The Insensitivity of NK: Diagnosis and Management

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Douglas K Devries, OD Disclosures

All Conflicts Have Been Mitigated

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Alcon Advisor and Speaker
Asecula Advisor
Azura Advisor
Bio Tissue Advisor and Speaker
Bruder Advisor
B&L Advisor and Speaker
Dompe Advisory and Speaker
Johnson and Johnson Advisor Speaker
Lumenis Advisor and Speaker\
Lenz- Advisor and Speaker
OcuSoft Advisor
Ophthalmic Resource Partner
Science Based Health Advisor and Speaker
Sight Science Advisor and Speaker
Sun Advisor and Speaker
Tarsus Advisor
Thea Advisor
TruKera Advisor
Versea Advisor
Visus AdvisorQuidel Advisor

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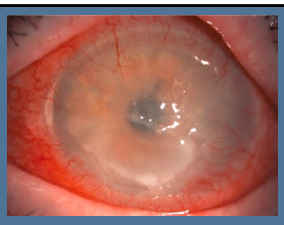

Neurotrophic Ulcer

End Stage NK

Mackie IA. In: Fraunfelder F, Roy FH, Meyer SM, eds. Current Ocular Therapy. WB Saunders; 1995.

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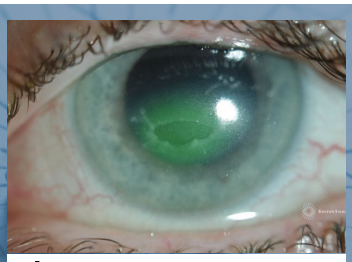
Neurotrophic Keratitis Definition



Hallmark: decreased sensation, decreased or no pain

- Degenerative corneal disease
- Damage to the trigeminal nerve (cranial nerve V)
- Loss of corneal sensation
- Breakdown of the corneal epithelium
- Impaired corneal healing
- Persistent epithelial defect → corneal ulceration → stromal melting and perforation
- *STAIN without PAIN*

Mastropasqua L, et al. J Cell Physiol. 2017;232(4):717-724.

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1. Dua HS, et al. Prog Retinal Eye Res. 2018;66:107-131.
2. Saad S, et al. Ocular Surf. doi:10.1016/j.jtos.2019.11.008.

Neurotrophic Keratitis

- Rare/orphan disease (ORPHA137596)[1]
  - Affects ≤ 5 individuals in 10,000
- NK Prevalence difficult to determine[1,2]
  - Estimated to be < 1.6/10,000
  - Best data are based on extrapolation from the most common conditions associated with NK
    - Herpes simplex keratitis: 6% develop NK
    - Herpes zoster keratitis: 12.8% develop NK
    - Postsurgical nerve damage: 2.8% develop NK

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Differential Diagnosis

- Loss of corneal sensation = *Neurotrophic Keratitis*
- *Neuropathic* pain (corneal neuralgia, keratoneuralgia):
  - *Pain without stain*
  - Pain in response to minimal or even no stimulus
- Diseases with overlapping features of NK; can lead to NK if corneal sensation is affected [1,2]
  - Dry eye disease
  - Contact lens-related disorders
  - Blepharitis
  - Exposure keratopathy
  - Stem cell deficiency
  - Topical drug toxicity
  - Mild chemical injury

1. Dua HS, et al. Prog Retinal Eye Res. 2018;66:107-131.
2. Sacchetti A, et al. Clinical Ophthalmology. 2014;8:571-579.

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CORNEAL NERVES: The Foundation of Ocular Surface Health

300 to 600 times more than skin and 20 to 40 times more than dental pulp

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1. CORNEAL NERVES: The Foundation of Ocular Surface Health

CORNEAL NERVE FUNCTIONS

The **CORNEAL NERVES** are a key element for the ocular surface health as they trigger 3 key ocular protection mechanisms:

1. Tear production
2. Reepithelization
3. Blinking reflex

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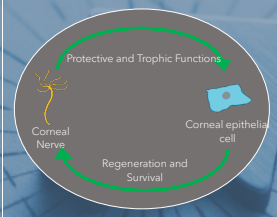
Corneal Innervation

- The cornea is the most sensitive and densely innervated tissue in the human body[1,2]
- Corneal nerve damage = loss of corneal sensation, epithelial breakdown, poor healing[1,2]



1. Sheha H. Clinical Ophthalmology. 2019;13:1973-1980.
2. Versura P, et al. Eye and Brain. 2018;10:37-45.
3. Dua HS, et al. Prog Retinal Eye Res. 2018;66:107-131.
4. Saad S, et al. Ocular Surf. doi:10.1016/j.jtos.2019.11.003.

