

A Color-Coded Approach to Recognizing Corneal Pathologies

Vermont Veterinary Medical Association Summer 2024 CE Conference

June 4th, 2024

Eric C. Ledbetter, DVM, DACVO

Cornell University, College of Veterinary Medicine,

Ithaca, NY, USA

Learning Objectives

- 1) To understand the basic pathologic responses of the cornea and the associated color change clinically observed with each
- 2) To be familiar with the potential etiologies of each discussed clinical corneal color change

Outline

- 1) Basic corneal anatomy and physiology
- 2) General corneal pathologies and their clinical recognition
 - a. Hemoglobin
 - b. Edema
 - c. Melanosis
 - d. Inflammatory cell infiltrate
 - e. Keratic precipitates
 - f. Fibrosis
 - g. Lipid deposition
 - h. Mineral deposition

1) Basic corneal anatomy and physiology

In animals, the cornea is composed of the following four primary layers: epithelium, stroma, Descemet's membrane, and endothelium. Optical clarity of the cornea is required for normal function and vision. The cornea is a transparent structure as a result of several of its tissue characteristics: avascular, no lymphatics, relatively dehydrated, highly organized stromal collagen lamellae, minimal lipid or mineral content, non-pigmented, relatively acellular, and non-keratinized surface epithelium.

Just as the normal physiologic and anatomic state of the cornea is optical clarity, virtually all pathologic responses of the cornea result in predictable alterations in corneal transparency. The corneal color change associated with this reduced transparency is often indicative of the underlying pathologic response and can assist in determining the etiology of the observed corneal disease. When a clinician is presented with an opaque cornea, it must be determined what is anatomically and physiologically faulty with the corneal tissue that resulted in the loss of transparency.

2) General corneal pathologies and their clinical recognition

Corneal pathologic color changes may be divided into the following categories:

1. Red
2. Blue
3. Black/brown
4. Yellow/green

5. Greasy tan
6. Grey/white and wispy
7. Crystalline white

Red

Red corneal discoloration results from the presence of hemoglobin pigment. The corneal hemoglobin may be within erythrocytes or extracellular. Sources of corneal hemoglobin include vascularization, intracorneal stromal hemorrhage, and vascular neoplasms. Corneal vascularization appears as linear red corneal opacities and is a common and non-specific response to chronic corneal injury or inflammation. The depth of corneal vessels may be divided into superficial vessels and deep vessels. Superficial vessels have a tree-like appearance and are bright-red, fine, branch repeatedly, and may be observed to cross the limbus. These vessels arise from conjunctival vessels and their presence suggests superficial corneal or ocular surface disease. Deep vessels have a hedge-like appearance and are dark, short, straight with no or few branches, and do not cross limbus. These vessels arise from anterior ciliary vessels and suggest deep corneal or intraocular disease.

Corneal stromal hemorrhage is a relatively uncommon condition and a complication of corneal vascularization with hemorrhage between stromal lamellae. Intracorneal hemorrhage appears as free blood within the stroma adjacent to corneal vessels. Advanced age and some systemic diseases (e.g., diabetes mellitus, hyperadrenocorticism, hypothyroidism, and systemic hypertension) may predispose animals to intracorneal hemorrhage.

Corneal vascular neoplasms are relatively rare conditions and include corneal hemangioma and hemangiosarcoma. These neoplasms may originate as a primary corneal mass or arise from the limbus and invade the cornea secondarily. Corneal vascular neoplasms appear as raised, irregular cornea surface masses that deform surrounding ocular tissues and progressively enlarge.

Blue

Blue discoloration of the cornea is the result of corneal edema (corneal stromal overhydration). When edematous, the cornea may also appear thickened concurrent with the blue “ground glass” appearance. Corneal edema may result from either corneal epithelial or corneal endothelial disease. The corneal stroma is a hydrophilic tissue that is sandwiched between two aqueous solutions: the precorneal tear film and the aqueous humor. The water-tight barriers of the corneal epithelium and endothelium help prevent overhydration and are composed of tight cellular junctions (zonula occludens and macula occludens). In addition, the corneal endothelium actively pumps water from the stroma into the aqueous humor using Na/K ATPase and carbonic anhydrase ion pumps.

