

Trypan Blue Versus Indocyanine Green

A clinical comparison of these dyes for capsular staining.

BY DAVID F. CHANG, MD

Staining the anterior capsule with dye is by far one of the most important advances in the management of complicated cataracts. With the FDA's recent approval of trypan blue, US surgeons are finally able to capitalize fully on this strategy (Figure 1). More than 5 years of worldwide experience has demonstrated that capsular staining is safe and effective for cataract surgery. Safety, however, depends on the specific dye used and its formulation. Uttley et al¹ reported on four eyes in which intraocular methylene blue, used for capsular staining, resulted in corneal decompensation that eventually required penetrating keratoplasty.

A HISTORY OF CAPSULAR STAINING

In 1998, Fritz² published a report on the use of sodium fluorescein dye to stain the anterior capsule for cases of mature cataract. Unfortunately, because of its small molecular size, fluorescein did not remain confined to the anterior chamber but diffused into both the lens and the vitreous.

Horiguchi et al³ first published a report on the use of

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0.5% indocyanine green (ICG) to stain the anterior capsule in 1998. They reported on a randomized, prospective study of 20 consecutive, mature, white cataracts in which one-half of the eyes received ICG dye and the other half did not. There were no statistically significant differences in laser flare-cell photometry, endothelial cell loss, or postoperative IOP spikes. Since it is only approved for choroidal angiography, lyophilized ICG (Akorn, Inc., Buffalo Grove, IL) is sold and packaged with a solvent that, because it is intended for IV injection, is of an inappropriate pH and osmolality for the anterior chamber. For this reason, Horiguchi et al mixed the dye using BSS Plus (Alcon Laboratories, Inc., Fort Worth, TX) and the supplied solvent in a 9:1 ratio. The OR personnel must be careful either to warm or vigorously

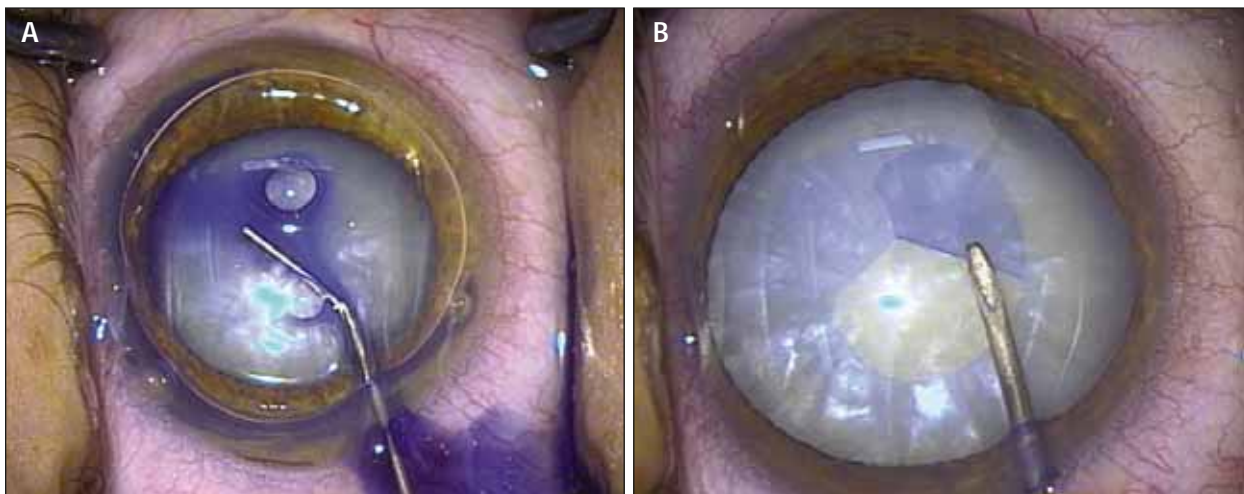


Figure 1. The surgeon injects trypan blue by means of a No. 30 cannula on a tuberculin syringe beneath an air bubble (A). The blue stain contrasts with the white cortex during the capsulorhexis step (B).



