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Drug treatment

Retina. 2013 Feb 7. [Epub ahead of print]

INTRAVITREAL RANIBIZUMAB INJECTION FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION IN PHAKIC VERSUS PSEUDOPHAKIC EYES.

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PURPOSE: To compare the effect of intravitreal ranibizumab injections for the treatment of neovascular age-related macular degeneration between phakic and pseudophakic eyes.

METHODS: We retrospectively reviewed the medical records of 110 patients with neovascular age-related macular degeneration receiving intravitreal ranibizumab therapy and categorized them into 2 subgroups: phakic group (75 eyes) and pseudophakic group (45 eyes). For all patients, the initial three loading injections were performed by month, and reinjection was performed as needed. Main outcome measures included best-corrected visual acuity and central macular thickness as assessed by optical coherence tomography.

RESULTS: The mean age of the patients was 72 ± 4.2 years, and the patients were followed up for an average of 18 ± 3.6 months. At the last visit, the average number of injections was 3.87 ± 1.18 in the phakic group and 3.62 ± 1.17 in the pseudophakic group. After injection, the mean logarithm of the minimum angle of resolution of best-corrected visual acuity improved from 0.88 ± 0.65 to 0.75 ± 0.66 in the phakic group and from 0.86 ± 0.54 to 0.74 ± 0.09 in the pseudophakic group. Average central macular thickness decreased from 561 ± 289 μm to 419 ± 216 μm in the phakic group and from 559 ± 232 μm to 429 ± 166 μm in the pseudophakic group. There was no statistically significant difference in the injection number, best -corrected visual acuity improvement was achieved, and central macular thickness improvement was achieved between the phakic group and pseudophakic group.

CONCLUSION: The therapeutic effect of intravitreal ranibizumab injection for neovascular age-related macular degeneration did not show differences between phakic and pseudophakic eyes.

PMID: 23400082 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging Retina. 2013 Jan 1;44(1):17-21. doi: 10.3928/23258160-20121221-07.

Ranibizumab versus photodynamic therapy for presumed ocular histoplasmosis syndrome.

Ramaiya KJ, Blinder KJ, Ciulla T, Cooper B, Shah GK.

BACKGROUND AND OBJECTIVE: To evaluate the efficacy of ranibizumab in the treatment of choroidal neovascularization secondary to presumed ocular histoplasmosis syndrome.

PATIENTS AND METHODS: Patients enrolled in the ranibizumab group received a monthly intravitreal injection of 0.5 mg of ranibizumab. Patients in the photodynamic therapy (PDT) group received a quarterly dosing of intravenous verteporfin coupled with PDT.

RESULTS: Mean change in ETDRS visual acuity at 1 year was 19.6 letters in the ranibizumab group versus 21 letters in the PDT group. All patients in the PDT group required rescue ranibizumab therapy. Four of five patients (80%) in the ranibizumab group and one of two patients (50%) in the PDT group showed a greater than 15 letter gain at 1 year.

CONCLUSION: Ranibizumab appears to be a safe and effective treatment option for choroidal neovascularization secondary to the presumed ocular histoplasmosis syndrome.

PMID: 23410808 [PubMed - in process]

Retina. 2013 Feb 7. [Epub ahead of print]

RANIBIZUMAB FOR CHOROIDAL NEOVASCULARIZATION ASSOCIATED WITH ADULT-ONSET FOVEOMACULAR VITELLIFORM DYSTROPHY: One-Year Results.

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PURPOSE: To evaluate the efficacy of intravitreal injections of ranibizumab for choroidal neovascularization associated with adult-onset foveomacular vitelliform dystrophy.

METHODS: Retrospective case series of 24 eyes affected with choroidal neovascularization associated with adult-onset foveomacular vitelliform dystrophy treated by intravitreal injections of ranibizumab (0.5 mg/0.05 mL). Best-corrected visual acuity, fundus examination, spectral domain optical coherence tomography, fundus autofluorescence, and fluorescein and indocyanine green angiography were performed for the diagnosis of adult-onset foveomacular vitelliform dystrophy and choroidal neovascularization. After initial 3 monthly injections of ranibizumab, patients were followed up monthly and retreated if neovascular activity persisted. Outcome measure was the proportion of patients losing fewer than 3 lines of visual acuity from baseline to 12 months (final visit).

RESULTS: At final visit, the mean number of ranibizumab injections was 4.5 ± 1.29. From baseline to final visit, 21 of 24 eyes (87.5%) lost fewer than 3 lines of visual acuity. Mean best-corrected visual acuity did not change significantly from baseline to final visit (0.37 ± 0.2 logarithm of the minimum angle of resolution vs. 0.30 ± 0.25 logarithm of the minimum angle of resolution, respectively; P = 0.115). Mean central macular thickness significantly decreased from baseline to final visit (327 ± 83 μm vs. 260 ± 57 μm, respectively; P = 0.001).

CONCLUSION: In this series, ranibizumab succeeded in stabilizing best-corrected visual acuity in patients with choroidal neovascularization associated with adult-onset foveomacular vitelliform dystrophy. Ranibizumab seems to be a reasonable therapeutic option in this condition.

PMID: 23400081 [PubMed - as supplied by publisher]

JAMA Ophthalmol. 2013 Feb 1;131(2):260-2. doi: 10.1001/jamaophthalmol.2013.1733.

Dramatic resolution of choroidal neovascular abnormalities after single aflibercept injection following years of ranibizumab use.

Chaikitmongkol V, Bressler NM.

PMID: 23411901 [PubMed - in process]

Retina. 2013 Feb 7. [Epub ahead of print]

INTRAVITREAL TISSUE PLASMINOGEN ACTIVATOR, PERFLUOROPROPANE (C3F8), AND RANIBIZUMAB OR PHOTODYNAMIC THERAPY FOR SUBMACULAR HEMORRHAGE SECONDARY TO WET AGE-RELATED MACULAR DEGENERATION.

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PURPOSE: To report a combined intravitreal treatment for submacular hemorrhage.

METHODS: This retrospective, noncomparative, interventional case series included 7 patients with neovascular age-related macular degeneration and 2 with idiopathic polypoidal choroidal vasculopathy, presenting with fovea-involving submacular hemorrhage ≥ 4 disk areas in size, of <10 days of duration. All patients received a single 0.05-mL intravitreal injection of 50 μg alteplase, 0.3 mL of 100% C3F8, and facedown positioning for 1 week. Patients with newly diagnosed age-related macular degeneration received 3 consecutive monthly intravitreal injections of 0.5 mg ranibizumab, followed by monthly retreatment as needed. Those with idiopathic polypoidal choroidal vasculopathy were treated with photodynamic therapy.

