

Delivering Corticosteroid Treatment for Patients With Uveitis-associated Macular Edema

Definition and Epidemiology of Noninfectious Uveitis

Uveitis is defined as inflammation of the uveal tissues of the eye, including the iris, ciliary body, and choroid. Other intraocular structures can also be involved in uveitis, including the sclera (termed scleritis), retina, retinal blood vessels, and the optic nerve.¹ The Standardization of Uveitis Nomenclature (SUN) working group guidance on uveitis terminology categorizes uveitis on the basis of location: anterior uveitis is localized primarily to the anterior segment of the eye, involving the iris and pars plicata; intermediate uveitis, localized to the vitreous cavity and pars plana; posterior uveitis, involving the choroid and retina; and panuveitis, defined as inflammation involving anterior, intermediate, and posterior uveal structures (Figure 1).²

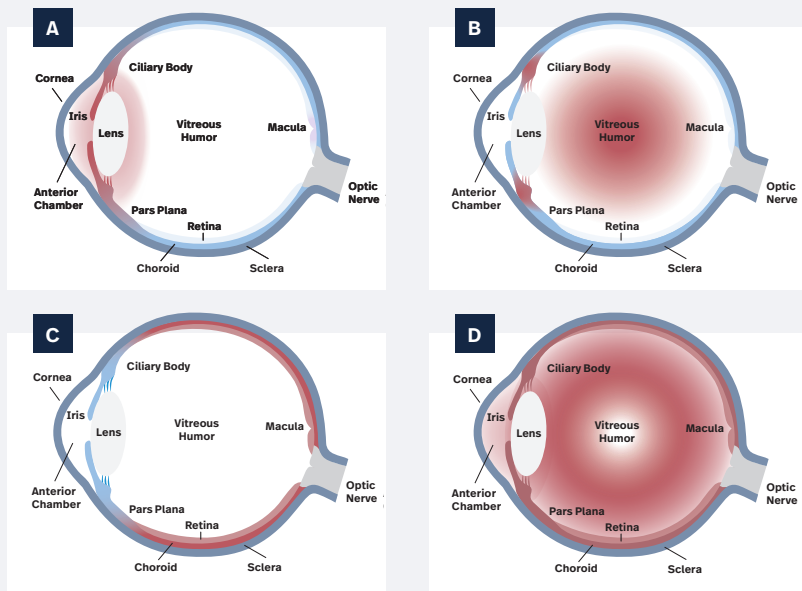


Figure 1. Uveitis classification system based on the location of inflammation.³

- A) Anterior uveitis involves the iris and/or ciliary body.
- B) Intermediate uveitis largely involves inflammatory cells in the vitreous and ciliary body.
- C) Posterior uveitis includes inflammation of the retina and/or choroid.
- D) Panuveitis includes inflammation of anterior uvea, the vitreous humor, and the retina or choroid.

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TARGET AUDIENCE

This educational activity is intended for ophthalmologists and ophthalmologists in residency or fellowship training.

LEARNING OBJECTIVES

Upon completion of this activity, participants will be able to:

1. Summarize risk factors for the development of NIU and associated ME as well as evidence supporting the need to promptly treat these conditions
2. Critically review drug delivery routes used in the treatment of uveitic ME and other ocular diseases, including their benefits and challenges
3. Interpret results of key trials examining SCS injections for the treatment of ocular diseases, particularly uveitic ME, and how new data may eventually influence practice
4. Describe proper techniques for SCS injection, solutions to common treatment challenges, and best practices for patient education and monitoring

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Essentially, uveitis results from an imbalance between inflammatory and inflammation-regulating mechanisms. Typically, resident macrophages and dendritic cells initiate acute inflammation. In autoimmune uveitis, self-reactive T cells from the thymus travel to the eye, where they encounter retinal antigens and become activated, initiating an inflammatory response in the eye.⁴

While uveitis may result from infection, systemic autoimmune diseases, or autoimmune diseases localized to the eye, noninfectious uveitis (NIU) is not associated with a pathogen.¹ NIU is often idiopathic but may also be associated with systemic autoimmune/inflammatory diseases or postoperative inflammation (**Table 1**).^{1,5-8} NIU can also arise following treatment with some antibiotics, and patients with

a history of COVID-19 may have an increased risk of NIU recurrence post-vaccination.⁹

NIU is a leading cause of vision loss in the developed world despite being relatively uncommon.¹ While uveitis accounts for 5% to 20% of legal blindness in the United States (US) and Europe,^{10,11} NIU has a reported prevalence of 58 to 121 per 100,000 in the US, 36.3 per 100,000 in Australia, and, in Europe, between 12.4 (Portugal) and 700 (Sweden) per 100,000.¹ Estimates per 100,000 for Asia include 152 in China, 317 to 730 in India, and 580 in Thailand.¹ Additionally, results from the US have indicated that NIU occurs more frequently in women than in men and that risk may increase with age (although results for the latter are variable).^{12,13}

STATEMENT OF NEED

Macular edema (ME), the accumulation of intra- or subretinal fluid in the macular region, has been noted as the most common sight-threatening complication of noninfectious uveitis (NIU), with visual impairment occurring in up to 40% of patients.^{1,2} Corticosteroids are first-line agents for addressing inflammation for most cases of acute uveitis, including NIU.² Intravitreal (IVT) corticosteroid administration has also been shown to be effective for the treatment of ME in NIU,³ even more so than periocular injections.⁴ Following IVT injection, the vitreous humor acts as a natural depot that permits slow drug release that may extend for as long as one month.⁵ However, IVT administration of corticosteroids can result in diffusion of the drug to non-target portions of the eye, such as the lens and ciliary body,⁵ resulting in steroid-associated off-target effects like elevated intraocular pressure or cataract.⁶ Other local side effects, such as sterile and infectious endophthalmitis, hypotony, IVT hemorrhage, and retinal detachment have also been reported with the use of IVT drug injection.^{6,7} One way to avoid the complications associated with IVT injections of corticosteroids could be drug administration into the suprachoroidal space (SCS), the region between the sclera and the choroid, which can accommodate up to 1 mL of fluid.^{8,10} SCS injections are a minimally invasive approach to directing pharmacotherapies, including corticosteroids, to target tissues.^{8,9} In fact, preclinical studies demonstrate that, compared with IVT administration, injection into the SCS results in a more posterior distribution of pharmacologic agents with higher drug exposures to the sclera, choroid, retinal pigment epithelium, and retina, coupled with lower exposure in the anterior segment.⁸ Clinical data have demonstrated both the efficacy and safety of SCS injection of triamcinolone acetonide for the treatment of ME secondary to NIU, among other conditions.¹¹⁻¹⁶ Ultimately, administration into the SCS may enable injected therapeutics to bypass the sclera without the risks associated with intraocular penetration.

The emergence of corticosteroid administration via the SCS for uveitic ME and other conditions has prompted high interest among retina specialists. A potential consideration for real-world use of the SCS injection technique, however, is overcoming the initial learning curve: more than half of retina specialists surveyed responded that training is the most important factor for integrating SCS administration into their practices.¹⁷ Because drug administration via the SCS is relatively new to the field of treatments for ME associated with NIU, there is an unmet need among

clinicians for understanding of both the concepts and practical aspects of using the SCS injection technique.

