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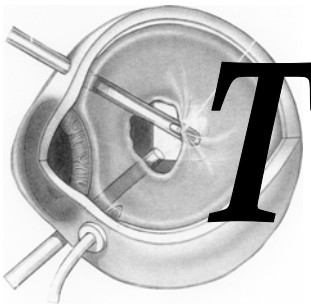

The Light Pipe

The newsletter of Georgia Retina, P.C.

Clinical Trials at Georgia Retina, P.C.

At Georgia Retina, P.C., we are committed to participating in current clinical trials that may potentially alter the way we manage and treat retinal diseases today. We are currently enrolling patients in many studies, and are actively evaluating several upcoming trials. The following is a brief description of each of the trials, which also includes the inclusion criteria of each study.

1) Anecortave Acetate Risk Reduction Trial (Alcon—Enrollment closed): The purpose of the study is to evaluate the safety and effectiveness of Anecortave Acetate vs. sham injections in stopping the progression of non-exudative (dry) AMD to exudative (wet) AMD in a multi-center, randomized, clinical trial. Anecortave acetate is a modified steroid compound that has been shown to have an angiostatic effect. It is injected into the retrobulbar space using a curved cannula through a superotemporal, subconjunctival incision. This trial is a 4 year study, with follow-up every 6 months to evaluate the status of the macula. Eligible participants must have:

Figure 1

- Exudative AMD in one eye and non-exudative AMD in the other eye (study eye)
- 20/40 or better vision in dry eye (study eye)
- At least 5 or more intermediate (>63 microns) or larger soft drusen within 3000 microns of foveal center (and/or confluent drusen within 3000 microns of foveal center) such as in Fig 1.

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Retisert – A New Implantable Steroid Device for Chronic Posterior Uveitis

Chronic posterior uveitis may be caused by a variety of infectious and non-infectious conditions. Once a medical workup has determined that the cause is non-infectious, there are a wide range of inflammatory diseases which can be responsible. These include sarcoidosis, pars planitis, birdshot retinochoroiditis, multifocal choroiditis with panuveitis, and many others. It is important to try to eradicate as much inflammation as possible, as low grade chronic inflammation results in considerable morbidity to patients, in the form of cataracts, glaucoma, cystoid macular edema, and posterior synechiae. The mainstay of treatment for these conditions is steroids which have well known ocular and systemic side effects that include gastric ulcers, fluid retention, weight gain, exacerbation of diabetes, aseptic necrosis of the hips, insomnia and others. Steroid sparing agents such as methotrexate, cyclophosphamide and cyclosporine are being used with increasing frequency. The drugs, of course, have their own side effects, such as bone marrow suppression in the case of methotrexate, and potential carcinogenicity as well as hemorrhagic cystitis with cyclophosphamide, which is an alkylating agent. Periocular injections or intravitreal injections of

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Endophthalmitis Risk After Cataract Surgery Is Increasing

Despite *the evolution* of cataract surgery from intracapsular cataract surgery (ICCE) to extracapsular cataract surgery to phacoemulsification with tunnel incisions to clear corneal phacoemulsification, the risks of your patient developing endophthalmitis is increasing rather than decreasing. This is important information. When cataract surgeons obtain a patient's informed consent, they may unknowingly provide the patient an inaccurate prediction of endophthalmitis risk. Interestingly, ten-year studies that began in the mid-1980's and a five-year study at the same time, which included tens of thousands of patients, revealed an endophthalmitis risk after cataract surgery ranging between .07 and .09. This means 7 to 9 patients out of 10,000 patients will develop endophthalmitis. Another study evaluated Medicare beneficiaries in 1986 and 1987, and found a risk rate of 0.08%.

Recently, researchers at the Wilmer Eye Institute and the Johns Hopkins School of Public Health have chosen to reevaluate the incidence of endophthalmitis after cataract surgery. Their article appears in the August, 2005 edition of *Ophthalmology*. Interestingly, of more recent cataract procedures, in **1994**, they found that the incidence of endophthalmitis was approximately 18 cases per 10,000 patients, and the risk in **2001** was approximately 25 cases per 10,000. Please take note that the risk in 1994 was much greater than the risk that was calculated 10 years earlier. Of even greater concern is that the risk in 2001 was found to be 37% higher.

