Drug treatment


Conbercept for patients with age-related macular degeneration: a systematic review.


Background: Conbercept is a novel vascular endothelial growth factor (VEGF) inhibitor for the treatment of wet age-related macular degeneration (AMD). This systematic review aims to assess the efficacy and safety of conbercept in the treatment of wet AMD.

Methods: PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure, VIP database, and Wanfang database were searched from their earliest records to June 2017. We included randomized controlled trials (RCTs) evaluating the efficacy and safety of conbercept in wet AMD patients. Outcomes included the mean changes from baseline in best-corrected visual acuity (BCVA) score (primary outcome), central retinal thickness (CRT), plasma level of vascular endothelial growth factor (VEGF) over time, and the incidence of adverse events (AEs).

Results: Eighteen RCTs (1285 participants) were included in this systematic review. Conbercept might improve BCVA compared to triamcinolone acetonide [MD = 0.11, 95% CI (0.08, 0.15)], and reduce CRT compared to the other four therapies (conservative treatment, ranibizumab, transpupillary thermotherapy, and triamcinolone acetonide). The incidence of AEs in patients receiving conbercept was significantly lower than those receiving triamcinolone acetonide [RR = 0.25, 95% CI (0.09-0.72)], but was similar to the other therapies. Conbercept seemed to be more effective than ranibizumab in lowering the plasma level of VEGF [MD = - 15.86, 95% CI (-23.17, -8.55)].

Conclusions: Current evidence shows that conbercept is a promising option for the treatment of wet AMD. Nevertheless, further studies are required to compare the efficacy, long-term safety and cost-effectiveness between conbercept and other anti-VEGF agents in different populations.

PMID: 29902977 DOI: 10.1186/s12886-018-0807-1
Intravitreal Bevacizumab with or without Triamcinolone for Wet Age-related Macular Degeneration: Twelve-month Results of a Prospective, Randomized Investigation.

Motarjemizadeh Q, Aidenloo NS, Abbaszadeh M, Sadrinia V.

Purpose: The purpose of this study is to compare the long-term outcomes of intravitreal bevacizumab (IVB) with a combination therapy including IVB/intravitreal triamcinolone acetonide (IVB/IVTA) in neovascular age-related macular degeneration (AMD).

Materials and Methods: This prospective, randomized clinical trial was conducted on 136 eyes of 136 patients with neovascular AMD. Eyes were randomly assigned to receive IVB alone (71 eyes) or in combination with IVTA (65 eyes). In the IVB group, three consecutive injections of 1.25 mg/0.05 ml of bevacizumab were administered 1 month apart, whereas in the IVB/IVTA group, 4 mg/0.05 mL of triamcinolone acetonide was added to bevacizumab in the first injection. Additional IVB injections were administered in eyes demonstrating active choroidal neovascularization. Best-corrected visual acuity (BCVA) and optical coherence tomography were performed at baseline as well as at all follow-up visits.

Results: No differences were seen between the patients receiving IVB and those receiving IVB/IVTA in terms of baseline BCVA (P = 0.97) and baseline central macular thickness (CMT) (P = 0.77). BCVA improved, and CMT reduced significantly in both study arms at almost all follow-up intervals. IVB/IVTA intervention, compared with IVB, was statistically more effective in improving BCVA (P = 0.01) and in reducing CMT (P = 0.02) after 12 months. The average number of reinjections was 1.25 ± 0.92 in the IVB group and 1.06 ± 1.01 in the IVB/IVTA group (P = 0.44).

Conclusion: Our results suggest that the synergistic effect of intravitreal triamcinolone and IVB for treatment of neovascular AMD shows itself most apparently after 8 months of follow-up.

PMID: 29899643 PMCID: PMC5974811 DOI: 10.4103/meajo.MEAJO_292_16

Basis and Design of a Randomized Clinical Trial to Evaluate the Effect of Levosulpiride on Retinal Alterations in Patients With Diabetic Retinopathy and Diabetic Macular Edema.


Background: Diabetic retinopathy (DR) and diabetic macular edema (DME) are potentially blinding, microvascular retinal diseases in people with diabetes mellitus. Preclinical studies support a protective role of the hormone prolactin (PRL) due to its ocular incorporation and conversion to vaso-inhibins, a family of PRL fragments that inhibit ischemia-induced retinal angiogenesis and diabetes-derived retinal vasopermeability. Here, we describe the protocol of an ongoing clinical trial investigating a new therapy for DR and DME based on elevating the circulating levels of PRL with the prokinetic, dopamine D2 receptor blocker, levosulpiride.

