

Issue 316

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This free weekly bulletin lists the latest published research articles on macular degeneration (MD) and some other macular diseases as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases.

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Drug treatment

Eye (Lond). 2017 Feb 17. [Epub ahead of print]

Aflibercept as a Second Line Therapy for Neovascular Age Related Macular Degeneration in Israel (ASLI) study.

Tiosano L, Segal O, Mathalone N, Pollack A, Ehrlich R, Klemperer I, Barak Y, Moroz I, Chowers I, Goldstein M.

Purpose: The purpose of this study is to evaluate an early switch to aflibercept in eyes with neovascular age-related macular degeneration (nvAMD) showing partial or lack of response for initial therapy with bevacizumab.

Methods: The Aflibercept as a Second Line Therapy for Neovascular Age Related Macular Degeneration in Israel (ASLI) was a prospective, multicenter, single-arm clinical trial. Eyes with nvAMD having incomplete response to 3-9 prior bevacizumab injections were recruited. Three monthly intravitreal aflibercept (2 mg) injections were administered, followed by two bi-monthly injections and a final examination at week 28. An optional injection was allowed at week 20.

Results: Forty-seven eyes of 46 patients (mean±SD age 76±8 years) were recruited. The mean number of prior bevacizumab injections was 5.5±2.9. The mean visual acuity improved from 60.3±10 ETDRS letters at baseline to 63.1±15 letters at week 28 ($P=0.02$, paired t-test). The central subfield thickness (CST) reduced from 409±127 micron at baseline to 330±110 microns at week 4 ($P=0.0002$; paired t-test), and 277±70 microns at week 28 ($P=0.00002$; paired t-test). Twenty-two eyes had three to five prior bevacizumab injections (mean 5.1±0.7), and 25 eyes had six to nine prior injections (7.32±1.2). Both groups had reduced CST from baseline to week 28 ($P=0.0004$ and $P=0.0007$; paired t-test, respectively). Thirty-five (75%) eyes required the optional additional aflibercept injection at week 20.

Conclusions: The ASLI study demonstrated improved BCVA and reduced CST following an early switch to aflibercept therapy in eyes with prior incomplete response to initial therapy with three to nine bevacizumab injections.

PMID: 28211882

Case Rep Ophthalmol. 2016 Dec 28;7(3):301-307.

Real-Life ILUVIEN (Fluocinolone Acetonide) Case Study: Rapid Drying of the Macula and Improved Vision within 2 Years after Therapy Initiation.

Quhill H, Quhill F.

IMPORTANCE: A case showing sustained structural and functional responses 2 years after a single treatment with ILUVIEN (0.2 µg/day fluocinolone acetonide, FAc) despite suboptimal responses to

ranibizumab.

OBSERVATIONS: A 68-year-old female patient with diabetic macular oedema (DME) from type 2 diabetes mellitus was first diagnosed in October 2010 and had a baseline visual acuity (VA) of 46 Early Treatment Diabetic Retinopathy Study (ETDRS) letters in the left eye. Central foveal thickness (CFT) was 712 microns. The patient was treated with 11 intravitreal injections of ranibizumab (5 in combination with a small-interfering RNA agent), and by March 2014, VA and CFT were largely unchanged (55 ETDRS letters and 774 microns). The patient was treated with ILUVIEN as she had a pseudophakic lens and a clearly suboptimal response to the prior therapy with ranibizumab. An implant releasing FAc at a dosage of 0.2 µg/day was administered in March 2014, and the optical coherence tomography indicated that the macula was dry after 7 days (CFT was below 300 microns). This was sustained at 6, 12, and 24 months after the treatment. VA improved by 5 letters within 7 days and by 15 letters within 14 days, and this was maintained after 24 months. Throughout the duration of this study, the intraocular pressure was ≤22 mm Hg, and no glaucoma medication was administered.

CONCLUSIONS AND RELEVANCE: In real-life UK practice, this DME patient showed a suboptimal response to multiple intravitreal injections of ranibizumab. When subsequently treated with a single injection of ILUVIEN, there were large and rapid improvements in VA and CFT that were maintained for the following 2 years.

PMID: 28203186 PMCID: PMC5260609

Ophthalmic Surg Lasers Imaging Retina. 2017 Feb 1;48(2):167-169.

Significant Bilateral Response in Diabetic Macular Edema After Single Unilateral Intravitreal Aflibercept Injection.

Rahimy E, Nyong'o O, Leng T.

Abstract

A 61-year-old patient with bilateral, treatment-naïve, diffuse diabetic macular edema (DME) that had been progressing during the previous 12 months received a single intravitreal injection of aflibercept (Eylea; Regeneron, Tarrytown, NY) to the left eye. At 2-week follow-up, noticeable bilateral improvement of the DME was observed by spectral-domain optical coherence tomography imaging with commensurate improvement of visual acuity to 20/30 bilaterally. [Ophthalmic Surg Lasers Imaging Retina. 2017;48:167-169.].

PMID: 28195620

Clin Ophthalmol. 2017 Feb 1;11:299-302. eCollection 2017.

Safety of bilateral same-day intravitreal injections of anti-vascular endothelial growth factor agents.

Ruão M, Andreu-Fenoll M, Dolz-Marco R, Gallego-Pinazo R.

PURPOSE: The aim was to evaluate the safety of bilateral same-day injections with intravitreal antiangiogenic drugs for macular diseases.

METHODS: Cross-sectional retrospective review of unilateral and bilateral same-day antiangiogenic injections was conducted between January 2011 and March 2016 in the Unit of Macula, University and Polytechnic Hospital La Fe (Valencia, Spain). A total of 8,172 injections were administered, among which 6,560 were unilateral and 1,612 were bilateral injections. Patients were included in the study regardless of the diagnosis. Ranibizumab and aflibercept were the antiangiogenic drugs used. The presence of endophthalmitis or retinal detachment was evaluated.

RESULTS: A total of 1 (0.012%) culture-proven endophthalmitis and 19 (0.233%) acute intraocular inflammations were registered. In the unilateral injections group, there were 18 (0.274%) acute intraocular inflammations and 1 (0.015%) culture-proven endophthalmitis. One (0.062%) of the 1,612 bilateral same-day injections had a unilateral acute intraocular inflammation, and there were no culture-proven endophthalmitis in this group.

CONCLUSION: Bilateral same-day injections are more convenient for patients and their caregivers than the unilateral injections administered on different days. In our study, the prevalence of culture-proven endophthalmitis and acute intraocular inflammation was lower in the bilateral injections than in the unilateral group. These data support the idea that bilateral same-day injections are a safe and valid treatment to use in our clinical practice.

