

AMERICAN JOURNAL OF OPHTHALMOLOGY®

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- xi **What the American Journal of Ophthalmology wants to publish.** *Richard K. Parrish II, Michael W. Stewart, Elizabeth A. Vanner, and Sarah L. Duncan Powers*

PERSPECTIVE

- xiii **International board members of the American Journal of Ophthalmology.** *Andrzej Grzybowski and Piotr Kanclerz*

This year marks the 100th anniversary of the “modern” *American Journal of Ophthalmology*. International influence was present since the beginnings of the *Journal*, as it had several foreign editorial board members and collaborators. Within the article, sketches of the deceased international board members are presented, particularly of Sir Stewart Duke-Elder, Pierre Amalric, Joaquin Barraquer, and Yasuo Tano.

ORIGINAL ARTICLES

- 1 **Corneal limbal stem cell deficiency in children with Stevens–Johnson syndrome.** *Se Hyun Choi, Mee Kum Kim, and Joo Youn Oh*

Limbal stem cell deficiency developed in 32% of children with Stevens-Johnson syndrome/toxic epidermal necrolysis and was associated with poor visual outcome. Since limbal stem cell deficiency significantly correlated with the severity of acute systemic manifestations, active treatment and follow-up are required for the patients presented with severe systemic conditions in the acute phase.

- 9 **Incidence and outcomes of intraoperative Descemet membrane perforations during deep anterior lamellar keratoplasty.** *Olivia S. Huang, Hla M. Htoon, Amy M. Chan, Donald Tan, and Jodhbir S. Mehta*

A retrospective audit of all deep anterior lamellar keratoplasty (DALK) cases was performed from 2004 to 2015 in a retrospective center. There were a total of 540 DALK cases, of which 101 cases (18.7%) had intraoperative Descemet membrane (DM) perforations. Cases with intraoperative DM perforations during DALK did not have increased rates of graft failure, graft rejection, subsequent surgery, or worse visual outcomes at postoperative years 1 and 3, compared to cases without perforations.

- 19 **Near-infrared autofluorescence in choroideremia: Anatomic and functional correlations.** *Johannes Birtel, Anna Paola Salvetti, Jasleen K. Jolly, Kanmin Xue, Martin Gliem, Philipp L. Müller, Frank G. Holz, Robert E. MacLaren, and Peter Charbel Issa*

Near-infrared fundus autofluorescence imaging allows the stratification of eyes in patients with choroideremia into 3 groups with distinct morphologic and functional characteristics. This may reflect different stages of degeneration of the retinal pigment epithelium. Including near-infrared fundus autofluorescence imaging in multimodal imaging of choroideremia would provide useful adjunctive information in the disease monitoring and patient stratification for clinical trials.

- 28 **Glaucoma specialist detection of optical coherence tomography suspicious rim tissue in glaucoma and glaucoma suspect eyes.** *Seung Woo Hong, Helen Koenigsman, Hongli Yang, Ruojin Ren, Juan Reynaud, Robert M. Kinast, Steven L. Mansberger, Brad Fortune, Shaban Demirel, Stuart K. Gardiner, and Claude F. Burgoyne*

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The authors objectively quantified glaucoma specialists' optic disc rim width estimates in glaucoma and glaucoma suspect eyes so as to assess their ability to detect sectors of rim tissue that were thin by optical coherence tomography (OCT) criteria. Among the 151 study eyes, OCT suspicious rim tissues most commonly occurred in the nasal sectors, which was also where the 5 clinicians most commonly missed its detection and where clinician-vs-OCT rim width discordance was greatest.

• **44 Orbital lymphoma—an international multicenter retrospective study.** *Tine Gadegaard Olsen, Frederik Holm, Lauge Hjorth Mikkelsen, Peter Kristian Rasmussen, Sarah E. Coupland, Bita Esmaeli, Paul T. Finger, Gerardo F. Graue, Hans E. Grossniklaus, Santosh G. Honavar, Jwu Jin Khong, Penelope A. McKelvie, Kaustubh Mulay, Lene Dissing Sjö, Geeta K. Vemuganti, Bradley A. Thuro, and Steffen Heegaard*

In this international retrospective study on orbital lymphoma spanning a period of 38 years, a total of 797 patients from 7 different eye cancer centers across the world were included. It represents the largest collection of orbital lymphoma cases presented to date. The focus of the study was to investigate the clinical features and survival outcomes of subtype-specific orbital lymphomas, with overall survival, disease-specific survival, and progression-free survival being the primary endpoints.