Methods: It is a prospective, randomized, double-blind, placebo-controlled trial enrolling male and female patients with type 2 diabetes having DME, non-proliferative DR (NPDR), proliferative DR (PDR) requiring vitrectomy, and DME plus standard intravitreal therapy with the antiangiogenic agent, ranibizumab. Patients are randomized to receive placebo (lactose pill, orally TID) or levosulpiride (75 mg/day orally TID) for 8 weeks (DME and NPDR), 1 week (the period before vitrectomy in PDR), or 12 weeks (DME plus ranibizumab). In all cases the study medication is taken on top of standard therapy for diabetes, blood pressure control, or other medical conditions. Primary endpoints in groups 1 and 2 (DME: placebo and levosulpiride), groups 3 and 4 (NPDR: placebo and levosulpiride), and groups 7 and 8 (DME plus ranibizumab: placebo and levosulpiride) are changes from baseline in visual acuity, retinal thickness assessed by optical coherence tomography, and retinal microvascular abnormalities evaluated by fundus
biomicroscopy and fluorescein angiography. Changes in serum PRL levels and of PRL and vasoinhibins levels in the vitreous between groups 5 and 6 (PDR undergoing vitrectomy: placebo and levosulpiride) serve as proof of principle that PRL enters the eye to counteract disease progression. Secondary endpoints are changes during the follow-up of health and metabolic parameters (blood pressure, glycated hemoglobin, and serum levels of glucose and creatinine). A total of 120 patients are being recruited.

Discussion: This trial will provide important knowledge on the potential benefits and safety of elevating circulating and intraocular PRL levels with levosulpiride in patients with DR and DME.

Ethics and dissemination: Ethics approval has been obtained from the Ethics Committees of the National University of Mexico (UNAM) and the Instituto Mexicano de Oftalmología, I.A.P. Dissemination will include submission to peer-reviewed scientific journals and presentation at congresses.


PMID: 29896154 PMCID: PMC5986911 DOI: 10.3389/fendo.2018.00242


The treat-and-extend injection regimen versus alternate dosing strategies in age-related macular degeneration: a systematic review and meta-analysis.

Okada M, Kandasamy R, Chong EW, McGuiness M, Guymer RH.

Purpose: To assess outcomes of the treat-and-extend (T&E) injection regimen for neovascular age related macular degeneration (AMD) as compared to either a monthly or a pro-re-nata (PRN) treatment strategy.

Design: Systematic review and meta-analysis

Methods: Studies that compared the T&E regimen with either monthly or PRN dosing for treatment-naïve AMD were included. Trial eligibility, data extraction and risk of bias were assessed according to Cochrane review methods. Estimates were pooled using random effects meta-analysis.

Results: Four eligible studies were identified, all using ranibizumab (total n=940 eyes), including two randomized controlled trials comparing T&E to monthly and two retrospective reviews comparing T&E to PRN. No studies evaluating aflibercept were identified. Improvements in vision and central retinal thickness were similar between T&E and monthly at 12 months, with a mean difference of -1.79 letters (95% CI: 3.70, 0.13) and 3.76 μm (95% CI: -13.78, 21.30) in favour of monthly injections. In contrast, visual gains were higher in the T&E compared to PRN group (difference of +6.18 letters, 95% CI: 3.28, 9.08). Fewer injections were required using the T&E regimen when compared to monthly (mean of -1.6 and -6.9 injections less at 12 and 24 months respectively). A mean of 1.44 more injections was required for the T&E compared to PRN regimen at 12 months, however this was achieved with fewer visits.

Conclusion: Despite the growing preference for the T&E regimen, there is limited head-to-head evidence comparing dosing strategies. The evidence available however, suggests that at 12 months, T&E is comparable to monthly and superior to PRN dosing for both efficacy and safety outcomes when using ranibizumab.

PMID: 29885297 DOI: 10.1016/j.ajo.2018.05.026


Ranibizumab for the Treatment of Diabetic Macular Oedema in the Real-World Clinical Setting in Portugal: A Multicentre Study.

