Three-dimensional reconstruction of a whole mount cornea confocal analysis from a EGFP-chimeric mouse demonstrating how green inflammatory cells migrate through the corneal stroma between the corneal epithelium and endothelium (blue) in response to lipopolyssacharide (red) deposits. Story, Page 2.
Researchers Exploit the Corneal Window for In Situ View of Inflammatory Reaction

UNDERSTANDING THE MOLECULAR AND CELLULAR EVENTS CHARACTERIZING AN INFLAMMATORY RESPONSE IN THE CORNEA IS FUNDAMENTAL FOR IDENTIFYING POTENTIAL STRATEGIES FOR CONTROLLING THAT PROCESS AND PREVENTING ITS VISION-THREATENING SEQUELAE OF SCARRING AND PERFORATION.

To that end, Victor L. Perez, M.D., and colleagues at The Cole Eye Institute are taking advantage of the cornea’s accessibility and transparency while applying innovative experimental methods and advanced in vivo and ex vivo imaging techniques to delineate the kinetic and dynamic interactions between infiltrating inflammatory cells and the cornea microenvironment.

“The cornea cannot afford to sustain an uncontrolled inflammatory response because its potential consequences include vision impairment and even blindness. Therefore, clinicians face the challenge of allowing the inflammatory response that is necessary to eradicate infection and promote healing while regulating it to avoid deleterious effects,” Dr. Perez says.

“We are fortunate that the eye uniquely offers a clear window for real-time visualization of immune responses. Now, we are exploiting that feature to gain insights into the mechanisms of the inflammatory response, and subsequently we will be able to apply that information with our sophisticated imaging techniques to perform elegant, comprehensive in vivo biological experiments that will provide us with answers to a variety of questions.”

In a recently published article in Investigative Ophthalmology & Visual Science, Dr. Perez and colleagues describe findings from their investigations of inflammatory cell recruitment and migration through the cornea in response to endotoxin-induced keratitis. That study was performed using chimeric mice engineered to express enhanced green fluorescent protein (EGFP) in their bone marrow-derived cells. Keratitis was induced by intrastromal injection of lipopolysaccharide (LPS), and the EGFP-positive hematopoietic cells were visualized within the cornea in serial studies via real-time fluorescent stereomicroscopy and ex vivo using confocal analysis with three-dimension reconstruction of whole mount corneas, a technique developed by Dr. Perez and his coworkers.

A neutralizing antibody for macrophage inflammatory protein-2 (MIP-2) was also injected into some animals prior to LPS injection to investigate the contribution of that chemokine for controlling inflammatory cell migration within the cornea, and conventional immunohistologic staining of frozen sections was performed to identify the types of infiltrating bone marrow-derived cells.

The results showed influxing inflammatory cells, identified as predominantly neutrophils, were first detected in the limbal area within 6 hours after LPS inoculation, although their migration into the central cornea was not seen until 24 hours. Interestingly, once the inflammatory cells infiltrated the cornea at the limbus, they traveled from all directions in an organized fashion toward the LPS deposits in a process that appeared to be directed in part by LPS-induced corneal production of MIP-2.

“Our studies indicate that once the immune cells reach the eye and extravasate from the limbal vessels, they do not migrate through the cornea in a random way, but rather the cornea appears to control their migratory route using chemotactic signals that direct them to the site of the inflammatory trigger. Identifying methods for regulating the inflammatory response within the eye so as to prevent sight-threatening damage is a next step for our laboratory, and the preliminary findings of this investigation suggest neutralization of MIP-2 may be a potential strategy,” Dr. Perez says.

The Cole Eye Institute investigators are also expanding their research of immunologic reactions in the cornea to characterize that process as it occurs in response to other inciting factors. They have recently completed an in vivo study of corneal transplants in a murine model. Future studies may focus on tracking and quantifying the immunologic response invoked after trauma secondary to chemical burns or in autoimmune disorders.
In an attempt to define better the relative efficacy and safety of trabeculectomy and drainage device surgery in eyes with uveitic glaucoma refractory to medication, Scott D. Smith, M.D., M.P.H., and colleagues at The Cleveland Clinic Cole Eye Institute undertook a retrospective study comparing outcomes of patients who underwent primary trabeculectomy with mitomycin C or implantation of an Ahmed glaucoma valve implant as a primary or secondary surgical procedure.

The results showed the two interventions were associated with comparably favorable success rates and similar safety profiles when they were performed against a background of careful attention to controlling intraocular inflammation pre- and postoperatively, reports Dr. Smith.

“There are a number of papers describing outcomes of trabeculectomy and glaucoma drainage device surgery in eyes with uveitic glaucoma, but importantly, there is a lack of studies that have directly compared the two procedures. Ideally, such an evaluation would be conducted in the setting of a prospective clinical trial,” Dr. Smith says.

“However, in the absence of those data, the findings from our retrospective review indicate that either trabeculectomy with mitomycin C or Ahmed glaucoma valve implantation can be a reasonable alternative for managing medically uncontrolled uveitic glaucoma, keeping in mind that patients who have had previously failed trabeculectomy have a lower probability of success with repeat surgery and should probably receive a drainage device,” he continues.

The study extracted data from the charts of patients with uveitic glaucoma operated on by Dr. Smith between 2000 and 2004. A total of 38 eyes from 27 patients with a minimum 1 year of follow-up were included; 26 of the eyes had undergone trabeculectomy with mitomycin C and 12 had received an Ahmed glaucoma valve implant. Mean follow-up for the group was almost 29 months. Patients selected for the trabeculectomy group all had undergone that procedure as a primary surgery with no history of any other glaucoma surgery.

Although the study was retrospective, the two surgical groups were well matched with respect to age, gender and race, and there were also no statistically significant differences between them in preoperative IOP and average number of glaucoma medications being used.

Outcomes were compared using data from follow-up at 3, 6 and 12 months and at the last available visit. For each of those time points, there was no significant difference between the study groups in mean IOP. Patients who had the drainage device surgery were using more glaucoma medications, on average, at 6 and 12 months, but there was no statistically significant difference in that endpoint between the surgical groups at the final visit.

