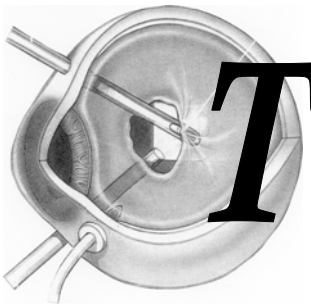
Volume I, Number 2 Summer 2000



The Light Pipe

The newsletter of Georgia Retina, P.C.

Photodynamic Therapy (PDT) - Beyond the Headlines

As you know Photodynamic therapy (PDT) with Visudyne (Verteporfin) was recently approved by the FDA for treatment of subfoveal choroidal neovascularization associated with age-related macular degeneration. The data from the multicenter **TAP (Treatment of ARMD with Photodynamic Therapy**) study was published in the October issue of the Archives of Ophthalmology. Georgia Retina was one of the centers in the Phase IIIb (**VIP** – Verteporfin in Photodynamic Therapy) study. We therefore began to develop experience with this technique, last summer.

The study was a prospective randomized trial, which included sham treatment of control patients. 609 patients were randomized and followed for 2 years. The primary outcome was "moderate visual loss" (15 letters or 3 lines on the ETDRS chart) and secondary outcome was "severe visual loss" (30 letters or 6 lines). 57% of placebo treated patients

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Our Practice News

The one constant at Georgia Retina is change. With the help of our wonderfully dedicated staff, we have been able to add to our treatment capabilities.

Our Northside / Saint Joseph's office was closed in May and early June for renovations, and reopened June 21. We are very pleased with its fresh new appearance, smooth patient flow. and new equipment.

We have acquired two new lasers. One is the Visudyne (689 nm) laser, which enables treatment to be performed to subfoveal neovascular membranes while minimizing damage to the overlying neurosensory retina (see accompanying article). The other is an 810 nm diode laser which treats the deeper tissues in the choroid. This is called transpupillary thermotherapy (TTT) which appears to be useful in poorly defined choroidal neovascularization and some relatively flat choroidal tumors, such as small malignant melanomas. The 810 nm laser can also be used to treat other retinal lesions which are partially obscured by vitreous or pre-retinal hemorrhage. Cyclophotocoagulation can be performed in the office with this laser using a special contact probe, in cases of severe glaucoma.

New digital photography systems have been installed at our Marietta and Riverdale offices. A similar system is already in place in Decatur. With these systems, test results can be discussed with patients during their visit. A significant bonus is the potential ability to network the offices digitally, so that immediate consultation can be obtained from a second physician at another office. We are proud to have developed the Georgia Retina Foundation, a non-profit organization that will fund clinical research. The Foundation may also be able to help defray hospitalization costs for selected indigent patients.

Of course, we still place a high priority on continuing medical education. Our Retinal Pearls seminars will be coming again soon. Watch your mail for announcements. We hope to see

Our Physicians

Michael S. Jacobson, M.D.

Scott I. Lampert, M.D.

Jay B. Stallman, M.D.

Charles L. Harris, M.D.

Clinical Challenges

Chief Complaint
"I've got the flu and I can't see."

Case History
R.F. is a 38 year old white woman who presented with acute onset of sudden vision loss. The patient states that she enjoyed perfect vision in her youth and had no prior surgery, trauma or disease until the onset of upper-respiratory symptoms. Twenty-four hours later she started to notice the onset of flashes and floaters followed by blurred vision, which progressed rapidly and significantly in both eyes. She specifically denied ocular pain, redness or photophobia. Regarding flu symptoms, the patient denied neck stiffness but she related achy muscles, a painful back, shaking chills and headache. She denied significant cough, sore throat, or diarrhea.

Medical History
Perfect health, other than being on a Weight Watchers diet which she began in October, and a recent fractured left foot (December 18, 1999). Medications: Oral contraceptives. Allergies: None. Family/Social History: She is an office manager, married with two children, smokes two packs per day. No alcohol use or recreational drug use.

