

DYES IN OPHTHALMOLOGY: A REVIEW**Kavitha Vivek D., Pradnya Deolekar, Mayakalyani Srivathsan, Azra Naseem*, Sonal Signapurkar, Pramila Yadav**

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Corresponding Author*Azra Naseem**Junior Resident, Department
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Medicine, Navi Mumbai,
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Stains and dyes are very effective diagnostic and therapeutic tools in ophthalmology. Although non-invasive, diagnostic dyes are objectively used to directly visualize, identify and track microscopic ocular structures for anterior and posterior segment disorders. These are very useful, both for anterior and posterior segment disorders. Diagnosis and management of retinal vascular disorders have been revolutionised, ever since the introduction of fluorescein. The term staining is used to describe epithelial disruption and other pathophysiological changes which can be seen when we use the dyes topically. The dyes used topically are called vital stains. Vital dyes represent an expanding area of research, and novel dyes deserve further investigation.

KEYWORDS: Dyes, Ophthalmology, Dyes in Eye, Indications for dyes.**INTRODUCTION**

Eye is the most accessible and easily visualized organ in the human body; due to this feature ophthalmic dyes have a significant role in ophthalmology to aid effective diagnosis of ocular conditions. These dyes are extensively used for the differential diagnosis in various ocular pathological conditions such as corneal abrasions, congestion, micro aneurysm, blood vessel proliferations in retina and ischemia.

The use of diagnostic dyes represents one of the most efficient, objective, non-invasive, and directly visible means we have of identifying and tracking ocular structures at the cellular level. They particularly are useful as both diagnostic modalities and as therapeutic adjuvants in both anterior and posterior segment disorders.^[1]

HISTORY

All living tissues and cells take up colours of vital dyes which are thus, considered important surgical tools to visualise the ocular tissues. Hoffer and McFarland in 1993 used the biocompatible dye fluorescein to stain the anterior capsule for capsulorhexis in mature cataracts.^[2] Subsequently, the use of vital dyes in cataract surgery has been widely reported. The use of a vital dye during vitreoretinal (VR) surgery was first reported by Abrams et al. In 1978, as a very useful aid in identifying vitreous.^[3] Chromovitrectomy is widely used since the year 2000.

Trypan blue has been used to stain the anterior capsule blue to make the procedure of capsulorhexis easier.^[4] Laboratories conduct pre-clinical investigations with reliable methods to study the toxicity of the dyes and these studies include functional, histological and biochemical analysis. The anterior segment analysis includes cell culture, specular and confocal microscopy. Retinal cell culture, electrophysiological tests and angiographic studies are conducted for posterior segment analysis.^[5,6]

Pfluger first described and used sodium fluorescein, often referred to as fluorescein to stain cornea and conjunctiva in rabbits in the 1882.^[7] Henrik Sjögren introduced Rose Bengal (RB) in 1933. Till then, fluorescein was in fact the primary dye used to stain the conjunctiva.^[8] Mogens Norn introduced Lissamine Green (LG), a vital stain with properties almost identical to those of RB in 1973.^[9]

Various dyes used in ophthalmology are as follows:**1. TRYPTAN BLUE^[10,11,12]**

It is available as a 0.06% ophthalmic solution for anterior capsular staining, 0.15% for posterior capsular surgeries and 0.06% for enucleation surgery for Tenon's capsule. It stains the anterior lens capsule making it clearly identifiable during surgery. The dye is injected onto and spread over the anterior lens capsule under an air bubble.

Indications

- To stain the anterior capsule of the lens during cataract surgeries. This is specially useful in eyes

with a decreased red reflex or weak zonules, as the dye can immediately allow the surgeon to detect a radial shift of the capsular bag.

- To stain and strip the Descemet's membrane in Descemet's stripping endothelial keratoplasty (DSEK).
- Aid in stripping the corneal endothelium from the donor button in Deep anterior lamellar keratoplasty (DALK).
- To stain the Tenon's capsule after enucleation surgeries.
- For posterior segment surgeries, to stain the epiretinal membrane (ERM).
- Useful adjunct in vitreoretinal surgery and in cases of proliferative vitreoretinopathy.
- In oculoplastics surgery, an extraocular indication has been described for staining Tenon's capsule during enucleation surgery.

Side effects

Spikes in Intraocular pressure (IOP), discolor high water content in hydrogen intraocular lens implants, stain the posterior lens capsule and anterior face of the vitreous, decrease in lens capsule elasticity and, increase the risk of capsular tears.

