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MD Research News

Issue 11

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Drug treatment

Acta Ophthalmol. 2011 Jan 14. doi: 10.1111/j.1755-3768.2010.02065.x. [Epub ahead of print]

Long-term efficacy and safety of ranibizumab administered pro re nata in Japanese patients with neovascular age-related macular degeneration in the EXTEND-I study.

Tano Y, Ohji M; on behalf of the EXTEND-I Study Group.

Department of Ophthalmology, Osaka University Medical School, Osaka, Japan Department of Ophthalmology, Shiga University of Medical Science, Shiga, Japan.

Purpose: To evaluate the long-term efficacy and safety of ranibizumab administered pro re nata (PRN) in Japanese patients with choroidal neovascularization secondary to age-related macular degeneration during the extension phase of the EXTEND-I study. Methods: EXTEND-I, an open-label, multicenter, Phase I/II study comprised: a single-injection (Group A); a multiple-injection (Groups A and B; the latter consisted of patients who did not participate in the single-injection phase); and an extension phase. In the extension phase, a PRN regimen of ranibizumab (0.3 or 0.5 mg) guided by monthly best-corrected visual acuity (BCVA) score and other ophthalmic examinations was employed. The efficacy variables included the mean BCVA change from Month 12 to the last visit in Group B. Safety was assessed in all patients. Results: In the extension phase, efficacy was assessed only in Group B patients. The number of ranibizumab injections per year in the 0.3 and 0.5 mg Group B patients was 4.19 and 4.27, respectively. The mean BCVA change (SD) from Month 12 to the last visit was -3.6 (14.82) letters for 0.3 mg (n = 28) and -2.2 (7.92) letters for 0.5 mg groups (n = 33) in Group B. Conjunctival haemorrhage and nasopharyngitis were the most commonly reported adverse events. Of the 13 serious adverse events reported, cerebral infarction (two incidences) was suspected to be study-drug related. Conclusions: Pro re nata regimen of ranibizumab guided by monthly BCVA and other ophthalmic examinations appears effective in sustaining the BCVA gained with 12 monthly injections while reducing the number of injections during the extension phase. Ranibizumab was well tolerated during the extension phase.

PMID: 21232078 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2011 Jan 14. doi: 10.1111/j.1755-3768.2010.02075.x. [Epub ahead of print]

Short-term effects of intravitreal bevacizumab (Avastin(®)) on retrobulbar hemodynamics in patients with neovascular age-related macular degeneration.

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Training and Research Hospital, Ankara, Turkey.

Purpose: To evaluate the short-term effects of intravitreal bevacizumab on retrobulbar hemodynamics in patients with neovascular age-related macular degeneration (AMD). Methods: This study was carried out at Ataturk Training and Research Hospital 1st Ophthalmology Clinic, Ankara. Fourteen patients with neovascular AMD, who were treated with intravitreal injection of bevacizumab, were included in this study. Peak systolic velocity (PSV), end-diastolic velocity (EDV) and resistivity index (RI) were measured with colour Doppler imaging (CDI) in the ophthalmic artery, central retinal artery (CRA) and posterior ciliary artery. Results: The mean age of the 14 patients was 78 ± 9 (64-87). Of the 14 patients, eight were men and six were women. Colour Doppler imaging measurements of EDV ($p = 0.015$) and RI ($p = 0.009$) parameters of CRA revealed statistically significant difference among all three periods. End-diastolic velocity values decreased at the end of the 1st week and returned close to preoperative values at the end of the 1st month after the procedure. Also, EDV of posterior ciliary artery (PCA) decreased at the end of the 1st week and returned close to preoperative values at the end of the 1st month after the procedure. Resistivity index of PCA showed a temporary increase at the end of the 1st week and returned close to preoperative values at the end of the 1st month after the procedure. Conclusion: Injection of bevacizumab decreased blood velocities of CRA and PCA and increased RI of CRA and PCA in the early postoperative period and returned to preoperative values at the end of the first month.

PMID: 21232081 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Retina. 2011 Jan 8. [Epub ahead of print]

EVALUATION OF SEGMENTATION PROCEDURES USING SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY IN EXUDATIVE AGE-RELATED MACULAR DEGENERATION.

Malamos P, Ahlers C, Mylonas G, Schütze C, Deak G, Ritter M, Sacu S, Schmidt-Erfurth U.

