

EXPLORE the CORNEA

By Linda Conlin, ABOC/NCLEC

Objectives:

1. Learn details of the corneal layers and the physiology of a healthy cornea.
2. Understand how corneal mechanisms affect contact lens wear.
3. Know corneal health problems and contraindications for contact lens wear.

Course Description:

This course describes the unique structure and function of the cornea through discussion of corneal anatomy including the recently identified Dua's layer, physiology, immunity and repair, and the effect of contact lens wear on the cornea. Our objectives are an in-depth look at the anatomy of the cornea, its physiology and function, and the effect of contact lens wear, on the cornea.

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The name cornea comes from the Medieval Latin word "corneatela", which means "horny web". As we will see later, that even before modern instruments, early physicians were able to identify some of the unique characteristics of this amazing tissue.

The cornea is transparent, of course. It is avascular, which means it has no blood vessels. It's shape is convex on the outside, and concave on the inside. At 43 diopters, the cornea makes up 70% of the total refractive power of the eye. The index of refraction is 1.37. The cornea also provides structural integrity and protection for the eye.

Water is 78% of what makes up the cornea. 15% is collagen, a fibrous protein. The remaining 2% is sulfates and salts. These seem like very simple components for such a complex structure!

We've been taught that the cornea has 5 layers, but a recent discovery indicates there may be a sixth layer! In 2013, Dr. Harminder Singh Dua identified a thin layer of corneal collagen between the stroma – the third layer – and Descemet's membrane – the fourth layer. Dr. Dua named the tissue after himself. It is strong, and air can't pass through it. But, some researchers argue that this it is actually part of Descemet's membrane, and not a separate layer, so it remains an unofficial sixth layer.

Take a look at this Dua's layer separated from Descemet's membrane.

The layer was discovered during a simulation of corneal surgery. Air bubbles were injected into the cornea, but bubbles below the layer couldn't be overinflated to bursting. This indicated that air wouldn't pass through. Electron microscopy showed that the layer was separate from Descemet's membrane. It's possible that tears in this layer have something to do with corneal hydrops – which is a rupture in Descemet's membrane that results in severe corneal edema often seen in keratoconus.

The size of the anterior cornea is generally 11.7mm in the vertical meridian and 10.6mm in the horizontal meridian. However, the posterior surface is 11.7mm in both meridians. The cornea thickens toward the periphery. The central thickness is 0.52mm, while the peripheral thickness is 0.67mm.

The radius of curvature of the central 1/3 of the cornea is different from front to back. The anterior radius of curvature is 7.8mm, while the posterior is 6.5. As we move away from the central area, the curve flattens, more nasally and superiorly. The cornea flattens slightly when the eyes converge as in reading, and tends to be flatter in men than women. Surprisingly, the corneal cap or apex isn't centered over the visual axis. It is decentered up and out, and slightly temporal to the pupil.

We can see the decentration of the corneal cap in this topography of a right eye spherical cornea. The steepest area, in red is decentered up and slightly out.

Let's take a closer look at the layers of the cornea. The mnemonic we learned to remember the 5 layers of the cornea is A B C D E. That stands for Anterior or epithelium, Bowman's membrane, Central stroma, Descemet's membrane and epithelium. The extra D for Dua's layer hasn't been added just yet.

We'll begin with a look at the epithelium. The most complex layer of the cornea, it has layers of flat, thin cells forming a hard, slippery tissue. It is continuous with the conjunctiva, but doesn't contain mucous containing goblet cells. The epithelium itself has layers. From back to front they are basal cells, wing or umbrella cells and surface cells that have a tight junction between them.

Epithelial cells have lots of mitochondria, the powerhouses of cells. They have a high glycogen content for stored energy, and filaments for strength. This is likely the "horny" part of the "horny web" for which the cornea was first named. Although some molecules will pass through the epithelium, sodium ions will not. Tiny finger-like microvilli and microplacae help hold onto the tear film. With a lack of oxygen, the glycogen is lost, and it becomes less sensitive.

The epithelium can repair itself through the movement and reproduction of cells. Older cells are shed, and new cells move in from the limbus. Through this process, the epithelium is completely replaced every year!

