Corneal neovascularization in contact lens wear

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Abstract
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CORNEAL NEOVASCULARIZATION IN CONTACT LENS WEAR

By

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A thesis submitted to the faculty of the
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ABSTRACT

Corneal neovascularization as a result of contact lens wear is a common finding among eye care practitioners. Blood vessels in the cornea can become sight threatening if they are allowed to progress far enough, therefore it is important to determine "how far" is "too far." This paper will discuss the factors in determining the distance a practitioner should allow corneal neovascularization to progress into the cornea. Included is a discussion of the results of a questionnaire received from thirty optometrists asking to what extent they allow neovascularization to progress before taking action to retard the progression. Also, since some practitioners questioned the difference between normal limbal vasculature and abnormal vessel growth, this issue will also be addressed. This discussion will describe the appearances and characteristics of abnormal vessel growth as opposed to normal changes of the limbal region. Furthermore, an extensive look at the possible factors responsible for the growth of new vessels into the cornea is included and methods of fitting lenses to minimize these factors and therefore reduce the progression of corneal neovascularization.

The Normal Limbus

Though the cornea is avascular in nature, the limbal area contains a series of vascular arcades having their origin in the superficial pericorneal plexus. The conjunctival vasculature forms a zone of
anastomosing loops, with the final branches of the arcades lying over the superficial limbal spur and immediately bending back forming venules which drain into the venous plexus. Some of these vessels appear whitish due to the absence of blood. However, with irritation they can fill up with blood quite rapidly.

Diagram of normal epibulbar vascular system at the limbus by retro-illumination and by direct focal illumination. U: unclear portion of cornea; A: artery; V: vein; P, P1, P2: Palisades zone; B: physiologic edema zone; C: terminal vessels of arcades; L.S: limbal spur; R: area between terminal vessels and end of palisade zone.

The limbal area is a major source of nutrition to the cornea. Limbal vessels originating from the episcleral branches of the anterior ciliary artery are essential to a healthy cornea. Other sources of nutrition include the aqueous present in the anterior chamber, and the precorneal tear layer rich in atmospheric oxygen. These three sources of nutrition are responsible for the metabolic needs of the cornea. Without proper metabolism the limbal vasculature is stimulated to send vessels into the normally clear corneal epithelium and stroma compensating for the loss in nutrition. This condition is called corneal neovascularization. 1,2

The terminal conjunctival arcades extend an average of one millimeter into the avascular cornea, and this is where abnormal vessel growth originates. These terminal arcades are often mistaken by some practitioners as corneal neovascularization. It is important to look for the terminal loops of the marginal arcade. Once these loops are identified, true corneal neovascularization can be easily observed and diagnosed with previous documentation of the normal limbus before contact lens wear. It is also important to realize that the length of one millimeter for the conjunctival terminal loops is merely an average. Two millimeter extensions are not uncommon, as well as half a millimeter. Therefore, it is important to recognize the appearance of normal vasculature. Many false diagnoses are due to this characteristic of the limbal vessels. 3,4,5,6.

The transitional conjunctival overlay causes the cornea to appear to be less than transparent if viewed with retro-illumination. Recognizing the translucency of this area will help the practitioner to distinguish normal conjunctival vessels and new corneal vessels. New corneal vessels are found in the transparent cornea. 7 Before one can diagnose a deviation from the norm, one must first be able to identify the norm.
Characteristics of Corneal Neovascularization

Before new vessel growth begins, a condition known as pericorneal injection occurs as a result of the engorgement of the limbal vascular arcades. These arcades, normally threadlike in appearance, become engorged with blood, and many invisible channels which are normally empty also fill with blood. The adjacent conjunctival vessels also become engorged, thus the name pericorneal injection. (See figure 2).


Once the perilimbal plexus is engored with blood, corneal neovascularization follows. Vascularization may move as fast as three hundred microns to five hundred microns per day and can be seen by using
retro-illumination in a biomicroscope. The new vessels appear as fine dark lines suspended in a clear cornea. 9.

The vessels invade the cornea at the exact depth the pathological process is occurring. If the new vessel growth process is in the superficial corneal tissue, the vessels will invade there. On the other hand, if the layers of the dense stroma are affected, new vessels will invade the stromal tissue. Stromal softening is a result of chronic edema in contact lens wear. Epithelial and stromal vessel penetration are categorized into generally two types of neovascularization: superficial and deep. 10,11. Superficial new vessel growth has its origin in the superficial limbal plexus which is characterized by having buds or loop formations. They proceed from the conjunctiva into the corneal epithelium which sometimes raises this tissue. However, vessels from the superficial limbal plexus may take a slightly deeper course and invade the area of Bowman's membrane. This will destroy Bowman's membrane allowing vessels to invade the anterior stromal region.