The authors speculate that the changes in how cataract surgery was performed may be a significant factor. There are other articles in the literature that demonstrate that there is an increased risk of endophthalmitis in patients who are having secondary lens implants. In their article they provided data from the American Society of Cataract and Refractive Surgery that clear cornea cataract surgery was performed by only 4% to 5% in 1992, 30% in 1997, and 47% by the year 2000. This risk in endophthalmitis seems to parallel the move towards clear corneal incisions. Since the data came from the government expenditures for Medicare beneficiaries and not actual individual doctors' offices, they were unable to distinguish the method of cataract surgery in these 500,000 Medicare patients. Of course, they conclude future studies will be necessary to assess if there is a significant relationship to the surgical technique employed. They also made some other interesting observations. Older age and black race carried an increased risk of endophthalmitis. In fact, the risk of developing endophthalmitis in a 90-year old patient was as high as 1 in 300, and 1 in 400 for the rest of the population.

Interestingly, they observed that the risk of endophthalmitis after penetrating keratoplasty has not changed appreciably over several decades. From our perspective, this suggests the increased incidence is not coming from the hospitals, but is more likely related to the surgical technique.

What can we do with this important information?

- We need to counsel our patients more accurately that the risk of endophthalmitis may be 1 out of 400, and not 1 out of 2,000, as we may have quoted in the past. Accordingly, we need to educate them that endophthalmitis is a rare but devastating complication.
- Accordingly, they need to be reminded that they need to contact their caregivers immediately if they experience increased pain, redness, discharge or decreased vision.
- From our experience, the best outcomes with endophthalmitis are the patients who are seen, diagnosed and treated as soon as the infection shows the earliest signs. This allows the best chance for vision recovery. Nonetheless, a virulent organism can still adversely influence the overall prognosis.

Perhaps we need to put greater emphasis on the actual creation of the sutureless incisions; specifically, better architecture of the scleral tunnel and the corneal incision must be accomplished. Truly, we need to try to cre-

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kenalog are very useful, but have a relatively short duration of action before they have to be repeated. Recently the FDA has approved a sustained release delivery system for the steroid fluocinolone, known as Retisert. The Retisert implant delivers continuous steroid therapy for 3 years.

The implant is a 1.5 mm PVA (polyvinyl alcohol) coated tablet with a tab to accept a suture. It is inserted via the pars plana and is suspended from the eye wall in a manner similar to the Vitrasert (ganciclovir) implant, used for CMV retinitis. This surgical procedure can have its own potential side effects such as retinal detachment, wound dehiscence, and endophthalmitis.

There have been two clinical trials published on Retisert. In a mixed group of patients, the disease recurrence rates were reduced from between 40 and 54% to between 7 and 14%. About 20% had increased visual acuity of 3 lines or better after 34 weeks. There was also a great reduction in the percentage of patients requiring systemic steroids. The average number of recurrences dropped from 2.5 episodes per year to no recurrences. The average number of periocular steroid injections dropped from 2.2 per year to 0.07. From the patient's standpoint there should be less inconvenience and less frequent need for office follow up. On the downside, more than 90% developed cataracts and about 64% had elevated IOP which was controlled either by medication or trabeculectomy surgery (19.4%).

The cost of the implant (made by Bausch and Lomb) is $18,250. This seems extremely high, but is not much more than some of the other new drugs which we routinely employ. For example, Macugen (Eyetech pharmaceuticals) costs about $20,000 for 2 years of treatment, if treatment were to be continued that long. If Retisert reduces time lost from work, and multiple office visits, it could be cost effective.

Overall, this is a promising therapy which has the potential to help patients with chronic posterior uveitis, especially those cases recalcitrant to therapy or intolerant of systemic medications.

New Cancer Treatment May be Helpful for Age Related Macular Degeneration

Recently, the FDA approved Avastin (bevacizumab) for the treatment of advanced colon cancer. Avastin is a VEGF antagonist made by Genentech. A study was published from the Bascom Palmer Eye Institute in Miami, where Avastin was used in an uncontrolled pilot, open label, study in nine patients with ARMD and subfoveal CNV. The drug is administered by intravenous infusion at two week intervals. Patients in this small study had visual acuity between 20/40 and 20/400 and were treated for 12 weeks. There were reportedly no serious adverse side effects, except a transient mild elevation of blood pressure at 6 weeks, but not at 12 weeks. In study eyes, there was an improvement in median visual acuity scores by 8 letters and mean visual acuity scores by 12 letters. On OCT examination the central retinal thickness decreased by about 160 microns. In fellow eyes the visual acuity also increased, and the retinal thickness measurements also decreased. Fluorescein angiography demonstrated a marked reduction or absence of hyperfluorescence due to the CNV.