PMID: 28203056 PMCID: PMC5295803

Arch Soc Esp Oftalmol. 2017 Feb 9. [Epub ahead of print]

Analysis and follow-up of type 1 choroidal neovascularisation with optical coherence tomography-angiography after antiangiogenic treatment. [Article in English, Spanish]

Torrecillas-Picazo R, Cerdà-Ibáñez M, Almor Palacios I, Hervás Hernandis JM, Ramón-Cosín R, Ruiz Del Rio N, Duch-Samper A.

AIM: To describe the characteristics of type 1 choroidal neovascularisation (CNV) in age-related macular degeneration (ARMD) using two different optical coherence tomography angiography (OCT-A) devices sequentially during a standard protocol of three intravitreal injections of an anti-vascular endothelial growth factor (anti-VEGF).

METHODS: The study included 6 eyes with naïve neovascular ARMD. Macular OCT-A images were acquired using AngioPlex Cirrus HD-OCT 5000 (Carl Zeiss Meditec, Inc., Dublin, USA) and DRI OCT Triton SS-OCT Angio (Topcon, Medical Systems, Inc. Oakland, NJ, USA). The macular OCT-A scan covered an area of 3×3mm. Distinct morphological patterns and quantifiable features of the neovascular membranes were studied on en face projection images, which were taken at different stages of the follow-up.

RESULTS: Treatment response could be estimated using the OCT-A criteria of CNV activity. Higher activity scores before treatment resulted in a greater decrease in the membrane area. The estimated net decline in area ranged from 83.5% to 1.4%. The OCT-A performed one-week after treatment revealed the greatest area reductions.

CONCLUSIONS: OCT-A provides new possibilities for the non-invasive assessment of features of neovascular networks and CNV structural morphology. Newly described activity criteria can also guide therapeutic decisions, and help in evaluating responses. Quantitative and qualitative information can be provided with this technique. However, further software development and future investigation are essential to define the role of this tool on a daily basis.

PMID: 28189273

J Fr Ophtalmol. 2017 Feb 9. [Epub ahead of print]

[Treatment of macular hematoma complicating AMD by vitrectomy, subretinal r-TPA injection, intravitreal injection of bevacizumab combined with gas tamponade: Report of 4 cases]. [Article in French]

Abboud M, Benzerroug M, Milazzo S.

INTRODUCTION: The occurrence of a subretinal hematoma in age-related macular degeneration (AMD) is a serious complication that can impact the visual prognosis with a poor functional recovery. The

management of this complication remains controversial. Several therapeutic methods have been described. We report the results of four patients treated with a protocol combining: vitrectomy, subretinal injection of r-TPA 0.025mg/0.3ml, intravitreal injection of 0.05ml of bevacizumab and retinal tamponade with 20% SF6 gas.

PATIENTS AND METHODS: Our series consists of four patients with a submacular hematoma complicating AMD, included in succession between October 2013 and October 2014 and treated with the same treatment protocol and by the same surgeon. All patients underwent surgery within eight days after the onset of the macular hematoma. Patients with a consultation period longer than eight days did not undergo this treatment. Face down postoperative positioning was then carried out for seven days by the patients.

RESULTS: We observed a shift in the macular hematoma in the four patients, which allowed the identification of secondary neovascularization responsible for the bleeding. The visual acuity improved in three patients from hand motion (HM) preoperatively to 2/10 at one month postoperatively. One patient maintained visual acuity 1/20 during the entire follow-up despite almost complete resorption of the subretinal hematoma. These visual acuities were stable at 6 months postoperatively.

DISCUSSION: Macular subretinal hematoma can cause severe visual loss by several mechanisms. The blood accumulates between the neurosensory retina and the retinal pigment epithelium, which causes a toxic effect on the surrounding tissues, thus resulting in a loss of photoreceptors and cellular destruction in the pigment epithelium and choriocapillaris, evolving into a fibroglial scar.

CONCLUSION: The therapeutic evaluation of this protocol in our series of four patients gives a favorable result. We observed an improvement in visual acuity in 3/4 of cases. This surgical technique appears to be effective in the treatment of this complication of AMD. However, a study on a larger scale is needed to confirm these results.

PMID: 28189348

Other treatment & diagnosis

Cochrane Database Syst Rev. 2017 Feb 16;2:CD006757. [Epub ahead of print]

Surgery for cataracts in people with age-related macular degeneration.

Casparis H, Lindsley K, Kuo IC, Sikder S, Bressler NM.

BACKGROUND: Cataract and age-related macular degeneration (AMD) are common causes of decreased vision that often occur simultaneously in people over age 50. Although cataract surgery is an effective treatment for cataract-induced visual loss, some clinicians suspect that such an intervention may increase the risk of worsening of underlying AMD and thus have deleterious effects on vision.

OBJECTIVES: The objective of this review was to evaluate the effectiveness and safety of cataract surgery compared with no surgery in eyes with AMD.

SEARCH METHODS: We searched CENTRAL (which contains the Cochrane Eyes and Vision Trials Register) (2016, Issue 11), Ovid MEDLINE, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily (January 1946 to December 2016), Embase (January 1980 to December 2016), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to December 2016), the ISRCTN registry (www.isrctn.com/editAdvancedSearch), ClinicalTrials.gov (www.clinicaltrials.gov), and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictpr/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 2 December 2016.

SELECTION CRITERIA: We included randomized controlled trials (RCTs) and quasi-randomized trials that enrolled participants whose eyes were affected by both cataract and AMD in which cataract surgery was

compared with no surgery.

DATA COLLECTION AND ANALYSIS: Two review authors independently evaluated the search results against the inclusion and exclusion criteria. Two review authors independently extracted data, assessed risk of bias for included studies, and graded the certainty of evidence. We followed methods as recommended by Cochrane.

MAIN RESULTS: We included two RCTs with a total of 114 participants (114 study eyes) with visually significant cataract and AMD. We identified no ongoing trials. Participants in each RCT were randomized to immediate cataract surgery (within two weeks of enrollment) or delayed cataract surgery (six months after enrollment). The risk of bias was unclear for most domains in each study; one study was registered prospectively. In one study conducted in Australia outcomes were reported only at six months (before participants in the delayed-surgery group had cataract surgery). At six months, the immediate-surgery group showed mean improvement in best-corrected visual acuity (BCVA) compared with the delayed-surgery group (mean difference (MD) -0.15 LogMAR, 95% confidence interval (CI) -0.28 to -0.02; 56 participants; moderate-certainty evidence). In the other study, conducted in Austria, outcomes were reported only at 12 months (12 months after participants in the immediate-surgery group and six months after participants in the delayed-surgery group had cataract surgery). There was uncertainty as to which treatment group had better improvement in distance visual acuity at 12 months (unit of measure not reported; very low-certainty evidence). At 12 months, the mean change from baseline between groups in cumulated drusen or geographic atrophy area size was small and there was uncertainty which, if either, of the groups was favored (MD 0.76, 95% CI -8.49 to 10.00; 49 participants; low-certainty evidence). No participant in one study had exudative AMD develop in the study eye during 12 months of follow-up; in the other study, choroidal neovascularization developed in the study eye of 1 of 27 participants in the immediate-surgery group versus 0 of 29 participants in the delayed-surgery group at six months (risk ratio 3.21, 95% CI 0.14 to 75.68; 56 participants; very low-certainty evidence). Quality of life was measured using two different questionnaires. Scores on the Impact of Vision Impairment (IVI) questionnaire suggested that the immediate-surgery group fared better regarding vision-related quality of life than the delayed-surgery group at six months (MD in IVI logit scores 1.60, 95% CI 0.61 to 2.59; low-certainty evidence). However, we could not analyze scores from the Visual Function-14 (VF-14) questionnaire from the other study due to insufficient data. No postoperative complication was reported from either study.

