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- **A6 Off-label use as a standard of care.** *Gary D. Novack and Ala Moshiri*

ORIGINAL ARTICLES

- **1 Incidence and Risk Factors of Glaucoma Following Pediatric Cataract Surgery With Primary Implantation.** *Youssef Abdelmassih, Pauline Beaujeux, Pascal Dureau, Catherine Edelson, and Georges Caputo*
Secondary glaucoma (SG) is a well-described complication after congenital cataract surgery. Sixteen percent of eyes included in our study developed SG with an estimated linear incidence rate of 3% per year. SG seems to have a bimodal incidence, 1 peak in the early postoperative period and another ≥ 2 years after surgery. Close follow-up should be maintained, especially in eyes that undergo this operation early, those that need multiple surgeries, or those where trypan blue was used.
- **7 Sickle cell maculopathy: microstructural analysis using OCTA and identification of genetic, systemic, and biological risk factors.** *Selim Fares, Sophie Hajjar, Marc Romana, Philippe Connes, Malik Acomat, Coralie Zorobabel, Kevin Zuber, Elise Boulanger-Scemama, Maryse Etienne-Julan, Thierry David, and Laurence Beral*
Factors associated with sickle cell maculopathy are poorly understood. This cross-sectional study describes associa-

tions between maculopathy and genetic, clinical, and biological factors in sickle cell disease. Further, this study evaluates microvascular macular alterations using optical coherence tomography angiography. HbSS genotype, abnormal coagulation, and hemolysis are associated with sickle cell maculopathy. Optical coherence tomography angiography detects early microvascular macular alterations before the onset of macular thinning.

- **18 Evolution of dome-shaped macula is due to differential elongation of the eye predominant in the peri-dome region.** *Lea Dormegny, Xuanli Liu, Elise Philippakis, Ramin Tadayoni, Zsolt Bocskei, Tristan Bourcier, Arnaud Sauer, Alain Gaudric, Claude Speeg-Schatz, and David Gaucher*

This study described the evolution of dome-shaped macula (DSM) in 58 eyes. Increase in macular bulge height was greater than eye elongation. Overall thinning of the peripheral choroid was observed. Thus, DSM might result from differential elongation of the eye predominant in the peri-dome region. “Mini-DSM” (with a bulge height inferior to 100 μm) presented with slower elongation, better visual prognosis, and fewer complications than “classic” DSM (with a bulge height superior to 100 μm).

- **30 COVID-19 and the unfinished agenda of VISION 2020.** *Lawson Ung, Jost B. Jonas, Thomas M. Lietman, and James Chodosh*

Amid growing concerns that COVID-19 will unravel decades of hard-earned progress in global public health, this perspective offers a reflection on the many resounding successes of VISION 2020 to date, and how a world without blindness can still be achieved in the post-pandemic era.

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- **36 Biosimilars for retinal diseases: an update.** *Ashish Sharma, Nilesh Kumar, Nikulaa Parachuri, Francesco Bandello, Baruch D. Kuppermann, and Anat Loewenstein*

Biologics have drastically improved the visual prognosis for retinal neovascular pathologies. The cost of the therapy though is a major barrier for wider adoption and adds to the financial stress. Biosimilars are intended to bring down the cost of therapy while maintaining efficacy and safety. This article aims to update the development of biosimilars that are in commercial use or near market realization.

- **43 The Tube Versus Trabeculectomy IRIS® Registry Study: Cohort selection and follow-up and comparisons to the randomized controlled trial.** *Elizabeth A. Vanner, Catherine Q. Sun, Matthew J. McSoley, Patrice J. Persad, William J. Feuer, Flora Lum, Scott P. Kelly, Richard K. Parrish, TA C. Chang, and Steven J. Gedde*

The Tube Versus Trabeculectomy (TVT) IRIS Registry 1-year follow-up analysis cohort contained 419 eyes: 236 tubes and 183 trabeculectomies, with many significant treatment group differences. There were also many significant differences compared to the TVT randomized controlled trial (RCT) cohort, such as more missing follow-up visits. Some TVT RCT inclusion and exclusion criteria could not be applied to the IRIS Registry data. Routine replication of RCT results with real-world data may be difficult or impossible.