Purpose: The purpose of this study was to evaluate the 2-year outcome of ranibizumab for diabetic macular oedema (DME) in the real-life clinical practice of five ophthalmology departments of the National Health Service (NHS) in Portugal.

Methods: This is a retrospective multicentre study. The clinical records on consecutive patients with DME from clinical practice treated with 0.5 mg intravitreal ranibizumab and followed up for 24 months were reviewed. Efficacy outcomes comprised the change in best corrected visual acuity (BCVA) and central macular thickness (CMT) evaluated by SD-OCT. Multivariate regression analysis was performed to explore predictors of BCVA.

Results: A total of 122 eyes of 93 patients were included. The median BCVA change by 24 months was +5.0 letters (IQR 12.0) (p < 0.001) and the CMT change was -89.0 µm (IQR 165.0) (p < 0.001). By 24 months, 21.4% of the eyes had gained ≥15 letters and 8.6% had lost ≥15 letters. The median number of injections given during follow-up was 5.0 (IQR 4.0). A greater baseline CMT and a more disrupted status of the external limiting membrane were predictive of worse BCVA at 24 months (p ≤ 0.015).

Conclusion: DME treatment with ranibizumab in the Portuguese NHS is associated with anatomic and functional improvement by 2 years; however, our results are below those reported in major clinical trials, and undertreatment is probably the cause.

PMID: 29886497 DOI: 10.1159/000489046

Other treatment and diagnosis

Yao Xue Xue Bao. 2016 Jul;51(7):1068-76.

Advances in the study of aptamer-based drug for targeting therapy.

[Article in Chinese]

Dou XQ, Fu J, Song HF.

Abstract: Aptamers are randomly selected from single-stranded oligonucleotide libraries by systematic evolution of ligands technology exponential enrichment(SELEX). They bind to various targets like metal ions, nucleic acids, proteins, small organic compounds, and even entire organisms. Candidate aptamers are predicted to be highly effective in producing targeting effects for certain diseases like cancer, macular degeneration, acute coronary syndrome, von Willebrand factor related disorder disease and so on. Aptamers may also serve as drug-carriers helping drugs to be released in specific regions and tissues. Compared with other types of targeting ligands, aptamers have an array of unique advantageous features, which make them promising to develop aptamer-drug conjugates(ApDCs) for targeted-oriented therapy. Deep investigation into Ap DCs discovery and development may promote the process of biological and biomedical analysis. In this review, we summarize the advances of drug discovery and drug delivery using aptamers in basic and clinical trials in recent years, and meanwhile analyze its advantages and challenges in biomedical studies.

PMID: 29897179


Analysis on the trend of innovation and development in the field of ophthalmology.

[Article in Chinese]


Objective: To systematically analyze the innovation and development trend in the field of ophthalmology.
Methods: The latest ophthalmology funding program from the National Eye Institute and National Natural Science Foundation of China, and funding project for 2012 to 2016 from the National Institutes of Health, National Natural Science Foundation of China and National key research and development plan of China was collected. Using the comparative analysis method, the major ophthalmology funding areas at home and abroad were analyzed. Papers published in 2012 to 2016 in the field of ophthalmology were collected from the Web of Science Core Collection, among which ESI highly cited papers and hot papers were particularly selected. Using bibliometric methods, the time trend of the number of papers and the citation frequency were analyzed. Using the co-occurrence cluster analysis method, the continued focuses and emerging concerns of ophthalmology papers was analyzed.

Results: The funding plan of the National Eye Institute mainly covers nine major diseases in ophthalmology. NSFC focuses on retinal damage and repair mechanisms. The National Key Research and Development Program of China focuses on research on high-end ophthalmic implants. NIH continues to focus on the molecular mechanisms of blinding eye disease such as diabetic retinopathy, age-related macular degeneration, glaucoma, corneal disease and cataracts, basic research in genetics, and advanced diagnostic techniques such as imaging. Latest areas of interest involve gene editing techniques and the application of stem cell technology in ophthalmology. In China, research and application of stem cells in ophthalmic diseases, intraocular sustained-release drug carrier, and precision medicine research in ophthalmology are emerging areas of funding. In 2012 to 2016, research topics of 168 papers collected by ESI focused on macular degeneration, retinal diseases, glaucoma and other eye diseases. How to quickly promote new drugs and new technological achievements to the clinical application is a problem in the field of ophthalmology. How to change the ophthalmology clinic model, so as to provide patients with convenient and quality service, has become a research topic that needs to be given attention to.