RESULTS: Mean (±SD) logarithm of the minimum angle of resolution visual acuity improved from 0.75 ± 0.35 at presentation to 0.35 ± 0.30 at a mean final follow-up of 15.1 months (P = 0.0078). Median Snellen acuity improved from 20/200 to 20/32. Visual acuity was stable in one case and improved in eight. The average size of submacular hemorrhage was 6.8 disk areas at presentation, reducing to 2.6 within 1 month (P = 0.0039). Subfoveal hemorrhage was displaced in all cases within 9 weeks. The mean pretreatment central retinal thickness of 669 μm reduced to 528 μm (P = 0.0039). One case developed transiently elevated intraocular pressure. Two developed breakthrough vitreous hemorrhage. No adverse events were attributed to tissue plasminogen activator.

CONCLUSION: Tissue plasminogen activator and C3F8, combined with intravitreal ranibizumab or photodynamic therapy, may result in anatomical clearance of submacular hemorrhage and improved visual acuity, in a condition with an otherwise poor visual prognosis.

PMID: 23400079 [PubMed - as supplied by publisher]

Jpn J Ophthalmol. 2013 Feb 15. [Epub ahead of print]

Two-year results of reduced-fluence photodynamic therapy combined with intravitreal ranibizumab for typical age-related macular degeneration and polypoidal choroidal vasculopathy.

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PURPOSE: To report the 2-year results of reduced-fluence photodynamic therapy (RF-PDT) combined with intravitreal ranibizumab (IVR) for typical age-related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV).

METHODS: Twenty-four previously untreated eyes of 23 AMD patients with decimal best-corrected visual acuity (BCVA) of less than 0.7 received the combined therapy, followed by retreatments as needed over the subsequent 2 years. When the BCVA was better than or equal to 0.7, only 3 monthly IVR injections were performed during the retreatment.

RESULTS: The BCVAs were maintained in 7 of 10 typical AMD eyes and in 13 of 14 PCV eyes at month 24. The mean BCVA improved in the PCV group ($P < 0.05$) but not in the typical AMD group. The central foveal thickness decreased in both groups ($P < 0.01$, $P < 0.001$). The mean numbers of the total PDT and IVR injections were 1.8 and 7.2 in the typical AMD group and 1.8 and 6.4 in the PCV group.

CONCLUSION: After RF-PDT combined therapy with administration of retreatments as needed that consisted of either 3 IVR injections alone or combined therapy, the BCVA was maintained in typical AMD and improved in PCV during a 2-year follow-up period.

PMID: 23413039 [PubMed - as supplied by publisher]

Indian J Ophthalmol. 2013 Feb;61(2):86. doi: 10.4103/0301-4738.107211.

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

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PMID: 23412534 [PubMed - in process]

Retina. 2013 Feb 12. [Epub ahead of print]

ANATOMIC AND PHARMACOKINETIC PROPERTIES OF INTRAVITREAL BEVACIZUMAB AND RANIBIZUMAB AFTER VITRECTOMY AND LENSECTOMY.

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PURPOSE: To determine the anatomic characteristics and pharmacokinetic properties of intravitreally placed bevacizumab and ranibizumab after pars plana lensectomy or pars plana vitrectomy and to compare these with nonoperated control eyes in a rabbit model.

METHODS: Three groups of six Dutch-belted rabbits each underwent pars plana vitrectomy, pars plana lensectomy, or served as nonsurgical controls. Twelve days after surgery, 3 rabbits from each group underwent intravitreal injection in one eye with 1.25 mg/0.05 mL I-124-bevacizumab or 0.5 mg/0.05 mL I-124-ranibizumab. Serial imaging with integrated positron emission and computed tomography (PET/CT) were obtained on Days 0, 2, 5, 7, 14, 21, 28, and 35. Measured radioactivity emission in becquerels/milliliter was used to calculate the half-lives for each agent.

RESULTS: The intravitreally placed radiolabeled agents were contained within the vitreous cavity for the duration of the study. The average clearance half-lives with standard error for bevacizumab and

ranibizumab after correction for radioactive decay were, respectively, 4.22 ± 0.07 days and 2.81 ± 0.05 days in unoperated eyes, 2.30 ± 0.09 days (P < 0.0001) and 2.13 ± 0.05 days (P < 0.0001) after vitrectomy, and 2.08 ± 0.07 days (P = 0.0001) and 1.79 ± 0.05 days (P < 0.0001) after lensectomy.

CONCLUSION: Intravitreal retention was longer for bevacizumab than ranibizumab within all study groups and was significantly reduced after vitrectomy and lensectomy for both agents. Consideration for more frequent intravitreal anti-vascular endothelial growth factor dosing regimens may be made for patients whose treated eyes have undergone previous vitrectomy or who are aphakic.

PMID: 23407351 [PubMed - as supplied by publisher]

Other treatment & diagnosis

JAMA Ophthalmol. 2013 Feb 14:1-8. doi: 10.1001/jamaophthalmol.2013.2578. [Epub ahead of print]

Validation of a Prediction Algorithm for Progression to Advanced Macular Degeneration Subtypes.

Seddon JM, Reynolds R, Yu Y, Rosner B.

IMPORTANCE: Risk score models predicting the progression of age-related macular degeneration (AMD) to its advanced forms may be useful for targeting high-risk individuals for lifestyle changes that reduce risk for AMD progression, helping with differential diagnosis of AMD and its subtypes, identifying high-risk subjects for participation in clinical trials, and selecting appropriate therapies.

OBJECTIVE: To develop and validate a predictive model for progression to advanced stages of AMD in 2 independent cohorts.

DESIGN: Participants in a validation cohort and an independent derivation population were classified into 5 stages of AMD based on ocular examination and fundus photographs at baseline. Progression was defined as either eye progressing from stage 1, 2, or 3 to either stage 4 or stage 5 at any follow-up visit to the end of the study. Cox proportional hazards models were used for progression analyses. Covariates included demographic and environmental factors, 6 variants in 5 genes, and baseline AMD grades in both eyes. The algorithm developed with the derivation sample was assessed for calibration and discrimination in the validation data set.

SETTING: Clinic populations and referrals.

PARTICIPANTS: The derivation population comprised 2914 subjects with 809 progressors. The independent validation cohort comprised 980 individuals with no, early, or intermediate AMD in at least one eye at baseline, of whom 294 progressed to advanced stages of geographic atrophy or neovascular disease.

MAIN OUTCOME MEASURE: Progression to advanced AMD.

RESULTS: For the model with all nongenetic and genetic factors, the respective C statistics for progression to advanced AMD in the derivation and validation samples were 0.858 and 0.750 at 5 years and 0.884 and 0.809 at 10 years, and models also discriminated risk for progression to geographic atrophy and neovascular disease separately. For unilateral or bilateral intermediate AMD, 5-year cumulative incidence rates of progression to advanced AMD were 10% with the low-risk score and 50% with the high-risk score; for unilateral advanced disease, the progression rates were 22% and 80% for the fellow eye.