REFERENCES

1. Massa H, Pipis SY, Adewoyin T, Vergados A, Patra S, Panos GD. Macular edema associated with non-infectious uveitis: pathophysiology, etiology, prevalence, impact and management challenges. *Clin Ophthalmol*. 2019;13:1761-1777.
2. Teper SJ. Update on the management of uveitic macular edema. *J Clin Med*. 2021;10(18):4133.
3. Koronis S, Stavarakas P, Balidis M, Kozels N, Tranos PG. Update in treatment of uveitic macular edema. *Drug Des Devel Ther*. 2019;13:667-680.
4. Thorne JE, Sugar EA, Holbrook JT, et al. Periocular triamcinolone vs. intravitreal triamcinolone vs. intravitreal dexamethasone implant for the treatment of uveitic macular edema: The PeriOcular vs. INTravitreal corticosteroids for uveitic macular edema (POINT) Trial. *Ophthalmology*. 2019;126(2):283-295.
5. Chiang B, Jung JH, Prausnitz MR. The suprachoroidal space as a route of administration to the posterior segment of the eye. *Adv Drug Deliv Rev*. 2018;126:58-66.
6. Tan HY, Agarwal A, Lee CS, et al. Management of noninfectious posterior uveitis with intravitreal drug therapy. *Clin Ophthalmol*. 2016;10:1983-2020.
7. Yap YC, Papathomas T, Kamal A. Results of intravitreal dexamethasone implant 0.7 mg (Ozurdex®) in non-infectious posterior uveitis. *Int J Ophthalmol*. 2015;8(4):835-838.
8. Habot-Wilner Z, Noronha G, Wykoff CC. Suprachoroidally injected pharmacological agents for the treatment of chorio-retinal diseases: a targeted approach. *Acta Ophthalmol*. 2019;97(5):460-472.
9. Naftali Ben Haim L, Moisseiev E. Drug delivery via the suprachoroidal space for the treatment of retinal diseases. *Pharmaceutics*. 2021;13(7):967.
10. Moisseiev E, Loewenstein A, Yiu G. The suprachoroidal space: from potential space to a space with potential. *Clin Ophthalmol*. 2016;10:173-178.
11. Yeh S, Khurana RN, Shah M, et al. Efficacy and safety of suprachoroidal CLS-TA for macular edema secondary to noninfectious uveitis: phase 3 randomized trial. *Ophthalmology*. 2020;127(7):948-955.
12. Yeh S, Kurup SK, Wang RC, et al. Suprachoroidal injection of triamcinolone acetonide, CLS-TA, for macular edema due to noninfectious uveitis: A randomized, phase 2 study (DOGWOOD). *Retina*. 2019;39(10):1880-1888.
13. Khurana RN, Merrill P, Yeh S, et al. Extension study of the safety and efficacy of CLS-TA for treatment of macular oedema associated with non-infectious uveitis (MAGNOLIA). *Br J Ophthalmol*. 2021;bjophthalmol-2020-317560.
14. Henry CR, Shah M, Barakat MR, et al. Suprachoroidal CLS-TA for non-infectious uveitis: an open-label, safety trial (AZALEA). *Br J Ophthalmol*. 2022;106(6):802-806.
15. Marashi A, Zazo A. Suprachoroidal injection of triamcinolone acetonide using a custom-made needle to treat diabetic macular edema post pars plana vitrectomy: a case series. *J Int Med Res*. 2022;50(4):3000605221089807.
16. Willoughby AS, Vuong VS, Cuneffare D, et al. choroidal changes after suprachoroidal injection of triamcinolone acetonide in eyes with macular edema secondary to retinal vein occlusion. *Am J Ophthalmol*. 2018;186:144-151.
17. CISION PR Newswire. New survey shows retina specialists believe suprachoroidal administration is an option for patients with macular edema associated with noninfectious uveitis. 2022. <https://www.prnewswire.com/news-releases/new-survey-shows-retina-specialists-believe-suprachoroidal-administration-is-an-option-for-patients-with-macular-edema-associated-with-noninfectious-uveitis-301545655.html>

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Table 1. Diseases and medications associated with NIU.^{1,7,9} BCG, Bacille Calmette–Guerin; HBV, hepatitis B virus; HLA, human leukocyte antigen; JIA, juvenile idiopathic arthritis; MMR, measles, mumps, and rubella; MS, multiple sclerosis; NIU, noninfectious uveitis.

Diseases/syndromes/conditions associated with NIU

- Acute posterior multifocal placoid pigment epitheliopathy
- Ampiginous choroiditis
- Behçet disease
- Birdshot choroiditis
- Diabetes
- HLA-B27-associated acute anterior uveitis
- Intermediate uveitis, non-pars planitis type
- Intermediate uveitis, pars planitis type
- JIA-associated chronic anterior uveitis
- MS-associated intermediate uveitis
- Multifocal choroiditis with panuveitis
- Multiple evanescent white dot syndrome
- Pregnancy
- Punctate inner choroidopathy
- Sarcoidosis
- Serpiginous choroiditis
- Sympathetic ophthalmia
- Tubulointerstitial nephritis and uveitis
- Vogt-Koyanagi-Harada disease

Medications and vaccines that increase risk for NIU

- Alendronate
- BCG Vaccine
- Bevacizumab
- Brimonidine
- Cidofovir
- Diethylcarbamazine
- Fluoroquinolones
- HBV Vaccine
- Infliximab
- Influenza Vaccine
- Metipranolol
- MMR Vaccine
- Prostaglandin analogues
- Ranibizumab
- Rifabutin Pamidronate
- Sulfonamides
- Varicella Vaccine

Additional risk factors

- Smoking
- Vitamin D deficiency
- Intraocular surgery
- Ocular trauma

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DATE OF ORIGINAL RELEASE

August 2024. Approved for a period of 12 months.

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Dr. Eichenbaum states that he has received grant/research support from 4DMT, Alkahest, Annexon, AsclepiX, Bayer, EyePoint, Gemini, Genentech, Gyroscope, Ionis, Iveric Bio, Kodiak, Mylan, NGM, Novartis, Ocular Therapeutix, Opthea, Recens Medical, Regeneron, Regenxbio, and Unity. He served as a consultant for Alimera, Allergan, Apellis, Bausch + Lomb, Coherus, Crinetics, DORC, EyePoint, Genentech, Gyroscope, Iveric Bio, KKR, Kodiak, Novartis, Opthea, Outlook, Recens Medical, Regeneron, Regenxbio, ReVive, US Retina, and Vial. He served on speaker's bureaus for Allergan, Apellis, Bausch + Lomb, Bayer, DORC, EyePoint, Genentech, and Novartis. He owns stocks in Boston Image Reading Center, Clearside, Hemera Biosciences, Network Eye, Outlook, ReVive, and US Retina.

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NIU and Uveitic Macular Edema

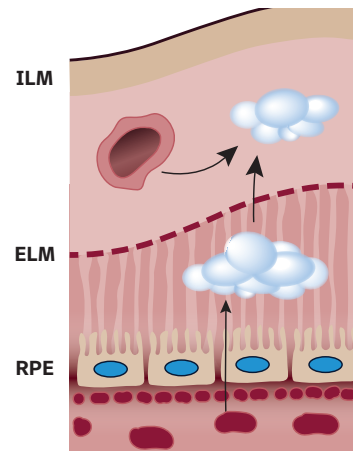
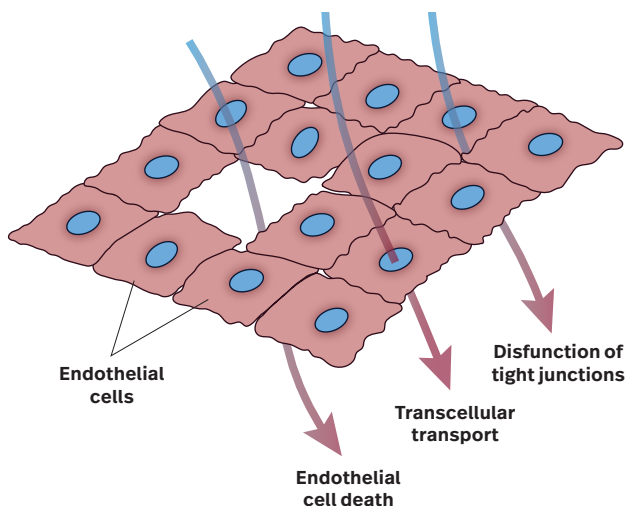
In some cases, NIU can be complicated by macular edema (ME), the accumulation of intra- or subretinal fluid in the macular region.⁵ Uveitic macular edema (UME) is the most common sight-threatening complication of NIU,¹⁴ with visual impairment occurring in up to 40% of patients.^{5,15} The most common cause of ME in patients with NIU is breakdown of blood-retinal barriers (BRBs) secondary to chronic inflammation (**Figure 2**).⁵ Breakdown of the BRB leads to the accumulation of extracellular fluid in either the intraretinal or the subretinal space.⁵ Several factors can contribute to BRB breakdown, including elevated levels of factors associated with chronic inflammation, including vascular endothelial growth factor (VEGF), which leads to the degradation of tight junction proteins in the retinal vasculature.¹⁶ Other factors involved in BRB breakdown include pro-inflammatory cytokines like tumor necrosis factor (TNF)- α , transforming growth factor (TGF)- β , angiotensin 2, interleukin (IL)-1, adenosine, histamine, and glucose.^{17,18} This chronic inflammatory state results in leakage of fluid into retinal tissue and the formation of cystic