For the purposes of this study, surgical failure was defined as IOP greater than 21 mm Hg with or without use of glaucoma medications, loss of light perception or need for further surgery to control IOP. Based on those criteria, the implant procedure was associated with a cumulative success rate of 100% at the last visit compared with 77% for eyes undergoing trabeculectomy with mitomycin C. However, the difference in those outcomes was not statistically significant.

“Although the success rate data favor the implant procedure numerically, our study population is too small to allow us to conclude with certainty that there is any real difference in outcomes between these two procedures,” Dr. Smith states.

Hypotony, which is the most common complication associated with these procedures and particularly in uveitic eyes, also occurred at similar rates in the trabeculectomy and Ahmed glaucoma valve groups (15.4% and 16.7%, respectively).

Dr. Smith adds there are a few other caveats to keep in mind when considering glaucoma surgery in uveitic eyes. Whatever procedure is performed, and particularly if trabeculectomy is chosen, success will be influenced greatly by adequate control of intraocular inflammation both before and after surgery.

“Postoperatively, patients need to be monitored carefully for inflammation and it should be treated aggressively with topical and/or systemic steroids as well as other systemic immunosuppressive agents if necessary,” he says.

Recognizing the trend for increasing use of intravitreal corticosteroid injections for the management of posterior segment inflammation and/or cystoid macular edema in uveitic eyes, Dr. Smith also notes drainage device implantation may be preferable if such treatment is being contemplated.

“Intraocular corticosteroids may increase the risk of endophthalmitis after trabeculectomy, and for that reason, implant surgery could be a better option,” he explains.
Ruthenium-106 Episcleral Plaque Radiotherapy Offers Benefits

By Arun D. Singh, M.D., Allan Wilkinson, Ph.D., Matt Kolar, M.S., and Peter Fleming, M.D.

Case report

A 60-year-old white male presented with complaints of flashing light sensation in the left eye of 2 weeks duration. A pigmented choroidal mass of the left eye was noted and he was referred to the Department of Ophthalmic Oncology at the Cleveland Clinic Cole Eye Institute for further evaluation and treatment.

Examination revealed blue irides and an absence of heterochromia or melanocytosis. The visual acuity was 20/20 OD and 20/40 OS. The anterior segments OU and fundus examination OD were unremarkable. The pertinent findings were limited to the fundus examination OS. A dome-shaped pigmented choroidal mass with indistinct margins was observed in the inferior quadrant. The mass was about 12 x 9 mm in basal dimension (Figure 1A). The posterior margin of the lesion was 3 mm from the optic disc and 4.5 mm from the foveola. Associated exudative retinal detachment extended into the macular region. The lesion had low internal reflectivity (Figure 1B) with absence of extra scleral extension. A diagnosis of choroidal melanoma OS was made and various therapeutic options including enucleation were discussed. Considering the size and location of the tumor plaque, radiotherapy was recommended.

A comparative analysis of dosimetry with ruthenium 106 (Model CCD; diameter 17.9, Bebig GmbH, Berlin, Germany) and iodine 125 (COMS guidelines; Model MED3631-A/M, North American Scientific Inc., Chatsworth, CA) was performed using the software Plaque Simulator, v 5.3.4, (Bebig GmbH, Berlin, Germany). A significant reduction in radiation dose to the optic disc and macula with ruthenium 106 plaque as compared with iodine 125 plaque was observed (Table 1). Therefore, ruthenium 106 plaque was recommended to the patient and surgery was performed without any complications.
Six months later, the tumor showed evidence of regression and complete resolution of exudative retinal detachment (Figure 2). There were no radiation complications.

**Comments**

The diagnostic accuracy of medium- and large-sized melanoma is more than 99% based on clinical examination and ancillary studies. The tumor in our patient could be classified as medium-sized choroidal melanoma based on COMS classification. Results of the COMS medium-sized tumor randomized trial have indicated similar survival in patients treated with enucleation or plaque radiotherapy. Only iodine 125 plaques were used in the COMS trial with overall efficacy of about 90% globe retention at 5 years (Figure 3A).

Similar tumor control rates have been reported with ruthenium 106 plaques, which have been used in Europe for more than 40 years (Figure 3B). Since ruthenium 106 is a beta emitter, it is most suitable for tumors that are 5 mm or less in height. Because of limited penetration of beta radiation (as compared with gamma radiation of iodine 125), in certain cases, the radiation dose distribution may be favorable with ruthenium 106 as compared with iodine 125 (Figure 4).

In our case, the total radiation dose to the optic disc (23 Gy) and macula (33 Gy) were well within threshold of tolerance (less than 40 Gy) with ruthenium 106 as compared with iodine-125 plaque (65 Gy and 78 Gy respectively). Other advantages with ruthenium 106 plaque included shorter duration of treatment and lower cost.

### Table 1. Comparison of dose distribution between iodine-125 plaque and ruthenium-106. The dose calculations for iodine-125 plaque were performed using COMS guidelines.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Iodine-125</th>
<th>Ruthenium-106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Point</td>
<td>85 Gy</td>
<td>85 Gy</td>
</tr>
<tr>
<td>Sclera</td>
<td>432 Gy</td>
<td>292 Gy</td>
</tr>
<tr>
<td>Macula</td>
<td>78 Gy</td>
<td>33 Gy</td>
</tr>
<tr>
<td>Optic disc</td>
<td>65 Gy</td>
<td>23 Gy</td>
</tr>
<tr>
<td>Duration</td>
<td>98 hrs</td>
<td>39 hrs</td>
</tr>
</tbody>
</table>

**References**

Some Medicare administrators have tried to limit payments for anesthesia care during the procedure that is the most frequently performed surgical procedure in the Medicare population today, explains Dr. Feldman.

“Efforts by anesthesiologists and ophthalmologists have so far succeeded in maintaining reimbursement levels,” he says. However, he acknowledges that having anesthesia staff present for all cataract surgeries is expensive and resource-intensive, so he is interested in facilitating a large national study of cost-effectiveness and outcomes of alternative approaches.

“Since cataract surgery is generally a very safe procedure, it would have to be a huge trial to get valid public health data,” he says.

The primary question he would like to study is whether there is a way to determine which patients do not actually benefit from monitored anesthesia care. “If we can identify the ones who do not really need it, can we increase the reimbursement for the others that do so we can provide those patients with the highest-quality care in a cost-effective manner? Can specially trained OR nurses monitor patients if an anesthesiologist or nurse anesthetist is available nearby?” he asks.