According to Graves, superficial new vessels form long slender buds (also known as spikes). These buds will meet, thus forming loops from which new buds then develop. New buds begin as endothelial tubes known as "pilots" which can only be seen with extremely high magnification and retro-illumination. New channels will develop while older channels will disappear. When these pilots become true buds and meet adjacent buds, these newly formed loops follow the general pattern of normal capillary vasculature. The new loops have afferent segments which are the arteriole side of the loops and efferent segments correspond to the venous portion of the capillary loop. 12,13,14.
FIGS. 591 and 592.—The Development of (Trachomatous) Pannus
(P. Thyeson; from K. P. Wilson).

As seen by the slit-lamp with direct illumination (on the right) and indirect illumination (on the left). P, the palisade zone; V. L., the zone of vascular loops; E. C. L., the zone of capillary end-loops.

![Diagram](image1)

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![Diagram](image2)

**Fig. 591.**—The normal limbus.

**Fig. 592.**—Early trachomatous pannus showing the extension of the end-capillary loops into the cornea and the characteristic faint subepithelial infiltrates of an early pannus.

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Figure 3: System of Ophthalmology. Edited by Sir Stewart Duke-Elder

Volume VIII: Disease of the Outer Eye Part 2 by Sir Stewart Duke Elder, GCVO, F.R.C.S. and Arthur Georger Leigh, M.D., FRCS

The evolution of superficial corneal vascularization. When two terminal loops meet, the circulation is reorganized. Thus the gradual meeting of the main loops at D in figure 3 leads to the abolition of the redundant efferent vessel E in figure 4.

Figure 4: See Duke-Elder (figure 2,3). Page 683.
Once a new loop is formed, its appearance is identical to the normal limbal capillary loops. It is critical to recognize the difference between neovascularization and the normal limbal vasculature. Proper documentation and possibly photos should be taken on the first time contact lens patient as a preventative precaution. By detecting the thin spearshaped buds projecting off of a loop, a simple differentiation can be made between normal limbal vasculature and new vessel growth. The distinguishing characteristic of superficial vessels can be observed to be continuous with the marginal arcade.

The second category for vessel growth known as "deep" neovascularization originates in the superficial layers of the cornea. When Bowman's membrane is destroyed by superficial neovascularization contact, vessels will invade the anterior stroma. If the condition is severe, vessels may continue on towards Descemet's membrane and eventually soften and destroy the membrane. According to Spicer, deep neovascularization can be divided into three categories: 1) terminal loops, 2) brush form (parallel branches), and 3) umbel type, the latter being the most serious and found in severe localized conditions such as severe ulcers. See Figure 5.
Once the cornea has been vascularized, evidence of the vessels will always remain. They appear as whitish lines which look somewhat like corneal nerves under direct focal illumination. However, corneal nerves are invisible with retro-illumination whereas white threadlike vessels can be easily detected. These white threadlike remnants of vessels are known as ghost vessels, and even after years empty of blood, the limbal region can be stroked and irritated causing vessel dilation and blood flow within these ghost vessels. 16, 17.

**Case Studies in Contact Lens Neovascularization**

Contact lens induced corneal neovascularization is the most common of the superficial type of vascular growth. However, deep stromal vascularization associated with cosmetic daily wear contact lenses has been documented. James Karesh, M.D. and associates reported three cases of deep stromal vascularization in 1983 which were associated with cosmetic daily wear contact lenses. 18.
Case 1 was a 25 year old woman who had been wearing hard contact lenses for ten years. Her wearing time was eighteen to twenty hours daily. Slit lamp examination showed that the lenses appeared to be minimally tight on the cornea, and central corneal edema was apparent in both eyes. There was both deep and superficial vascular growth into the cornea approximately two millimeters. 19.

Case 2 was a 30 year old woman who for four years wore daily wear soft contact lenses. Her wearing schedule was approximately sixteen hours per day, and she never wore them continuously. The lenses were fit moderately tight. Both deep and superficial neovascularization was observed extending two to three millimeters into the cornea. 20.

Case 3 was a 17 year old boy who had been wearing soft contact lenses for almost three years. He was found to have deep corneal vascularization projecting into the cornea three to four millimeters, and 360 degrees bilaterally. The vessels not only were found within the deep stroma, but also were found in Descemet's membrane which caused an increased thickening of the cornea. 21. All three of these patients had normal corneas prior to contact lens wear, and other possible causes of deep stromal vascularization were not indicated. However, by far the majority of corneal new vessel growth is of the superficial type due to daily contact lens wear.