• **58 The natural history of inherited retinal dystrophy due to biallelic mutations in the RPE65 gene.** *Daniel C. Chung, Mette Bertelsen, Birgit Lorenz, Mark E. Pennesi, Bart P. Leroy, Christian P. Hamel, Eric Pierce, Juliana Sallum, Michael Larsen, Knut Stieger, Markus Preising, Richard Weleber, Paul Yang, Emily Place, Emily Liu, Grace Schaefer, Julie DiStefano-Pappas, Okan U. Elci, Sarah McCague, Jennifer A. Wellman, Katherine A. High, and Kathleen Z. Reape*

This multicenter, retrospective, cross-sectional study is the largest single cohort of patients with biallelic RPE65-associated inherited retinal disease evaluated over time to date. Cross-sectional data demonstrated that, on average, visual acuity was markedly impaired, but stable, during the first decade of life; decreased between 15 and 20 years of age; and decreased more rapidly from 20 years of age forward. Visual field decreased and structural abnormalities increased with age, consistent with progressive retinal degeneration in these patients.

• **71 En face optical coherence tomography imaging of the photoreceptor layers in hydroxychloroquine retinopathy.** *Seong Joon Ahn, Jooyoung Joung, and Byung Ro Lee*

En face optical coherence tomography imaging of the photoreceptor layers was useful to detect retinopathy and evaluate its progression in hydroxychloroquine retinopathy. The en face imaging enabled quantitative evaluation of progression of the photoreceptor defects and functional correlation between photoreceptor status and visual field results in the retinopathy. The imaging may be a helpful adjunct for screening and follow-up tests of hydroxychloroquine retinopathy.

• **82 Clinical and biological factors associated with recurrences of severe toxoplasmic retinochoroiditis confirmed by aqueous humor analysis.** *Alexandre Matet, Luc Paris, Christine Fardeau, Céline Terrada, Emmanuelle Champion, Arnaud Fekkar, Nathalie Cassoux, Valérie Toutou, Phuc LeHoang, and Bahram Bodaghi*

The risk of toxoplasmic retinochoroiditis recurrence is higher immediately after an episode and in eyes with longer disease-free intervals after the first episode. Eyes with more intense bands on immunoblot of the aqueous humor are also at higher risk of subsequent recurrences.

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• **94 Incidence of management changes at the postoperative week 1 visit after cataract surgery: Results from the perioperative care for intraocular lens study.**

Durga S. Borkar, Inês Laíns, Emily A. Eton, Nicole Koullis, Giannis A. Moustafa, Tavé van Zyl, and Carolyn E. Kloek, on behalf of the Perioperative Care for IntraOcular Lens Study Group

In this study including 1272 eyes of 1009 patients, the incidence of unexpected management changes at the postoperative week one visit in asymptomatic patients after cataract surgery with no intraoperative complications and a routine postoperative day one examination was 0.9%. The most common finding prompting a management change was an asymptomatic intraocular pressure elevation. This study provides novel information for guiding postoperative visit schedules after cataract surgery for the appropriate subgroup of patients.

• **101 Prevalence of normal-tension glaucoma in the Chinese population: A systematic review and meta-analysis.**

Jing Zhao, Marisse Masis Solano, Catherine E. Oldenburg, Tianshu Liu, Yaxing Wang, Ningli Wang, and Shan C. Lin

Normal tension glaucoma is very common in the Chinese population and its prevalence may be underestimated. It comprises the majority of primary open-angle glaucoma in the Chinese population-based studies. Regular eye examinations with vigilance in detecting this disease should be added to public health guidelines.