Comprehensive Ocular Examination
Visual acuity: 20/400 OU; pupils: 3 mm, equally reactive without afferent defect; motility: normal, no strabismus; visual fields: multiple bitemporal paracentral scotomas; slit lamp examination: unremarkable, anterior vitreous: normal, rare nonpigment cell; tension: 12 mmHg OD and 13 mmHg OS; funduscopic examination: C/D OD - 0.1; vessels: mild arterial attenuation, venous engorgement, and vascular tortuosity; macula: OD - feathery edge superficial white lesions which partially obscures retinal vessels, nasal hemi-macula and rare lesions temporally (figure 1) OS - same white lesions, peripheral retina: normal, fovea: increased orange reflex (figure 2).

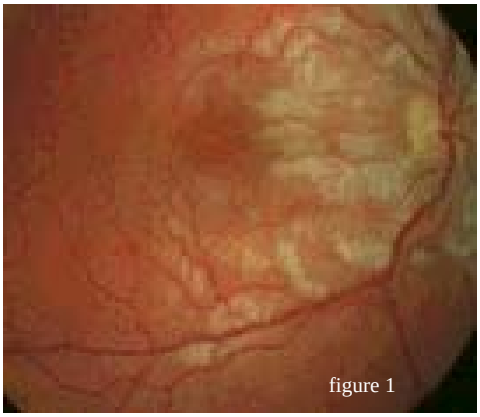
figure 1

wide angle of right fundus

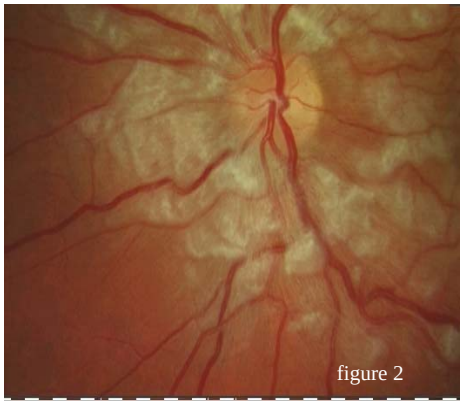
figure 2

close up of left disc

Impression
1. Profound decreased vision, both eyes, of sudden onset.
2. Preceding flu-like illness.

The differential diagnosis of a "crop" of white lesions in the posterior pole is extensive. The diagnoses one should consider in the evaluation of this patient include AMPPE, Purtscher's retinopathy, cotton wool spots arising from autoimmune disease, hematologic disorders, thromboembolic disease or other causes. Systemic laboratory investigations were done, including a sed rate, also an MRI scan and lumbar puncture, all of which were normal. With these laboratory tests, we can essentially exclude hematologic disorders and autoimmune
diseases such as lupus. Remaining possibilities include Purtscher's retinopathy, AMPPE, and thromboembolic disease. At this point, the patient was referred for a retinal consultation. Closer inspection of the white lesions reveals that they are not typical AMPPE lesions because they are superficial and not at the level of the RPE. Furthermore, the confluence of the lesions is something not frequently observed in AMPPE. Purtscher's retinopathy can be excluded due to lack of risk factors such as pancreatitis or fat emboli from long bone fracrtures. This patients' fracture was of her foot rather than of a long bone. This history is therefore more of a "red herring".
The diagnosis may already be self-evident to many of you. This patient is a 39 year old woman on oral

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Retina Q & A *Location, Location, Location!*

How do I know I am seeing a patient who is a good candidate for photodynamic therapy? Patients keep asking. *-D.P.*

When evaluating such a patient, our initial focus is not whether a patient is a photodynamic therapy (PDT) candidate. The most important issue is to recognize those patients who have a subretinal neovascular membrane (SRNV). Furthermore, the fundamental principle is to assume all patients over age 55 who exhibit hemorrhage, exudate, or serous detachment have a SRNV until proven otherwise. **Fluorescein angiography is the only way to make this determination.** Do not forget that patients can have a SRNV in the absence of drusen or significant RPE atrophy or pigmentary migration. In addition, older patients with unexplained decreased vision may have a SRNV. Cataract or opacification of the posterior capsule can sometimes make recognition of this much more difficult. Don't underestimate the value of an Amsler grid. Test your patients with it. Detection of an asymptomatic central scotoma of which the patient was not aware can help guide you to the correct diagnosis.