2. ROSE BENGAL^[13,14,15]

Rose bengal is a pink stain derived as an analogue of fluorescein. Its disodium salt in ophthalmic solutions has been used as a diagnostic agent in suspected damage to conjunctival and corneal cells.

Indications

- Diagnostic agent in routine ocular examinations, when superficial conjunctiva or corneal tissue change is suspected, as an aid in the diagnosis of keratoconjunctivitis sicca, keratitis, dry eyes, abrasions or corruptions as well as the detection of foreign bodies.
- Diagnosis of Meibomian gland dysfunction.

Side effects

Stinging, burning sensation in the eye

3. INDOCYANINE GREEN (ICG)^[16,17,18]

The dye has a high affinity for collagen type IV (which is found in basement membrane) and laminin. Both of these are found in a high concentration in the internal limiting membrane (ILM) of the retina. Hence, the dye is the used for staining the ILM during vitreoretinal procedures.

Indications

- For staining the anterior capsule during cataract surgery.
- In chromovitrectomy, to visualise the ILM.
- In Indocyanine Green Angiography (ICGA), to visualise choroidal circulation, and help in the diagnosis of conditions like polypoidal choroidal

vasculopathy, choroidal neovascular membrane, age related macular degeneration (wet), and posterior uveitis

Side effects

- For use in anterior capsule staining in cataract surgery, the dye has to be reconstituted and diluted. This has to be followed by filtration before use to prevent undissolved particles from entering the eye.
- The property of decomposition is a major deterrent in using ICG in posterior segment surgeries, since it can cause retinal toxicity which is worsened on exposure to light.
- Can remain in the vitreous after surgery.
- Can seep through the macular hole during surgery, and cause RPE damage post-operatively.
- Can deposit permanently on the optic disc after surgery.
- Use in intraocular surgery is not approved by the FDA.

4. BRILLIANT BLUE [10,19]

Brilliant blue G; also known as Coomassie or acid blue is a disclosing agent used in ophthalmological surgery to stain the internal limiting membrane (ILM).

Indications

- Staining the ILM in posterior segment surgeries.

Side effects

- Retinal break
- Retinal tear
- Retinal hemorrhage
- Retinal detachment
- Development of cataract
- Atrophic changes have been reported in a very few cases of subretinal migration of the dye.

5. LISSAMINE GREEN^[20,21]

Lissamine green (LG) is also known as acid green S, wool green S or C and fast light green. LG is available in impregnated paper strips containing 1.5mg of the dye.

Indications

- Lissamine green (LG) is a vital stain which stains membrane degenerate cells, dead cells and mucus. It is replacing rose bengal (RB) as the premier dye for conjunctival staining.
- It is recommended that the dye be used in dry eye assessment, examination of prospective Contact Lens (CL) wearers (particularly with skin conditions), symptomatic CL wearers, further investigation of any patient with fluorescein staining and in refractive surgery preoperative assessments.

Side effects

Short term blurring, transient stinging, staining of eyelids in case of overspill, tearing following application.

6. FLUORESC EIN^[1,22,23]

Fluorescein is a diagnostic contrast agent particularly used in various ophthalmic procedures

Indications

- Applanation tonometry, gonioscopy, contact lens fittings to angiography or angiography of retina and iris vasculature.
- Fluorescein produces remarkable contrast to determine any corneal abrasions, epithelial keratitis, herpes simplex keratitis, or corneal foreign bodies.

Side effects

Paresthesia of lips, change in taste (orally), severe eye-stinging and irritation (ophthalmic), severe nausea, vomiting, abdominal pain, chest pain, and extravasation.

CONCLUSION

The use of vital stains, particularly fluorescein and lissamine green, is a must in ophthalmology. Fluorescein is to be used to stain the cornea and lissamine green to stain the conjunctiva, even in the asymptomatic patients. Some circumstances may warrant the use of RB, but lissamine green might be a better option. Various patterns of staining that may occur with common ocular surface disruptions should be familiarised and used to determine the aetiology and managed appropriately.

