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MD Research News

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Drug Treatment

Eur J Ophthalmol. 2012 Aug 6:0. doi: 10.5301/ejo.5000190. [Epub ahead of print]

Information used to decide on retreatment of exudative age-related macular degeneration with anti-VEGF in clinical practice.

Manousaridis K, Manjunath V, Talks J.

Ophthalmology Department, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals, NHS Foundation Trust, Newcastle upon Tyne - UK.

Purpose: To record the information used in order to make a retreatment decision in patients with exudative age-related macular degeneration (AMD) and to assess if an optical coherence tomography (OCT)-only follow-up clinic would suffice.

Methods: Two hundred patients under treatment with intravitreal anti-vascular endothelial growth factor injections (anti-VEGF) for exudative AMD were included. Each patient had previously received at least 3 intravitreal anti-VEGF injections (loading dose) (range 3-24 injections). Clinicians seeing the patients beyond the third injection were asked to document the criteria used to make a retreatment decision.

Results: Overall, in 171 (85.5%) cases the retreatment decision was based on OCT findings of intraretinal or subretinal fluid alone. Diagnosis of recurrence requiring treatment would have been missed in 12 cases (6%), if OCT-only data had been used and funduscopy or visual function criteria had been omitted. Decision was based solely on functional criteria in only 2% of the cases. The retreatment decision was based on evaluation of morphologic funduscopic or OCT criteria in 187 (93.5%) cases.

Conclusions: With the increasing number of patients having follow-up after anti- VEGF treatment, efficient systems of follow-up are required. Although most retreatment decisions could have been made by qualitative assessment of OCT images alone, the examination has considerable limitations. Optical coherence tomography in combination with color fundus photography could serve as screening tools for a rational implementation of other invasive imaging techniques such as fundus fluorescein angiography and indocyanine green angiography in decision-making.

PMID: 22890600 [PubMed - as supplied by publisher]

BMJ. 2012 Aug 13;345:e5182. doi: 10.1136/bmj.e5182.

The relative clinical effectiveness of ranibizumab and bevacizumab in diabetic macular oedema: an indirect comparison in a systematic review.

Ford JA, Elders A, Shyangdan D, Royle P, Waugh N.

Health Services Research Unit, University of Aberdeen, Health Services Building, Aberdeen AB25 2ZD, UK.

OBJECTIVE: To indirectly compare the effectiveness of ranibizumab and bevacizumab in the treatment of diabetic macular oedema.

DESIGN: Systematic review and indirect comparison.

DATA SOURCES: Medline (1996-September 2011), Embase (1996-September 2011), and the Cochrane Central Register of Controlled Trials (Issue 4, 2011).

SELECTION CRITERIA FOR STUDIES : Randomised trials evaluating ranibizumab or bevacizumab in diabetic macular oedema with a common comparator and sufficient methodological similarity to be included within an indirect comparison were eligible for inclusion.

MAIN OUTCOME MEASURES: The primary outcome was the proportion of patients with an improvement in best corrected visual acuity of more than two lines on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale. Secondary outcomes included mean changes in best corrected visual acuity and in central macular thickness, and adverse events. Best corrected visual acuity was converted to logMAR units, a linear scale of visual acuity with positive values representing increasing visual loss. Indirect comparisons were done using Bayesian methods to estimate relative treatment effects of bevacizumab and ranibizumab.

RESULTS: Five randomised controlled trials with follow-up of 6-12 months and a common comparator (multiple laser treatment) were sufficiently similar to be included in the indirect comparison. Generally studies were small, resulting in wide credible intervals. The proportions of patients with an improvement in best corrected visual acuity of >2 lines were 21/77 participants (27%) for bevacizumab and 60/152 participants (39%) for ranibizumab (odds ratio 0.95 (95% credible interval 0.23 to 4.32)). The wide credible intervals cannot exclude a greater improvement, or worse outcome, for either drug. The mean change in best corrected visual acuity non-significantly favoured bevacizumab (treatment effect -0.08 logMAR units (-0.19 to 0.04)). The difference in mean change in central macular thickness was not statistically significant between ranibizumab and bevacizumab (treatment effect -6.9 μm (-88.5 to 65.4)).

CONCLUSIONS: Results suggest no difference in effectiveness between bevacizumab and ranibizumab, but the wide credible intervals cannot exclude the possibility that either drug might be superior. Sufficiently powered, direct head to head trials are needed.

PMID: 22890029 [PubMed - in process] PMCID:PMC3418219

Clin Ophthalmol. 2012;6:1073-1082.

Retinal ganglion cell function after repeated intravitreal injections of ranibizumab in patients with age-related macular degeneration.

Nishimura T, Machida S, Harada T, Kurosaka D.

Department of Ophthalmology, Iwate Medical University School of Medicine, Morioka, Iwate, Japan.

BACKGROUND: The purpose of this study was to evaluate the safety of intravitreal ranibizumab injection in patients with age-related macular degeneration.

