



# Ophthalmology Update

Richmond Eye Associates, P.C.

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## Ophthalmic Topics of Interest to the Medical Physician

### Controversies in Ophthalmology

This issue applies recent clinical research to areas of controversy in Ophthalmology.

#### Inside This Issue

|  |   |
|--|---|
| Routine Laboratory Testing Prior to Cataract Surgery | 1 |
| Night Light Use and the Risk of Myopia in Children   | 1 |
| Inhaled Steroids and Cataract Risk                   | 2 |
| Clinical Pearl: Roth Spots - Endocarditis Only?      | 2 |
| Does Plaquenil Usage Carry any Real Retinal Risk?    | 3 |
| Office locations, addresses, and phone numbers       | 4 |

#### Is Routine Laboratory Testing Necessary Prior to Cataract Surgery?

Cataract extraction with lens implant is one of the most commonly performed surgical procedures in the United States today, and is one of the largest single expenses to Medicare in total dollars. Not only is the population aging, but the functional ability of older individuals is being preserved through advances in medicine in general. Thus, good vision remains a top priority for our older patients, many of who remain productive in the work force. Cataract surgery today is characterized as a rapid, painless, and effective procedure, with visual recovery complete within weeks.

Typically performed in an outpatient, ambulatory surgery setting, cataract surgery usually involves two operating room staff, a nurse anesthetist, and the surgeon. The nurse anesthetist sedates the recumbent patient with rapid, short acting intravenous agents, and a local anesthetic is then given in the periorcular space of the operated eye. The surgery proceeds shortly thereafter, and often is completed within 15 to 20 minutes. In many cases the patient awakens during surgery or

near its completion, but remains comfortable. The anesthetist monitors the patient throughout.

Many ambulatory surgery centers or community hospitals dictate what pre-operative evaluation is necessary prior to any monitored care anesthesia cases. Often preoperative laboratory testing is required within 2 to 4 weeks of the procedure, including CBC, EKG, CXR, serum electrolytes, BUN, creatinine, and glucose. It has been estimated that over 150 million dollars are spent annually in pre-operative laboratory testing for cataract surgery.

**“Over 150 million dollars are spent each year on preoperative cataract lab testing.”**

A large, randomized, prospective study<sup>1</sup> published in the New England Journal of Medicine looked at whether or not routine preoperative laboratory testing was beneficial

*Continued on page 4 . . .*

#### **In the Next Issue of**

#### **Ophthalmology Update:**

##### **The Best Ophthalmic Drugs for:**

- Seasonal Allergic conjunctivitis
- Acute conjunctivitis
- Dry eye
- Blepharitis

#### Does Night Light Use Cause Myopia in Children?

The prevalence of myopia (nearsightedness) in the general population is increasing, reaching 70-90% in some Asian populations. A study published in Nature in May 1999<sup>1</sup>, “Myopia and Ambient Lighting at Night”, attempts to correlate the development of myopia in children with exposure to ambient lighting at night during the first 2

years of life (night light or room light use). In this study, 479 children in a pediatric ophthalmologist’s practice at Children’s Hospital of Philadelphia were enrolled. The parents were asked to complete a questionnaire asking how the children’s rooms were lit before age 2. At the time of the study, the children

*Continued on page 3 . . .*

## The Controversy of Inhaled Corticosteroids and Cataract Risk

Intranasal corticosteroids are among the most effective medical treatments for the millions of patients with asthma and seasonal allergic respiratory disorders. A study recently published in the *Journal of Allergy and Clinical Immunology* essentially gives a green light for the use of intranasal steroids in patients under the age of 70 as not increasing the risk of cataract development.

In this retrospective study<sup>1</sup>, 286,078 patients under age 70 were classified as users of only nasal steroids, users of only oral steroids, and non-users of either. The United Kingdom General Practice Research Database was used. Computerized medical records were used to identify the diagnosis of cataract. The incidence of cataract was found to be similar between intranasal steroid users and non-users. However, oral steroid use was found to be associated with approximately twice the risk of cataract development, and this risk increased to a 4-fold risk in those with 10 or more prescriptions for oral steroids.