In 1983, Toft and Friend developed a theory of the balance in regeneration of the epithelium. It's called the XYZ theory. Z represents cells that are lost. X represents cells that are created through cell division in the basal layer, and Y represents stem cells that move in from the limbus. The new cells, minus the old cells, create a balance. $(X + Y) - Z = \text{BALANCE}$.

Besides normal cell replacement, there is some fast action when the epithelium is damaged. Healthy cells at the edge of the wound detach and move in to cover the wound. When the cells come in contact with each other, the movement stops. I like to think of them as tiny bumper cars! The cells then anchor in place and begin to reproduce. They establish tight junctions between each other. Within 7 days, the new cells will adhere to Bowman's layer. For all of this to take place, however, some part of the limbus must be unharmed to provide stem cells.

This slide illustrates the healing process. Cells move in, reproduce, and adhere to Bowman's layer. If Bowman's layer hasn't been injured, healing of the epithelium is complete within 7 to 14 days.

Here's another look at this amazing healing process. Cells at the edge of the wound detach and move across the wound until they meet each other. They then anchor in place and reproduce, producing tight junctions. Healing is complete with adhesion to Bowman's layer.

Now, let's look at the basal cells of the epithelium. They become thicker with diabetes, pathology and age. They are anchored to Bowman's layer with filaments and plaques. Edema and lipid solvents will compromise the adhesion to Bowman's layer.

We just heard how important it is for the epithelium to anchor to Bowman's membrane, so let's take a closer look at Bowman's. It is also known as the anterior limiting lamina, and is composed of collagen fibers rather than cells that form a weave in the periphery. Giving strength to the peripheral cornea, it could be the reason for the "web" part of the "horny web" name. Bowman's membrane is strong, but it will not regenerate upon injury or infection.

Now we come to the stroma, the thickest layer of the cornea. The stroma contains layers of collagen bundles and can repair itself through cell migration and modification. Scars in the stroma are transparent which contributes to the overall transparency of the cornea.

This illustration shows how the collagen bundles are layered in the stroma. Notice that they aren't neatly stacked, but crisscross each other somewhat.

Next is Descemet's membrane, also called the posterior limiting lamina. It is a strong, resistant collagen sheet that forms the basal lamina of the endothelium. The posterior 2/3 of the membrane form after birth, and it thickens with age. While it doesn't regenerate upon injury, endothelial cells form an identical basal lamina.

More isn't always better! With aging, there is an overproduction of material similar to the basal lamina. This overproduction results in an excretion of material in the periphery known as Hassal Henle Warts. While the discovery of these excretions was important, I wouldn't want warts named after me! When the warts are in the central area, they are known as gutatta.

We can clearly see these warts in this slide of Gutatta.

Last but not least is the endothelium. It is composed of a single layer of cube shaped cells that become flatter with age. The cells don't regenerate, but as cells die, existing cells enlarge and change shape to fill the void, although the density of the endothelium decreases. This is known as polymegathism. Like the epithelium, the endothelium has microvilli and abundant mitochondria. It gets its nutrition and oxygen from the aqueous fluid.

This illustration shows how the endothelium repairs itself. Although the cell area increases, the cell density decreases.

How does the cornea maintain its transparency? First, it has to be somewhat dehydrated – about 80% of maximum hydration. It does this by preventing salts and metabolites from entering the stroma, and it pumps out bicarbonates, which are metabolic waste.

Other factors contributing to transparency are the lack of blood vessels and pigments, nerve fibers that don't have a myelin coating – the white, fatty substance that insulates nerve fibers, the uniform spacing of collagen fibers and tight junctions between cells.

How does the cornea survive without the blood that all of our other tissues need? The answer is the vascular arcade, a group of blood vessels that extend 1mm into the peripheral cornea. You can see them at the top of the illustration.

As you can see in this picture, capillaries get to the limbus, then turn back and away from the cornea.

We all know how much even a minor injury to the cornea can hurt! That's because the cornea is one of the most heavily innervated parts of the body. The anterior ciliary, cervical sympathetic and posterior ciliary nerves all join to form the pericorneal plexus. A plexus is a network of interlacing nerves.

Fibers from the Cervical Sympathetic Nerve supply almost the entire eye to warn of injury. For that reason, it is called the "Sentinel of the Eye."