CONCLUSIONS AND RELEVANCE: The risk prediction model was validated in an independent study of progression from no, early, or intermediate stages to advanced subtypes of AMD and will be useful for research, clinical trials, and personalized medicine.

PMID: 23411794 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2013 Feb 14. [Epub ahead of print]

Fundus autofluorescence and microperimetry in progressing geographic atrophy secondary to age-related macular degeneration.

Pilotto E, Guidolin F, Convento E, Spedicato L, Vujosevic S, Cavarzeran F, Midena E.

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PURPOSE: To prospectively analyse microperimetry, standard short-wavelength fundus autofluorescent (SW-FAF) and near infrared-wavelength FAF (NIR-FAF) changes in eyes with geographic atrophy (GA) secondary to age-related macular degeneration.

METHODS: Twenty consecutive eyes (14 patients) affected by GA were enrolled. Repeated microperimetric examinations and FAF images were obtained over a mean follow-up period of 12.3±4.5 months.

RESULTS: GA area was always wider on NIR-FAF versus SW-FAF images (5.05±2.40 mm(2) vs 4.45±2.41 mm(2), p=0.005 baseline; 5.78±2.87 mm(2) vs 5.21±2.77 mm(2), p<0.0001 follow-up). Mean retinal sensitivity significantly decreased during follow-up from 7.68±3.92 dB to 6.71±4.37 dB (p=0.0013). 47.3% of the relative dense scotomas (≤5 dB) progressed to dense scotoma (0 dB). Retinal areas showing relative dense scotoma and characterised by hypo-SW-FAF or hyper-NIR-FAF at baseline had a higher risk of evolving to dense scotoma compared with normo-FAF and hyper-FAF on SW-FAF (OR=2.62 and 2.77, respectively), or normo-FAF at NIR-FAF (OR=2.96).

CONCLUSIONS: SW-FAF, compared with NIR-FAF, underestimates GA area at baseline and at follow-up. The enlargement rate of progression based on NIR-FAF is not greater than on SW-FAF. Different SW-FAF and NIR-FAF patterns show different relative risk of progression from relative to dense scotoma. Microperimetry, SW-FAF and NIR-FAF should be combined to obtain adequate morphological and functional prospective information.

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Ophthalmic Surg Lasers Imaging Retina. 2013 Jan 1;44(1):73-6. doi: 10.3928/23258160-20121221-16.

Carbon nanotube bucky paper as an artificial support membrane for retinal cell transplantation.

Leng T, Fishman HA.

BACKGROUND AND OBJECTIVE: Transplantation of epithelial cells on a substrate to rescue diseased retinal cells is an experimental therapy for age-related macular degeneration. Carbon nanotube bucky paper was tested for cell transplantation into the retina.

MATERIALS AND METHODS: Bucky paper was prepared and human RPE cells cultured on its surface demonstrating its utility as a cell transplantation substrate. Bucky paper was implanted underneath 9 rabbit retinas using a standard 3-port pars plana vitrectomy and subretinal bleb. A 1 mm retinotomy was created through which Bucky paper precut to fit was inserted with the subretinal forceps, into the subretinal bleb. The retina was reattached by airfluid exchange.

RESULTS: By light microscopy, RPE cells demonstrated normal morphology and growth patterns on the bucky paper surface. Scanning electron microscopy confirmed a confluent monolayer of cells, and indicated the formation of microvilli on the apical surface. Bucky paper remained flat in the subretinal space after 2 weeks, the retina fully attached without edema or inflammation.

CONCLUSION: Bucky paper possesses the necessary attributes for therapeutic cell transplantation in the eye.

PMID: 23410811 [PubMed - in process]

Retina. 2013 Feb 7. [Epub ahead of print]

MULTIMODAL EVALUATION OF FOVEAL SPARING IN PATIENTS WITH GEOGRAPHICATROPHY DUE TO AGE-RELATED MACULAR DEGENERATION.

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PURPOSE: To compare the ability of spectral domain optical coherence tomography (SD-OCT), blue light fundus autofluorescence (FAF), and near-infrared fundus autofluorescence (NIR-FAF) to evaluate foveal involvement in geographic atrophy as a result of age-related macular degeneration.

METHODS: All consecutive patients with geographic atrophy underwent FAF (excitation λ = 488 nm; emission λ > 500 nm), NIR-FAF (excitation λ = 787 nm; emission λ > 800 nm), and simultaneous SD-OCT scanning (Spectralis HRA + OCT; Heidelberg Engineering). Two readers independently graded foveal involvement on FAF, NIR-FAF, and SD-OCT and measured the width of foveal sparing. In eyes with an intergrader agreement of foveal sparing by at least one among FAF, NIR-FAF, and SD-OCT, microperimetry (Spectral OCT/SLO; OPKO-OTI) was analyzed.

RESULTS: A total of 158 eyes (83 patients; 53 women, 30 men, mean age 69.2 ± 4.8 years) with geographic atrophy were included. Spectral domain OCT showed the highest intergrader agreement of foveal involvement (k = k' = 0.8, P = 0.001 vs. k = k' = 0.7, P = 0.01 for NIR-FAF and k = k' = 0.5, P = 0.01 for FAF). In 74 eyes (46.8%) foveal sparing was present according to interobserver agreement. Width of the foveal sparing was larger on SD-OCT than on NIR-FAF and FAF (1,334 ± 943 μm vs. 1,228 ± 912 μm, P < 0.001 and 1,201 ± 922 μm, P < 0.001, respectively). Retinal fixation was predominantly central and stable in 97.3% of eyes with foveal sparing.

CONCLUSION: Spectral domain OCT is an appropriate imaging modality for evaluating the presence and extent of foveal sparing, followed by NIR-FAF and FAF.

PMID: 23400084 [PubMed - as supplied by publisher]

Retina. 2013 Feb 11. [Epub ahead of print]

SENSITIVITY AND SPECIFICITY OF DETECTING RETICULAR PSEUDODRUSEN IN MULTIMODAL IMAGING IN JAPANESE PATIENTS.

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PURPOSE: To identify reticular pseudodrusen (RPD) in age-related macular degeneration using multiple imaging modalities, including the blue channel image of fundus photography, infrared reflectance (IR), fundus autofluorescence, near-infrared fundus autofluorescence, confocal blue reflectance, indocyanine green angiography, and spectral-domain optical coherence tomography (SD-OCT), and to compare the sensitivities and specificities of these modalities for detecting RPD.

METHODS: This study included 220 eyes from 114 patients with newly diagnosed age-related macular degeneration. Patients underwent fundus photography, IR, fundus autofluorescence, near-infrared fundus autofluorescence, confocal blue reflectance, indocyanine green angiography, and SD-OCT in both eyes. Eyes were diagnosed with RPD if they showed reticular patterns on at least two of the seven imaging modalities.

