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MD Research News

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This free weekly bulletin lists the latest published research articles on macular degeneration (MD) as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term “macular degeneration”.

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Drug treatment

J Telemed Telecare. 2013 Sep 4. [Epub ahead of print]

A teleconsultation network improves the efficacy of anti-VEGF therapy in retinal diseases.

Azzolini C, Torreggiani A, Eandi C, Donati S, Oum MA, Vinciguerra R, Bartalena L, Tartaglia V.

Department of Surgical and Morphological Sciences, Section of Ophthalmology, University of Insubria, Ospedale di Circolo, Varese, Italy.

Abstract: We investigated the care of patients with age-related macular degeneration (AMD) managed via a physician-to-physician teleconsultation network for ophthalmology. Eleven groups of ophthalmologists took part in the study. The groups were located in 10 cities across Italy. Each group was based on a Retina Centre located at a university or hospital, with one or two expert ophthalmologists (20 expert ophthalmologists in total). In each region containing a Retina Centre, 6-10 general ophthalmologists (94 ophthalmologists in total) referred patients via the network for a period of three months between June 2011 and December 2012. An automatic grading system quantified the risk of disease progression, and a remote booking system allowed the referring ophthalmologist to make appointments directly with the appropriate Retina Centre. There were 360 network patients and 318 control patients (consecutive patients undergoing usual care during the previous three months). The time delay before therapy was significantly shorter in the network patients (mean 5.5 days) compared with the usual care patients (mean 28.7 days; $P < 0.0001$). There was a significant improvement in visual acuity in the network patients after treatment (first visit = 0.29 logMAR; after treatment = 0.22 logMAR; $P < 0.05$). In contrast, there was no improvement in the usual care patients (first visit = 0.29 logMAR; after treatment = 0.27 logMAR; $P > 0.05$). The telemedicine network allows regional ophthalmologists to quantify the risk of disease progression, and to send patients to a Retina Centre quickly and easily, when required.

PMID: 24162839 [PubMed - as supplied by publisher]

Semin Ophthalmol. 2013 Oct 30. [Epub ahead of print]

Branch Retinal Vein Occlusion: Treatment Modalities: An Update of the Literature.

Chatziralli IP, Jaulim A, Peponis VG, Mitropoulos PG, Moschos MM.

Department of Ophthalmology, Barts and the London NHS Trust , London , UK .

Background: Retinal vein occlusion is the second most common retinal vascular disorder after diabetic retinopathy and is considered to be an important cause of visual loss. In this review, our purpose is to

update the literature about the treatment alternatives for branch retinal vein occlusion.

Methods: Eligible papers were identified by a comprehensive literature search of PubMed, using the terms "branch retinal vein occlusion," "therapy," "intervention," "treatment," "vitrectomy," "sheathotomy," "laser," "anti-VEGF," "pegaptanib," "bevacizumab," "ranibizumab," "triamcinolone," "dexamethasone," "corticosteroids," "non-steroids," "diclofenac," "hemodilution," "fibrinolysis," "tPA," and "BRVO." Additional papers were also selected from reference lists of papers identified by the electronic database search.

Results: Treatment modalities were analyzed.

Conclusions: There are several treatment modalities for branch retinal vein occlusion and specifically for its complications, such as macular edema, vitreous hemorrhage, retinal neovascularization, and retinal detachment, including anti-aggregative therapy and fibrinolysis, isovolemic hemodilution, vitrectomy with or without sheathotomy, peripheral scatter and macular grid retinal laser therapy, non-steroid agents, intravitreal steroids, and intravitreal anti-vascular endothelial growth factors (anti-VEGFs).

PMID: 24171809 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Ophthalmic Surg Lasers Imaging Retina. 2013 Nov 1:S30-S32. doi: 10.3928/23258160-20131101-05. [Epub ahead of print]

Retinal Pigment Epithelial Detachment With Disgorgement in Age-Related Macular Degeneration Observed With OCT.

Kadasi LM, Adhi M, Liang MC, Duker JS.

Abstract: This report describes a rare appearance of retinal pigment epithelial changes in a 71-year-old woman with known long-standing, non-exudative age-related macular degeneration. She presented with visual distortion in her right eye and was found to have a retinal pigment epithelial detachment (RPED) on optical coherence tomography (OCT). Over the following 8 years, sequential OCT imaging revealed an appearance and progression of a break in the existing RPED, disgorgement of material from within the RPED, and appearance of hyper-reflective spots within the inner retinal layers, suggesting pigment epithelial cell migration. Visual acuity remained stable over this period. The RPED resolved spontaneously without treatment. The patient later developed new intraretinal hemorrhage, which was treated with intravitreal bevacizumab. [Ophthalmic Surg Lasers Imaging Retina. 2013;44:S30-S32.].