Once it is established that a patient has a subretinal neovascular membrane, then the question is, what are the options? **The location and character of the SRNV defines the appropriate course of management.** Prompt referral for SRNV evaluation and treatment is always the best plan, since SRNVs can grow as much as 10 – 100 microns per day. Therefore, a juxtafoveal or extrafoveal SRNV can become a subfoveal SRNV in a short period of time. Nonetheless, reduced vision of longstanding duration may not preclude treatment unless subretinal fibrosis evolves. If subretinal fibrosis evolves, then most modalities are of little value.

For **juxtafoveal** and **extrafoveal** subretinal neovascular membranes, conventional argon or krypton laser photocoagulation remain the best treatment options. For **subfoveal** subretinal neovascular membranes, as defined by angiography, there are a variety of treatment options. The treatments are tailored to the patient's situation and the patient's desires. Options include: **foveal translocation**, which is best for well-defined subretinal neovascular membranes without significant surrounding disease and which do not extend inferior to the fovea; **photodynamic therapy (PDT)**, which is only useful for subretinal neovascular membranes with greater than or equal to 50% classic features; and **transpupillary thermotherapy (TTT),** which may prove best for poorly defined subretinal neovascular membranes. No one treatment is superior in all cases.

In addition to SRNV treatment, over the past few years we have been utilizing a variety of surgical techniques that permit better evaluation of subretinal neovascular membranes specifically for patients with significant submacular hemorrhages which typically obstruct angiographic visualization of the presence and/or extent of the subretinal neovascular membrane. **Pneumatic displacement of the subretinal hemorhage**, combined with tissue plasminogen activator (tPA) injection, may help "steam-roll" blood out from under the fovea. A valuable option for refractory patients may be surgical intervention with vitrectomy, in which tPA is directly injected under the retina and the blood clot is evacuated.

If you have a patient who m you suspect has an SRNV, please have the patient evaluated with **IMMEDIATE** fluorescein angiography. **Remember that time is of the essence in the evaluation of these patients. Even with all the new treatments, and despite all the media hype about them, early detection and conventional laser treatment still produces the best visual result.**

If you have a retinal question about a specific patient or general patient management, please submit it to us. We will be happy to answer promptly. If we feel your questions would be of broad interest, we will include is in a future newsletter.

MSJ

From the Administrator's Desk...

We want to know...

As I am sure we all know, keeping everyone happy when managing a doctor's schedule isn't easy today! Insurance companies dictate at which hospital the patient can have surgery, and the hospitals tell us when the OR is available. Many of our patients can't drive and their children can only get off work at certain times to bring them, and then have to take them to the internist first! We have also learned that detachments seem to come in spurts and they all need to be worked in on the same day.

Although we try our best to maintain a smooth patient flow, the need to accomodate urgent patients and to comfort those with alarming diagnoses may result in our running behind. We continue to "tweek" our schedule with the hope that we will evolve the perfect system.

In the meantime, please let me know if you or one of your patients has run into a snag when trying to schedule an appointment. It will help in our "tweeking" process and I will do my best to help. We do appreciate the feedback!

I can be reached at our Decatur office at (404) 299-5209.

Barbara Wright
Practice Administrator

ROP Zones

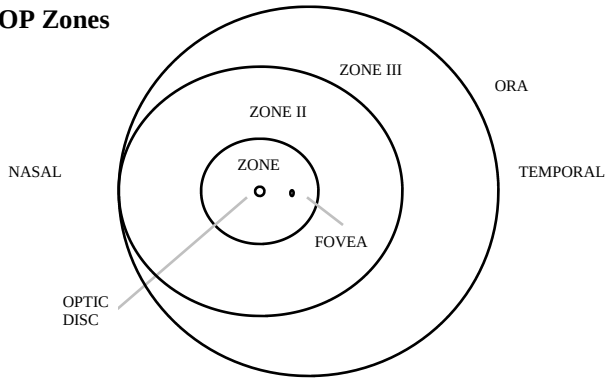

figure 3

ROP Screening

We are pleased to announce as of May 2000, Georgia Retina has been providing the retinopathy of prematurity screening examinations for the neonates at DeKalb Medical Center. Initially described in 1942, retinopathy of prematurity (ROP) has become more prevalent due to advances in neonatology and subsequent increased survival of premature infants. ROP affects between 10-16% of the high risk premature infants-usually considered to include those infants of 32 weeks gestation or less and those who weigh 1500 grams or less. In 1999, DeKalb Medical Center had 164 infants who met screening criteria.