RESULTS: Thirty-seven eyes were diagnosed with RPD. However, SD-OCT and IR had the highest

sensitivity (94.6%), and at the same time, SD-OCT had a high specificity (98.4%). The blue channel of color fundus photography, confocal blue reflectance, and indocyanine green angiography had a specificity of 100% but had lower sensitivity than that of SD-OCT and IR.

CONCLUSION: For detecting RPD, IR and SD-OCT had the highest sensitivity. Although SD-OCT had the highest sensitivity and specificity, RPD detection should be confirmed using more than one modality for increased accuracy.

PMID: 23403515 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2011;21 Suppl 6:S69-74. doi: 10.5301/EJO.2010.6059.

Macular edema: miscellaneous.

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Abstract: This article provides the reader with practical information to be applied to the various remaining causes of macular edema. Some macular edemas linked to ocular diseases like radiotherapy after ocular melanomas remained of poor functional prognosis due to the primary disease. On the contrary, macular edemas occurring after retinal detachment or after some systemic or local treatment use are often temporary. Macular edema associated with epiretinal membranes or vitreomacular traction is the main cause of poor functional recovery. However, the delay to observe a significant improvement of vision after surgery should be long, as usually observed in tractional myopic vitreoschisis. Finally, some circumstances of macular edemas such as hemangiomas or macroaneurysms should be treated, if symptomatic, with the treatments currently used in diabetic macular edema or exudative macular degeneration.

PMID: 23264332 [PubMed - in process]

Eur J Ophthalmol. 2011;21 Suppl 6:S62-8. doi: 10.5301/EJO.2010.6058.

Postsurgical cystoid macular edema.

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Abstract: Cystoid macular edema (CME) is a primary cause of postoperative reduced vision. It may occur even when the intraoperative course is successful for operations such as cataract and vitreoretinal surgery. Its incidence following modern cataract surgery is 0.1%-2.35%. This risk is increased if there are certain preexisting systemic or ocular conditions and when there are intraoperative complications. The etiology of CME is not completely understood. Prolapsed or incarcerated vitreous and postoperative inflammatory processes have been proposed as causative agents. Pseudophakic CME is characterized by poor postoperative visual acuity. Fluorescein angiography is indispensable in the workup of CME, showing the classical perifoveal petaloid staining pattern and late leakage of the optic disk. Optical coherence tomography is a useful diagnostic tool, which displays cystic spaces in the outer nuclear layer. The most important differential diagnoses include age-related macular degeneration and other causes of CME such as diabetic macular edema. Most cases of pseudophakic CME resolve spontaneously. The value of prophylactic treatment is doubtful. First-line treatment of postsurgical CME should include topical nonsteroidal anti-inflammatory drugs and corticosteroids. Oral carbonic anhydrase inhibitors can be considered complementary. In cases of resistant CME, periocular or intraocular corticosteroids present an option. Antiangiogenic agents, though experimental, should be considered for nonresponsive persistent

CME. Surgical options should be reserved for special indications.

PMID: 23264331 [PubMed - in process]

Neurosci Lett. 2013 Feb 8. pii: S0304-3940(13)00017-7. doi: 10.1016/j.neulet.2012.12.055. [Epub ahead of print]

Mesenchymal stem cells from trabecular meshwork become Photoreceptor-like cells on amniotic membrane.

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Abstract: Stem cell therapy is a promising approach for treatment of degenerative retinal disorders such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD). In this study, human mesenchymal stem cells (MSCs) were isolated from the trabecular meshwork (TM), the major functional tissue of the anterior chamber angle in the eye, were characterized and differentiated into photoreceptor cells on amniotic membrane (AM). After isolation of trabecular meshwork and culture of the stromal segment of this tissue, fibroblast-like cells (CD105(+), CD90(+), CD44(+), CD166(+) cells) capable of differentiation toward mesenchymal and photoreceptor lineages were obtained. The isolated cells were seeded on amniotic membrane and were treated with induction medium. Immunocytochemistry and quantitative real time RT-PCR (qPCR) were used to detect expression of photoreceptor genes such as rhodopsin, recoverin, CRX, and peripherin; and the bipolar cell marker protein kinase C alpha (PKC-alpha). As a result, immunocytochemistry revealed that the differentiated TMMSCs expressed rhodopsin, CRX and PKC proteins. qPCR showed the expression of rhodopsin (rod like photoreceptor-specific marker), and CRX genes were significantly higher in TMMSCs differentiated on AM than those differentiated on tissue culture polystyrene (TCPS). In conclusion, our findings suggested that a combination of TMMSCs (as a new source) and basement membrane support from AM might be a suitable source of cells for subretinal transplantation in regenerative therapy for retinal disorders such as AMD and RP.

PMID: 23403103 [PubMed - as supplied by publisher]

Pathogenesis

Ophthalmology. 2013 Feb 12. pii: S0161-6420(12)01068-8. doi: 10.1016/j.ophtha.2012.11.002. [Epub ahead of print]

Increased Expression of CD200 on Circulating CD11b+ Monocytes in Patients with Neovascular Age -related Macular Degeneration.

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OBJECTIVE: Dysregulation of retinal microglial activity has been implicated in the pathogenesis of neovascular age-related macular degeneration. Microglia activity can be regulated through the membrane protein CD200 and its corresponding receptor, the CD200 receptor (CD200R). Because both the ligand and the receptor are expressed on a broad spectrum of cell types, we set out to study the expression of CD200 and CD200R on CD11b+ monocytes, granulocytes, and subsets of T lymphocytes.

DESIGN: Prospective, case-control study.

PARTICIPANTS: The study population consisted of 62 patients with neovascular age-related macular degeneration (AMD) and 44 age-matched controls without AMD.

METHODS: The participants were aged 60 years or older, had no history of immune dysfunction or cancer, and were not receiving immune-modulating therapy. All participants were subjected to a structured interview, and detailed retinal imaging was performed: fundus autofluorescence imaging, digital color fundoscopy, and spectral-domain optical coherence tomography. Fluorescein and indocyanine green angiography were performed in patients with suspected neovascular AMD. Visual acuity was measured in both eyes. Fresh venous blood was obtained and stained with monoclonal antibodies and analyzed using flow cytometry within 6 hours of phlebotomy.

MAIN OUTCOME MEASURES: The percentage of CD11b+ monocytes, granulocytes, and CD4+/CD8+ T lymphocytes positive for CD200 or CD200R in patients and controls, respectively.

RESULTS: Patients with neovascular AMD had a higher percentage of CD11b+CD200+ monocytes and CD200+ monocytes compared with controls. Multiple regression analysis revealed that the intergroup differences observed were independent of age. Moreover, an age-related increment in CD200 expression on monocytes was observed in controls with healthy eyes, but not in patients with neovascular AMD. We did not find any differences in CD200 and CD200R expression between patients with subretinal fibrosis and patients without subretinal fibrosis.

