



The donut-hole technique for dense cataracts

Why pneumatic retinopexy fails

Ostrich eggshell as a substitute bone-graft implant

Nd:YAG vs argon-YAG in Filipino eyes

The changing pattern of retinoblastoma

Childhood cataract: Profile at the Philippine General Hospital

A case of hidden eye

Brief reports on malignant melanoma and retinal dysplasia

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Published quarterly, Number One of Volume One is dated January–March 1969. Entered as a third-class mail matter at the Manila Post Office on February 13, 1969. Journal International Standard Serial Number: PHISSN 0031 - 7659. Vol. 29 No.1, March 2004.

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**ANNOUNCEMENTS**

## PAO 2004 annual conference on November 18-20

The Philippine Academy of Ophthalmology (PAO) will hold its 2004 annual convention on November 18 to 20 at the Shangri-La Hotel in Mandaluyong.

With the theme "Look the Future in the Eye," the convention focuses on pediatric ophthalmology and strabismus to draw attention to the growing number of blind and visually impaired children in the country.

"They are our hope and future," says PAO President Dr. Marcelino D. Banzon, citing the appropriateness of the theme. Yet, they are also the "most vulnerable" to the many causes of blindness and visual impairment, which are easily preventable with early screening and management, he adds.

Prominent international pediatric ophthalmologists and strabismologists have been invited to shed light on the different ophthalmic disease entities affecting children. Among them are Dr. Kenneth Wright, Dr. Mohamad S. Jaffar, Dr. Ken K. Nischal, Dr. John W. Shore, and Dr. Sonal Farzavandi. Meanwhile, Dr. Tekeyuki Akahoshi and Dr. Abhay Vasavada will share more pearls on phacoemulsification. The opening session will have as speaker Victoria Garchitorena, president of Ayala Foundation.

Dr. Ma. Dominga B. Padilla, who heads this year's organizing committee, said PAO's 2004 meeting will have many "firsts." It will feature two new courses on topics that are becoming more and more important to ophthalmologists—ophthalmic photography and computerization of the ophthalmic practice. The annual photography contest will also include a category on digital photography. Also, all registered participants will get CDs containing a compilation of selected lectures.

## Joint PAO-AAO meeting eyed for 2005

The Philippine Academy of Ophthalmology will mark the 60th year of organized ophthalmology in the Philippines with a proposed joint meeting with the American Academy of Ophthalmology.

Dr. Romulo N. Aguilar, former PAO president and head of the committee undertaking preparations for the celebrations, said the proposal has been accepted by the AAO and a memorandum of understanding is due to be signed soon.

Dr. Aguilar said this marks the first time that the AAO is holding a joint meeting with a national ophthalmology organization, having done so in the past only with supranational organizations.

The meeting is slated November 28 to December 1 at the Shangri-La Hotel in Mandaluyong.

The convention is also expected to draw participants from the Asia-Pacific region.

It will serve as a fitting highlight of the PAO's celebration of 60 years of organized ophthalmology in the country. Organized ophthalmology began in the Philippines in 1945 with the founding of the Philippine Ophthalmological and Otolaryngological Society.

Dr. Aguilar is joined in the anniversary celebration committee by Drs. Salvador Salceda, Alejandro de Leon, Marcelino Banzon, Ma. Dominga Padilla, Carlos Naval, Winston Villar, Teresita Castillo, Reynaldo Santos, Heriberto Guballa, Mary Rose Pe-Yan, and Ronald Yutangco.

## 2nd PAO-SERI confab

The Philippine Academy of Ophthalmology (PAO) and Singapore Eye Research Institute (SERI) will hold their second joint conference on July 29 and 30, 2005.

The two-day conference will have a mix of prominent local and Singaporean ophthalmologists to speak on glaucoma and conditions affecting the retina.

On the first day, clinical topics will be discussed while, on the second day, research methodology will be tackled.

For the first time, the residents' research paper contest will be presented at the PAO-SERI conference instead of the PAO annual convention.

Sponsored by Novartis, the research paper contest is open to all senior residents in ophthalmology. Those who want to take part have until April 31, 2005 to submit their paper to the PAO (+63-2-8135324, [www.pao.org.ph](http://www.pao.org.ph)).

In charge of organizing the PAO-SERI conference is PAO's Adhoc committee on research. Dr. Franklin Kleiner is the chair while Drs. Jessica Marie Abaño, Leo Cubillan, Heriberto Guballa, Patricia Khu, Ruben Lim Bon Siong, and Reynaldo Santos are members. The committee is advised by Dr. Alejandro De Leon.

Dr. Manuel Delfin chairs the subcommittee that will oversee the contest. He is assisted by Drs. Santiago Antonio Sibayan and Lee Versoza, and advised by Drs. Guballa and Kleiner.



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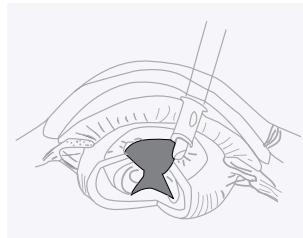
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**ORIGINAL ARTICLE 118**

*A phacoemulsification chopping technique that attacks the posterior plate*

M C D Reyes, L G Verzosa

Creating a donut-shaped nucleus before chopping it off offers a safe technique when dealing with dense cataracts that have tough posterior plate.

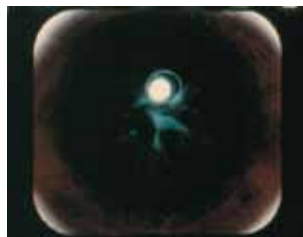


**ORIGINAL ARTICLE 127**

*Ostrich eggshell as an onlay bone-graft substitute for orbital blow-out fractures*

RA Yadao, et al.

Ostrich eggshell has shown biocompatibility and stability as a substitute bone graft for orbital floor defects. But further studies are needed to establish whether fibrovascularization and implant resorption or extrusion would occur in the long run.

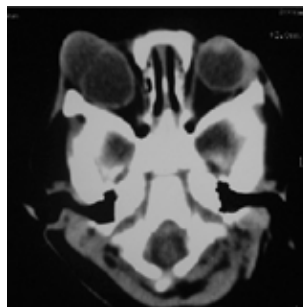


**ORIGINAL ARTICLE 140**

*Profile of childhood cataract cases at the Philippine General Hospital*

J V Tecson, A P D Santiago

Rubella infection is the major identifiable cause of childhood cataract. But the disease remains idiopathic in more than 60 percent of cases.



**CASE REPORT 144**

*The hidden eye*

R M Joaquin-Quino, et al.

The second documented case of cryptophthalmos in the Philippines is diagnosed at the University of the Philippines-Philippine General Hospital.

## EDITORIAL

# Our thirst for new knowledge

*Our resource limitations in the face of the wealth of studies provided by developed countries should not discourage us from pursuing our own research. Research will not only add to the current volume of information we have but also help us formulate appropriate treatment approaches, preventive programs, or health policies.*

Medical research is one of the most potent productive forces in society. Developing novel mechanisms in the understanding and new strategies in the treatment of diseases are the results of endless research and countless studies, both inside laboratories and in clinical settings. The United States (US) National Institutes of Health (NIH) is spending \$20.3 billion for research in 2004, apportioned among 27 institutions and centers.<sup>1</sup> The US pharmaceutical industry spent more than \$24 billion for Research and Development (R & D) in 1999 for nearly twice the number of biomedical research projects the US government undertook.<sup>2</sup> These expenditures accounted for 20.8% of sales in the industry. From 1985 and 1995, the industry's investments in R & D nearly tripled; they have provided the largest share of all US expenditures for R & D since 1980.<sup>2</sup>

The question may be asked: Why is the US spending so much on biomedical research when expenses for pharmaceuticals make up a small segment of the total daily per capita expenditures of Americans: \$0.64 versus \$8.45 for housing and \$7.94 for food?<sup>3</sup> The answer can be found in the editorial of S.J. Giorgianni<sup>4</sup> in connection with the 150th anniversary of Pfizer Corporation in 1999: "Modern medical technology makes it possible to manage more diseases and treat them more effectively and with greater degree of safety than ever before. As a result, people with chronic or debilitating disease can have their quality of life transformed from merely existing to robust, active living. They live productively within the fabric of society because of research."

Knowledge and innovation are powerful forces that improve the lives of people. Today's advances in medicine are the results of a forward-looking investment in biomedical research. The global leadership of the US in discovery, learning, and innovation, for instance, rests on investments in fundamental research and education. As proof of this success, the US publishes about one third of the world's scientific literature, the 15 European Union (EU) countries another third, and the rest of the world the remaining third.<sup>5</sup> The US produced the most number of papers in all fields worldwide; consequently its work are the most cited at an average of 13.5 per paper.<sup>6</sup> Among the top ten nations according to output of published journal articles in science between 1992 and 2002<sup>7</sup> as indexed by ISI (Table 1), the US ranked number 1, followed by Japan and Germany.

