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MD Research News

Issue 33

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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

Arch Ophthalmol. 2011 Jun;129(6):709-17.

Estimated cases of legal blindness and visual impairment avoided using ranibizumab for choroidal neovascularization: non-Hispanic white population in the United States with age-related macular degeneration.

Bressler NM, Doan QV, Varma R, Lee PP, Suñer IJ, Dolan C, Danese MD, Yu E, Tran I, Colman S.

Wilmer Eye Institute, Maumenee 752, Johns Hopkins Hospital, 600 N Wolfe St, Baltimore, MD 21287. nmboffice@jhmi.edu.

OBJECTIVE: To estimate the number of non-Hispanic white individuals in the United States avoiding legal blindness and visual impairment from neovascular age-related macular degeneration (AMD) with ranibizumab availability.

METHODS: Modeling of visual acuity outcomes from phase 3 ranibizumab trials to incidence rates of neovascular AMD from population-based studies.

RESULTS: If no treatment were given, of the 103 582 individuals developing neovascular AMD for which ranibizumab would be indicated and available, 16 268 would become legally blind in 2 years. Monthly ranibizumab would reduce the incidence of legal blindness in 2 years by 72% (95% confidence interval [CI], 70% to 74%) to 4484 individuals. If no treatment were given, 34 702 would become visually impaired. Monthly ranibizumab would reduce the incidence of visual impairment in 2 years by 37% (95% CI, 35% to 39%) to 21 919 cases.

CONCLUSIONS: Ranibizumab should have a substantial effect on reducing the magnitude of legal blindness and visual impairment within 2 years after diagnosis of neovascular AMD among non-Hispanic white individuals in the United States. Although racial subgroups other than non-Hispanic whites were not considered (because there is limited information in the literature regarding incidence rates of choroidal neovascularization in other populations) and although these results assume access to and application of monthly ranibizumab for 2 years, the number of individuals developing legal blindness or vision impairment from neovascular AMD should be reduced dramatically if monthly ranibizumab is applied when indicated.

PMID: 21670337 [PubMed - in process]

Clin Experiment Ophthalmol. 2011 Jun 13. doi: 10.1111/j.1442-9071.2011.02613.x. [Epub ahead of print]

Retinal venular calibre dilatation after intravitreal ranibizumab treatment for neovascular age-related macular degeneration.

Wickremasinghe SS, Guymer RH, Wong TY, Kawasaki R, Wong W, Qureshi S.

Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital Melbourne, Australia Singapore Eye Research Institute, National University of Singapore, Singapore.

Background: To describe the changes in retinal vascular calibre in response to intravitreal ranibizumab injections in patients with neovascular age-related macular degeneration (AMD). Design: Prospective interventional case series. Participants: Treatment naïve patients with neovascular AMD were recruited over a one-year period. Methods: Each patient received three monthly intravitreal injections according to a "loading dose". Retinal arteriolar and venular calibre was measured from digital fundus photographs and summarized as Central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE) at baseline and three months. Main Outcome Measure: CRAE and CRVE changes from baseline to three months. Results: 74 eyes of 71 patients had good quality images for grading vessel calibre at baseline and at three months in treated (study) eyes and 51 eyes of 51 patients had good quality images in fellow (control) eyes. Over three months, in study eyes treated with ranibizumab, there was a significant increase in CRVE over baseline, +6.20μm, p = 0.005, but no significant change in CRAE, +0.86μm, p = 0.55). In control eyes, there was no change in CRVE, -0.82μm, p = 0.70) or CRAE, 0.34μm, p = 0.75. Conclusion: Intravitreal ranibizumab has a significant vasodilational effect on retinal venular calibre in eyes treated for neovascular AMD. The reason for this change is unclear, but may relate to changes in blood flow or inflammatory changes within the retina.

PMID: 21668787 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2011 Jun 9. [Epub ahead of print]

Ocular Complications After Anti-Vascular Endothelial Growth Factor Therapy in Medicare Patients With Age-Related Macular Degeneration.

Day S, Acquah K, Mruthyunjaya P, Grossman DS, Lee PP, Sloan FA.

Department of Ophthalmology, Duke Eye Center, Durham, North Carolina.

PURPOSE: To determine longitudinal rates of ocular complications after anti-vascular endothelial growth factor (VEGF) treatment for neovascular age-related macular degeneration (AMD) in a nationally representative longitudinal sample.

DESIGN: Retrospective, longitudinal case-control study.

METHODS: Using the Medicare 5% claims database, diagnoses of neovascular AMD and anti-VEGF injections of ranibizumab, bevacizumab, or pegaptanib were identified from International Classification of Diseases and Current Procedural Terminology procedure codes. Six thousand one hundred fifty-four individuals undergoing anti-VEGF treatment for neovascular AMD (total of 40 903 injections) were compared with 6154 matched controls with neovascular AMD who did not undergo anti-VEGF treatment. Propensity score matching was used to match individuals receiving anti-VEGF injections with controls. Rates of postinjection adverse outcomes (endophthalmitis, rhegmatogenous retinal detachment, retinal tear, uveitis, and vitreous hemorrhage) were analyzed by cumulative incidence and Cox proportional hazards model to control for demographic factors and ocular comorbidities.

RESULTS: At the 2-year follow-up, the rates of endophthalmitis per injection (0.09%; P < .01), uveitis (0.11%; P < .01), and vitreous hemorrhage per injection (0.23%; P < .01) were significantly higher in the

anti-VEGF treatment group. With Cox proportional hazards modeling, the anti-VEGF treatment group had a 102% higher risk of severe ocular complications overall and a 4% increased risk per injection, both of which were statistically significant (P < .01).