CONCLUSIONS: The surface expression of CD200 on circulating CD11b+ monocytes was found to be increased in patients with neovascular AMD compared with controls with healthy eyes. This novel finding supports the notion that altered regulation of the inflammatory response plays an integral role in the pathogenesis of AMD.

PMID: 23410964 [PubMed - as supplied by publisher]

Exp Eye Res. 2013 Feb 11. pii: S0014-4835(13)00027-4. doi: 10.1016/j.exer.2013.01.015. [Epub ahead of print]

Role of Heparan Sulfate in Ocular Diseases.

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Abstract: Heparan sulfate (HS), a ubiquitous and structurally diverse cell surface polysaccharide and extracellular matrix component, is a factor common to several major eye pathologies. Its multitude of functions and variable distribution among the different ocular tissues makes it an important contributor to a variety of disease states. Although HS facilitates the pathogenesis of many disorders, its role in each varies. Unique functions of HS have been particularly noted in viral and bacterial keratitis and age-related macular degeneration. Combined, these pathologies comprise a large portion of conditions leading to visual impairment worldwide. Given this prevalence of diseases facilitated by HS, it is prudent to take an in-depth look at this compound in the context of these pathologic states. While the initial part of the review will discuss the pathogenic aspects of HS, it is also important to consider the wider implications of such roles for HS. The remainder of the article will specifically address one such implication, the possibility for future use of novel HS-based therapeutics to combat these eye pathologies.

PMID: 23410824 [PubMed - as supplied by publisher]

Med Hypotheses. 2013 Feb 11. pii: S0306-9877(13)00041-8. doi: 10.1016/j.mehy.2013.01.018. [Epub ahead of print]

Elevated norepinephrine may be an etiological factor in a wide range of diseases: Age-related macular degeneration, systemic lupus erythematosus, atrial fibrillation, metabolic syndrome.

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Abstract: The neurotransmitter norepinephrine (NE) participates in a broad range of physiological functions, both in the brain and in the periphery, where it is a principal output molecule of the sympathetic nervous system. NE receptors are present in nearly all, if not all, organs of the body, which may allow this molecule to play a role in a variety of disease processes. This paper examines the hypothesis elevated NE signaling, through genetics and/or environmental factors, is an etiological factor in a variety of diseases outside of the brain, including age-related macular degeneration, systemic lupus erythematosus, atrial fibrillation, and metabolic syndrome. Lines of evidence presented to assess the hypothesis include: (1) studies of noradrenergic drugs modulating the four diseases; (2) association of these diseases with bipolar disorder, hypertension, and obesity, where the latter three conditions may involve elevated NE signaling; and (3) association with psychological stress, since NE is released in response to stress. Many of the studies cited tend to support the hypothesis, or are at least consistent with it. If the hypothesis is correct, perhaps a large number of individuals would benefit from chronically taking drugs that systemically diminish noradrenergic signaling, thereby helping prevent or treat a wide variety of diseases.

PMID: 23410497 [PubMed - as supplied by publisher]

PLoS One. 2013;8(2):e56099. doi: 10.1371/journal.pone.0056099. Epub 2013 Feb 8.

7-ketocholesterol induces inflammation and angiogenesis in vivo: a novel rat model.

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Abstract: Accumulation of 7-Ketocholesterol (7KCh) in lipid deposits has been implicated in a variety of chronic diseases including atherosclerosis, Alzheimer's disease and age-related macular degeneration. 7KCh is known to be pro-inflammatory and cytotoxic to various types of cultured cells but little is known about its effects in vivo. In this study we have investigated the effects of 7KCh in vivo by implanting biodegradable wafers into the anterior chamber of the rat eye. The wafers were prepared using a mixture of two biodegradable polymers with different amounts of 7KCh. The 7KCh-containing implants induced massive angiogenesis and inflammation. By contrast, no angiogenesis and very little inflammation were observed with cholesterol-containing implants. The neovessel growth was monitored by fluorescein angiography. Neovessels were observed 4 days post implantation and peaked between 7 to 10 days. The angiography and isolectin IB(4) labeling demonstrated that the neovessels originated from the limbus and grew through the cornea. Immunolabeling with anti-CD68 suggested that the 7KCh-containing implants had extensive macrophage infiltration as well as other cell types. A significant increase in VEGF was also observed in 7KCh-containing implants by fluorescent immunolabeling and by immunoblot of the aqueous humor (AH). Direct measurement of VEGF, IL-1β and GRO/KC demonstrated a marked elevation of these factors in the AH of the 7KCh-implants. In summary this study demonstrates two important things: 1) 7KCh is pro-angiogenic and pro-inflammatory in vivo and 2) implants containing 7KCh may be used to create a novel angiogenesis model in rats.

PMID: 23409131 [PubMed - in process]

Gerontology. 2013 Feb 8. [Epub ahead of print]

Retinal Microenvironment Imbalance in Dry Age-Related Macular Degeneration: A Mini-Review.

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Background: Age-related macular degeneration (AMD) is the leading cause of blindness in the western world. To prevent what will certainly be a tremendous health and economic burden, effective therapeutics for AMD are urgently needed. To develop these agents in a timely fashion, the molecular pathways that cause disease progression must be elucidated.

Objective: To briefly describe the clinical features of AMD, and review the current understanding of the molecular basis of AMD.

Methods: A literature review.

Results: The discussion will primarily focus on the interplay of oxidative stress and complement dysregulation and the resulting chronic proinflammatory state thought to be central in AMD pathogenesis.

Conclusions: Oxidative stress and complement dysregulation play a substantive role in the development of AMD.

PMID: 23406680 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2013 Feb 12. pii: iovs.11-9095v1. doi: 10.1167/iovs.11-9095. [Epub ahead of print]

Suppression of Laser-induced Choroidal Neovascularization by a CCR3 Antagonist.

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PURPOSE: To evaluate the efficacy of a novel CCR3 antagonist for laser injury-induced choroidal neovascularization (CNV) in mice.

METHODS: We evaluated YM-344031, a novel and selective small molecule CCR3 antagonist. CNV was induced by laser injury in C57BL/6J mice, and its volume was measured after 7 days by confocal microscopy. Leakage from the CNV was also measured after 7 days by fluorescein angiography. The CCR3 antagonist was administered by gavage at 1 hour before and 1 day after the laser injury, or intravitreous injection immediately after the laser injury. After the laser injury, ELISA, western blot analysis and real-time RT-PCR for VEGF-A expression in the RPE/choroid, and immunohistochemistry for CCR3, CCL11, Ki67, and Rac1 was performed.

