the choroid, the blood speed data obtained do not reflect blood flow or vascular resistance changes in the optic nerve head, but only in the choroid. The blood flow through the paraoptic branches is only a fraction of the flow through the much larger posterior ciliary arteries.

Colour Doppler findings in the short posterior ciliary arteries are thus, in practice, not relevant to the optic nerve head circulation, and, by extension, to a study of patients with NAION. Hayreh⁵ points out that researchers have been misled to believe that blood flow evaluation in these arteries provides information about the optic nerve circulation. Also, measurements of the ophthalmic artery circulation are not at all relevant to the optic nerve head nor to studies of NAION. Optic nerve head blood flow is only a minuscule fraction of ophthalmic artery flow.

The question arises as to the relevance of central retinal artery blood flow characteristics to the optic nerve head circulation and to NAION. Kaup *et al*¹ report reduced blood speed in the central retinal artery in their patients with NAION. A similar finding was reported by Flaharty *et al*⁶ who also used colour Doppler imaging. Hayreh⁵ points out that the central retinal artery supplies only the surface nerve fibre layer of the optic nerve head and thus has no

real role in the blood supply to the regions of the nerve head associated with NAION. Arnold,³ reviewing fluorescein angiographic findings in NAION, does note, however, that in some cases impaired filling patterns in the surface vasculature have been observed. Kaup *et al*¹ suggest that involvement of the central retinal artery in NAION may be secondary to the oedema of the optic nerve surrounding the artery.

How, then, can the optic nerve head microcirculation relevant to NAION be reliably evaluated? With fluorescein angiography, the filling of the laminar and retrolaminar regions of the nerve head is obscured by fluorescence from the surface. Several laser Doppler techniques have been used to study NAION, most recently by Collignon-Robe *et al*.⁷ The issue becomes one of penetration depth of the probing laser beam and the relative contributions of the various depths sampled to the analysed signal. Collignon-Robe *et al* did report circulatory decreases of up to 20% in NAION, but what remains unclear is the relative contribution to the signal from the more anterior layers of the nerve head not directly associated with the occlusive vasculopathy. A Doppler signal derived solely from a deeper region would probably have shown more of a decrease in circulation.

In summary, clinical evaluation of the optic nerve circulation in NAION remains an elusive goal yet to be fully achieved.

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Preoperative glaucoma assessment

Conjunctival markers as predictable markers for preoperative glaucoma assessment

P-J Pisella

Glaucoma and the conjunctiva

Filtering surgery throughout its development has mainly focused on the ocular surface, most particularly the conjunctiva. Similarly, all doctors treating patients with glaucoma should also concentrate on the status of the patient's ocular surface, not only at the time of surgery but especially before. The glaucomatous patient is the primary category of patients who may have side effects from long term topical treatment.

Currently, it is well known that the chronic use of eye drops has a cumulative toxic effect on the conjunctival epithelium. Broadway *et al*^{1,2} have shown the role of medical treatment as a risk factor for filtering surgery failure. They

clearly showed that the success rate was considerably lower (55%) in patients treated with one or more drugs for glaucoma for at least 3 years than in other patients (94%, $p < 0.001$). Later, Baudouin *et al*³ showed the major component of conjunctival toxicity inside a bottle of eyedrops for glaucoma—preservatives, with few differences between the various types, but particularly well studied in benzalkonium chloride (BAK), still the most frequently found preservative in eye drops.³ The toxic effect of BAK on the epithelium has long been known,⁴ but the relationship between the presence of BAK in eye drops and changes in the conjunctival epithelial profile has been

described only more recently. Briefly, BAK toxicity is twofold: (1) an indirect toxicity on the lipid layer of the lacrimal tear film is found because of the soap effect of quaternary ammonium and, as a consequence, an increase in functional and clinical signs of dry eye; (2) a direct cytotoxic effect on conjunctival epithelial cells is clearly shown experimentally, in vivo and in vitro.^{5,6} In this way, subclinical inflammation takes place inside the conjunctiva and plays a major part in fibrosis development after filtering surgery. These results were confirmed throughout the world and prompted manufacturers of ophthalmic solutions to produce, when chemically possible, eye drops for glaucoma without preservatives in single-dose or filtering multi-dose bottle forms. In fact, the main family of anti-glaucoma drugs available without preservative remains the β blockers.