CONCLUSIONS: Rates of endophthalmitis, uveitis, and vitreous hemorrhage were higher in the group treated with anti-VEGF injection than in the control group, although these nevertheless were rare in both groups. The overall risk of severe ocular complications was significantly higher in the anti-VEGF treatment group.

PMID: 21664593 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2011 Jun 16. [Epub ahead of print]

Treatments for macular degeneration: summarising evidence using network meta-analysis.

Fadda V, Maratea D, Trippoli S, Messori A.

Area Vasta Centro Toscana, ESTAV, Prato, Italy.

PMID: 21680571 [PubMed - as supplied by publisher]

Curr Opin Biotechnol. 2011 Jun 13. [Epub ahead of print]

Polymer therapeutics as nanomedicines: new perspectives.

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Abstract

A growing number of polymer therapeutics have entered routine clinical use as nano-sized medicines. Early products were developed as anticancer agents, but treatments for a range of diseases and different routes of administration have followed - recently the PEGylated-anti-TNF Fab Cimzia(®) for rheumatoid arthritis and the PEG-aptamer Macugen(®) for age related macular degeneration. New polymer therapeutic concepts continue to emerge with a growing number of conjugates entering clinical development, for example PEGylated-aptamers and a polymer-based siRNA delivery system. 'Hot' topics of the past 2 years include; emerging issues relating to polymer safety, the increasing use of biodegradable polymers, design of technologies for combination therapy, potential biomarkers for patient individualisation of treatment and Regulatory challenges for 'follow-on/generic' polymer therapeutics.

PMID: 21676609 [PubMed - as supplied by publisher]

Indian J Ophthalmol. 2011 Jul-Aug;59(4):318-9.

Intravitreal ranibizumab for the treatment of choroidal neovascularization secondary to ocular toxoplasmosis.

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Department of Cornea and Anterior Segment, The Eye Super Specialities, Ghatkopar - East, Mumbai - 400 077, India.

Abstract

The purpose of the study was to report a case of choroidal neovascularization (CNV) secondary to ocular toxoplasmosis in an 18-year-old female patient. She was treated with a single intravitreal injection of ranibizumab. The CNV resolved as confirmed by fluorescein angiography and optical coherence tomography (OCT). The visual acuity improved to 20/30, which was maintained till the last follow-up visit at two years, without requisition of a repeat injection.

PMID: 21666322 [PubMed - in process]

Indian J Ophthalmol. 2011 Jul-Aug;59(4):306-8.

Combination treatment of low fluence photodynamic therapy and intravitreal ranibizumab for choroidal neovascular membrane secondary to angioid streaks in Paget's disease - 12 month results.

Prabhu VV, Morris RJ, Shah PK, Narendran V.

Department of Retina and Vitreous, Aravind Eye Hospital and Postgraduate Institute of Ophthalmology, Coimbatore, Tamilnadu, India.

Abstract

Angioid streaks also called Knapp striae are small breaks in the Bruch's membrane and have been reported with a host of systemic diseases. Rupture of streaks or development of secondary choroidal neovascular membrane (CNVM) carries a dismal visual prognosis. We report the successful treatment of CNVM secondary to Paget's disease using low fluence photodynamic therapy (PDT) and intravitreal ranibizumab.

PMID: 21666317 [PubMed - in process]

Other treatment & diagnosis

Stem Cells. 2011 Jun 14. doi: 10.1002/stem.676. [Epub ahead of print]

Towards Stem Cell-Based Therapies for Retinal Neurodegenerative Diseases.

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Abstract

Loss of sight due to irreversible retinal neurodegeneration imposes a significant disease burden on both patients and society. Glaucoma and age-related macular degeneration are the commonest neurodegenerative blinding diseases in the developed world, and both are becoming increasingly prevalent as populations age. Our heavy reliance on our sense of sight means that visual loss often severely restricts day-to-day life, making it difficult to function without additional support. Visual impairment also limits employment possibilities, adding to the economic burden. Current therapies for many degenerative retinopathies are limited in their efficacy, often treating the effects of disease rather than the underlying causes. Consequently, the development of novel adjunctive neuroprotective and neuroregenerative treatments are important goals. Evidence from animal models suggests that stem cells could be useful as part of novel new treatment strategies for eye disease. The accessibility of the eye and extensive repertoire of available surgical techniques may facilitate the translation of stem cell-based therapies, for example via transplantation, to the retina more rapidly than to other parts of the central nervous system. This concise review will examine how cell therapies are being applied experimentally for neuroregenerative and neuroprotective treatment of currently incurable degenerative retinal diseases. Furthermore, recent progress towards clinical translation of such therapies will be highlighted.

PMID: 21674700 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2011 Jun 10. [Epub ahead of print]

Automatic detection of diabetic retinopathy and age-related macular degeneration in digital fundus images.

Agurto C, Barriga ES, Murray V, Nemeth S, Crammer R, Bauman W, Zamora G, Pattichis MS, Soliz P.

VisionQuest Biomedical LLC, Albuquerque, New Mexico;

Purpose: To describe and evaluate the performance of an algorithm that automatically classifies images with pathologies commonly found in diabetic retinopathy (DR) and age-related macular degeneration (AMD).

Methods: Retinal digital photographs (N=2247) of 3 fields of view (FOV) were collected of the eyes from 822 patients at two centers: The Retina Institute of South Texas (RIST) and The University of Texas Health Science Center San Antonio (UTHSCSA). Ground truth was provided for the presence of pathologies including: microaneurysms, hemorrhages, exudates, neovascularization in the optic disc and elsewhere, drusen, abnormal pigmentation, and geographic atrophy. The algorithm was used to report on the presence or absence of pathology. A detection threshold was applied to obtain different values of sensitivity and specificity with respect to ground truth and construct a Receiver Operating Characteristic (ROC) curve.