Now that we know the structure of the cornea, let's see what it does. The cornea functions to refract and transmit light – remember that it has 43 diopters of refracting power. It protects the internal structures of the eye and contains the intraocular pressure. The cornea can also absorb and deliver topical drugs to the body.

But HOW does the cornea function? Glucose and oxygen provide nutrition. Glucose supplied by the aqueous humor breaks down to ATP - adenosine triphosphate which provides energy. Oxygen is supplied mainly through tear film, limbal capillaries and aqueous humor. It is important to note that the epithelium consumes oxygen 10 times faster than the stroma. The aqueous humor also provides amino acids to synthesize proteins. Waste diffuses through the epithelium.

Earlier, we saw how the different layers of the cornea heals, but here's a look at the results of increasing degrees of injury. There is no corneal opacity resulting from an injury that involves only the epithelium. Remember that it heals very quickly! An injury involving Bowman's membrane and the superficial stroma results in a nebula – a cloudy spot on the cornea. An injury to 1/3rd of the stroma results in a macula – an opaque spot. And an injury involving more than half of the stroma results in a leucoma or scar.

I mentioned that the cornea can also be a drug delivery system, but only under certain conditions. The drug has to be in a form that is water and lipid soluble. It has to be of a molecular size, weight and concentration that will pass through the cornea. It has to have a compatible ionic form, and a pH and surface agents that won't be harmful. And it has to have the right tonicity or osmotic pressure to pass through the cornea.

What happens when we place a contact lens on the cornea? The presence of the lens results in changes to corneal structure, form and function.

The contact lens affects the function of the epithelium. The cell metabolisms shift from aerobic – with oxygen – to anaerobic – without oxygen. The shift increases lactate – an acid – and carbon dioxide production. That in turn, shifts the normal pH to more acidic which results in stromal hydration. Are you seeing the chain of events? Reduced oxygen leads to epithelial thinning, reduced adhesion of epithelium to basement membrane, epithelial edema and punctate epithelial erosion, that is, areas of epithelial cell loss.

As we saw, most of the changes to the cornea occur because of a continued lack of oxygen, and studies had similar findings with both soft and rigid lenses.

The specific changes that occur are a reduction in oxygen uptake by the epithelium, an increase in epithelial and stromal thickness, endothelial polymegathism because cells are dying, asteeptening of the cornea and a decrease in corneal sensitivity.

Exactly what happens when there is a lack of oxygen? There is another chain of events. First, we should know that the primary source of oxygen for the cornea is the atmosphere. When the cornea isn't getting enough oxygen from the atmosphere, such as when a contact lens is in the way, it uses stored oxygen from the stroma. In a short time, the stored oxygen is gone, and the epithelium and stroma switch to anaerobic respiration. That switch produces less energy in the form of ATP, and more carbon dioxide and lactic acid.

The carbon dioxide and lactic acid build up because they diffuse out of the cornea more slowly. That buildup causes the stroma to uptake water from the aqueous. If there isn't enough oxygen available to produce the energy needed to pump the water out of the stroma, the result is corneal edema.

The swollen stroma is a less effective barrier against blood flow from the limbal blood vessels resulting in neovascularization – the encroachment of blood vessels into the cornea.

Other effects include microcysts – spaces in the tissue filled with fluid, blebs or blisters, striae or stretch marks, folds, polymegathism and reduced endothelial cell density.

Epithelial thinning is another consequence of reduced oxygen to the cornea. When the corneal metabolism slows, less ATP – energy – is available. Less energy results in slower production of new cells. Fewer new cells results in thinning of the epithelium.

In the endothelium, increased acidity from the buildup of lactic acid or acidosis, causes endothelial blebs.

And, as mentioned before, the decreased metabolism in the endothelium results in cell death and polymegathism in an attempt to repair the damage.

Overall, the reduced cell metabolism leads to reduced cell production. Cells die faster than they can be replaced. The $(X+Y) - Z$ balance is off resulting in corneal thinning.

The theory for reduced corneal sensitivity in contact lens wearers is that the constant stimulation of the highly innervated cornea by a contact lens leads to an adaptive response. With an adaptive response, some nerves stop firing, which results in a decreased response to all mechanical stimuli.

In summary, there may actually be six layers of the cornea instead of the previously identified 5. Each layer of the cornea has a unique structure and function. Contact lens wear can disrupt that structure and function mostly due to decreased oxygen supply.