The retina is normally fully vascularized by the 38-40th week of gestation. Premature infants with less time *in utero* do not develop mature retinal vasculature. Incomplete vascularization of the retina can result in neovascularization, vitreous hemorrhage and traction retinal detachment.

The location and severity of ROP are important criteria for evaluation and treatment. As you may recall the more immature the retina, and the greater the extent of the disease, the poorer the prognosis. Accordingly, a standard clarification has been established. Zones describes the distance that the normal vessels have developed as they expand outward from the disc towards the periphery. (figure 3) Zones quantify the degree of retinal vasculature immaturity and stages define the severity of ROP. A threshold for treatment has been established by the Cryo-ROP study.

Cryotherapy to the avascular retina had been the mainstay of treatment unless retinal detachment had occurred and then extensive vitrectomy surgery would be necessary. Recently indirect laser photocoagulation has shown promise in supplanting cryotherapy as it causes fewer complications and is easier to apply when ROP involves the posterior retina (zone 1). We have had extensive experience with both modes of treatment. In the past babies have been transferred to other facilities to receive treatment. Now Georgia Retina is pleased to be able to provide cryopexy or laser treatment at DeKalb Medical Center avoiding the danger of transporting these fragile babies to other facilities.

CLH

(Continued from page 2)

contraceptives who smokes two packs per day. As you know, such patients are at increased risk for thromboembolic events. Believe it or not, the data shows that this patient is at a *25-50 fold* increased risk of dying from a thrombotic event such as myocardial infarction, stroke, and/or pulmonary embolus. Beyond age 40, her mortality risk more than doubles. This case represents retinal vascular thrombosis (cotton wool spots) due to oral contraceptives and tobacco abuse. Dehydration secondary to aggressive dieting and the flu-like syndrome may have been an inciting factor. While I have seen a number of patients with a few cotton wool spots in either eye in women who use oral contraceptives and smoke, I have never seen a case of this magnitude.

Clinical Course

Oral contraceptives and smoking were stopped. Over the next 3 weeks the cotton wool spots and retinal edema had subsided, leaving visible cotton wool spots which were for the most part no longer confluent. Her visual acuity improved to 20/40 OD and 20/60 OS. There was remarkable resolution of the cotton wool spots. This case highlighted our awareness of the dangers of oral contraceptives in patients over age 30 or in patients who smoke. One month later, her visual acuity was 20/40 OD and 20/30 OS. The right optic nerve exhibited mild pallor, probably secondary to loss of nerve fiber layer tissue. No retinal pigmentary changes were evident in the areas where the cotton wool spots were present. Her central scotomas primarily temporal to fixation, persist.

MSJ

(Continued from page 1)
versus 43% of PDT patients had moderate visual loss. 27% of placebo vs. 17% of PDT patients had severe visual loss. In the subgroup of patients with lesions consisting of greater than 50% classic CNV, 33% of treated patients had moderate vision loss, versus 61% of controls. Only 6% of treated patients improved 3 lines, compared to 2% of controls. This data shows benefit of this treatment for primarily subfoveal lesions that are at least 50% classic CNV. Treated lesions were less likely to grow and were more likely to show cessation of fluorescein leakage than untreated lesions. Patients in the study had to have 20/200 or better vision.

In preparation for treatment, we instruct patients to bring a hat, gloves, sunglasses and a long sleeve shirt to protect them from exposure to the sun. Exposure to the sun in the first few days can result in a serious phototoxic skin burn. Additionally, it may be wise for patients to discontinue any antioxidant vitamins, which act as free radical scavengers, before the treatment. These could theoretically reduce the efficacy of the treatment, since Visudyne works through damage to the vascular endothelium, mediated by free oxygen. Furthermore, the package insert advises the discontinuation of aspirin or other platelet aggregation inhibitors, since the final event in the mechanism of action of the drug is thrombosis of the abnormal vessels. Neither of these two recommendations was addressed or studied in the trials which led to FDA approval, so their significance is uncertain.