AUTHORS' CONCLUSIONS: At this time, it is not possible to draw reliable conclusions from the available data as to whether cataract surgery is beneficial or harmful in people with AMD after 12 months. Although cataract surgery provides short-term (six months) improvement in BCVA in eyes with AMD compared with no surgery, it is unclear whether the timing of surgery has an effect on long-term outcomes. Physicians must make recommendations to their AMD patients regarding cataract surgery based on experience and clinical judgment until large controlled trials are conducted and their findings published. There is a need for prospective RCTs in which cataract surgery is compared with no surgery in people with AMD to better evaluate whether cataract surgery is beneficial or harmful in all or a subset of AMD patients. However, ethical considerations preclude withholding surgery, or delaying it for several years, if it may be a potentially beneficial treatment. Designers of future trials are encouraged to utilize existing standardized systems for grading cataract and AMD and for measuring key outcomes: visual acuity, change in visual acuity, worsening of AMD, quality of life measures, and adverse events.

PMID: 28206671

BMJ Open. 2017 Feb 14;7(2):e012790. doi: 10.1136/bmjopen-2016-012790.

Healthcare experiences of patients with age-related macular degeneration: have things improved? Cross-sectional survey responses of Macular Society members in 2013 compared with 1999.

Boxell EM, Amoaku WM, Bradley C.

OBJECTIVE: To investigate healthcare experiences of patients with age-related macular degeneration (AMD) and determine whether a previous survey and Royal College of Ophthalmologists (RCOphth)

management guidelines brought improvements.

DESIGN: Cross-sectional survey of Macular Society members in 2013 compared with previous 1999 survey.

SETTING: UK Postal Questionnaires.

PARTICIPANTS: 1169 respondents in 2013 (1187 in 1999).

INTERVENTION: Publication of 1999 survey results (2002), and RCOphth AMD guidelines (2009).

MAIN OUTCOME MEASURES: Respondents answered questions about experiences at diagnosis. Five questions were replicated from the 1999 survey for direct comparison in the 2013 survey which included additional questions based on 2009 RCOphth recommendations for information and support provision for patients with AMD.

RESULTS: Most 2013 survey respondents were given the name of their macular condition (91%), felt the healthcare professional was interested in them (71%) and were satisfied overall with the diagnostic consultation (76%). These outcomes show significant improvement since 1999. Within the 2013 sample, multivariable analyses showed gradual trends of improvement over time in: provision of written information, Macular Society information and receiving appropriate help, support and advice at diagnosis. Only overall satisfaction with the diagnostic consultation (but not the other nine areas of information and support provision studied) significantly improved in the time after publication of the RCOphth 2009 guidelines. There were no significant improvements associated with the publication of the 1999 survey results. Low information and support provision remained, for example, 44% of respondents diagnosed after the RCOphth 2009 guidelines reported not receiving information on what to do if vision deteriorated. Lack of such information at diagnosis was significantly associated with registration as sight impaired ($p < 0.01$). Reports of general practitioner (GP) knowledge of AMD remained low: 39% reported their GP was 'not at all well informed'. The 2013 respondents reported lower levels of help and support from GPs than 1999 respondents ($p < 0.001$).

CONCLUSIONS: Patients diagnosed with AMD after 1999 (vs before 1999) reported better experiences at diagnostic consultation. However, information and support provision at diagnosis, and satisfaction with GPs remained low.

PMID: 28196945

Retina. 2017 Feb 10. [Epub ahead of print]

DYNAMISM OF DOT SUBRETINAL DRUSENOID DEPOSITS IN AGE-RELATED MACULAR DEGENERATION DEMONSTRATED WITH ADAPTIVE OPTICS IMAGING.

Zhang Y, Wang X, Godara P, Zhang T, Clark ME, Witherspoon CD, Spaide RF, Owsley C, Curcio CA.

PURPOSE: To investigate the natural history of dot subretinal drusenoid deposits (SDD) in age-related macular degeneration, using high-resolution adaptive optics scanning laser ophthalmoscopy.

METHODS: Six eyes of four patients with intermediate age-related macular degeneration were studied at baseline and 1 year later. Individual dot SDD within the central 30° retina were examined with adaptive optics scanning laser ophthalmoscopy and optical coherence tomography.

RESULTS: A total of 269 solitary SDD were identified at baseline. Over 12.25 ± 1.18 months, all 35 Stage 1 SDD progressed to advanced stages. Eighteen (60%) Stage 2 lesions progressed to Stage 3 and 12 (40%) remained at Stage 2. Of 204 Stage 3 SDD, 12 (6.4%) disappeared and the rest remained. Twelve new SDD were identified, including 6 (50%) at Stage 1, 2 (16.7%) at Stage 2, and 4 (33.3%) at Stage 3. The mean percentage of the retina affected by dot SDD, measured by the adaptive optics scanning laser ophthalmoscopy, increased in 5/6 eyes (from 2.31% to 5.08% in the most changed eye) and decreased slightly in 1/6 eye (from 10.67% to 10.54%). Dynamism, the absolute value of the areas affected by new

and regressed lesions, ranged from 0.7% to 9.3%.

CONCLUSION: Adaptive optics scanning laser ophthalmoscopy reveals that dot SDD, like drusen, are dynamic.

PMID: 28196054

Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):1054-1062.

Classification of Exudative Age-Related Macular Degeneration With Pachyvessels on En Face Swept-Source Optical Coherence Tomography.

Ng DS, Bakthavatsalam M, Lai FH, Cheung CY, Cheung GC, Tang FY, Tsang CW, Lai TY, Wong TY, Brelén ME.

PURPOSE: The purpose of this study was to classify exudative maculopathy by the presence of pachyvessels on en face swept-source optical coherence tomography (SSOCT).