Results: The system achieved an average area under the ROC curve (AUC) of 0.89 for detection of DR and of 0.92 for detection of sight-threatening DR (STDR). With a fixed specificity of 0.50, the system's sensitivity ranged from 0.92 for all DR cases to 1.00 for clinically significant macular edema (CSME).

Conclusions: A computer-aided algorithm was trained to detect different types of retinal pathologies. The cases of hard exudates within 1 disc diameter (DD) of the fovea (surrogate for CSME) were detected with very high accuracy (sensitivity = 1, specificity = 0.50) whereas mild non-proliferative DR was the most challenging condition (sensitivity= 0.92, specificity= 0.50). The algorithm was also tested on images with signs of AMD, achieving a performance of AUC = 0.84 (sensitivity= 0.94, specificity= 0.50).

PMID: 21666234 [PubMed - as supplied by publisher]

Work. 2011;39(1):63-6.

The multi-disciplinary nature of low vision rehabilitation~-- A case report.

Markowitz M, Markowitz RE, Markowitz SN.

Private Practice, Toronto, Ontario, Canada.

Abstract

This paper presents the case of a 47-year-old female with low vision secondary to high myopic macular degeneration who remains active in the work force as a spiritual and religious care coordinator for a large institution. An ophthalmologist with a specialty in low vision rehabilitation initially assessed the client. The ophthalmologist prescribed optical devices which used residual retinal vision available at preferred retinal loci. This availed better vision for viewing targets located at far, near and intermediate distances from the client. An optician provided and dispensed the devices prescribed to the client. Additionally, the ophthalmologist made a referral to an occupational therapist. The occupational therapist conducted a series of sessions to further enhance reading and writing skills and a work place assessment aimed at optimizing workplace conditions in order to achieve optimal functional vision. This case illustrates and emphasizes the multi-disciplinary nature of low vision rehabilitation, which involved in this case co-operation between ophthalmology, occupational therapy and opticianry.

PMID: 21673429 [PubMed - in process]

Ophthalmic Physiol Opt. 2011 Jul;31(4):375-380. doi: 10.1111/j.1475-1313.2011.00848.x. Epub 2011 May 24.

Depressive symptoms and quality of life in people with age- related macular degeneration.

Mathew RS, Delbaere K, Lord SR, Beaumont P, Vaegan, Madigan MC.

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Citation information: Mathew RS, Delbaere K, Lord SR, Beaumont P, Vaegan & Madigan MC. Depressive symptoms and quality of life in people with age- related macular degeneration. Ophthalmic Physiol Opt 2011, 31, 375-380. doi: 10.1111/j.1475-1313.2011.00848.x

Purpose: To examine quality of life and associated factors in people with Age-Related Macular Degeneration (AMD).

Methods: One hundred and forty-five AMD participants (mean age 78.0 ± 7.7 years) and 104 age- and gender- matched controls (mean age 78.1 ± 5.8 years) comprised the study populations for this case-control study. Depressive symptoms were measured with the Goldberg Anxiety and Depression (GAD) scale; general health and daily functioning was assessed with the Medical Outcomes Study Short Form 36 (SF-36) and questions relating to assistance required for daily living activities.

Results: People with AMD performed more poorly than controls on the GAD depression scale, and physical functioning subscale of SF-36. 44.4% of people with AMD had clinically significant depressive symptoms compared to 17.5% of controls ($p < 0.001$). Multiple regression analysis revealed that AMD was independently associated with depressive symptoms and a path model indicated that AMD led to depressive symptoms both directly and indirectly via reduced general health and social functioning.

Conclusion: Psychological and functional outcome measures are reduced in people with AMD. Earlier recognition and treatment of depressive symptoms in people with AMD may be crucial to maintaining quality of life in this group.

PMID: 21679317 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging. 2011 Jun 9;42:e56-8. doi: 10.3928/15428877-20110602-04.

Diffuse retinal pigment epithelial disease in an adult with cystic fibrosis.

Goren JF, Shah SP, Janzen GP, Gross NE, Duker JS.

Abstract

An adult with cystic fibrosis presented for decreased vision in the right eye of several months' duration. Biomicroscopy and fluorescein angiography demonstrated bilateral large subretinal drusenoid deposits concentrated temporal to the fovea, as well as a small subretinal hemorrhage associated with focal leakage of fluid within the macula in the right eye. Optical coherence tomography demonstrated subretinal fluid consistent with choroidal neovascular membrane in the right eye with the absence of fluid in the left eye. The retinal manifestations of bilateral diffuse drusen associated with choroidal neovascular membrane may be consistent with autosomal dominant drusen, age-related macular degeneration, and type II glomerulonephritis, or alternatively may be a unique finding associated with cystic fibrosis. To the authors' knowledge, these findings have not previously been described in association with cystic fibrosis.

PMID: 21661668 [PubMed - in process]

Epidemiology & pathogenesis

Stroke. 2011 Jun 16. [Epub ahead of print]

Age-Related Macular Degeneration and the Risk of Stroke: The Rotterdam Study.

Wieberdink RG, Ho L, Ikram MK, Koudstaal PJ, Hofman A, de Jong PT, Vingerling JR, Breteler MM.

From the Departments of Epidemiology, Neurology, and Ophthalmology, Erasmus Medical Center, Rotterdam, the Netherlands; the Department of Ophthalmology, Academic Medical Center, Amsterdam, the Netherlands; and The Netherlands Institute for Neuroscience, Royal Netherlands Academy of Arts and Sciences, Amsterdam, the Netherlands.