In spite of this apparent safety of intranasal steroid use, a 1998 study<sup>2</sup> published in *JAMA*, showed that prolonged administration of high dose intranasal steroids increased the risk of cataract extraction in patients age 70 and older. In this study, the provincial health insurance plan database of Quebec was used to identify patients who had

cataract extraction with at least five years of prior follow-up. All prescriptions for oral and inhaled corticosteroids were identified.

Of 10,214 patients with cataract extraction, 3677 had 5 years of prior follow-up data. 21, 868 control cases were selected. In patients with no oral steroid use but with 3 years of inhaled steroid use, the risk of cataract extraction was 3 fold that of those not exposed to inhaled steroids. After 2 years of use, high dose inhaled steroid users also had a 3 fold increase in cataract extraction. With oral steroid use, the risk of cataract extraction increased after only 1 year of exposure.

In reality, many patients are exposed to both inhaled and oral corticosteroids. In a 1996 study from the *Annals of Pharmacotherapy*<sup>3</sup>, the use of inhaled steroids seems to offset the risk of cataract extraction in patients otherwise using oral steroids for steroid-dependent asthma. While in this study the long-term use of inhaled steroids appeared relatively safe, the addition of any oral corticosteroids as pulse therapy or any pattern of regular use increased the risk of posterior subcapsular cataract (PSC - a particularly visually significant type of cataract commonly found in the young, in diabetics, and in steroid users.)

### **Intranasal and Oral Steroid Use and Cataract**

- **After 3 years of use, intranasal steroid use increases the risk of cataract extraction in the elderly 3 fold.**
- **In younger patients, intranasal steroid use appears safe, but more long-term studies are needed.**
- **Regular and pulse oral steroid use increases the risk of cataract in all age ranges.**
- **Reducing oral steroid use by adding intranasal steroids appears to reduce the overall risk of cataract compared to oral use alone.**

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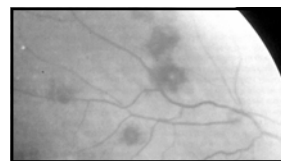
## Clinical Pearl: Differential Diagnosis of Roth Spots

Roth Spots are commonly seen retinal lesions which may be visible with direct ophthalmoscopy, as performed by a medical physician through an undilated pupil. Once felt to be pathognomonic for subacute bacterial endocarditis, it is now known that Roth Spots are found in a variety of medical conditions.

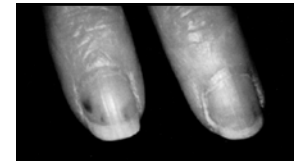
Roth Spots are characterized as a round, oval, or flame shaped retinal hemorrhage with a white center. Prior to pathological studies, it was inferred that the white center was focal retinitis from septic emboli. Now it is believed that Roth Spots result from the rupture of retinal capillaries with exudation of whole blood, followed by platelet fibrin thrombus formation that appears as the pale white center.

### **The differential diagnosis of Roth Spots now includes:**

- Subacute Bacterial Endocarditis (as a hallmark finding)
- Leukemia (with the white centers actually being leukocyte aggregates)
- Profound anemia
- Thrombocytopenia
- Sepsis
- Hypertension
- Diabetes
- Carbon monoxide poisoning
- Intracranial hemorrhage
- Oral contraceptive use
- Birth trauma
- Physical abuse during childhood



**Retinal Roth Spots**



**Splinter Hemorrhages**

- Prolonged intubation
- Ocular toxoplasmosis
- Multiple myeloma
- HIV retinopathy
- Systemic lupus

Typical physical findings in subacute bacterial endocarditis include fever, chills, heart murmur, splenomegaly, and fundoscopic and peripheral signs of septic embolization including Janeway lesions (painless erythematous palm lesions), Osler's nodes (tender purple-red fingertip and toe lesions), and splinter hemorrhages beneath the nail beds. Roth Spots are actually reported in only 5% or less of endocarditis patients.