- **53 One-year results of arcuate keratotomy in patients with low to moderate corneal astigmatism using a low-pulse-energy femtosecond laser.** *Luca Schwarzenbacher, Daniel Schartmüller, Veronika Röggl, Elias Meyer, Christina Leydolt, and Rupert Menapace*

The study assessed corneal astigmatism reduction and corneal optical quality after surface-penetrating femtosecond laser arcuate keratotomies considering anterior and posterior corneal curvature, total corneal refractive power

astigmatism, and corneal higher-order aberrations, over the follow-up period of 1 year.

- **66 Perspective on vision: the visual system as a Black Box.** *August Colenbrander*

Vision is a complex phenomenon. Its input are visual stimuli; the output is visually guided behavior. Clarity about the relationships between different aspects in different settings is essential for understanding the consequences of vision loss.

- **74 Three-Year Outcomes of Cionni-Modified Capsular Tension Ring Implantation in Children Under 8 Years Old With Ectopia Lentis.** *Lei Cai, Xiaoyan Han, Yongxiang Jiang, Xiaodi Qiu, Dongjin Qian, Yi Lu, and Jin Yang*

Severe zonular laxity in children increases the difficulty of cataract extraction, IOL implantation, and the risk of serious complications. Sclera-fixated MCTR and an IOL implanted in the capsular bag combined with posterior capsulectomy and anterior vitrectomy are safe and effective procedures for treating young children with ectopia lentis.

- **84 Adaptive optics imaging in patients affected by pseudoxanthoma elasticum.** *Vittoria Murro, Dario Pasquale Mucciolo, Dario Giorgio, Laura Pavese, Federica Boraldi, Daniela Quaglino, Lucia Finocchio, Andrea Sodi, Gianni Virgili, and Fabrizio Giansanti*

Adaptive optics imaging in pseudoxanthoma elasticum-related retinopathy shows the presence of photoreceptors within the angioid streaks, allowing us to differentiate 3 types of angioid streaks based on size and reflective features, and to identify the very small comet lesions not identifiable using other retinal imaging techniques.

- **96 Clinical Characteristics of Idiopathic Intracranial Hypertension in Patients Over 50 Years of Age: A**

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Multicenter Clinical Cohort Study. *Peter A. Downie, John J. Chen, M. Tariq Bhatti, Andrew T. Melson, Gregory P. Van Stavern, Collin M. McClelland, Bruce R. Lindgren, Jibran A. Sharieff, and Michael S. Lee*

This retrospective study compares the clinical features and outcomes of patients with idiopathic intracranial hypertension who were 50 years old and older to those in a control population 50 years old and younger. The older cohort experienced a disease course and outcome similar to the younger group and were managed in a similar fashion to typical individuals.

• **102 Surgical Outcomes of Superotemporal Versus Inferonasal Placement of Aurolab Aqueous Drainage Implant in Refractory Pediatric Glaucoma.** *George Varghese Puthuran, Hiruni Kaushalya Wijesinghe, Steven J. Gedde, Kousalya Pavani Chiranjeevi, Iswarya Mani, Subbaiah Ramasamy Krishnadas, Alan Lee Robin, and Paul Palmberg*

The low profile of the nonvalved Aurolab aqueous drainage implant makes it particularly suitable for inferonasal placement when the superotemporal quadrant is compromised by multiple previous surgeries for glaucoma or other conditions. However, in children and when compared with placement of the device in the superotemporal quadrant, inferonasal placement entails more complications, such as tube exposure, patch graft melt, which necessitates resurgery, and with a greater incidence of reoperation for glaucoma.

• **112 A service coverage analysis of primary congenital glaucoma care across the United States.** *Daniel M. Vu, Justin Stoler, Adam L. Rothman, and Ta Chen Chang*

Long travel times represent a barrier to appropriate subspecialty care. A cross-sectional geospatial service coverage analysis was performed to estimate the number of infants at risk of delayed primary congenital glaucoma evaluation based on travel time to the nearest pediatric ophthalmologist and glaucoma specialist in the United

States. American Community Survey population data and both American Glaucoma Society and American Association for Pediatric Ophthalmology and Strabismus members' office locations were extracted for the analysis.