METHODS: Consecutive patients with signs of exudative maculopathy underwent SSOCT, fluorescein and indocyanine green angiography (ICGA), ultra-widefield fundus color photography, and autofluorescence examinations. Images were analyzed in a masked fashion by two sets of four examiners in different sessions: (1) the presence of pachyvessels in en face OCT and (2) features of exudative maculopathy in conventional imaging modalities. Quantitative data obtained were subfoveal choroidal thickness (SFCT) and choroidal vascularity index (CVI), which was the ratio of choroidal vessels lumen area to a specified choroidal area from binarized cross-sectional OCT scans.

RESULTS: Pachyvessels was observed in 38 (52.1%) of 73 eyes. The pachyvessels group was associated with younger age (69.1 ± 9.4 years, odds ratio [OR] = 0.95, 95% confidence interval [95% CI] = 0.90-0.97, $P = 0.04$), presence of polypoidal lesions (OR = 3.27, 95% CI = 1.24-8.62, $P = 0.01$), increased SFCT (OR = 1.08, 95% CI = 1.02-1.14, $P < 0.01$), and increased CVI (65.4 ± 5.3 , OR = 1.12, 95% CI = 1.02-1.23, $P = 0.01$). In multivariate regression, CVI significantly correlated with pachyvessels (OR = 1.24, 95% CI = 1.03-1.55, $P = 0.04$).

CONCLUSIONS: Exudative maculopathy could be classified based on differences in choroidal vasculature morphology. Current results implied that choroidal hemodynamics may be relevant to variable natural history and treatment response in neovascular AMD and polypoidal choroidal vasculopathy.

PMID: 28195603

EURASIP J Bioinform Syst Biol. 2014 Oct 7;2014:18. eCollection 2014.

Discovering irregular pupil light responses to chromatic stimuli using waveform shapes of pupillograms.

Nakayama M, Nowak W, Ishikawa H, Asakawa K, Ichibe Y.

BACKGROUND: The waveforms of the pupillary light reflex (PLR) can be analyzed in a diagnostic test that allows for differentiation between disorders affecting photoreceptors and disorders affecting retinal ganglion cells, using various signal processing techniques. This procedure has been used on both healthy subjects and patients with age-related macular degeneration (AMD), as a simple diagnostic procedure is required for diagnosis.

RESULTS: The Fourier descriptor technique is used to extract the features of PLR waveform shapes of pupillograms and their amplitudes. To detect those patients affected by AMD using the extracted features, multidimensional scaling (MDS) and clustering techniques were used to emphasize stimuli and subject differences. The detection performance of AMD using the features and the MDS technique shows only a

qualitative tendency, however. To evaluate the detection performance quantitatively, a set of combined features was created to evaluate characteristics of the PLR waveform shapes in detail. Classification performance was compared across three categories (AMD patients, aged, and healthy subjects) using the Random Forest method, and weighted values were optimized using variations of the classification error rates. The results show that the error rates for healthy pupils and AMD-affected pupils were low when the value of the coefficient for a combination of PLR amplitudes and features of waveforms was optimized as 1.5. However, the error rates for patients with age-affected eyes was not low.

CONCLUSIONS: A classification procedure for AMD patients has been developed using the features of PLR waveform shapes and their amplitudes. The results show that the error rates for healthy PLRs and AMD PLRs were low when the Random Forest method was used to produce the classification. The classification of pupils of patients with age-affected eyes should be carefully considered in order to produce optimum results.

PMID: 28194168 PMCID: PMC5270378

Surv Ophthalmol. 2017 Feb 8. [Epub ahead of print]

Retinal Angiomatous Proliferation.

Tsai AS, Cheung N, Gan AT, Jaffe GJ, Sivaprasad S, Wong TY, Cheung CM.

Abstract: Retinal angiomatous proliferation (RAP) is a unique variant of neovascular age-related macular degeneration (nAMD). Published studies have estimated that up to 15% of patients with nAMD have RAP. Clinical features frequently associated with RAP include bilateral disease, presence of pigment epithelial detachments and reticular pseudodrusen. RAP is more frequently associated with the development of retinal pigment epithelial tears and geographic atrophy that can lead to severe vision loss. Recent advances in retinal and choroidal imaging technology have furthered our understanding of RAP. Although indocyanine green angiography remains the gold-standard diagnostic tool, optical coherence tomography has improved the precision by which nAMD with RAP lesions can be diagnosed, staged and monitored. Anti-vascular endothelial growth factor therapy is currently the first line of treatment. Other treatment options including combination of photodynamic therapy with anti-angiogenic agent intravitreal injections or corticosteroids may also achieve a reasonable therapeutic outcome; however, RAP may portend a more guarded visual prognosis than typical choroidal neovascularization because of variable treatment response and dependence on the disease stage. Future basic and clinical research is needed to clarify the pathophysiology, definition and classification, optimal treatment regimen and long-term outcome of RAP.

PMID: 28189495

Pathogenesis

Exp Mol Med. 2017 Feb 17;49(2):e294.

Ig-like domain 6 of VCAM-1 is a potential therapeutic target in TNF α -induced angiogenesis.

Kim TK, Park CS, Na HJ, Lee K, Yoon A, Chung J, Lee S.

Abstract: Tumor necrosis factor alpha (TNF α)-induced angiogenesis plays important roles in the progression of various diseases, including cancer, wet age-related macular degeneration, and rheumatoid arthritis. However, the relevance and role of vascular cell adhesion molecule-1 (VCAM-1) in angiogenesis have not yet been clearly elucidated. In this study, VCAM-1 knockdown shows VCAM-1 involvement in TNF α -induced angiogenesis. Through competitive blocking experiments with VCAM-1 Ig-like domain 6 (VCAM-1-D6) protein, we identified VCAM-1-D6 as a key domain regulating TNF α -induced vascular tube formation. We demonstrated that a monoclonal antibody specific to VCAM-1-D6 suppressed TNF α -induced endothelial cell migration and tube formation and TNF α -induced vessel sprouting in rat aortas. We also

found that the antibody insignificantly affected endothelial cell viability, morphology and activation. Finally, the antibody specifically blocked VCAM-1-mediated cell-cell contacts by directly inhibiting VCAM-1-D6-mediated interaction between VCAM-1 molecules. These findings suggest that VCAM-1-D6 may be a potential novel therapeutic target in TNF α -induced angiogenesis and that antibody-based modulation of VCAM-1-D6 may be an effective strategy to suppress TNF α -induced angiogenesis.

PMID: 28209985

Mol Ther. 2017 Feb 12. [Epub ahead of print]

Systemic Injection of RPE65-Programmed Bone Marrow-Derived Cells Prevents Progression of Chronic Retinal Degeneration.

Qi X, Pay SL, Yan Y, Thomas J Jr, Lewin AS, Chang LJ, Grant MB, Boulton ME.