RESULTS: Both oral administration and intravitreous injection of YM-344031 significantly suppressed the CNV volume ($p<0.0001$ and $p<0.01$, respectively). Pathologically significant leakage was significantly less common in YM-344031-injected mice ($p<0.0001$). The mean VEGF protein level was significantly increased in vehicle-injected eyes after the laser injury ($p<0.05$). Although the YM-344031-injected eyes did not show VEGF-A suppression after the laser injury, VEGF-164mRNA upregulation was significantly suppressed in YM-344031-injected mice ($P<0.05$). And intravitreous injection of YM-344031 appeared to suppress CCR3, CCL11 (eotaxin), Ki67, and Rac1 expression after the laser injury.

CONCLUSIONS: The present data suggest that the CCR3 antagonist YM-344031 can suppress CNV, via suppression of the upregulation of VEGF-164mRNA in VEGF isoform after the laser injury. Although our

findings may warrant further investigation, YM-344031 may have potential as a new therapy for age-related macular degeneration.

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Invest Ophthalmol Vis Sci. 2013 Feb 12. pii: iovs.12-10821v1. doi: 10.1167/iovs.12-10821. [Epub ahead of print]

Amyloid-β increases capillary bed density in the adult zebrafish retina.

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Purpose: Amyloid-beta (Aβ) is an endogenous peptide that becomes dysregulated in age-related macular degeneration (AMD) and Alzhiemer's disease. Both of these disorders are marked by extracellular deposits that contain Aβ, highly branched capillary networks, and neurodegeneration. Although Aβ has been implicated in AMD and Alzheimer's pathology for decades, its non-pathological function has remained unclear. We recently showed that high levels of monomeric Aβ induce blood vessel branching in embryonic zebrafish brain, and here we report that a similar mechanism may contribute to aberrant blood vessel branching in the retina of adult zebrafish.

Methods: Transgenic zebrafish expressing enhanced green fluorescence protein (EGFP) in their endothelial cells were sedated and small intraocular injections of PBS were made into one eye and either Aβ or γ-secretase inhibitor were injected into their opposite eye. A week later the eyes were enucleated and high resolution maps of the retina vasculature were created using confocal microscopy. Comparisons were made between the treatment groups using the general linear model ANOVA.

Results: We found that Aβ significantly affects capillary blood vessels in the retina. Small volumes of Aβ injected into the eyes of adult zebrafish induced the formation of significantly more endothelial tip cells, and capillary bridges - some with loops - near the circumferential vein. These effects were dose-dependent and increased capillary bed density, though there was no effect on larger arterial vessels.

Conclusion: This study reveals a previously unknown role for Aβ in regulating capillary bed density, providing a new insight into the normal biological function Aβ will help in the development of therapeutic interventions for AMD and Alzheimer's disease.

PMID: 23404118 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2011;21 Suppl 6:S3-9. doi: 10.5301/EJO.2010.6049.

Blood-retinal barrier.

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Abstract: The blood-ocular barrier system is formed by 2 main barriers: the blood-aqueous barrier and the blood-retinal barrier (BRB). The BRB is particularly tight and restrictive and is a physiologic barrier that regulates ion, protein, and water flux into and out of the retina. The BRB consists of inner and outer components, the inner BRB being formed of tight junctions between retinal capillary endothelial cells and the outer BRB of tight junctions between retinal pigment epithelial cells. The BRB is essential to maintaining the eye as a privileged site and is essential for normal visual function. Methods of clinical evaluation of the BRB are reviewed and new directions using optical coherence tomography are presented. Alterations of the

BRB play a crucial role in the development of retinal diseases. The 2 most frequent and relevant retinal diseases, diabetic retinopathy and age-related macular degeneration (AMD), are directly associated with alterations of the BRB. Diabetic retinopathy is initiated by an alteration of the inner BRB and neovascular AMD is a result of an alteration of the outer BRB. Macular edema is a direct result of alterations of the BRB.

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Eur Heart J. 2013 Feb 10. [Epub ahead of print]

The eye and the heart.

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Abstract: The vasculature of the eye and the heart share several common characteristics. The easily accessible vessels of the eye are therefore-to some extent-a window to the heart. There is interplay between cardiovascular functions and risk factors and the occurrence and progression of many eye diseases. In particular, arteriovenous nipping, narrowing of retinal arteries, and the dilatation of retinal veins are important signs of increased cardiovascular risk. The pressure in the dilated veins is often markedly increased due to a dysregulation of venous outflow from the eye. Besides such morphological criteria, functional alterations might be even more relevant and may play an important role in future diagnostics. Via neurovascular coupling, flickering light dilates capillaries and small arterioles, thus inducing endothelium-dependent, flow-mediated dilation of larger retinal vessels. Risk factors for arteriosclerosis, such as dyslipidaemia, diabetes, or systemic hypertension, are also risk factors for eye diseases such as retinal arterial or retinal vein occlusions, cataracts, age-related macular degeneration, and increases in intraocular pressure (IOP). Functional alterations of blood flow are particularly relevant to the eye. The primary vascular dysregulation syndrome (PVD), which often includes systemic hypotension, is associated with disturbed autoregulation of ocular blood flow (OBF). Fluctuation of IOP on a high level or blood pressure on a low level leads to instable OBF and oxygen supply and therefore to oxidative stress, which is particularly involved in the pathogenesis of glaucomatous neuropathy. Vascular dysregulation also leads to a barrier dysfunction and thereby to small retinal haemorrhages.

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Brain. 2013 Feb 8. [Epub ahead of print]

Microcystic macular degeneration from optic neuropathy: not inflammatory, not trans-synaptic degeneration.

Barboni P, Carelli V, Savini G, Carbonelli M, La Morgia C, Sadun AA.

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PMID: 23396580 [PubMed - as supplied by publisher]

Epidemiology

Retina. 2013 Feb 12. [Epub ahead of print]

TEN-YEAR INCIDENCE OF AGE-RELATED MACULAR DEGENERATION ACCORDING TO DIABETIC RETINOPATHY CLASSIFICATION AMONG MEDICARE BENEFICIARIES.

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PURPOSE: To compare the longitudinal incidence over 10 years of dry and wet age-related macular degeneration (AMD) in a U.S. sample of Medicare beneficiaries with no diabetes mellitus, diabetes mellitus without retinopathy, nonproliferative diabetic retinopathy (NPDR), and proliferative diabetic retinopathy (PDR).

METHODS: Using Medicare claims data, the 10-year incidence of dry and wet AMD from 1995 to 2005 in beneficiaries older than 69 years with newly diagnosed diabetes mellitus (n = 6,621), NPDR (n = 1,307), and PDR (n = 327) compared with each other and matched controls without diabetes for each group.

RESULTS: After controlling for covariates, newly diagnosed NPDR was associated with significantly increased risk of incident diagnosis of dry AMD (hazard ratio, 1.24; 95% confidence interval: 1.08-1.43) and wet AMD (hazard ratio 1.68; 95% confidence interval: 1.23-2.31). Newly diagnosed PDR was associated with significantly increased risk of wet AMD only (hazard ratio 2.15; 95% confidence interval: 1.07-4.33). Diabetes without retinopathy did not affect risk of dry or wet AMD. There was no difference in risk of wet AMD in PDR compared with NPDR.