spaces in the outer plexiform layer or within all layers of the retina.^{5,18} Inflammation may also lead to swelling of Muller cells, which contributes to cystoid ME.^{5,18} These cells also produce vessel-permeabilizing factors such as VEGF and TNF- α .¹⁹ ME may complicate anterior, intermediate, or posterior uveitis and can disrupt retinal layers or lead to serous retinal detachment.^{5,20}

Consequences of NIU and ME

The development of ME in patients with NIU adversely affects visual and quality of life outcomes. The presence of ME strongly predicts worsening best corrected visual acuity (BCVA) at baseline and over time.²² Patients also experience poorer visual outcomes with longer duration of uveitis.²² Along with uveitis-associated loss of BCVA, patients with NIU experience higher rates of ocular complications, such as cataract, visual disturbances, retinal disorders, and glaucoma.¹⁴

Figure 2. Disruption of the BRB and the development of ME. Figure adapted from Ento Key 2019.²¹ BRB, blood-retinal barrier; ELM, external limiting membrane; ME, macular edema; IGF, insulin-like growth factor; IL, interleukin; ILM, internal limiting membrane; RPE, retinal pigment epithelium; TGF, transforming growth factor; TNF, tumor necrosis factor; VEGF, vascular endothelial growth factor.



BRB permeability increased via elevated levels of:

- Adenosine
- Glucose
- Histamine
- IGF-1
- ILs
- Prostaglandins
- TGF- β
- TNF- α
- VEGF

Uveitis also compromises functional vision, such as the ability to drive, and significantly reduces quality of life measures such as mental health outcomes, vision-related social functioning, and the ability to attend to daily activities independently.²³

In the clinical setting, uveitic ME should be suspected in any patient with uveitis and a complaint of decreased vision.¹⁸ Other symptoms of uveitic ME include a disturbance in contrast sensitivity, difficulty in reading, metamorphopsia, micropsia, and a positive relative scotoma.^{18,24} Slit-lamp examination supplemented by biomicroscopy may reveal increased macular thickness, loss of the normal foveal reflex, cystic spaces, and an associated epiretinal membrane. There also may be an overlying vitreous haze and signs of inflammation (eg, vasculitis, chorioretinitis, choroiditis, disc edema, inferior snowballs, snow banking).^{18,24}

Imaging in UME

Optical imaging is the mainstay of monitoring uveitis and UME, particularly optical coherence tomography (OCT) to assess anatomical changes in the retina, and fluorescein angiography (FA) to visualize vascular leakage.²⁵ Newer multimodal imaging techniques permit visualization of subtle pathologic changes that may support better management of patients with uveitis,²⁵ and these approaches may have predictive value in estimating a patient's disease trajectory.²⁶

Ocular Coherence Tomography

OCT (**Figure 3**) is the gold standard technique for the diagnosis and monitoring of UME, regardless of its etiology, because

it is noninvasive, reproducible, and sensitive. It accurately quantifies retinal macular thickness using mapping and may show fluid accumulation at either the inner or outer plexiform layer. It also can demonstrate intraretinal fluid accumulation between retinal septa—which typically appears as a cystoid shape—and enables analysis of the optic nerve head and the thickness of optic fibers that could be damaged in uveitic glaucoma.¹⁶

In addition to monitoring anatomical changes in the retina, OCT measures can correlate with visual outcomes. In a study of patients with NIU who received a triamcinolone acetonide injectable suspension, eyes responsive to treatment (ie, showed a decrease in central subfield thickness [CST] $\geq 50 \mu\text{m}$ at 4 weeks) had a greater improvement in BCVA at 24 weeks vs eyes that did not qualify as treatment responders (14.6 vs 6.5 letters, $P=0.006$).²⁷ Additionally, OCT can identify disorganization of the retinal inner layers (DRIL) in patients with uveitic ME, which is a significant predictor of poorer BCVA outcomes.²⁸

More recently, there have been a number of advances in OCT that have increased its utility. Swept-source OCT (SS-OCT) operates at about two times the speed of spectral domain OCT and permits scanning of a wider field of view in a similar amount of time. SS-OCT also allows visualization of structures beyond the vascular arcades and the posterior pole. Thickness maps from large scan patterns can be used to identify perivascular thickening, which is correlated with vascular leakage demonstrated by FA.²⁹ Ultra-widefield (UWF) OCT permits clear visualization of the vitreous, the vitreoretinal interface, the retinal layers, and the choroid beyond the anterior border of the vortex veins. It has the potential improve understanding of posterior segment inflammatory diseases and responses to treatment.³⁰

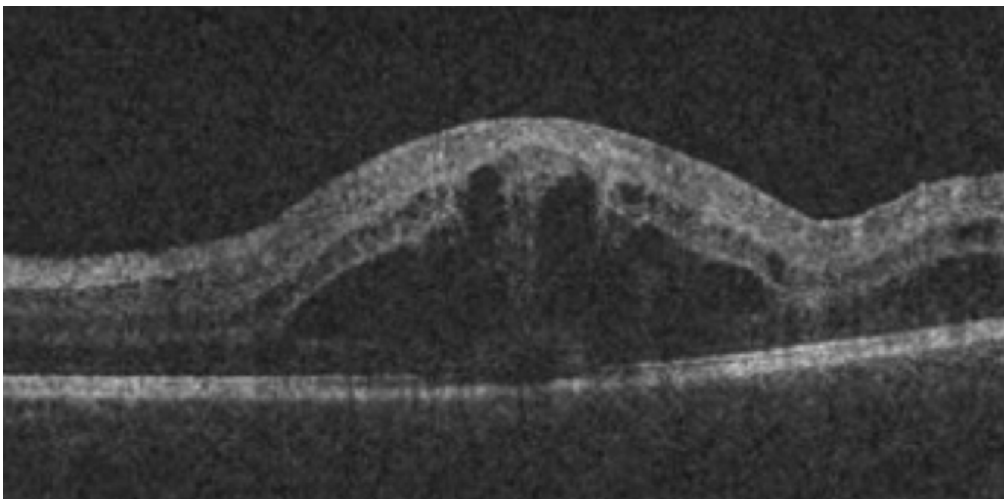


Figure 3. OCT of a retina with diffuse and cystoid ME (Image courtesy of Dr. Steven Yeh, MD). ME, macular edema; OCT, optical coherence tomography.



Figure 4. UWFA of a fundus (OD) with active vasculitis with leakage and staining.³³ UWFA, ultra-widefield fluorescein angiography.