What are the clinical manifestations of this toxicity, and how can the doctor easily detect a conjunctival profile with major risk for surgical failure?

The answer is simple, as all clinicians know that in most cases this is difficult to detect. A clinical examination of the ocular surface does not provide sufficient information to diagnose an inflammatory profile of the conjunctiva, because, in many

patients, the ophthalmologist sees a "white" eye with no clinical inflammation. Of course, changes can be seen in the precorneal tear film, with instability indicated by a short break-up time, and in some cases moderate superficial punctate keratitis is detectable, suggesting chronic inflammation of the corneconjunctival surface caused by long term topical treatment, particularly when the staining is predominantly located both on the nasal conjunctiva and on the inferior part of the cornea.⁷ However, these clinical findings are present when the deleterious effect of preservatives has already taken hold, or in other words, when the risk factors for surgical failure are high. To achieve maximum efficacy and increase considerably the rate of success in filtering surgery, a preclinical test to detect local changes in the ocular surface early would be useful and could also serve in determining the best time for surgery. Impression cytology, which studies the main cellular populations of the conjunctival epithelium—the epithelial cells, the goblet cells and the antigen-presenting cells—has advanced in this direction. Several markers on these cells help improve the understanding of the cellular mechanism of toxicity and of other chronic ocular surface diseases such as dry eye or rosacea.⁸ Human leucocyte antigen (HLA) DR was systematically overexpressed in all of these conditions and is now currently used as the main inflammatory marker of the conjunctiva. Moreover, Baudouin *et al* have also shown a high level of HLA-DR expression by epithelial cells taken from the conjunctiva of patients treated for only 6 months with topical eye drops, but with no clinical signs

of toxicity.⁹ Furthermore, mucin detection, indirectly evaluated by goblet cell density evaluation, was also shown to be associated with these processes, with an earlier decrease in these cells. These results were tested in pathologies such as dry eye and ocular rosacea, but also in cases of ocular surface aggression with topical eye drops for glaucoma and in contact lens wearers; MUC5AC expression was routinely used for detection of both secreted mucin and cells. Finally, we obtained a conjunctival profile of subclinical inflammation with a high level of expression of HLA-DR antigens and a considerable decrease in goblet cells, suggesting conjunctival epithelial metaplasia caused by inflammatory processes. This profile evaluation could be a useful tool for clinicians seeking to evaluate the success rate of filtering surgery and to predict a switch from preserved to unpreserved drugs when possible, or the use of topical anti-inflammatory agents before surgery. However, this technique requires a high level of laboratory technology, and the scientific knowledge necessary for interpretation is time-consuming, thus may not be used routinely by all. However, these studies open the door to ocular surface evaluation for subclinical detection of the earliest epithelial changes. In the near future, this approach could greatly benefit from new imaging technology exploring the anterior segment, such as confocal microscopy or very-high-frequency ultrasound imaging.^{10 11} Fundamental research could finally join clinical practice, with direct benefits for our patients.

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Intraocular pressure

Intraocular pressure-lowering efficacy of bimatoprost 0.03% and travoprost 0.004% in patients with glaucoma or ocular hypertension

R Noecker

The efficacy of bimatoprost and travoprost in patients with glaucoma and ocular hypertension

Dr Cantor's article¹ (see page 1370) on the efficacy of bimatoprost and travoprost in patients with glaucoma and ocular hypertension shows again that both these drugs are efficacious

in lowering intraocular pressure (IOP). The study is a prospective, randomised investigator-blinded trial, which has results similar to those found in studies carried out with the drugs in this class.

Dr Cantor found that bimatoprost lowered IOP slightly more than travoprost in this study population. This is the first relatively large two-arm study to show this in a head-to-head design. The current study supports others who have shown that bimatoprost is somewhat more efficacious than travoprost.

What is reassuring about this study is that there are no surprises, and the results appear to be consistent with what has been seen in the collection of other studies comparing drugs in this class. The relative degrees of IOP reduction, rates of hyperaemia and clinical success parameters are within the range reported in smaller studies and larger multiple comparison studies.^{2–6}

What has differed from study to study is the cohort of patients examined, and the treatment of the data both from the standpoints of study design and statistical treatment. These factors can influence the results to some extent, but taken in the context of the body of