Conclusions: Based on the multidimensional analysis of innovation and development in the field of ophthalmology, cross application and integration of ophthalmology and high-tech fields such as advanced imaging technology, stem cell technology, gene editing technology, molecular targeting, and artificial intelligence will provide a strong basis for the enhancement of China's ophthalmology research innovation and international competitiveness. Research efforts for ophthalmic transformation should be strengthened, in order to realize the clinical application of the achievements as soon as possible.

PMID: 29895120

Pathogenesis


Loss of NAMPT in aging retinal pigment epithelium reduces NAD+ availability and promotes cellular senescence.

Jadeja RN, Powell FL, Jones MA, Fuller J, Joseph E, Thounaojam MC, Bartoli M, Martin PM.

Abstract: Retinal pigment epithelium (RPE) performs numerous functions critical to retinal health and visual function. RPE senescence is a hallmark of aging and degenerative retinal disease development. Here, we evaluated the temporal expression of key nicotinamide adenine dinucleotide (NAD+)-biosynthetic genes and associated levels of NAD+, a principal regulator of energy metabolism and cellular fate, in mouse RPE. NAD+ levels declined with age and correlated directly with decreased nicotinamide phosphoribosyltransferase (NAMPT) expression, increased expression of senescence markers (p16INK4a, p21Waf/Cip1, ApoJ, CTGF and β-galactosidase) and significant reductions in SIRT1 expression and activity. We simulated in vitro the age-dependent decline in NAD+ and the related increase in RPE senescence in human (ARPE-19) and mouse primary RPE using the NAMPT inhibitor FK866 and demonstrated the positive impact of NAD+-enhancing therapies on RPE cell viability. This, we confirmed in vivo in the RPE of mice injected sub-retinally with FK866 in the presence or absence of nicotinamide mononucleotide. Our data confirm the importance of NAD+ to RPE cell biology normally and in aging and demonstrate the potential utility of therapies targeting NAMPT and NAD+ biosynthesis to prevent or
alleviate consequences of RPE senescence in aging and/or degenerative retinal diseases in which RPE dysfunction is a crucial element.

PMID: 29905535 DOI: 10.18632/aging.101469


Oxysterol Signatures Distinguish Age-Related Macular Degeneration from Physiologic Aging.


Abstract: Macrophage aging is pathogenic in numerous diseases, including age-related macular degeneration (AMD), a leading cause of blindness in older adults. Although prior studies have explored the functional consequences of macrophage aging, less is known about its cellular basis or what defines the transition from physiologic aging to disease. Here, we show that despite their frequent self-renewal, macrophages from old mice exhibited numerous signs of aging, such as impaired oxidative respiration. Transcriptomic profiling of aged murine macrophages revealed dysregulation of diverse cellular pathways, especially in cholesterol homeostasis, that manifested in altered oxysterol signatures. Although the levels of numerous oxysterols in human peripheral blood mononuclear cells and plasma exhibited age-associated changes, plasma 24-hydroxycholesterol levels were specifically associated with AMD. These novel findings demonstrate that oxysterol levels can discriminate disease from physiologic aging. Furthermore, modulation of cholesterol homeostasis may be a novel strategy for treating age-associated diseases in which macrophage aging is pathogenic.

PMID: 29903570 DOI: 10.1016/j.ebiom.2018.05.035


Berberine Protects Human Retinal Pigment Epithelial Cells from Hydrogen Peroxide-Induced Oxidative Damage through Activation of AMPK.