• **120 Pigmented Paravenous Chorioretinal Atrophy: Clinical Spectrum and Multimodal Imaging Characteristics.** *Eun Kyoung Lee, Sang-Yoon Lee, Baek-Lok Oh, Chang Ki Yoon, Un Chul Park, and Hyeong Gon Yu*

Pigmented paravenous chorioretinal atrophy can present with a variable expressivity. Interocular asymmetry was common not only in fundus appearance but also in electroretinography finding. Most patients exhibited no apparent changes in fundus appearance and retained stable vision over time. Nevertheless, some eyes with macular involvement manifest poor visual prognosis. Multimodal imaging can provide insights into its clinical characteristics to facilitate the diagnosis, classification, and follow-up of these patients.

• **133 Individualized corneal cross-linking with riboflavin and UV-A in ultrathin corneas: the sub400 protocol.** *Farhad Hafezi, Sabine Kling, Francesca Gilardoni, Nikki Hafezi, Mark Hillen, Reyhaneh Abrishamchi, Jose Alvaro P. Gomes, Cosimo Mazzotta, J. Bradley Randleman, and Emilio A. Torres-Netto*

Standard corneal cross-linking is limited to corneas with a stromal thickness of more than 400 μm . We present the clinical validation of the sub400 protocol based on an algorithm that we had developed and published previously. The algorithm predicts corneal cross-linking penetration depth and provides fluences adapted to the individual patient's stromal thickness. The sub400 protocol successfully prevented keratoconus progression in ultrathin corneas (214-400 μm) in 90% of cases after 1 year of follow-up.

• **143 Genetic influence on choroidal volume.** *Sungsoon Hwang, Moonil Kang, Don-Il Ham, and Mingui Kong*

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Macular choroidal volume is highly heritable with an estimated heritability of 0.76.

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- **150 Refractive and visual outcome of misaligned toric intraocular lens after operative realignment.** Annika Müller-Kassner, Tsvetina Sartory, Michael Müller, Kleopatra Varna-Tigka, Wolfgang J. Mayer, Thomas Kreuzer, Anna Schuh, Siegfried Priglinger, Thomas Kohlen, and Mehdi Shajari

This retrospective analysis demonstrates that realignment of misaligned toric IOLs improves visual acuity and reduces residual refractive errors. Especially for high cylinder power IOLs, better refractive outcomes can be seen when performing a back-calculation before realignment.

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- **158 Ophthalmology and Ethics in the COVID-19 Era.** Kenneth M. Prager, Lora R. Dagi Glass, Marlene Wang, Royce W.S. Chen, Jeffrey M. Liebmann, and George A. Cioffi

The Department of Ophthalmology and the Medical Ethics Committee at Columbia University Irving Medical Center present 4 case scenarios to guide the teaching and application of ethics in ophthalmology during the COVID-19 era.

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- **163 Determinants of optical coherence tomography parameters in a population-based study.** S. Ramyashri, Harsha L. Rao, Ganesh Babu Jonnadula, Uday K. Addepalli, Nikhil Choudhari, Sirisha Senthil, and Chandrasekhar Garudadri

This is an observational cross-sectional study examining the determinants of optical coherence tomography (OCT) parameters in a normal population from the L V Prasad Eye Institute - Glaucoma Epidemiological and Molecular Genetic Study (LVPEI-GLEAMS). Age, sex, axial length, disc area, and signal strength of the OCT scan were significantly associated with OCT measurements, which

needs to be considered while interpreting OCT results for glaucoma and nonglaucoma subjects.