“Can the example of LASIK, which does not use anesthesia, be applied? Or does the difference in average demographic – a healthy 37-year-old versus a 70-year-old with multiple health problems – make that not valid?” he continues.

Currently, more than 90 percent of the 1.5 million cataract procedures performed in the United States each year involve local anesthesia with monitoring by an anesthesiologist or nurse anesthetist. Topical anesthesia with no injections and only mild sedation is the norm. The cost of this monitored care exceeds $150 million per year.

If Medicare were to limit monitored anesthesia care just to patients in whom it has been documented as medically necessary without further study, patient outcomes could suffer, Dr. Feldman fears.

“Cataract surgery procedures should be deemed by their very nature to require either general, regional or monitored anesthesia care. The surgical procedure itself justifies anesthesia care and there should be no need for a justifying diagnosis,” he explains.

“Microsurgical techniques such as this require the full attention and focus of operating surgeons. Surgeons should not be distracted by patient comfort and safety concerns, and they are not the best people to address airway management and resuscitation complications,” he says.

Dr. Feldman recently conducted an economic evaluation of anesthesia in cataract surgery in which he found that while Medicare reimburses 83 percent of commercial rates for non-anesthesia care, it only reimburses 38.9 percent of anesthesia services. Further, since Medicare only allows four base units to be billed, the actual reimbursement rate is closer to 29 percent of commercial average. For cataract surgery overall, anesthesia care accounted for $194 out of a total cost of $2,502 (7.8 percent).

“This compared with $1,272 for the surgeon and $822 to the facility,” he observes.

“A prospective, randomized multi-center trial could truly test the hypothesis that preoperative evaluation and intraoperative and postoperative management by anesthesia personnel improve patient satisfaction and efficiency and prevent untoward medical events in an identifiable subset of cataract patients,” Dr. Feldman says.

Patient satisfaction, incidence of adverse medical events and efficiency levels of a control group receiving traditional anesthesia monitoring care would be compared with one receiving nursing monitoring.

“A scientific public health analysis of anesthesia care for cataract surgery would help determine appropriate and cost-effective medical care for elderly patients,” he concludes.
A 69-YEAR-OLD WHITE MALE WAS REFERRED TO THE DEPARTMENT OF OPHTHALMIC ONCOLOGY AT THE COLE EYE INSTITUTE FOR EVALUATION OF AN ASYMPTOMATIC FUNDUS MASS. HIS LAST EYE EXAM WAS 10 YEARS PRIOR. THE PATIENT REPORTED A REMOTE HISTORY OF MILD OCULAR TRAUMA; MEDICAL HISTORY WAS SIGNIFICANT FOR DIABETES, HYPERTENSION AND HYPERCHOLESTEROLEMIA.

Examination revealed best corrected visual acuity of 20/25+ OD, 20/20 OS and normal IOPs, pupils, peripheral fields and extraocular movements. External examination and slit-lamp microscopy was remarkable for mild cortical changes.

A clear vitreous was present.

What is the differential diagnosis and what further tests are required? See Page 8.
Differential diagnosis

The main differential for this melanotic choroidal mass is a benign choroidal nevus versus a malignant melanoma. To differentiate these entities, several tests were ordered. B-scan ultrasonography revealed a medium-high reflective lesion, 2.8 mm in height, without extra-scleral extension (Figure 2). Indocyanine green (ICG) angiography revealed early hypofluorescence that persisted into late phases (Figure 3). The mass demonstrated no intrinsic choroidal vasculature. Given the above information, what is the final diagnosis and what is the proposed management?

Diagnosis

There is a lack of consensus on how best to differentiate a benign choroidal nevus and a malignant melanoma. Many studies have used size criteria (linear dimensions as well as area and volume) to classify lesions as benign or malignant. The Collaborative Ocular Melanoma Study (COMS), a multi-center prospective study, used linear dimensions to categorize choroidal melanomas as lesions greater than 1 mm in height (H) and 5 mm in largest basal diameter (LBD). Given this classification, our patient’s lesion should be considered as a choroidal melanoma. However, a COMS prospective, nonrandomized observational study of small choroidal melanomas found that about two-thirds of the lesions defined as small choroidal melanoma did not grow after 5 years of follow up (Figure 4). This raises questions about the accuracy of the initial diagnosis given that malignant lesions should exhibit growth. A critical review of published studies suggests that one can exclude the diagnosis of melanoma with high certainty in a lesion smaller than 1 mm (H) and 5 mm (LBD). Lesions larger than this still have a higher likelihood of being benign. This highlights the limitations of relying solely on size as a determinant of malignancy in choroidal melanocytic lesions.

Several authors have focused on lesion characteristics to determine predictors of growth potential. COMS found that larger initial size, presence of orange pigment, absence of drusen and absence of RPE changes adjacent to the tumor all predicted tumor growth (Table 1). While the larger size and location of our patient’s lesion are risk factors for growth, the presence of drusen and RPE changes and lack of orange pigmentation lower the risk of malignancy.

Several studies have also examined the ability of fluorescein angiography, ultrasonography and ICG angiography to differentiate nevi and melanoma of the choroid. Mueller et al reported that microcirculation patterns within the choroidal lesion detected by confocal ICG angiography predicted the growth of small choroidal melanocytic tumors. Our patient’s lesion showed no microcirculation pattern.

Given the above information, what is the final diagnosis and what are the treatment options?

Table 1. Statistically significant risk features predictive of growth as observed in small melanoma study of the COMS.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Dimensions</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>&gt; 2.0-3.0</td>
<td>4-17</td>
</tr>
<tr>
<td>Diameter</td>
<td>&gt; 8.0</td>
<td>5</td>
</tr>
<tr>
<td>Drusen</td>
<td>Present</td>
<td>0.24</td>
</tr>
<tr>
<td>Area of RPE changes</td>
<td>Present</td>
<td>0.23</td>
</tr>
<tr>
<td>Orange pigment</td>
<td>Present</td>
<td>2-6</td>
</tr>
</tbody>
</table>

Figure 2: B-scan ultrasonogram reveals a dome-shaped choroidal mass 2.8 mm in height without extra-scleral extension (A). Medium-high reflectivity is seen in A scan (B).