Ultra-widefield Fluorescein Angiography

FA is a mainstay in optical imaging and is conventionally useful for determining locations and severity of inflammation, as well as involvement of retinal vessels and the optic disc. It also supports quantification of retinal vascular leakage.¹⁷ Ultra-widefield fluorescein angiography (UWFA) provides the ability to monitor the same clinical signs as traditional FA but visualizes a larger portion of the retina, allowing clinicians to detect peripheral nonperfusion and far peripheral neovascularization elsewhere (defined as a new blood vessel >1 disc diameter away from the optic disc (**Figure 4**)).^{31,32} Peripheral vascular leakage visualized with UWFA is highly specific and sensitive for prediction of clinically active uveitis and is an important parameter for following status.²⁹ This approach has also been shown to be useful in correlating vascular leakage with macular thickness. Eyes with peripheral vascular leakage on UWFA are likely to have uveitic ME, and such patients will need more aggressive therapy.¹⁷

Treating NIU and ME

The diagnostic and therapeutic management of UME is challenging due to the complex diagnostic workup, its usually recurrent nature, and the fact that it may be refractory to conventional treatment.⁵ Corticosteroids are the first-line short-term treatment for NIU-associated ME. Because uveitis is, at its core, an inflammatory disease, corticosteroids provide broad inhibition across multiple inflammatory pathways. Additionally, corticosteroids can be administered using a variety of methods, allowing clinicians to tailor treatment based on a patient's individual needs.

While steroids are considered first-line in the treatment of NIU and ME, both local and systemic steroids are associated with long-term side effects; systemic corticosteroids are associated with diabetes, osteoporosis, and hypertension, while local ocular corticosteroids can induce intraocular pressure (IOP) increase and cataract formation.⁵ Thus, while corticosteroids are useful in reducing uveitis-related inflammation and ME, the goal for treating NIU and ME is steroid-free remission from corticosteroids to steroid-sparing immunomodulatory therapy.

Systemic Corticosteroid Administration

Systemic corticosteroids are considered to be very effective in controlling uveitic ME, with a rapid onset of action to resolve severe inflammation. The most commonly used systemic corticosteroids to treat NIU-associated ME are oral prednisone and intravenous methylprednisolone.³⁴ Despite their efficacy, systemic steroids are also associated with clinically significant systemic adverse events (AEs), especially when they are administered for extended periods.^{35,36} Systemic corticosteroids have lower risk for local side effects, such as glaucoma and cataract, but they may result in other complications, including hypertension, diabetes, osteoporosis, Cushing syndrome, atherosclerosis, mood changes, and infections resulting from immunosuppression.^{35,36} As a result, systemic steroids are typically used for short periods to control acute or breakthrough inflammation or in patients with bilateral uveitic ME.^{35,36} Patients being treated with systemic steroids should be closely monitored for development of the above complications.³⁶

Local Corticosteroid Administration

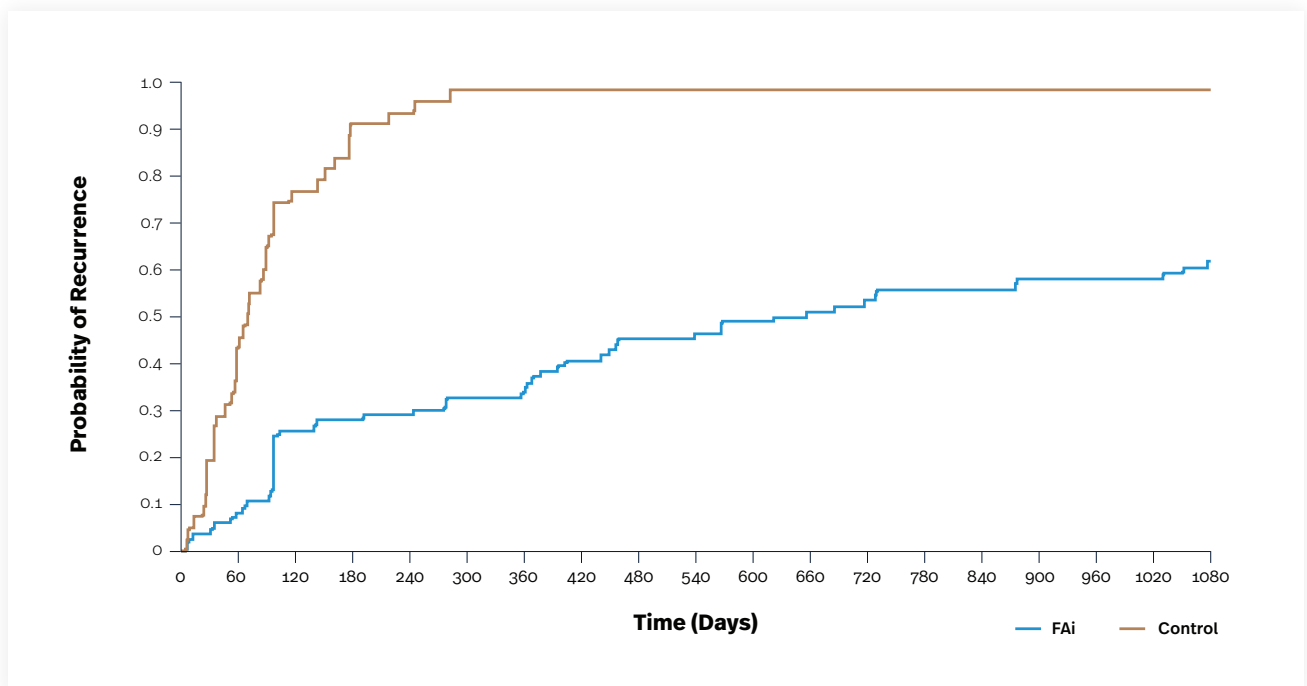
TOPICAL ADMINISTRATION

Topical corticosteroid drops are first-line agents for addressing inflammation for most cases of acute anterior uveitis.¹⁵ However, this route of administration limits use to only milder cases of ME associated with anterior uveitis.¹⁵ While topical corticosteroids can be useful in milder, anterior cases of uveitis, they do carry a risk for steroid-related AEs, such as cataracts and elevated IOP.³⁶

PERIOcular ADMINISTRATION

Periocular corticosteroids can be delivered via many routes, including sub-Tenon, subconjunctival, orbital floor, trans-septal, and retrobulbar injections. All of these approaches have been demonstrated to be effective in clinical studies.³⁶ Periocular or posterior sub-Tenon triamcinolone acetonide has demonstrated efficacy for the management of ME, vitritis, retinal vasculitis, and chorioretinitis in cases of NIU.³⁷ It is typically administered at a dose of 40 mg/mL, which remains effective for about 3 months. Inflammation resolution and visual acuity (VA) improvement to $\geq 20/40$ with this treatment were seen more often in anterior uveitis than in intermediate or posterior/panuveitis. As with other corticosteroids, major ocular complications with periocular steroid delivery include cataract formation or progression and elevated IOP.³⁷

Figure 5. Probability of uveitis recurrence by days from treatment in patients treated with IVT injection of the 0.18-mg FAi or sham control.⁴² FAi, fluocinolone acetonide implant; IVT, intravitreal.



INTRAVITREAL ADMINISTRATION

Intravitreal (IVT) corticosteroid administration is also effective for the treatment of ME associated with NIU, particularly in patients with unilateral involvement.³⁶ Results from the Multicenter Uveitis Steroid Treatment (MUST) research group showed that IVT corticosteroid injections were more effective than periocular injections in the treatment of ME secondary to uveitis.³⁸

In addition to IVT administration of a corticosteroid itself, IVT corticosteroid implants can provide consistent, long-term inflammation control. A 0.7-mg dexamethasone IVT implant is approved for the treatment of NIU involving the posterior segment of the eye.³⁹ In the 26-week Intravitreal Dexamethasone Implant (HURON) clinical trial, 229 eyes with noninfectious intermediate or posterior uveitis received a single treatment with the 0.7-mg dexamethasone implant (n=77), a 0.35-mg dexamethasone implant (n=76), or a sham procedure (n=76).⁴⁰ At 6 months, eyes treated with the single IVT dexamethasone implant demonstrated significantly decreased intraocular inflammation (eg, vitreous haze) and improved VA, an outcome achieved by 47% of eyes with the 0.7-mg dexamethasone implant and 36% with the 0.35-mg implant vs 12% with the sham implantation procedure ($P < 0.001$). Regarding the safety of IVT dexamethasone implants, the incidence of elevated IOP and cataract formation did not differ significantly from that of the placebo group.⁴⁰

Another US Food and Drug Administration (FDA)-approved corticosteroid IVT implant is the 0.18-mg fluocinolone acetonide implant (FAi) for the management of noninfectious intermediate, posterior, and panuveitis. The FAi delivers a low daily corticosteroid dose for 3 years and can be injected in an office-based procedure.³⁹ In a 3-year prospective, randomized, sham injection-controlled clinical trial of patients with NIU, eyes injected with 0.18-mg FAi had a significantly reduced probability of uveitis occurrence vs sham treatment at all time points analyzed (6, 12, and 36 months; **Figure 5**).^{41,42}

Additionally, patients in the FAI-treated group had a decreased need for adjunctive therapies for uveitis, such as systemic corticosteroids or immunosuppressants. While the FAI-treated group had higher rates of cataract, the rate of use of IOP-lowering medications during the study was similar to that of the sham treatment group.