What factors account for the variations in biomedical research productivity worldwide? Per capita gross national product (GNP) and R&D expenditure were the two most important factors among ten social and economic indicators studied in a multiple regression model.<sup>8</sup> This means that a nation should have the resources and finances to conduct research with major scientific impact. The relationship between national research funding and English proficiency on publication output in developed countries was also studied showing significant results ( $p=0.04$ ;  $p<0.01$ , respectively). These two variables explained approximately 71.5% of the variation in publication rate ( $r=0.85$ ;  $p<0.01$ ).<sup>9</sup> Normalized for population size, English-speaking nations and certain northern European countries had the highest rate of publication while Asian countries had generally low rates of publication.<sup>9</sup>

In terms of frequency of citations, the US ranked first, followed by the United Kingdom (UK) and Germany (Table 2).<sup>10</sup> Japan ranked fourth, largely because many of the articles were written in the native language. In ophthalmic research from 1991 to 2000,

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the US contributed 51.5%, followed by UK (11.3%), and Japan (6.5%).<sup>11</sup>

Research output of developing countries is lower primarily because of limited government funding. In the Philippines, sources of research funding include university grants, select government agencies like the Department of Health (DOH), local and international nongovernment organizations (NGOs), and local and international foundations. Funds are generally limited to the areas of interest sponsored by these organizations. Another factor affecting research output in developing countries is the lack of investigators with doctorate degrees especially in the basic sciences. In the last survey of the top 20 universities in Asia, none of the universities in the Philippines was included because of low research output and few professors with PhD.<sup>12</sup>

Table 1. Top 10 nations in research output.

Rank	Country	Number of Papers*
1	United States	2,702,477
2	Japan	697,468
3	Germany	641,695
4	England	589,894
5	France	475,536
6	Canada	357,199
7	Italy	299,843
8	Russia	264,062
9	People's Republic of China	206,698
10	Australia	205,441

\*Published journal articles in 22 main fields of science, based on papers indexed by Thomson ISI between 1992 and 2002.  
Source: ISI Essential Science Indicators

Table 2. Top 20 countries cited in clinical medicine (1992-2002).

Rank	Country	Number of Papers	Number of Times Cited	Citations per Paper
1	USA	636,932	8,600,922	13.50
2	Great Britain	149,783	1,683,670	11.24
3	Germany	143,293	1,116,097	7.79
4	Japan	143,770	1,083,033	7.53
5	France	102,532	886,302	8.64
6	Canada	70,337	885,042	12.58
7	Italy	77,417	770,101	9.95
8	Netherlands	51,716	670,650	12.97
9	Sweden	42,830	504,669	11.78
10	Australia	43,885	432,168	9.85
11	Switzerland	33,227	382,419	11.51
12	Belgium	25,270	292,120	11.56
13	Scotland	22,357	276,513	12.37
14	Spain	39,633	267,987	6.76
15	Finland	21,217	267,752	12.62
16	Denmark	20,869	260,791	12.50
17	Israel	22,136	180,228	8.14
18	Austria	20,728	173,965	8.39
19	Norway	13,081	137,982	10.55
20	Taiwan	15,203	80,317	5.28

Source: ISI Essential Science Indicators

Our resource limitations in the face of the wealth of studies provided by developed countries should not discourage us from pursuing our own research. Diseases affect different groups of people differently and there may be genetic, cultural, or environmental factors that play a role in the development of certain disorders, which we can identify when we conduct studies among our own people. The same holds true for the effect of some drugs. There are also diseases that may be unique to Filipinos by virtue of certain genetic, environmental, or cultural predisposition. Research will not only add to the current volume of information we have but also help us formulate appropriate treatment approaches, preventive programs, or health policies.

The search for new knowledge is often triggered by a simple observation in clinical practice. The inability to fully comprehend why an event transpired or why an illness arises leads to several questions and the formulation of a research question. If the case is rare or presents in an atypical manner, it may be reported in a widely circulated medical journal. If the case or several cases present as diagnostic dilemmas or management problems, they may lead to further laboratory or clinical investigations. This questioning and searching for answers to understand a particular disease is what leads to research. Medical research will lead to innovative thinking and discovery. The application of scientific knowledge obtained from research will not only improve health and overall quality of life but also educate and inform those who use and benefit from these discoveries.

In this issue, several local studies will give the readers insights into some of the conditions intrinsic to Filipinos. Long-term observation of retinoblastoma (*The Epidemiologic Pattern of Retinoblastoma*, pages 135-138) covering three periods highlights the varying patterns of this disease entity in children and the factors accounting for this change. A study on the different causes of pediatric cataract (*Profile of Childhood Cataract*, pages 139-142) provides an example of how blindness can be prevented in this group of patients and why there is a need to formulate a policy of screening for these disorders. Again, research consisting of systematic observation and deductive thinking led to increased understanding of these diseases.

—The Editor in Chief

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ORIGINAL ARTICLE

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# A phacoemulsification chopping technique that attacks the posterior plate

## ABSTRACT

### Objective

To describe a technique for nuclear fragmentation during phacoemulsification that addresses the tough posterior plate in 3+ to 4+ nuclear sclerosis.

### Surgical Technique

The technique involves creating a central crater, flipping the nucleus out into the supracapsular space, and creating another crater through the posterior surface that will eventually connect with the anterior crater to produce a central hole. The donut-shaped nucleus is then chopped and the fragments are aspirated with greater ease.

### Results

The technique was performed successfully in seven eyes of six patients with only minor problems. Phacoemulsification times were longer than usual because of the additional sculpting, but clinical results were not adversely affected.

### Conclusion

For dense or hard cataracts for which the surgeon anticipates a tough posterior plate, this technique is a safe alternative to the usual chopping techniques.

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Presented at the Philippine Academy of Ophthalmology Annual Convention, November 2003 and at the Vitreoretina Society of the Philippines Meeting, March 2004.

**Key words:** *Cataract, Phacoemulsification, Chopping, Nuclear fragmentation*

The authors have no financial or proprietary interest in any product used or cited in this study.

PHILIPP J OPHTHALMOL 2004; 29(3): 118-121

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THE PREVALENCE of the brunescient cataract has always been higher in the Asia-Pacific region because of its closeness to the equator. In Manila, Philippines, 43% of cataracts are brunescient compared with 20% in Tampa, Florida and 9% in Rochester, New York.<sup>1</sup> This presents a challenge for the Asian surgeon.

The problem with the brunescient cataract is its thicker dimension. When chopping is done with a 1.5mm chopping tip, as with a Steinert chopper, only the superficial layers are split, leaving a posterior plate.<sup>2</sup>

Different techniques have been described to handle the brunescient cataract. There was a general shift from horizontal to vertical cutting conceptualized by Vladimir Pfeifer of Slovenia and further developed by David Dillman and Louis Nichamin.<sup>2</sup> Horizontal chopping, according to Dr. David Chang, creates a compressive force while vertical chopping creates a shearing force, forming sharp fracture lines like broken glass.<sup>3</sup> He recommended horizontal chopping for softer cataracts and vertical chopping for harder cataracts.

Newer techniques, such as Maloney's supracapsular flip<sup>4</sup> and Joo and Kim's bevel down technique<sup>5</sup> were developed in the late 1990s to better handle the brunescient cataract. None of the techniques illustrate how to specifically handle the posterior plate.

This paper describes a technique that attacks the posterior plate by combining crater formation with nuclear flipping, creating a donut and making subsequent chopping less difficult.

### SURGICAL TECHNIQUE

The procedure was performed by 2 surgeons (MCDR and LGV) at a tertiary center on 7 eyes of 6 patients who had age-related cataracts with moderate to dense (2+ to 4+) nuclear sclerosis. Patients were 54 to 76 years old (average of 67); five were female and one was male. None of the patients had ocular problems other than the cataract, except one who had chorioretinal scars off the macula. The study conformed to the tenets of the Declaration of

Table 1. Settings for surgeon 1.

Surgeon 1	Vacuum (mm Hg)	Power (%)	Pulses/sec
Sculpt	30	40	0
Segment Removal	270	25	20
Dual Linear Segment Removal	150	45	0

Table 2. Settings for surgeon 2.

Surgeon 2	Vacuum (mm Hg)	Power (%)	Pulses/sec
Sculpt	300	40	0
Segment Removal	300	50	10
Dual Linear Segment Removal	300	40	10

Helsinki. All participants signed an informed consent.

Patients were placed under general anesthesia (5 eyes) or local anesthesia (2 eyes). Two sideports were created, one either at 6 or 12 o'clock, and the other 120 degrees counterclockwise from the first sideport. When necessary, 0.1 ml trypan blue (Blue Rhexis, Contact Care, Butsarat, India) was used to stain the anterior capsule. Sodium hyaluronate 3.0% chondroitin sulfate 4.0% (Viscoat, Alcon Laboratories, Fort Worth, TX, USA) was injected into the anterior chamber. A temporal clear corneal incision was made. A 5-6 mm continuous curvilinear capsulorhexis was created to make room for the nuclear flip (Figure 1). Hydrodissection and hydrodelineation were done with Balanced Salt Solution (BSS, Alcon Laboratories, Fort Worth, TX, USA).

The Storz Millennium (Bausch & Lomb, New York, NY, USA) was the phacoemulsification machine used. Settings are detailed in Tables 1 and 2. A well half the diameter of the capsulorhexis was made in the center, which was at least 1/2 to 3/4 the thickness of the center of the nucleus (Figure 2).