MATERIALS AND METHODS: We examined retinal ganglion cell function using the photopic negative response of the electroretinogram (ERG) in patients with age-related macular degeneration (AMD) treated with intravitreal injections of ranibizumab. We studied 32 eyes of 32 patients with AMD and aged 50-84 years with a mean of 71 years. An intravitreal ranibizumab injection was given three times at monthly intervals. Additional injections were given according to an optical coherence tomography-guided variable dosing regimen. ERG recordings were made before treatment (baseline) and at 3, 6, 9, and 12 months postoperatively. Full-field cone ERGs were elicited by red stimuli on a blue background. The focal macular ERGs were elicited by a 15 degree white stimulus spot centered on the macular region. We measured the amplitudes of the a and b waves, oscillatory potentials, and the photopic negative response of the full-field cone and focal macular ERGs.

RESULTS: Visual acuity was significantly better than the baseline acuity, and macular thickness was significantly reduced after the intravitreal injections of ranibizumab. The amplitudes and implicit times of each wave of the full-field cone ERGs were not significantly changed after intravitreal ranibizumab injections. However, the amplitudes of each wave of the focal macular ERGs were increased after the injections. The implicit times of the a and b waves of the focal macular ERGs were significantly shortened after intravitreal injections of ranibizumab. The ratio of the full-field and focal photopic negative response/b-wave amplitude was not significantly changed after the injections.

CONCLUSION: The amplitudes of the focal macular ERGs, including the photopic negative response improved after repeated intravitreal ranibizumab injections, accompanied by a recovery of visual acuity and macular structure. The results of the full-field cone ERGs indicate that retinal ganglion cell function was not altered by repeated intravitreal ranibizumab injection.
PMID: 22888205 [PubMed - as supplied by publisher] PMCID: PMC3413340

Am J Ophthalmol. 2012 Sep;154(3):429-435.e2.

Uveitis, the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT), and Intravitreal Biologics for Ocular Inflammation.

Yeh S, Albini TA, Moshfeghi AA, Nussenblatt RB.

Emory Eye Center, Emory University School of Medicine, Atlanta, Georgia.

PURPOSE: To provide perspective on the implications of the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT) on intravitreal biologic agents in uveitis and retinal diseases in which ocular inflammatory pathways are central to their pathogenesis.
DESIGN: Interpretative essay.

METHODS: Literature review and interpretation.

RESULTS: Besides the clear importance of CATT from a patient treatment perspective in age-related macular degeneration (AMD), these data highlight the critical relevance of highly specific protein immunotherapies offered with biologic agents. The CATT trial also provides a reminder regarding the importance of rigorous efficacy and safety monitoring required when administering intravitreal biologic therapy. Within the field of uveitis, systemic and local biologics have been used to effectively treat uveitis, targeting pathways implicated in both angiogenesis and inflammation (eg, tumor necrosis factor-α [TNF-α] and interleukin-2 pathways), and research on intravitreal biologic therapy for uveitis and AMD will continue to expand. With over 25 ongoing clinical trials on intravitreal biologic therapy for AMD, enthusiasm for vanguard biologic therapies should be tempered by judicious monitoring for adverse events.

CONCLUSION: The importance of the CATT trial encompasses day-to-day treatment decisions for AMD, as well as lessons on how biologics for ocular disease should be implemented into clinical practice. Specifically, the introduction of intravitreal biologic therapies into clinical practice for uveitis, AMD, and other ocular diseases in which inflammation is involved should be guided by a clear understanding of the immunotherapeutic agent and its molecular target and with rigorous monitoring for both patient benefit and patient safety.

PMID: 22898344 [PubMed - in process]

Clin Exp Optom. 2012 Aug 13. doi: 10.1111/j.1444-0938.2012.00771.x. [Epub ahead of print]

Macular oedema due to letrozole: A first case report.

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Abstract
A 72-year-old woman presented with unexplained, progressive, painless visual loss in the right eye during the past six months. At presentation visual acuity (VA) was 3/60 in the right eye and 6/6 in the left eye. Anterior segment examination and intraocular pressures were normal. Dilated fundoscopy revealed significant macular oedema in the right eye and a normal fundus appearance in the left eye. Her medical history was noteworthy for breast ductal carcinoma in situ, for which she had undergone right mastectomy three years earlier. She had not received chemotherapy or radiotherapy but she had been under treatment with letrozole 2.5 mg/day over the past three years. She did not receive any other medication. Optical coherence tomography showed intraretinal fluid and a significant increase in retinal thickness in the foveal and parafoveal areas, while fluorescein angiography detected foveal hyperfluorescence and leakage of the dye in the late phase. Multifocal electroretinogram showed a decreased response in both eyes. In suspicion of letrozole-related retinopathy, the patient was advised to stop the medication. The patient agreed to receive an intravitreal injection of 0.05 ml/0.5 mg ranibizumab. One month later, VA in the right eye was 6/9 and macular oedema had apparently improved. This is the first reported case of letrozole-associated macular oedema treated with intravitreal ranibizumab.