BACKGROUND AND PURPOSE: Age-related macular degeneration (AMD) and stroke are both frequent diseases in the elderly. A link between AMD and stroke has been suggested, because both disorders have many risk factors in common. The aim of this study was to investigate the association between AMD and stroke and the subtypes cerebral infarction and intracerebral hemorrhage in the general elderly population.

METHODS: This study was part of the population-based Rotterdam Study and included 6207 participants aged ≥55 years who were stroke-free at baseline (1990 to 1993). Signs of AMD were assessed on fundus photographs at baseline and at regular follow-up examinations and were categorized in 5 stages (0 to 4) representing an increasing severity. Late AMD (Stage 4) was subdivided into dry and wet AMD. Follow-up for incident stroke was complete up to January 1, 2007. Data were analyzed using time-dependent Cox regression models adjusted for age, sex, and potential confounders.

RESULTS: During a median follow-up of 13.6 years, 726 participants developed a stroke (397 cerebral infarction, 59 intracerebral hemorrhage, 270 unspecified). Late AMD was associated with an increased risk of any stroke (hazard ratio, 1.56; 95% CI, 1.08 to 2.26) due to a strong association with intracerebral hemorrhage (hazard ratio, 6.11; 95% CI, 2.34 to 15.98). In contrast, late AMD was not associated with cerebral infarction. Earlier AMD stages were not associated with risk of stroke or any of its subtypes.

CONCLUSIONS: We found that late AMD is strongly associated with intracerebral hemorrhage, but not with cerebral infarction, in the general elderly population.

PMID: 21680903 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2011 Jun 14. [Epub ahead of print]

Risk Factors for Four-Year Incidence and Progression of Age-Related Macular Degeneration: The Los Angeles Latino Eye Study.

Choudhury F, Varma R, McKean-Cowdin R, Klein R, Azen SP; Los Angeles Latino Eye Study Group.

Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California.

PURPOSE: To identify risk factors for 4-year incidence and progression of age-related macular degeneration (AMD) in adult Latinos.

DESIGN: Population-based prospective cohort study.

METHODS: Participants, aged 40 or older, from The Los Angeles Latino Eye Study (LALES) underwent standardized comprehensive ophthalmologic examinations at baseline and at 4 years of follow-up. Age-related macular degeneration was detected by grading 30-degree stereoscopic fundus photographs using the modified Wisconsin Age-Related Maculopathy Grading System. Multivariate stepwise logistic regression was used to examine the independent association of incidence and progression of AMD and baseline sociodemographic, behavioral, clinical, and ocular characteristics.

RESULTS: Multivariate analyses revealed that older age (OR per decade of age: 1.52; 95% CI: 1.29, 1.85) and higher pulse pressure (OR per 10 mm Hg: 2.54; 95% CI: 1.36, 4.76) were independently associated with the incidence of any AMD. The same factors were associated with early AMD, soft indistinct drusen, and retinal pigmentary abnormalities. Additionally, presence of clinically diagnosed diabetes mellitus was independently associated with increased retinal pigment (OR: 1.66; 95% CI: 1.01, 2.85), and male gender was associated with retinal pigment epithelial depigmentation (OR 2.50; 95% CI: 1.48, 4.23). Older age (OR per decade of age: 2.20; 95% CI: 1.82, 2.67) and current smoking (OR: 2.85; 95% CI: 1.66, 4.90) were independently associated with progression of AMD.

CONCLUSIONS: Several modifiable risk factors were associated with 4-year incidence and progression of AMD in Latinos. The results suggest that interventions aimed at reducing pulse pressure and promoting smoking cessation may reduce incidence and progression of AMD, respectively.

PMID: 21679916 [PubMed - as supplied by publisher]

Prev Chronic Dis. 2011 Jul;8(4):A84. Epub 2011 Jun 15.

Smoking and visual impairment among older adults with age-related eye diseases.

Zhang X, Kahende J, Fan AZ, Barker L, Thompson TJ, Mokdad AH, Li Y, Saaddine JB.

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INTRODUCTION: Tobacco use is the leading preventable cause of death in the United States. Visual impairment, a common cause of disability in the United States, is associated with shorter life expectancy and lower quality of life. The relationship between smoking and visual impairment is not clearly understood. We assessed the association between smoking and visual impairment among older adults with age-related eye diseases.

METHODS: We analyzed Behavioral Risk Factor Surveillance System data from 2005 through 2008 on older adults with age-related eye diseases (cataract, glaucoma, age-related macular degeneration, and diabetic retinopathy; age ≥50 y, N = 36,522). Visual impairment was defined by self-reported difficulty in recognizing a friend across the street or difficulty in reading print or numbers. Current smokers were respondents who reported having smoked at least 100 cigarettes ever and still smoked at the time of interview. Former smokers were respondents who reported having ever smoked at least 100 cigarettes but currently did not smoke. We used multivariate logistic regressions to examine the association and to adjust for potential confounders.

RESULTS: Among respondents with age-related eye diseases, the estimated prevalence of visual impairment was higher among current smokers (48%) than among former smokers (41%, P < .05) and respondents who had never smoked (42%, P < .05). After adjustment for age, sex, race/ethnicity, education, and general health status, current smokers with age-related eye diseases were more likely to have visual impairment than respondents with age-related eye diseases who had never smoked (odds ratio, 1.16, P < .05). Furthermore, respondents with cataract who were current smokers were more likely to have visual impairment than respondents with cataract who had never smoked (predictive margin, 44% vs 40%, P = .03), and the same was true for respondents with age-related macular degeneration (65% of current smokers vs 57% of never smokers, P = .02). This association did not hold true among respondents with glaucoma or diabetic retinopathy.

CONCLUSION: Smoking is linked to self-reported visual impairment among older adults with age-related eye diseases, particularly cataract and age-related macular degeneration. Longitudinal evaluation is needed to assess smoking cessation's effect on vision preservation.