Abstract: Age-related macular degeneration (AMD) is the leading cause of central vision loss in the elderly with less effective treatment, especially for dry AMD (90% of AMD). Although the etiology of this disease is not well elucidated, increasing evidences indicate that excessive reactive oxygen species (ROS) impairing the physiological functions of retinal pigment epithelium (RPE) cells may be one of the main causes. Therefore, it could be a great strategy to find some drugs that can effectively protect RPE cells from oxidative damage which is desired to treat and slow the process of AMD. In the present study, a well-known traditional Chinese medicine berberine (BBR) was found to suppress hydrogen peroxide (H₂O₂)-induced oxidative damage in D407 cells, a human RPE cell line. Pre-treatment of D407 cells with BBR significantly suppressed H₂O₂-induced cell apoptosis by restoring abnormal changes in nuclear morphology, preventing the decline of mitochondrial membrane potential, reducing lactate dehydrogenase release and inhibiting caspase 3/7 activities induced by H₂O₂. Western blot analysis showed that BBR was able to stimulate the phosphorylation/activation of AMPK in a time- and dose-dependent manner in D407 cells, while treatment of cells with AMPK pathway inhibitor Compound C, or knockdown of the AMPK by specific siRNA blocked the effect of BBR. Similar results were obtained in primary cultured human RPE cells. Taken together, these results demonstrated that BBR was able to protect RPE cells against oxidative stress via the activation of AMPK pathway. Our findings also indicate the potential application of BBR in AMD treatment.

PMID: 29895743 DOI: 10.3390/ijms19061736

Age-related macular degeneration changes the processing of visual scenes in the brain.


Abstract: In age-related macular degeneration (AMD), the processing of fine details in a visual scene, based on a high spatial frequency processing, is impaired, while the processing of global shapes, based on a low spatial frequency processing, is relatively well preserved. The present fMRI study aimed to investigate the residual abilities and functional brain changes of spatial frequency processing in visual scenes in AMD patients. AMD patients and normally sighted elderly participants performed a categorization task using large black and white photographs of scenes (indoors vs. outdoors) filtered in low and high spatial frequencies, and nonfiltered. The study also explored the effect of luminance contrast on the processing of high spatial frequencies. The contrast across scenes was either unmodified or equalized using a root-mean-square contrast normalization in order to increase contrast in high-pass filtered scenes. Performance was lower for high-pass filtered scenes than for low-pass and nonfiltered scenes, for both AMD patients and controls. The deficit for processing high spatial frequencies was more pronounced in AMD patients than in controls and was associated with lower activity for patients than controls not only in the occipital areas dedicated to central and peripheral visual fields but also in a distant cerebral region specialized for scene perception, the parahippocampal place area. Increasing the contrast improved the processing of high spatial frequency content and spurred activation of the occipital cortex for AMD patients. These findings may lead to new perspectives for rehabilitation procedures for AMD patients.

PMID: 29905126 DOI: 10.1017/S0952523817000372

Epidemiology

Einstein (Sao Paulo). 2018 Jun 7;16(2):eAO4240.

Qualitative assessment of online information about age-related macular degeneration available in Portuguese.

[Article in English, Portuguese]

Agi J, Kasahara N, Lottenberg CL.

Objective: To evaluate the quality of online information on age-related macular degeneration available in Portuguese.

Methods: The search term “age-related macular degeneration” was used to browse the web using four different search engines. The first 40 websites appearing on match lists provided by each search engine were recorded and those listed in at least three tab pages selected. The Sandvik Severity Index was used as to assess website quality.

Results: Quality of information available on selected websites was rated average (mean Sandvik Score 7.08±2.23).

Conclusion: Most websites disseminating information about age-related macular degeneration were of average quality. The need to readjust web-based information to target lay public and promote increased understanding was emphasized.

**Six-Year Incidence and Risk Factors of Age-Related Macular Degeneration in Singaporean Indians: The Singapore Indian Eye Study.**


**Abstract:** We aimed to determine the 6-year incidence and risk factors of age-related macular degeneration (AMD) in first and second generations of Singaporean Indians. Baseline examination was conducted in 2007-9 and 6-year prospective follow-up examination of this Indian population in 2013-5. All participants underwent interviews with questionnaires and comprehensive medical and eye examinations. Incidence was age-standardized to Singaporean 2010 census. Risk factors associated with AMD incidence were assessed and compared between first and second generations of immigrants. Among 2200 persons who participated in the follow-up examination (75.5% response rate), gradable fundus photographs were available in 2105. The 6-year age-standardized incidences of early and late AMD were 5.26% and 0.51% respectively. Incident early AMD was associated with cardiovascular disease history (HR 1.59, 95% CI 1.04-2.45), underweight body mass index (BMI) (HR 3.12, 95% CI 1.37-7.14) (BMI of <18.5 vs 18.51-25 kg/m2), heavy alcohol drinking (HR 3.14 95% CI 1.25-7.89) and ARMS2 rs3750847 homozygous genetic loci carrier (HR 2.52, 95% CI 1.59-3.99). We found a relatively low incidence of early AMD in this Singaporean Indian population compared to Caucasian populations. Both first and second-generation Indian immigrants have similar incidence and risk factor patterns for early AMD.