Since this initial report of the use of Avastin, multiple case series have been reported showing often dramatic resolution of edema in many conditions, including branch vein occlusions, central retinal vein occlusions, diabetic retinopathy, and exudavtive macular degeneration with CNV. We have now had a great deal of experience using it and many of your patients may have benefited from it. Clinical trials may be undertaken to evaluate systemic bevacizumab, either alone or as an adjunct to locally administered VEGF inhibitors as well as photodynamic therapy.

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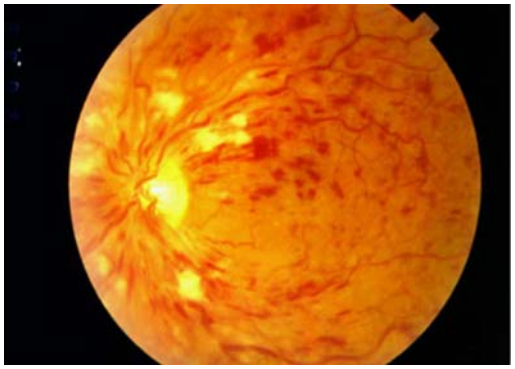

- Hyperpigmentation within 3000 microns of the foveal center
- No geographic atrophy (hypopigmentation ≥125 µm)
- No intraocular surgery in the study eye within 60 days prior to enrolling in the study
- Be ≥ 50 years old and in overall good health

2) CRVO Study (Eyetech-Enrollement closed): The purpose of this study is to determine the safety, efficacy, and pharmacokinetics of intravitreous injection of Macugen (an anti-Vascular Endothelial Growth Factor aptamer) vs. sham injections in patients with recent vision loss due to macular edema secondary to CRVO in a randomized, controlled, clinical trial. Injections are administered every 6 weeks for 30 weeks, with the final study visit at 52 weeks. Eligible participants must have:

- CRVO dx within 6 months from study entry (Figure 2)
- Macular edema ≥ 250 µm as determined by OCT
- 20/50-20/400 vision in study eye and 20/200 vision or better in fellow eye
- IOP of 21 mmHg or less
- No prior PRP or sector scatter photocoagulation
- No prior systemic, intravitreous, or subtenon's corticosteroid for ophthalmic conditions
- No intraocular surgery with the exception of cataract within 12 months of study entry
- Cataract and YAG surgeries are excluded within 3 months of study entry
- Blood pressure must be ≤140 systolic and ≤90 diastolic

3) SCORE study (Enrollment open): The **S**tandard Care versus **CO**rticosteroid for **RE**tinal Vein Occlusion (SCORE) Study is a randomized, multi-center, clinical trial, funded by the National Eye Institute (NEI), designed to compare the efficacy and safety of the standard care treatment for patients with macular edema associated with central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) **versus** intravitreal injection(s) of triamcinolone acetonide. Small case series of patients treated with intravitreal injection(s) of triamcinolone acetonide (Kenalog, Bristol-Myers-Squibb) for macular edema associated with CRVO and BRVO appear promising despite concerns regarding adverse events related to steroids such as cataract and glaucoma. As current treatment ("standard care") for macular edema associated with CRVO and BRVO is limited, intravitreal injection(s) of triamcinolone acetonide have been used with increasing frequency in the past several years. The SCORE Study is being conducted to evaluate the potential long-term benefits and risks of this treatment compared with standard care treatment. Additionally, a new, sterile, preservative-free and endotoxin-free formulation of intravitreal triamcinolone acetonide has been developed for use in the SCORE Study. Eligibility criteria include:

- Patients with CRVO or BRVO with associated macular edema of 2 to18 months duration
- Best-corrected visual acuity between 20/40 and 20/320
- No history of systemic corticosteroids within 4 months of study entry
- Macular edema ≥250 µm as shown by OCT
- Patients with a history of grid laser photocoagulation for macular edema are eligible if the treatment was deemed inadequate.
- No prior history of intravitreal corticosteroid injection.