Abstract: Bone marrow stem and progenitor cells can differentiate into a range of non-hematopoietic cell types, including retinal pigment epithelium (RPE)-like cells. In this study, we programmed bone marrow-derived cells (BMDCs) ex vivo by inserting a stable RPE65 transgene using a lentiviral vector. We tested the efficacy of systemically administered RPE65-programmed BMDCs to prevent visual loss in the superoxide dismutase 2 knockdown (Sod2 KD) mouse model of age-related macular degeneration. Here, we present evidence that these RPE65-programmed BMDCs are recruited to the subretinal space, where they repopulate the RPE layer, preserve the photoreceptor layer, retain the thickness of the neural retina, reduce lipofuscin granule formation, and suppress microgliosis. Importantly, electroretinography and optokinetic response tests confirmed that visual function was significantly improved. Mice treated with non-modified BMDCs or BMDCs pre-programmed with LacZ did not exhibit significant improvement in visual deficit. RPE65-BMDC administration was most effective in early disease, when visual function and retinal morphology returned to near normal, and less effective in late-stage disease. This experimental paradigm offers a minimally invasive cellular therapy that can be given systemically overcoming the need for invasive ocular surgery and offering the potential to arrest progression in early AMD and other RPE-based diseases.

PMID: 28202390

J Neurodegener Dis. 2017;2017:4810232. Epub 2017 Jan 18.

Disturbed Matrix Metalloproteinase Pathway in Both Age-Related Macular Degeneration and Alzheimer's Disease.

Hussain AA, Lee Y, Zhang JJ, Francis PT, Marshall J.

Purpose: Abnormal protein deposits including β -amyloid, found in ageing Bruch's membrane and brain, are susceptible to degradation by matrix metalloproteinases (MMPs). In ageing Bruch's membrane, these MMPs become less effective due to polymerisation and aggregation reactions (constituting the MMP Pathway), a situation much advanced in age-related macular degeneration (AMD). The likely presence of this MMP Pathway in brain with the potential to compromise the degradation of β -amyloid associated with Alzheimer's disease (AD) has been investigated.

Methods: Presence of high molecular weight MMP species (HMW1 and HMW2) together with the much larger aggregate termed LMMC was determined by standard zymographic techniques. Centrifugation and gel filtration techniques were used to separate and quantify the distribution between bound and free MMP species.

Results: The MMP Pathway, initially identified in Bruch's membrane, was also present in brain tissue. The various MMP species displayed bound-free equilibrium and in AD samples, the amount of bound HMW1 and pro-MMP9 species was significantly reduced ($p < 0.05$). The abnormal operation of the MMP Pathway in AD served to reduce the degradation potential of the MMP system.

Conclusion: The presence and abnormalities of the MMP Pathway in both brain and ocular tissues may therefore contribute to the anomalous deposits associated with AD and AMD.

PMID: 28197357 PMCID: PMC5286539

Cell Rep. 2017 Feb 14;18(7):1606-1613.

FGF21 Administration Suppresses Retinal and Choroidal Neovascularization in Mice.

Fu Z, Gong Y, Liegl R, Wang Z, Liu CH, Meng SS, Burnim SB, Saba NJ, Fredrick TW, Morss PC, Hellstrom A, Talukdar S, Smith LE.

Abstract: Pathological neovascularization, a leading cause of blindness, is seen in retinopathy of prematurity, diabetic retinopathy, and age-related macular degeneration. Using a mouse model of hypoxia-driven retinal neovascularization, we find that fibroblast growth factor 21 (FGF21) administration suppresses, and FGF21 deficiency worsens, retinal neovessel growth. The protective effect of FGF21 against neovessel growth was abolished in adiponectin (APN)-deficient mice. FGF21 administration also decreased neovascular lesions in two models of neovascular age-related macular degeneration: very-low-density lipoprotein-receptor-deficient mice with retinal angiomatous proliferation and laser-induced choroidal neovascularization. FGF21 inhibited tumor necrosis α (TNF- α) expression but did not alter Vegfa expression in neovascular eyes. These data suggest that FGF21 may be a therapeutic target for pathologic vessel growth in patients with neovascular eye diseases, including retinopathy of prematurity, diabetic retinopathy, and age-related macular degeneration.

PMID: 28199833

Oxid Med Cell Longev. 2017;2017:3187594. Epub 2017 Jan 19.

Sirtuins Expression and Their Role in Retinal Diseases.

Balaiya S, Abu-Amero KK, Kondkar AA, Chalam KV.

Abstract: Sirtuins have received considerable attention since the discovery that silent information regulator 2 (Sir2) extends the lifespan of yeast. Sir2, a nicotinamide adenine dinucleotide- (NAD-) dependent histone deacetylase, serves as both a transcriptional effector and energy sensor. Oxidative stress and apoptosis are implicated in the pathogenesis of neurodegenerative eye diseases. Sirtuins confer protection against oxidative stress and retinal degeneration. In mammals, the sirtuin (SIRT) family consists of seven proteins (SIRT1-SIRT7). These vary in tissue specificity, subcellular localization, and enzymatic activity and targets. In this review, we present the current knowledge of the sirtuin family and discuss their structure, cellular location, and biological function with a primary focus on their role in different neuroophthalmic diseases including glaucoma, optic neuritis, and age-related macular degeneration. The potential role of certain therapeutic targets is also described.

PMID: 28197299 PMCID: PMC5288547

Oxid Med Cell Longev. 2017;2017:9208489. Epub 2017 Jan 18.

Retinal Diseases Associated with Oxidative Stress and the Effects of a Free Radical Scavenger (Edaravone).

Masuda T, Shimazawa M, Hara H.

Abstract: Oxidative stress plays a pivotal role in developing and accelerating retinal diseases including age-related macular degeneration (AMD), glaucoma, diabetic retinopathy (DR), and retinal vein occlusion (RVO). An excess amount of reactive oxygen species (ROS) can lead to functional and morphological

impairments in retinal pigment epithelium (RPE), endothelial cells, and retinal ganglion cells (RGCs). Here we demonstrate that edaravone, a free radical scavenger, decreased apoptotic cell death, oxidative damage to DNA and lipids, and angiogenesis through inhibiting JNK and p38 MAPK pathways in AMD, glaucoma, DR, and RVO animal models. These data suggest that the therapeutic strategy for targeting oxidative stress may be important for the treatment of these ocular diseases, and edaravone may be useful for treating retinal diseases associated with oxidative stress.

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J Nat Sci. 2017 Jan;3(1).

Insights from Genetic Model Systems of Retinal Degeneration: Role of Epsins in Retinal Angiogenesis and VEGFR2 Signaling.

Dong Y, Cai X, Wu Y, Liu Y, Deng L, Chen H.