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- **172 Uveal melanoma in BAP1 tumor predisposition syndrome: estimation of risk.** Nakul Singh, Rahul Singh, Randy Chris Bowen, Mohamed H. Abdel-Rahman, and Arun D. Singh

The BAP1 Tumor Predisposition Syndrome (BAP1-TPDS, MIM 614327) is a recently recognized autosomal dominant syndrome with predisposition to uveal melanoma. In patients with germline BAP1 pathogenic variant, the point prevalence of uveal melanoma was estimated to be 2.8%. Quantification of the risk of developing uveal melanoma can enhance counseling regarding surveillance.

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- **178 Automated Evaluation of Parapapillary Choroidal Microvasculature in Pseudoexfoliation Syndrome and Pseudoexfoliation Glaucoma.** Masoud Aghsaei Fard, Mona Safizadeh, Amirreza Shaabani, Rahele Kafieh, Sahar Hojati, Marjan Afzali, Yanin Suwan, Robert Ritch, and Sasan Moghimi

In this cross-sectional study, parapapillary choroidal microvasculature was measured by optical coherence tomography angiography. A progressive decrease in outer parapapillary choroidal microvasculature from the control group to those with pseudoexfoliation syndrome to those with pseudoexfoliation glaucoma in the present study suggests deep peripapillary vasculopathy in pseudoexfoliation syndrome.

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- **185 Potential functional restoration of corneal endothelial cells in Fuchs endothelial corneal dystrophy by ROCK inhibitor (Ripasudil).** Ursula Schlötzer-Schrehardt, Matthias Zenkel, Maria Strunz, Andreas Gießl, Hannah Schondorf, Heather da Silva, Gregory A. Schmidt, Mark A. Greiner, Naoki Okumura, Noriko Koizumi, Shigeru Kinoshita, Theoflos Tourtas, and Friedrich E. Kruse

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This laboratory study investigated the effect of the ROCK inhibitor ripasudil on corneal endothelial cell–Descemet membrane lamellae surgically obtained from patients with Fuchs dystrophy. The findings demonstrated that ripasudil can activate endothelial cell cycle progression, promote cell migration, and enhance endothelial pump and barrier function without inducing adverse phenotypic changes, thereby verifying ripasudil as a potent tool in regenerative therapies in Fuchs dystrophy patients.

• **200 The Association Between Keratoconus and Body Mass Index: A population-Based Cross-Sectional Study Among Half a Million Adolescents.** *Elior Eliasi, Maxim Bez, Jacob Megreli, Eva Avramovich, Naomi Fischer, Adiel Barak, and Hagai Levine*

The prevalence of overweight and obese adolescents has risen dramatically in the past decades. In this nationwide cross-sectional study that included 579,946 male and female adolescents, the odds of having keratoconus for adolescents in overweight and obese groups were much higher compared with adolescents of normal weight. These findings suggest that obesity should be considered a risk factor for the development of keratoconus.

• **207 Comparative Study of Long-Term Graft Survival Between Penetrating Keratoplasty and Deep Anterior Lamellar Keratoplasty.** *Anshu Arundhati, Milton C. Chew, Li Lim, Jodhbir Singh Mehta, Stephanie Shuang Lang, Hla Myint Htoon, and Donald T. Tan*

This study compares the 10-year long-term graft survival for deep anterior lamellar keratoplasty to that of penetrating keratoplasty (PK). Results demonstrated that DALK results in significantly higher graft survival than PK as well as a lower rate of long-term complications, including graft rejection and failure.

• **217 Retinal Fluid Volatility Associated With Interval Tolerance and Visual Outcomes in Diabetic Macular**

Edema in the Vista Phase III Trial. *Justis P. Ehlers, Atsuro Uchida, Duriye Damla Sevgi, Ming Hu, Kim Reed, Alyson Berliner, Robert Vitti, Karen Chu, and Sunil K. Srivastava*

This study evaluated retinal fluid volatility as measured by changes in the retinal fluid index and identified that increased volatility during initial loading phase was associated with fluid recurrence following treatment extension.