PMID: 22882318 [PubMed - as supplied by publisher]

Surv Ophthalmol. 2012 Sep;57(5):415-29.

Corneal Neovascularization: An Anti-VEGF Therapy Review.

Chang JH, Garg NK, Lunde E, Han KY, Jain S, Azar DT.

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Abstract
Corneal neovascularization is a serious condition that can lead to a profound decline in vision. The abnormal vessels block light, cause corneal scarring, compromise visual acuity, and may lead to inflammation and edema. Corneal neovascularization occurs when the balance between angiogenic and antiangiogenic factors is tipped toward angiogenic molecules. Vascular endothelial growth factor (VEGF), one of the most important mediators of angiogenesis, is upregulated during neovascularization. In fact, anti-VEGF agents have efficacy in the treatment of neovascular age-related macular degeneration, diabetic

retinopathy, macular edema, neovascular glaucoma, and other neovascular diseases. These same agents have great potential for the treatment of corneal neovascularization. We review some of the most promising anti-VEGF therapies, including bevacizumab, VEGF trap, siRNA, and tyrosine kinase inhibitors.

PMID: 22898649 [PubMed - in process]

Oftalmologia. 2012;56(1):51-7.

[Antiangiogenic agents in ARMD treatment]. [Article in Romanian]

Coroi MC, Demea S, Todor M, Apopei E.

Spitalul Clinic Judeţean de Urgenţă Oradea.

Abstract
The aim of antiangiogenic agents in the treatment of age related senile macular degeneration is to destroy coroidian neoformation vessels by minimally affecting the central vision. We present a case of important central vision recovery after 3 intravitreal injections of Avastin. The therapeutic decision and patient monitoring have been made using imagistical investigations such as OCT and AFG. A modern therapeutic approach of neovascular forms of age related macular degeneration, backed up by AFG and OCT is a modern treatment method of this disabling illness which brings patients optimal functional and structural improvement.

PMID: 22888687 [PubMed - in process]

Other treatment & diagnosis

Invest Ophthalmol Vis Sci. 2012 Aug 16. [Epub ahead of print]

Street-Crossing Decision-Making: A Comparison between Patients with Age-Related Macular Degeneration and Normal Vision.

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Purpose: To determine whether the street-crossing decisions of subjects with Age-related macular degeneration (AMD) are as accurate and precise as those made by young and older subjects with normal vision.

Methods: Street-crossing decisions in 13 AMD subjects, 20 young and 20 older control subjects with normal vision were measured along an unsignalized street for nine different gap times. After calculating the discriminability (d') of the street-crossing decision variable for all gap pairs and entering these d' values into a one-dimensional scaling model, the means of each distribution of the decision variable relative to a "center of gravity" were estimated and plotted against gap time. The resultant plot was a non-linear function. Street-crossing decision accuracy was computed for each subject as the difference between the x-intercept of the non-linear function (tCOG) and subject's measured street-crossing time. Street-crossing decision-making precision was computed as the value of the slope of the non-linear function at tCOG.

Results: We found that all subjects were precise in their street-crossing decisions (p=0.55). Significant differences in street-crossing accuracy were found as a function of age (p=0.003). Compared to either the

older normally-sighted (p=0.018) or AMD subjects (p=0.019), the young normally-sighted subjects made the least accurate street-crossing decisions. No significant difference in accuracy was found between the AMD and age-matched normally-sighted subjects (p=0.90).

Conclusions: Our data suggests that age and central vision loss did not significantly affect a subject's precision in their street-crossing decisions. Age, but not central vision loss, significantly affected a subject's accuracy in their street-crossing decisions.

PMID: 22899756 [PubMed - as supplied by publisher]

Surv Ophthalmol. 2012 Sep;57(5):389-414.

Evaluation of Age-related Macular Degeneration With Optical Coherence Tomography.

Keane PA, Patel PJ, Liakopoulos S, Heussen FM, Sadda SR, Tufail A.

NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, UK; Doheny Eye Institute, Keck School of Medicine of the University of Southern California, Los Angeles, California, USA.

Abstract
Age-related macular degeneration (AMD) is the leading cause of severe visual loss in people aged 50 years or older in the developed world. In recent years, major advances have been made in the treatment of AMD, with the introduction of anti-angiogenic agents, offering the first hope of significant visual recovery for patients with neovascular AMD. In line with these advances, a new imaging modality-optical coherence tomography (OCT)-has emerged as an essential adjunct for the diagnosis and monitoring of patients with AMD. The ability to accurately interpret OCT images is thus a prerequisite for both retina specialists and comprehensive ophthalmologists. Despite this, the relatively recent introduction of OCT and the absence of formal training, coupled with rapid evolution of the technology, may make such interpretation difficult. These problems are compounded by the phenotypically heterogeneous nature of AMD and its complex morphology as visualized using OCT. We address these issues by summarizing the current understanding of OCT image interpretation in patients with AMD and describe how OCT can best be applied in clinical practice.

