Correspondence

β -adrenergic receptor subtypes and intraocular pressure

SIR, I read with interest the recent article by Trope and Clark¹ concerning the distribution of β_1 and β_2 receptors in the pigmented ciliary process of the sheep. Although the data presented indicate that β_2 receptors predominate in the ciliary processes of this animal, I believe that the results cannot be readily extrapolated to man in respect of physiological or pharmacological control of intraocular pressure and that comment is justified on some of the data quoted in the discussion section to support such extrapolation.

In particular the human volunteer study by Alm *et al.*² in which 0.5% timolol eye drops produced a slightly greater oculohypotensive effect than 3% metoprolol is quoted to support the greater influence of β_2 receptors in intraocular pressure control. In order to justify this conclusion it would be necessary to administer the β_1 selective agent, metoprolol, and the nonselective agent timolol, at equivalent β_1 receptor antagonist doses, and this does not appear to have been the case in the study quoted. When administered systemically timolol is approximately 10 times as potent as metoprolol in the inhibition of exercise tachycardia. Moreover there is evidence that timolol is much better absorbed across the cornea than metoprolol: in rabbits topical administration of 0.25% timolol give higher aqueous humour levels than 4% metoprolol.³ Therefore, the ratio of topical concentrations used by Alm *et al.*—6:1 metoprolol to timolol—would probably considerably favour timolol in terms of β_1 adrenoceptor antagonist activity and consequently complicate any interpretation of the relative influence of β_1 and β_2 adrenoceptors.

In this context I have studied the oculohypotensive activity of a β_2 selective adrenoceptor antagonist, ICI 118,551,⁴⁻⁶ in normal volunteers in comparison with the nonselective antagonist, propranolol (Inderal). When administered orally at equivalent β_2 antagonist doses, ICI 118,551 produced only one-third of the intraocular pressure

reduction of propranolol (Fig. 1). Changes in cardiovascular parameters were minor and could not account for the differential effects on intraocular pressure. I believe that these results support the conclusion that β_1 receptors are the major β receptors involved in intraocular pressure control in the in-vivo physiological situation in man.

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SIR, We disagree with A. Rushton that β_1 receptors are the major β receptor subtypes in the ciliary processes. Rushton appears to be unaware of other published works supporting our findings that β_2 receptors are the major receptor subtype in the ciliary processes of both animals and humans.¹⁻⁴ Our radioligand study complements these reports.⁵

Fig. 1 Supine intraocular pressure levels following administration of ICI 118,551 and propranolol. The data are presented as adjusted means of 8 subjects. The differences between the post-propranolol values and the post-ICI 118,551 values are statistically significant for all time points subsequent to the first.

Despite Rushton's poor response with the orally administered β_2 blocker ICI 118,551, β_2 specific blockers used topically on the eye have been reported to lower intraocular pressure potentially in animal eyes.⁶ Furthermore we are not at all surprised that he found ICI 118,551 less potent than ($\pm$) propranolol. We have found that ICI 118,551 binds 10 times less potently to receptors in the ciliary processes than ($\pm$) propranolol (Trope GE, Clark B, paper in preparation). (Kd for ICI 118,551 = 5.5×10^{-8} , Kd for ($\pm$) propranolol 7.9×10^{-9} .) Despite this finding we still feel that a trial of Topical ICI 118,551 on patients with glaucoma is probably indicated in view of this drugs β_2 specific blocking effects and its cardioprotective action.⁷

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Angioid streaks in thalassaemia major

SIR, I read with interest the paper on angioid streaks in a case of thalassaemia major.¹ I thought it appropriate to call to your attention a paper entitled 'Laser treatment of choroidal neovascular membranes in angioid streaks.'²

Case 1 describes a 50-year-old man with a history of thalassaemia intermedia and haemochromatosis (as a result of his anaemia). Fundus examination revealed peripapillary angioid streaks in both eyes with dense disciform macular scarring in the left.

We noted in the case cited in our paper that haemochromatosis can occasionally accompany thalassaemia intermedia. Haemochromatosis also results in the clinical manifestation of iron overload in the tissues. The 2 haemolytic disorders combined could cause iron deposition on Bruch's membrane and the resultant angioid streaks. Yet neither thalassaemia intermedia nor haemochromatosis effects a primary disturbance in the elastic tissue of the body. The brittle lamina basalis in this case may have occurred because of iron deposition, and thus Bruch's

membrane is probably quite similar to that in a patient with sickle cell disease.

We were interested to find that you also noted the similarity between the 2. We mentioned that the mechanism of the breaks in Bruch's membrane in the eyes of patients with sickle cell disease is not primary elastic tissue degeneration either, since no elastic tissue defect occurs with this disease. It has been conjectured that the haemolysis of sickled red cells leads to iron deposition on Bruch's membrane, which would lead to the brittleness of the lamina basalis.

We were pleased to find that your paper also supports the iron deposition theory with reference to development of angioid streaks. Congratulations on an excellent paper.

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Book reviews

Pathobiology of Ocular Disease: A Dynamic Approach. Eds. ALEC GARNER and GORDON K. KLINTWORTH. Pp. 1760. SFr. 650.00. (In two parts). Marcel Dekker: New York. 1982.

The aim of the work, as explained in the editors' preface, is to bring a new, dynamic approach to the study of ophthalmic pathology, concentrating on disease mechanisms rather than on descriptive pathology, which is stressed in other books on the subject.

The work is in 2 volumes totalling 55 chapters, written by a host of experts, who are recognised authorities in the field of their contributions, including the 2 editors, who have taken an active part in the writing.

The size of the work allows only a brief survey here of the contents. The first chapter, appropriately, is on ultrastructure, and is in a subsection headed 'Basic principles'; it is followed by a discussion on inflammation in general, incorporating recent and important advances. Infection of the eye is dealt with in 8 contributions, each one discussing a particular class of agents such as micro-organisms, viruses, etc. The techniques and methods described in this section often belong to disciplines other than histopathology. Principles of laboratory investigations in ocular infection are discussed and practical details are given, such as the selection of culture media. All aspects of trauma are covered in an extensive chapter, and another substantial contribution deals with development, normal and abnormal, featuring valuable tabulations of various defects. A section on glaucoma includes experts' accounts of anterior and posterior segment changes in this condition and a discussion