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Etiology

INFECTIOUS[1,2]
- Herpes (simplex, zoster)
- Leprosy

IATROGENIC
- Trauma to ciliary nerves by laser treatment and surgery
- Corneal incisions
- LASIK or PRK

SYSTEMIC DISEASE[1,2]
- ***Diabetes***
- Multiple sclerosis
- Vitamin A deficiency

CORNEAL DYSTROPHIES[1,2]
- Lattice
- Granular

TOXIC[1,2]
- Chemical burns
- Carbon disulfide exposure
- Hydrogen sulfide exposure

TOPICAL MEDICATIONS[1,2]
- Anesthetics (abuse)
- Timolol
- Betaxolol
- Sulfacetamide
- Diclofenac sodium
- Ketorolac

MISC[2]
- ***Contact Lenses***
- Increasing age
- Adie syndrome
- Limbal stem cell failure (chronic)

FIFTH-NERVE PALSY[1,2]
- Trigeminal neuralgia surgery
- Neoplasia (acoustic neuroma)
- Aneurysms
- Facial trauma
- Congenital
- Riley-Day syndrome
- Goldenhar-Gorlin syndrome
- Möbius syndrome
- Familial corneal hypesthesia

1. Dua, HS, et al. Prog Retinal Eye Res. 2018;66:107-131.
2. Medscape. Neurotrophic keratitis. https://emedicine.medscape.com/article/1194889-overview

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Chronic Comorbidities May Worsen Prognosis of NK

Chronic comorbidities can also confound the diagnosis of NK, increasing the need for a thorough diagnostic work-up, including a confirmatory test.

- Dry Eye
- Blepharitis
- Exposure Keratitis
- Topical Drug Toxicity
- Mild Chemical Injury
- Contact Lens-Related Disorder
- Limbal Cell Deficiency

Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. Clin Ophthalmol. 2014;8:571-579.

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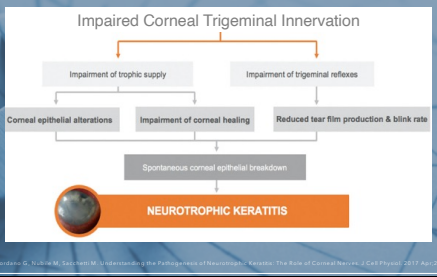
Nerve Malfunction: Central to NK



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Etiologies: Impairment of Trigeminal Innervation

- Herpetic Corneal Disease (HSV/VZV)
- Damage to CN V – h/o stroke, tumor, brain injury/surgery
- H/o ***LASIK*** or other ***ocular surgery***
- Iatrogenic injury (h/o contact lenses)
- Chronic use of topical medications (e.g., *PGA* timolol, betaxolol)
- Some corneal dystrophies
- Limbal stem cell deficiency long standing/diseased epithelium (chemical burns)
- Systemic Diseases: ie, ***diabetes mellitus***, multiple sclerosis, Riley-Day syndrome
- Multiple ocular surgeries
- Ocular cicatricial pemphigoid

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Diagnosing NK

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Diagnostic Considerations

- Clinical History
- Corneal sensitivity testing
- Complete eye exam (slit lamp/DFE – eg, r/o diabetic retinopathy)
- ***Corneal staining***
- Schirmer test (can be impaired as a result of reduction in corneal sensitivity)
- Corneal cultures (r/o secondary infection)
- In vivo confocal microscopy (affected sub-basal nerves)
- Evaluation for systemic immune disorders

Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. Clin Ophthalmol. 2014;8:571-579.

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Corneal Sensation

- Greatest in the central cornea
  - 5 to 6 times as many nerve fibers compared to peripheral
  - Drops rapidly as distance increases from the central cornea
- Falls with increasing age
- Is not affected by iris color
- More sensitive in the temporal limbus than the inferior limbus
- Reduction has been reported in diabetes (types 1 and 2)

Faulkner WJ, Varley GA. Corneal diagnostic techniques. In: Krachmer JH, Mannis MJ, Holland EJ, eds. Cornea. 2nd ed. Vol. 1 Philadelphia: Elsevier/Mosby; 2005:229-235. External Disease and Cornea, Section 8, Basic and Clinical Science Course, AAO, 2010.