PMID: 22898648 [PubMed - in process]

Arch Ophthalmol. 2012 Aug 13:1-7. doi: 10.1001/archophthalmol.2012.2491. [Epub ahead of print]

Optical Coherence Tomographic Imaging of Sub-Retinal Pigment Epithelium Lipid.

Mukkamala SK, Costa RA, Fung A, Sarraf D, Gallego-Pinazo R, Freund KB.

OBJECTIVE: To describe an optical coherence tomographic finding of layered hyperreflective bands beneath the retinal pigment epithelium (RPE), the so-called onion sign believed to represent lipid within a vascularized pigment epithelial detachment.

METHODS: This retrospective observational case series involved reviewing clinical histories of patients with the onion sign. Imaging studies analyzed included spectral-domain optical coherence tomography, color and red-free photographs, near infrared reflectance, fundus autofluorescence, and blue-light fundus autofluorescence.
RESULTS: A total of 22 eyes of 20 patients with sub-RPE hyperreflective bands were identified. There were 15 women and 5 men with a mean patient age of 76 years (range, 60-92 years). Snellen best-

corrected visual acuities ranged from 20/25 to counting fingers, with a median of 20/80. Two patients had bilateral involvement, and 3 of 17 eyes had multifocal onion signs in the same eye. All eyes had neovascular age-related macular degeneration, with type 1 (sub-RPE) neovascularization. In all patients, the onion sign correlated with areas of yellow-gray exudates seen clinically that appeared bright on red-free and near infrared reflectance imaging. No specific fundus autofluorescence or blue-light fundus autofluorescence pattern was identified.

CONCLUSIONS: The onion sign refers to layered hyperreflective bands in the sub-RPE space usually associated with chronic exudation from type 1 neovascularization in patients with age-related macular degeneration. With an associated bright near infrared reflectance, these bands may correspond to lipid, collagen, or fibrin. Because the onion sign colocalizes to areas of exudation that are known to consist of lipoprotein, we propose that this finding may represent layers of precipitated lipid in the sub-RPE space. To our knowledge, this is the first report of lipid detected in the sub-RPE space on clinical examination.

PMID: 22892986 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2012 Sep;154(3):427-8.

Toward personalized medicine for age-related macular degeneration.

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Department of Ophthalmology, University Paris Est Creteil (UPEC), Creteil, France.

PMID: 22898343 [PubMed - in process]

Br J Ophthalmol. 2012 Aug 15. [Epub ahead of print]

16 Gy low-voltage x-ray irradiation followed by as needed ranibizumab therapy for age-related macular degeneration: 12 month outcomes of a 'radiation-first' strategy.

Moshfeghi AA, Morales-Canton V, Quiroz-Mercado H, Velez-Montoya R, Zavala-Ayala A, Shusterman EM, Kaiser PK, Sanislo SR, Gertner M, Moshfeghi DM.

Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Palm Beach Gardens, Florida, USA.

BACKGROUND AND OBJECTIVE: To describe 'radiation-first' combination treatment with a non-invasive, low-voltage x-ray irradiation system followed by as needed ranibizumab for neovascular age-related macular degeneration (AMD).

STUDY DESIGN AND METHODS: Phase I study of non-invasive, low-voltage 16 Gy x-ray irradiation delivered in three beams via the inferior pars plana in patients with active neovascular AMD. Ranibizumab was administered as needed per protocol. Patients were followed monthly for safety and efficacy over 12 months.

RESULTS: 13 patients were enrolled and completed 12 months follow-up. Safety was good with no serious ocular/non-ocular adverse events or radiation-related ocular complications. 11 patients lost <15 Early Treatment of Diabetic Retinopathy Study (ETDRS) letters, seven gained ≥0 ETDRS letters and 0 gained ≥15 ETDRS letters. Patients received a total of 31 subsequent ranibizumab injections (of possible 156) over the 12 months following x-ray irradiation. Mean time to first injection was 3.9 months. One patient received no ranibizumab injections, three patients received one injection, four patients received two injections, and

five patients received three or more injections.

CONCLUSIONS: After 12 months, non-invasive, low-voltage x-ray irradiation with as needed ranibizumab rescue therapy demonstrated good safety with a visual acuity stabilising effect and reduction in retinal thickness in patients with neovascular AMD.

PMID: 22895887 [PubMed - as supplied by publisher]

J Biomed Opt. 2012 Jul;17(7):070505.

Ultrahigh-speed non-invasive widefield angiography.

Blatter C, Klein T, Grajciar B, Schmoll T, Wieser W, Andre R, Huber R, Leitgeb RA.

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Abstract
Retinal and choroidal vascular imaging is an important diagnostic benefit for ocular diseases such as age-related macular degeneration. The current gold standard for vessel visualization is fluorescence angiography. We present a potential non-invasive alternative to image blood vessels based on functional Fourier domain optical coherence tomography (OCT). For OCT to compete with the field of view and resolution of angiography while maintaining motion artifacts to a minimum, ultrahigh-speed imaging has to be introduced. We employ Fourier domain mode locking swept source technology that offers high quality imaging at an A-scan rate of up to 1.68 MHz. We present retinal angiogram over ~48 deg acquired in a few seconds in a single recording without the need of image stitching. OCT at 1060 nm allows for high penetration in the choroid and efficient separate characterization of the retinal and choroidal vascularization.