A Steinert chopper was inserted through the second sideport to hook the nucleus, inverting and landing it on the capsular bag or the supracapsular space (Figure 3). A spatula in the other side port aided in the flipping when necessary. Central sculpting was performed on the posterior plate (Figure 4) creating another well that eventually connected with the anterior well to form a central hole, causing the nucleus to assume a donut or ring shape (Figure 5). Vertical chopping was done either with the Steinert chopper and the phaco tip or with a Nagahara and a Steinert chopper. The nuclear fragments were emulsified at the iris plane.

Hydroxypropyl methyl cellulose 2% (Viscolon, Contact Care, Butsarat, India) was injected to inflate the capsular bag. The incision was extended to 5.1mm in 6 patients and a polymethylmetacrylate (PMMA) intraocular lens (IOL) with 5.25mm optic (Texel, Eagle Optics, Mumbai, India) was inserted. The clear corneal incision was not extended in 1 patient and a foldable hydrogel IOL (Hydroview 1.5, Bausch & Lomb, New York, NY, USA) with 6.0 mm optic and PMMA haptics was inserted. A final irrigation/aspiration was done, followed by reformation of the anterior chamber and a check for leaks. Postoperatively, patients were given topical antibiotic and steroid eye drops.

Data collected included preoperative visual acuity, nuclear sclerosis grading, phacoemulsification time, incidence of complications (zonulysis, posterior capsular tear, corneal edema), and one-week-postoperative visual acuity.

### RESULTS

Average effective phaco time was 2:31 minutes. Five out of the seven eyes had visual acuity of 6/15 (20/30) or

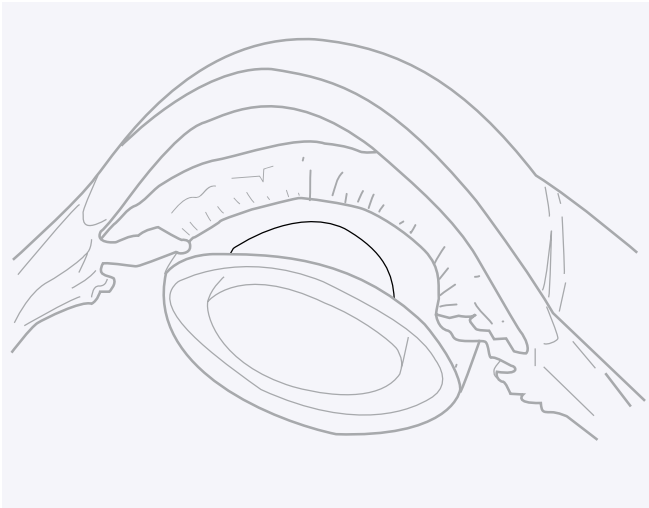


Figure 1. Creation of a 5-6 mm capsulorhexis.

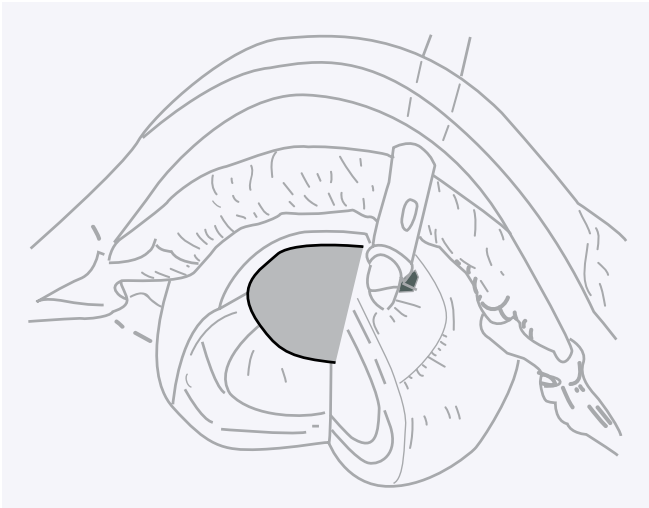


Figure 2. Central nuclear sculpting forming a crater 1/2 to 3/4 depth.

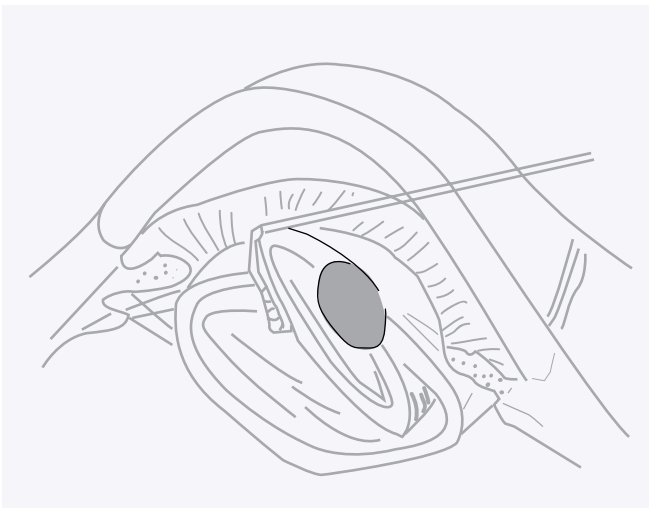


Figure 3. Nuclear flipping with a Steinert chopper.

better one week postoperatively. Two eyes of one patient had 1/4 to 1/2 quadrant zonulysis after the nuclear flip, and the IOL was inserted in the ciliary sulcus. Four eyes had transient corneal edema, which resolved within a week. None of the patients had posterior capsular tear or iris damage. One patient developed postoperative vitritis. Individual patient characteristics and results are detailed in Table 3.

### DISCUSSION

The chopping technique combines crater formation with a nuclear flip, allowing the surgeon to sculpt the posterior plate. This makes vertical chopping less difficult by debulking the central nucleus.

Zonulysis and transient corneal edema were the two most common complications found with this technique. Two of the patients developed zonulysis during the flip,

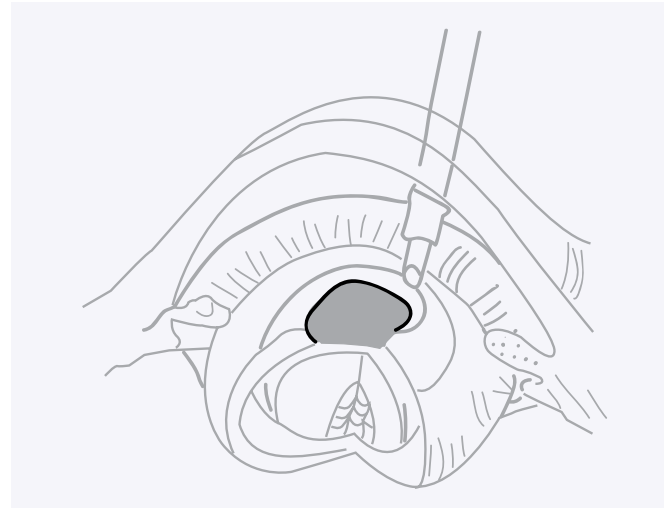


Figure 4. Sculpting of the posterior nucleus after flipping.

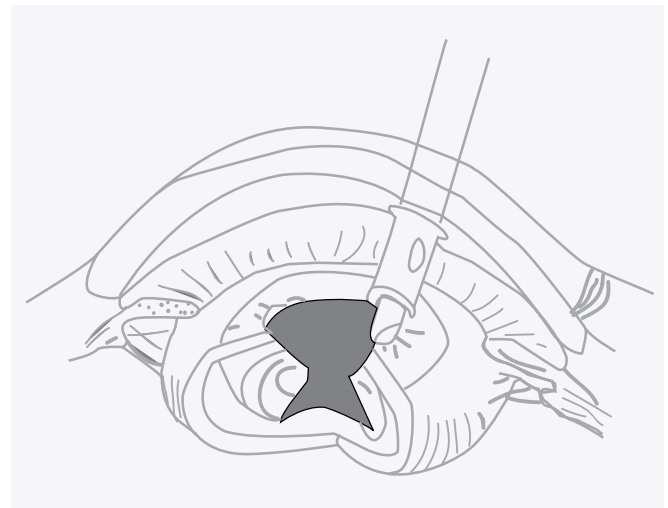


Figure 5. Formation of a donut.

Table 3. Patient characteristics and results.

Eye #	Age	Sex	Nuclear Sclerosis	Preop VA	Postop VA	Phaco Time	PC Rupture	Zonulysis	Corneal Edema	Others	Surgeon
1	76	F	2+	20/100	20/30	1:03	No	No	Yes		LGV
2	75	F	3+	20/50	20/50	0:48	No	No	No	Vitritis	LGV
3	62	M	4+	HM	20/30	6:10	No	Yes	Yes		MCDR
4	62	M	3+	HM	20/25	3:35	No	Yes	Yes		MCDR
5	54	F	2+	5/200	20/25	1:40	No	No	No		MCDR
6	73	F	3+	HM	20/70	2:09	No	No	Yes		MCDR
7	60	F	3+	HM	20/25	2:14	No	No	No		MCDR

which was attributed to the small capsulorhexis (5 mm) and the landing of the nucleus on the capsular bag after the flip instead of on the supracapsular space. Chopping in the supracapsular space places less stress on the ciliary zonules. Zonulysis occurred in the two eyes of one patient who may have had inherent zonular weakness. He also had the hardest cataract of all the eyes in this study.