PMID: 24170230 [PubMed - as supplied by publisher]

Retina. 2013 Oct 30. [Epub ahead of print]

AN IMPROVED OPTICAL COHERENCE TOMOGRAPHY-DERIVED FUNDUS PROJECTION IMAGE FOR DRUSEN VISUALIZATION.

Chen Q, Leng T, Zheng LL, Kutzscher L, De Sisternes L, Rubin DL.

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PURPOSE: To develop and evaluate an improved method of generating en face fundus images from three-dimensional optical coherence tomography images which enhances the visualization of drusen.

METHODS: We describe a novel approach, the restricted summed-voxel projection (RSVP), to generate en face projection images of the retinal surface combined with an image processing method to enhance drusen visualization. The RSVP approach is an automated method that restricts the projection to the retinal pigment epithelium layer neighborhood. Additionally, drusen visualization is improved through an image processing technique that fills drusen with bright pixels. The choroid layer is also excluded when creating the RSVP to eliminate bright pixels beneath drusen that could be confused with drusen when geographic atrophy is present. The RSVP method was evaluated in 46 patients and 3-dimensional optical coherence tomography data sets were obtained from 8 patients, for which 2 readers independently identified drusen as the gold standard. The mean drusen overlap ratio was used as the metric to determine the accuracy of visualization of the RSVP method when compared with the conventional summed-voxel projection technique.

RESULTS: Comparative results demonstrate that the RSVP method was more effective than the conventional summed-voxel projection in displaying drusen and retinal vessels, and was more useful in detecting drusen. The mean drusen overlap ratios based on the conventional summed-voxel projection method and the RSVP method were 2.1% and 89.3%, respectively.

CONCLUSION: The RSVP method was more effective for drusen visualization than the conventional summed-voxel projection method, and it may be useful for macular assessment in patients with nonexudative age-related macular degeneration.

PMID: 24177190 [PubMed - as supplied by publisher]

Retina. 2013 Oct 28. [Epub ahead of print]

MACULAR EPIRETINAL BRACHYTHERAPY IN TREATED AGE-RELATED MACULAR DEGENERATION (MERITAGE): Month 24 Safety and Efficacy Results.

Petrarca R, Dugel PU, Bennett M, Barak A, Weinberger D, Nau J, Jackson TL.

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PURPOSE: To evaluate the safety and efficacy of epimacular brachytherapy for the treatment of chronic, active neovascular age-related macular degeneration.

METHODS: A prospective, multicenter, interventional noncontrolled clinical trial recruited 53 participants with previously treated neovascular age-related macular degeneration. Participants underwent pars plana vitrectomy with a single 24 Gray dose of epimacular brachytherapy, delivered using an intraocular cannula containing a Strontium 90/Yttrium 90 source that was positioned over the active lesion. Participants were retreated with ranibizumab, administered monthly as needed, using predefined retreatment criteria. Coprimary outcomes at 24 months were the proportion of participants losing <15 Early Treatment of Diabetic Retinopathy Study letters and mean number of ranibizumab retreatments.

RESULTS: Over 24 months, 68.1% lost <15 letters with a mean of 8.7 ranibizumab retreatments. Mean change in visual acuity was -6.3 (standard deviation, 18.9) letters. There was one case of nonproliferative radiation retinopathy.

CONCLUSION: The apparent reduction in ranibizumab retreatment was less evident in Year 2 than Year 1, with the moderate reduction in visual acuity extending into the second year. Although radiation retinopathy occurred in one case, it was not vision threatening and safety remained acceptable.

PMID: 24169101 [PubMed - as supplied by publisher]

Semin Ophthalmol. 2013 Oct 30. [Epub ahead of print]

Feasibility of Telemedicine in Detecting Diabetic Retinopathy and Age-Related Macular Degeneration.

Vaziri K, Moshfeghi DM, Moshfeghi AA.