PMID: 21672408 [PubMed - in process]

Clin Experiment Ophthalmol. 2011 Jun 13. doi: 10.1111/j.1442-9071.2011.02620.x. [Epub ahead of print]

Filtering blue light reduces light-induced oxidative stress, senescence, and accumulation of extracellular matrix proteins in human retinal pigment epithelium cells.

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Department of Ophthalmology, Ludwig-Maximilians-University, Munich, Germany GSF-National Research Center for Environment and Health, Neuherberg, Germany.

Purpose: Cumulative light exposure is significantly associated with aging and the progression of age-related macular degeneration. To prevent the retina from blue-light damage in pseudophakia, blue-light-absorbing intraocular lenses (IOLs) have been developed. This study compares the possible protective effects of a blue-light-absorbing IOL to an untinted UV-absorbing IOL with regard to light-induced oxidative stress and senescence of human retinal pigment epithelium (RPE).

Methods: As primary human RPE cells were exposed to white light, either a UV- and blue-light-absorbing IOL or UV-absorbing IOL was placed in the light beam. After 60 min of irradiation, cells were investigated by electron microscopy for viability, induction of intracellular reactive oxygen species, and senescence-associated β-galactosidase activity. Expression and secretion of matrix metalloproteinases 1 and 3 and their mRNA were determined by real-time PCR and enzyme-linked immunosorbent assay.

Results: Light exposure induced structural damage, decreased RPE cell viability, and increased reactive oxygen species, senescence-associated β-galactosidase activity, and matrix metalloproteinases 1 and 3 expression and secretion. Although both types of IOL significantly reduced these effects, the protective effects of the UV- and blue-light-absorbing IOL were significantly stronger than those of the UV-absorbing IOL.

Conclusions: The UV- and blue-light-absorbing IOL demonstrated significantly better protection against light-induced oxidative stress, senescence, and structural damage than the UV-absorbing IOL. These in vitro findings support the hypothesis that the UV- and blue-light-absorbing IOL may prevent retinal damage in clinical use.

PMID: 21668780 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2011 Jun 15. doi: 10.1111/j.1755-3768.2011.02170.x. [Epub ahead of print]

Assessment of macular pigment optical density (MPOD) in patients with unilateral wet age-related macular degeneration (AMD).

Tsika C, Tsilimbaris MK, Makridaki M, Kontadakis G, Plainis S, Moschandreas J.

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Purpose: To compare the macular pigment optical density (MPOD) of patients with unilateral wet age-related macular degeneration (AMD) with the MPOD of bilateral dry AMD patients and healthy elderly individuals.

Methods: The MPOD of 34 patients with unilateral wet AMD was measured in their fellow eye that had the dry form of the disease (study group). The MPOD of the study group was compared with the MPOD of 33 patients with bilateral dry AMD (patients' control group) and 35 elderly subjects without any signs of retinal

disease (control group). None of the subjects was under carotenoid supplementation. The MPOD was measured with Heterochromatic Flicker Photometry [QuantifEYE™- MPS 9000 (ZeaVision(©))]. The statistical package SPSS v 17.0 was used for the analysis.

Results: The overall mean MPOD was 0.52 (SD 0.15). Patients with unilateral wet AMD have significantly higher levels of MPOD in their fellow eye compared with patients with bilateral dry AMD (0.58 versus 0.48, p = 0.026). Mean MPOD of patients with bilateral dry AMD does not differ significantly from that of healthy elderly subjects (0.48 versus 0.50, p = 0.865). In this population sample, no correlation with age was observed, while women have slightly but significantly higher levels of MPOD (0.55 versus 0.49, p = 0.029).

Conclusion: In the present study, the mean MPOD at the fellow eye of patients with unilateral wet AMD was found to be significantly higher than that of patients with bilateral dry AMD, while no other significant difference emerged between groups. Further investigation is demanded to clarify the role of macular pigment in AMD progression.

PMID: 21672183 [PubMed - as supplied by publisher]

Eye Contact Lens. 2011 Jun 11. [Epub ahead of print]

Ozone Depletion and Solar Ultraviolet Radiation: Ocular Effects, a United Nations Environment Programme Perspective.

Cullen AP.

From the School of Optometry (A.P.C.), University of Waterloo, Waterloo, Ontario, Canada.

PURPOSE: To describe he role played by the United Nations Environmental Effects Panel with respect to the ocular effects of stratospheric ozone depletion and present the essence of the Health Chapter of the 2010 Assessment.

METHODS: A consideration of solar ultraviolet radiation (UVR) at the Earth's surface as it is affected by atmospheric changes and how these influence sunlight-related eye diseases. A review of the current Assessment with emphasis on pterygium, cataract, ocular melanoma, and age-related macular degeneration.

RESULTS: Although the ozone layer is projected to recover slowly in the coming decades, continuing vigilance is required regarding exposure to the sun. Evidence implicating solar UVR, especially UVB, in every tissue of the eye continues to be amassed.

CONCLUSION: The need for ocular UV protection existed before the discovery of the depletion of the ozone layer and will continue even when the layer fully recovers in approximately 2100.

PMID: 21670695 [PubMed - as supplied by publisher]

Eye Contact Lens. 2011 Jun 10. [Epub ahead of print]

An Epidemiological Perspective of UV Exposure-Public Health Concerns.

Lucas RM.

From the National Centre for Epidemiology and Population Health, The Australian National University, Canberra, Australia.