Other ophthalmic findings of subacute bacterial endocarditis include conjunctival hemorrhages, retinal cotton wool spots, central retinal artery occlusion, ischemic optic neuropathy, and cranial nerve palsies.

## The Risk of Retinal Toxicity with Plaquenil Use.

Plaquenil (hydroxychloroquine) is a commonly used drug for rheumatoid arthritis, systemic lupus, and other auto-immune diseases. Antimalarial drugs (4-aminoquinolone derivatives) such as Plaquenil and chloroquine have a high affinity for melanin granules, and thus tend to accumulate in the choroid, ciliary body, and retinal pigment epithelium of the eye. While retinal toxicity is reported with Plaquenil, it appears to be exceedingly rare. Chloroquine is known to be more retinal toxic, but is less frequently used due to other systemic toxicities. Is the risk of retinal toxicity from Plaquenil enough to justify frequent ophthalmic testing, and are retinal complications reversible if they are discovered?

It has been felt in the past that Plaquenil in a dosage of 400 mg per day or less has negligible toxicity risk. However significant toxicity has been reported recently as dosages within this range. In the September 1999 Archives of Ophthalmology<sup>1</sup>, a case was reported of a 45 year old woman taking 400 mg of Plaquenil daily for 6 years. She presented to the ophthalmologist with best corrected visual acuity of 20/50 bilaterally, poor color vision, severe central scotomas bilaterally on visual field testing, and typical fundoscopic pigmentary changes as a “bull’s-eye pattern” of the macula.

Of significance in this patient is that the Plaquenil dosage was 8.5 mg/kg (patient weight of 103 lbs.). Other studies have found that a safer cutoff dosage of Plaquenil is 6.5 mg/kg of body weight/day. Nevertheless, some case reports have demonstrated toxicity with dosages as low as 200 mg per day! Renal insufficiency, liver disease, and especially long term use (more than 10 years) have been found to be additional risk factors for retinal toxicity, possibly accounting for these variations. At a dosage of 6.5 mg/kg per day or 400 mg/day or less, retinal toxicity will develop in only 1% or less of cases.

In cases such as above, where there are visible retinal changes, significant visual field defects, and reduced visual acuity, discon-

tinuation of the drug will not allow for the recovery of visual loss. In fact, in some cases the findings will progress further. It is important to diagnose possible toxicity before findings are so clinically apparent. The goal of ophthalmic examination is to identify signs of toxicity before there is irreversible retinal damage. The most sensitive testing for this appears to be serial static (automated) visual field testing, possibly using a red test object. A baseline visual field should be done before or shortly after the initiation of Plaquenil. This should then be repeated in 9 to 12 month intervals to look for subtle declines in sensitivity in within the central 10 to 20 degrees of fixation. If a decline is discovered, the visual field test should be repeated for verification, and there should be strong consideration for stopping the drug.

Another important finding to follow is the appearance of the macula. Baseline fundus photos can be compared to future fundoscopic examinations to search for evidence of a pigmentary retinopathy (often very subtle). Color vision testing is usually performed, but it is less sensitive than visual field testing in cases of toxicity. Patients can self-monitor their vision at home at weekly intervals at home with an Amsler grid. There is some evidence that fading of the squares may indicate early toxicity.

Fluorescein angiography is not routinely obtained as a baseline test. However, if there is evidence of an macular disorder prior to initiating Plaquenil, a baseline fluorescein angiogram may be important for future comparison. In some cases, it may be difficult to distinguish Plaquenil retinopathy from other retinal disorders without the fluorescein angiogram.

Thus, it appears that regularly scheduled examinations to rule out Plaquenil toxicity are justified, and the early detection of toxicity can help to prevent progressive visual loss.

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<sup>1</sup>Maturi RK et al. Arch Ophthalmol 1999;117:1262-1263.

## Night Light Use and the Risk of Myopia (from page 1)

ranged from age 2 to 16 (median of 8). The authors found a strong correlation between ambient illumination at night ( $P < .00001$ ) and the development of myopia. 16% of parents had kept the child’s room fully illuminated at night, and 55% of these children were myopic. 50% of the parents used a night light, and 34% of these children were myopic. 34% of the parents reported no illumination in the child’s room, and 10% of these children were myopic. Children with medical eye problems were excluded from the study.

