Stem cells are looked upon as either an ethical train wreck or the gateway to the alleviation of all human illness, depending on which side of the political spectrum one resides. This unfortunate notoriety has resulted in an unprecedented coverage in the media, but has not done much to advance the cause of this technology. Yet recent ophthalmologic research suggests that the medical applications of stem cells hold notable promise for the treatment of ocular degenerative conditions, and that realization of this potential may come about in the near future.

What are stem cells?
First of all, there is a good deal of confusion among the public and even some professionals as to what stem cells are, and there is even more misunderstanding over their therapeutic potential. Stem cells are undifferentiated cells that possess a self-renewing capacity and have the ability to give rise to multiple cell types. They exist throughout the body of adult organisms, although the most potent stem cells are thought to be derived from embryos. It has been argued by individuals concerned over the ethical question of the destruction of human embryos that embryonic stem cell research is on the one hand immoral and on the other hand unnecessary. This is surely incorrect, since in the long run the understanding of the breadth and limitations of this technology will require a thoroughgoing analysis of the embryonic stem cell. But for the time being, a viable alternative to embryonic stem cells exists.

What makes them so intriguing?
Adult stem cells possess some unique advantages. These cells are derived from adult tissues and cultured using special procedures that favour their growth and isolation from a large non-stem cell population. Even if at present they seem to lack the versatility of embryonic stem cells, the fact that they can be generated from the patient’s own tissues means there will be no immunological barrier to their acceptance. This relative lack of plasticity has a positive side, in that adult stem cells are less prone to malignant transformation, a problem that has bedeviled work with embryonic stem cells. Moreover, because their development does not require the elimination of human embryos, a much wider range of funding support is open to investigations in this area. Although restrictions are placed on US National Institute of Health (NIH) grant funding involving the use of embryonic stem cells, no such limitations apply to adult stem cells. And even the astronomical cost of tailoring cell lines for each individual patient is becoming less of a barrier as the cost of other treatment options spirals into the stratosphere.

Homing in on the retina
At the 2007 meeting of the Association for Research in Vision and Ophthalmology (ARVO), a review of the abstracts for “stem cells” reveals 123 hits, indicating a wide range of interest in the application of this technology to disorders of the eye. Although it was long believed that bone marrow, muscle, skin and digestive tract were the only source of adult stem cells, they have recently been cultured from adult brain, heart, bone, fat, pancreas and eye. Moreover the limbus, conjunctiva, ciliary epithelium, and retina have all been found to harbour potentially useful stem cells. The retina is the site of macular degeneration (or age related macular degeneration; AMD) and retinitis pigmentosa (RP), and as such it is a prime target of research using adult stem cells. So far, results are mixed. In animal models of this disease, transplantation of cells has resulted in some alleviation of the disease state, and transplants into the fovea of patients with macular degeneration produced clinical improvement. However, transplants of foetal retinal cells showed poor synaptic integration and did not improve vision in patients with RP.

In short...
John Morrow discusses the potential applications of stem cell therapy in ophthalmology. Marred by controversy, this area of therapy must be viewed in a more positive light, according to Mr Morrow, since recent research suggests that stem cells hold promise for the treatment of ocular degenerative conditions, particularly retina diseases.
Neural stem cells can be obtained from the brain and expanded to large populations in the rat animal model. When cultured in the presence of factors which induce cell division, they do show some differentiation into photoreceptors when transplanted into adult retinas.

Many scientists working in the field feel that the best line of attack is the use of endogenous stem cells, derived from ciliary epithelium and glial cells growing in the retina. The glial cells, especially, express a number of markers of retinal function, and with proper stimulation could represent a viable therapeutic approach.

Is there evidence to support stem cell therapy?
Dr Martin Friedlander and his colleagues from Scripp’s Institute discussed at the ARVO meeting the reconstruction of a damaged retina with adult stem cells derived from autologous bone marrow or cord blood. Such stem cells selectively target sites of neovascularization and gliosis where they provide neurotrophic effects. These cells are seen to activate astrocytes, a hallmark of many ocular diseases, and participate in normal development. When the stem cells (derived from mice or humans) are injected intravitreally they can migrate into the abnormally growing vasculature and stabilize the growing blood vessels. This allows them to function more normally, preventing retinal vascular degeneration ordinarily observed in mouse models. This novel application of stem cells offers the possibility of treatment of a number of degenerative diseases of the eye. Friedlander is currently directing a $17 million program on the use of stem cells to treat eye diseases.

An unusual approach to AMD was explored by Dr Y. Yodoi and his colleagues at Kyoto University in Japan. Following the hypothesis that a patient’s own stem cells contribute to the neovascularization that is the hallmark of the disease, they measured the migration of haematopoietic stem cells in patients and controls, finding a significant increase of these cells in the circulation of patients manifesting the disease.

These examples provide an idea of the range of applications of stem cell technology to diseases of the eye. While the field is in its infancy and routine stem cell therapies lie years in the future, the potential for treatments are exciting, and the next few years, regardless of the political debate surrounding stem cells, should yield innovative therapies. Friedlander has stated publicly that he intends to have stem cell therapies in the clinic in the next five years. I feel, however, that it is highly unlikely that therapies using embryonic stem cells will have progressed to the clinic within this time frame.