PMID: 22894461 [PubMed - in process]

Arch Ophthalmol. 2012 Aug 1;130(8):1028-1037.

Baseline Traits of Low Vision Patients Served by Private Outpatient Clinical Centers in the United States.

Goldstein JE, Massof RW, Deremeik JT, Braudway S, Jackson ML, Kehler KB, Primo SA, Sunness JS; for the Low Vision Research Network Study Group.

OBJECTIVE: To characterize the traits of low vision patients who seek outpatient low vision rehabilitation (LVR) services in the United States.

METHODS: In a prospective observational study, we enrolled 764 new low vision patients seeking outpatient LVR services from 28 clinical centers in the United States. Before their initial appointment, multiple questionnaires assessing daily living and vision, physical, psychological, and cognitive health states were administered by telephone. Baseline clinical visual impairment measures and disorder diagnoses were recorded.

RESULTS: Patients had a median age of 77 years, were primarily female (66%), and had macular disease (55%), most of which was nonneovascular age-related macular degeneration. More than one-third of the patients (37%) had mild vision impairment with habitual visual acuity (VA) of 20/60 or greater. The VA correlated well with contrast sensitivity (r = -0.52) but poorly with self-reported vision quality. The intake

survey revealed self-reported physical health limitations, including decreased endurance (68%) and mobility problems (52%). Many patients reported increased levels of frustration (42%) and depressed mood (22%); memory and cognitive impairment (11%) were less frequently endorsed. Patients relied on others for daily living support (87%), but many (31%) still drove.

CONCLUSIONS: Most patients seeking LVR are geriatric and have macular disease with relatively preserved VA. The disparity between VA and subjective quality of vision suggests that LVR referrals are based on symptoms rather than on VA alone. Patients seen for LVR services have significant physical, psychological, and cognitive disorders that can amplify vision disabilities and decrease rehabilitation potential.

PMID: 22893074 [PubMed - as supplied by publisher]

Isr Med Assoc J. 2012 Jun;14(6):363-6.

Factors associated with early detection of choroidal neovascularization in age-related macular degeneration in the clinic setting.

Lichtinger A, Caraza M, Galbinur T, Chowers I.

Department of Ophthalmology, Hadassah-Hebrew University Medical Center and Hadassah-Hebrew University Medical School, Jerusalem, Israel.

BACKGROUND: Delayed diagnosis of choroidal neovas cularization (CNV) in age-related macular degeneration (AMD) adversely affects visual outcome.

OBJECTIVES: To identify factors associated with early detection of CNV in the clinic setting.

METHODS: Demographic and clinical data and lesion characteristics were retrospectively collected from 76 consecutive AMD patients who had a history of CNV in one eye and presented with CNV in the second eye. These data were evaluated for association with visual acuity (VA) at the time of presentation.

RESULTS: Better VA was associated with a history of CNV in the fellow eye ($P < 0.0001$), adherence to follow-up every 4 months ($P = 0.015$), younger age ($P = 0.03$), smaller lesion ($P < 0.0001$), and non-subfoveal location ($P = 0.048$). VA of the fellow eye did not correlate with VA at presentation with CNV.

CONCLUSIONS: These data suggest that patients' experience of CNV, regardless of VA, facilitates early diagnosis in the fellow eye. Adherence to follow-up in the routine clinic setting also facilitates early detection of CNV.

PMID: 22891397 [PubMed - in process]

Optom Vis Sci. 2012 Aug 9. [Epub ahead of print]

Contour Enhancement Benefits Older Adults with Simulated Central Field Loss.

Kwon M, Ramachandra C, Satgunam P, Mel BW, Peli E, Tjan BS.

Department of Psychology (MYK, BST), Neuroscience Graduate Program (BWM, BST), Department of Biomedical Engineering (CR, BWM), University of Southern California, Los Angeles, California, and Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts (PNS, EP).

PURPOSE: Age-related macular degeneration is the leading cause of vision loss among Americans aged >65 years. Currently, no effective treatment can reverse the central vision loss associated with most age-related macular degeneration. Digital image-processing techniques have been developed to improve image visibility for peripheral vision; however, both the selection and efficacy of such methods are limited. Progress has been difficult for two reasons: the exact nature of image enhancement that might benefit peripheral vision is not well understood, and efficient methods for testing such techniques have been elusive. The current study aims to develop both an effective image enhancement technique for peripheral vision and an efficient means for validating the technique.

METHODS: We used a novel contour-detection algorithm to locate shape-defining edges in images based on natural-image statistics. We then enhanced the scene by locally boosting the luminance contrast along such contours. Using a gaze-contingent display, we simulated central visual field loss in normally sighted young (aged 18-30 years) and older adults (aged 58-88 years). Visual search performance was measured as a function of contour enhancement strength ["Original" (unenhanced), "Medium," and "High"]. For preference task, a separate group of subjects judged which image in a pair "would lead to better search performance."