If a contact lens is properly fit and used correctly on a healthy cornea, corneal neovascularization is minimal. Even with chronic over-wear, the latent period for vascularization is usually a matter of years. Extended wear contact lens wearers experience the shortest latency period, as well as patients wearing contact lenses on diseased corneas. 22. It is extremely important for the clinician to carefully

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assess and document the patient's limbal vasculature prior to fitting and dispensing contact lenses. Ghost vessels can easily be overlooked by the practitioner if he/she does not carefully look for them in the pre-fitting examination. When the lenses are dispensed to the patient, in only a short matter of time these ghost vessels will fill with blood during normal contact lens wear. 23,24,25.

Mechanisms Leading to Contact Lens Induced Neovascularization.

"There is no single hypothesis that satisfactorily accounts for all aspects of this complex phenomenon." 26. The previous statement, made by Charles McMonnies, senior research consultant at the Cornea and Contact Lens Research Unit at the University of New South Wales, definitely indicates a need for more research in extended wear soft contact lenses. McMonnies has been extensively researching the ocular responses to contact lenses, and primarily limbal vasculature responses. There are several mechanisms working together that contribute to corneal neovascularization.

One mechanism is the loss of compactness of corneal tissue due to edema. In a healthy, non-edematous cornea, tissue is thought to be very tightly compacted together, physically obstructing vascular growth. Edema creates a situation where the tissue loses its compactness and vessels are easily able to penetrate. Chronic edema may cause a breakdown of stromal ground substance resulting in stromal thinning. Stromal softening occurs when collagenases, elastases and proteases are released from filtrating neutrophils. 27

It is likely that peripheral edema is a much higher risk factor than central edema due to the fact that with hard contact lenses central edema may occur while the peripheral cornea experiences no vascularization. On the other hand, soft lenses that indeed cause peripheral edema has a
higher chance of causing corneal new vessel growth. McMonnies also believes a hard lens which decenters and covers a portion of the limbus may cause peripheral edema leading to neovascularization.

Another possible mechanism causing corneal vascularization is closely associated with the loss of compactness of the cornea due to edema, is the concept of stromal softening. Stromal softening occurs when collagenases, elastases, and proteases are released from infiltrating neutrophils. There is an actual breakdown of individual collagen fibrils which may facilitate the migration of vessels into the avascular cornea.

In association with contact lenses, chronic epithelial disturbances may facilitate the invasion of new vessels by stimulating the production of enzymes which softens the cornea through the process of collagenolysis.

A third possible mechanism leading to neovascularization of the cornea is the involvement of vasostimulating factors. According to Maurice et al, the avascular cornea may contain a vascular growth inhibiting substance, and a vaso-stimulating factor may function by neutralizing this normally present growth inhibiting factor. The sources of vaso-stimulating substances include leukocytes, damaged or disturbed epithelial cells and hypoxic metabolism. Contact lens wear may induce leukocyte infiltration (an inflammatory response) or epithelial disturbances leading to corneal neovascularization. Tight fitting lenses cause the production of lactic acid and other products of hypoxic metabolism which may contribute to new vessel growth. Contact lenses which cause a retention of metabolic waste products and tissue debri present a high risk for neovascularization. Therefore, achieving proper lens movement to activate the tear pump is extremely important in successful contact lens wear. A healthy normal epithelial layer of the
cornea is essential to a contact lens patient.

According to McMonnies, "Hypoxia and associated anaerobic metabolism leading to lactic acid production are commonly associated with contact lens wear without corneal vascularization. If lactic acid initiates or contributes to corneal vascularization, then it may only under circumstances that lead to its accumulation within corneal tissue."

Imre mentions that reduced venous drainage may cause an increase in lactic acid, and could possibly induce corneal neovascularization.

There are various forms of epithelial damage that may occur with contact lens wear such as 3-9 staining and superficial punctate keratitis, a more common finding with soft contact lens wear. Some chronic epithelial disturbances may facilitate the invasion of new vessels by stimulating the production of enzymes which softens the cornea through the process of collagenolysis. These epithelial disturbances do not usually induce new vessel growth because the vasostimulating factor is not produced in a large enough quantity or the removal of lenses eliminates the build-up of vasostimulating substance needed to trigger the vascularization process. Collin found, however, limbal epithelial damage may increase the likelihood of vascularization of the cornea. A more effective and complete drainage mechanism is essential to the limbal cornea rather than in the central cornea.

