

KEY POINTS:

- *We discovered a novel ocular glymphatic system*, which selectively transports solutes and fluids from the retina, along axons, across the lamina cribrosa, to the lymphatic system.
- *The pressure gradient between the eyes and the brain is key* to this transport and clearance is stimulated by pupil movement.
- *Damage caused by glaucoma can impact this system*, potentially preventing proper clearance of neurotoxic solutes.

REFERENCES

1. Agre P, Preston GM, Smith BL, Jung JS, Raina S, Moon C, Guggino WB, Nielsen S. Aquaporin CHIP: the archetypal molecular water channel. *Am J Physiol*. 1993 Oct;265(4 Pt 2):F463-76. doi: 10.1152/ajprenal.1993.265.4.F463. PMID: 7694481.
2. A. S. Thrane, V. Rangroo Thrane, M. Nedergaard, Drowning stars: reassessing the role of astrocytes in brain edema. *Trends in neurosciences* 37, 620-628 (2014).
3. M. Amiry-Moghaddam, O. P. Ottersen, The molecular basis of water transport in the brain. *Nature reviews. Neuroscience* 4, 991-1001 (2003).
4. J. J. Iliff et al., A paravascular pathway facilitates CSF flow through the brain parenchyma and the clearance of interstitial solutes, including amyloid beta. *Science translational medicine* 4, 147ra111 (2012).
5. L. Xie et al., Sleep drives metabolite clearance from the adult brain. *Science (New York, N.Y.)* 342, 373-377 (2013).
6. Jessen NA, Munk AS, Lundgaard I, Nedergaard M. The Glymphatic System: A Beginner's Guide. *Neurochem Res*. 2015;40(12):2583-2599. doi:10.1007/s11064-015-1581-6
7. A. Louveau et al., Structural and functional features of central nervous system lymphatic vessels. *Nature* 523, 337-341 (2015).
8. A. Alm, S. F. Nilsson, Uveoscleral outflow--a review. *Exp Eye Res* 88, 760-768 (2009).
9. A. S. Huang, A. Camp, B. Y. Xu, R. C. Pentead, R. N. Weinreb, Aqueous Angiography: Aqueous Humor Outflow Imaging in Live Human Subjects. *Ophthalmology* 124, 1249-1251 (2017).
10. Y. H. Yucel et al., Identification of lymphatics in the ciliary body of the human eye: a novel "uveolymphatic" outflow pathway. *Exp Eye Res* 89, 810-819 (2009).
11. E. Mathieu et al., Evidence for Cerebrospinal Fluid Entry Into the Optic Nerve via a Glymphatic Pathway. *Invest Ophthalmol Vis Sci* 58, 4784-4791 (2017).
12. X. Wang et al., An ocular glymphatic clearance system removes beta-amyloid from the rodent eye. *Science translational medicine* 12 (2020).
13. C. Pan et al., Shrinkage-mediated imaging of entire organs and organisms using uDISCO. *Nat Methods* 13, 859-867 (2016).
14. M. D. Roberts et al., Remodeling of the connective tissue microarchitecture of the lamina cribrosa in early experimental glaucoma. *Invest Ophthalmol Vis Sci* 50, 681-690 (2009).
15. A. S. Verkman, J. Ruiz-Ederra, M. H. Levin, Functions of aquaporins in the eye. *Progress in retinal and eye research* 27, 420-433 (2008).
16. E. A. Nagelhus et al., Aquaporin-4 water channel protein in the rat retina and optic nerve: polarized expression in Muller cells and fibrous astrocytes. *The Journal of neuroscience : the official journal of the Society for Neuroscience* 18, 2506-2519 (1998).
17. T. M. Mathiisen, K. P. Lehre, N. C. Danbolt, O. P. Ottersen, The perivascular astroglial sheath provides a complete covering of the brain microvessels: an electron microscopic 3D reconstruction. *Glia* 58, 1094-1103 (2010).
18. R. N. Weinreb, T. Aung, F. A. Medeiros, The pathophysiology and treatment of glaucoma: a review. *Jama* 311, 1901-1911 (2014).
19. L. Guo et al., Targeting amyloid-β in glaucoma treatment. *Proceedings of the National Academy of Sciences* 104, 13444-13449 (2007).
20. M. A. Meraz-Rios, D. Toral-Rios, D. Franco-Bocanegra, J. Villeda-Hernández, V. Campos-Peña, Inflammatory process in Alzheimer's Disease. *Front Integr Neurosci* 7, 59-59 (2013).

News from the European Glaucoma Society Guidelines 2020 – How, why, & what to avoid?