RESULTS: We found that although contour enhancement had no significant effect on search time and accuracy in young adults, Medium enhancement resulted in significantly shorter search time in older adults (about 13% reduction relative to Original). Both age-groups preferred images with Medium enhancement over Original (2-7 times). Furthermore, across age-groups, image content types, and enhancement strengths, there was a robust correlation between preference and performance.

CONCLUSIONS: Our findings demonstrate a beneficial role of contour enhancement in peripheral vision for older adults. Our findings further suggest that task-specific preference judgments can be an efficient surrogate for performance testing.

PMID: 22885784 [PubMed - as supplied by publisher]

Clin Exp Optom. 2012 Aug 13. doi: 10.1111/j.1444-0938.2012.00789.x. [Epub ahead of print]

Positive impact of Australian 'blindness' tobacco warning labels: findings from the ITC four country survey.

Kennedy RD, Spafford MM, Behm I, Hammond D, Fong GT, Borland R.

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BACKGROUND: Smokers with greater knowledge of the health effects of smoking are more likely to quit and remain abstinent. Australia has communicated the causal association of smoking and blindness since the late 1990s. In March 2007, Australia became the first country to include a pictorial warning label on cigarette packages with the message that smoking causes blindness. The current study tested the hypothesis that the introduction of this warning label increased smokers' knowledge of this important health effect.

METHODS: Six waves of the International Tobacco Control Four Country Survey were conducted, as a telephone survey of 17,472 adult smokers in Australia, Canada, United Kingdom and the United States, with three waves before and three waves after the blindness health warning was introduced in Australia. The survey measured adult smokers' knowledge that smoking causes blindness.

RESULTS: Australian smokers were significantly more likely to report that smoking causes blindness, compared to Canadian, UK and US smokers, where there were neither health campaigns nor health warnings labels about blindness. After the introduction of the blindness warning, Australian smokers were more likely than before the blindness warning to report that they know that smoking causes blindness (62 versus 49 per cent; OR = 1.68, 95% CI: 1.03, 2.76, p = 0.04). In Australia, smokers aged over 55 years were less likely than those aged 18 to 24 to report that smoking causes blindness (OR = 0.43; 95% CI: 0.29, 0.62, p < 0.001).

CONCLUSION: While more smokers report that smoking causes blindness in Australia compared to other countries, which have not had national social marketing campaigns, further gains in knowledge were found after pictorial warning labels were introduced in Australia. Findings suggest there is still a need to educate the public about the causal association of smoking and blindness. More education may be needed to redress the knowledge gap in older Australian smokers as the incidence of age-related macular degeneration increases with age.

PMID: 22882362 [PubMed - as supplied by publisher]

Oftalmologia. 2012;56(1):36-44.

[New aspects in age related macular degeneration]. [Article in Romanian]

Turlea C.
Clinica de Oftalmologie Timisoara.

Abstract
Being the leading cause of blindness in modern world Age Related Macular Degeneration has beneficiated in the last decade of important progress in diagnosis, classification and the discovery of diverse factors who contribute to the etiology of this disease. Treatments have arised who can postpone the irreversible evolution of the disease and thus preserve vision. Recent findings have identified predisposing genetic factors and also inflamatory and imunological parameters that can be modified trough a good and adequate prevention and therapy This articole reviews new aspects of patology of Age Related Macular Degeneration like the role of complement in maintaining inflamation and the role of oxidative stress on different structures of the retina.

PMID: 22888685 [PubMed - in process]

Oftalmologia. 2012;56(1):30-5.

[Future methods of treatment in age related macular degeneration].[Article in Romanian]

Turlea C.
Clinica de Oftalmologie Timisoara.

Abstract
In the present time the treatment of Age Related Macular Degeneration (ARMD) begins to develop. Many medical therapies are presently tested in the two types of ARMD, geographic atrophy and exudative ARMD. In atrophic ARMD, new drugs are aimed to spare photoreceptors and the retinal pigment epithelium, to prevent oxidative damage on the retina and to suppress the inflammation process. In exudative ARMD, new therapies are already in use and in progress, especially the anti-VEGF factors, and others try to improve visual prognosis in targeting other mechanism or cells involved in the angiogenesis process. This article reviews and summarizes the available data, presented in several scientific meetings, congresses or given directly by the companies involved.

PMID: 22888684 [PubMed - in process]

Pathogenesis

Vision Res. 2012 Aug 7. [Epub ahead of print]

Photopic and scotopic multifocal pupillographic responses in age-related macular degeneration.

Rosli Y, Bedford SM, James AC, Maddess T.

Program of Biomedical Science, School of Diagnostic and Applied Health Sciences, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur, Malaysia; The ARC Centre of Excellence in Vision Science, John Curtin School of Medical Research, Australian National University, Canberra, ACT 0200, Australia.