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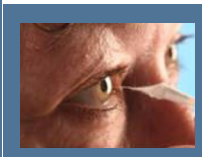
Corneal Sensitivity Testing



QUALITATIVE

- Examples: Cotton swab, cotton wisp, dental floss, tip of a tissue
- Basic scoring systems may be developed using simple tests for sensation
- Descriptive scales: normal, hypoesthesia, anesthesia

QUANTITATIVE

- Examples: Cochet-Bonnet esthesiometer
- Often used in basic research and clinical trial settings
- May be limited in general clinical practice

Versura P, Giannaccare G, Pellegrini M, et al. Neurotrophic keratitis: current challenges and future prospects. Eye Brain. 2018;10:37-45.

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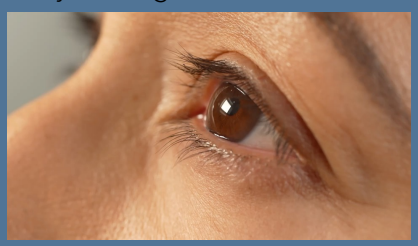
Video Workshop Presentation of Corneal Sensitivity Testing with Dental Floss



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Video Workshop Presentation of Corneal Sensitivity Testing on NK Patient

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1. CORNEAL NERVES: The Foundation of Ocular Surface Health

CORNEAL SENSITIVITY TESTING

Non-contact esthesiometry is the test for **screening and monitoring** of **patients at risk for neurotrophic dysfunction** associated with ocular surface disease

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3. Paradigm Shift to Proactive Approach in OSD Management

CONVENIENT, EASY & QUICK TEST

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3. Paradigm Shift to Proactive Approach in OSD Management

KEY FEATURES

- Non-Contact (noninvasive)
- Standardized stimulation levels for assessing 6 corneal health status: from suspected hypersensitivity to very severe hyposensitivity
- Electronic precise positioning system
- Quantifiable and repeatable method for consistent and reliable patient monitoring
- Quick and easy to use
- Designed for seamless placement on a slit lamp
- No consumables or calibration required

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3. Paradigm Shift to Proactive Approach in OSD Management

CORNEAL SENSITIVITY TEST RESULTS

Stimulus Level- threshold	Corneal status*
Level 1	Corneal hypersensitivity (suspect)
Level 2	Regular corneal sensitivity
Level 3	
Level 4	Corneal hyposensitivity (suspect)
Level 5	Severe corneal hyposensitivity
None (Level 6)	Very severe corneal hyposensitivity

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Mackie Severity Classification

Stage	Clinical Features
1	✓ Punctate epitheliopathy (punctate corneal fluorescein/LG staining) ✓ Decreased TBUT ✓ Stromal haze
2	✓ Persistent epithelial defect with smooth rolled edges ✓ Stromal opacity
3	✓ Stromal thinning/ulceration ✓ Corneal perforation

Mackie, IA. (1995) Neuroparalytic keratitis. WB Saunders.
Dua HS, Said DG, Messmer EM, et al. Neurotrophic keratopathy. Prog Retin Eye Res. 2018;66:107-131.

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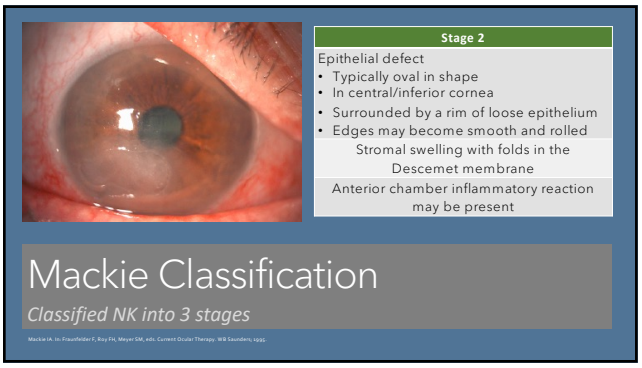

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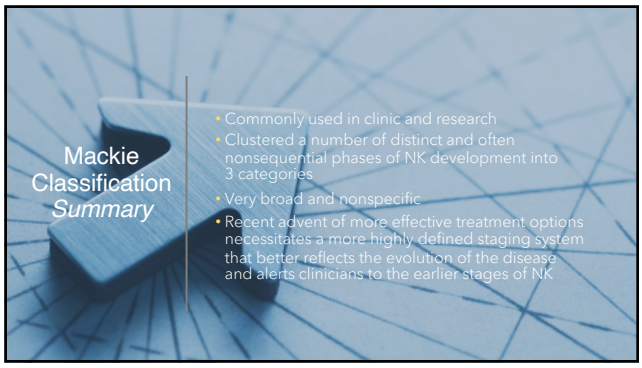