• **111 Using Kalman filtering to forecast disease trajectory for patients with normal tension glaucoma.**

Gian-Gabriel P. Garcia, Koji Nitta, Mariel S. Lavieri, Chris Andrews, Xiang Liu, Elizabeth Lobaza, Mark P. Van Oyen, Kazuhisa Sugiyama, and Joshua D. Stein

Kalman filtering, a form of machine learning, was used to forecast values of mean deviation and pattern standard deviation on standard perimetry 24 months into the future

for a cohort of patients with normal tension glaucoma. This technique outperformed conventional glaucoma forecasting techniques and generated forecasts of mean deviation that were within 1 decibel of the actual value obtained in clinic for 50.4% of the patients studied.

• **120 Macula vessel density and thickness in early primary open-angle glaucoma.**

Huiyuan Hou, Sasan Moghimi, Linda M. Zangwill, Takuhei Shoji, Elham Ghahari, Rafaella C. Penteadó, Tadamichi Akagi, Patricia Isabel C. Manalastas, and Robert N. Weinreb

Thickness and vessel density of ganglion cell complex were characterized and compared in preperimetric and early primary open-angle glaucoma eyes. Both thickness loss and vessel density dropout were detectable in preperimetric and early glaucoma eyes compared to healthy eyes. Compared to vessel density loss, thickness loss was similar in preperimetric glaucoma but greater in early perimetric glaucoma. However, thickness and vessel density measurements showed similar efficiency to detect early glaucoma.

• **133 Assessment of circumferential angle closure with swept-source optical coherence tomography: A community based study.**

Natalia Porporato, Mani Baskaran, Tin A. Tun, Rehana Sultana, Marcus C.L. Tan, Joanne H.M. Quah, John Allen, David S. Friedman, Ching-Yu Cheng, and Tin Aung

This large community-based study (N = 1857 subjects) evaluated the diagnostic performance of swept-source optical coherence tomography (SS-OCT, CASIA SS-1000; Tomey Corporation, Nagoya, Japan) for angle closure detection, in comparison with gonioscopy as reference standard. Manually graded SS-OCT images detected gonioscopy-defined angle closure with about 80% sensitivity and specificity, exhibiting moderate performance for angle closure detection (AUC 0.84, CI 95% 0.81-0.88).

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• **140 Early detection of glaucomatous visual field progression using pointwise linear regression with binomial test in the central 10 degrees.** *Shotaro Asano, Hiroshi Murata, Masato Matsuura, Yuri Fujino, and Ryo Asaoka*
In the current study, the usefulness of the binomial pointwise linear regression to evaluate glaucomatous visual field progression in the central 10 degrees was investigated. The binomial pointwise linear regression detected the visual field progression significantly earlier compared with mean deviation trend analysis and the permutation test analysis applied to pointwise linear regression.

• **150 Clinical outcomes of Descemet membrane endothelial keratoplasty in eyes with a glaucoma drainage device.** *Rénuka S. Birbal, C. Maya Tong, Isabel Dapena, John S. Parker, Jack S. Parker, Silke Oellerich, and Gerrit R.J. Melles*
This retrospective study evaluates the feasibility and clinical outcomes of Descemet membrane endothelial keratoplasty in eyes with a glaucoma drainage device. Taking the complexity of these eyes into consideration, Descemet membrane endothelial keratoplasty provided acceptable clinical outcomes. However, the presence of a glaucoma drainage device may reduce graft survival times and pose a risk for more frequent regrafting.

• **159 Residual iris retraction syndrome after artificial iris implantation.** *Christian S. Mayer, Andrea E. Laubichler, Michael Masyk, Philipp Prahs, Daniel Zapp, and Ramin Khoramnia*
Little is known about the long term effect on the remnant iris after artificial iris implantation. Artificial iris implantation may lead to morphological changes on the remnant iris and enlargement of the residual pupillary aperture with secondary complications. The residual iris can disappear almost completely and irreversibly. It seems that there is a

risk for iris retraction when the device is implanted in the ciliary sulcus without suture fixation to the sclera.