Figure 3: Indocyanine green angiogram (ICG) reveals hypofluorescence both in early (A) and late (B) phases. The mass lacks intrinsic choroidal vasculature.
Management

Given the size (indicative of melanoma) and appearance (indicative of nevus), a diagnosis of indeterminate choroidal melanocytic lesion was made. Options of observation (to document growth) and treatment with combination of plaque radiotherapy and transpupillary thermotherapy (sandwich therapy) were offered. Patients’ needs and wishes must also be taken into account when formulating a treatment plan, and this patient is an avid hunter who is right eye dominant.

Final disposition

Given his current excellent level of vision, high risk for visual loss if treated, one-in-three odds of the lesion eventually growing and 1% risk of tumor-related mortality, our patient preferred the option of observation. He was advised to return in 3 months, or earlier if he noticed any visual symptoms.

Time to Tumor Growth


References

GENETICS
STUDIES OF THE MOLECULAR GENETICS OF EYE DISEASES
Objective: To map the genes for inherited eye diseases. To screen candidate genes for mutations in a variety of genetic ocular disorders, including ocular malformations, congenital cataracts and retinal dystrophies. Contact: E. Traboulsi, M.D., at (216) 444-4363 or S. Crowe, C.O.T., at (216) 445-3840
THE GENETICS OF STRABISMUS
Objective: To discover the genes that cause some strabismus syndromes, including those for accommodative esotropia, congenital esotropia, congenital ocular fibrosis syndrome, intermittent esotropia, Brown syndrome and Duane syndrome. Contact: E. Traboulsi, M.D., at (216) 444-4363 or S. Crowe, C.O.T., at (216) 445-3840
PEDIATRICS
INFANT APHAKIA TREATMENT STUDY
Objective: To determine whether infants with a unilateral congenital cataract are more likely to develop better vision following cataract extraction surgery if (1) they undergo the primary implantation of an IOL or (2) they are treated primarily with a contact lens. Contact: E. Traboulsi, M.D., at (216) 444-4363 or S. Crowe, C.O.T., at (216) 445-3840
REFRACTIVE SURGERY
VISION THERAPY: A PROGRESSIVE CONTROLLED STUDY ON THE EFFECTIVENESS OF VISION THERAPY IN ELIMINATING ASTHENOPHIA IN A SYMPTOMATIC POPULATION
Eligibility Criteria: Patients who are 18 to 35 years of age and have any of the following symptoms: eye strain, occasional blurred vision when using a computer or performing other near work, occasional headaches, have words run together or fall asleep when doing prolonged computer work or near work. If eligible, participation will involve approximately three visual assessments at the Cleveland Clinic Division of Ophthalmology at Beachwood and required equipment for therapy. Compensation of $100 will be allotted for travel expenses. Contact: D. Tucker, O.D., at (216) 831-0120 or L. Slaby, C.O.A., at (330) 963-4843
LADARVISION SYSTEM USE OF THE REFRACTIVE DATA FROM A WAVEFRONT MEASUREMENT DEVICE (WMD) FOR THE CORRECTION OF REFRACTIVE ERROR-LASIK
Rationale: In an effort to improve outcomes in LASIK surgery, Alcon Surgical has developed a product, the LADARwave Custom Cornea Wavefront System, designed to measure refractive errors, including a method of characterizing aberrations of the visual system, generically referred to as a Wavefront Measurement Device (WMD). This clinical study is currently enrolling only hyperopic patients. Contact: R. Krueger, M.D., at (216) 445-8585 or R. Scott at (216) 444-0680
ACRYSOF ANGLE-SUPPORTED PHAKIC INTRAOCULAR LENS
Objective: To collect information on the safety and effectiveness of the artificial lens ACRYSOF for the correction of severe myopia. This study lens will be implanted behind the cornea in the anterior chamber. The lens is made of a soft acrylic material that allows the lens to be folded for implantation and therefore can be inserted through a smaller incision than other rigid lens designs. Participation in this study will last about 3 years. Contact: R. Krueger, M.D., at (216) 445-8585 or R. Scott at (216) 444-0680
RETINAL DISEASES
A PHASE III, MULTI-CENTER, RANDOMIZED, DOUBLE-MASKED, ACTIVE TREATMENT-CONTROLLED STUDY OF THE EFFICACY AND SAFETY OF RHFUFA V2 (RANIBIZUMAB) COMPARED WITH VERTEPORFIN (VISUDYNE) PHOTODYNAMIC THERAPY IN SUBJECTS WITH PREDOMINANTLY CLASSIC SUBFoveAL NEOVASCULAR AGE-RELATED MACULAR DEGENERATION
Objective: To evaluate the efficacy of intravitreal injections of ranibizumab administered monthly compared with verteporfin PDT in preventing vision loss, as measured by the proportion of subjects who lose fewer than 15 letters in visual acuity at 12 months compared with baseline. Contact: P. Kaiser, M.D., at (216) 444-6702 or L. Holody, C.O.A., at (216) 445-3762
PROTOCOL B7A-MC-MBDL REDUCTION IN THE OCCURRENCE OF CENTER-THREATENING DIABETIC MACULAR EDEMA
Objective: The primary objective of this study is to test the hypothesis that oral administration of 32 mg per day of ruboxistaurin for approximately 36 months will reduce, relative to placebo, the occurrence of center-threatening diabetic macula edema as assessed by fundus photography in patients with non-clinically significant macular edema and nonproliferative diabetic retinopathy at baseline. Contact: P. Kaiser, M.D., at (216) 444-6702 or C. Rosal, R.N., B.S.N., at (216) 445-1256
AN EVALUATION OF EFFICACY AND SAFETY OF POSTERIOR JUXTASCERAL ADMINISTRATIONS OF ANECORTAVE ACETATE FOR DEPOT SUSPENSION (15 MG OR 30 MG) VERSUS SHAM ADMINISTRATION IN PATIENTS AT RISK FOR DEVELOPING SIGHT-THREATENING CHOROIDAL NEOVASCULARIZATION DUE TO EXUDATIVE AGE RELATED MACULAR DEGENERATION (AMD) AART
Objective: To evaluate the effectiveness of anecortave acetate in stopping the progression of the “dry” or early form of AMD to the “wet” or advanced form. Depot administration or sham treatment (like an injection) will be every six months for four years for a total of nine visits. Patients must have “wet” AMD in one eye and “dry” AMD in the other. Vision in the “dry” eye must be equivalent to 20/40 or better. Contact: P. Kaiser, M.D., at (216) 444-6702 or L. Schaaf, R.N., at (216) 445-4086
THE STANDARD CARE VERSUS CORTICOSTEROID FOR RETINAL VEIN OCCLUSION STUDY
Objective: To evaluate the effectiveness of triamcinolone acetonide injections for treatment of macular edema versus standard treatment. Patients will have 11 to 13 visits over a period of up to three years. Contact: P. Kaiser, M.D., at (216) 444-6702 or L. Holody, C.O.A., at (216) 445-3762