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PURPOSE: The purpose of this study was to evaluate standardized automated segmentation procedures of spectral domain optical coherence tomography (SD-OCT) in imaging of age-related macular degeneration.

METHODS: Twenty-nine eyes of 29 patients with neovascular age-related macular degeneration were included. Three groups were assigned, according to the predominant localization of extravasated fluid in the intra-, subretinal, and subretinal pigment epithelium (RPE) compartment. Automated segmentation procedures were evaluated in B scans of 512 × 128 × 1024 and 200 × 200 × 1024 scan patterns using SD-OCT (Cirrus). Alignment errors at the internal limiting membrane, actual RPE, and extrapolation of the physiologic RPE (RPE fit) were graded using a standardized classification system.

RESULTS: The rate of severe alignment failures was 56% and 41% for the 512 × 128 and the 200 × 200 raster pattern, respectively. Internal limiting membrane and actual RPE boundaries were most correctly delineated in 200 × 200 raster pattern. Retinal pigment epithelium fit alignment was generally poor in 50% of scans. Retinal thickness values defined by internal limiting membrane and actual RPE segmentation were 90% accurate and not compromised by RPE fit misalignment. Subretinal fluid was demarcated most reliably. Alignment errors may occur together with a large spectrum of morphologic alterations.

CONCLUSION: Automated algorithms of SD-OCT demonstrate a substantial rate of alignment failures in the assessment of exudative age-related macular degeneration pathologies, which are usually associated with misinterpretation of boundaries at the (sub) RPE level.

PMID: 21221050 [PubMed - as supplied by publisher]

Arch Ophthalmol. 2011 Jan;129(1):40-7.

Drusen analysis in a human-machine synergistic framework.

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OBJECTIVES: To demonstrate how human-machine intelligence can be integrated for efficient image analysis of drusen in age-related macular degeneration and to validate the method in 2 large, independently graded, population-based data sets.

METHODS: We studied 358 manually graded color slides from the Netherlands Genetic Isolate Study. All slides were digitized and analyzed with a user-interactive drusen detection algorithm for the presence and quantity of small, intermediate, and large drusen. A graphic user interface was used to preprocess the images, choose a region of interest, select appropriate corrective filters for images with photographic artifacts or prominent choroidal pattern, and perform drusen segmentation. Weighted κ statistics were used to analyze the initial concordance between human graders and the drusen detection algorithm; discordant grades from 177 left-eye slides were subjected to exhaustive analysis of causes of disagreement and adjudication. To validate our method further, we analyzed a second data set from our Columbia Macular Genetics Study.

RESULTS: The graphical user interface decreased the time required to process images in commercial software by 60.0%. After eliminating borderline size disagreements and applying corrective filters for photographic artifacts and choroidal pattern, the weighted κ values were 0.61, 0.62, and 0.76 for small, intermediate, and large drusen, respectively. Our second data set demonstrated a similarly high concordance.

CONCLUSIONS: Drusen identification performed by our user-interactive method presented fair to good agreement with human graders after filters for common sources of error were applied. This approach exploits a synergistic relationship between the intelligent user and machine computational power, enabling fast and accurate quantitative retinal image analysis.

PMID: 21220627 [PubMed - in process]

Retina. 2011 Jan 8. [Epub ahead of print]

INNER SEGMENT-OUTER SEGMENT JUNCTIONAL LAYER INTEGRITY AND CORRESPONDING RETINAL SENSITIVITY IN DRY AND WET FORMS OF AGE-RELATED MACULAR DEGENERATION.

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PURPOSE: To investigate a relationship between the inner segment-outer segment (IS-OS) junctional layer integrity and the overlying retinal sensitivity assessed by Spectral OCT/SLO (spectral-domain optical coherence tomography) and microperimetry testing in patients with dry and wet forms of age-related macular degeneration (AMD).

METHODS: Spectral-domain optical coherence tomography examination and microperimetry testing were performed in 55 eyes of 43 consecutive patients with AMD. Microperimetry maps were registered onto three-dimensional retinal topography maps, and point-to-point analysis of correlation between microperimetric retinal sensitivities and corresponding status of the underlying IS-OS junctional layer was performed. In addition, the analysis of correlation between the best-corrected visual acuity and the integrity

of IS-OS layer in the center of fovea was also performed.

