Many surgeons make use of dyes and other agents to improve visualization of intraocular structures during vitreoretinal surgery. Substances currently employed for this purpose in the United States include the vital stains trypan blue and indocyanine green (ICG) and the corticosteroid triamcinolone acetonide. Outside the United States, brilliant blue G dye is also used for this purpose, but this dye has not yet received US regulatory approval. Other dyes are in the pipeline for potential use in ophthalmic surgery.

The biggest advantage to the use of any of the available agents is improved intraoperative visualization of membranes to facilitate peeling. We cannot peel what we cannot see. With a good stain the surgeon can identify the entire extent of the membrane in question and peel it more completely than might be possible without a visualization aid.

None of the currently available agents—trypan blue, ICG, or triamcinolone—is perfect; each has its limitations, and each has different preferred applications. This article reviews the current state of visualization aids available for use in vitreoretinal surgery and presents some of the pluses and minuses of each.

**INDOCYANINE GREEN**

ICG (IC-Green, Akorn) is a water-soluble tricarbocyanine dye that is indicated for use in ophthalmic angiography.1 It has been used off-label to stain the internal limiting membrane (ILM) for the past decade.2,3 The dye binds to plasma proteins, and therefore provides robust staining of the ILM. Early investigators2,3 reported that the dye greatly facilitated ILM peeling because it provided a stark contrast between the stained ILM and the unstained underlying retina. Subsequent in vitro work showed that long exposure of retinal pigment epithelium...
(RPE) cells to low concentrations of ICG produced toxicity, and clinical experience showed that ICG had a dose-dependent toxic effect on the retina.

Because of the possibility of toxicity to the RPE, many surgeons are reluctant to use ICG dye in macular hole surgery. That being said, however, in clinical practice the toxicity of ICG is idiosyncratic. When I have used ICG as a standard stain, toxicity occurred only rarely. Why it occurs in one patient and not another when all cases are executed in a similar way is unexplained. Perhaps this variability is related to genetic or other traits that have yet to be elucidated.

To minimize the toxic effect of ICG on the retina, it is recommended that the dye be injected in the lowest concentration possible, that repeated injections of ICG onto bare retina be avoided, that dye should be injected far from the macular hole to prevent exposure to the RPE, that surgery time should be kept as short as possible to minimize exposure, and that the light pipe be kept as far from the retina as possible to minimize phototoxicity.5 If these cautions are observed, ICG can be used in many cases without adverse sequelae.

**TRIAMCINOLONE ACETONIDE**

Triamcinolone is a synthetic glucocorticoid corticosteroid with a wide variety of applications in ophthalmology. There are two ophthalmic commercial preparations of triamcinolone (Trivaris injectable suspension 80 mg/mL, Allergan; Triesence injectable suspension 40 mg/mL, Alcon). Of the two, Trivaris is specifically labeled with an indication for visualization during vitrectomy; both products are labeled for intravitreal injection for treatment of uveitis and other ocular inflammatory conditions.6,7 Still, many ophthalmologists use Kenalog-40 (Bristol-Myers Squibb) injectable suspension, a formulation that has been used off label for a variety of ophthalmic applications for many years.9,10

Triamcinolone is not actually a stain or dye, but it functions in much the same manner. Diluted to provide a fine dusting on the macula, it improves intraoperative visualization. Its crystal particles settle on the surface of the membrane to be peeled, whether this is the ILM or the epiretinal membrane (ERM).9,10 As the membrane is peeled, the crystals embedded on its surface can be seen, so the surgeon knows what has been peeled and what remains.

Triamcinolone works well for staining both the ILM and ERM, and it is preferred for these purposes by many surgeons because it is associated with few toxicity issues, other than potential intraocular pressure (IOP) elevation in patients who are sensitive to steroids.

In these times of tightening budgets, there is also a cost factor that may favor triamcinolone—especially the off-label formulation—in surgery centers where there are fixed reimbursement rates per case. While no medical decision should be made solely on the basis of cost, these days we must be cognizant of expenditures, and there should be a clear benefit for use of a substance that costs more when a less expensive option is available.

I use some form of visualization aid in every case that involves ILM peeling. Currently, because of some recent cases in which I encountered toxicity with use of ICG, I tend to use triamcinolone to improve membrane visualization in ILM peeling.

**TRYPAN BLUE**

Trypan blue is a diazo dye whose commercial formulation (MembraneBlue; 0.15% trypan blue ophthalmic solution, Dutch Ophthalmic USA) is indicated for staining ERM during ophthalmic surgery.11 This commercial formulation is the only ophthalmic dye approved by the US Food and Drug Administration as an intraoperative visualization aid, according to the manufacturer.12

Toxicity has been reported with high concentrations of the dye in in vivo studies, but trypan blue has been widely used in the anterior segment for more than a decade and the posterior segment more recently, and the package labeling cautions only that excess dye should be removed.11

Trypan blue is most effective for staining the ERM. This is because the dye is not absorbed by living cells, such as those of the ILM, but is absorbed by dead cells. The ERM is dead tissue, and therefore cells in the ERM are well-stained by trypan blue. Its use for this purpose was first described in 2002.14 Investigators found it to be a valuable adjunct in surgical management of proliferative vit-
blue is indicated for staining of the ILM, and the combination dye is indicated for staining of both ILM and ERM.11

In human donor eye studies, bromophenol blue, Evans blue, and light green dyes were shown to stain the ILM. ERMs were strongly stained with 0.5% Evans blue and moderately stained with 0.5% light green, fast green, brilliant blue, and bromophenol blue dyes.16 Further preclinical work is required to determine whether these dyes will offer safety and additional functionality for applications in intraocular surgery.

CONCLUSION

The greatest advantage of use of any of these visualization aids is improved intraoperative identification of membranes of interest, whether ILM or ERM, and the discrimination of these membranes from surrounding intraocular structures. The better these membranes can be identified, the better they can be peeled and removed, and the lower the chance that further surgery will be needed. The choice of visualization agents, within the broad categories outlined above, is largely a matter of personal preference and comfort level. Whatever one’s choice, with these dyes available to us it may be better to use one and be safe than to skip this simple adjunctive step and be sorry later.

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1. AC-Green [package insert]. Akorn; Lake Forest, IL; 2010.

OTHER DYES

Two other useful blue dyes are available for ophthalmic use in Europe but are not approved for use in the United States: brilliant blue G (ILM-Blue, DORC International) and a mixture of trypan blue and brilliant blue G (MembraneBlue Dual, D.O.R.C. International). Brilliant