For a complete list, go to www.clevelandclinic.org/eye/research
A SIX-MONTH PHASE 3, MULTICENTER, MASKED, RANDOMIZED, SHAM-CONTROLLED TRIAL (WITH SIX-MONTH OPEN-LABEL EXTENSION) TO ASSESS THE SAFETY AND EFFICACY OF 700 µG AND 350 µG DEXAMETHASONE POSTERIOR SEGMENT DRUG DELIVERY SYSTEM

Objective: To evaluate the safety and efficacy of the 700 µg DEX PS DDS Applicator System and 350 µg DEX PS DDS Applicator System compared with a Sham DEX PS DDS Applicator System (needle-less applicator) for six months in patients with macular edema following branch retinal vein occlusion or central retinal vein occlusion. The safety of the 700 µg DEX PS DDS Applicator System will be assessed for an additional 6 months in patients who qualify for treatment in an open-label safety extension.

Contact: P. Kaiser, M.D., at (216) 444-6702 or L. Schaaf, R.N., at (216) 445-4086

GLAUCOMA

ADVANCED IMAGING FOR GLAUCOMA

Objective: Advanced Imaging for Glaucoma (AIG) is a multi-center bioengineering partnership sponsored by the National Eye Institute. This partnership includes four clinical centers: the Cleveland Clinic Foundation (CCF), University of Pittsburgh Medical Center/University of Pittsburgh School of Medicine (UPMC), the University of Miami (Bascom Palmer Eye Institute) and the University of Southern California. The goal of the partnership is to develop advanced imaging technologies to improve the detection and management of glaucoma. The advanced imaging technologies include optical coherence tomography, scanning laser polarimetry and scanning laser tomography. The technologies will be evaluated in a longitudinal five-year clinical trial composed of glaucoma suspects, glaucoma patients and normal subjects.

Contact: S. Smith, M.D., M.P.H., at (216) 444-4821 or R. Scott (216) 444-0680

Programs in Ophthalmic Education 2005–2006

PHYSICIANS ARE CORDIALLY INVITED TO ATTEND THE FOLLOWING OPHTHALMIC CONTINUING MEDICAL EDUCATION COURSES AT THE CLEVELAND CLINIC COLE EYE INSTITUTE. ALL COURSES WILL BE HELD IN THE JAMES P. STORER CONFERENCE CENTER ON THE FIRST FLOOR OF THE COLE EYE INSTITUTE EXCEPT THE APRIL 29 REFRACTIVE SURGERY COURSE, WHICH WILL BE HELD AT THE CLEVELAND CLINIC WESTON, FL, CAMPUS NEAR FORT LAUDERDALE IMMEDIATELY PRIOR TO THE ASSOCIATION FOR RESEARCH IN VISION AND OPHTHALMOLOGY MEETING.

For more information, contact Jane Sardelle, program coordinator, at 216/444-2010 or 800/223-2273, ext. 42010, or sardelj@ccf.org.

Saturday, February 11, 2006
7:00 a.m. to 2:00 p.m.

6TH UVEITIS UPDATE

Course Directors:
Careen Y. Lowder, M.D., Ph.D.
Uveitis Department
Cole Eye Institute
Victor L. Perez, M.D.
Cornea and Uveitis Departments
Cole Eye Institute

Guest Faculty:
Janet L. Davis, M.D.,
Professor, Bascom Palmer Eye Institute
Miami, FL
Douglas A. Jabs, M.D., M.B.A.
Alan C. Woods Professor
Departments of Ophthalmology and Medicine
The Johns Hopkins University
School of Medicine
Baltimore, MD
James Rosenbaum, M.D.
The Edward E. Rosenbaum
Professor of Inflammation Research
Professor of Ophthalmology, Medicine and Cell Biology
Oregon Health & Sciences University
Portland, OR

Russell Van Gelder, M.D., Ph.D.
Associate Professor
Washington University
St. Louis, MO

Cleveland Clinic Faculty:
Gary S. Hoffman, M.D., M.S.
Professor of Medicine,
Chairman and Harold C. Schott Chair
Department of Rheumatic and Immunologic Diseases
Director, Center for Vasculitis Care and Research
The Cleveland Clinic Foundation
Cleveland, OH

Brian Mandell, M.D., Ph.D., FACR
Vice Chairman of Medicine for Education
Professor of Medicine,
Lerner College of Medicine of CWRU
Center for Vasculitis Care and Research
The Cleveland Clinic Foundation
Cleveland, OH

Continued on page 12
Description:
This course will present comprehensive ophthalmologists with information on the newest medical and surgical modalities in the treatment of patients with inflammatory and infectious ocular diseases. Special emphasis will be placed on the pathophysiology of diseases and evidence-based treatments. Case presentations will allow audience participation and interaction with faculty.

Objectives:
At the conclusion of this course, participants should be able to:
1. Review the use of nonspecific drugs, including immunosuppressive therapy.
2. Describe the current clinical trials in ocular inflammatory diseases.
3. Identify newer therapies for noninfectious posterior uveitis syndromes.
4. Evaluate and determine which laboratory tests to order in patients with uveitis.
5. Diagnose and formulate a treatment plan for patients with various uveitis syndromes.

Registration fee: $100. Receive a $25 discount by registering online.

Saturday, March 4, 2006
7:00 a.m. to 1:30 p.m.

NEURO-OPHTHALMOLOGY UPDATE:
IN CASE, AFTER CASE, AFTER CASE ...