RESULTS: Retinal sensitivity was inversely and strongly correlated with the integrity of IS-OS layer in both dry and wet forms of AMD (correlation coefficient [r] = -0.75 [95% confidence interval, 0.49-0.88], P < 0.001, and -0.79 [95% confidence interval, 0.61-0.89], P < 0.001, respectively). The correlation between the best-corrected visual acuity and the integrity of IS-OS layer in the center of fovea was less significant (r = -0.58 [95% confidence interval, 0.19-0.79], P = 0.02, for dry AMD, and r = -0.6 [95% confidence interval, 0.32-0.78], P = 0.015, for wet AMD).

CONCLUSION: Retinal sensitivity consistently correlated with the status of underlying IS-OS junctional layer in both dry and wet forms of AMD. Loss of IS-OS layer is significantly associated with poor retinal sensitivity, assessed by microperimetry. Compared with visual acuity, functional testing with microperimetry appears to more consistently correlate with changes in the outer retina, such as IS-OS junctional integrity, especially, in patients with wet AMD.

PMID: 21221051 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2010 Dec 30. pii: 00A20131-8306-4E65-B736-0BEC7CB4E96A. [Epub ahead of print]

Loss of chance: a new kind of damage to ophthalmologic patients from Europe to Italy.

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Abstract. This work was inspired by a recent juridical development in Italy, whose purpose is to prevent rejection of damage claims whenever it is not possible to prove a causal link between iatrogenic illicit behavior and damage to the patient, despite the fact that the patient has clearly suffered physical or mental injury. In view of this, some European countries-e.g., France and Germany-have recently come up with a new damage interpretation called loss of chance, i.e., the missed opportunity to get a more favorable outcome through different or more timely and efficient therapies. Although the problem has been thoroughly discussed on several levels, no countries have conformed their legislation accordingly, leaving it up to the courts to settle issues of damage claims where loss of chance can be applied and to resolve doubts about the limits of applicability of this new type of damage interpretation. The concept of loss of chance seems to be applicable to many cases in ophthalmologic practice. For example, glaucoma and macular degeneration are common, serious, and potentially blinding diseases in which delayed diagnosis and therapy reduce the chances not only to limit injuries, but also to stop future progress of the disease. Hence, the authors emphasize that a good practice is the only way for ophthalmologists to avoid malpractice claims related to the new developments in tort law in Italy and in other European countries following the creation of new definitions of damage.

PMID: 21218390 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2011 Jan 8. [Epub ahead of print]

Measuring macular pigment optical density in vivo: a review of techniques.

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BACKGROUND: Macular pigment has been the focus of much attention in recent years, as a potential modifiable risk factor for age-related macular degeneration. This interest has been heightened by the ability to measure macular pigment optical density (MPOD) in vivo.

METHOD: A systematic literature search was undertaken to identify all available papers that have used in vivo MPOD techniques. The papers were reviewed, and all relevant information was incorporated into this article.

RESULTS: Measurement of MPOD is achievable with a wide range of techniques, which are typically categorized into one of two groups: psychophysical (requiring a response from the subject) or objective (requiring minimal input from the subject). The psychophysical methods include heterochromatic flicker photometry and minimum motion photometry. The objective methods include fundus reflectometry, fundus autofluorescence, resonance Raman spectroscopy and visual evoked potentials. Even within the individual techniques, there is often much variation in how data is obtained and processed.

CONCLUSION: This review comprehensively details the procedure, instrumentation, assumptions, validity and reliability of each MPOD measurement technique currently available, along with their respective advantages and disadvantages. This leads us to conclude that development of a commercial instrument, based on fundus reflectometry or fundus autofluorescence, would be beneficial to macular pigment research and would support MPOD screening in a clinical setting.

PMID: 21221629 [PubMed - as supplied by publisher]

Arq Bras Oftalmol. 2010 Oct;73(5):474-9.

Possible mechanisms of retinal function recovery with the use of cell therapy with bone marrow-derived stem cells.

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Abstract

Bone marrow has been proposed as a potential source of stem cells for regenerative medicine. In the eye, degeneration of neural cells in the retina is a hallmark of such widespread ocular diseases as age-related macular degeneration (AMD) and retinitis pigmentosa. Bone marrow is an ideal tissue for studying stem cells mainly because of its accessibility. Furthermore, there are a number of well-defined mouse models and cell surface markers that allow effective study of hematopoiesis in healthy and injured mice. Because of these characteristics and the experience of bone marrow transplantation in the treatment of hematological disease such as leukemia, bone marrow-derived stem cells have also become a major tool in regenerative medicine. Those cells may be able to restore the retina function through different mechanisms: A) cellular differentiation, B) paracrine effect, and C) retinal pigment epithelium repair. In this review, we described these possible mechanisms of recovery of retinal function with the use of cell therapy with bone marrow-derived stem cells.