• **167 Changes in ganglion cell–inner plexiform layer thickness and retinal microvasculature in hypertension: An optical coherence tomography angiography study.** *Hyung Bin Lim, Min Woo Lee, Jae Hyeong Park, Kyeongmin Kim, Young Joon Jo, and Jung Yeul Kim*
Ganglion cell–inner plexiform layer (GC-IPL) thickness and retinal microvascular metrics measured using optical coherence tomography angiography in chronic hypertension were significantly decreased. Chronic hypertension was closely related to GC-IPL thinning, which may have been caused by a reduction in retinal blood flow.

• **177 Automated detection of the stromal demarcation line using optical coherence tomography in keratoconus eyes after corneal cross-linking.** *Shady T. Awwad, Maamoun Abdul Fattah, Manal Shokr, and Ahmad R. Dhaini*
This is a reliability analysis study that evaluated the role of a novel automated detection software as compared to human operators in assessing the presence and depth of stromal demarcation line on optical coherence tomography in keratoconus eyes post cross-linking. As a result, detection of demarcation line can be further optimized and standardized by an ultrafast and accurate automated software detection tool, providing a reliable indicator for treatment success.

• **184 Choroidal microvascular dropout in primary angle closure glaucoma.** *Harsha L. Rao, Shruthi Sreenivasaiah, Mohammed Riyazuddin, Srilakshmi Dasari, Shivani Dixit, Jayasree P. Venugopal, Zia S. Pradhan, Narendra K. Puttaiah, Sathi Devi, Robert N. Weinreb, Kaweh Mansouri, and Carroll A.B. Webers*
Choroidal microvascular dropout (CMvD) was seen in 58.3% of primary open-angle glaucoma (POAG) and

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35.7% of primary angle-closure glaucoma (PACG) eyes ($P = .07$). CMvD in POAG was associated with lower pretreatment intraocular pressure and greater severity of glaucoma damage, whereas CMvD in PACG eyes was associated only with greater severity of visual field damage. CMvD was also more frequently seen in eyes with initial parafoveal scotoma on visual fields both in POAG and PACG.

• **193 Assessment of the impact of an Endpoint Committee in the Ocular Hypertension Treatment Study.** Mae O. Gordon, Eve J. Higginbotham, Dale K. Heuer, Richard K. Parrish II, Alan L. Robin, Patricia A. Morris, Deborah A. Dunn, Bradley S. Wilson, and Michael A. Kass, for The Ocular Hypertension Treatment Study
The impact of a masked Endpoint Committee on estimates of the incidence of primary open-angle glaucoma (POAG), treatment efficacy, and statistical power of the Ocular Hypertension Treatment Study–Phase 1, 1994–2002 was assessed. Endpoint Committee adjudication of endpoints improved accuracy of POAG incidence estimates, increased statistical power, and increased calculated treatment effect by 23%. An Endpoint Committee should be considered in therapeutic trials when common ocular and systemic comorbidities, other than the target condition, could compromise study results.

• **200 The impact of prefilled syringes on endophthalmitis following intravitreal injection of ranibizumab.** Philip P. Storey, Zujaja Tauqeer, Yoshihiro Yonekawa, Bozho Todorich, Jeremy D. Wolfe, Sumit P. Shah, Ankoor R. Shah, Takashi Koto, Ashkan M. Abbey, Yuki Morizane, Priya Sharma, Edward H. Wood, Mio Morizane-Hosokawa, Pooja Pendri, Maitri Pancholy, Shawn Harkey, Karen W. Jeng-Miller, Anthony Obeid, Durga S. Borkar, Eric Chen, Patrick Williams, Annabelle A. Okada, Makoto Inoue, Fumio Shiraga, Akito Hirakata, Chirag P. Shah, Jonathan

Prenner, and Sumir Garg, for the Post-Injection Endophthalmitis (PIE) Study Group

In an international, multicenter study of 243 754 intravitreal injections of ranibizumab, prefilled syringes were associated with lower rates of culture-positive endophthalmitis, including from oral flora, and improved visual outcomes compared to conventional preparation of the medication.