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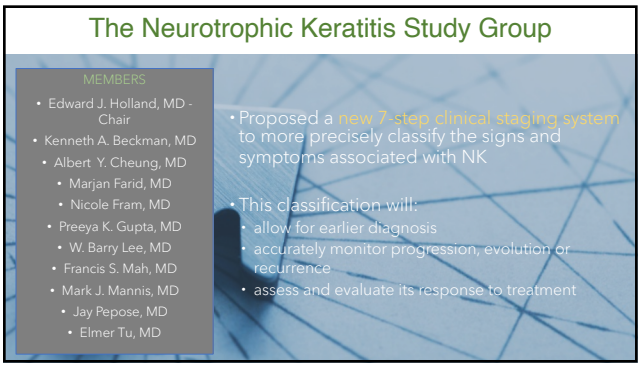

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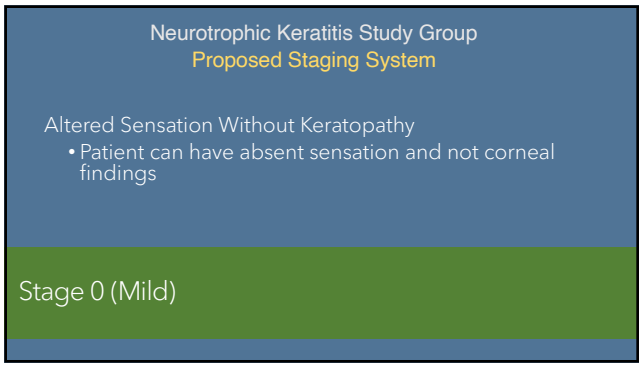

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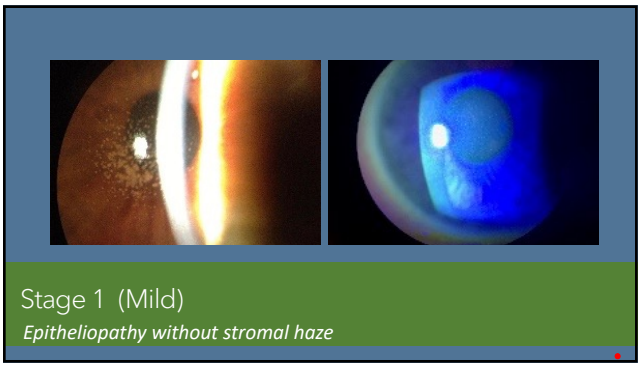

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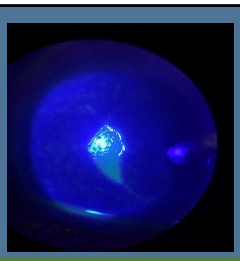
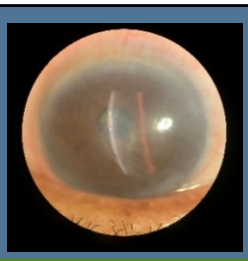

Stage 2 (Moderate)

Epitheliopathy with stromal haze

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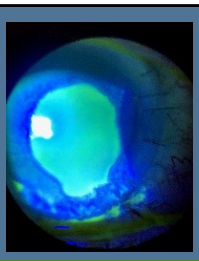

Stage 3 (Severe)

Persistent or recurrent epithelial defects

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Stage 4 (Severe)

Persistent or recurrent epithelial defect and stromal scarring without corneal ulceration

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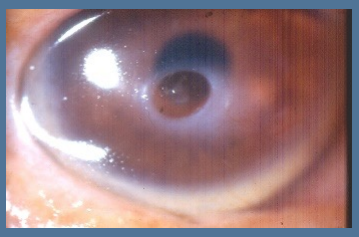

Stage 5 (Severe)

Persistent or recurrent epithelial defect with corneal ulceration

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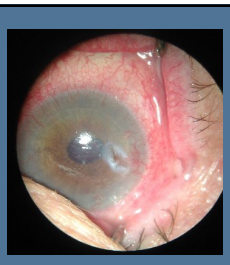

Stage 6 (Severe)

Corneal perforation

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Topics for Discussion

- Mackie Classification versus Neurotrophic Keratitis Study Group 7-stage grading
  - When to use each?
- How to differentiate early NK from dry eye
  - Exam flow, staff flow
- When to manage?
- When to treat/refer?