Figure 2. This eye has a mature, white cataract. The intense staining with trypan blue is advantageous when corneal clarity is suboptimal, such as after a penetrating keratoplasty (A). Persistent staining helps the surgeon to judge the placement of a horizontal chopper (B). Visible staining of the capsule with trypan blue persists even after the completion of phacoemulsification (C).

shake the mixture in order to fully dissolve the ICG powder. Otherwise, large, undissolved particles will remain suspended in the solution.

In 1999, Melles et al⁴ published their use of 0.1% trypan blue dye to stain the anterior capsule in a series of 30 patients with mature cataracts. As with the aforementioned study by Horiguchi et al, there was no clinical evidence of increased inflammation, corneal endothelial impairment, or elevated IOP, but there was no control group. After receiving CE Marking that year, trypan blue 0.06% has been distributed internationally by DORC International BV (Zuidland, the Netherlands) as Vision Blue. Because it is specifically intended for capsular staining, Vision Blue is packaged in an appropriately small vial of solution that is formulated for intraocular use and requires no mixing.

LABORATORY AND CLINICAL STUDIES

Laboratory and animal studies have supported the safety of both ICG and trypan blue. ICG was shown to be nontoxic in rabbits and was safely used to count cells on human donor keratoplasty buttons.⁵ Investigators reported similar findings with trypan blue, which was used to examine the endothelium in more than 32,000 donor corneas by the Dutch National Eye Bank.⁴ To gain CE Marking in Europe, Gerritt Melles, MD, employed a standard cytotoxicity study with cultured fibroblasts to evaluate four different dyes: trypan blue; ICG; methylene blue; and gentian violet. Trypan blue had the best score with the lowest toxicity (data on file with DORC International BV).

Since these initial reports, ophthalmic surgeons have adopted both of these dyes worldwide for capsular staining. For example, Vision Blue has been available in 60 countries, with approximately 700,000 units sold by DORC International BV prior to the dye's US release.

There are no published reports of anterior segment complications directly attributable to either dye. One prospective, randomized, controlled study found no difference in endothelial cell loss when trypan blue was used.⁶ Even so, there has been concern that ICG, when used for peeling the internal limiting membrane, may be toxic to the retinal photoreceptors and may cause new visual field defects.⁷ A recent study in vitrectomized rabbits found no retinal toxicity from the commercially available 0.06% concentration of trypan blue.⁸ Trypan-blue staining of an expandable hydrophilic acrylic IOL has been reported, however.^{9,10} This particular lens model has the highest water content of the hydrogel class.

With respect to efficacy, the benefit of improved visualization of the capsule is clinically obvious, but one randomized study demonstrated that better visualization improves a surgeon's ability to complete the capsulorhexis in mature cataracts. Dada et al^{11,12} randomized 50 eyes to capsular staining with five different agents (10 eyes each): 0.1% trypan blue; 0.001% gentian violet; 0.5% ICG; 2% fluorescein; and autologous hemocoloration. The first three dyes provided superior visualization of the capsule and higher success rates in completing a capsulorhexis with no cases of extended capsular tears. The last two groups both had poorer visualization of the capsulorhexis and an extension rate of 20%.

In 2000, I reported on one of the first clinical comparisons of ICG and trypan blue for capsular staining.¹³ Trypan blue provided a significantly darker and more intense staining of the capsule (Figure 1), particularly helpful qualities when other complicating factors such as corneal edema are present. In addition, trypan blue provided more persistent, longer-lasting staining of the anterior capsule (Figure 2). This attribute greatly facilitates nuclear emulsification in mature white and brown lenses,



Figure 3. Brunescant nuclei require dark staining for adequate contrast.

where poor visualization makes the disruption of the capsulorhexis with the phaco tip or chopper more likely. As reported from a retrospective study,¹⁴ I performed ICG staining in 18 consecutive mature white cataracts between June 1998 and October 1999, and, in the US and abroad, I used trypan blue in 16 cases of consecutive mature lenses between November 1999 and November 2000. I performed a planned, can-opener capsulotomy for extracapsular cataract extraction for one eye in each group. I successfully completed a capsulorhexis in 15 of 17 eyes and 15 of 15 eyes stained with ICG and trypan blue dye, respectively, that subsequently underwent phacoemulsification. Both dyes provided excellent visualization of the capsule and were not associated with complications. Staining with trypan blue was definitely more intense and persistent.