IVT corticosteroids also provide anatomical benefit. In a study comparing CST in patients with UME randomized to receive IVT triamcinolone acetonide, the IVT dexamethasone implant, or periocular triamcinolone, all treatment groups demonstrated improved CST at 8 weeks, with the IVT triamcinolone acetonide and dexamethasone implant providing significantly superior CST reductions vs periocular triamcinolone.³⁸

Beyond injectable IVT corticosteroid implants, a surgically implanted, 0.59-mg fluocinolone acetonide IVT implant is also FDA-approved for the treatment of NIU.³⁹ The 0.59-mg fluocinolone acetonide IVT implant is secured at pars plana through an incision with a 20-gauge needle and then steadily releases the drug over 3 years: 0.6 µg/day initially for 1 month, then a steady rate between 0.3 and 0.4 µg/day.³⁹ The MUST trial showed that, through 54 months, visual outcomes for the 0.59-mg fluocinolone acetonide

implant were similarly favorable to systemic corticosteroid treatment for intermediate uveitis, posterior uveitis, and panuveitis with regard to improved BCVA, reduced intraocular inflammation, and control of ME.^{39,43} In a 7-year, follow-up study of MUST trial participants, 94% of eyes treated with the 0.59-mg fluocinolone acetonide implant showed resolved ME.⁴⁴

SUPRACHOROIDDAL ADMINISTRATION

The suprachoroidal space (SCS) is located between the sclera and the choroid that traverses the circumference of the posterior segment of the eye (**Figure 6**).⁴⁵ Injection into the SCS is a more recent mode of corticosteroid delivery in the treatment of uveitis,⁴⁵ and the procedure is minimally invasive.^{46,47} The SCS can accommodate up to 1 mL of fluid and may enable bypassing the sclera without the risk of intraocular penetration.⁴⁸ Preclinical data indicate that injection into the SCS results in a more posterior distribution of drug vs IVT administration, with higher exposures to the sclera, choroid, retinal pigment epithelium (RPE) cells, and retina, as well as lower exposure to off-target anterior segment tissues (**Figure 7**).^{46,49}

Figure 6. The suprachoroidal space.⁵⁰

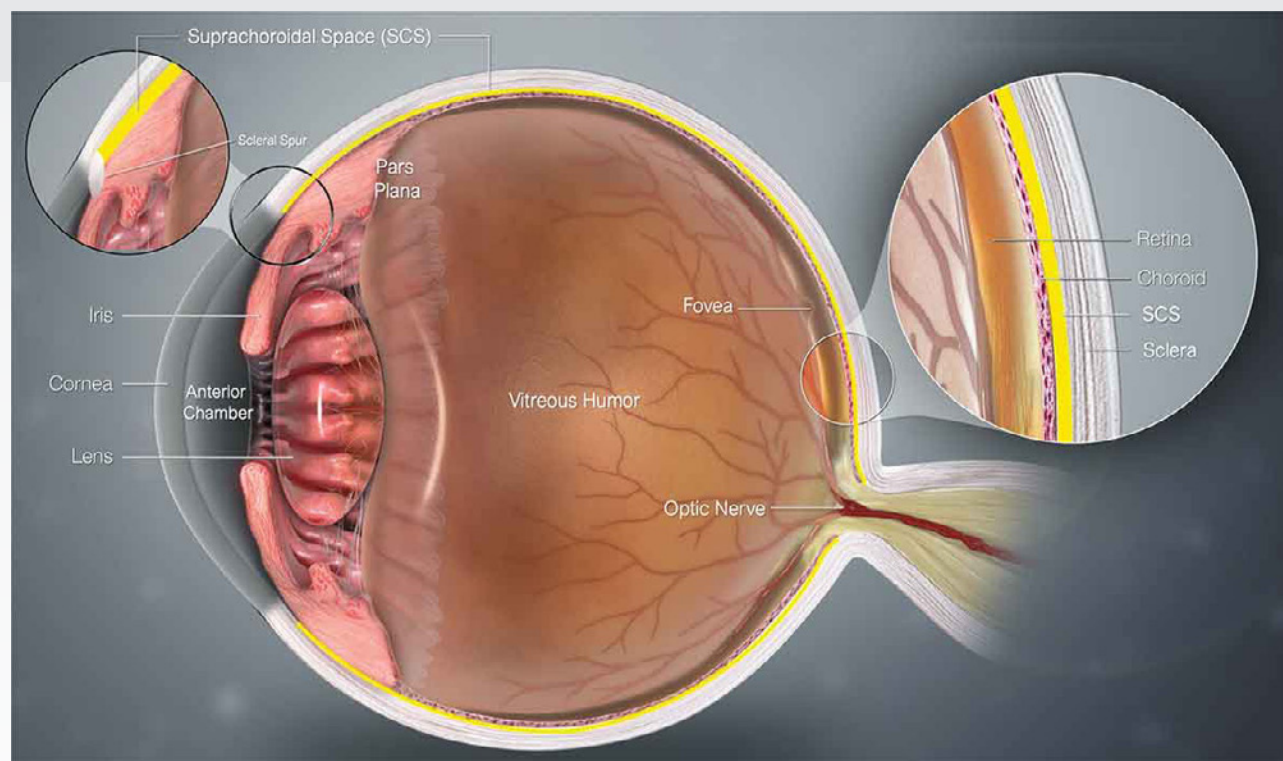
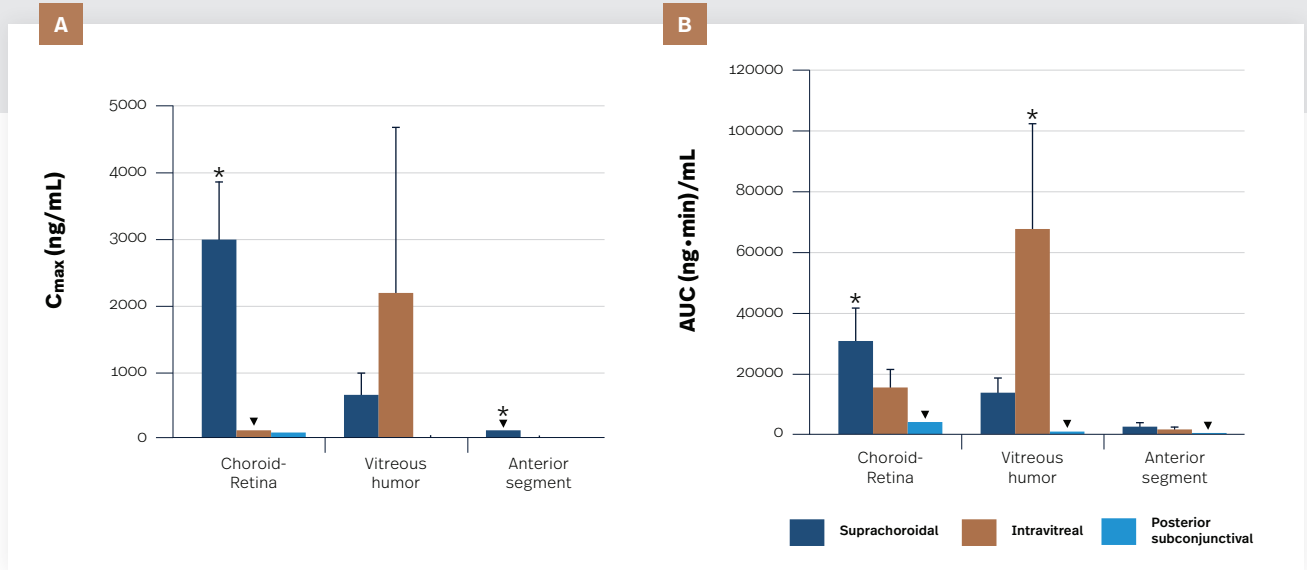