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Abstract: Age-related macular degeneration and diabetic retinopathy are important causes of visual impairment and blindness in the world. Because of recent advances and newly available treatment modalities along with the devastating consequences associated with late stages of these diseases, much attention has been paid to the importance of early detection and improving patient access to specialist care. Telemedicine or, more specifically, digital retinal imaging utilizing telemedical technology has been proposed as an important alternative screening and management strategy to help meet this demand. In this paper, we perform a literature review and analysis that evaluates the validity and feasibility of telemedicine in detecting diabetic retinopathy and age-related macular degeneration. Understanding both the progress and barriers to progress that have been demonstrated in these two areas is important for future telemedicine research projects and innovations in telemedicine technology.

PMID: 24171781 [PubMed - as supplied by publisher]

Pathogenesis

J Biol Chem. 2013 Oct 29. [Epub ahead of print]

Identification of a Novel Lipofuscin Pigment (iisoA2E) in Retina and Its Effects in the Retinal Pigment Epithelial Cells.

Li J, Yao K, Yu X, Dong X, Gan L, Luo C, Wu Y.

Zhejiang University, China.

Abstract: Lipofuscin accumulation in retinal pigment epithelial (RPE) cells of the eye implicates the etiologies of Stargardt's disease and age-related macular degeneration, a leading cause of blindness in the elderly. Here, we have identified a previously unknown RPE lipofuscin component. By 1D- and 2D-NMR techniques and mass spectrometry, we confirmed that this compound is a new type of pyridinium bisretinoid presenting an unusual structure, in which two polyenic side-chains are attached to adjacent carbons of a pyridinium ring. This pigment is a light-induced isomer of isoA2E, rather than A2E, referred to as iisoA2E. This pigment is a fluorescent lipofuscin compound with absorbance maxima at ~430 and 352 nm detected in human, pig, mouse, and bovine eyes. Formation of iisoA2E was found in reaction mixtures of all-trans-retinal and ethanolamine. Excess intracellular accumulation of this adduct in RPE cells in vitro leads to a significant loss of cell viability and caused membrane damage. Phospholipase D-mediated phosphodiester cleavage of A2PE series generated isoA2E and iisoA2E, in addition to A2E, thus corroborating the presence of isoA2PE and iisoA2PE that may serve as biosynthetic precursors of isoA2E and iisoA2E.

PMID: 24169698 [PubMed - as supplied by publisher]

ASN Neuro. 2013 Oct 27. [Epub ahead of print]

Pigment epithelium-derived factor reduces apoptosis and pro-inflammatory cytokine gene expression in a murine model of focal retinal degeneration.

Wang Y, Subramanian P, Shen D, Tuo J, Becerra SP, Chan CC.

Abstract: Age-related macular degeneration (AMD) is a neurodegenerative disease causing irreversible central blindness in the elderly. Apoptosis and inflammation play important roles in AMD pathogenesis. Pigment epithelium-derived factor (PEDF) is a potent neurotrophic and anti-inflammatory glycoprotein that protects the retinal neurons and photoreceptors against cell death caused by pathological insults. We studied the effects of PEDF on focal retinal lesions in Ccl2-/-/Cx3cr1-/- on C57BL/6N [Crb1rd8] (DKO rd8) mice, a model for progressive, focal retinal degeneration. First, we found a significant decrease in PEDF transcript expression in DKO rd8 mouse retina and retinal pigment epithelium (RPE) than wild type (WT, C57BL/6N). Next, cultured DKO rd8 RPE cells secreted lower levels of PEDF protein in the media than WT. Then the right eyes of DKO rd8 mice were injected intravitreously with recombinant human PEDF protein (1 µg), followed by a subconjunctival injection of PEDF (3 µg) 4 weeks later. The untreated left eyes served as controls. The effect of PEDF was assessed by fundoscopy, ocular histopathology and A2E levels, as well as apoptotic and inflammatory molecules. The PEDF-treated eyes showed slower progression or attenuation of the focal retinal lesions, fewer and/or smaller photoreceptor and RPE degeneration, and significantly lower A2E, relative to the untreated eyes. Additionally, lower expression of apoptotic and inflammatory molecules were detected in the PEDF-treated than untreated eyes. Our results establish that PEDF potently stabilizes photoreceptor degeneration via suppression of both anti-apoptotic and anti-inflammatory pathways. The multiple beneficial effects of PEDF represent a novel approach for potential AMD treatment.

PMID: 24160756 [PubMed - as supplied by publisher]

Genetics

Curr Genomics. 2013 May;14(3):166-72. doi: 10.2174/1389202911314030002.