Corneal edema may result from either corneal epithelial or corneal endothelial disease. Corneal epithelial disease results in a loss of the epithelial barrier function with tears imbibed into the stroma. Corneal epithelial disease often produces focal edema that is relatively mild and the cornea is typically fluorescein stain positive. Corneal epithelial diseases that may result in corneal edema include ulcerative keratitis, corneal lacerations, and corneal foreign bodies.

Corneal endothelial disease can be either a primary or secondary dysfunction of the active ion pumps with simultaneous loss of endothelium barrier functions. Endothelial disease ultimately results in aqueous humor being imbibed into the corneal stroma. Corneal endothelial disease often produces diffuse edema with the

potential to be marked and the cornea is typically fluorescein negative. Corneal endothelial diseases that may result in corneal edema include the endothelial dystrophies (primary genetic dysfunction of the endothelium) and endothelial degenerations (secondary damage to the endothelium that may occur as a sequela to uveitis, glaucoma, lens luxation, persistent pupillary membranes, or intraocular surgery).

Black/Brown

Black or brown corneal discoloration is a result of melanin pigment that may be intracellular or extracellular. In general, sources of melanin pigment for deposition in the cornea may include limbal melanocytes, conjunctiva, uvea, neoplasms, and fungi. Specific situations associated with the presence of corneal melanin include corneal epithelial or stromal melanin deposition; endothelial pigment from congenital anomalies, deflated iris cysts, or anterior synechiae; iris prolapse; symblepharon; limbal melanomas; and dematiaceous fungi.

Corneal epithelial or stromal deposition of melanin is most frequently the result of chronic corneal inflammation or irritation. Diverse conditions may produce chronic keratitis, including keratoconjunctivitis sicca, eyelid or ciliary abnormalities, and immune-mediated keratitis. In these situations, the migration of limbal melanocytes into the cornea occurs with intra- or extracellular melanin deposition.

It should be noted that corneal sequestrum, a condition that is primarily observed in domestic cats, also appears as a black or brown corneal discoloration. Feline corneal sequestra have an unknown color source that is not believed to be associated with melanosis.

Yellow/Green

A yellow or green discoloration of the cornea is a result of inflammatory cell infiltrates in the corneal epithelium or stroma. These infiltrates may be diffuse or focal. When focal, the condition is commonly referred to as a corneal stromal abscess. Inflammatory cell infiltrates of the cornea are induced by infections, foreign bodies, and autoimmune corneal conditions.

Greasy Tan

A greasy tan corneal discoloration results from keratic precipitates. Keratic precipitates are inflammatory cell deposits adherent to the corneal endothelium. They are most commonly observed on the ventral endothelial surface and may appear to shimmer due to the presence of phagocytosed lipids. Keratic precipitates indicate active or inactive anterior uveitis.

There are two basic types of keratic precipitates: non-granulomatous and granulomatous. Non-granulomatous keratic precipitates are composed of lymphocytes or neutrophils and appear as fine, round, whitish, and widely spaced deposits (“salt and pepper precipitates”). Granulomatous keratic precipitates are composed of macrophages and epithelioid cells and appear as larger, coalescent, and yellowish deposits (“mutton fat precipitates”).

Gray/White and Wispy

A gray-white and wispy discoloration of the cornea results from scarring (corneal fibrosis and stromal collagen disorganization). This non-specific corneal change typically appears as a flat white or gray color tone with indistinct borders and a feathery appearance. Corneal scarring can develop secondary to any corneal injury or insult. Once formed, corneal scars may be permanent.

Crystalline White

Crystalline white corneal discoloration results from lipid or mineral deposition in the corneal epithelium or stroma. These deposits have a well-defined and refractile (“sparkly”) appearance. Lipid or mineral corneal deposition may result from primary or secondary corneal conditions. Primary diseases that cause lipid deposition in the cornea are the inherited corneal dystrophies. Secondary diseases that result in either lipid or mineral deposition include corneal degeneration (deposition secondary to keratitis and corneal vascularization) and systemic diseases where these substances originate from elevated levels in the systemic vasculature.

Summary

The eight general corneal pathologies and their associated corneal color change are:

- Hemoglobin = Red
- Edema = Blue
- Melanosis = Black/brown
- Inflammatory cell infiltrate = Yellow/green
- Keratic precipitates = Greasy tan
- Fibrosis = Gray/white and wispy
- Lipid deposition = Crystalline white
- Mineral deposition = Crystalline white

Recognition of these basic corneal color changes assists the clinician in determining the underlying pathologic response occurring within the cornea and its etiology.