Pharmacological Therapy and Prophylaxis

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For the majority of patients with age-related macular degeneration (AMD) no therapy is currently available. The disadvantage of existing therapy forms, such as laser coagulation or surgery, lies in the inevitable trauma they cause to surrounding tissues. In addition, a large proportion of patients do not respond to photodynamic therapy (PDT), and those who do generally still have visual loss after treatment. Most current therapies are also directed against neovascular AMD, while there is no current therapy for dry forms of the disease. Because of this, new therapy forms are desperately needed.

Owing to the chronic nature of this disease, long-term therapy is required for patients suffering from AMD. The eye, however, offers the unique opportunity for local application with the potential for avoiding systemic toxicities of therapeutic treatment. This is particularly advantageous for patients with AMD, the majority being elderly.

Preventative pharmacologic measures could not only prevent the development of early disease forms, including drusen and lipofuscin formation, but could also inhibit the progression from early to late forms of the disease (Holz and Miller 2003). In neovascular AMD, therapies are directed at new vessel formation and endothelial permeability, whereas the purpose of therapies directed against geographic atrophy is to inhibit the growth of the atrophic area.

Owing to better understanding of basic disease mechanisms at the molecular level, there are many new perspectives in pharmacological therapies for AMD. Substances that affect choroidal neovascularization (CNV) have recently been given particular attention. The majority of current projects undertaken by the pharmaceutical industry have concentrated upon inhibitors or antibodies against pro-angiogenic substances. This strategy is based on the assumption that CNV is the result of an imbalance between negative and positive regulators of angiogenesis. A large amount of work in ophthalmology has concentrated on the inhibition of the key vascular growth factor VEGF.

Other pharmacological therapies exploit neurotropic or neuroprotective factors intended to improve the survival of retinal pigment epithelium (RPE) and neuronal cells of the retina while having positive effects upon both 'dry' and 'wet' forms of the disease. A further strategy attempts to detoxify substances within the RPE. With age, lipofuscin granules accumulate in the RPE and contain substances such as A2-E and proteins that are modified through exposure to light. Both of these substances interfere with normal cellular metabolism and have toxic properties (Holz et al. 1999; Schütz et al. 2000). With knowledge of the molecular mechanisms of AMD, strategies are being developed that can inhibit or halt the development of such toxic substances. Despite this, much remains unknown about the causal relationships between lipofuscin accumulation, focal and diffuse drusen, and the development of later forms of the disease.

14.1 Vitamins and Minerals

Age is the most important known risk factor for AMD. Because of this, it has been assumed that, as in other degenerative processes, a deficiency in essential molecules may play a part in this disease. It is therefore possible that aged patients, in particular, may consume a diet deficient in which key elements that support reparative and antioxidative enzymes, resulting in a predisposition to disease.

The recommendation of antioxidants for AMD patients is based on the assumption that exposure to light enhances the production of free radicals in an environment that already has a high flux of oxygen and polyunsaturated fatty acids in the outer layers of the retina, the RPE, and Bruch's membrane (Spaide et al. 1999). Peroxidized lipids can induce new vessel growth and may, in fact, be responsible for the development of AMD (Spaide et al. 1999). The association between smoking and AMD supports the role of such a mechanism in the development of this disease (Klein et al. 1993). If the balance between pro-oxidative and antioxidative substances could be tipped in favor of pro-oxidative ones through the application of exogenous compounds, it is thought that oxidative stress could be