There were 4 cases of transient corneal edema, which has been reported in previous studies as a more common complication of the supracapsular flip in the early part of the learning curve.<sup>4</sup> In all cases, the corneal edema resolved within one week.

The vitritis in one of the patients was a result of retained viscoelastic material during the procedure and not of the chopping technique itself. Vitritis has not been reported with the supracapsular flip or with the crater-and-chop technique.

Phacoemulsification time was rather long because of the sculpting required to form the central hole. Thus, we do not recommend this technique for softer cataracts.

We did not experience other complications of the nuclear flip like iris damage in suboptimally dilated pupils and IOL decentration because of the large capsulorhexis reported in other studies.<sup>4, 6</sup>

This technique is suited for cataracts with 3+ and 4+

nuclear sclerosis, where a posterior plate would cause a problem for the surgeon. We do not recommend it for less than 3+ nuclear sclerosis because of the added phacoemulsification time required for sculpting the plate. The technique should be done with a large capsulorhexis and in the supracapsular space to avoid zonulysis.

Subsequent studies to evaluate the technique should include the measurement of endothelial cell loss, which is said to be higher in a supracapsular nuclear flip than with other chopping techniques. This technique may also be compared with the crater-and-chop or quick-chop technique for harder cataracts with regard to complication rates, particularly posterior capsular tear and zonulysis, in a randomized trial.

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ORIGINAL ARTICLE

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# Causes of failure of pneumatic retinopexy

## ABSTRACT

### Objective

To determine the causes of failure in eyes that underwent pneumatic retinopexy at the University of the Philippines-Philippine General Hospital (UP-PGH).

### Methods

A retrospective review of pneumatic retinopexy procedures performed at the UP-PGH from January 1996 to December 2002 was undertaken. Seventeen cases were analyzed as to preoperative and intraoperative variables: age; sex; preoperative visual acuity; presence of proliferative vitreoretinopathy (PVR); extent of retinal detachment; presence of macular detachment; presence, number, and type of lattice degeneration; previous cataract surgery; surgeon factor; and intraoperative use of cryotherapy. Two-tailed Fisher's exact test and Chi square test were used in the analysis of statistical significance.

### Results

The following variables were shown to be significantly correlated with failure: eyes with breaks outside the 11-1 o'clock meridians ( $p = 0.02$ ), eyes with less than or equal to 3 quadrants of retinal detachment ( $p = 0.05$ ), and preoperative visual acuity worse than 5/60 ( $p < 0.100$ ).

### Conclusion

Failure in eyes with retinal breaks outside the 11-1 o'clock meridians suggested poor patient compliance with regard to postoperative posture. In eyes with less than or equal to three quadrants of detachment, failure may ensue as a result of spillover of subretinal fluid to uninvolved quadrants. Future success with pneumatic retinopexy will rely ultimately on careful patient selection, surgeon familiarity with the technique, and patient cooperation.

**Key words:** *Pneumatic retinopexy, Retinal detachment, Proliferative vitreoretinopathy*

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Presented at the Annual Meeting of the Philippine Academy of Ophthalmology, November 2003, and at the Vitreoretina Society of the Philippines Meeting, March 2004.

The authors have no proprietary or financial interest in any product used or cited in this study.

INTRODUCED by Hilton and Grizzard<sup>1</sup> in 1986, pneumatic retinopexy uses intravitreal gas to temporarily tamponade retinal breaks in rhegmatogenous retinal detachments. The reported single-operation success rates in a series of at least 100 eyes performed between 1986 and 1990 ranged from 69% to 84%.<sup>2</sup> The study identified the following causes of failure: new or missed breaks (14.9%), reopened initial breaks (11.2%), and breaks that never closed (4.6%). Risk factors for failure were male gender, preoperative visual acuity worse than 20/50, four quadrants or total retinal detachment, aphakia or pseudophakia, and additional pathologic findings. Despite the relatively low success rates as initial intervention, pneumatic retinopexy remains a useful alternative to scleral buckling. It offers reduced tissue trauma, less complications related to surgical technique, and lower expense.<sup>1,3</sup> Disorders of muscle balance and changes in refraction are not experienced.<sup>4</sup> Overall morbidity with pneumatic retinopexy is likely to be lesser than that of scleral buckling.<sup>5</sup>

This study evaluated the causes of and determined the risks for failure of pneumatic retinopexy done at the University of the Philippines-Philippine General Hospital (UP-PGH).

## METHODOLOGY

A retrospective review of pneumatic retinopexies performed at the UP-PGH from January 1996 to December 2002 was undertaken. Twenty-six cases of unilateral pneumatic retinopexy operations were identified. Data were extracted from patient charts and recorded in a computer database. These included patient characteristics (age, sex, and laterality) and preoperative and surgical variables.

### Preoperative variables

- Duration of blurring of vision prior to surgery
- Time between consultation and surgery
- Visual acuity
- Intraocular pressure
- Refraction
- Proliferative vitreoretinopathy (PVR) classification
- Extent of retinal detachment
- Presence of macular detachment
- Presence, number, type, and location of breaks
- Approximate size of breaks (e.g. <1 clock-hour)
- Presence and location of lattice degeneration
- Previous cataract surgery
- History of trauma

### Surgical variables

- Type of anesthesia
- Surgeon (consultant, fellow, resident)

- Amount and concentration of perfluoropropane (C<sub>3</sub>F<sub>8</sub>) injected
- Anterior chamber paracentesis
- Use of cryotherapy or postoperative laser photocoagulation
- Intraoperative complications

The types and number of surgeries required to attach the retina and the causes of failure were recorded. Preoperative and postoperative visual-acuity changes were computed using the logMAR scale.

Most of the data on preoperative variables like proliferative-vitreoretinopathy (PVR) classification and number and location of breaks were extrapolated from the preoperative drawings.

Case records analyzed were those of eyes with rhegmatogenous retinal detachment that had been treated with pneumatic retinopexy as a primary procedure. All cases fulfilled the indications for the use of pneumatic retinopexy, which were a single break no larger than 1 clock-hour located within the superior 8 clock-hours of the retina or a group of small breaks within 1 clock-hour and no PVR worse than Grade B.

Success was defined as anatomic reattachment achieved with a single operation and maintained for a minimum of 30 days. Patients with persistent detachment for 12 days or more were classified as failures.

Nine cases were excluded from the analysis for the following reasons: large breaks (> 1 clock-hour in size, 2 cases), 2 small holes that were 2 clock-hours apart (1 case), PVR Grade CP type 1 involving 2 clock-hours of the ocular fundus (2 cases), and short duration (< 2 weeks) of follow-up (4 cases).

The causes of failure of retinal attachment after a single pneumatic retinopexy procedure were determined. Two-tailed Fisher's exact test and Chi square test were used in the analysis of statistical significance.

## RESULTS

Seventeen cases were analyzed, 11 (65%) right eyes and 6 (35%) left eyes. There were 12 (71%) males and 5 (29%) females with mean age of 45.6 ± 14.6 years. The mean duration of blurring of vision prior to consultation was 46.0 ± 56.0 days. The mean number of days from consultation to surgery was 6.5 ± 9.5.

Only 6 of 17 eyes were attached with a single operation, giving a success rate of 35%. This included one case that underwent a second C<sub>3</sub>F<sub>8</sub> injection 2 days after the initial pneumatic retinopexy procedure. Out of the 11 eyes that failed the initial procedure, 9 were reoperated (5 by scleral buckling, 3 by combined pars plana vitrectomy with scleral buckling, and 1 by pars plana vitrectomy with lensectomy), of which 8 were reattached successfully for a success rate

of 88.9%. The lone failure underwent a combined pars plana vitrectomy with scleral buckling. Two of the scleral buckling surgeries used adjunctive C<sub>3</sub>F<sub>8</sub>. If the two cases that did not have subsequent surgery were excluded, the ultimate success rate would be 93.3% (14 of 15 eyes ultimately reattached).

The causes of failure were the inability of the primary break to close in 7 cases (41%) and new or missed breaks in 4 (24%).

The following preoperative and surgical variables were significantly correlated with failure: eyes with breaks outside the 11-1 o'clock meridians ( $p=0.02$ ), eyes with less than or equal to 3 quadrants of retinal detachment ( $p=0.05$ ) and preoperative visual acuity worse than 5/60 ( $p < 0.100$ ) (Table 1). Five out of the six eyes where the initial operation was successful had preoperative macular detachment. All these had improvement in visual acuity, showing a logMAR difference of 0.37 to 1.30 (logMAR preop – logMAR final). The eye without macular detachment suffered visual loss (logMAR difference = -0.14) secondary to cystoid macular edema. All eyes that were subsequently reattached with a second surgery had improved vision. The logMAR difference ranged from 0.7 to 1.86.