CONCLUSION: Elderly individuals with NPDR or PDR may be at higher risk of AMD compared to those without diabetes mellitus or diabetic retinopathy.

PMID: 23407352 [PubMed - as supplied by publisher]

Indian J Ophthalmol. 2013 Feb;61(2):53-8. doi: 10.4103/0301-4738.107191.

The British Asian Community Eye Study: Outline of results on the prevalence of eye disease in British Asians with origins from the Indian subcontinent.

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Background: Asians from the Indian Subcontinent form the largest ethnic minority in the United Kingdom. Data on the prevalence of visually-impairing eye conditions in this population are vital for planning eye health care services.

Materials and Methods: This survey was based in the two London boroughs with the largest Asian populations. Subjects originating from the Indian Subcontinent were identified from GP practice records. All subjects were asked about demographic details and were given a full ophthalmological examination. The severity of cataract, glaucoma, diabetic retinopathy, and age-related maculopathy was recorded. Blindness was defined as logMAR visual acuity of 0.99 (Snellen equivalence 20/200 in the better eye) or worse, 'low vision' was defined as Snellen equivalence of 20/63 or worse (logMAR 0.5 or higher), and visual impairment was defined as visual acuity worse than 20/40.

Results: The median age was 56 years. Two hundred and eighty four subjects did not attend for eye examination. Of the 922 examined, 128 subjects (13.9%) were 'visually impaired,' 39 (4.2%) had 'low vision,' and 6 (0.7%) were bilaterally blind. The overall prevalence of cataract, open-angle glaucoma, age-related macular degeneration, and diabetic retinopathy were 77%, 1.0%, 8.7%, and 8.8%, respectively.

Conclusion: Visual impairment rates amongst Asians seem to be similar to Caucasian populations in the

UK. The prevalence of cataract and diabetic retinopathy is higher, while the risk of ARMD and OAG are comparable. In view of the high cataract prevalence, a more detailed assessment of the visual profile and factors limiting healthcare accessibility in this community are needed.

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Long-term Blood Pressure and Age-Related Macular Degeneration: The ALIENOR Study.

Cougnard-Gregoire A, Delyfer MN, Korobelnik JF, Rougier MB, Malet F, Le Goff M, Dartigues JF, Colin J, Barberger-Gateau P, Delcourt C.

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PURPOSE: To explore the association of age-related macular degeneration (AMD) with long-term average blood pressure (BP) parameters, including pulse pressure (PP).

Methods: The Alienor study is a population-based study on age-related eye diseases in 963 residents of Bordeaux (France), aged 73 years or more. AMD was graded from non mydriatic color retinal photographs, in three exclusive stages: no AMD (1015 eyes); large soft distinct drusen and/or large soft indistinct drusen and/or reticular drusen and/or pigmentary abnormalities (early AMD, 276 eyes); late AMD (66 eyes). BP parameters were measured at 4 occasions over a 7-year period. PP was defined as systolic BP minus diastolic BP. Associations of AMD with blood pressure parameters were estimated using Generalized Estimating Equation logistic regressions. Statistical analyses included 702 subjects (1357 eyes) with complete data.

Results: After adjustment for age, gender, educational level, smoking, body mass index, plasma HDL- and LDL-cholesterol, CFH Y402H, ApoE2, ApoE4 and ARMS2 A69S polymorphisms, elevated PP was significantly associated with an increased risk of late AMD (OR=1.37 for a 10 mmHg-increase, 95 % confidence interval (CI): [1.03-1.82]). Associations were similar for late atrophic and late neovascular AMD (OR= 1.39 [1.01-1.92], p=0.04 and OR= 1.43 [0.90-2.23], p=0.13, respectively). Association with early AMD was in the same direction but did not reach statistical significance (OR=1.12, 95% CI: 0.98-1.28). Early and late AMD were not significantly associated with systolic or diastolic blood pressure, hypertension or use of anti-hypertensive medications.

Conclusions: This study suggests that high pulse pressure may be associated with increased risk for AMD.

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Retina. 2013 Feb 7. [Epub ahead of print]

SYSTEMIC RISK FACTORS ASSOCIATED WITH POLYPOIDAL CHOROIDAL VASCULOPATHY AND NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

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PURPOSE: To compare the association of systemic risk factors between neovascular age-related macular degeneration (nAMD) and polypoidal choroidal vasculopathy (PCV).

METHODS: Seven hundred and three patients (235 with nAMD and 468 with PCV) were included. Associated systemic conditions, including hypertension, cardiovascular disease, stroke, diabetes mellitus,

and end-stage renal disease, were investigated through an interview and questionnaire.

RESULTS: The prevalence of diabetes mellitus and end-stage renal disease in nAMD was significantly higher than that in PCV ($P < 0.001$ and $P = 0.021$, respectively, multivariate logistic regression analysis). Moreover, in diabetic patients with nAMD or PCV, the more severe form of diabetic retinopathy was more prevalent in nAMD cases than in PCV cases ($P = 0.006$, multivariate logistic regression analysis).

CONCLUSION: Diabetes mellitus and end-stage renal disease are more prevalent in patients with nAMD than in those with PCV. Specific systemic conditions might be associated with the development of nAMD.

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The Relationship of Atherosclerosis to the 10-Year Cumulative Incidence of Age-related Macular Degeneration: The Beaver Dam Studies.

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OBJECTIVE: To describe the relationships of intima-media thickness (IMT), plaque in the carotid artery, angina, myocardial infarction (MI), and stroke to the 10-year cumulative incidence of early and late age-related macular degeneration (AMD) and progression of AMD.

DESIGN: Cohort study.

PARTICIPANTS: A total of 1700 persons aged 53 to 96 years who participated in both the Epidemiology of Hearing Loss Study and the Beaver Dam Eye Study in 1998-2000, with photographs gradable for AMD at 5 -year (2003-2005) and 10-year (2008-2010) follow-up examinations.

METHODS: The IMT and presence of plaque were assessed using B-mode ultrasonography of the carotid artery. Presence of angina, MI, and stroke were defined on the basis of a self-reported history of physician diagnosis. The presence and severity of AMD were determined by systematic grading of stereoscopic color fundus photographs.

MAIN OUTCOME MEASURES: Age-related macular degeneration.