Abstract: The retina is a light sensitive tissue that contains specialized photoreceptor cells called rods and cones which process visual signals. These signals are relayed to the brain through interneurons and the fibers of the optic nerve. The retina is susceptible to a variety of degenerative diseases, including age-related macular degeneration (AMD), diabetic retinopathy (DR), retinitis pigmentosa (RP) and other inherited retinal degenerations. In order to reveal the mechanism underlying these diseases and to find methods for the prevention/treatment of retinal degeneration, animal models have been generated to mimic human eye diseases. In this paper, several well-characterized and commonly used animal models are reviewed. Of particular interest are the contributions of these models to our understanding of the mechanisms of retinal degeneration and thereby providing novel treatment options including gene therapy, stem cell therapy, nanomedicine, and CRISPR/Cas9 genome editing. Role of newly-identified adaptor protein epsins from our laboratory is discussed in retinal angiogenesis and VEGFR2 signaling.

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Oral Bisphosphonates and Risk of Wet Age-Related Macular Degeneration.

Grzybowski A, Iribarren R, Iribarren G, Honda S.

PMID: 28190512

Am J Ophthalmol. 2017 Feb 9. [Epub ahead of print]

Oral Bisphosphonates and Risk of Wet Age-Related Macular Degeneration.

Mammo Z, Guo M, Maberley D, Matsubara J, Etminan M.

PMID: 28190509

Curr Opin Struct Biol. 2017 Feb 9;44:111-118. [Epub ahead of print]

The lectin self of complement factor H.

Blaum BS.

Abstract: Complement, a part of the humoral innate immune system, is divided into three pathways. The classical and mannose-binding lectin pathways are triggered by specific recognition of foreign targets.

Conversely, the alternative pathway (AP) is actively down-regulated on host tissue. Glycosaminoglycans (GAGs) and sialylated glycans mediate host recognition of the AP as self-associated molecular patterns (SAMPs) to the regulatory protein factor H (FH). This review summarizes the more recent years of research on SAMP recognition by FH from a structural biology point of view and discusses implications for two complement-associated conditions, age-related macular degeneration (AMD) and atypical hemolytic uremic syndrome (aHUS). Taking into account crystal structures that elucidated FH binding to a bacterial evasion protein and to the thioester domain of C3b, the target of FH-mediated AP restriction, a novel atomistic model for the mechanism by which FH prevents AP activation on self surfaces is proposed.

PMID: 28189794

Epidemiology

Ophthalmology. 2017 Feb 14. [Epub ahead of print]

Vitreomacular Adhesion and the Risk of Neovascular Age-Related Macular Degeneration.

Maggio E, Polito A, Guerriero M, Prigione G, Parolini B, Pertile G.

PURPOSE: To assess the prevalence of vitreomacular adhesion (VMA) in consecutive naïve eyes diagnosed with exudative age-related macular degeneration (AMD) in comparison with eyes with nonexudative AMD and age-matched controls, and to evaluate prospectively the incidence of vitreomacular interface changes over time and their influence on choroidal neovascularization (CNV) development.

DESIGN: Retrospective cross-sectional analysis and longitudinal cohort study conducted at Sacrocuore Hospital, Negrar, Verona, Italy.

PARTICIPANTS: A total of 1067 eyes examined at Sacrocuore Hospital between August 2008 and June 2015 met the inclusion criteria and were evaluated in this study.

METHODS: Eyes were classified into 3 groups: 403 eyes of 364 patients (mean [standard deviation; SD] age 77.8 [8.0] years) affected by exudative AMD; 350 eyes of 298 subjects (mean [SD] age 78.1 [8.2] years) with nonexudative AMD; and 314 eyes of 214 subjects (mean [SD] age 74.2 [8.2] years) with no signs of AMD enrolled as the control group. The vitreomacular interface status was evaluated by spectral-domain optical coherence tomography (OCT) and was graded according to the OCT-based International Classification System developed by the International Vitreomacular Traction Study Group by 2 independent masked observers.

RESULTS: VMA was present in 101 (25.1%) eyes with exudative AMD, 84 (24.0%) eyes with nonexudative AMD, and 84 (26.8%) eyes with no signs of AMD (no statistical difference was found; $P = 0.3384$). Spontaneous release of VMA (RVMA) was found in 15 (15.3%) eyes with exudative AMD, 21 (28.0%) eyes with nonexudative AMD, and 10 (24.4%) eyes with no signs of AMD over a mean follow-up of 25.5, 25.9, and 24.1 months, respectively. The incidence of RVMA in exudative AMD eyes was significantly lower compared with nonexudative ($P = 0.0207$) and lower, but not statistically significant, with respect to eyes with no signs of AMD ($P = 0.1013$). In eyes with nonexudative AMD, de novo development of CNV occurred in 91 eyes (30.6%). There was no significant difference regarding the rate of CNV development in the presence or absence of VMA ($P = 0.0966$).

CONCLUSIONS: The present study found no significant difference in the prevalence of VMA in eyes affected by AMD compared with age-matched controls and no difference in the rate of de novo CNV development in eyes with or without VMA. Conversely, a lower incidence of RVMA over time was found in eyes affected by exudative AMD. The results of this study suggest that VMA might be a consequence rather than a causative factor in the development of CNV.

PMID: 28214102

Retina. 2017 Feb 10. [Epub ahead of print]

ANGIOGRAPHIC SUBTYPES OF POLYPOIDAL CHOROIDAL VASCULOPATHY IN TAIWAN: A Prospective Multicenter Study.

Yeung L, Kuo CN, Chao AN, Chen KJ, Wu WC, Lai CH, Wang NK, Hwang YS, Chen CL, Lai CC.

PURPOSE: To determine the incidence and clinical characteristics of angiographic subtypes of polypoidal choroidal vasculopathy (PCV).

METHODS: It is a prospective, multicenter, cross-sectional study. Patients with newly diagnosed exudative macular degeneration are classified into PCV, age-related macular degeneration (AMD), and retinal angiomatous proliferation. Polypoidal choroidal vasculopathy is further classified into two subtypes depending on the presence (Type 1: polypoidal choroidal neovascularization) or absence (Type 2: typical PCV) of feeder vessels on indocyanine green angiography.

RESULTS: We enrolled 169 patients: 76 (45%) with PCV, 75 (44.4%) with AMD, and 14 (8.3%) with retinal angiomatous proliferation. Of the patients with PCV, 20 (26%) were classified as Type 1 PCV and 56 (74%) were classified as Type 2 PCV. The Type 1 PCV had a similar mean age compared to the AMD group (73.1 ± 9.6 vs. 75.6 ± 8.8 years, $P = 0.281$) and the Type 2 PCV (68.8 ± 9.6 years) was younger than the AMD group ($P < 0.001$). Type 1 PCV presented with worse visual acuity compared with the AMD. Both PCV subtypes had a higher incidence of hemorrhagic complications (85% and 75% respectively).

CONCLUSION: Type 2 PCV is more common than Type 1 PCV in Taiwan. Our results support the hypothesis that polypoidal choroidal neovascularization and typical PCV may be distinct entities.

PMID: 28196060

Genetics

Genet Epidemiol. 2017 Feb 15. [Epub ahead of print]

Genetic risk models: Influence of model size on risk estimates and precision.