## DISCUSSION

In this study, the single operation attachment rate with pneumatic retinopexy of 35% is far below that reported in literature (60 to 84%).<sup>2</sup> Similarity, in a multicenter study comparing pneumatic retinopexy with scleral buckling, 2 centers each had a single-operation success rate for pneumatic retinopexy of 43% (3 of 7 eyes).<sup>6</sup> This underscores the effect of a small sample size on the outcome. Furthermore, a low success rate in the small series may imply less experience with the technique. The success in the larger series reported may reflect an increase in the success rate with familiarity of the procedure.

The ultimate success rate in this study, defined as successful reattachment of the retina after at least 2 surgeries, was 93.3%, comparable with those in other reports (92 to 100%).<sup>2, 3, 6, 7</sup> This finding validated the conclusion that eyes which fail the initial pneumatic retinopexy procedure can be reattached with subsequent surgery and that an initial attempt with pneumatic retinopexy does not lower the chances of ultimate anatomic success.<sup>2, 6</sup>

Failure in eyes with retinal breaks outside the 11-1 o'clock meridians was found to be statistically significant compared to eyes with breaks within the 11-1 o'clock meridians. Grizzard and associates found no similar correlation.<sup>2</sup> This finding in our study may suggest postural problems by the patients with retinal breaks outside the superior 2 clock-hours. These patients were required to tilt their head or lie on their side unlike those with breaks within the 11-1 o'clock meridians who maintained an

upright posture most of the time.

In the 3 eyes with total retinal detachment, the retina was reattached with the initial procedure. Failure was significantly correlated in eyes with less than 4 quadrants of retinal detachment. A possible explanation is the spillover of subretinal fluid to the attached areas. This phenomenon has been observed by various authors.<sup>8, 9, 10</sup> Yeo et al.<sup>8</sup> first reported the extension of the detachment to the previously uninvolved macula. Poliner et al.<sup>11</sup> first documented the occurrence of new retinal detachment in previously uninvolved quadrants within 2 days of the pneumatic retinopexy procedure. Chen et al.<sup>10</sup> observed the shift of subretinal fluid leading to failure by opening a break in a previously attached area of the retina. According to Algvere et al.,<sup>9</sup> the most serious and only significant complication in their series was the development of rhegmatogenous or tractional detachments in previously uninvolved inferior retinal quadrants in 24% of cases. These were attributed to vitreous inflammation induced by the gas, ocular motion, patient posture, among other causes.

A preoperative visual acuity worse than 5/60 correlated with failure at  $p < 0.10$ . A vision of worse than 6/15 (20/50) was noted by other authors<sup>2</sup> and believed to be also a risk factor in scleral buckling.

Grizzard et al.<sup>2</sup> found that failure in eyes with PVR was statistically significant compared with failure in eyes without PVR, making them conclude that eyes with early signs of PVR, such as star folds or rolled posterior edges, should not be subjected to pneumatic retinopexy. We found no such correlation. A possible reason is that Grizzard, et al., included patients with stage C-1 PVR. In our study, the 2 eyes excluded from the analysis because of C-1 PVR had previous cataract surgery and failed the initial pneumatic retinopexy procedure. Both remained detached after 2 to 5 subsequent surgeries.

The success of the procedure was not correlated with age and sex. On the contrary, Grizzard et al.<sup>2</sup> found a significant failure correlation among male patients. This was attributed to patient's poor maintenance of correct postoperative posture or to differences in ocular pathology. There have been no reports regarding the effect of age on the outcome.

The possibility that the presence of lattice degeneration could affect the anatomic outcome has not been previously suggested. Although there was no statistically significant correlation of failure with the presence of lattice associated with the primary breaks in this study, the procedure failed in all 5 eyes with breaks associated with lattice. The failure could be related to inability to visualize the breaks within the lattice or the development of new breaks within the lattice.

Twenty-four percent of the eyes in our study had new

Table 1. Eyes in which initial pneumatic retinopexy procedure failed.

Variables	No. of eyes	% Failed	p value
<i>Age</i>			
19-35	6	50.0	0.35 <sup>3a</sup>
41-66	11	72.7	
<i>Sex</i>			
Male	12	58.3	0.39 <sup>3a</sup>
Female	5	80.0	
<i>Pre-operative VA</i>			
Worse than 5/60	13	76.9	0.06 <sup>3b*</sup>
6/60 or better	4	25.0	
<i>PVR Grade</i>			
No PVR	6	50.0	0.35 <sup>3a</sup>
PVR A, B	11	72.7	
<i>Quadrants detached</i>			
4 and total	3	0	0.05 <sup>4b</sup>
1, 2, 3	14	78.6	
<i>Macular status</i>			
Macula attached	2	50.0	1.00 <sup>4a</sup>
Macula detached	15	66.7	
<i>No. of breaks</i>			
1	16	68.8	0.35 <sup>4a</sup>
2	1	0	
<i>Location break</i>			
11-1 o'clock	7	28.6	0.02 <sup>4b</sup>
Elsewhere	10	90.0	
<i>Location</i>			
Anterior	13	69.2	0.58 <sup>4a</sup>
Posterior	4	50.0	
<i>Type of break</i>			
Hole	11	63.6	1.00 <sup>4a</sup>
Tear	6	66.7	
<i>Break associated with lattice</i>			
Yes	5	100.0	0.17 <sup>4a</sup>
No	12	50.0	
<i>Lattice found elsewhere</i>			
Yes	3	66.7	1.00 <sup>4a</sup>
No	14	64.3	
<i>Previous cataract surgery</i>			
Yes	3	100.0	0.61 <sup>4a</sup>
No	14	57.1	
<i>Surgeon<sup>1</sup></i>			
Consultant	4	75.0	0.45 <sup>4a</sup>
Fellow	10	50.0	
Resident	2	100.0	
<i>Intraoperative cryotherapy<sup>2</sup></i>			
Yes	9	55.6	0.33 <sup>4a</sup>
No	4	100.0	

<sup>1</sup>One lacking entry for "surgeon"

<sup>2</sup>Eyes with posterior breaks excluded

<sup>3</sup>Chi-square test

<sup>4</sup>Two-tailed Fisher's exact test

<sup>a</sup>Not statistically significant

<sup>b</sup>Statistically significant

<sup>\*</sup>Statistically significant at  $p < 0.100$

or missed breaks. Other series reported 7 to 23%.<sup>2,4,6-7,9-10</sup> Some investigators believed that unrelieved vitreous traction was the major cause of new tears.<sup>4,7</sup> Extension of the original tears had been noted after gas injection.<sup>4</sup> Others theorized it as the result of transmitted vitreous traction 180 degrees away from the gas bubble.<sup>7</sup>

In a review by Grizzard et al.,<sup>2</sup> out of 161 failures in 676 eyes, the immediate cause of failure was new or missed breaks in 12.8%, reopened breaks in 3.6% and breaks that never closed in 1.0%. In our series, inability to close the primary break was the most frequent cause of failure in 7 of 11 failures (41%). Nonclosure of the break was believed to be secondary to persistent vitreous traction (3 cases) and inadequate scar formation around the break (1 case). There were three other failures resulting from nonclosure of the break. Whether these failures were the result of delayed absorption of the subretinal fluid remains in question. However, delayed absorption of subretinal fluid should not be mistaken for failure of the procedure.<sup>10</sup>

Previous cataract surgery did not correlate with failure. In this study, the initial pneumatic retinopexy failed in all eyes with a history of cataract surgery, including the 2 excluded from the analysis. Of the 3 eyes included in the analysis, all had no posterior capsule, 2 were pseudophakic (PCIOL) and one was aphakic. The poor surgical outcome of pneumatic retinopexy for pseudophakic and aphakic eyes is well documented. Success rates in these cases are variable, ranging from 25% to 67%.<sup>2,4,6,9-10</sup> Nevertheless, Tornambe and Hilton<sup>6</sup> still recommend pneumatic retinopexy in pseudophakic and aphakic patients regardless of whether the posterior capsule is intact or not, as most of these eyes that failed the procedure initially were ultimately reattached with good vision.

Surgeon experience was also evaluated as a possible factor but did not correlate with success.

Although the procedure failed in all eyes that were not treated with preoperative cryotherapy, our study failed to show any significant correlation. Similarly, Grizzard et al.<sup>2</sup> did not find any significant difference in eyes treated with cryotherapy, but these were compared to eyes treated with postinjection focal laser. In our study, the two groups were not compared.

Brinton and Hilton<sup>12</sup> outlined the indications for the use of cryopexy and laser. Cryopexy is generally recommended for eyes with small or hard-to-find breaks, media opacities, pigment atrophy, far peripheral tears, and 11 to 1 o'clock tears with no laser indirect ophthalmoscope available. Laser delivered through an indirect ophthalmoscope or by the slit-lamp is performed in a two-session procedure for very posterior and extensive or large breaks (to minimize retinal pigment epithelial dispersion). In our study, two eyes with posterior breaks were successfully treated with laser delivered by slit-lamp alone. Both

cryotherapy and laser were applied in four eyes. One eye was successfully attached and 3 failed. To our knowledge, there have been no reports on the use of a combination of cryotherapy and laser.