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NK Treatment

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Severity-Based Therapy

Stage	Therapy
1	• Preservative-free artificial tears formulations • Punctal occlusion • Hydrogel contact lens (consider large diameter) • Recombinant human NGF (rhNGF, cenegermin) • Serum/plasma/platelet rich plasma
2	Supportive therapies plus: • rhNGF • Scleral lens (± serum/plasma) • Amniotic membrane • Botulinum induced ptosis, Tarsorrhaphy
3	• rhNGF • Keratoplasty + scleral lens, tarsorrhaphy, neurotization

Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. Clin Ophthalmol. 2014;8:571-579. Sheha H, Tighe S, Hashem O, Hayashida Y. Update on cenegermin eye drops in the treatment of neurotrophic keratitis. Clin Ophthalmol .2019;13:1973-1980. Published Oct 7, 2019.

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Therapeutic Bandage Contact Lens

PROS

- Inexpensive
- Mechanical protection
- Surface hydration

CONS

- **Risks**
- Infection
- Hypopyon formation
- Reactive iritis
- **Requires frequent follow-up**
- Use with caution!

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Serum/Plasma Therapy

Serum/plasma have reported efficacy as primary or adjunct therapy

- Reported success of serum alone (20-50% concentration) ranges from 71 to 100% within 90 days (Guadilla et al. *Arch Soc Esp Offalmol* 2013; Jeng and Dupps Cornea 2009; Pflugfelder *AJO* 2006)
- Umbilical cord serum may be more effective and has higher concentrations of substance P and NGF than peripheral blood serum (Yoon KC et al. *Ophthalmology* 2007)
- Epithelial defect healed in 97.4% of stage 2-3 NK after 11 weeks of plasma rich in growth factors (PRGF) (Sanchez-Avila RM et al. *Int Ophthalmol* 2018)
- Serum can be used safely in combination with SiH CL. No inflammation or CL deposits were observed (Choi JA *ECL* 2011)

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Amniotic Membrane

- Randomized clinical trial reported healing of refractory neurotrophic ulcers with conventional therapy (lubrication plus BCL or tarsorrhaphy) or amniotic membrane transplant (AMT). Healing rates were similar in the 2 groups: 67% with conventional therapy and 73% with AMT (Khokhar S et al. *Cornea* 2005)
- AMT was also equivalent to autologous serum (AS) in healing neurotropic ulcers: 70% for AS and 73% for AMT (Turkoglu E et al. *Semin Ophthalmol* 2014)
- Multilayer AMT recommended for deep ulcers and Descemetoceles (Kruse F et al. *Ophthalmology* 1999)

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Amniotic Membrane

- Self-retaining or in O.R.
- Single or multi-layer graft or patch
- Heal acute defect
- Restore stromal thickness
- Re-establish epithelial integrity
- Consider amniotic membrane extract

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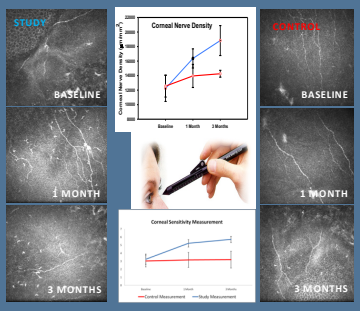
Lasting Effect by Increasing Corneal Nerve Density



Jain T, et al. Journal of ophthalmology. 2017 Aug 15;2017.

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Scleral Lenses

- Use of fluid filled scleral contact lenses for treatment of NK initially reported decades ago (Romero-Rangel et al. *AJO* 2000)
- Nonhealing corneal epithelial defects with BCL healed without recurrence in all 9 eyes treated with PROSE scleral lens (Ling J et al. *Am J Ophthalmol* 2013)
- Overnight wear (with close monitoring) may accelerate healing (Lim P et al. *AJO* 2013)

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The Latest Treatment Options

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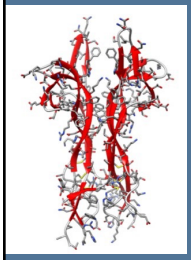
Active Ingredient Structurally Identical to Human Nerve Growth Factor Produced in Ocular Tissues



- Naturally occurring neurotrophin is responsible for differentiation, growth, and maintenance of neurons[1]
- The regenerative potential of nerve growth factor (NGF) was discovered by Nobel-prize winning scientists in the early 1950s[1]
- Cenegermin-bkbj, a novel recombinant human nerve growth factor (rhNGF), is STRUCTURALLY IDENTICAL to the NGF protein[2]

46

1. Lambiase A, Rama P, Bonini S, Caprioglio G, Aloe L. Topical treatment with nerve growth factor for corneal neurotrophic ulcers. N Engl J Med 1998;338:1174-80. 2. Voelker R. New Drug Treats Rare, Debilitating Neurotrophic Keratitis. JAMA. 2018;320(13):1309.