Course Director:
Gregory S. Kosmorsky, D.O.
Department of Neuro-Ophthalmology
Cole Eye Institute

Guest Faculty:
Eric Eggenberger, D.O.
Professor, Department of Neurology and Ophthalmology
Michigan State University
East Lansing, MI

Steven Galetta, M.D.
Van Meter Professor of Neurology
Director, Neuro–Ophthalmology Division
University of Pennsylvania
School of Medicine
Philadelphia, PA

Steven Newman, M.D.
University of Virginia Medical Center
Professor
Department of Ophthalmology
Charlottesville, VA

Description:
This course will feature a panel of experts who will present a breadth of neuro-ophthalmologic cases from the "sublime to the ridiculous." Entirely case based, this discussion of clinical pearls and literature reviews will help neuro-ophthalmologists, general ophthalmologists and neurologists recognize and treat a broad range of neuro-ophthalmologic disorders.

Objectives:
At the conclusion of this course, participants should be able to:
1. Identify common neuro-ophthalmologic disorders.
2. Evaluate the most appropriate diagnostic approach for various signs and symptoms.
3. Organize seemingly disparate signs and symptoms into a cogent neuro-ophthalmic diagnosis.

Registration fee: $100. Receive a $25 discount by registering online.

Saturday, April 29, 2006
7:00 a.m. to 6:30 p.m.

REFRACTIVE SURGERY:
BEYOND LASIK AND EXCIMER LASERS

This course will be held at The Cleveland Clinic Weston, FL campus near Fort Lauderdale immediately prior to the Association for Research in Vision and Ophthalmology meeting.

Course Director:
Ronald R. Krueger, M.D., M.S.E.
Medical Director, Refractive Surgery
Cole Eye Institute

Cole Eye Institute Faculty:
Steven E. Wilson, M.D.
Director, Corneal Research
Cole Eye Institute
Constance Cox, M.D.
William J. Dupps, M.D., Ph.D.
Cornea, External Disease & Refractive Surgery Fellows

Guest Faculty:
Randall J. Olson, M.D.
John A. Moran Presidential Professor
Chair of Ophthalmology and Visual Sciences
Director, John A. Moran Eye Center
University of Utah
Salt Lake City, UT

Yaron S. Rabinowitz, M.D.
Director of Ophthalmology Research
Cedars-Sinai Medical Center
Clinical Professor of Ophthalmology
University of California Los Angeles
School of Medicine
Los Angeles, CA

Description:
There is more to refractive surgery than just LASIK and excimer lasers. This course will cover the various other futuristic technologies used, including synthetic implants and femtosecond lasers.

Objectives:
At the conclusion of this course, participants should be able to:
1. Identify and differentiate keratoconus suspect patients seeking refractive surgery.
2. Review the treatment options for keratoconus suspect patients.
3. Describe the benefits and limitations of using femtosecond lasers in refractive surgery.
4. Determine the indications, techniques and complications of phakic IOLs.
5. Identify the indications, techniques and complications of presbyopic lens exchange.
6. Review the status of accommodating and multifocal IOLs.

Registration fee: $100. Receive a $25 discount by registering online.
Saturday, May 20, 2006  
7:00 a.m. to 5:00 p.m.  

NEW DEVELOPMENTS IN RETINA: TRIALS, DRUGS AND NEW TECHNIQUES  

Course Directors:  
Peter K. Kaiser, M.D.  
Vitreoretinal Department  
Cole Eye Institute  
Jonathan E. Sears, M.D.  
Vitreoretinal Department  
Cole Eye Institute  

Guest Faculty:  
Allen C. Ho, M.D.  
Professor of Ophthalmology  
Thomas Jefferson University  
Retina Service  
Wills Eye Hospital  
Philadelphia, PA  
Jason S. Slakter, M.D.  
Vitreous-Retina-Macula  
Consultants of New York  
Clinical Professor of Ophthalmology  
New York University  
New York, NY  

Description:  
This meeting is designed for retinal specialists and general ophthalmologists who diagnose and treat retinal disease. The lectures will update participants on the newest clinical trials in retina especially in age-related macular degeneration and diabetic retinopathy. In addition, faculty members, who are all experts in the field of retina, will offer current treatment options for vitreoretinal conditions normally seen in clinical practice with particular emphasis on the newly released drugs.  

Objectives:  
At the conclusion of this course, participants should be able to:  
1. Describe recent clinical trials in age-related macular degeneration and diabetic retinopathy.  
2. Distinguish the differences between the new anti-VEGF drugs.  
3. Compare various treatment modalities and clinical trial results.  
4. Describe the use of steroids in age-related macular degeneration and diabetic retinopathy.  
5. Explain how new imaging devices are enhancing retinal diagnosis.  

Registration fee: $100. Receive a $25 discount by registering online.

Thursday, June 15, 2006  
(Poster Reception)  
5:00 p.m. to 7:30 p.m.  

Friday, June 16, 2006  
(Meeting/Graduation Ceremony)  
7:00 a.m. to midnight  

ANNUAL RESEARCH, RESIDENTS & ALUMNI MEETING  

Course Directors:  
Hilel Lewis, M.D.  
Chairman, Division of Ophthalmology  
Director, Cole Eye Institute  
Careen Y. Lowder, M.D., Ph.D.  
Uveitis Department  
Cole Eye Institute  

Keynote Speaker:  
Paul R. Lichter, M.D.  
F. Bruce Fralick  
Professor of Ophthalmology  
Chair, Department of Ophthalmology and Visual Sciences  
Director, University of Michigan Kellogg Eye Center  
Ann Arbor, MI  

Description:  
This program provides a scientific forum to present clinical and basic science research of the Cole Eye Institute residents, fellows, staff, alumni and invited ophthalmologists.  

The goal of this meeting is to pursue and present the highest-quality, original, thought-provoking clinical research papers. In addition to the educational aspects of the program and learning about new and ongoing investigations, this event offers an excellent opportunity to meet current residents, fellows, new faculty and invited ophthalmologists and to make and renew friendships.  

Objectives:  
At the conclusion of this course, participants should be able to:  
1. Recognize the most up-to-date concepts and treatments in research and clinical ophthalmology.  
2. Identify current basic science research in age-related macular degeneration.  
3. Explain the rationale and status of the most current treatments for uveitic and diabetic macular edema.  
4. Discuss outcomes of complicated glaucoma and cataract surgery.  
5. Describe the latest techniques in refractive surgery.  

