and there is transudation of fluid into the tissue spaces. This results in orbital oedema, proptosis, paresis of ocular movement and retinal oedema. Retinal arterioles and veins at this stage are of normal calibre or dilated due to the relative anoxia of the vessel walls. The extremely low tolerance of ganglion cells to ischaemia produces the loss of vision.[3]

The acute stage is followed by gradual absorption of oedema, narrowing and sclerosis of previously ischaemic retinal arterioles, and ganglion cell degeneration producing optic atrophy.[3]

We are however not aware of any previous report of cavernous sinus thrombosis in this syndrome. Our patient was a healthy male with controlled hypertension. There were no other predisposing factors for venous thrombosis. The cavernous sinus thrombosis in his case was a late event as shown by normal neuroimaging on the day of surgery and 1-week postoperative. It was unilateral and nonprogressive. We believe that stagnation of blood flow and ischaemic damage to vessel walls resulting from prolonged collapse of vascular channels in this patient led to the onset of thrombosis in the orbital circulation with retrograde extension to the cavernous sinus.

This case represents a serious but potentially avoidable sequence of ocular events following prone position surgery. The importance of proper head positioning, such that the eye is not subjected to sustained pressure against the headrest, cannot be overemphasized.

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Sir,

Ocular and systemic side effects of latanoprost

We have read with considerable interest the paper by Konstas *et al*.[1] The authors concluded that latanoprost had a 'similar safety than timolol as monotherapy in the treatment of exfoliation glaucoma (XFG)'. However, according to the paper's Table 3, there were significantly more cases of conjunctival hyperaemia in patients receiving latanoprost compared with those receiving timolol regimen. This can be reasonably explained because prostaglandins including latanoprost, as potent vasodilators, act directly on vascular smooth muscle, attenuating responses of vasoconstrictive stimuli, and enhancing microcirculation,[2] thereby leading to conjunctival hyperaemia. The latter might be further aggravated by the fact that prostaglandins can promote angiogenesis.

Moreover, in Table 4 there was one case of upper respiratory tract infection in a patient treated with latanoprost. Although this systemic side effect has not reached statistical significance when compared with the timolol group, it can be attributed to latanoprost, because it has been shown that local administration of antiglaucoma drops results in systemic absorption through the nasal mucosa,[3] and prostaglandins, released by cyclooxygenase (COX)-2 (one of the key isoenzymes in the production of prostaglandins), induce immune suppression,[4] thereby leading to defective elimination of pathogens. Notably, disturbances of the immune system can induce disease in virtually any portion of the eye; examples include conjunctivitis, keratitis, keratoconjunctivitis, scleritis, uveitis, optic neuritis, and orbital inflammation. Therefore, patients under latanoprost treatment should be aware of potential systemic and/or topical infective side effects.

From another extreme viewpoint, although the authors have not administered latanoprost for an extended period of time, it should be noted that prostaglandins are implicated both in cell proliferation, and inhibition of immune surveillance; therefore these agents could favour a potential malignant growth. It is already known that

COX-2 overexpression enhances prostaglandin synthesis, may inhibit apoptosis, increases invasiveness of malignant cells, and can be mutagenic and tumorigenic *in vitro*.[5,6] Tumour-derived COX-2 and prostaglandins may play an important role in antagonising the host immune response and therefore facilitating tumour growth and spread.[4] Of note, *Helicobacter pylori* (*H. pylori*) infection, involved in the pathogenesis of glaucoma,[3,7] increases COX-2 and prostaglandin expressions, which might be one of the mechanisms leading to *H. pylori*-induced carcinogenesis. Moreover, prostaglandins promote angiogenesis, thereby contributing to invasiveness of a variety of tumours.[8] In particular, prostaglandins enhance the proliferation and invasion of malignant cells via activation of major intracellular signal transduction pathways such as PI3K/Akt. Additionally, the synthetic machinery and receptors for prostaglandins, prominently expressed by T lymphocytes in tissues at the boundary of normal tissue with tumour cells, may play a central role in prostanoid-driven tumorigenesis. In view of all the above-mentioned data, ophthalmologists should consider and be aware of prostaglandin-induced infective side effects, and of their long-term, although still speculative and rare, oncogenic properties.

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Sir,

Reply to J Kountouras *et al*

The authors would like to thank Drs Kountouras, Zavos and Chatzopoulos for their letter regarding our paper published in *Eye* (2004) on the treatment of exfoliation glaucoma with latanoprost *vs* timolol. We appreciate their interest in this manuscript, their obvious effort to respond regarding potential side effects of prostaglandins, and their concern for ophthalmic patients.

The authors are correct in stating that glaucoma medicines 'when instilled topically' can be absorbed systemically through the nasal mucosa. Also, we heartily agree that ophthalmologists should be aware of potential systemic and ocular side effects from latanoprost as well as from any glaucoma medication. However, the authors' statements that the upper respiratory infection in our study was attributable to latanoprost specifically and that prostaglandins are apt to cause ocular immune disease and cancer are difficult to support.

In general, the effects of prostaglandins in the body are dependent upon three factors:

(1) the appropriate receptor at the target tissue
(2) the specific class of prostaglandin
(3) the tissue levels of the prostaglandin

Latanoprost is an F_2a prostaglandin analog with a very high specificity to FP receptors. Such receptors have generally higher concentrations in the eye, smooth muscle cells, and corpus luteum. The authors' conclusions about latanoprost, as an F_2a prostaglandin analog, appear generally based on research of other prostaglandin subtypes and are not generally applicable to latanoprost. Making such a direct comparison of other prostaglandin research to specific clinical effects of an F_2a prostaglandin analog is hazardous and potentially misleading.