PMID: 21225138 [PubMed - in process]

Acta Ophthalmol. 2011 Jan 14. doi: 10.1111/j.1755-3768.2010.02074.x. [Epub ahead of print]

The predictive value of subjective symptoms and clinical signs for the presence of treatment-requiring exudative age-related macular degeneration.

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Purpose: The introduction of vascular endothelial growth factor inhibitors for the treatment of exudative age-related macular degeneration (AMD) has increased the referral rates of AMD patients with visual

symptoms to treating centres considerably. However, a large proportion of the referred patients do not qualify for treatment implying that considerable resources could be saved if these patients could be identified on the basis of the clinical data available in the referring nonspecialized setting. Methods: A prospective observational study of 1682 consecutive patients referred with suspicion of exudative AMD qualifying for intravitreal angiostatic treatment. On the basis of the structured interviewing about symptoms, ophthalmoscopy, optical coherence tomography scanning, and fluorescein angiography, the patients were divided into two groups: one qualifying for and another not qualifying for treatment. Multiple logistic regression was used to identify independent parameters predicting the need for treatment. Results: The presence of metamorphopsia, dyschromatopsia, retinal haemorrhages and exudates, central retinal thickness, and the absence of micropsia were highly significant individual determinants of treatment-requiring AMD. Sudden onset and worsening of symptoms and the presence of a central dark spot covaried with the occurrence of retinal haemorrhages, whereas reduced visual acuity and blurred vision covaried with the presence of both haemorrhages and exudates. Conclusion: Patients with treatment-requiring AMD can be reliably identified by questioning about the presence of metamorphopsia and dyschromatopsia and the absence of micropsia, combined with ophthalmoscopical detection of retinal haemorrhages and exudates. This information may improve the triage of patients considered for referral.

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Invest Ophthalmol Vis Sci. 2011 Jan 12. [Epub ahead of print]

Wet vs. dry age-related macular degeneration in patients with central field loss : different effects on Maximum Reading Speed.

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PURPOSE. To describe new efficient predictors of Maximum Reading Speed (MRS) in age-related macular degeneration (AMD) patients with Central Field Loss. Type of AMD disease (wet vs. dry) was scrutinized because this factor seems to offer a promising model of differential visual adaptation induced by different temporal courses of disease progression. METHODS. Linear mixed-effects (lme) analyses were performed on a dataset initially collected to assess the effect of interline spacing on MRS. MRS was measured with MNRead-like French sentences in 89 eyes (64 dry and 25 wet) from 61 patients with AMD. MP1 microperimetry examination was performed for each eye. Eyes were only included if they had a dense macular scotoma including the fovea, which ensured that patients used eccentric viewing. RESULTS. Analyses show the unique contributions, i.e. after adjusting for the effects of other factors, of 3 new factors. a) MRS is higher for wet eyes than for dry eyes. b) An advantage of similar amplitude is found for phakic eyes compared to pseudo-phakic eyes. c) MRS decreases when distance between fixation PRL and fovea increases. In addition, the instantaneous slope of the relationship between scotoma area and MRS is much shallower than reported in two previous studies. CONCLUSION. The 4 effects described above improve our ability to reliably predict MRS for AMD patients. The wet/dry difference is a major result that might result from the different time-courses of the two types of disease, thus involving different types of visuo-motor and attentional adaptation processes.

PMID: 21228374 [PubMed - as supplied by publisher]

Retina. 2011 Jan 8. [Epub ahead of print]

PUBLICATION RATES OF REGISTERED CLINICAL TRIALS IN MACULAR DEGENERATION.

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Brunswick, New Jersey; †UMDNJ-Robert Wood Johnson Medical School, Piscataway, New Jersey; and ‡Boston University Medical School, Boston, Massachusetts.

PURPOSE: The purpose of this study was to evaluate the rate of publication of registered clinical trials concerning age-related macular degeneration (AMD).

METHODS: The National Institute of Health's ClinicalTrials.gov registry was searched to identify all trials concerning AMD. Trials that were actively recruiting, not interventional, terminated, or did not actually concern AMD were excluded. Only trials completed 2 or more years before this analysis was started were included, to allow for adequate time to pass before publication was expected to occur. PubMed.gov was then searched to evaluate the publication status of each study.