Abstract

Over the last 30 years, many countries have developed strong sun protection programs, spurred on by rap-

idly increasing skin cancer incidence and concerns about stratospheric ozone depletion. More recently, considerable concern has arisen about widespread vitamin D insufficiency, creating a "sun exposure dilemma," since in most regions vitamin D predominantly derives from endogenous synthesis in the skin initiated by exposure to ultraviolet (UV) radiation. Little attention has been paid to whether a similar dilemma exists for UV-related eye conditions.For the eyes, to our current knowledge, exposure to UV radiation has only adverse effects. There is strong evidence that acute high dose exposure to UV radiation causes photokeratitis and photoconjunctivitis, while even low dose chronic exposure to UV radiation is a risk factor for cataract, pterygium, and squamous cell carcinoma of the cornea and conjunctiva. There is weaker evidence in relation to other conditions, including ocular melanoma and age-related macular degeneration. Ultraviolet radiation-related eye diseases are common, disabling, and cause a considerable disease burden worldwide.The "correct" public health message for optimal sun exposure is not clear cut, with too many variables-ambient UV radiation, personal skin type, age, weight, clothing habits, medication, and others-for a blanket sun safety message. In addition, there remain many unknowns, including strong evidence supporting or refuting the very many proposed health benefits of vitamin D. More evidence is required to define disease burdens for UV-induced eye diseases, to evaluate the decrease in disease burden from sun protective measures and to elucidate any beneficial effects of exposure of the eye to UV radiation, to provide appropriate advice to the public.

PMID: 21670693 [PubMed - as supplied by publisher]

Oncotarget. 2011 Jun 10. [Epub ahead of print]

RIP Kinase-Mediated Necrosis as an Alternative Mechanism of Photoreceptor Death.

Murakami Y, Miller JW, Vavvas DG.

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Abstract

Photoreceptor cell death is the terminal event in a variety of retinal disorders including age-related macular degeneration, retinitis pigmentosa, and retinal detachment. Apoptosis has been thought to be the major form of cell death in these diseases, however accumulating evidence suggests that another pathway, programmed necrosis is also important. Recent studies have shown that, when caspase pathways are blocked, receptor interacting protein (RIP) kinases promote necrosis and overcome apoptosis inhibition. Therefore, targeting of both caspase and RIP kinase pathways are required for effective photoreceptor protection. Here, we summarize the current knowledge of RIP kinase-mediated necrotic signaling and its contribution to photoreceptor death.

PMID: 21670490 [PubMed - as supplied by publisher]

Genetics

J Hum Genet. 2011 Jun 16. doi: 10.1038/jhg.2011.54. [Epub ahead of print]

Copy number polymorphisms in new HapMap III and Singapore populations.

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Abstract

Copy number variations can be identified using newer genotyping arrays with higher single nucleotide polymorphisms (SNPs) density and copy number probes accompanied by newer algorithms. McCarroll et al. (2008) applied these to the HapMap II samples and identified 1316 copy number polymorphisms (CNPs). In our study, we applied the same approach to 859 samples from three Singapore populations and seven HapMap III populations. Approximately 50% of the 1291 autosomal CNPs were found to be polymorphic only in populations of non-African ancestry. Pairwise comparisons among the 10 populations showed substantial differences in the CNPs frequencies. Additionally, 698 CNPs showed significant differences with false discovery rate (FDR)<0.01 among the 10 populations and these loci overlap with known disease-associated or pharmacogenetic-related genes such as CFHR3 and CFHR1 (age related macular degeneration), GSTTI (metabolism of various carcinogenic compounds and cancers) and UGT2B17 (prostate cancer and graft-versus-host disease). The correlations between CNPs and genome-wide association studies-SNPs were investigated and several loci, which were previously unreported, that may potentially be implicated in complex diseases and traits were found; for example, childhood acute lymphoblastic leukaemia, age-related macular degeneration, breast cancer, response to antipsychotic treatment, rheumatoid arthritis and type-1 diabetes. Additionally, we also found 5014 novel copy number loci that have not been reported previously by McCarroll et al. (2008) in the 10 populations.Journal of Human Genetics advance online publication, 16 June 2011; doi:10.1038/jhg.2011.54.

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Implication of CD21, CD35, and CD55 in the Pathogenesis of Age-Related Macular Degeneration.

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PURPOSE: To determine a possible implication of CD21, CD35, and CD55 in the pathogenesis of age-related macular degeneration (AMD) by assessing the difference in expression rates of these factors on AMD patients and a control group.

DESIGN: Case-control study.

METHODS: Fifty unrelated AMD patients and 48 unrelated sex- and age-matched control subjects participated in this case-control study. Samples of fresh EDTA-blood were stained and flow cytometry was chosen to measure fluorescence emissions. The association between exudative AMD and CD21, CD35, and CD55 was evaluated from all patients who completed the study.

RESULTS: Our study shows CD35 to be expressed in a significantly higher frequency in AMD patients on monocytes (P = .00586), lymphocytes (P = .000605), and granulocytes (P < .000033). In contrast, the expression rate of CD21 (P > .05) and CD55 (P > .05) are similar in both groups.

CONCLUSION: More regulative factors of the complement system are involved in pathogenesis of AMD. Our study underlines the key role of the complement system in AMD and shows the involvement of the whole immune system through more regulative factors.

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Missing X and Y: a review of participant ages in population-based eye studies.

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Abstract

Ophthalmic population-based studies have been used to establish the frequency of eye disease and the associated environmental and genetic factors that cause vision impairment and blindness. Most of these studies have concentrated on the diseases of aging; cataract, Age-related Macular Degeneration, glaucoma, and diabetic retinopathy. Other studies have identified eye diseases in children but few studies of young adult eye disease exist. We conducted a systematic review of the ophthalmic literature to identify potential population-based eye studies and then note the age of participants in the studies. We then summarised the disease specific to young adults to show there is a need for further research to identify eye disease in this important and often-neglected group in the community. 84 large population based studies have been conducted worldwide; nine in North America, two in South America, 17 in Africa, 35 in Asia, 11 in Australia and the Pacific, six in Europe, four in the Middle East and one that covered three continents. No studies specifically examined young adults. 26% of studies included young adults as part of all ages examined but none of these examined a large number of young adults.