PMID: 29891972 DOI: 10.1038/s41598-018-27202-w

**Genetics and gene therapy**


Genotype-phenotype correlations of low frequency variants in the complement system in renal disease and age-related macular degeneration.


**Abstract:** Genetic alterations in the complement system have been linked to a variety of diseases, including atypical hemolytic uremic syndrome (aHUS), C3 glomerulopathy (C3G), and age-related macular degeneration (AMD). We performed sequence analysis of the complement genes CFH, CFI, and C3 in 866 aHUS/C3G and 697 AMD patients. In total we identified 505 low frequency alleles, representing 121 unique variants, of which 51 are novel. CFH contained the largest number of unique low frequency variants (n=64; 53%), followed by C3 (n=32; 26%) and CFI (n=25; 21%). A substantial number of variants were found in both patients groups (n=48; 40%), while 41 (34%) variants were found only in aHUS/C3G and 32 (26%) variants were AMD-specific. Genotype-phenotype correlations between the disease groups identified a higher frequency of protein-altering alleles in SCR20 of Factor H (FH), and in the serine protease domain of Factor I (FI) in aHUS/C3G patients. In AMD a higher frequency of protein-altering alleles was observed in SCR3, SCR5 and SCR7 of FH, the SRCR domain of FI, and in the MG3 domain of C3. In conclusion, we observed a substantial overlap of variants between aHUS/C3G and AMD, however, there is a distinct clustering of variants within specific domains. This article is protected by copyright. All rights reserved.

PMID: 29888403 DOI: 10.1111/cge.13392
Stem cells


Generation of Transplantable Retinal Pigmented Epithelial (RPE) Cells for Treatment of Age-Related Macular Degeneration (AMD).

Surendran H, Rathod RJ, Pal R.

Abstract: Age-related macular degeneration (AMD) is the foremost cause of blindness in people over the age of 60 worldwide. Clinically, this disease starts with distortion in central vision eventually leading to legal blindness. Vision loss has a significant impact on quality of life and incurs a substantial cost to the economy. Furthermore, AMD is a complex and progressive neurodegenerative disorder that triggers visual impairment due to the loss of retinal pigmented epithelium (RPE) and the light-sensitive photoreceptors that they support, protect and provide nutrition. Currently, there is no curative treatment for the most common form of this disease, i.e., dry AMD. A novel approach to treat AMD involves the transplantation of RPE cells derived from human induced pluripotent stem cells (iPSCs) in the outer retina. These iPSC-derived RPE cells not only show characteristics similar to native RPE but also could replace as well as regenerate damaged pathologic RPE and produce supportive growth factors and cytokines. Several clinical trials are being conducted taking advantage of a variety of cell- and tissue engineering-based approaches. Here, we present a simple, cost effective, and scalable cell-culture model for generation of purified RPE thus providing the foundation for developing an allogeneic cell therapy for AMD.

PMID: 29896658 DOI: 10.1007/7651_2018_140

Ophthalmology. 2018 Jun 5. pii: S0161-6420(18)30024-1. [Epub ahead of print]

Transplantation of Human Embryonic Stem Cell-Derived Retinal Pigment Epithelial Cells in Macular Degeneration.


Purpose: Transplantation of human embryonic stem cell (hESC)-derived retinal pigment epithelial (RPE) cells offers the potential for benefit in macular degeneration. Previous trials have reported improved visual acuity (VA), but lacked detailed analysis of retinal structure and function in the treated area.

Design: Phase 1/2 open-label dose-escalation trial to evaluate safety and potential efficacy (clinicaltrials.gov identifier, NCT01469832).

Participants: Twelve participants with advanced Stargardt disease (STGD1), the most common cause of macular degeneration in children and young adults.

Methods: Subretinal transplantation of up to 200,000 hESC-derived RPE cells with systemic immunosuppressive therapy for 13 weeks.

Main Outcome Measures: The primary end points were the safety and tolerability of hESC-derived RPE cell administration. We also investigated evidence of the survival of transplanted cells and measured retinal structure and function using microperimetry and spectral-domain OCT.