Potential complications of pneumatic retinopexy are cataract, glaucoma, vitreous inflammation, endophthalmitis,<sup>1</sup> subretinal gas,<sup>13</sup> and vitreous hemorrhage.<sup>3</sup> Cataract may be induced by direct trauma to the lens during injection or secondary to the cataractogenic effect of the gases.<sup>14</sup> Glaucoma may result from the expansion of perfluoropropane (C<sub>3</sub>F<sub>8</sub>) gas, which is most rapid in the first six hours after injection.<sup>1</sup> No intraoperative complications were noted in this series.

Postoperative PVR was documented in only one patient in this study. Other series reported 3 to 10%.<sup>1, 3, 6-7, 9-10</sup> In the randomized controlled clinical trial comparing pneumatic retinopexy and scleral buckling by Tornambe and Hilton,<sup>6</sup> PVR developed with similar frequency (3 and 5%) in both groups. They suggested that neither perfluoropropane nor sulfur hexafluoride stimulated the development of PVR in the human eye with RD. Pigments in the vitreous similar to "tobacco dust" were seen. These pigments were frequently seen with cryosurgery and not a specific feature of gas injection.<sup>1</sup>

Future success with pneumatic retinopexy will rely ultimately on careful patient selection, surgeon familiarity with the technique, and patient cooperation.

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ORIGINAL ARTICLE

# Ostrich eggshell as an onlay bone-graft substitute for orbital blow-out fractures

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## ABSTRACT

### Objective

To assess the biological behavior of an ostrich eggshell implant as an onlay graft on the orbital floor.

### Methods

This is an experimental study of 12 rabbits implanted with ostrich eggshell (6 rabbits with 5mm- and 6 rabbits with 10mm-diameter grafts) subperiosteally in the right orbital floor. The right orbit was harvested en bloc 1, 2, and 3 months after onlay. Radiographic studies were done one day after implantation and prior to harvest. The specimens were submitted for gross and microscopic studies.

### Results

All animals showed normal wound healing. The grafts were stable and no foreign body reaction was observed 1, 2 and 3 months postimplantation. The size of the ostrich eggshell implants remained the same. There was no change in radiodensity at 3 months observation.

### Conclusion

The results of this study support the potential application of ostrich eggshell as bone substitute for orbital floor fractures.

*Key words: Eggshell, Blow-out, Implant, Orbit, Graft*

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The authors have no proprietary or financial interest in any product used or cited in this study.

PHILIPP J OPHTHALMOL 2004; 29(3): 127-130

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THE MANAGEMENT of orbital floor fractures has been controversial for many years.<sup>1,2</sup> Some orbital floor fractures require only observation while others require surgical reduction. When surgery is performed, the herniated, displaced orbital tissues are freed and repositioned into the orbit. To prevent reherniation, an implant is used to span the orbital floor defect.

Several forms of implants are available but none possesses the ideal characteristics; each has its own advantages and drawbacks. Autografts are preferred by most plastic and craniofacial surgeons,<sup>3</sup> but bone harvesting procedures are associated with increased morbidity such as bleeding, infection, and pain at the donor graft site.<sup>4,5</sup> Allograft is associated with transmission of hepatitis and AIDS.<sup>6</sup> Alloplastic implants such as silicone, polyethylene, hydroxyapatite, and metal alloy plates are preferred by ophthalmologists, but these materials are expensive.

In an earlier study by Dupoirieux<sup>7</sup> on the use of chicken eggshell as bone substitute in maxillofacial surgery, he concluded that the eggshell is biocompatible and suggested its use for filling limited bone defects in nonweight-bearing areas. A 1999 follow-up study by the same author using ostrich eggshell as onlay graft on rabbit mandibles showed similar results.<sup>8</sup> The eggshell had the mechanical strength for load-bearing areas. Other advantages cited were:

1. Ease of trimming with a dental burr;
2. Ease of sterilization by autoclaving without altering its biological properties;
3. Conformity of the form and thickness of the implant to the curvature of the human orbit.

The ostrich (*Struthio camelus*) has the largest egg of any living bird with a mean weight of 1.5 kg and mean size of 16 cm x 12 cm. The shell is about 2 mm thick and is strong to stand a force of up to 55 kg.<sup>8</sup> The composition of avian eggshells differs slightly among species, but is mainly a mineral matrix (over 97%) composed of calcium carbonate (97.4%), magnesium phosphate (1.9%), and tricalcium phosphate (0.7%).

This study evaluated the clinical and histological responses to ostrich eggshell when used as onlay graft on the orbital floor in rabbits.

## METHODOLOGY

Empty ostrich eggs bought from Gross Ostrich farm in San Antonio, Nueva Ecija were fragmented with a dental burr to sizes 5 mm x 2 mm (diameter x thickness) and 10 mm x 2 mm. The membranes were peeled from the inner surface with forceps and the implants were then bleached in a 10% solution of sodium hypochlorite (NaClO) for 24 hours. The implants were subsequently washed with sterile water and sterilized by autoclaving.

Twelve white rabbits weighing 2 to 2.5 kg each were

equally divided into two groups. One group was implanted with ostrich eggshells measuring 5 mm in diameter, and the other group with ostrich eggshells measuring 10mm in diameter. The animals were anesthetized with ketamine 10mg/kg (Ketaject, Astrapin Pharma, Pfaffen-Schwabenheim, Germany) intramuscularly. The right eye was prepped with 10% povidone-iodine solution. A subciliary incision was done followed by division of the orbicularis oculi muscle. After elevation of muscle-skin flap, the periosteum was incised 2 mm from the inferior orbital rim and the implant was laid down on the orbital floor. The periosteal division was closed with 5-0 chromic gut suture (Ethilon, Johnson & Johnson, New Brunswick, NJ, USA) and the skin with 6-0 silk (Ethilon, Johnson & Johnson, New Brunswick, NJ, USA). Antibiotic ointment was applied over the skin incision and cefazolin 50 mg/kg (Megacef, Oboi Laboratories, Mumbai, India) was injected intramuscularly. The skin sutures were removed 5 days after the operation.

The right orbit was harvested en bloc at 1, 2, and 3 months after implantation for each group (2 per group/month). The eyeball was enucleated to facilitate gross examination. Specimens were fixed in 10% formalin, partially decalcified in dilute nitric acid and then infiltrated with paraffin for sectioning. Histologic sections of the specimens were stained with hematoxylin and eosin for examination with light microscopy.

Radiographic studies of the orbit (left and right oblique views) were obtained immediately after implantation and prior to harvesting.

Treatment of the rabbits adhered to the guidelines of the Association for Research in Vision and Ophthalmology.

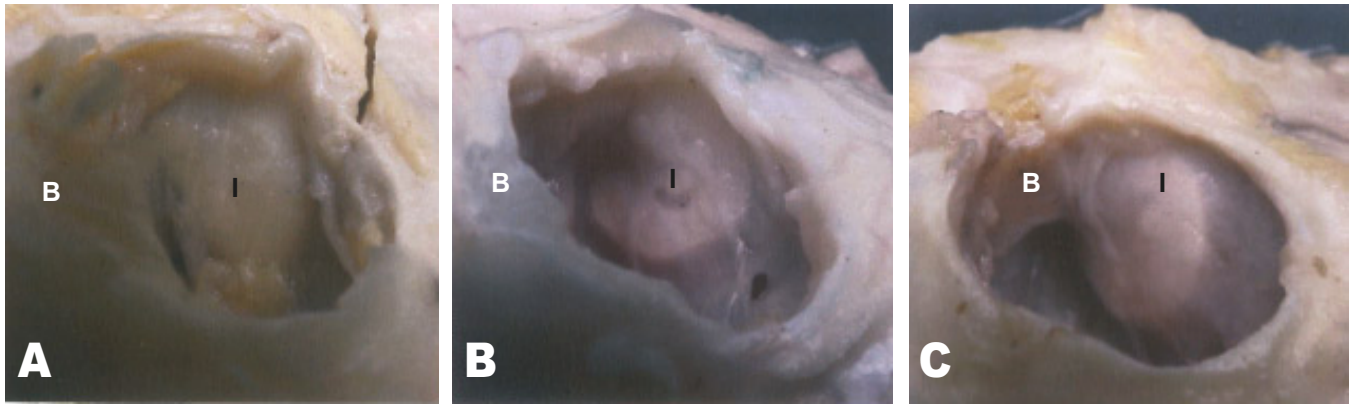
## RESULTS

No wound infection was encountered in all experimental animals. One rabbit belonging to the 5 mm implant group died 3 days after implantation because of unknown causes and was excluded from the study.