In relation to contact lenses, it is true some degree of hypoxia frequently occurs resulting in lactic acid production but that in itself rarely induces corneal neovascularization. However, if a tight fitting lens indents the limbal conjunctival vessels restricting venous drainage, a large increase in the lactic acid concentration around the peripheral cornea will result and may trigger neovascularization. Also, a hard contact lens which is decentered and rides over the limbus will also restrict venous drainage and cause the same hypoxic condition. 
McMonnies has found that chronic limbal hyperemia is common among contact lens wearers. Possible factors causing the hyperemia include a residual foreign body response, damaged or dirty lenses, reactions to poorly fitting lenses and adverse reactions to solutions. Limbal hyperemia occurs if a lens is fit too tight compressing the conjunctival limbal veins, which is often painless and unnoticed by the contact lens wearer. This may explain the finding of vascularization in asymptomatic patients who have never experienced a time when they were intolerant to contact lens wear or any acute inflammation due to other conditions. This type of vascularization may possibly have been a chronic process. However, neovascularization may not occur with several years of contact lens wear and can be hypothesized that an individual's susceptibility may be the most important factor.

In summary, McMonnies states:

"An important consideration in the occasional finding of corneal vascularization in contact lens wear may be the presence of systemic or local factors that increase individual susceptibility for those patients to develop this complication. However, apart from individual susceptibility, it is proposed that with hard contact lenses, risk of corneal vascularization may be greatest when there is hypoxia, lens decentration causing peripheral edema and/or restriction of venous drainage, epithelial disturbances, limbal hyperemia, and overwear. All these factors apply to soft lens wear except that soft lenses may be more likely to induce peripheral and venous
drainage restriction or otherwise cause a greater degree of chronic limbal hyperemia.”

Partial Summary of Contact Lens Fittings that may Induce Corneal Vascularization:

1. Soft lenses that are thicker in the periphery, such as high minus lenses or prism ballast lenses.
2. Decentered hard contact lens which locates over the limbus.
3. Any contact lens which causes epithelial damage, such as a hard lens without an adequate blend, a hard lens with an inadequate edge (chipped or excessively sharp), a soft lens which is dirty causing SPK, or is damaged. In essence, any staining of the cornea using fluorescence is implying a risk factor to corneal neovascularization.
4. A contact lens, hard or soft, which does not exhibit adequate movement to activate the tear pump allowing removal of metabolic waste material from the surface of the cornea.
5. Any tight fitting soft contact which impinges on the conjunctival vessels of the limbus. Look for blanching of vessels at the edge of the lens.
6. An inadequate tear reservoir under a hard contact lens using fluorescein and slit lamp techniques.
7. Any lens or solutions which cause excessive limbal hyperemia (allergic reactions).
8. An excessive wearing schedule not allowing adequate time daily for the cornea to recover from the contact lens induced changes.
Possible Ways to Prevent Corneal Vascularization

1. Adequate movement of both hard and soft contacts.
2. Using proper solutions to prevent any hypersensitivity reactions.
3. No limbal vessel restrictions or impingements with soft lenses (do not fit tight).
4. Contact lenses with thin edges.
5. Adequate tear reservoir under a hard contact lens with feathering of the reservoirs edge. (Proper Blending Techniques.)
6. Lenses that are clean and undamaged. Follow a strict cleaning regime.
7. Fluorescein corneal evaluation to rule out staining before the initial fitting.
8. A hard contact which centers on the cornea.
9. Adequate amount of time daily to allow the cornea to recover from contact lens induced changes.
10. A lens with an adequate Dk value. (However, regardless of the Dk value, the contact lens must have adequate movement to remove the metabolic wastes from the surface of the cornea. If there is no movement, or inadequate movement, the cornea is at risk to vascularization and edema, regardless of the oxygen transmissability of the contact lens.)
11. In summary: A properly fitting contact lens will reduce the chance of inducing corneal neovascularization to a minimum.

The Progression of Corneal Vascularization: How Far is Too Far?

To many practitioners, a slight amount of corneal vascularization is an acceptable and expected finding in their contact lens patients. Indeed,
corneal vascularization is a slow moving, seemingly unthreatening condition that if it stays where it should, it can be left alone and the patient can continue to wear his/her lenses with minimal concern. However, when should the practitioner take action to stop the progression of corneal vascularization? How far into the cornea is too far? These questions are of interest to practitioners who fit contact lenses, and the answers have been inconsistent ones ultimately left up to the judgement of the individual practitioner. According to Mathea R. Allensmith, MD, at about 1 mm from the limbus, the corneal structure changes, leaving greater space between the fibrils in the periphery than in the center. As vessels grow towards the center of the cornea, they are usually halted at the point the fibrils become denser. This 1 mm area is where arcus senilis occurs, and is apparently stopped by the physical barrier of closely packed fibrils. Allensmith states, "This area of about a millimeter is about as far into the cornea as neovascularization should be allowed to go in the elective contact lens wearer." Allensmith published this finding in the Journal of the American Optometric Association in 1984, and this is one of the few articles in which the author suggests an actual distance of intrusion based on seemingly logical scientific reasoning.