Abstract
We compared photopic and scotopic multifocal pupillographic stimuli in age-related macular degeneration (AMD). Both eyes of 18 normal and 14 AMD subjects were tested with four stimulus variants presented at photopic and 126 times lower luminances. The multifocal stimuli presented 24 test regions/eye to the central 60°. The stimulus variants had two different check sizes, and when presented either flickered (15Hz) for 266ms, or were steady for 133ms. Mean differences from normal of 5 to 7dB were observed in the central visual field for both photopic and scotopic stimuli (all $p<0.00002$). The best areas under receiver operating characteristic plots for exudative AMD in the photopic and scotopic conditions were 92.9±8.0 and 90.3±5.7% respectively, and in less severely affected eyes 83.8±9.7% and 76.9±8.2%. Damage recorded at photopic levels was possibly more diffusely distributed across the visual field. Sensitivity and specificity was similar at photopic and scotopic levels.

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J Immunother. 2012 Aug 13. [Epub ahead of print]

Targeted Tumor Therapy With a Fusion Protein of an Antiangiogenic Human Recombinant scFv and Yeast Cytosine Deaminase.

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Abstract
In adults, endothelial cell division occurs only in wound healing, during menstruation, or in diseases such as wet age-related macular degeneration or development of benign or malignant tissues. Angiogenesis is one of the major requirements to supply the fast developing tumor tissue with oxygen and nutrients, and enables it to spread into other tissues far from its origin. We selected the extradomain B (ED-B), a splice variant of fibronectin, which is exclusively expressed in ovaries, uterus, during wound healing, and in tumor tissues, as a target for the development of an innovative antiangiogenic, prodrug-based targeted tumor therapy approach. We designed a fusion protein termed L19CDy-His, consisting of the antibody single

chain fragment L19 for targeting ED-B and yeast cytosine deaminase for the conversion of 5-fluorocytosine into cytotoxic 5-fluorouracil. We purified high amounts of the fusion protein from Pichia pastoris that is stable, enzymatically active, and retains 75% of its activity after incubation with human plasma for up to 72 hours. The binding of L19CDy-His to ED-B was confirmed by an enzyme-linked immunosorbent assay and quantified by surface plasmon resonance spectroscopy determining a KD value of 81±7 nM. L19CDy-His successfully decreased cell survival of the murine ED-B-expressing teratocarcinoma cell line F9 upon addition of the prodrug 5-fluorocytosine. Our data demonstrate the suitability of targeting ED-B by L19CDy-His for effective prodrug-based tumor therapy.
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Epidemiology

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[Case-control study of risk factors in age-related macular degeneration]. [Article in Chinese]

Tian J, Fang K, Qin XY, Chen Q, Li J, Yu WZ, Hou J, Chen da F, Hu YH, Li XX.

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OBJECTIVE: To examine the potential influence factors of age-related macular degeneration (AMD).

METHODS: A nationwide multicenter case-control study conducted between Jan. 2008 and May 2010. A total of 545 AMD patients and 480 controls, aged 50 years or older consented to participate in the study. Questionnaires were designed to collect information about demographic characteristics (age, gender), family history, disease history, and behavior factors (smoking, drinking). Moreover, physical examinations, biochemical examinations and ophthalmology examinations were conducted for each participant.

RESULTS: The subjects who had AMD family history were 4.21 times more likely to have AMD (P<0.001). The subject who had the history of tracheitis /asthma were 1.87 times more likely to have AMD (P=0.008). Both smoking and drinking were risk factors to AMD (OR= 1.91,P < 0.001; OR=1.53, P = 0.003, respectively). Total protein (P = 0.004), high-density lipoprotein cholesterol ester (P = 0.016) and apolipoprotein A1 (P = 0.012) were associated with AMD.

CONCLUSION: Family history, smoking, drinking and history of tracheitis /asthma are the risk factors of AMD. Total protein, high-density lipoprotein cholesterol ester and apolipoprotein A1 are associated with AMD.

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Genetics

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Association of Pattern Dystrophy With an HTRA1 Single-Nucleotide Polymorphism.

Jaouni T, Averbukh E, Burstyn-Cohen T, Grunin M, Banin E, Sharon D, Chowers I.

OBJECTIVE: To evaluate if adult-onset foveomacular vitelliform dystrophy (AOFVD) and butterfly-shaped pigment dystrophy (BSPD) are associated with risk single-nucleotide polymorphisms (SNPs) for age-related macular degeneration (AMD).

