Mechanisms of Photoreceptor Death in Retinal Degenerations: From the Cell Biology of the 1990s to the Ophthalmology of the 21st Century?

In the inaugural review article for the Mechanisms of Ophthalmologic Disease section in the January 1996 issue of the ARCHIVES, Dr Adler[1] begins with the statement, "There is still no effective treatment for retinal degenerative diseases such as retinitis pigmentosa (RP), in which the loss of photoreceptor cells causes visual loss and eventually blindness." It is surprising that no mention is made of "A Randomized Trial of Vitamin A and Vitamin E Supplementation for Retinitis Pigmentosa," an article by Berson et al[2] published in the June 1993 issue of the ARCHIVES. Also in 1993, the National Eye Institute issued a report of this trial's results and recommended that patients with RP take vitamin A palmitate (C. Kupfer, MD, written communication, June 14, 1993).

This treatment trial was initiated prior to the discovery that RP may involve "genes by the dozen, mutations by the score."[1] No evidence was found that the beneficial effect of vitamin A was confined to one or another genetic type. Since we now know that this trial must have included patients from many different pedigrees with numerous genetic abnormalities, it could be inferred that if the treatment provided a beneficial effect for the group, then some phenotypes might benefit more from treatment than others. The clinician often has no way of determining which phenotype or genetic mutation a given patient has, let alone whether the patient will respond to treatment.

Dr Adler's informative article outlines some theoretically possible future treatments for RP such as neurotrophic growth factors, or pharmacological intervention on metabolic genetic pathways, which may come to fruition in the 21st century. Until researchers have developed future treatments, ophthalmologists are left with vitamin A palmitate. While this treatment is not without controversy,[3] it would seem prudent for ophthalmologists to offer vitamin A palmitate to patients with RP.

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1. Adler R. Mechanisms of photoreceptor death in retinal degenerations: from the cell biology of the 1990s to the ophthalmology of the 21st century? *Arch Ophthalmol.* 1996;114:79-83.
2. Berson EL, Rosner B, Sandberg MA, et al. A randomized trial of vitamin A and vitamin E supplementation for retinitis pigmentosa. *Arch Ophthalmol.* 1993; 111:761-772.
3. Berson EL, Bird AC. Retinal photoreceptor dystrophies: LI Edward Jackson Memorial Lecture. *Am J Ophthalmol.* 1995;120:683-684.

In reply

The goals of my contribution to the Mechanisms of Ophthalmic Disease series were to review recent advances in our understanding of cellular and molecular mechanisms of retinal degenerations and to discuss possible avenues for research into new therapeutic strategies for these devastating disorders. It would have been beyond the scope and space limitations of the article to review the literature on previously described or proposed therapeutic approaches, such as the use of vitamin A in RP or antioxidant treatments for macular degeneration. The opening sentence of my article was actually meant to indicate that no cure is currently available for these diseases, but Dr Crane's comments suggest that the wording of that statement was ambiguous. I would like to thank Dr Crane very much for pointing this out, and for the opportunity to clarify such possible misunderstanding.

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Apoptotic Photoreceptor Cell Death After Traumatic Retinal Detachment in Humans

In a recent article in the ARCHIVES, Chang et al[1] ascribed photoreceptor cell degeneration in patients with traumatic retinal detachment as being due to apoptosis. They based this claim on terminal deoxynucleotidyl transferase–mediated biotinylated deoxyuridine triphosphate nick end labeling (TUNEL)–positive labeling of photoreceptor nuclei in 7 (46.7%) of 15 eyes that were enucleated within 2 days after trauma. Furthermore, they found nicked nuclear DNA as early as 8 hours after trauma. This is of great interest since apoptosis is thought to represent genetically programmed cell death, which may be triggered by a variety of biochemical and other physiological factors. If apoptosis is found to be an important mechanism of photoreceptor cell degeneration soon after traumatic retinal detachment in humans, then it may be impossible to reverse the consequent degeneration. This may serve as an indication for the need for very early intervention in trauma. Such information might have an impact on how soon to operate on primary retinal detachments.

However, greater caution should be exercised prior to such judgments. While the 2 features described above are characteristic of apoptosis, their presence may not always be specific to this mechanism. This is important, since, in the purest sense, apoptosis connotes a preprogrammed mode of cell degeneration and a state of irre-