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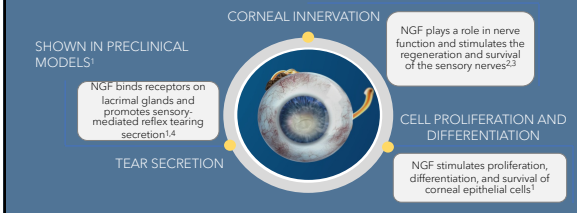
Endogenous NGF Maintains Corneal Integrity By Three Mechanisms

Endogenous Nerve growth factor acts through specific high-affinity (ie, TrkA) and low-affinity (ie, p75NTR) nerve growth factor receptors in the anterior segment of the eye to support corneal innervation and integrity.[1]



1. Mastropasqua L, Massaro-Giordano G, Nubile M, Sacchetti M. Understanding the pathogenesis of neurotrophic keratitis: the role of corneal nerves. J Cell Physiol. 2017 Apr;232(4):717-724. 2. Müller LJ, Marfurt CF, Kruse F, Tervo TM. Corneal nerves: structure, contents and function. Exp Eye Res. 2003 May;76(5):521-42. 3. Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. Clin Ophthalmol. 2014;8:571-9. 4. Musi S, Colafrancesco V, Sornelli F, et al. Nerve Growth Factor in the Developing and Adult Lacrimal Glands of Rat With and Without Inherited Retinal Degeneration. Cornea. 2010;29:1163–1168.

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Cenegermin-bkbj Clinical Data

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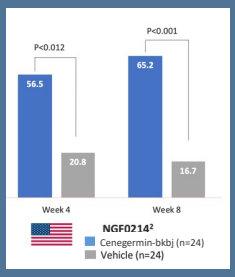
Clinical Trials: Efficacy



Complete Corneal Healing* in up to 65.2% of patients receiving cenegermin at Week 8

*Complete corneal healing defined as 0-mm staining in the lesion area and no other persistent staining in the rest of the cornea after 8 weeks of treatment (last post-baseline observation carried forward; chi-squared test).

The formulation that was tested in REPARO (Study NGF0212) did not include the antioxidant methionine and is not the final formulation of cenegermin-bkbj that is on the market. Methionine is an excipient added to the commercial formulation to improve its stability. More than one study was conducted with the final commercial formulation. No difference in safety was seen in either of the trials.

49 1. Bonini S, Lambiase A, Rama P, et al. Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. Ophthalmology. 2018;125:1332-1343. 2. Chao W, J. BDC, R. D et al. Data on file. Healing of persistent epithelial defects or corneal ulcers by recombinant human nerve growth factor eye drops in patients with stage 2 or 3 neurotrophic keratitis. Presented at: Congress of the European Society of Ophthalmology (SOE) 10-13 June 2017, Barcelona, Spain. 2017. 3. cenegermin-bkbj ophthalmic solution 0.002% (20 mcg/ml) [US package insert]. Boston, MA: Dompé U.S. Inc.; 2018.

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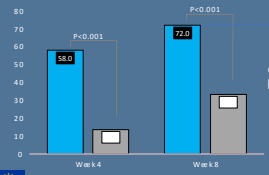
Clinical Trials: Efficacy



80%

of patients who achieved complete corneal healing* in Study NGF0212 (REPARO) were still healed 48 weeks after completing one 8-week cenegermin treatment cycle

*Complete corneal healing defined as 0-mm staining in the lesion area and no other persistent staining in the rest of the cornea after 8 weeks of treatment.

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Safety: The most common adverse reaction was eye pain following instillation which was reported in approximately 16% of patients. Other adverse reactions occurring in 1-10% of cenegermin-bkbj patients and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing[3]

50 1. Bonini S, Lambiase A, Rama P et al. Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. Ophthalmology. 2018;125:1332-1343. 2. NGF0212 (REPARO) CSR- Data on file. 3. cenegermin-bkbj ophthalmic solution 0.002% (20 mcg/ml) [US package insert]. Boston, MA: Dompe U. S. Inc.; 2018.

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Clinical Trials: Pooled Safety Report

- No serious adverse reaction related to the treatment occurred in any clinical trials
- The majority of adverse reactions were mild and transient ocular reactions that did not require treatment discontinuation or any corrective treatment

16%

The most common adverse reaction was **eye pain** following instillation, which was reported in approximately 16% of patients.

