

# Introduction

*Age*-related macular degeneration (AMD) is defined as the loss of macular function from the degenerative changes that is related to aging. It occurs most frequently in adults over 60 years of age. The condition can be bilateral, but the onset is usually asymmetric. (*Fine et al, 2000*)

It is characterized in the early stages by drusen, pigmentary changes and degeneration of the retinal pigment epithelium (RPE). In the later stages, there is atrophy of the photoreceptors and RPE (geographic atrophy or dry form) and choroidal neovascularisation (CNV or wet form). (*Tezel et al, 2004*)

With the exception of smoking avoidance, no preventive strategy has been established. High-dose supplementation with vitamins C and E, beta-carotene, and zinc recently showed to slow the progression of dry AMD. (*Age-Related Eye Disease Study Research Group, 2001*)

Many lines of treatment are available as Prostaglandin E<sub>1</sub> (PGE<sub>1</sub>) infusions, which are able to stop the gradual vision loss in dry AMD and, further, to stabilize or improve visual acuity. (*Heidrich et al, 1989*)

Thermal laser photocoagulation for CNV has been the standard of care for many years. Photodynamic therapy (PDT) with verteporfin represents a major advance in the treatment of subfoveal choroidal neovascularisation. . (*Mittra and Singerman, 2002*)

Surgical treatment was done by removing CNV membranes by submacular membranectomy. Other surgical treatments include intraoperative lysis of feeder vessels, pneumatic displacement of submacular blood and translocation of the macula to an extramacular and healthier area of the RPE. (*Thomas et al, 1992*)

Pegaptanib Sodium (Macugen) is a highly selective anti-vascular endothelial growth factor -agent with both anti-angiogenic and anti-permeability properties. Both intravitreal ranibizumab (Lucentis) and bevacizumab (Avastin) have successfully been used to treat CNV. (*Avery et al, 2006*)

Regenerative treatment concerns about using stem cells hoping to restore lost vision in degenerative retinal diseases. Stem Cells are defined as cells with the capacity of self-renewal and to generate differentiated cells that compose an organ, including retina. Extensive efforts expended on the transplantation of neural and retinal stem cells have shown that this method has promise as a strategy for therapy of diseased retinas. (*Klassen et al. 2007*)

Stem cells can form progeny that can differentiate, i.e. develop into one of the different types of cells that comprise the living organism. There are three sources of stem cells (embryonic, adult, and fetal). (*Kim SY, et al 2005*)

Multipotent stem cells exist in many tissues and organs of the body, such as the brain, retina, liver, muscles, cornea, and bone marrow. In recent years, these multipotent stem cells have been isolated and cultured in vitro from different parts of the mammalian retina (*Klassen et al., 2004*)

Human Embryonic stem cells can be stimulated to generate neural progeny by factors such as retinoic acid, increased beta-catenin signaling, and feeder cells. They can generate eye-like structures in vitro containing lens, neural retina, and pigmented retinal cells. (*Zhao et al., 2002*)

Retinal progenitor (stem) cells have been isolated from ciliary margin of adult retina of different ages or from fetal retina then after transplantation, stem cells integrate and migrate into retina depending on the age, disease, or injury status of the recipient retina. (*Coles et al., 2004*)

There are two methods for implanting stem cells in the retina. Stem cells injected into the vitreous do not generally integrate well with the retina unless an outer nuclear layer (ONL) lesion or discontinuity of the photoreceptors is present. This is because retinal injury stimulates signaling mechanisms and the release of growth factors that guide the migration, proliferation and differentiation of stem cells into damaged areas. (*Zhang et al., 2003*)

Stem cells implanted sub-retinally form a protective sheet over photoreceptors. They readily integrate with and thicken the ONL. The thickness of the ONL is one measurement of photoreceptor density. Increased ONL density combined with the appearance of new cells expressing photoreceptor specific markers such as recoverin, rhodopsin and cone opsin have been presented as evidence that stem cells can differentiate into retinal photoreceptors. (*Meyer et al., 2005*)

In AMD photoreceptor degeneration initially leaves the inner retinal circuitry intact, and newly transplanted stem cells (if they differentiate into new photoreceptors) need only make single short synaptic connections to contribute to the retinal network. (*MacLaren et al. 2006*)