Figure 7. Pharmacokinetic parameters over 360 minutes following suprachoroidal, IVT, or posterior conjunctival injection of sodium fluorescein in Sprague Dawley rats.⁴⁹ **A)** Maximum concentration of sodium fluorescein by injection type across ocular tissues. **B)** AUC for sodium fluorescein concentration over 360 minutes by injection type across ocular tissues. * $P < 0.05$ vs the other two groups. AUC, area under the concentration-vs-time curve; C_{max} , maximum concentration; IVT, intravitreal.



Clinical trials have demonstrated both the efficacy and safety of SCS injection of triamcinolone acetonide (SCS-TA) for the treatment of ME secondary to NIU (Figure 8),⁵¹⁻⁵⁴ diabetic ME, post pars plana vitrectomy,⁵⁵ and ME secondary to retinal vein occlusion.⁵⁶ In a phase 2 study of the safety and efficacy of a single suprachoroidally injected triamcinolone acetonide formulation (CLS-TA; 4.0 or 0.8 mg) in 22 patients with NIU and ME, both BCVA and CST measures improved significantly at months 1 and 2, and there were no corticosteroid-related IOP increases.⁵⁴ These results were confirmed in phase 3 data in 160 patients with ME secondary to NIU who received either CLS-TA or suprachoroidal sham treatment at baseline and week 12.⁵³ Over 24 weeks, 47% of patients receiving CLS-TA gained ≥ 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters vs 16% in the control arm ($P < 0.001$) and had a $153\text{-}\mu\text{m}$ CST reduction from baseline vs an $18\text{-}\mu\text{m}$ reduction in the control arm ($P < 0.001$) (Figure 8).⁵³

When followed out to 48 weeks, patients with uveitic ME from the phase 3 trial who were treated with CLS-TA or sham at baseline and week 12 had a median time to rescue for uveitis of 257 days in the CLS-TA arm vs 55.5 days in the sham arm.⁵² Furthermore, 50% of patients in the CLS-TA arm did not require rescue therapy until 9 months after the last treatment.

To assess safety of CLS-TA, an open-label, prospective multicenter study evaluated 38 patients with NIU, with and without ME, who received 2 injections of CLS-TA (4 mg) 12 weeks apart.⁵¹ Through 24 weeks, there were no serious ocular AEs, and the most commonly reported AEs included cataract formation, IOP elevation >10 mmHg vs baseline, and IOP elevation >30 mmHg vs baseline, though overall, IOP remained stable throughout the study.

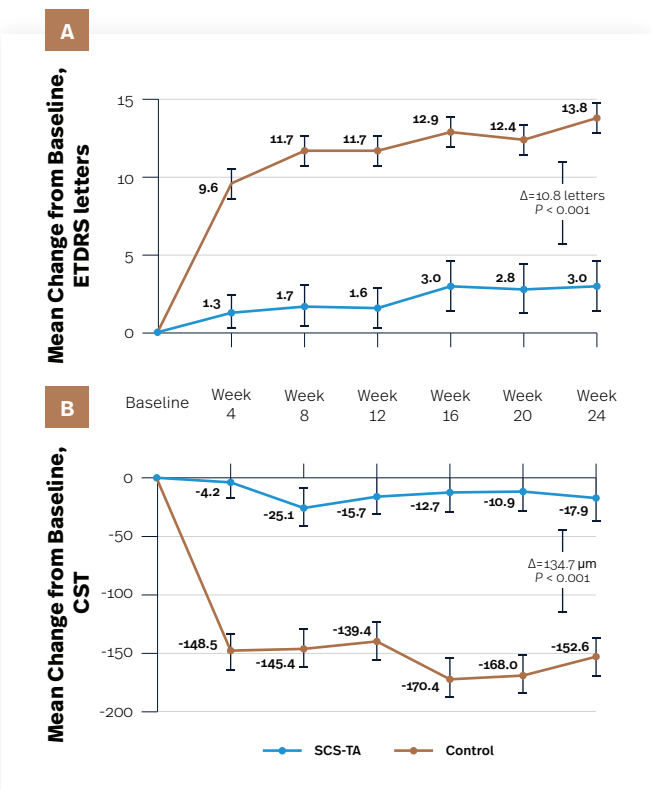


Figure 8. Efficacy of SCS-TA for ME secondary to NIU in the PEACHTREE trial: changes in BCVA (A) and CST (B) over 24 weeks.⁵³ BCVA, best corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment of Diabetic Retinopathy Study; ME, macular edema; NIU, noninfectious uveitis; SCS-TA, suprachoroidal space injection of triamcinolone acetonide.

NON-STEROID IMMUNOMODULATORS/ IMMUNOSUPPRESSANTS

Because of their known side effect profile, steps should be taken to limit steroid exposure. To reduce overall steroid exposure, patients can transition from systemic steroids to steroid-sparing immunomodulating therapy for long-term use.

A number of anti-inflammatory agents are emerging for use in NIU (**Table 2**), and once on an immunomodulator, steroid use can be reduced to only local administration;³⁴ in fact, concurrent anti-inflammatory and local corticosteroid therapy may even speed UME resolution.⁵⁷

Table 2. Emerging anti-inflammatory therapies for NIU.⁵⁸

| Drug | Target | Structure | Dosage and Route of Administration | Uveitis Type |
|--------------|---------------|---------------------------|---|---|
| Adalimumab | TNF- α | mAb, fully humanized | LD: 80 mg SC MD: 40 mg SC every other week | Noninfectious non-anterior uveitis |
| Infliximab | TNF- α | mAb, mouse-human chimeric | LD: 5 mg/kg IV at weeks 0, 4, and 6 MD: 5 mg/kg IV every 4 to 8 weeks Max. dose: 10 mg/kg IV for adults, 20 mg/kg IV for children every 4 weeks | JIA-related uveitis, Behçet, VKH, sarcoidosis, pars planitis, birdshot retinocho-roidopathy, idiopathic uveitis |
| Golimumab | TNF- α | mAb, fully humanized | MD: 50 mg SC monthly Max. dose: 100 mg SC monthly | Refractory uveitis |
| Certolizumab | TNF- α | mAb, fully humanized | 200 mg SC every 2 weeks | Refractory uveitis |
| Tocilizumab | IL-6 | mAb, fully humanized | 4 to 12 mg/kg IV every 2-4 weeks | Non-infectious non-anterior uveitis, Behçet, birdshot, JIA-related uveitis |
| Rituximab | CD-20 | mAb, mouse-human chimeric | LD: 500 mg or 1000 mg IV at 0 and 2 weeks MD: Repeat at 6-12 months if needed | Refractory uveitis, JIA-related uveitis, Behçet, VKH, Wegener's granulomatosis |

CD, cluster of differentiation; IL, interleukin; IV, intravenously; JIA, juvenile idiopathic arthritis; LD, loading dose; mAb, monoclonal antibody; Max, maximum; MD, maintenance dose; NIU, noninfectious uveitis; SC, subcutaneously; TNF- α , tumor necrosis factor α ; VKH, Vogt-Koyanagi-Harada disease.

