NK
INFO TOOL

BLINK AND YOU'LL MISS IT: SAVING CORNEAL SENSATION IN NEUROTROPHIC KERATOPATHY

Neurotrophic Keratopathy

Neurotrophic keratopathy (NK), also known as neurotrophic keratitis, is a disease that affects corneal sensitivity.[1] Neurotrophic keratopathy is rare, affecting approximately 5 in 10,000 patients.[2] If NK remains undetected and untreated, it can progress and lead to blindness.[3]

Neurotrophic keratopathy is defined as dysfunction of corneal sensory innervation that results in dysregulation of the corneal nerve and cellular function.[1,4-6] Corneal nerves act in maintaining corneal epithelial cells via the protective blink reflex and tear secretion. Corneal nerves release neuropeptides that provide trophic support for epithelial cells. In turn, corneal epithelial cells support the neurons through their release of neurotrophic factors, including nerve growth factor **(Figure)**.[1,4-6] Loss of this neuronal homeostasis leads to loss of corneal sensation (the hallmark of NK), corneal epithelial breakdown, and, ultimately, keratolysis if left untreated.[1,5,6] **Table 1** gives an overview of the causes of NK.[1,6]

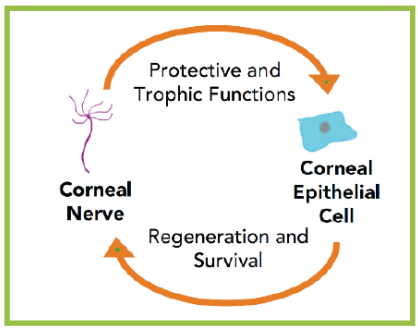

Figure. Corneal nerves and corneal epithelial cells interact in a mutually supportive relationship to maintain neuronal homeostasis[1,4-6]

Table 1. Overview of the Causes of Neurotrophic Keratopathy[1,6]

Infectious and Noninfectious Keratitis • Herpes simplex keratitis • Herpes zoster keratitis • Acanthamoeba keratitis • Chemical injury • Thermal injury • Contact lenses	**Iatrogenic** • Ocular surgery • Keratoplasty • Corneal refractive surgery • Collagen cross-linking • Retinal photocoagulation • Orbital surgery • Surgery affecting trigeminal nerve	**Congenital Diseases** • Familial dysautonomia • Goldenhar-Gorlin syndrome • Congenital corneal hypoesthesia • Möbius syndrome
Systemic Diseases • Diabetes • Multiple sclerosis • Leprosy	**Medication Induced** • Anesthetic abuse • Topical medication toxicity • Chronic use of antipsychotic drugs • Chronic use of antihistamines	**Trigeminal Nerve Palsy** • Traumatic injury • Intracranial and orbital malignancy • Postsurgical palsy • Aneurysm and cerebrovascular accident

Clinical signs of NK include punctate epithelial erosions, irregular corneal epithelium, epithelial defects, subepithelial haze, stromal scarring and ulceration, and corneal perforation.[1,3] These have been traditionally classified by Mackie as NK stages 1 to 3 **(Table 2)**.[1,3,7]

Table 2. Stages of Neurotrophic Keratopathy[1,3,7]

Stage	Examination Findings	Corneal Sensation
1: Mild	• Punctate keratopathy • Epithelial hyperplasia and irregularity • Superficial neovascularization • Stromal scarring	Reduced or aberrant corneal sensation
2: Moderate	• Persistent epithelial defect • Loose and opaque epithelium around the defect • Rolled edges of defect • Stromal swelling • Anterior chamber reaction • Sterile hypopyon (rare)	Corneal anesthesia
3: Severe	• Stromal involvement (thinning, perforation)	Corneal anesthesia

Treatment of NK depends on its severity and is often a stepwise approach, involving a combination of drugs, devices, and surgical procedures.[1,2,6] Recombinant human nerve growth factor (cenegermin) is the only US Food and Drug Administration–approved therapy for NK and has been shown to promote corneal healing.[8-10] Other treatments include artificial tears, serum drops, and anti-inflammatory drugs, tarsorrhaphy, punctal plugs, and amniotic membrane grafts.[1,2,6]

References

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GETTING A FEEL FOR CORNEAL SENSITIVITY TESTING

Raising Suspicion for Neurotrophic Keratopathy

It is imperative to identify and treat NK and other diseases affecting the corneal sensation early to avoid disease progression, invasive measures, and adverse patient outcomes.

Any of the following should raise suspicion of reduced or absent corneal sensitivity[1,2]:

- Persistent or painless epithelial defect
- Vision changes not ascribed to the retina or lens
- Photophobia
- History of the following:
  - Herpetic eye disease
  - Trigeminal nerve damage
  - Corneal procedures
- Risk factors:
  - Poorly controlled diabetes
  - Reduced blink

Corneal Sensitivity Testing

Methods of assessing corneal sensation[3]:

- "Wisp" of cotton, dental floss
  - Performed easily in the clinic
  - Patient's reaction is noted and compared between each eye
- Cochet-Bonnet esthesiometer
  - Different lengths (60 to 5 mm) of nylon filament applied to the cornea
  - The longer the length, the higher the sensitivity
- Belmonte noncontact gas esthesiometer
  - Cornea stimulated with calibrated air jet; blink response is observed
  - Used only in study settings

If you suspect possible lowered ocular surface sensitivity, DELAY ADMINISTERING ANESTHETIZING EYE DROPS and refer to the clinic physician.

Qualitative Method

Using a cotton-tipped applicator or dental floss, compare the sensation in each eye. Approach the patient from the side and test all 4 quadrants **(Figure)**.[4] Document the sensation in each section as normal, reduced, or absent.

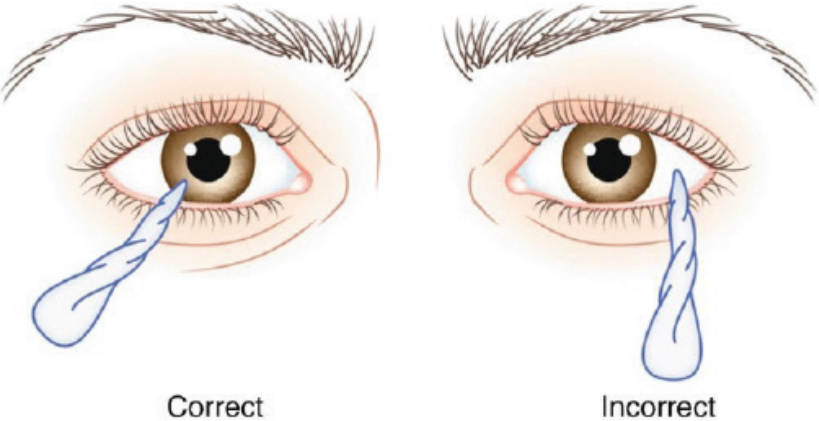

Figure. Testing corneal reflex[4]

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1. Dana R, Farid M, Gupta PK, et al. Expert consensus on the identification, diagnosis, and treatment of neurotrophic keratopathy. *BMC Ophthalmol.* 2021;21(1):327.
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