RESULTS: Three hundred and eight-six studies were initially identified, and 64 (16.5%) were included in the final evaluation. Three hundred and twenty-one studies were not included for the following reasons: 171 did not involve AMD or were not interventional; 141 were not completed by January 1, 2007; and 9 trials were terminated. Of the 64 trials included, 35 (54%) were published. Early phase trials were published at a lower rate (41.6% [15/36]) than late-phase trials (71.4% [20/28]). This difference was statistically significant (P = 0.02). The sponsor type, date of study initiation, and location did not influence the publication rate.

CONCLUSION: Using broad study parameters, 54% of registered interventional clinical trials in AMD have been reported in the peer-reviewed literature.

PMID: 21221049 [PubMed - as supplied by publisher]

Genetics

Acta Ophthalmol. 2011 Jan 14. doi: 10.1111/j.1755-3768.2010.02080.x. [Epub ahead of print]

Complement factor H Y402H gene polymorphism and response to intravitreal bevacizumab in exudative age-related macular degeneration.

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Purpose: To determine whether different complement factor H (CFH) genotypes play a role in treatment of age-related macular degeneration (AMD) with intravitreal bevacizumab. Methods: In this prospective study, we included 197 patients with exudative AMD and treated with 1.25 mg intravitreal bevacizumab at 6-week intervals until choroidal neovascularization (CNV) was no longer active. In all patients, ophthalmological examinations, visual acuity, optical coherence tomography (OCT), fundus photography and fluorescein angiography were performed. Single nucleotide polymorphism (SNP) genotyping was performed using restriction fragment length polymorphism (RFLP) analysis of polymerase chain reaction (PCR) products. Results: Age, gender and baseline mean visual acuity were similar among the three CFH genotypes. There was no significant difference in underlying lesion type of CNV, lesion size, number of injections or macula thickness. When examining the effect of genotype on post-treatment visual acuities, we observed a significant worse outcome for distance and reading visual acuity in the CFH 402HH genotype group. The number of patients who lost 3 or more lines in distance and reading visual acuity testing was significantly higher in the CFH 402HH (41%, 46%) genotype group than in patients with the CFH 402YY (28%, 26%) and CFH 402YH (26%, 24%) genotype. Conclusions: In addition to the higher risk for exudative AMD in patients with the CFH 402HH genotype that was found in previous studies, our results show that the CFH 402HH genotype also correlates with lower visual acuity outcome after treatment with bevacizumab, suggesting that pharmacogenetics of CFH plays a role in response to treatment of wet AMD.

PMID: 21232084 [PubMed - as supplied by publisher]

Pathogenesis & epidemiology

Neurobiol Dis. 2011 Jan 7. [Epub ahead of print]

CCR2/CCL2-mediated inflammation protects photoreceptor cells from amyloid-β-induced apoptosis.

Bruban J, Maoui A, Chalour N, An N, Jonet L, Feumi C, Tréton J, Sennlaub F, Behar-Cohen F, Mascarelli F, Dinet V.

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Abstract

Age-related macular degeneration is characterized by the formation of drusen containing amyloid-β (Aβ) and the degeneration of photoreceptors. To explore the largely unknown role of Aβ in the retina, we investigated the effects on photoreceptors of the oligomeric form of Aβ(1-42). Subretinal injection of the Aβ peptide induced misplaced expression of recoverin and synaptophysin in the photoreceptors, oxidative stress in their inner and outer segments, and finally apoptosis. Aβ did not induce cell death in purified photoreceptor cell cultures, but did so in retinal cell cultures, thereby suggesting that the cellular environment plays a role in Aβ-induced photoreceptor apoptosis. Subretinal injection of Aβ was followed by activation and migration of microglial cells and then by photoreceptor apoptosis. Microglial cells phagocytosed rhodopsin-containing debris and Aβ in the subretinal space. Quantitative RT-PCR allowed us to identify a specific gene expression profile associated with the Aβ-induced progression of retinal degeneration and consistent with oxidative stress, inflammation, and an apoptotic program. The gene most highly upregulated in Aβ-injected retinas was that for the chemokine CCL2, and its absence or that of its cognate receptor CCR2 greatly reduced migration of activated microglial cells to the site of retinal injury and profoundly worsened photoreceptor degeneration and disorganization of the retinal pigment epithelium in Aβ-injected retinas. Our study pinpoints the roles of Aβ and of CCL2/CCR2 axis-dependent inflammation in photoreceptor apoptosis.