Results: Focal areas of subretinal hyperpigmentation developed in all participants in a dose-dependent manner in the recipient retina and persisted after withdrawal of systemic immunosuppression. We found no evidence of uncontrolled proliferation or inflammatory responses. Borderline improvements in best-corrected VA in 4 participants either were unsustained or were matched by a similar improvement in the untreated contralateral eye. Microperimetry demonstrated no evidence of benefit at 12 months in the 12 participants. In one instance at the highest dose, localized retinal thinning and reduced sensitivity in the
area of hyperpigmentation suggested the potential for harm. Participant-reported quality of life using the 25-item National Eye Institute Visual Function Questionnaire indicated no significant change.

**Conclusions**: Subretinal hyperpigmentation is consistent with the survival of viable transplanted hESC-derived RPE cells, but may reflect released pigment in their absence. The findings demonstrate the value of detailed analysis of spatial correlation of retinal structure and function in determining with appropriate sensitivity the impact of cell transplantation and suggest that intervention in early stage of disease should be approached with caution. Given the slow rate of progressive degeneration at this advanced stage of disease, any protection against further deterioration may be evident only after a more extended period of observation.

PMID: 29884405 DOI: 10.1016/j.ophtha.2018.04.037

**Diet, lifestyle and low vision**


**Carotenoids in human nutrition and health.**

Eggersdorfer M, Wyss A.

**Abstract**: Carotenoids are naturally occurring pigments found in most fruits and vegetables, plants, algae, and photosynthetic bacteria. Humans cannot synthesize carotenoids and must ingest them in food or via supplementation. Carotenoids have a range of functions in human health. They primarily exert antioxidant effects, but individual carotenoids may also act through other mechanisms; for example, β-carotene has a pro-vitamin A function, while lutein/zeaxanthin constitute macular pigment in the eye. The benefit of lutein in reducing progression of age-related macular eye disease and cataracts is strengthening; an intake recommendation would help to generate awareness in the general population to have an adequate intake of lutein rich foods. There is evidence that carotenoids, in addition to beneficial effects on eye health, also produce improvements in cognitive function and cardiovascular health, and may help to prevent some types of cancer. Despite the evidence for the health benefits of carotenoids, large population-based supplementation studies have produced mixed results for some of the carotenoids. To establish and confirm the health benefits of the different carotenoids more research, including clinical studies, is needed.

PMID: 29885291 DOI: 10.1016/j.abb.2018.06.001

**Case Reports**


**Blinding spontaneous suprachoroidal haemorrhage in anticoagulant taking wet-AMD patients.**

[Article in Hungarian]

Ecsedy M, Csákány B, Kovács I, Resch M, Nagy Z, Récsán Z.

**Abstract**: We present cases of blinding spontaneous suprachoroidal haemorrhage in anticoagulant taking wet-AMD patients. A retrospective study has been performed to present the clinical course, management and final outcome of spontaneous suprachoroidal haemorrhage in 7 eyes of six age-related macular degeneration patients seen in our clinic from January 2016 to April 2017. All patients were on chronic oral anticoagulant therapy because of cardiovascular disorder. In one patient, haematological disorder was also present modifying significantly the haemostasis. All eyes received prior anti-VEGF treatment for exsudative AMD. Acute angle closure glaucoma - with no response to topical and oral IOP lowering therapy - was the most frequent ocular complication in our cases. The final visual prognosis was usually very poor. The risk of spontaneous suprachoroidal haemorrhage is increased in wet-AMD patients who are on anticoagulant
therapy. To prevent this blinding condition, a stronger communication between ophthalmologists and cardiologists would be beneficial, with an ophthalmological check-up in this group of patients before and during the use of anticoagulants. Orv Hetil. 2018, 159(24): 985-990.

PMID: 29888658 DOI: 10.1556/650.2018.30966

**Letters**


**Generational Differences in Lifetime Exposure to Lead and the Decreasing Incidence of Age-Related Macular Degeneration.**

Fuller-Thomson E.

Letter: https://jamanetwork.com/journals/jamaophthalmology/article-abstract/2684570

PMID: 29902290 DOI: 10.1001/jamaophthalmol.2018.2163

Cruickshanks KJ.

Reply: https://jamanetwork.com/journals/jamaophthalmology/article-abstract/2684572

PMID: 29902287 DOI: 10.1001/jamaophthalmol.2018.2175