12/75= 16%
7/23=30.4% (US trial)
5/52= 9.6% (REPARO)

1-10%

Other adverse reactions occurring in 1-10% of patients taking cenegermin-bkbj and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation, and tearing.

Source: Data on file, pooled analysis of NGF0212/REPARO and NGF0214

1. Bonini S, Lambiase A, Rama P, et al. Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. Ophthalmology 2018;125:1332-1343. 2. cenegerm in-bkbj ophthalmic solution 0.002% (20 mcg/ml) [US package insert]. Boston, MA: Dompé U.S. Inc.; 2018.

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Study Conclusions

After 8 weeks of treatment, 6 times daily

In most patients across two clinical studies cenegermin-bkbj ophthalmic solution 0.002% was well tolerated and more effective than vehicle in promoting complete corneal healing of moderate or severe NK.

50 clinical trial sites in Europe and the US

Study NGF0214 (N=24 per group)

US patients with NK in one or both eyes

NCT02227147

65.2% completely healed

Vehicle response rate 16.7%

Of patients who healed after one 8-week course of treatment…

80%

Remained healed for 1 year*

*Based on REPARO, the study with longer follow-up

52 1. Bonini S, Lambiase A, Rama P et al. Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. Ophthalmology. 2018;125:1332-1343. 2. Chao W, J. BDC, R. D et al. Data on file. Healing of persistent epithelial defects or corneal ulcers by recombinant human nerve growth factor eye drops in patients with stage 2 or 3 neurotrophic keratitis. Presented at: Congress of the European Society of Ophthalmology (SOE) 10-13 June 2017, Barcelona, Spain. 2017. 3. cenegermin-bkbj ophthalmic solution 0.002% (20 mcg/ml) [US package insert]. Boston, MA: Dompé U.S. Inc.; 2018.

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The Latest Research

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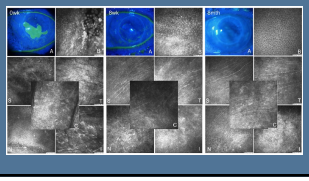
Recent Research

- Pedrotti et al performed a prospective case series, n=18, 14/18 cleared at 8 weeks and stayed clear at 4 and 8 mo follow-up. In vivo corneal microscopy was used to evaluate corneal nerve regeneration.
- Significant peripheral corneal nerve growth and branching was seen at 2 mo, and central advancement across the 8 months. Corneal sensitivity improved. The nerve regeneration was partially visible at 8 weeks and continued after treatment with the hypothesis that the initial growth sustained further regeneration (Journal of Rare Diseases 2022).



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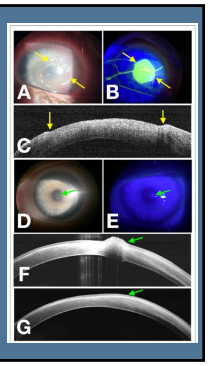
Recent Research

- Bonzano et al evaluated anterior segment OCT in 16 NK patients, half treated with 50% autologous serum and half with cenegermin.
- The corneal wound healing process was followed, including size and depth measured at the thinnest part of the cornea. Mean time to wound closure (slit lamp) was 3.9 weeks +/- 0.5 weeks and 5.9 weeks +/- 1.9 weeks in the AS arm.
- AS-OCT healing process: corneal epithelial hypertrophy, opaque reflective scar tissue followed by improvements in stromal thickness.
- Both treatments both improved NK, but cenegermin resolved quicker, possibly due to peripheral nerve regeneration. (*Frontiers in Pharmacology* 2022)



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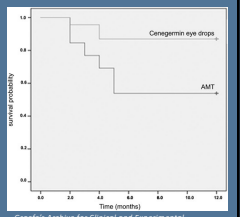
Recent Research

- Sacchetti et al evaluated 2 groups, Amniotic membrane transplant and cenegermin with 12 months f/u: 13/15 AMT and 23/24 cenegermin remained cleared. There was less recurrence in the cenegermin group.
- Patient satisfaction and satisfaction with treatment outcomes were significantly better in the cenegermin group using a specifically designed patient reported satisfaction questionnaire.
- Similar to other studies, there was approximately a 13% recurrence rate. Survival analysis (recurrence) favored cenegermin. BCVA was statistically significantly improved.