Registration fee: $100. Receive a $25 discount by registering online.
THE COLE EYE INSTITUTE DISTINGUISHED LECTURE SERIES PROVIDES A FORUM FOR RENOWNED RESEARCHERS IN THE VISUAL SCIENCES TO PRESENT THEIR LATEST FINDINGS. THIS SERIES OF LECTURES FEATURES ADVANCES IN MANY AREAS OF OPHTHALMIC RESEARCH PRESENTED BY NOTED BASIC AND CLINICAL SCIENTISTS FROM THROUGHOUT THE WORLD. AMPLE OPPORTUNITY FOR QUESTIONS AND ANSWERS IS PROVIDED.

ALL LECTURES ARE HELD ON THURSDAYS FROM 7 TO 8 A.M. IN THE JAMES P. STORER CONFERENCE ROOM ON THE FIRST FLOOR OF THE COLE EYE INSTITUTE, CLEVELAND CLINIC FOUNDATION. REGISTRATION IS NOT REQUIRED. FOR QUESTIONS, PLEASE CALL 216/444-5832.

January 19, 2006
ON AND OFF PATHWAYS IN THE RETINA AND VISUAL SYSTEM
Ralph F. Nelson, Ph.D.
Senior Investigator
Basic Neurosciences Program
National Institute of Neurological Disorders and Stroke
National Institutes of Health
Bethesda, MD

February 9, 2006
GENETIC REGULATION OF THE EYE’S AXIAL LENGTH
Olof H. Sundin, Ph.D.
Assistant Professor of Ophthalmology
Wilmer Eye Institute
The Johns Hopkins University School of Medicine
Baltimore, MD

March 16, 2006
IS IT FEASIBLE TO GENERATE AN ARTIFICIAL CORNEA?
James D. Zieske, Ph.D.
Associate Professor
Department of Ophthalmology
Schepens Eye Research Institute
Harvard Medical School
Boston, MA

April 20, 2006
THE ROLE OF MACROPHAGES IN CONTROLLING ANGIOGENESIS IN THE EYE
Thomas A. Ferguson, Ph.D.
Professor
Department of Ophthalmology and Visual Sciences
Department of Pathology and Immunology
Washington University of St. Louis, School of Medicine
St. Louis, MO

May 18, 2006
OCULAR SURFACE CELL DYNAMICS
M. Elizabeth Fini, Ph.D.
Professor and Scientific Director
Evelyn F. and William L. McKnight Vision Research Center
Walter G. Ross Chair in Ophthalmic Research
Bascom Palmer Eye Institute
University of Miami
Miller School of Medicine
Miami, FL

June 8, 2006
MOLECULAR BASIS OF CORNEAL CLARITY AND AVASCULARITY
Dimitri T. Azar, M.D.
Associate Chief of Ophthalmology
Director of Cornea, External and Refractive Surgery
Massachusetts Eye and Ear Infirmary
Professor Ophthalmology
Harvard Medical School
Boston, MA

July 20, 2006
CELLULAR REMODELING OF THE RETINA IN RESPONSE TO DETACHMENT
Steven K. Fisher, Ph.D.
Professor
Department of Molecular, Cellular and Developmental Biology
Neuroscience Research Institute
University of California, Santa Barbara
Santa Barbara, CA

September 14, 2006
PATHOGENIC MECHANISMS IN UVEORETINITIS
John V. Forrester, M.D.
Cockburn Professor and Head
Department of Ophthalmology
University of Aberdeen
Institute of Medical Sciences
Foresthill
Aberdeen, Scotland

October 19, 2006
CIRCADIAN CLOCKS AND NEUROMODULATORS IN THE RETINA
P. Michael Iuvone, Ph.D.
Professor
Department of Pharmacology
Emory University
Atlanta, GA

November 16, 2006
MAKING SENSE OF NEURONAL DIVERSITY: A BOTTOM-UP VIEW OF THE RETINA
Richard H. Masland, Ph.D.
Charles A. Pappas Professor of Neuroscience
Harvard Medical School
Investigator, Howard Hughes Medical Institute
Boston, MA
Applications of anterior segment surgery

endophthalmitis, posterior segment complications of anterior segment surgery

Specialty/Research Interests: Vitreoretinal眼banking, cataracts, stem cell transplantation, artificial corneas, retinal diseases, diabetic retinopathy, retinal detachment, ocular surface disease, limbal stem cell transplantation, artificial corneas, keratoconus, cataracts, corneal transplantation, corneal disease, corneal vascularization, corneal dystrophy

Specialty Interests: Vitreoretinal surgery

Director, Cole Eye Institute

Specialty/Research Interests: Vitreoretinal surgery for complicated retinal detachment and trauma, age-related macular degeneration, diabetic retinopathy, retinal photocoagulation, instrument development

Bela Anand-Apte, M.B.B.S., Ph.D. Ophthalmic Research Department

Research Interests: Age-related macular degeneration, inherited retinal diseases

Marc A. Feldman, M.D. Ophthalmic Anesthesia

Specialty Interests: Ophthalmic surgery anesthesia, preoperative assessment, resident education

Richard E. Gans, M.D., F.A.C.S. Comprehensive Ophthalmology Department

Specialty Interests: Cataract, glaucoma, diabetes

Philip N. Goldberg, M.D. Comprehensive Ophthalmology Department

Specialty Interests: Cataract, glaucoma

Frondic A. Gutman, M.D. Vitreoretinal Service

Specialty Interests: Retinal vascular diseases, laser therapy, diabetic retinopathy

Stephanie A. Hagstrom, Ph.D. Ophthalmic Research Department

Research Interests: Inherited forms of retinal degeneration, including macular degeneration and retina pigmentosa

Joe G. Hollyfield, Ph.D. Ophthalmic Research Department

Research Interests: Retinal degeneration, retinal diseases

Bennie H. Jeng, M.D. Cornea and External Disease Department

Specialty/Research Interests: Corneal transplantation, ocular surface disease, limbal stem cell transplantation, artificial corneas, keratoconus, cataracts

Peter K. Kaiser, M.D. Vitreoretinal Service

Specialty/Research Interests: Vitreoretinal diseases, age-related macular degeneration, retinal detachment, diabetic retinopathy, endophthalmitis, posterior segment complications of anterior segment surgery