Shan Y, Tromp G, Kuivaniemi H, Smelser DT, Verma SS, Ritchie MD, Elmore JR, Carey DJ, Conley YP, Gorin MB, Weeks DE.

Abstract: Disease risk estimation plays an important role in disease prevention. Many studies have found that the ability to predict risk improves as the number of risk single-nucleotide polymorphisms (SNPs) in the risk model increases. However, the width of the confidence interval of the risk estimate is often not considered in the evaluation of the risk model. Here, we explore how the risk and the confidence interval width change as more SNPs are added to the model in the order of decreasing effect size, using both simulated data and real data from studies of abdominal aortic aneurysms and age-related macular degeneration. Our results show that confidence interval width is positively correlated with model size and the majority of the bigger models have wider confidence interval widths than smaller models. Once the model size is bigger than a certain level, the risk does not shift markedly, as 100% of the risk estimates of the one-SNP-bigger models lie inside the confidence interval of the one-SNP-smaller models. We also created a confidence interval-augmented reclassification table. It shows that both more effective SNPs with larger odds ratios and less effective SNPs with smaller odds ratios contribute to the correct decision of whom to screen. The best screening strategy is selected and evaluated by the net benefit quantity and the reclassification rate. We suggest that individuals whose upper bound of their risk confidence interval is above the screening threshold, which corresponds to the population prevalence of the disease, should be screened.

PMID: 28198095

Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):1076-1083.

Identification of ANGPT2 as a New Gene for Neovascular Age-Related Macular Degeneration and Polypoidal Choroidal Vasculopathy in the Chinese and Japanese Populations.

Ma L, Brelen ME, Tsujikawa M, Chen H, Chu WK, Lai TY, Ng DS, Sayanagi K, Hara C, Hashida N, Chan VC, Tam PO, Young AL, Chen W, Nishida K, Pang CP, Chen LJ.

PURPOSE: We determine the angiopoietin 2 (ANGPT2) gene as a new susceptibility gene for neovascular age-related macular degeneration (nAMD) and polypoidal choroidal vasculopathy (PCV).

METHODS: A total of 34 haplotype-tagging single-nucleotide polymorphisms (SNPs) were first genotyped in an exploratory Hong Kong Chinese cohort. Suggestive SNPs were replicated in a Shantou Chinese cohort and an Osaka Japanese cohort, with a total of 2343 subjects. The SNP rs800292 in the complement factor H (CFH) gene was genotyped in all the subjects. Genetic association and gene-gene interaction were analyzed.

RESULTS: In the Hong Kong cohort, four SNPs in ANGPT2 (rs13255574, rs4455855, rs13269021, and rs11775442) were nominally associated with nAMD and PCV. The four ANGPT2 SNPs showed the same trends of association in the Shantou and Osaka cohorts. Combining the data from the 3 study cohorts revealed that SNPs rs4455855 and rs13269021 achieved study-wise significance ($P < 0.0016$), conferring an approximately 1.3-fold of increased risk for nAMD and PCV. Interaction analysis revealed the CFH SNP rs800292 has a highly significant interaction with the ANGPT2 SNP rs13269021 in nAMD and PCV in the combined analysis. Subsequent stratification analysis confirmed the interaction.

CONCLUSIONS: This study reveals ANGPT2 as a new susceptibility gene for nAMD and PCV, and it may affect disease susceptibility in association with CFH. Thus, this report provides new insights into the genetic architecture of nAMD and PCV.

PMID: 28192798

Genome Res. 2017 Feb 16. [Epub ahead of print]

Genome surgery using Cas9 ribonucleoproteins for the treatment of age-related macular degeneration.

Kim K, Park SW, Kim JH, Lee SH, Kim D, Koo T, Kim KE, Kim JH, Kim JS.

Abstract: RNA-guided genome surgery using CRISPR-Cas9 nucleases has shown promise for the treatment of diverse genetic diseases. Yet, the potential of such nucleases for therapeutic applications in nongenetic diseases is largely unexplored. Here, we focus on age-related macular degeneration (AMD), a leading cause of blindness in adults, which is associated with retinal overexpression of, rather than mutations in, the VEGFA gene. Subretinal injection of preassembled, Vegfa gene-specific Cas9 ribonucleoproteins (RNPs) into the adult mouse eye gave rise to mutagenesis at the target site in the retinal pigment epithelium. Furthermore, Cas9 RNPs effectively reduced the area of laser-induced choroidal neovascularization (CNV) in a mouse model of AMD. Genome-wide profiling of Cas9 off-target effects via Digenome-seq showed that off-target mutations were rarely induced in the human genome. Because Cas9 RNPs can function immediately after in vivo delivery and are rapidly degraded by endogenous proteases, their activities are unlikely to be hampered by antibody- and cell-mediated adaptive immune systems. Our results demonstrate that in vivo genome editing with Cas9 RNPs has the potential for the local treatment for nongenetic degenerative diseases, expanding the scope of RNA-guided genome surgery to a new dimension.

PMID: 28209587

Stem Cells

Stem Cells Transl Med. 2017 Feb;6(2):444-457. Epub 2016 Sep 9.

Multimodal Delivery of Isogenic Mesenchymal Stem Cells Yields Synergistic Protection from Retinal Degeneration and Vision Loss.

Bakondi B, Girman S, Lu B, Wang S.

Abstract: We previously demonstrated that subretinal injection (SRI) of isogenic mesenchymal stem cells (MSCs) reduced the severity of retinal degeneration in Royal College of Surgeons rats in a focal manner. In contrast, intravenous MSC infusion (MSCIV) produced panoptic retinal rescue. By combining these treatments, we now show that MSCIV supplementation potentiates the MSCSRI-mediated rescue of photoreceptors and visual function. Electrophysiological recording from superior colliculi revealed 3.9-fold lower luminance threshold responses (LTRs) and 22% larger functional rescue area from combined treatment compared with MSCSRI alone. MSCIV supplementation of sham (saline) injection also improved LTRs 3.4-fold and enlarged rescue areas by 27% compared with saline alone. We confirmed the involvement of MSC chemotaxis for vision rescue by modulating C-X-C chemokine receptor 4 activity before MSCIV but without increased retinal homing. Rather, circulating platelets and lymphocytes were reduced 3 and 7 days after MSCIV, respectively. We demonstrated MSCSRI-mediated paracrine support of vision rescue by SRI of concentrated MSC-conditioned medium and assessed function by electroretinography and optokinetic response. MSC-secreted peptides increased retinal pigment epithelium (RPE) metabolic activity and clearance of photoreceptor outer segments *ex vivo*, which was partially abrogated by antibody blockade of trophic factors in concentrated MSC-conditioned medium, or their cognate receptors on RPE. These data support multimodal mechanisms for MSC-mediated retinal protection that differ by administration route and synergize when combined. Thus, using MSCIV as adjuvant therapy might improve cell therapies for retinal dystrophy and warrants further translational evaluation.