• **228 Ten-year progression from intermediate to exudative age-related macular degeneration and risk factors: Bundang AMD Cohort Study Report 1.** *Kwangsic Joo, Yong Seok Mun, Sang Jun Park, Kyu Hyung Park, and Se Joon Woo*

The clinical features of age-related macular degeneration (AMD) in Asians are fewer drusen and more cases of polypoid choroidal vasculopathy than whites. This retrospective cohort study shows the 10-year progression to exudative AMD and environmental and genetic factors associated with AMD progression in 418 Koreans with intermediate AMD.

• **238 Risk factors for blindness in children with primary congenital glaucoma—follow-up of a registry cohort.** *Rayan Alshigari, Alia Freidi, Ches Souru, Deepak P. Edward, and Rizwan Malik*

The follow-up of 196 children with primary congenital glaucoma from a registry identified the severity of corneal clouding at baseline to be a risk factor for both blindness and blindness in at least one eye. The presence of diffuse corneal clouding, Descemet breaks, horizontal corneal diameter, and axial length, although not significant in multivariable regression, also showed some differences between groups.

• **246 Vitreous Structure and Visual Function in Myopic Vitreopathy Causing Vision-Degrading Myodesopsia.** *Justin H. Nguyen, Jeannie Nguyen-Cuu, Jonathan Mamou, Brittany Routledge, Kenneth M.P. Yee, and J. Sebag*

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Increasing axial myopia is associated with proportionately greater vitreous echodensity and degradation in contrast sensitivity function (CSF). Posterior vitreous detachment aggravates these effects, resulting in 59% increased vitreous echodensity and 77% CSF degradation compared to controls ($P < .001$). Limited vitrectomy normalizes visual function.

• **254 Long-Term Review of Penetrating Keratoplasty: A 20-Year Review in Asian Eyes.** *Arundhati Anshu, Lim Li, Hla Myint Htoon, Laura de Benito-Llopis, Lang Stephanie Shuang, Mehta Jodhbir Singh, and Tan Donald Tiang Hwee*

This is a prospective cohort study involving the Singapore Corneal Transplant Study and reviewed long-term outcomes of optical, therapeutic and tectonic penetrating keratoplasties performed at the Singapore National Eye Centre from 1991 to 2010. A total of 1,206 primary penetrating keratoplasties were performed. The overall rates of corneal graft survival at 1, 5, 10, 15, and 20 years were 91%, 66.8%, 55.4%, 52%, and 44%, respectively. Graft survival for optical grafts was significantly better than therapeutic and tectonic grafts.

• **267 Automated quantitative assessment of retinal fluid volumes as important biomarkers in neovascular age-related macular degeneration.** *Tiarnan D.L. Keenan, Usha Chakravarthy, Anat Loewenstein, Emily Y. Chew, and Ursula Schmidt-Erfurth*

Quantitative measures of intraretinal fluid and subretinal fluid are important biomarkers in neovascular age-related macular degeneration. Accurate volumes can be extracted efficiently and automatically from macular optical coherence tomography scans by artificial intelligence algorithms to guide the treatment of exudative macular diseases. These automated quantitative measures of retinal fluid volume have substantial advantages over manual qual-

itative assessments in both clinical practice and research. For consistency between studies, we propose the nanoliter as a convenient unit.

• **282 Population-based frequency of ophthalmic adverse events in melanoma, other cancers, and after immune checkpoint inhibitor treatment.** *David Braun, Darios Getahun, Vicki Y. Chiu, Anne L. Coleman, Gary N. Holland, Fei Yu, Lynn K. Gordon, and Michel M. Sun*

The frequency of ophthalmic immune-related adverse events (OirAEs) after immune checkpoint inhibitor treatment was evaluated for patients in the Kaiser Permanente Southern California health care system. Particularly elevated risk of specific OirAEs was observed in patients undergoing immune checkpoint inhibitor treatment for malignant melanoma and patients with previous history of uveitis. Evidence-based guidelines for management of these patients will likely need to reflect differing risk stratifications based on underlying cancer diagnosis and history of prior autoimmune disease.

