver essential nutrients. The lacrimal glands secrete the aqueous layer of the tear film, while the meibomian glands produce lipids crucial for tear film stability and prevention of evaporative loss. Together, these components protect the eye from environmental pathogens, mechanical insults, and oxidative stress, while engaging in neuroimmune interactions that support rapid immune surveillance and tissue repair. A comprehensive understanding of this anatomy is essential for clinicians and researchers aiming to develop more precise therapeutic strategies and surgical techniques to enhance patient outcomes and preserve visual function.

ETHICAL DECLARATIONS

Ethical approval: This study was a narrative review, and no ethical approval was required.

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