Graefe's Archive for Clinical and Experimental Ophthalmology (2022)

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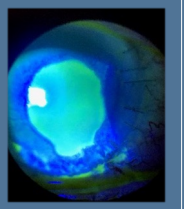
Treatment Summary

- Neurotrophic keratopathy is caused by a number of conditions
- Severity ranges from diffuse epitheliopathy to corneal ulceration and perforation
- Base treatment on severity stage
- Efficacy of many therapies are based on low level of evidence
- rhNGF is a validated, highly effective FDA-approved therapy that should be considered a first-line option
- A proactive approach to minimize recurrent corneal epithelial breakdown, stromal scarring and thinning and vision loss is recommended



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CASE STUDIES

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Case 1: LASIK NK Case

Patient Information	• 53-year-old woman • Works in our billing office and sits in front of a computer all day
Medical History	• Hx LASIK OU 4-2017 • Hx right side trigeminal neuralgia, 6-2017 had rhizotomy which did not help but resulted in right side facial and eye numbness • Complains of decreased vision As the day progresses, her central more than peripheral vision becomes hazy Uses artificial tears and notices it helps her vision for a brief period Feels no pain Later in the day, the vision is so bad she just covers the right eye • Being referred for a large central corneal abrasion OD

Case courtesy of Francis Mah, MD

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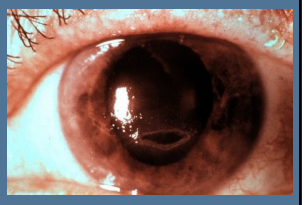
Case 1: LASIK NK Case

Rx	• Currently using ciprofloxacin 3-4x/day
VA	• OD: 20/40 ph no improvement • OS: 20/40 ph 20/20



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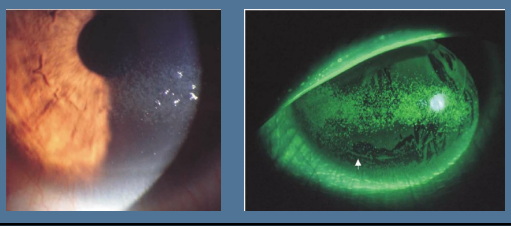
Case 1: LASIK NK Case

- Healed within 2 weeks using ointment QID OD



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Case 1: LASIK NK Case

- However, during the next 12 months, every time she stopped the ointment, she would form another abrasion. She didn't like the ointment because it blurred her vision.
- She developed an abrasion 4 times within the year.
- Self-retaining AMT was used; ointment was used, but she kept breaking down when she decreased the ointment use.
- She was fitted for a scleral lens, but she couldn't tolerate it.
- Finally, we discussed tarsorrhaphy.

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Case 1: LASIK NK Summary

- cenegermin launched in early 2019
- 1/28/2019 we prescribed cenegermin 6 x a day OD
- 2/11/2019 she was approved by her insurance
- 2/20/2019 she started cenegermin
- 2/21/2019 she saw the oculoplastic surgeon to have the tarsorrhaphy taken down
- 3/20/2019 she was already healed
- 6/3/2022 she remains healed on artificial tears; VA 20/25

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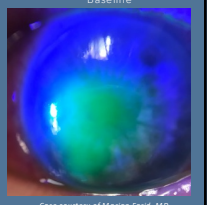
Case 2

Patient Information	• 75-year-old man with 3- to 4-month nonhealing epithelial defect
Medical History	• h/o bilateral LASIK • h/o Herpes Zoster Ophthalmicus • 1 previous history of "corneal abrasion" 1 year ago that healed after 2 weeks with aggressive lubrication, antibiotic gtts
Previous Treatments	• BCL • Amniotic Membrane (self retaining) – Prokera x 2 • Autologous serum gtts
Concomitant Medications	• Antibiotic gtts • Artificial tears • Valtrex 1 gm BID
Corneal Sensitivity	• Absent
Diagnosis	• Nonhealing neurotrophic corneal epithelial defect

Baseline



Case courtesy of Marjan Farid, MD

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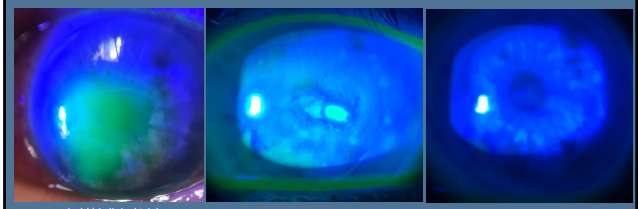
Case 2—what to expect

Baseline	Week 4	Week 8
• >5 mm central lesion, started cenegermin-bkbj	• Central lesion reduced in size, incomplete closure	• Central lesion resolved, slight haze



cenegermin-bkbj clinical trial

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THANK YOU!

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