Conclusions

ME—the accumulation of intra- or subretinal fluid in the macular region—is a frequent and sight-threatening complication of NIU. Ocular imaging is crucial for proper diagnosis and monitoring of uveitis, and multimodal imaging with a variety of tools (eg, advanced options for OCT, UWFA) has significantly improved initial characterization of disease and monitoring of both inflammation and alterations in the structure of the retina and associated tissues.

Treatment in patients with uveitic ME is focused on gaining durable control over inflammation and preserving vision while minimizing both local and systemic AEs/complications. Novel targeted approaches for delivery of corticosteroids to the eye have emerged, and the number of nonsteroidal, targeted anti-inflammatory biologics that can be employed as alternatives to systemic corticosteroid delivery have grown. These have the potential to improve both efficacy and safety for patients who require long-term anti-inflammatory therapy that is both potent and well-tolerated to control their disease.

REFERENCES

- Joltikov KA, Lobo-Chan AM. Epidemiology and risk factors in non-infectious uveitis: a systematic review. *Front Med (Lausanne)*. 2021;8:695904.
- Okada AA, Palestine AG, Kramer M, Jabs DA, Standardization Of Uveitis Nomenclature Sun Working G. Reply to comment on: classification criteria for Behcet disease uveitis. *Am J Ophthalmol*. 2022;235:339-340.
- Rosenbaum JT, Dick AD. The eyes have it: a rheumatologist's view of uveitis. *Arthritis Rheumatol*. 2018;70(10):1533-1543.
- Merida S, Palacios E, Navea A, Bosch-Morell F. New immunosuppressive therapies in uveitis treatment. *Int J Mol Sci*. 2015;16(8):18778-18795.
- Massa H, Pipis SY, Adewoyin T, Vergados A, Patra S, Panos GD. Macular edema associated with non-infectious uveitis: pathophysiology, etiology, prevalence, impact and management challenges. *Clin Ophthalmol*. 2019;13:1761-1777.
- Murray PI, Rauz S. The eye and inflammatory rheumatic diseases: The eye and rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis. *Best Pract Res Clin Rheumatol*. 2016;30(5):802-825.
- Agarwal M, Dutta Majumder P, Babu K, et al. Drug-induced uveitis: a review. *Indian J Ophthalmol*. 2020;68(9):1799-1807.
- Yeh S, Shantha JG. The burden of noninfectious uveitis of the posterior segment: a review. *Retina Today*. 2016;July/August:47-51.
- Kumar A, Miller DC, Sun Y, Arnold BF, Acharya NR. Risk of noninfectious uveitis after coronavirus disease 2019 vaccination in a United States claims database. *Ophthalmology*. 2023;130(12):1269-1278.
- Bodaghi B, Cassoux N, Wechsler B, et al. Chronic severe uveitis: etiology and visual outcome in 927 patients from a single center. *Medicine (Baltimore)*. 2001;80(4):263-270.
- de Smet MD, Taylor SR, Bodaghi B, et al. Understanding uveitis: the impact of research on visual outcomes. *Prog Retin Eye Res*. 2011;30(6):452-470.
- Gonzalez MM, Solano MM, Porco TC, et al. Epidemiology of uveitis in a US population-based study. *J Ophthalmic Inflamm Infect*. 2018;8(1):6.
- Thorne JE, Suhler E, Skup M, et al. Prevalence of noninfectious uveitis in the United States: a claims-based analysis. *JAMA Ophthalmol*. 2016;134(11):1237-1245.
- Dick AD, Tundia N, Sorg R, et al. Risk of ocular complications in patients with noninfectious intermediate uveitis, posterior uveitis, or panuveitis. *Ophthalmology*. 2016;123(3):655-662.
- Teper SJ. Update on the management of uveitic macular edema. *J Clin Med*. 2021;10(18):4133.
- Fardeau C, Champion E, Massamba N, LeHoang P. Uveitic macular edema. *Eye (Lond)*. 2016;30(10):1277-1292.
- Agarwal A, Pichi F, Invernizzi A, Gupta V. Disease of the year: differential diagnosis of uveitic macular edema. *Ocul Immunol Inflamm*. 2019;27(1):72-88.
- Sood G, Patel BC. Uveitic macular edema. *StatPearls*. 2024.
- Bringmann A, Wiedemann P. Muller glial cells in retinal disease. *Ophthalmologica*. 2012;227(1):1-19.
- Otani T, Yamaguchi Y, Kishi S. Serous macular detachment secondary to distant retinal vascular disorders. *Retina*. 2004;24(5):758-762.
- Mechanisms of macular edema and therapeutic approaches. Accessed February 6, 2024. <https://entokey.com/mechanisms-of-macular-edema-and-therapeutic-approaches-2/>
- Kempen JH, Altaweel MM, Holbrook JT, et al. Randomized comparison of systemic anti-inflammatory therapy versus fluocinolone acetonide implant for intermediate, posterior, and panuveitis: the multicenter uveitis steroid treatment trial. *Ophthalmology*. 2011;118(10):1916-1926.
- Naik RK, Rentz AM, Foster CS, et al. Normative comparison of patient-reported outcomes in patients with noninfectious uveitis. *JAMA Ophthalmol*. Feb 2013;131(2):219-25.
- Feldman BH, Garg PG, Shah VA, et al. Cystoid macular edema. American Academy of Ophthalmology. 2024. https://eyewiki.aao.org/Cystoid_Macular_Edema
- Srivastava S. Ultra-widefield imaging in the management of uveitis. *Retina Today*. 2017;October:48-52.
- Khochtali S, Krifa H, Zina S, et al. Multimodal imaging of acute foveolitis following COVID-19 vaccination. *Ocul Immunol Inflamm*. 2022;30(5):1214-1217.
- Ciulla TA, Kapik B, Barakat MR, et al. Optical coherence tomography anatomic and temporal biomarkers in uveitic macular edema. *Am J Ophthalmol*. 2022;237:310-324.
- Liu Z, Tao QQ, Li XR, Zhang XM. Disorganization of the retinal inner layers as a predictor of visual acuity in eyes with macular edema secondary to uveitis. *Int J Ophthalmol*. 2021;14(5):725-731.
- Munk MR. Ocular imaging in uveitis. Presented at American Academy of Ophthalmology Uveitis Subspecialty Day; September 30, 2022; Chicago, IL.
- Marchese A, Cicinelli MV, Amato A, et al. The next steps in ocular imaging in uveitis. *Ocul Immunol Inflamm*. 2023;31(4):785-792.
- Witmer MT, Kiss S. The clinical utility of ultra-wide-field imaging. *Rev Ophthalmol*. 2012. <https://www.reviewofophthalmology.com/article/the-clinical-utility-of-ultra-wide-field-imaging>
- Shukla UV, Tripathy K. Diabetic retinopathy. *StatPearls*. 2024.
- Chi Y, Guo C, Peng Y, Qiao L, Yang L. A prospective, observational study on the application of ultra-wide-field angiography in the evaluation and management of patients with anterior uveitis. *PLoS One*. 2015;10(3):e0122749.
- Valdes LM, Sobrin L. Uveitis therapy: the corticosteroid options. *Drugs*. 2020;80(8):765-773.
- Emami-Naeini P. Treating uveitic macular edema: a review of local and systemic treatments for UME and insights on when to use them. 2024. <https://www.retina-specialist.com/article/treating-uveitic-macular-edema>
- Koronis S, Stavrakas P, Balidis M, Kozeis N, Tranos PG. Update in treatment of uveitic macular edema. *Drug Des Devel Ther*. 2019;13:667-680.
- Li B, Li H, Zhang L, Zheng Y. Efficacy and safety of adalimumab in noninfectious uveitis: a systematic review and meta-analysis of randomized controlled trials. *Front Pharmacol*. 2021;12:673984.
- Thorne JE, Sugar EA, Holbrook JT, et al. Periocular triamcinolone vs. intravitreal triamcinolone vs. intravitreal dexamethasone implant for the treatment of uveitic macular edema: the periocular vs. intravitreal corticosteroids for uveitic macular edema (POINT) trial. *Ophthalmology*. 2019;126(2):283-295.
- Li YH, Hsu SL, Sheu SJ. A review of local therapy for the management of cystoid macular edema in uveitis. *Asia Pac J Ophthalmol (Phila)*. 2021;10(1):87-92.
- Lowder C, Belfort R, Jr., Lightman S, et al. Dexamethasone intravitreal implant for noninfectious intermediate or posterior uveitis. *Arch Ophthalmol*. 2011;129(5):545-553.
- Jaffe GJ, Foster CS, Pavesio CE, Paggiarino DA, Riedel GE. Effect of an injectable fluocinolone acetonide insert on recurrence rates in chronic noninfectious uveitis affecting the posterior segment: twelve-month results. *Ophthalmology*. 2019;126(4):601-610.
- Jaffe GJ, Pavesio CE, Study Investigators. Effect of a fluocinolone acetonide insert on recurrence rates in noninfectious intermediate, posterior, or panuveitis: three-year results. *Ophthalmology*. 2020;127(10):1395-1404.
- Multicenter Uveitis Steroid Treatment Trial Research Group, Kempen JH, Altaweel MM, et al. Benefits of systemic anti-inflammatory therapy versus fluocinolone acetonide intraocular implant for intermediate uveitis, posterior uveitis, and panuveitis: fifty-four-month results of the Multicenter Uveitis Steroid Treatment (MUST) Trial and Follow-up Study. *Ophthalmology*. Oct 2015;122(10):1967-75. doi:10.1016/j.ophtha.2015.06.042
- Tomkins-Netzer O, Lightman SL, Burke AE, et al. Seven-year outcomes of uveitic macular edema: the multicenter uveitis steroid treatment trial and follow-up study results. *Ophthalmology*. 2021;128(5):719-728.
- Chiang B, Jung JH, Prausnitz MR. The suprachoroidal space as a route of administration to the posterior segment of the eye. *Adv Drug Deliv Rev*. 2018;126:58-66.
- Habot-Wilner Z, Noronha G, Wykoff CC. Suprachoroidally injected pharmacological agents for the treatment of chorio-retinal diseases: a targeted approach. *Acta Ophthalmol*. 2019;97(5):460-472.
- Naftali Ben Haim L, Moisseiev E. Drug delivery via the suprachoroidal space for the treatment of retinal diseases. *Pharmaceutics*. 2021;13(7):967.
- Moisseiev E, Loewenstein A, Yiu G. The suprachoroidal space: from potential space to a space with potential. *Clin Ophthalmol*. 2016;10:173-178.
- Tyagi P, Kadam RS, Kompella UB. Comparison of suprachoroidal drug delivery with subconjunctival and intravitreal routes using noninvasive fluorophotometry. *PLoS One*. 2012;7(10):e48188.
- Hancock SE, Wan CR, Fisher NE, Andino RV, Ciulla TA. Biomechanics of suprachoroidal drug delivery: From benchtop to clinical investigation in ocular therapies. *Expert Opin Drug Deliv*. 2021;18(6):777-788.
- Henry CR, Shah M, Barakat MR, et al. Suprachoroidal CLS-TA for non-infectious uveitis: an open-label, safety trial (AZALEA). *Br J Ophthalmol*. 2022;106(6):802-806.
- Khurana RN, Merrill P, Yeh S, et al. Extension study of the safety and efficacy of CLS-TA for treatment of macular oedema associated with non-infectious uveitis (MAGNOLIA). *Br J Ophthalmol*. 2022;106(8):1139-1144.
- Yeh S, Khurana RN, Shah M, et al. Efficacy and safety of suprachoroidal CLS-TA for macular edema secondary to noninfectious uveitis: phase 3 randomized trial. *Ophthalmology*. 2020;127(7):948-955.
- Yeh S, Kurup SK, Wang RC, et al. Suprachoroidal injection of triamcinolone acetonide, CLS-TA for macular edema due to noninfectious uveitis: a randomized, phase 2 study (DOGWOOD). *Retina*. 2019;39(10):1880-1888.
- Marashi A, Zazo A. Suprachoroidal injection of triamcinolone acetonide using a custom-made needle to treat diabetic macular edema post pars plana vitrectomy: a case series. *J Int Med Res*. 2022;50(4):3000605221089807.
- Willoughby AS, Vuong VS, Cunefare D, et al. Choroidal changes after suprachoroidal injection of triamcinolone acetonide in eyes with macular edema secondary to retinal vein occlusion. *Am J Ophthalmol*. 2018;186:144-151.
- Lin D, Hu J, Wu K, et al. Synergistic effect of combined sub-tenon triamcinolone and intravitreal anti-VEGF therapy for uveitic macular edema. *Drug Des Devel Ther*. 2022;16:1055-1066.
- Busto-Iglesias M, Rodriguez-Martinez L, Rodriguez-Fernandez CA, et al. Perspectives of therapeutic drug monitoring of biological agents in non-infectious uveitis treatment: a review. *Pharmaceutics*. 2023;15(3):766.