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Common Variants near FRK/COL10A1 and VEGFA are Associated with Advanced Age-related Macular Degeneration.

Yu Y, Bhangale TR, Fagerness J, Ripke S, Thorleifsson G, Tan PL, Souied EH, Richardson AJ, Merriam JE, Buitendijk GH, Reynolds R, Raychaudhuri S, Chin KA, Sobrin L, Evangelou E, Lee PH, Lee AY, Leveziel N, Zack DJ, Campochiaro B, Campochiaro P, Smith RT, Barile GR, Guymer RH, Hogg R, Chakravarthy U, Robman LD, Gustafsson O, Sigurdsson H, Ortmann W, Behrens TW, Stefansson K, Uitterlinden AG, van Duijn CM, Vingerling JR, Klaver CC, Allikmets R, Brantley MA Jr, Baird PN, Katsanis N, Thorsteinsdottir U, Ioannidis JP, Daly MJ, Graham RR, Seddon JM.

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Abstract

Despite significant progress in the identification of genetic loci for age-related macular degeneration (AMD), not all of the heritability has been explained. To identify variants which contribute to the remaining genetic susceptibility, we performed the largest meta-analysis of genome-wide association studies to date for advanced AMD. We imputed 6,036,699 SNPs with 1000-Genomes reference genotypes on 2594 cases and 4134 controls with follow-up replication of top signals in 5640 cases and 52,174 controls. We identified two new common susceptibility alleles, rs1999930 on 6q21-q22.3 near FRK/COL10A1 (odds ratio 0.87; P=1.1x10 (-8)) and rs4711751 on 6p12 near VEGFA (odds ratio 1.15, P=8.7x10(-9)). In additional to the two novel loci, ten previously reported loci in ARMS2/HTRA1 (rs10490924), CFH (rs1061170, and rs1410996), CFB (rs641153) C3 (rs2230199), C2 (rs9332739), CFI (rs10033900), LIPC (rs10468017), TIMP3 (rs9621532) and CETP (rs3764261) were confirmed with genome-wide significant signals in this

large study. Loci in the recently reported genes ABCA1 and COL8A1 were also detected with suggestive evidence of association with advanced AMD. The novel variants identified in this study suggest that angiogenesis (VEGFA) and extracellular collagen matrix (FRK/COL10A1) pathways contribute to the development of advanced age-related macular degeneration.

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Disease-causing mutations in genes of the complement system.

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Abstract

Recent studies have revealed profound developmental consequences of mutations in genes encoding proteins of the lectin pathway of complement activation, a central component of the innate immune system. Apart from impairment of immunity against microorganisms, it is known that hereditary deficiencies of this system predispose one to autoimmune conditions. Polymorphisms in complement genes are linked to, for example, atypical hemolytic uremia and age-dependent macular degeneration. The complement system comprises three convergent pathways of activation: the classical, the alternative, and the lectin pathway. The recently discovered lectin pathway is less studied, but polymorphisms in the plasma pattern-recognition molecule mannan-binding lectin (MBL) are known to impact its level, and polymorphisms in the MBL-associated serine protease-2 (MASP-2) result in defects of complement activation. Recent studies have described roles outside complement and immunity of another MBL-associated serine protease, MASP-3, in the etiology of 3MC syndrome, an autosomal-recessive disorder involving a spectrum of developmental features, including characteristic facial dysmorphism. Syndrome-causing mutations were identified in MASP1, encoding MASP-3 and two additional proteins, MASP-1 and MAp44. Furthermore, an association was discovered between 3MC syndrome and mutations in COLEC11, encoding CL-K1, another molecule of the lectin pathway. The findings were confirmed in zebrafish, indicating that MASP-3 and CL-K1 underlie an evolutionarily conserved pathway of embryonic development. Along with the discovery of a role of C1q in pruning synapses in mice, these recent advances point toward a broader role of complement in development. Here, we compare the functional immunologic consequences of "conventional" complement deficiencies with these newly described developmental roles.

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Pre-clinical

Birth Defects Res C Embryo Today. 2011 Jun;93(2):182-93. doi: 10.1002/bdrc.20203.

Zebrafish models to study hypoxia-induced pathological angiogenesis in malignant and nonmalignant diseases.

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Abstract

Most in vivo preclinical disease models are based on mouse and other mammalian systems. However,

these rodent-based model systems have considerable limitations to recapitulate clinical situations in human patients. Zebrafish have been widely used to study embryonic development, behavior, tissue regeneration, and genetic defects. Additionally, zebrafish also provides an opportunity to screen chemical compounds that target a specific cell population for drug development. Owing to the availability of various genetically manipulated strains of zebrafish, immune privilege during early embryonic development, transparency of the embryos, and easy and precise setup of hypoxia equipment, we have developed several disease models in both embryonic and adult zebrafish, focusing on studying the role of angiogenesis in pathological settings. These zebrafish disease models are complementary to the existing mouse models, allowing us to study clinically relevant processes in cancer and nonmalignant diseases, which otherwise would be difficult to study in mice. For example, dissemination and invasion of single human or mouse tumor cells from the primary site in association with tumor angiogenesis can be studied under normoxia or hypoxia in zebrafish embryos. Hypoxia-induced retinopathy in the adult zebrafish recapitulates the clinical situation of retinopathy development in diabetic patients or age-related macular degeneration. These zebrafish disease models offer exciting opportunities to understand the mechanisms of disease development, progression, and development of more effective drugs for therapeutic intervention. Birth Defects Research (Part C) 93:182-193, 2011. © 2011 Wiley-Liss, Inc.