• **209 Amniotic membrane transplantation in acute severe ocular chemical injury: A randomized clinical trial.** Medi Eslani, Alireza Baradaran-Rafii, Albert Y. Cheung, Khaliq H. Kurji, Hamidreza Hasani, Ali R. Djalilian, and Edward J. Holland

In a prospective randomized parallel-controlled clinical trial, 60 eyes with Roper-Hall grade IV ocular chemical injury were randomly assigned to either standard medical therapy or amniotic membrane transplantation onto the entire ocular surface in addition to medical therapy. In comparison to conventional medical therapy, combined amniotic membrane transplantation and medical therapy does not accelerate corneal epithelialization or affect final visual acuity and neovascularization in severe chemical injuries.

• **216 Comparison of topical 5-fluorouracil and interferon alfa-2b as primary treatment modalities for ocular surface squamous neoplasia.** Nandini Venkateswaran, Carolina Mercado, Anat Galor, and Carol L. Karp

Ocular surface squamous neoplasia is the most common nonpigmented malignancy of the ocular surface. Treatment options for ocular surface squamous neoplasia include surgical excision with cryotherapy or medical management with chemotherapeutic agents including interferon alfa-2b, 5-fluorouracil, and mitomycin C. In this retrospective study comparing topical 5-fluorouracil 1% and interferon alfa-2b, both agents were both found to be viable and

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effective treatment modalities for ocular surface squamous neoplasia, exhibiting high clinical resolution rates and low rates of recurrence.

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- **223 Binocular visual function with staged implantation of diffractive multifocal intraocular lenses with three add powers.** *Hiroko Bissen-Miyajima, Yuka Ota, Kunihiko Nakamura, Manabu Hirasawa, and Keiichiro Minami*

This prospective study compared binocular visual function following the staged implantation of multifocal intraocular lens with add power of +4.0 diopter (D) in the first eye and +4.0 D, +3.25 D, or +2.75 D in the fellow eye. The current results demonstrate preferable binocular distance-corrected visual acuity at intermediate distance, in addition to at distance and near, without decrease of contrast sensitivity when the fellow eye received a lower-diopter additional lens.

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- **230 Association of age-related macular degeneration with mortality in patients with acquired immunodeficiency syndrome; role of systemic inflammation.** *Douglas A. Jabs, Mark L. Van Natta, Garrett Trang, Norman G. Jones, Jeffrey M. Milush, Ryan Cheu, Nichole R. Klatt, Ronald P. Danis, and Peter W. Hunt*

Patients with AIDS and age-related macular degeneration (AMD) have increased mortality versus those without AMD. Plasma levels of the inflammatory biomarkers C-reactive protein, interleukin-6, and interferon- γ inducible protein-10 also were associated with increased mortality. In a regression model, biomarker levels attenuated the relationship between AMD and mortality, suggesting that the increased mortality observed with AMD may be attributable, at least in part, to systemic inflammation.

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- **238 National study of ocular hospitalizations in Medicare beneficiaries.** *Alisa J. Prager, Nicholas J. Volpe, and Dustin D. French*

This study looks at characteristics of Medicare beneficiaries hospitalized for a primary ophthalmic condition using the 2015 National Medicare 100% Inpatient Limited Dataset. This study found that the majority of primary ophthalmic admissions were for nontraumatic disorders of the eye and adnexa. Patients admitted for eye conditions were more likely to have comorbidities such as hypertension, diabetes, AIDS, lymphoma, rheumatologic diseases, and psychiatric conditions such as depression compared to the general Medicare inpatient population.

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- **246 Endophthalmitis incidence of cancer patients after cataract surgery: A nationwide matched cohort study in Taiwan.** *Chiun-Ho Hou, Jiahn-Shing Lee, Ken-Kuo Lin, Shu-Hao Chang, Wen-Kuan Huang, Chang-Fu Kuo, and Lai-Chu See*

Rates of endophthalmitis after cataract surgery were compared in a cancer cohort and matched noncancer cohort from the National Health Insurance Research Database of Taiwan. Endophthalmitis developed within 3 months after 110 cataract procedures in the cancer cohort and after 108 procedures in the noncancer cohort. The rates were similar between cohorts and did not significantly differ in relation to cancer site or type of cancer treatment. There was no significant difference in the endophthalmitis rates in all time periods after cancer diagnosis.

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- **257 Diagnosis, clinical presentations, and outcomes of *Nocardia* endophthalmitis.** *Jayanth Sridhar, Thomas A.*

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