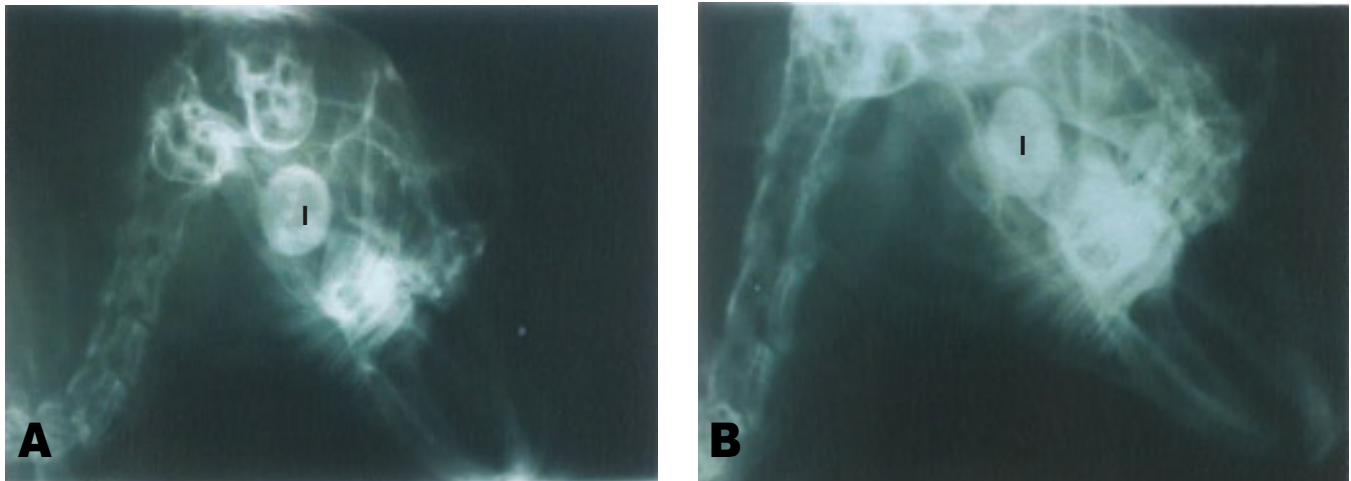
On gross examination (Figure 1), the implants were easily distinguished from the surrounding bone and maintained normal contour in all cases. Observing through the intact periosteum, there were no signs of graft extrusion and none was mobile. The diameter and thickness of the ostrich eggshell grafts did not change 1, 2, and 3 months after implantation.

On radiological examination (Figure 2), no signs of extrusion, new bone formation, or resorption were seen.

Histological sections (Figure 3) showed no inflammatory cells or foreign body reaction, no bone or vascular ingrowth into the implant, and no resorption or autolysis. Fibrous encapsulation was not observed in all specimens.



**Figure 1.** Gross examination of ostrich eggshell implants through intact periosteum at 1 (A), 2 (B), and 3 (C) months. The implant (I) is easily distinguished from the surrounding bone (B).



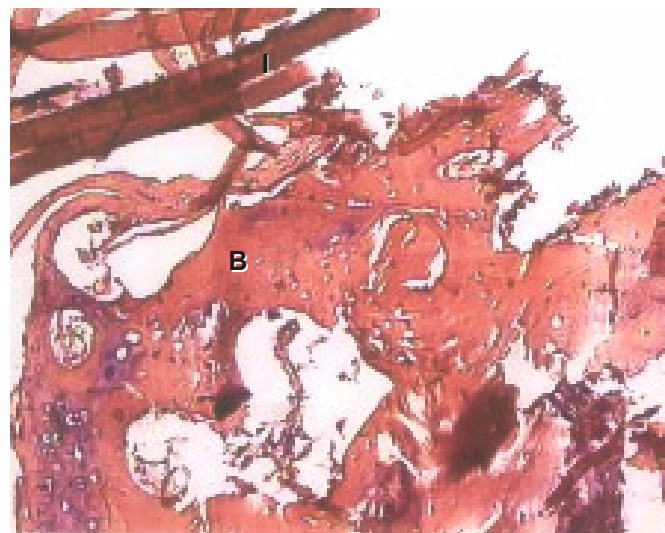
**Figure 2.** Radiographs taken 1 day (A) and 3 months (B) postoperatively show no change in radiodensity of implants (I).

### DISCUSSION

The ideal orbital implant should provide good structural support over the defect, be nonreactive and well tolerated by surrounding tissues, be easily cut and positioned, be readily available, and associated with minor complications.<sup>9-10</sup>

Implants made from ostrich eggshell have desirable handling characteristics. They can easily be cut and shaped with a dental burr to cover different types of orbital defects.

The biocompatibility of an implant is based on the reaction of the surrounding tissue. The presence of giant cells and the more specific polymorphonuclear cells and necrotic tissue usually denotes foreign body reaction.<sup>11</sup> This study showed neither foreign body giant cells, polymorphonuclear cells, nor tissue necrosis. Thus, we surmised the ostrich eggshell implant to be a biocompatible material. This is supported by an earlier study of Dupoirieux in 1995, where the eggshell was placed as an intramuscular pouch in rodents. The biocompatibility of the eggshell implant was expected because the calcium



**Figure 3.** Histological examination of an eggshell onlay graft (I) shows no foreign body reaction and no fibrovascular ingrowth (B- orbital floor bone). (H & E, original magnification x 12.5).

carbonate, which is a natural component of bone, has already been shown to be biocompatible.<sup>7,8</sup>

Implant extrusion can occur in all types of grafts. Dense alloplastic materials have higher incidence of extrusion when compared to bone grafts and porous alloplastic implants such as those made from hydroxyapatite and polyethylene.<sup>12</sup> These latter implants permit fibrovascular integration as well as bone ingrowth, preventing displacement.<sup>13</sup> The same characteristic of these porous implants also creates problems such as difficulty in mobilizing the implant during reoperation or explantation. The growth of orbital tissue into an implant may result in limitation of ductions of the globe due to adhesions of extraocular muscles or orbital fibroadipose tissue to the implant.<sup>10</sup>

The lack of porosity in eggshell implant prevents the invasion of a fibrovascular network that could help anchor the implant to the underlying bone. In this study, however, all the eggshell implants remained immobile. The tight fibrovascular adhesion between the orbital bone and the periosteum surrounding the implants kept them in place even though no capsule growth surrounding the implants was observed.

Both the 5-mm and 10-mm implants behaved similarly with regard to positional stability. Kohn<sup>14</sup> reported that larger implants have higher incidence of complications such as lacrimal obstruction and cutaneous erosion secondary to implant migration and extrusion. These were not observed in this study although longer follow up is necessary as implant extrusion has been reported within months to years after surgery.<sup>15</sup>

Resorption is a realistic concern with bone grafts and other natural implants.<sup>13</sup> Zins et al<sup>16</sup> reported bone resorption of 11.6% to 53.3% as early as 10 weeks in experimental animals. In their study, resorption of bones placed in the craniofacial region of the rabbits and monkeys was measured by computing for the difference in the percent total graft area before and at 5, 10, and 20 weeks after implantation. In our study, gross examination showed that the dimensions (diameter and thickness) of the eggshell grafts did not change. Radiographic examination similarly showed no change in the radiodensity of the eggshell grafts at 1, 2, and 3 months after implantation. The process of resorption is related to vascularization and composition of an implant.<sup>17</sup> Since eggshell implants are inert and no

vascularization occurred, it is not surprising that they did not undergo resorption during the study period.

The incidence of infection with eggshell implant was not established in this study because the graft was placed onlay on an intact orbital floor. Creating an orbital floor defect was attempted but abandoned because of technical difficulties. The surgical field was small and deep, allowing only minimal maneuvering of surgical instruments. The procedure would also compromise the orbital soft tissues and the globe.

This study is limited by its short time frame. Future studies should consider prolonging the harvest time to observe whether fibrovascularization and implant resorption or extrusion would eventually occur. Nevertheless, the ostrich eggshell implant has demonstrated biocompatibility and stability and can be used as bone-substitute graft for orbital floor defects.

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## ORIGINAL ARTICLE

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# A prospective, randomized comparison of Nd:YAG and sequential argon-YAG laser iridotomy in Filipino eyes

## ABSTRACT

### Objective

This study compared Nd:YAG laser alone versus sequential argon-Nd:YAG laser iridotomy in terms of success in attaining patency, differences in visual acuity and intraocular pressure, and rate of complications in dark irides of Filipinos.

### Methods

A prospective, randomized, controlled trial was performed involving patients requiring laser iridotomy who were randomized either to Nd:YAG laser or sequential argon-Nd:YAG laser iridotomy. Iris-perforation success rate, the average number of laser shots and amount of laser energy used, the intraocular pressure (IOP) after laser treatment, and the rate of complications were compared. The prelaser pupil size was correlated with the iris perforation success rate.

### Results

Forty-one eyes underwent laser iridotomy (23 Nd:YAG and 18 sequential). All eyes had patent iridotomies. There was no difference between the two groups in terms of the number of Nd:YAG laser shots delivered ( $p = 0.97$ ) and amount of Nd:YAG energy used ( $p = 0.64$ ). The total amount of laser energy used was higher in the sequential group ( $p = 0.003$ ). There was no significant difference in the IOP and complication rates after treatment. A positive correlation was seen between prelaser pupil size and number of Nd:YAG shots needed to enlarge ( $r = 0.38$ ,  $p = 0.01$ ).

### Conclusion

Nd:YAG laser alone and sequential argon-Nd:YAG have comparable success in attaining patency of laser iridotomy, IOP control, and rate of complications in dark irides of Filipinos.