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Diet

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Reducing the Genetic Risk of Age-Related Macular Degeneration With Dietary Antioxidants, Zinc, and {omega}-3 Fatty Acids: The Rotterdam Study.

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OBJECTIVE: To investigate whether dietary nutrients can reduce the genetic risk of early age-related macular degeneration (AMD) conferred by the genetic variants CFH Y402H and LOC387715 A69S in a nested case-control study.

METHODS: For 2167 individuals (≥55 years) from the population-based Rotterdam Study at risk of AMD, dietary intake was assessed at baseline using a semiquantitative food frequency questionnaire and genetic variants were determined using TaqMan assay. Incident early AMD was determined on fundus photographs at 3 follow-up visits (median follow-up, 8.6 years). The synergy index was used to evaluate biological interaction between risk factors; hazard ratios were calculated to estimate risk of early AMD in strata of nutrient intake and genotypes.

RESULTS: Five hundred seventeen participants developed early AMD. Significant synergy indices supported the possibility of biological interaction between CFH Y402H and zinc, β-carotene, lutein/zeaxanthin, and eicosapentaenoic/docosahexaenoic acid (EPA/DHA) and between LOC387715 A69S and zinc and EPA/DHA (all P < .05). Homozygotes of CFH Y402H with dietary intake of zinc in the highest tertile reduced their hazard ratio of early AMD from 2.25 to 1.27. For intakes of β-carotene, lutein/zeaxanthin, and EPA/DHA, these risk reductions were from 2.54 to 1.47, 2.63 to 1.72, and 1.97 to 1.30, respectively. Carriers of LOC387715 A69S with the highest intake of zinc and EPA/DHA reduced their risk from 1.70 to 1.17 and 1.59 to 0.95, respectively (all P trends <.05).

CONCLUSIONS: High dietary intake of nutrients with antioxidant properties reduces the risk of early AMD in those at high genetic risk. Therefore, clinicians should provide dietary advice to young susceptible individuals to postpone or prevent the vision-disabling consequences of AMD.

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Serum Lutein Response Is Greater from Free Lutein Than from Esterified Lutein during 4 Weeks of Supplementation in Healthy Adults.

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BACKGROUND: Current data suggest great variability in serum response following lutein ingestion from various sources.

OBJECTIVE: To compare the relative serum response during supplementation with free lutein (fL) and lutein esters (Le).

METHODS: 72 volunteers (23-52 years; body mass index [BMI] >20 and <30 kg/m(2); baseline serum lutein <20 µg/dL [<352 nmol/L]) were identified. Subjects, matched for gender, age, and BMI, were randomly assigned to the fL or Le group. fL and Le capsules contained 12.2 mg of free lutein or 27 mg of lutein ester (equivalent to 13.5 mg free lutein), respectively. Fasting blood was obtained at baseline and after 7, 14, 21, and 28 days of supplementation. Supplements were consumed with standard portions of dry, ready-to-eat cereal and 2% cow's milk.

RESULTS: Absolute changes in serum lutein, per mg daily dose, were significantly greater in fL vs. Le after 21 days (p = 0.0012) and remained so after 28 days (p = 0.0011) of supplementation. Serum lutein Area Under the Curve [AUC((day 0-28))] response was 17% greater for fL vs. Le (p = 0.0187). Regression models were used and determined that (1) baseline serum lutein levels and (2) the form of lutein ingested (fL > Le) influence the serum lutein response during supplementation, while subject age, gender, BMI, and serum lipids do not affect serum response.

CONCLUSIONS: These results suggest that the relative serum lutein response will be significantly greater from supplements containing free lutein than from supplements containing lutein esters. These findings should be useful for future clinical trials exploring the effectiveness of lutein supplementation in the prevention of or protection against age-related macular degeneration and/or cataracts.

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Antioxidant Effect of Trans-Resveratrol in Cultured Human Retinal Pigment Epithelial Cells.

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Abstract Purpose: Oxidative damages to the retinal pigment epithelium (RPE) have been suggested to play a key role in the pathogenesis of age-related macular degeneration. trans-Resveratrol (3,4',5-trihydroxystilbene) is a nonflavonoid dietary polyphenol with various pharmacological effects, including antioxidant activity. The purpose of this study was to evaluate the potential protective effect of resveratrol against hydrogen peroxide induced oxidative stress in cultured human RPE cells.

Methods: Human retinal D407 RPE cells were pretreated with resveratrol at 3 different concentrations (25, 50, and 100 µM) for 24 h and exposed for 1 h to 500 µM hydrogen peroxide. Cell viability, cytotoxicity, and the level of intracellular reactive oxygen species (ROS) were determined in basal and oxidative stress conditions. The concentration of reduced glutathione and the activities of catalase, superoxide dismutase, and glutathione peroxidase were also examined under both experimental conditions.

Results: Resveratrol in culture media had no cytotoxic effect at a concentration of 25-100 μM but showed a protective effect against hydrogen peroxide-induced cytoxicity. Pretreatment with resveratrol induced a significant, dose-dependent increase of superoxide dismutase, glutathione peroxidase, and catalase activities. Moreover, resveratrol significantly enhanced the level of reduced glutathione under both basal and oxidative stress conditions. The significant inhibition of the intracellular ROS generation supports the hypothesis that resveratrol can also contribute to the antioxidant defense by directly scavenging the ROS in RPE cells.

Conclusions: Our results indicate that treatment of RPE cells with resveratrol at micromolar concentrations confers a marked protection against oxidative stress. These data suggest that dietary supplementation of resveratrol may contribute to the prevention of RPE degeneration induced by oxidative stress.

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