Miriam Kolko

John Thygesen

Miriam Kolko¹ and John Thygesen²

¹ Department of Drug Design And Pharmacology, University of Copenhagen, Departments of Ophthalmology, Copenhagen University Hospital, Rigshospitalet-Glostrup, Copenhagen, Denmark

² Assoc. professor emer, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark, Director Copenhagen Eye & Glaucoma Clinic, Kgs. Lyngby, Member of the board of the European Glaucoma Society Foundation, Mentor of European Glaucoma Society (EGS) Education Committee, Chair of European Glaucoma Society (EGS) Angle-Closure SIG

EGS guidelines: History

In December 2020, the 5th edition of the European Glaucoma Society (EGS) Guidelines became available. Since the first edition of the EGS guidelines was published in 1998,

the EGS has been continuously working to update the evidence-based guidelines for dealing with the increasing number of glaucoma patients. The Danish Glaucoma Guidelines from 1997 greatly inspired the first edition,

especially regarding classification and terminology.

5th edition EGS guidelines: How?

For the 5th edition, the process began by identifying

EGS Guideline Recommendations:

- SLT can be offered as first choice treatment for early primary or moderate open angle glaucoma or OH
- Iridotomy in PAC suspects has a weak recommendation
- Iridotomy in PAC and PACG of patients below 50 years has a strong recommendation
- Iridotomy or lens extraction in PAC and PACG of patients above 50 years has a strong recommendation



Things to avoid*:

- IOP correction algorithms based on OCT
- Glaucoma diagnosis based on OCT alone
- Glaucoma progression based on OCT alone
- Replacement of gonioscopy with anterior chamber imaging

*EGS guidelines for the full list

Figure 1. Selected guidelines updates in the 5th edition. Abbreviations: EGS: European Glaucoma Society, SLT: Selective Laser Trabeculoplasty, PAC: Primary Angle Closure, PACG: Primary Angle Closure Glaucoma, IOP: Intraocular Pressure, OCT: Optical Coherence Tomography, OH: Ocular Hypertension

important clinical questions within treatments and diagnostic technologies (Figure 1). Following the identification of these critical questions, the best available evidence was identified and evaluated by invited experts. All evidence was then assessed according to the strength of evidence and the level of recommendation. Relevant evidence was collected in 2019 in cooperation with the US-Cochrane Eyes and Vision Group (CEV-US) by conducting an overview of systematic reviews of glaucoma interventions and diagnostic technologies. Unlike previous editions of the EGS guidelines, the 5th edition contains only references to high-quality systematic reviews, landmark glaucoma trials, and population-based studies. The reason for the stringent restriction is to avoid biased selection of publications.

A large group of international glaucoma experts, methodologists, and evidence-based experts from CEV-US, patient representatives and external reviewers from the Latin American Glaucoma Society, the American Glaucoma Society, and the World Glaucoma Association were involved in the completion of the EGS guidelines, 5th edition. From the Nordic countries, Anders Heijl, Gauti Jóhannesson,

Anja Tuulonen, Miriam Kolko and John Thygesen were invited by the guideline committee.

The mission statement of the EGS guidelines is to provide a guideline for “the best care for people with, or at risk of, glaucoma and to promote their well-being and quality of life within a sustainable health care system.” The guidelines are financed by an unrestricted grant from the EGS Foundation.

5th edition EGS guidelines: Why?

The purpose of the EGS Guidelines is to support ophthalmologists in the management of people with or at risk of glaucoma. The guidelines highlight that they should be considered as a guide rather than strict decision-making procedures! Decision-making should always be individualized according to patients' needs and circumstances, ideally guided by the best available documentation.

5th edition EGS guidelines: What's new?

The 5th edition is divided into two parts. Part one consists of the key questions and evidence-based recommendation. For all key questions the level of evidence is reported as very low, low, moderate, or high, and the strength of recommendation is

provided as “strong” or “weak.” If a recommendation is “strong,” it can be translated into that most patients should receive the intervention, whereas if a recommendation is “weak” the limited evidence of the intervention should be discussed with the patients and their values and preferences considered. In addition to the key questions, things to avoid are highlighted as a new feature in the 5th edition (Figure 1). Moreover, patients' major concerns are summarized, e.g., the importance of taking the anxiety of glaucoma patients into consideration and remembering the potential information gaps when consulting glaucoma patients. Finally, part one includes glaucoma epidemiology, landmark randomized clinical trials, and considerations of cost-effectiveness when managing glaucoma.

Part two consists of patient examination, classification, and terminology, as well as treatment options. Some examples of changes since the latest edition of EGS guidelines include phasing out the use of cup-disc ratio, the removal of the classification “normal tension glaucoma,” and introducing rho kinase inhibitors.

5th edition EGS guidelines: How to get them?

The 5th edition of the EGS guideline can be downloaded from the EGS website: www.eugs.org/eng/guidelines.asp. Hard copies will be available from some of the EGS congress sponsors.

Santen has given support to the authors Miriam Kolko and John Thygesen. No company has had influence on the content of the present article.

WWW.SANTEN.COM