RESULTS: The 10-year cumulative incidence of early AMD was 15.7%, and the 10-year cumulative incidence of late AMD was 4.0%. After adjusting for age, sex, body mass index, smoking status, age-related maculopathy susceptibility 2 (ARMS2) and complement factor H (CFH) genotypes, and other factors, mean IMT was associated with the 10-year incidence of early AMD (odds ratio [OR] per 0.1 mm IMT, 1.11; 95% confidence interval [CI], 1.00-1.21; $P = 0.03$) and late AMD (OR per 0.1 mm IMT, 1.27; CI, 1.10-1.47; $P = 0.001$). Mean IMT was associated with the 10-year incidence of pure geographic atrophy (OR per 0.1 mm IMT, 1.31; CI, 1.05-1.64; $P = 0.02$) but not exudative AMD (OR per 0.1 mm IMT, 1.14; CI, 0.97-1.34; $P = 0.11$). Similar associations were found for maximum IMT. The number of sites with plaque was related to the incidence of late AMD (OR per 0.1 mm IMT, 2.79 for 4-6 sites vs. none; CI, 1.06-7.37; $P = 0.04$) but not to early AMD. A history of angina, MI, or stroke was not related to any incident AMD outcome.

CONCLUSIONS: In these population-based data, carotid artery IMT and carotid plaques had a weak relationship to the incidence of late AMD that was independent of systemic and genetic risk factors. Angina, MI, and stroke were not related to AMD. It is unclear whether the carotid IMT is a risk indicator of processes

affecting Bruch's membrane and the retinal pigment epithelium, or a measure of atherosclerosis affecting susceptibility to AMD.

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Genetics

Mutagenesis. 2013 Mar;28(2):197-204. doi: 10.1093/mutage/ges071.

The 3895-bp mitochondrial DNA deletion in the human eye: a potential involvement in corneal ageing and macular degeneration.

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Abstract: In human skin, the 3895-bp deletion of mitochondrial DNA (mtDNA(3895)) is catalysed by ultraviolet (UV) light through the generation of reactive oxygen species. Given its function in vision, the human eye is exposed to oxidising UV and blue light in its anterior (cornea, iris) and posterior (retina) structures. In this study, we employed a highly sensitive quantitative PCR technique to determine mtDNA (3895) occurrence in human eye. Our analysis shows that the mtDNA(3895) is concentrated in both the cornea and the retina. Within the cornea, the highest mtDNA(3895) level is found in the stroma, the cellular layer conferring transparency and rigidity to the human cornea. Moreover, mtDNA(3895) accumulates with age in the stroma, suggesting a role of this deletion in corneal ageing. Within the retina, mtDNA(3895) is concentrated in the macular region of both the neural retina and the retinal pigment epithelium, supporting the hypothesis that this deletion is implicated in retinal pathologies such as age-related macular degenerescence. Taken together, our results imply that UV and blue light catalyse mtDNA(3895) induction in the human eye.

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Diet

J Nutr. 2013 Feb 13. [Epub ahead of print]

High Concentrations of Plasma n3 Fatty Acids Are Associated with Decreased Risk for Late Age-Related Macular Degeneration.

Merle BM, Delyfer MN, Korobelnik JF, Rougier MB, Malet F, Féart C, Le Goff M, Peuchant E, Letenneur L, Dartigues JF, Colin J, Barberger-Gateau P, Delcourt C.

INSERM, ISPED, Centre INSERM U897-Epidemiologie-Biostatistique, Bordeaux, France.

Abstract: High dietary intakes of n3 (Ω3) PUFA and fish have been consistently associated with a decreased risk for age-related macular degeneration (AMD). We assessed the associations of late AMD with plasma n3 PUFA, a nutritional biomarker of n3 PUFA status. The Antioxydants Lipides Essentiels Nutrition et Maladies Occulaires (Alienor) Study is a prospective, population-based study on nutrition and age-related eye diseases performed in 963 residents of Bordeaux (France) aged ≥73 y. Participants had a first eye examination in 2006-2008 and were followed for 31 mo on average. Plasma fatty acids were measured by GC from fasting blood samples collected in 1999-2001. AMD was graded from non-mydriatic color retinal photographs at all examinations and spectral domain optical coherence tomography at follow-up. After adjustment for age, gender, smoking, education, physical activity, plasma HDL-cholesterol, plasma TGs, CFH Y402H, apoE4, and ARMS2 A69S polymorphisms, and follow-up time, high plasma total n3 PUFA was associated with a reduced risk for late AMD [OR = 0.62 for 1-SD increase (95% CI: 0.44-0.88); P = 0.008]. Associations were similar for plasma 18:3n3 [OR = 0.62 (95% CI: 0.43-0.88); P = 0.008]

and n3 long-chain PUFA [OR = 0.65 (95% CI: 0.46-0.92); P = 0.01]. This study gives further support to the potential role of n3 PUFAs in the prevention of late AMD and highlights the necessity of randomized clinical trials to determine more accurately the value of n3 PUFAs as a means of reducing AMD incidence.

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Oral Docosahexaenoic Acid in the Prevention of Exudative Age-Related Macular Degeneration: The Nutritional AMD Treatment 2 Study.

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OBJECTIVE: To evaluate the efficacy of docosahexaenoic acid (DHA)-enriched oral supplementation in preventing exudative age-related macular degeneration (AMD).

DESIGN: The Nutritional AMD Treatment 2 study was a randomized, placebo-controlled, double-blind, parallel, comparative study.

PARTICIPANTS: Two hundred sixty-three patients 55 years of age or older and younger than 85 years with early lesions of age-related maculopathy and visual acuity better than 0.4 logarithm of minimum angle of resolution units in the study eye and neovascular AMD in the fellow eye.

METHODS: Patients were assigned randomly to receive either 840 mg/day DHA and 270 mg/day eicosapentaenoic acid (EPA) from fish oil capsules or the placebo (olive oil capsules) for 3 years.

MAIN OUTCOME MEASURES: The primary outcome measure was time to occurrence of choroidal neovascularization (CNV) in the study eye. Secondary outcome measures in the study eye were: incidence of CNV developing in patients, changes in visual acuity, occurrence and progression of drusen, and changes in EPA plus DHA level in red blood cell membrane (RBCM).

RESULTS: Time to occurrence and incidence of CNV in the study eye were not significantly different between the DHA group (19.5±10.9 months and 28.4%, respectively) and the placebo group (18.7±10.6 months and 25.6%, respectively). In the DHA group, EPA plus DHA levels increased significantly in RBCM (+70%; P<0.001), suggesting that DHA easily penetrated cells, but this occurred unexpectedly also in the placebo group (+9%; P = 0.007). In the DHA-allocated group, patients steadily achieving the highest tertile of EPA plus DHA levels in RBCM had significantly lower risk (-68%; P = 0.047; hazard ratio, 0.32; 95% confidence interval, 0.10-0.99) of CNV developing over 3 years. No marked changes from baseline in best-corrected visual acuity, drusen progression, or geographic atrophy in the study eye were observed throughout the study in either group.

CONCLUSIONS: In patients with unilateral exudative AMD, 3 years of oral DHA-enriched supplementation had the same effect on CNV incidence in the second eye as did the placebo. However, RBCM fatty acid measurements revealed that CNV incidence was significantly reduced in DHA-supplemented patients showing a steadily high EPA plus DHA index over 3 years.

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