The **treatment procedure** requires that the patient is weighed in the office, and their height measured, so that body surface area may be calculated. This calculation is applied to a nomogram to calculate the proper dose of the drug. A separate calculation of the laser spot size is performed by superimposing a reticle over the lesion on a conventional film angiogram. Factors such as the magnification of the contact lens used must be taken into account. On the computerized digital imaging system, a special software package uses MPS (Macular Photocoagulation Study) rings to measure the lesion size.

The dye is reconstituted from powder form and an IV infusion pump is used to infuse the dye over 10 minutes. The infusion must be closely monitored since extravasation of the dye can lead to skin necrosis that may require skin grafts. The irradiance and fluence of the laser must be set, and exactly five minutes later, the dye is photoactivated by a non-thermal low-energy infrared laser. The exposure lasts 83 seconds, and is painless and comfortable for the patient. Only topical anesthetic is required. While performing the treatment, no visible color change is seen in the retina. It is technically challenging to keep the aiming beam properly positioned over the lesion for the full duration, and does require some encouragement of the patients to help them maintain their fixation.

For the TAP and VIP study, patients were not required to have follow-up examination sooner than three months. We have elected to see patients more frequently to both better understand behavior of the treated lesions, and to reassure patients. Often there is little change within the first few weeks. Data so far suggests that most patients (about 90%) will have persistent leakage on fluorescein angiography at 3 months, and will require re-treatment every three months.

The treatment is quite expensive. The cost of the dye is about $1558.00 per vial for each treatment. This, plus the cost of the laser procedure itself will add up quickly, given the prevalence of ARMD. Of course, the dye is excited only by one specific wavelength laser (689 nm), which is dedicated to that dye. There are several other dyes in development. Purlytin (“Photopoint”) - tin-ethyl etiopurin (SnET2) is a dye in phase III trials being conducted by Pharmacia-Upjohn, as is Lu-Tex (Lutecium-texaphryn) or “Optrin” being studied by Pharmacylics and Alcon. Purlytin is excited at 664nm and Lu-tex is excited at 732 nm. In a few years, both the Visudyne and the lasers dedicated to it may be obsolete.

Regarding **reimbursement**, some Medicare carriers, in an attempt to reduce access to this treatment, are trying to enforce regulations, which apply criteria from the study, to determine when the treatment may be utilized. (i.e., They may not pay for anyone with vision of 20/400 or worse.) A patient with a very small lesion associated with subretinal blood might be an excellent candidate for the treatment, but would be prohibited from having it by HCFA, unless they were to pay for it themselves as a “non-covered service”. We are strongly opposed to this and feel the government is trying prevent doctors from using their medical judgement. The government is trying to practice medicine, by doing so. Unfortunately many patients will be unable to afford this treatment which can cost as much as 10,000 annually.

JBS

We participate in the following insurance plans :

Aetna US Healthcare
Aetna Select Choice HMO, Elect PPO
Aetna Managed Choice POS
Aetna Open Choice PPO
Aetna US Healthcare Medicare
AHI Healthcare Systems
American's Health Plan
Americare Health Alliance of Georgia
BCBS of Georgia
Beech Street PPO, WC
Blue Choice PPO, POS and HMO
Blue Choice Platinum (red silo)
Cadeusus Health Care Corp
Capp Care
Champus Tricare (Humana)
Cigna (PPO, HMO & Medicare)
Corvel Corporation
Community Care Network (CCN)
Evolutions HEalthcare SystemGalaxy
Emorycare through CIGNA
First Health
Formost
Galaxy Health Network
Georgia First
Georgia Better Healthcare
Grad y Healthcare, Inc - Medicare
Health Payors Organization
Healthstar
Health Network America
Health Management Network, Inc.
Highway to Health
Humana (HMO and POS)
Managed Care Strategies
Medicaid - EDS
Medicare - BCBS of Alabama
Medicare Railroad
Medical Resource Network
National Preferred Provider Network
Network Atlanta
One Health Plan
PPO USA Network
Preferred Health Network
Preferred Plan of GA PPO, EPO
Private Healthcare Systems PHCS
Promina Health Systems
Pronet
Prudential Healthcare HMO, PPO
Prudential Emory & Select Care
Railroad Medicare
State Health Benefit Plan
United Healthcare
(Metrahealth PPO, EPO, POS)
USA Managed Care Organization

Other plans are pending, please call to see if we are participating

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