• **292 Comparison Between Graders in Detection of Diabetic Neovascularization With Swept Source Optical Coherence Tomography Angiography and Fluorescein Angiography.** *Hasenin Al-kharsan, Jonathan F. Russell, Thomas A. Lazzarini, Nathan L. Scott, John W. Hinkle, Nimesh A. Patel, Nicolas A. Yannuzzi, Benjamin J. Fowler, Rehan M. Hussain, Anita Barikian, Jayanth Sridhar, Stephen R. Russell, Luis J. Haddock, William E. Smiddy, Seenu M. Hariprasad, Yingying Shi, Liang Wang, William Feuer, Giovanni Gregori, and Philip J. Rosenfeld*

After a brief introductory training session for the detection of diabetic neovascularization using optical coherence tomography angiography (OCTA), ophthalmologists with various levels of clinical experience were able to use OCTA as effectively as fluorescein angiography for the identification of neovascularization in diabetic

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retinopathy, which builds on previous work suggesting that OCTA is a clinically useful diagnostic imaging platform for diabetic retinopathy.

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- **301 Minimally Invasive 360-Degree Approach to Intraconal Orbital Tumors.** *Joel Caballero-García, Carlos Aparicio-García, Yurledys Jhohana Linares-Benavides, Misael López-Sánchez, Franklyn Alain Abreu-Perdomo, and Juvenal Huanca-Amaru*

Anterior orbitotomies for deep intraconal tumors, especially in the orbital apex, are characterized by a lack of good illumination and visualization. On the other hand, classical craniotomies are more invasive methods. We performed a retrospective interventional case series of patients treated with a 360-degree minimally invasive approach to the orbit and offer a practical algorithm for approach selection. This less invasive philosophy can be safe and efficient in patients with select orbital intraconal tumors.

-
- **310 Matched cohort study of Cataract surgery with and without trabecular microbypass stent implantation in primary angle-closure glaucoma.** *Ali Salimi, Mohamed Abu-Nada, and Paul Harasymowycz*

This clinical matched-cohort study compared one-year surgical outcomes of phacoemulsification alone versus phacoemulsification with implantation of two iStent stents or iStent *inject* in primary angle-closure glaucoma eyes. Compared to phacoemulsification alone, phacoemulsification with implantation of iStent or iStent *inject* yielded significantly greater reductions in intraocular pressure and medication use and was more protective against early postoperative intraocular pressure spikes. Thus, iStent and iStent *inject* could be viable options for treating patients with primary angle-closure glaucoma.

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- **321 Correlations Between Choriocapillaris and Choroidal Measurements and the Growth of Geographic Atrophy Using Swept Source OCT imaging.** *Yingying Shi, Qinqin Zhang, Hao Zhou, Liang Wang, Zhongdi Chu, Xiaoshuang Jiang, Mengxi Shen, Marie Thulliez, Cancan Lyu, William Feuer, Luis de Sisternes, Mary K. Durbin, Giovanni Gregori, Ruikang K. Wang, and Philip J. Rosenfeld*
Statistically significant correlations were observed between the enlargement rates of geographic atrophy (GA) and the choriocapillaris (CC) flow deficits (FDs) throughout the entire scan area outside the area of GA, even though the greatest FDs were located adjacent to the margins of GA, suggesting that CC flow impairment was widespread in the maculae of AMD patients with GA and those CC FDs may be associated with a decrease in choroidal vascular volume.

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- **332 Comparison of Methods for Measuring Cyclo-deviation.** *Laura Liebermann, Sarah R. Hatt, David A. Leske, Lindsay D. Klaehn, Andrea M. Kramer, and Jonathan M. Holmes*

Synoptophore cross-in-circle targets and the largest (of right or left) single-Maddox rod are similar to the double-Maddox rods when measuring subjective cyclodeviation. Fusible synoptophore targets and summed single-Maddox rod values differ from the double-Maddox rod. Objective evaluation of fundus photographs may be useful for assessing anatomic torsion but, as expected, measurements disagree with those of the double-Maddox rod. Further study is needed to understand relationships with symptoms and their treatment.

CORRESPONDENCE

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- **343 Comment on: allogenic simple limbal epithelial transplantation versus amniotic membrane grafting in the early management of severe-grade ocular chemical**

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