PMID: 28191768

Stem Cells Transl Med. 2017 Feb;6(2):490-501. Epub 2016 Aug 24.

Directing Differentiation of Pluripotent Stem Cells Toward Retinal Pigment Epithelium Lineage.

Choudhary P, Booth H, Gutteridge A, Surmacz B, Louca I, Steer J, Kerby J, Whiting PJ.

Abstract: Development of efficient and reproducible conditions for directed differentiation of pluripotent stem cells into specific cell types is important not only to understand early human development but also to enable more practical applications, such as in vitro disease modeling, drug discovery, and cell therapies. The differentiation of stem cells to retinal pigment epithelium (RPE) in particular holds promise as a source of cells for therapeutic replacement in age-related macular degeneration. Here we show development of an efficient method for deriving homogeneous RPE populations in a period of 45 days using an adherent, monolayer system and defined xeno-free media and matrices. The method utilizes sequential inhibition and activation of the Activin and bone morphogenetic protein signaling pathways and can be applied to both human embryonic stem cells and induced pluripotent stem cells as the starting population. In addition, we use whole genome transcript analysis to characterize cells at different stages of differentiation that provides further understanding of the developmental dynamics and fate specification of RPE. We show that with the described method, RPE develop through stages consistent with their formation during embryonic development. This characterization- together with the absence of steps involving embryoid bodies, three-dimensional culture, or manual dissections, which are common features of other protocols-makes this process very attractive for use in research as well as for clinical applications.

PMID: 28191760

Diet, lifestyle and low vision

Nutrients. 2017 Feb 9;9(2).

Lutein and Zeaxanthin-Food Sources, Bioavailability and Dietary Variety in Age-Related Macular Degeneration Protection.

Eisenhauer B, Natoli S, Liew G, Flood VM.

Abstract: Lutein and zeaxanthin (L/Z) are the predominant carotenoids which accumulate in the retina of the eye. The impact of L/Z intake on the risk and progression of age-related macular degeneration (AMD), a leading cause of blindness in the developed world, has been investigated in cohort studies and clinical trials. The aims of this review were to critically examine the literature and evaluate the current evidence relating to L/Z intake and AMD, and describe important food sources and factors that increase the bioavailability of L/Z, to inform dietary models. Cohort studies generally assessed L/Z from dietary sources, while clinical trials focused on providing L/Z as a supplement. Important considerations to take into account in relation to dietary L/Z include: nutrient-rich sources of L/Z, cooking methods, diet variety and the use of healthy fats. Dietary models include examples of how suggested effective levels of L/Z can be achieved through diet alone, with values of 5 mg and 10 mg per day described. These diet models depict a variety of food sources, not only from dark green leafy vegetables, but also include pistachio nuts and other highly bioavailable sources of L/Z such as eggs. This review and the diet models outlined provide information about the importance of diet variety among people at high risk of AMD or with early signs and symptoms of AMD.

PMID: 28208784

Ophthalmic Physiol Opt. 2017 Mar;37(2):202-211.

What do patients think about the role of optometrists in providing advice about smoking and nutrition?

Downie LE, Douglass A, Guest D, Keller PR.

PURPOSE: Tobacco smoking and nutrition are key lifestyle factors with long-term effects on eye health. However, little is known about patients' perceptions and experiences in these areas in relation to the care received from optometrists. The main aim was to survey patients' perceptions and prior experience regarding the role of optometrists in enquiring and providing advice about tobacco smoking and nutrition.

METHODS: An anonymous, paper-based survey was distributed to a convenience sample of 225 adults attending the University of Melbourne eye care clinic. Respondents provided demographic and other information (age, sex, length of time since last eye examination, country of most recent eye examination, smoking status and intake of nutritional supplements) and indicated their level of agreement (using a five-step Likert scale) with a series of statements relating to the care provided by optometrists in the areas of health, smoking and nutrition. The statements were designed to assess the perceived scope of practice of optometrists and the extent to which patients expect, and feel comfortable, discussing these issues with their optometrist.

RESULTS: 220 completed surveys were returned. Most respondents (>80%) agreed that they visit their optometrist to quantify their refractive error and to examine their eye health. About two-thirds of respondents indicated that they expect their optometrist to ask about their general health, with almost half expecting their optometrist to communicate with their general medical practitioner. Approximately one-third of respondents indicated having been routinely questioned about their smoking status, diet and nutritional supplement intake by their optometrist. This was despite about half expecting their optometrist to question them about these factors and almost three out of four respondents indicating that they felt comfortable talking with their optometrist about these lifestyle behaviours.

CONCLUSIONS: This study provides novel insight into patients' perceptions and experience with

optometric practice in the areas of tobacco smoking and nutrition. The majority of respondents expected their optometrist to examine their eye health, ask them about their smoking and diet habits, and indicated feeling comfortable discussing these topics with their primary eye care provider. These findings suggest that brief advice interventions relating to tobacco use and diet are likely to be acceptable to deliver in optometry practice.

PMID: 28211179

Ophthalmic Physiol Opt. 2017 Mar;37(2):225-233.

Visual impairment in older institutionalised Canadian seniors with dementia.

Chriqui E, Law C, Kergoat MJ, Leclerc BS, Kergoat H.

PURPOSE: To estimate the prevalence of visual impairment (VI) in a sub-population of Canadian long-term care facilities, i.e. residents affected by dementia.

METHODS: This study was conducted in the long-term care facility units at the Institut universitaire de gériatrie de Montréal. All residents ≥ 65 years old (y.o.), having a clinical diagnosis of dementia, and able to understand French or English, were eligible for participation in the study. All residents participating in the study received a complete eye exam by an experienced optometrist. For the purpose of the study, VI was defined as a distance visual acuity (VA) $< 6/12$ (0.30 logMAR, 20/40) in the better seeing eye.

RESULTS: One hundred and fifty residents, 68-102 y.o. took part into the study. All participants had a diagnosis of dementia recorded in their clinical chart. VI was present in 37.3% (95% CI: 29.1-46.1%) ($n = 50$) of residents in whom monocular VA could be measured. Ocular refraction for their better seeing eye improved the VA to $\geq 6/12$ (0.30 logMAR, 20/40) in 40% ($n = 20$) of those 50 residents. When VI remained after refraction, it was due in order of frequency to cataract, age-related macular degeneration, and primary open angle glaucoma.

CONCLUSIONS: Our data showed that an appreciable proportion (37.3%) of older residents with dementia also have VI, and that VI can be corrected in many by updating their refraction. Others could potentially be helped through cataract surgery. It is therefore important to offer regular eye care services to those residents, knowing that many are not able to express their visual needs.

PMID: 28211177

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