PMID: 21220018 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2011 Jan 7. [Epub ahead of print]

Prevalence of age-related macular degeneration in Spain.

Spanish Eyes Epidemiological (SEE) Study Group.

Aim To estimate the prevalence of age-related maculopathy (ARM) and age-related macular degeneration (AMD) in the Spanish population aged ≥65 years. Methods Individuals were selected by random stratified sampling of census data from eight Spanish health districts encompassing a wide geographic area. Participants underwent an ophthalmologic evaluation including fundus imaging, and ARM and AMD were defined according to the International ARM Epidemiological Study Group classification. The age- and gender-adjusted prevalences and CIs for ARM and neovascular and atrophic forms of AMD were calculated. Results Of the 3028 individuals invited to participate, 2132 attended the ophthalmologic evaluation (840 men (70.9% response) and 1292 women (69.7% response); 978 aged 65-74 years (77.6% response), 1154 aged ≥75 years (65.3% response)). The overall prevalence of ARM and AMD was 10.3% (95% CI 8.7% to 11.8%) and 3.4% (95% CI 2.5% to 4.3%), respectively. AMD increased from 1.3% in individuals aged 65-74 years to 8.5% in those aged ≥80 years. Neovascular and atrophic AMD accounted for 1.9% and 1.5% of individuals, respectively. Conclusions The prevalence of AMD in this large, population-based Spanish sample was similar to that observed in other large-scale population-based studies. However, the prevalence of ARM was lower than found in similar studies.

PMID: 21216795 [PubMed - as supplied by publisher]

Arch Ophthalmol. 2011 Jan;129(1):75-80.

Prevalence of Age-Related Macular Degeneration in the US Population.

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OBJECTIVE: To examine the prevalence of age-related macular degeneration (AMD) in non-Hispanic white, non-Hispanic black, Mexican American, and other racial/ethnic groups.

DESIGN: A US nationally representative, population-based, cross-sectional study involving a total of 5553 persons aged 40 years and older from the 2005-2008 National Health and Nutrition Examination Survey. The main outcome measure was AMD determined by the grading of 45° digital images from both eyes using a standardized protocol.

RESULTS: In the civilian, noninstitutionalized, US population aged 40 years and older, the estimated prevalence of any AMD was 6.5% (95% confidence interval, 5.5-7.6) and the estimated prevalence of late AMD was 0.8% (95% confidence interval, 0.5-1.3). Non-Hispanic black persons aged 60 years and older had a statistically significantly lower prevalence of any AMD than non-Hispanic white persons aged 60 years and older (odds ratio = 0.37; 95% confidence interval, 0.21-0.67).

CONCLUSIONS: Overall, the prevalence of any AMD in the 2005-2008 National Health and Nutrition Examination Survey was 6.5%, which is lower than the 9.4% prevalence reported in the 1988-1994 Third National Health and Nutrition Examination Survey. While this finding might be explained in part by possible methodological differences, these estimates are consistent with a decreasing incidence of AMD and suggest important public health care implications.

PMID: 21220632 [PubMed - in process]

East Mediterr Health J. 2010 Sep;16(9):942-6.

Causes of blindness in people aged 50 years and over: community-based versus hospital-based study.

Al-Akily SA, Bamashmus MA, Al-Mohammadi KA.

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Abstract

The causes of blindness in Yemen were determined in people aged 50+ years in both a community- and hospital-based study and documented using WHO/PBL criteria. In the community sample of 707 individuals in a rural area of Taiz governorate the prevalence of bilateral blindness was 7.9% and the main causes were cataract (71.4%) and age-related macular degeneration (ARMD) (14.3%). Corneal opacities and uncorrected aphakia were rare (1 case each) and there were no cases of diabetic retinopathy. Unilateral blindness was found in 8.6% of the community sample. In a case-notes review of 1320 new patients attending an eye clinic in Sana'a, bilateral blindness was documented in 26.5% and unilateral blindness in 9.0% (main causes: cataract, glaucoma, ARMD, diabetic retinopathy, corneal opacities and trauma.

PMID: 21218720 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2011 Jan 12. [Epub ahead of print]

Regulation of ocular angiogenesis by Notch signaling: implications in neovascular age-related macular degeneration.