CLINICAL INDICATIONS

In addition to the white cataract, capsular dye should be considered whenever the red reflex is compromised.¹⁵ Examples include corneal scars or edema, dense anterior cortical spokes, a mature brown nucleus, vitreous hemorrhage, and asteroid hyalosis. Trypan blue is superior for the brunescent lens in particular (Figure 3), because ICG does not provide adequate color contrast with this hue of nucleus. The enhanced visibility of a capsulorhexis' edge stained with trypan blue is also very helpful when removing traumatic cataracts, for which the surgeon must place capsule retractors or capsular tension rings. Others have reported on dye-aided anterior and posterior capsulorhexes in pediatric cataracts.¹⁶⁻¹⁸

Another underused application of capsular dye is for teaching phaco techniques.^{19,20} Not only can staining

help beginning residents find and grasp the anterior capsular flap, but it is particularly valuable for any surgeon learning new phaco techniques such as phaco flip or phaco chop. With the latter method, a stained capsulorhexis' edge helps the transitioning surgeon to avoid overly distending it with the chopper's shaft or misplacing the horizontal chopper's tip peripherally, outside the capsular bag (Figure 2B).

Finally, surgeons sometimes find the capsular flap unexpectedly difficult to visualize when performing the capsulorhexis. It is important to recognize that one can stop and perform capsular staining even after the capsulorhexis has been initiated,²¹ because the dye preferentially stains the capsule and not the cortex.²² When irrigating out the dye in this situation, it is important not to allow the chamber to become shallow, or the tear may extend peripherally.

STAINING TECHNIQUES

Many surgeons continue to inject capsular dye beneath an air bubble, as originally described by Horiguchi et al³ and Melles et al⁴ (Figure 1A). The ophthalmologist fills the anterior chamber with air using a 30-gauge cannula inserted through a tiny paracentesis. He then draws several drops of dye into a tuberculin syringe and places them on the anterior capsular surface by means of the same cannula. Although the dye is not toxic to the endothelium, the bubble prevents excessive dilution and helps to confine the dye to the capsular surface. After waiting at least 10 to 15 seconds, the surgeon can easily irrigate out the dye with BSS before injecting viscoelastic.

Laureano and Coroneo²³ suggested simply omitting the air bubble. Takayuki Akahoshi, MD, has described an alternate technique of mixing ICG with viscoelastic (see Dr. Akahoshi's article in this issue), and Kayikicioglu et al²⁴ have used a similar viscoelastic-mixing technique with 0.4% trypan blue. Finally, Robert Osher, MD, has popularized the technique of isolating a puddle of dye on the anterior capsule beneath a partition of cohesive or viscoadaptive viscoelastic (eg, Healon5 [Advanced Medical Optics, Inc., Santa Ana, CA]).²⁵ This method intensifies the staining compared with the bubble technique in which the bubble's meniscus and surface tension displace the dye from the central anterior capsular surface.

CONCLUSION

Both ICG and trypan blue have been safely and successfully used to enhance visualization of the anterior capsule. Unlike ICG, trypan blue does not require mixing, and it provides superior, more prolonged capsular visualization. Now that trypan blue is the first and only product

to receive FDA approval for capsular staining, it is clearly the dye of choice. ■

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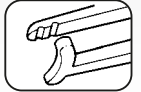


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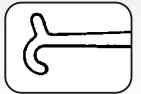
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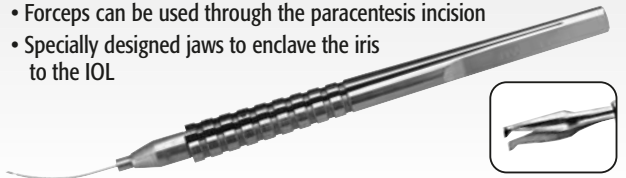
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