While at first glance these results seem impressive, in fact the study is so flawed with design errors that no conclusion can be drawn from the data. The authors admit that the study has limitations, but go on to recommend that “it seems prudent that infants and young children sleep at night without artificial lighting in the bedroom, while the present findings are evaluated more comprehensively.” It is this author’s, and other’s<sup>2</sup>, opinion that even this recommendation is not warranted.

### Flaws of the Night Light Study:

- Most obvious, no data was collected regarding the refractive status of the parents! Since myopia is known to be inherited, and myopic individuals have poorer vision at night, the final true conclusion of this study may be that **myopic parents** are

more likely to use night lights in their children’s rooms, and their children are myopic through genetic inheritance.

- No information was given regarding how the children were selected to be included in the study. While some were excluded due to medical ophthalmic problems, this was **not** a group of patients examined consecutively. This introduces unacceptable selection bias on the part of the observer as well as the participating parent.
- No correlation was made between the age of the child and the development of myopia. Myopia developing in a 16 year old is of a different nature than that developing in a 2 year old.
- This group of patients does not represent a valid cross-section of the general population, since the parents were voluntarily visiting a hospital-based pediatric ophthalmologist.
- Fully 16% of the sample used full room illumination at night, which seems abnormally high, also indicating selection bias.
- Human eyelids effectively block all ambient light when closed, questioning the plausibility of this hypothesis.

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<sup>1</sup>Quinn GE et al. Nature. 1999; 399: 113-114.

<sup>2</sup>Appen et al. Arch Ophthalmol. 2000(5); 118: 701-702.

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*Ophthalmology Update*

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**Pre-operative Labs (page 1)**

in the safety of cataract surgery. This multicenter study included 9 surgery centers evenly divided between ambulatory surgery centers, academic medical centers, and community hospitals. 19,557 private practice cataract procedures were randomized to having routine preoperative testing, or no routine testing. History and physical examinations were performed preoperatively on all patients, and patients in the no-test group did not undergo lab testing unless they presented with a new or worsening medical problem that would have warranted such testing anyway.

The medical outcomes were assessed for a total of 9408 patients who had preoperative testing, and 9411 who did not. Intra-operative medical complications, and medical complications occurring within the first week were recorded. The overall rates of intra and post-operative complications were found to be the same, or about 3%, for both groups. The most common medical events in both groups were hypertension and arrhythmia requiring treatment. There was found to be no significant difference between the two groups. The authors of the study concluded that routine preoperative laboratory testing prior to cataract surgery did not significantly increase the safety of the procedure. Instead, targeted laboratory tests based on the history and physical evaluation were recommended.

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Schein OD et al: The value of routine preoperative medical testing before cataract surgery. N Engl J Med 342:168,2000.

**Steroids and Cataract (page 2)**

The first and second studies cited above look at different outcomes in regard to cataract development. The first study looked at the development of any cataract in a younger, under age 70, patient group. The second study looked at the final endpoint of cataract development, cataract extraction, in an older population. Clearly, cataract develops over a long period of time, and neither study examines the outcome of a lifetime of steroid use, whether oral or intranasal. With intranasal steroids gaining acceptance and more widespread and long-term use, an increased risk of cataract development may extend into the younger, under 70 age group. The effects of very long-term intranasal steroid use need to be monitored. However, in cases of steroid dependent conditions, intranasal steroid use appears to lower the risk of cataract development compared to oral steroid use.

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<sup>1</sup>Derby L, et al. Risk of cataract among users of intranasal corticosteroids. J Allergy Clin Immunol 2000;105(5):912-916.

<sup>2</sup>Garbe E et al. Association of inhaled corticosteroid use with cataract extraction in elderly patients. JAMA 1998;280:539-543.

<sup>3</sup>Levy HB et al. Annals of Pharmacotherapy 1996;30:1324-1327.