Epigenetics in ocular diseases.

Liu MM, Chan CC, Tuo J.

Laboratory of Immunology, National Eye Institute, National Institutes of Health, Bethesda, MD ; Johns Hopkins University School of Medicine, Baltimore, MD, USA.

Abstract: Epigenetics pertains to heritable alterations in gene expression that do not involve modification of the underlying genomic DNA sequence. Historically, the study of epigenetic mechanisms has focused on DNA methylation and histone modifications, but the concept of epigenetics has been more recently extended to include microRNAs as well. Epigenetic patterning is modified by environmental exposures and may be a mechanistic link between environmental risk factors and the development of disease. Epigenetic dysregulation has been associated with a variety of human diseases, including cancer, neurological disorders, and autoimmune diseases. In this review, we consider the role of epigenetics in common ocular diseases, with a particular focus on DNA methylation and microRNAs. DNA methylation is a critical regulator of gene expression in the eye and is necessary for the proper development and postmitotic survival of retinal neurons. Aberrant methylation patterns have been associated with age-related macular degeneration, susceptibility to oxidative stress, cataract, pterygium, and retinoblastoma. Changes in histone modifications have also been observed in experimental models of diabetic retinopathy and glaucoma. The expression levels of specific microRNAs have also been found to be altered in the context of ocular inflammation, retinal degeneration, pathological angiogenesis, diabetic retinopathy, and ocular neoplasms. Although the complete spectrum of epigenetic modifications remains to be more fully explored, it is clear that epigenetic dysregulation is an important contributor to common ocular diseases and may be a relevant therapeutic target.

PMID: 24179439 [PubMed]

Diet & lifestyle

Surv Ophthalmol. 2013 Nov-Dec;58(6):585-609. doi: 10.1016/j.survophthal.2012.12.002.

Iron, zinc, and copper in retinal physiology and disease.

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Abstract: The essential trace metals iron, zinc, and copper play important roles both in retinal physiology and disease. They are involved in various retinal functions such as phototransduction, the visual cycle, and the process of neurotransmission, being tightly bound to proteins and other molecules to regulate their structure and/or function or as unbound free metal ions. Elevated levels of "free" or loosely bound metal ions can exert toxic effects, and in order to maintain homeostatic levels to protect retinal cells from their toxicity, appropriate mechanisms exist such as metal transporters, chaperones, and the presence of certain storage molecules that tightly bind metals to form nontoxic products. The pathways to maintain homeostatic levels of metals are closely interlinked, with various metabolic pathways directly and/or indirectly affecting their concentrations, compartmentalization, and oxidation/reduction states. Retinal deficiency or excess of these metals can result from systemic depletion and/or overload or from mutations in genes involved in maintaining retinal metal homeostasis, and this is associated with retinal dysfunction and pathology. Iron accumulation in the retina, a characteristic of aging, may be involved in the pathogenesis of retinal diseases such as age-related macular degeneration (AMD). Zinc deficiency is associated with poor dark adaptation. Zinc levels in the human retina and RPE decrease with age in AMD. Copper deficiency is associated with optic neuropathy, but retinal function is maintained. The changes in iron and zinc homeostasis in AMD have led to the speculation that iron chelation and/or zinc supplements may help in its treatment.

PMID: 24160731 [PubMed - in process]

J Ophthalmol. 2013;2013:862806. doi: 10.1155/2013/862806. Epub 2013 Sep 12.

Efficacy of Ethanol Extract of Fructus lycii and Its Constituents Lutein/Zeaxanthin in Protecting Retinal Pigment Epithelium Cells against Oxidative Stress: In Vivo and In Vitro Models of Age-Related Macular Degeneration.

Xu X, Hang L, Huang B, Wei Y, Zheng S, Li W.

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Abstract: Age-related macular degeneration (AMD) is a major cause of blindness worldwide. Oxidative stress plays a large role in the pathogenesis of AMD. The present study was to evaluate the effects of Fructus lycii ethanol extract on AMD in mice and to investigate whether combination of lutein and zeaxanthin, two carotenoid pigments in Fructus lycii, could protect human retinal pigment epithelial ARPE-19 cells treated with hydrogen peroxide (H2O2) in vitro. We found that severe sediment beneath retinal pigment epithelium and thickened Bruch membrane occurred in AMD mice. However, Fructus lycii ethanol extract improved the histopathologic changes and decreased the thickness of Bruch membrane. Furthermore, the gene and protein expression of cathepsin B and cystatin C was upregulated in AMD mice but was eliminated by Fructus lycii ethanol extract. Investigations in vitro showed that ARPE-19 cell proliferation was suppressed by H2O2. However, lutein/zeaxanthin not only stimulated cell proliferation but also abrogated the enhanced expression of MMP-2 and TIMP-1 in H2O2-treated ARPE-19 cells. These data collectively suggested that Fructus lycii ethanol extract and its active components lutein/zeaxanthin

had protective effects on AMD in vivo and in vitro, providing novel insights into the beneficial role of Fructus lycii for AMD therapy.