Doctor Juan J. Arentsen stated in a book from the International Ophthalmology Clinics, "Under various stimuli, neovascularization will originate from limbal arcades; if it invades the cornea for more than 2 mm, it should be considered abnormal." Does this imply that any growth less than 2 mm into the cornea is normal? This would imply Allensmith's 1 mm intrusion limit to be the absolute limit that vascularization should be allowed to progress, is actually perfectly normal. Which statement is more clinically correct?
To possibly help in answering this question of corneal vascularization progression, the authors sent a survey instrument to 55 optometrists around the state of Oregon, and 30 responded. The questionnaire asked:

1) "How far do you feel vessels should invade the cornea before a change of lens type is indicated?"

2) "How far do you feel vessels should invade the cornea before contact lens wear is terminated?"

The optometrist was also given the option to elaborate on the subject if he/she wanted to do so.

The answer to the first question from the questionnaire ranged from zero to three millimeters, and the average distance was 1.43 mm (see Graph A). With regard to contact lens wear termination, the distances ranged from zero millimeters to five millimeters, with the average being 2.53 mm (see Graph B).

A few of the practitioners elaborated on their answers. These elaborations were as follows:

**Practitioner A:** "Not too worried if vessels are superficial (epithelial) but any mid stromal vessels indicate termination no matter the extent."

**Practitioner B:** "I do not want any blood vessels in the cornea at all."

**Practitioner C:** "Essentially any progressing vessel growth is an indication to change. I will not ultimately terminate wear (especially in an aphake) if I think it has stopped progressing (verified by close follow up care)."

**Practitioner D:** "We do not see neovascularization with hard contact lenses or gas perms."

**Practitioner E:** "It is important to not only evaluate the amount of..."
neovascularization but also look at other areas. Look to determine if
the neo has open spokes radiating toward the optical center or if they
are looping back toward the limbus. Also the degree of filling of the
vessels are important. If I have a patient with 2 mm of
neovascularization but the ends are looped back and with very
minimal filling, I would not take this person out of this lens."

Practioner F: "Vessels in the cornea are abnormal at any distance."

As one can see, there seems to be many different opinions concerning
corneal neovascularization among practitioners. The range of answers
speak for themselves: a range of 0 mm to 5 mm before termination of
contact lens wear is indicated certainly tells us that there exists no clear
cut answer to this question at the present time. It is the opinion of the
authors that an answer to the question "How far should practitioners allow
corneal vascularization to progress?" needs to be determined. Extensive
clinical research is needed in this area, and if and when the answer is
determined, it must be supported by solid scientific evidence, absent of
opinions. At the present time, there only exists opinions with little
scientific evidence supporting these opinions. It also can be argued that a
definitive answer may not exist, and only guidelines exist that
practitioners can use to make a judgement.

CONCLUSION

Every optometrist who fits contact lenses has most likely been faced
with the finding of corneal neovascularization. On the other hand, many
optometrists have thought that they were observing neovascularization
where in actuality they were observing a perfectly avascular cornea and an
irregular limbus intruding a little more than usual.

Careful slit lamp documentation is essential for preventative contact
lens wear problems. It is very important practitioners learn to identify what is normal limbal vasculature and what is abnormal. In addition, it is essential to understand all of the factors that elicit growth of blood vessels into the cornea which occurs when a contact lens is on the eye. Having an understanding of the risk factors will allow the practitioner to have a better understanding of the necessity of an adequately fitting contact lens. These factors must be weighed carefully before a decision can be made regarding the proper care for the patient.

Furthermore, at the present time there are only opinions as to how far neovascularization should be allowed to progress before contact lens wear is altered or terminated. However, in all actuality a definitive answer may not exist. Instead there may simply be guidelines for expectations in combination with the various types of neovascularization which help the informed optometrist make a judgement.
Graph A

# of O.D.'s

Neovascularization (mm)

Ave. 1.43mm
GRAPH B

# of O.D.'s

Neovascularization (mm)

Ave. 2.53mm
References