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Purpose: Wet age-related macular degeneration (AMD), which accounts for the majority of AMD-related vision loss, is characterized by choroidal neovascularization (CNV). The underlying mechanism of CNV is poorly understood but evidence indicates pathological recruitment of normal angiogenic signaling pathways, e.g., the Vegf pathway. Recent evidence suggests that the Vegf pathway regulates angiogenesis in concert with Notch signaling. Here, we examined the role of Notch signaling in CNV in the backdrop of Notch signaling mediated-regulation of retinal angiogenesis. Methods: Choroid sclera complexes, following laser-induced CNV, were examined for changes in CNV lesion volume and pro and anti-angiogenic gene expression after perturbation in Notch signaling. Retinal vessels and angiogenic gene expression in retinal endothelial cells were analyzed in postnatal rats following perturbations in Notch signaling. Notch signaling was activated and inhibited by intra-vitreal or systemic injection of Jagged1 peptide and gamma secretase inhibitor, DAPT, respectively. Results: We demonstrate that the activation of the canonical Notch pathway reduced the volume of CNV lesions as it attenuated the development of post-retinal retinal vasculature. In contrast, inhibition of Notch pathway exacerbated CNV lesions as it led to the development of hyper-dense retinal vasculature. Furthermore, we identified genes associated with pro-angiogenesis (Vegfr2, Ccr3, and Pdgfb) and anti-angiogenesis (Vegfr1 and Unc5b) as targets of Notch signaling-mediated vascular homeostasis, the disruption of which might underlie CNV. Conclusion: Our study suggests that Notch signaling is a key regulator of CNV and thus a molecular target for therapeutic intervention in wet AMD.

PMID: 21228388 [PubMed - as supplied by publisher]

Lymphology. 2010 Sep;43(3):128-34.

Specific role of lymphatic marker podoplanin in retinal pigment epithelial cells.

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Abstract

Podoplanin is a small transmembrane glycoprotein widely known to be a marker for lymphatic endothelial cells. In this study, we identify a novel localization of podoplanin in the retinal pigment epithelium (RPE), a cellular monolayer critically involved in the visual process. Using a small interfering RNA (siRNA)-mediated gene silencing approach, we have also demonstrated, for the first time, that podoplanin depletion in human RPE cells leads to a marked reduction of cell aggregates and tight junctions. Additionally, the podoplanin-depleted cells also exhibit a significantly lower rate of proliferation. These data together indicate that podoplanin plays a crucial role in RPE cell functions. Further investigation on this factor may reveal novel mechanisms and therapeutic strategies for RPE-related eye diseases, such as proliferative retinopathy and age-related macular degeneration.

PMID: 21226415 [PubMed - in process]

Biol Aujourdhui. 2010;204(4):311-319. Epub 2011 Jan 10.

[Role of chemokines in the development of age-related macular degeneration.]

[Article in French]

Raoul W, Lelièvre E, Auvynet C, Feumi C, Combadière C, Sennlaub F.

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Abstract

Age-related macular degeneration (AMD) is the main cause of irreversible blindness in industrialized nations. Recent research has emphasized the importance of inflammatory processes in pathogenesis of this disease. Chemotactic cytokines also named chemokines are important mediators of inflammation and might have a role in development of this disease. They appear to be crucial in the subretinal microglia / macrophage accumulation observed in AMD and may participate in the development of retinal degeneration and in choroidal neovascularization. This paper reviews the possible implication of chemokines in the development of AMD.

PMID: 21215248 [PubMed - as supplied by publisher]

Biol Aujourdhui. 2010;204(4):267-272. Epub 2011 Jan 10.

[New prospects for chemokines.]

[Article in French]

Rostène W.

Abstract

Chemokines are small secreted proteins belonging to the cytokine family which were initially discovered for their chemoattractant properties for immune cells. Recently it was shown that chemokines and their G-protein-coupled receptors can be constitutively expressed or induced in several organs and different cell types. Thus chemokines have been shown to regulate immune functions involving infection and inflammation, stem cell migration during development, to be implicated in oncogenic, neovascularization and atherosclerosis processes, to modulate neuronal excitability regulating neurotransmitter release, and to play a key role in the pathogenesis of various neurodegenerative diseases such as Parkinson's disease or age-related-macular degeneration and in pain. Some of these recent advances concerning chemokine functions will be highlighted in this broad appeal symposium which aims to introduce this emerging field. This introductory chapter will examine the basic properties of the various chemokine systems and their receptors.

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