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REFERENCES

1. Kim J. The use of vital dyes in corneal disease. *Curr Opin Ophthalmol*, 2000; 11: 241-7.
2. Hoffer KJ, McFarland JE. Intracameral subcapsular fluorescein staining for improved visualization during capsulorhexis in mature cataracts. *J Cataract Refract Surg*, 1993; 19: 566.
3. Abrams GW, Topping T, Machermer R. An improved method for practice vitrectomy. *Arch Ophthalmol*, 1978; 96: 521-5.
4. Jacobs DS, Cox TA, Wagoner MD, Ariyasu RG, Karp CL, American Academy of Ophthalmology, et al. Capsule staining as an adjunct to cataract surgery: A report from the American Academy of Ophthalmology. *Ophthalmology*, 2006; 113: 707-13.
5. Mencucci R, Pellegrini-Giampietro DE, Paladini I, Favuzza E, Menchini U, Scartabelli T. Azithromycin: Assessment of intrinsic cytotoxic effects on corneal epithelial cell cultures. *Clin Ophthalmol*, 2013; 7: 965-71.
6. Januschowski K, Mueller S, Spitzer MS, Schramm C, Doycheva D, Bartz-Schmidt KU, et al. Evaluating retinal toxicity of a new heavy intraocular dye, using a model of perfused and isolated retinal cultures of bovine and human origin. *Graefes Arch Clin Exp Ophthalmol*, 2012; 250: 1013-22.
7. Wise RJ, Pflüger. For nutrition of the cornea. *Klin monthly Ophthalmology*, 1882; 20: 69-81.
8. Sjögren H, Kenntnis Z. The keratoconjunctivitis sicca [keratitis filiformis in hypofunction of the tear glands]. *Acta Ophthalmol*, 1933; 13: 40-5.
9. Norn MS. Lissamine green. Vital staining of cornea and conjunctiva. *Acta Ophthalmol (Copenh)*, 1973; 51: 483-91.
10. Atul Kumar, M B Thirumalesh. Use of dyes in ophthalmology. *Journal of Clinical Ophthalmology and research*, 2012; 1(1): 55-8.
11. Trypan Blue Dye: Capsular Staining for Cataract Surgery and More, American Academy of Ophthalmology, <https://www.aao.org/current-insight/trypan-blue-dye-capsular-staining-cataract-surgery>
12. Kumar Sanjiv. Effect of Class IV LASER on Bell's Palsy: A case series. *Journal of Clinical Ophthalmology and Research*, 2013; 1(1): 55-8.
13. Yokoi, Norihiko. "Vital staining for disorders of conjunctiva and lids". *Atarashii Ganka*, 2012; 29: 1599-1605.
14. Ervin AM, Wojciechowski R, Schein O. "Punctal occlusion for dry eye syndrome". *Cochrane Database Syst Rev.*, June 26, 2017; 9(6): CD006775. doi:10.1002/14651858.CD006775.pub3. PMC 5568656. PMID 28649802.
15. Dhaliwal RS, Dhaliwal KVS, Singh M, Kakkar A. Stains and dyes in Ophthalmology. *Glob J Cataract Surg Res Ophthalmol*, 2022; 1: 81-7.
16. Safe and Efficient ILM peeling, Retinal Physician, <https://www.retinalphysician.com/newsletter/surgica-l-maneuvers/january-2017>
17. The role of ICG in Macular Hole Surgery, Retinal Physician, <https://www.retinalphysician.com/supplements/2004/october-2004/advanced-vitreoretinal-techniques-technology/the-role-of-icg-in-macular-hole-surgery>
18. Khurana, A. K. "Ocular therapeutics". *Comprehensive ophthalmology*. Khurana, Aruj K., Khurana, Bhawna. (6th ed.). New Delhi: Jaypee, The Health Sciences Publisher, 2015; 460.
19. Brilliant blue G selectively stains the internal limiting membrane/brilliant blue G-assisted membrane peeling. *Retina*, 2006; 26(6): 631-6.
20. Abelson MB, Ousler GW, Nally LA, Emory TB. Dry eye syndromes: Diagnosis, clinical trials, and pharmaceutical treatment[†] improving clinical trials.[†] Lacrimal Gland, Tear Film, and Dry Eye Syndromes 3. In: Sullivan D, et al., editors. Kluwer Academic/Plenum Publishers, 2002; 1079-86.
21. Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. *Cornea*, 2003; 22: 640-50.
22. Dada VK, Sharma N, Sudan R, Sethi H, Dada T, Pangtey MS. Anterior capsule staining for capsulorhexis in cases of white cataract: Comparative clinical study. *J Cataract Refract Surg*, 2004; 30: 326-33.

23. Wilhelm F, Melzig M, Görscher T, Franke G. Differential value of various vital stains of corneal endothelium. *Ophthalmologie*, 1995; 92: 496-8.