Gregory S. Kosmorsky, D.O. Neuro-Ophthalmology Department

Specialty Interests: Neuro-ophthalmology, cataract, refractive surgery

Ronald R. Krueger, M.D., M.S.E. Refractive Surgery Service

Specialty/Research Interests: Refractive surgery, lasers, refractive corneal pathology, lamellar corneal transplants, investigational clinical trials

Roger H.S. Langston, M.D. Cornea and External Disease Department

Specialty Interests: Cataract, glaucoma, diabetes

Careen Y. Lowder, M.D., Ph.D. Uveitis Department

Specialty/Research Interests: Uveitis, intraocular inflammatory diseases, pathology

Andreas Marcotty, M.D. Pediatric Ophthalmology and Strabismus Service

Specialty Interests: Pediatric ophthalmology, adult strabismus

Shari Martyn, M.D. Comprehensive Ophthalmology Department

Specialty Interests: Cataract, glaucoma, diabetes

David M. Meisler, M.D. Cornea and External Disease Department

Specialty/Research Interests: Corneal and extracellular diseases, inflammatory and infectious diseases of the cornea, corneal transplantation, refractive surgery

Michael Millstein, M.D. Comprehensive Ophthalmology Department

Specialty Interests: Cataract, glaucoma, refractive surgery

Neal S. Peachey, Ph.D. Ophthalmic Research Department

Research Interests: Visual loss associated with hereditary retinal degeneration

Victor L. Perez, M.D. Cornea and External Disease Department

Specialty/Research Interests: Medical and surgical treatments of autoimmune inflammatory conditions of the cornea and ocular surface, uveitis, corneal transplantation, cataract surgery

Julian D. Perry, M.D. Oculoplastic and Orbital Surgery Department

Specialty/Research Interests: Aesthetic facial surgery/fat transplantation and repositioning, acellular human dermal graft matrix, new bovine hydroxyapatite orbital implant, thyroid eye disease/rate of strabismus after decompression surgery for dysthyroid orbitopathy

Edward J. Rockwood, M.D. Glaucoma Department

Specialty/Research Interests: Glaucoma, glaucoma laser surgery, combined cataract and glaucoma surgery, glaucoma filtering surgery with antimetabolite therapy, glaucomatous optic nerve damage, congenital glaucoma

Allen S. Roth, M.D. Comprehensive Ophthalmology Department

Specialty Interests: Corneal transplantation, refractive surgery, cataract and implant surgery

Jonathan E. Sears, M.D. Vitreoretinal Service

Specialty/Research Interests: Pediatric and adult vitreoretinal diseases, pediatric retinal detachment, inherited vitreoretinal disorders, retinopathy of prematurity, other acquired proliferative diseases

David B. Sholiton, M.D. Comprehensive Ophthalmology Department

Specialty Interests: Cataract and implant surgery, glaucoma, ocuroplasics

Arun D. Singh, M.D. Ophthalmic Oncology Department

Specialty/Research Interests: Adult and pediatric ocular tumors, uveal melanoma, genetics of retinoblastoma, retinal capillary hemangioma, von Hippel-Lindau disease

Scott D. Smith, M.D., M.P.H. Glaucoma Department

Specialty/Research Interests: Glaucoma, cataract, prevention of eye disease, international ophthalmology, congenital glaucoma

Elias I. Traboulsi, M.D. Pediatric Ophthalmology and Strabismus Department

Center for Genetic Eye Diseases

Specialty/Research Interests: Ocular diseases of children, genetic eye diseases, strabismus, retinoblastoma, congenital cataracts, childhood/congenital glaucoma

Steven E. Wilson, M.D. Cornea and External Disease and Refractive Surgery Department

Specialty/Research Interests: Corneal and external disease, refractive surgery, corneal healing

216/444-2020

The Cleveland Clinic Cole Eye Institute

www.clevelandclinic.org/eye
Ophthalmology Update, a publication of The Cleveland Clinic Cole Eye Institute, provides information for ophthalmologists about state-of-the-art diagnostic and management techniques and current research. Please direct any correspondence to:

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Ophthalmology Update is written for physicians and should be relied upon for medical education purposes only. It does not provide a complete overview of the topics covered and should not replace the independent judgment of a physician about the appropriateness or risks of a procedure for a given patient.

Physicians who wish to share this information with patients need to make them aware of any risks or potential complications associated with any procedures.

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Ophthalmic Pearl

Proper Patient Selection Is Key to Outstanding Intacs Outcomes

By Bennie H. Jeng, M.D.

The recent FDA approval of Intacs intrastromal corneal segments for the treatment of keratoconus has been exciting news for patients with keratoconus as well as corneal surgeons. Proper patient selection is essential to achieving outstanding outcomes.

Intacs are indicated for keratoconus patients who have clear central corneas. Although it may seem insignificant, any scarring in the central cornea will distort the topography, even after Intacs placement, and the effect of the Intacs will be suboptimal. Even a small amount of subepithelial scarring at the apex of a cone will lead to less-than-optimal results.

The other major selection criterion, as in any surgical procedure, is patient expectations. While uncorrected visual acuity almost always improves with Intacs placement, it is imperative that patients realize Intacs are intended to improve best corrected visual acuity, either with spectacles or contact lenses. They are not designed to give perfect vision without correction.

It is also important to emphasize that best corrected visual acuity may not be 20/20. Studies demonstrate that the average patient will achieve two lines of improvement in best corrected visual acuity. However, for a young, active person, which describes many patients with keratoconus, the difference between 20/50 and 20/30 is tremendous. In addition, for patients who would otherwise be facing corneal transplantation because of contact lens intolerance, Intacs can often restore the ability to wear a contact lens.

As for the technical aspects of the procedure itself, a critical evaluation of the current literature on techniques to position Intacs suggests that no one method is clearly superior over another. In my experience, however, I have found that a temporal incision with a thicker segment placed inferiorly to provide greater flattening along with a thinner segment (or no segment) superiorly works well for asymmetric cones, while symmetric segments with a temporal incision works well for central cones.

While I use a manual dissection technique, others who use the femtosecond laser to create the channels have also demonstrated excellent technical outcomes.