METHODS: This was a tertiary referral center-based cross-sectional study including 35 consecutive patients with BSPD and AOFVD, 317 patients with AMD, and 159 unaffected individuals. Demographics, clinical information, and ophthalmic imaging studies were collected. Sequencing was performed for the peripherin/RDS and BEST1 genes, and genotyping was performed for SNPs in the genes for complement factor H (CFH) (rs1061170), HTRA1 (rs11200638), and complement component 3 (C3) (rs2231099).
RESULTS: Adult-onset foveomacular vitelliform dystrophy and BSPD were diagnosed in 24 (68.6%) and 11 (31.4%) of the 35 patients, respectively. The mean (SD) age of patients with pattern dystrophy (PD) was 75.3 (10) years and median visual acuity was 0.7. Pattern dystrophy was associated with the HTRA1 risk allele compared with unaffected individuals (odds ratio, 1.72; 95% CI, 1.11-2.66; P = .03). The HTRA1 SNP showed similar prevalence in patients with AMD and PD. The CFH risk allele was significantly less common in patients with PD compared with patients with AMD (odds ratio, 0.47; 95% CI, 0.28-0.76; P = .002). No mutations in peripherin/RDS or BEST1 were detected.
CONCLUSIONS: The AOFVD and BSPD phenotypes are associated with an HTRA1 risk SNP. These phenotypes often present in elderly individuals who do not carry peripherin/RDS gene mutations and are associated with retinal pigment epithelium alterations and increased risk for choroidal neovascularization. Further research is required to evaluate if AOFVD and BSPD phenotypes in aged individuals are associated with AMD.
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BMC Neurol. 2012 Aug 13;12(1):73. [Epub ahead of print]
Severe and rapidly progressing cognitive phenotype in a SCA17-family with only marginally expanded CAG/CAA repeats in the TATA-box binding protein gene: A case report.
Nielsen TT, Mardosiene S, Løkkegaard A, Stokholm J, Ehrenfels S, Bech S, Friberg L, Nielsen JK, Nielsen JE.

BACKGROUND: The autosomal dominant spinocerebellar ataxias (SCAs) confine a group of rare and heterogeneous disorders, which present with progressive ataxia and numerous other features e.g. peripheral neuropathy, macular degeneration and cognitive impairment, and a subset of these disorders is caused by CAG-repeat expansions in their respective genes. The diagnosing of the SCAs is often difficult due to the phenotypic overlap among several of the subtypes and with other neurodegenerative disorders e.g. Huntington's disease,
CASE PRESENTATION: We report a family in which the proband had rapidly progressing cognitive decline and only subtle cerebellar symptoms from age 42. Sequencing of the TATA-box binding protein gene revealed a modest elongation of the CAG/CAA-repeat of only two repeats above the non-pathogenic threshold of 41, confirming a diagnosis of SCA17. Normally, repeats within this range show reduced penetrance and result in a milder disease course with slower progression and later age of onset. Thus, this case presented with an unusual phenotype.
CONCLUSIONS: The current case highlights the diagnostic challenge of neurodegenerative disorders and the need for a thorough clinical and paraclinical examination of patients presenting with rapid cognitive decline to make a precise diagnosis on which further genetic counseling and initiation of treatment modalities can be based.
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Crystal structure of the globular domain of C1QTNF5: Implications for late-onset retinal macular degeneration.
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Abstract
Autosomal dominant late-onset retinal macular degeneration (L-ORMD) is caused by a single S163R

mutation in the C1q and tumor necrosis factor-related protein 5 (C1QTNF5) gene. The C1QTNF5 gene encodes a secreted and membrane-associated protein involved in adhesion of retinal pigmented epithelial cells (RPE) to Bruch's membrane. The crystal structure of the trimeric globular domain of human C1QTNF5 at 1.34Å resolution reveals unique features of this novel C1q family member. It lacks a Ca(2+)-binding site, displays a remarkable non-uniform distribution of surface electrostatic potentials and possesses a unique sequence (F(181)F(182)G(183)G(184)W(185)P(186)) that forms a hydrophobic plateau surrounded by Lys and Arg residues with a solvent cavity underneath. S(163) forms a hydrogen bond with F(182) in a hydrophobic area extending to the hydrophobic plateau. The pathogenic mutation S163R disrupts this hydrogen bonding and positively charges these hydrophobic areas. Thus, our analysis provides insights into the structural basis of the L-ORMD disease mechanism.

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Diet

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Estimated flavonoid intake of the elderly in the United States and around the world.

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Abstract
The aging population has been growing fast in the United States and worldwide. The morbidity of age-related chronic degenerative diseases has also been increasing in parallel. Numerous studies have reported that consumption of flavonoid-rich fruits and vegetables is inversely associated with such chronic diseases as Alzheimer's disease, age-related macular degeneration, cardiovascular disease, and osteoporosis. In establishing flavonoids as one of the contributors to the protective effects, the very first step is to estimate flavonoid intake from various dietary sources. Estimation of flavonoid intake from dietary sources has been feasible since 2003 when the U.S. Department of Agriculture (USDA) released the database for the flavonoid content of selected foods. Since then, several articles have been published in which flavonoid intake in various subpopulation groups was estimated from relatively large, current databases of flavonoid concentration data. However, information is still limited on the intake by seniors in the United States and worldwide. This review summarizes the most current estimates of flavonoid intake by seniors in the United States and elsewhere.

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Association of vitamin d deficiency and age-related macular degeneration in medicare beneficiaries.

Day S, Acquah K, Platt A, Lee PP, Mruthyunjaya P, Sloan FA.

PMID: 22893083 [PubMed - in process]