PMID: 24163760 [PubMed] PMCID: PMC3791792 Free PMC Article

Indian J Ophthalmol. 2013 Oct 30. [Epub ahead of print]

Dietary and lifestyle risk factors associated with age-related macular degeneration: A hospital based study.

Nidhi B, Mamatha BS, Padmaprabhu CA, Pallavi P, Vallikannan B.

Department of Molecular Nutrition, CSIR-Central Food Technological Research Institute, CSIR, Mysore, Karnataka, India.

Aim: To establish the frequency, associations and risk factors for age-related macular degeneration (AMD) in hospital population of South India.

Materials and Methods: In this cross-sectional hospital based study, 3549 subjects (2090 men and 1459 women) above 45 years of age were screened randomly for AMD. Participants underwent ocular evaluation and were interviewed for lifestyle variables and dietary intake of carotenoids by structured food frequency questionnaire. AMD was defined according to the international classifications and grading system.

Results: Either form of AMD was detected in 77 (2.2%) participants. Of which, early and late AMD was present in 63 (1.8%) and 14 (0.4%) subjects, respectively. Binary logistic analysis showed that the incidence of AMD was significantly higher with increasing age (Odds ratio [OR] 1.17; 95% CI 1.13-1.22) and diabetes (OR 3.97; 95% CI 2.11-7.46). However, AMD was significant among heavy cigarette smokers (OR 5.58; 95% CI 0.88-7.51) and alcoholics (OR 4.85; 95% CI 2.45-12.22). Dietary lutein/zeaxanthin (L/Z) and b-carotene intake were associated ($P < 0.001$) with the reduction in risk for AMD, with an OR of 0.38 and 0.65, respectively.

Conclusions: Higher dietary intake of carotenoids, especially L/Z, was associated with lower risk for AMD. Risk of AMD is higher with increasing age and was prevalent among subjects with diabetes. Cessation of smoking and alcohol may reduce the risk of AMD in this population.

PMID: 24178404 [PubMed - as supplied by publisher]

Nepal J Ophthalmol. 2013 Jul;5(10):195-200. doi: 10.3126/nepjoph.v5i2.8728.

A study on plasma homocysteine level in age-related macular degeneration.

Ghosh S, Saha M, Das D.

Introduction: Age-related macular degeneration (AMD) related to adverse vascular changes is the most frequent cause of irreversible visual impairment in the elderly. Elevated plasma concentrations of serum homocysteine have been shown to increase the risk of vascular disease.

Objective: To assess the relationship between plasma homocysteine level and age related macular degeneration.

Materials and methods: A case control study was conducted in a tertiary eye care hospital with 32 diagnosed AMD patients. The patients were compared for plasma homocysteine levels with a control group of 32 patients without AMD. A 1.5 ml of fasting venous blood sample was obtained from each participant. Plasma homocysteine level was measured by high performance liquid chromatography. The main outcome measure was hyperhomocysteinemia, defined as a plasma homocysteine level above 15 µmol/l.

Results: Hyperhomocysteinemia was found in 10 blood samples (83.3 %) of patients in the wet AMD group, in 16 (80 %) blood samples in the dry AMD group, and in 12 blood samples (37%) of controls. The mean ± SD homocysteine level in the AMD group was 16.86 ± 3.52 µmol/L, while in the non-AMD control group it was 14.53 ± 4.08 µmol/L. This difference was statistically significant (p-value = 0.0186). In the individual analysis, it was also found out that the homocysteine level differed significantly between cases and controls in only the wet variety of AMD.

Conclusion: Hyperhomocysteinemia was significantly associated with the wet AMD variety but not with the dry AMD. Thus, homocysteine by oxidative stress and vascular dysfunction can be an important risk factor in the pathogenesis of AMD.

PMID: 24172554 [PubMed - in process]