Additional information about patient eligibility criteria and the SCORE Study can be found online at http://spitfire.emmes.com/study/score/

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4) AMD (Eyetech-Enrollment open): The purpose of this study is to compare Macugen (Intravitreal anti-VEGF) plus Photodynamic Therapy with Visudyne to Macugen plus sham PDT. This is a 54 week study with Macugen injected every 6 weeks. Eligible participants must have:

- CNV due to AMD, predominantly classic lesion
- VA between 20/40 and 20/200 in study eye and better than 20/800 in fellow eye
- The greatest linear dimension of the lesion must be ≤5400
- No prior PDT with Visudyne in study eye
- No prior AMD thermal laser
- IOP of 21mmHg or less
- No Intraocular surgery within 3 months of trial entry in the study eye
- No history of intravitreal corticosteroids
- ≥50 years of age and in overall good health

AREDS II (National Eye Institute—Enrollment open): This is a randomized, prospective, National Eye Institute approved study of vitamin supplements plus LCPUFA (long chain polyunsaturated fatty acids (omega-3)), or lutein in ARMD. These substances were not studied in AREDS I (Age-Related Eye Disease Study), which is of course, the trial that produced the recommendations for the use of Ocuvite PreserVision. Eligible participants must be:

55-80 years of age at qualification
Have large drusen in both eyes, or large drusen in one eye and advanced AMD in fellow eye

Genentech SAILOR (Enrollment—Open): This is a randomized, controlled, clinical trial to evaluate the effect of LUCENTIS (Placebo, 0.3 and 0.5 mg doses) in patients with subfoveal choroidal neovascular membranes due to ARMD. This is a larger scale study, compared to MARINA, which will enroll both naïve lesions and previously treated subfoveal lesions. Elligible eyes may have:

Lesion size ≤ 12 disc areas in size
Vision between 20/40 to 20/320 is study eye
No previous Avastin treatment
Minimum of 30 day washout since last previous treatment of lesion
No current vitreous hemorrhage
No fibrosis or atrophy involving center of fovea in study eye

For a more detailed description of the individual studies, please contact Starr Hendricks at (404) 299-0529.

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ate an internal tunnel incision that is a functioning one-way valve for a correctly structured incision. We believe the eye is pressurized and maintains its pressure. Pressure inside the eye keeps the wound closed, and the greater the pressure the more tightly the wound is closed. Therefore, those eyes in which there is low pressure, a leaky wound, a vitreous wick, or a thermal burn probably are all at an increased risk of endophthalmitis, as the wound integrity does not insure maintenance of pressure, and the one-way valve effect is compromised, allowing movement of fluid in and out of the eye. As the pressure drops, organisms may enter the eye. Hopefully, this documented increased risk of endophthalmitis is a transient phenomenon. Perhaps as cataract surgeons better engineer the creation of scleral tunnels and clear corneal incision entries, the risk of endophthalmitis may decrease. Otherwise, as the population ages, and since the risk of endophthalmitis increases with age, there is potential that the risk of endophthalmitis may actually even increase further.

We participate in the following insurance plans :

Aetna U.S. Healthcare
American Preferred Provider
BCBS of Georgia
Beech Street
Blue Choice
CCN PPO
Choice Care Network
Cigna
Companion Workers' Comp Plan
Corvel
Coventry Healthcare
Evolutions Healthcare System
First Health PPO
First Medical Network
Focus Workers' Comp PPO
Galaxy Health Network
Great-West
Health Network of America
Humana
Integrated Health Plan
Kaiser MultiChoice POS
Managed Care 2000
Managed Care Strategies
Medicaid, Peachcare for Kids, Georgia
Better Healthcare
Medical Resource Network
Medicare
Medicare Railroad
Multiplan PPO
National Preferred Provider Network
National Provider Network
Phystar
Preferred Plan of Georgia
Private HealthCare Systems
Southcare PPO
Synergy Health Network
Three Rivers Provider Network
TriCare PPO, HMO
State Health
USA Managed Care Organization
WellCare Medicare HMO

Other plans are pending, please call to see if we are participating (770) 907-9400.

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