Continuing Medical Education Post Assessment

- Risk factors for noninfectious uveitis (NIU) include:**
 - Diabetes
 - Autoimmune disease
 - Prior ocular surgery
 - All of the above
- The most sight-threatening complication of NIU is:**
 - Increased intraocular pressure (IOP)
 - Geographic atrophy
 - Macular edema (ME)
 - Ischemic optic neuropathy
- In the MUST trial, the presence of macular edema (ME) in patients with NIU strongly predicted:**
 - Poor visual outcomes
 - Cataract
 - Vitreous haze
 - Anterior cell flare
- Optical coherence tomography (OCT) is the gold standard in evaluating and monitoring uveitic ME because it:**
 - Is invasive
 - Can accurately measure macular thickness
 - Visualizes fluid accumulation
 - B and C
- When treating patients with systemic corticosteroids for uveitic ME, what is the maximum recommended maintenance dose of prednisone to minimize serious and long-term adverse effects?**
 - ≤5 mg per day
 - ≤7.5 mg per day
 - ≤10 mg per day
 - ≤12 mg per day
- True or false: In the POINT trial, the use of intravitreal (IVT) triamcinolone and the IVT dexamethasone implant in patients with UME resulted in greater reductions in central subfield thickness (CST) than did periocular triamcinolone.**
 - True
 - False
- Which of the following are advantages of drug delivery to the suprachoroidal space (SCS)?**
 - Suspension formulations with high solubility exhibit sustained pharmacodynamics
 - Injected fluids spread circumferentially and posteriorly between the sclera and choroid around the globe
 - Compartmentalizes drug therapies away from the vitreous and anterior segment to enhance safety
 - B and C
- Patients with ME secondary to NIU who received suprachoroidal triamcinolone acetonide injection experienced which of the following benefits?**
 - Reduced CST
 - Decreased visual haze
 - Improved best corrected visual acuity (BCVA)
 - A and C
- Which of the following are true about suprachoroidal corticosteroid delivery?**
 - The sclera has minimal resistance during suprachoroidal injections
 - As the plunger of the microneedle is depressed gently, there should be an increase of resistance as the needle enters the SCS
 - Medication should be administered with a very steady, slow, deliberate pace over about 5 seconds, because patients may feel pressure due to the expansion of the SCS
 - Patient selection and preparation are not important considerations for suprachoroidal steroid injection
- In a recent study evaluating sub-Tenon triamcinolone acetonide (STA) injection combination with IVT anti-vascular endothelial growth factor (VEGF) versus STA injection alone for uveitic ME, the addition of anti-VEGF therapy was found to:**
 - Decrease the incidence of ME resolution
 - Speed the resolution of ME compared to STA monotherapy
 - Increase side effects and worsen ME
 - Significantly decrease IOP