**Key words:** *Glaucoma, Laser iridotomy, Nd: YAG laser, Argon laser*

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The authors have no proprietary or financial interest in any product used or cited in this study.

PRIMARY angle-closure glaucoma is common among Asians, particularly Singaporeans who have the highest incidence.<sup>1</sup> In the Philippines where prevalence studies are lacking, only limited data can be obtained regarding glaucoma occurrence. At the University of the Philippines-Philippine General Hospital (UP-PGH), approximately 1,500 glaucoma consultations were recorded in 2000, about half of them angle-closure cases (De Jesus A, Chief Resident's Annual Report 2000, PGH Department of Ophthalmology and Visual Sciences).

Laser iridotomy (LI) for primary angle-closure glaucoma is currently the treatment procedure of choice.<sup>2</sup> Pupillary block of any degree, determined clinically significant, is an indication for LI.<sup>3</sup> It may be performed using argon laser or Neodymium: Yttrium-Aluminum-Garnet (Nd:YAG) laser, both of which have their own advantages and disadvantages.<sup>4,6</sup>

Aside from pitfalls inherent in the technique, several factors including racial differences in iris pigmentation and thickness affect treatment outcomes. Dilated pupils and miotic resistant pupils increase iris thickness, posing a problem in LI. A study involving Korean eyes has suggested that LI may not be helpful in cases with dilated and miotic-resistant pupils with formation of extensive peripheral anterior synechiae (PAS).<sup>7</sup> A review of sequential argon-Nd:YAG to treat primary angle-closure glaucoma among Singaporeans revealed that eyes with mid-dilated pupils and more than 6 clock hours of PAS required further medical or surgical treatment for uncontrolled IOP despite a patent LI.<sup>8</sup>

Although initial studies showed no significant long-term differences between LI created with Nd:YAG or argon laser,<sup>9</sup> the former has shown clinical advantages in creating a patent iridotomy. One-hundred-percent success rates have been reported with Nd:YAG laser<sup>10-12</sup> while 20 to 58% failure rates were reported for argon laser.<sup>11, 13, 14</sup> Success rates may vary in the thicker and more heavily pigmented Asian irides, which require higher energy levels to penetrate the iris. As a result, more complications and failures have been reported, including iridotomy closure, iris bleeding, transient IOP elevation, and corneal endothelial edema.

A technique utilizing both argon and Nd:YAG lasers has been devised to combine the advantages of both lasers while avoiding the disadvantages. The argon laser creates preparatory stretch burns and the Nd:YAG laser completes the perforation.<sup>15</sup> Such method may be the ideal iridotomy technique for Asian irides.<sup>10, 15-17</sup> A study comparing blue, hazel, and thick brown irides found that the amount of Nd:YAG energy required varied directly with the pigmentation of the iris.<sup>18</sup> Initial studies reported 100-percent success rate for this technique.<sup>10,17</sup>

This study determined whether Nd:YAG laser alone or

the sequential argon-Nd:YAG laser were comparable in terms of success in attaining patency of laser iridotomy, control of IOP, and incidence of complications encountered in dark, Filipino irides treated at the UP-PGH. We compared the average number of laser shots and amount of laser energy used for both techniques and correlated the prelaser pupil size with the iris perforation success rate.

## METHODOLOGY

The study protocol and informed consent form were approved by the PGH Institutional Review Board.

All patients seen consecutively at the Glaucoma Clinic of the UP-PGH from June 2001 to October 2002 were screened for possible inclusion into the study. Included were eyes with primary angle-closure glaucoma, the fellow eye of an angle-closure attack, narrow occludable angle, uveitic or inflammatory glaucoma with pupillary block. For those with bilateral involvement, eyes were randomly selected for each procedure. Patients with comorbid systemic diseases such as diabetes and hypertension were included provided that no ocular complications were evident.

Angle-closure glaucoma caused by neovascularization of angles or by ciliary block mechanism, previous intraocular surgery, previous laser surgery, and those unable to tolerate the procedure were excluded.

All patients underwent a standard eye examination which included history taking, visual acuity determination, IOP measurement, slit-lamp biomicroscopy, gonioscopy, and fundus examination.

A laser iridotomy protocol form was filled up and followed for each patient. Baseline ocular examination was performed at least one hour before laser treatment with particular attention to pupil size, IOP, and peripheral anterior synechiae. All eyes were pretreated with 1 drop 2% pilocarpine and 0.5% apraclonidine (Iopidine, Alcon Laboratories, Forth Worth TX, USA) 1 hour before laser surgery. If IOP was greater than 20 mm Hg, 1 tablet of dichlorphenamide 50 mg (Oratrol, Alcon Laboratories, Forth Worth, TX, USA) was given per orem. If the cornea was edematous due to very high IOP, oral hyperosmotic glycerol 1.5 cc/kg was added.

Using a table of random values, each eye was assigned to undergo either Nd:YAG or sequential argon-YAG treatment. Immediately before the procedure, topical anesthetic was administered. If the cornea was still edematous, topical glycerine was added to the anesthetized eye.

An Abraham iridotomy contact lens (Ocular Instruments, Bellevue, WA, USA) with cellulose gel was used for either technique. The choice of iridotomy site was based on the following parameters: (1) superior quadrants of the iris covered by the upper lid, preferably superonasal;

(2) as far peripherally as possible clearing the arcus senilis beyond the outer radial one-third of the iris; (3) thinner looking area or crypt. The 3- and 9-o'clock positions and visible vessels were avoided. The actual iridotomy site was drawn on the protocol form.

Laser iridotomy was performed by six senior residents using standardized parameters to minimize interobserver variability. All measures of visual acuity, IOP, pupillary size, slit-lamp biomicroscopy, gonioscopy on follow-up were done by one clinician (KMEB).

#### **Nd:YAG laser iridotomy**

Nd:YAG laser settings: 2.5 mJ power, 1 pulse per burst. Technique: The beam was focused within the iris stroma and not on the surface of the iris. 2.5mJ was the starting power used. If a patent iridotomy was not attained after several shots, the laser parameters were modified to power of 1-10 mJ and 1-3 pulses per burst until patency was achieved. When intraoperative bleeding occurred, gentle pressure was applied on the eye with the lens. When plasmod aqueous precluded completion of the procedure, intensive steroid eye drops were given and the patient was brought back for completion of laser in 24 hours.

#### **Sequential argon-Nd:YAG laser iridotomy**

Settings: 800-1000 mW power (equivalent to 1000 mJ per second), 50 micron spot size, 0.02 second exposure time. Chipping technique was done as follows: The beam was focused within the iris stroma. The first shot was made on the projected final iridotomy site. The subsequent shots were directed immediately adjacent to and around the first shot, forming a rosette pattern. Successful priming using argon laser was defined as the creation of a charred and thinned out area. If this was not reached, argon laser parameters were modified to achieve this end point with power of 1200-2500 mW and exposure time of 0.02 to 0.1 second. The Nd:YAG technique followed as described above, aiming at the center or thinnest part of the argon-treated area of the iris.

The final end point for both techniques was the creation of an iridotomy 100 to 500 micrometers in size through which the aqueous mixed with pigment flowing into the anterior chamber could be visualized, with the iris falling backwards and the peripheral anterior chamber deepening. Patency was confirmed by direct visualization of the lens through the iridotomy and not just by transillumination through the pupil or iridotomy.

Immediately after the laser treatment, 1 drop of apraclonidine 0.5% was administered. Topical steroid eyedrops were given for 7 days. In cases of posterior synechiae formation, pupillary dilation was done.

Visual acuity, IOP, and iridotomy patency were monitored at 1 hour, 2 hours, 3 hours, 24 hours, 1 week, 1

month, 3 months, and 6 months postlaser. The occurrence of complications was monitored.

Analysis of variance (ANOVA) and Kruskal-Wallis test were used to determine differences in parameters between the two treatments. Correlation studies were also performed.

## **RESULTS**

Forty-one eyes of 41 patients (8 males and 33 females) were included in the study. Twenty-three patients were assigned to the Nd:YAG group, 18 to the sequential laser group. The mean patient age was 62 years (range of 42 to 86 years). Thirty-one patients had a diagnosis of narrow occludable angle, 9 had intermittent angle-closure glaucoma, and 1 had chronic angle-closure glaucoma. There was no significant difference in preoperative parameters between the treatment groups (Table 1).

In the Nd:YAG group 22 (95.65%) patients were seen on day 1, 15 (65.22%) on week 1, 10 (43.48%) at 1 month, and 2 (8.69%) at 3 months. Three (13%) out of 23 patients completed the six-month follow-up.

In the sequential group, 8 (44.44%) patients were seen on day 1, 15 (83.33%) on week 1, 11 (61.11%) at 1 month and 2 (16.67%) at 3 months. Two (11.11%) out of 18 patients completed the six-month follow-up.

All eyes had patent iridotomies at the end of each session.

The mean number of Nd:YAG laser shots needed to perforate the iris (initial gush of fluid) was  $14.52 \pm 19.35$  for the Nd:YAG only group and  $14.33 \pm 14.76$  for the sequential group. There was no statistically significant difference between the two treatments ( $p = 0.97$ ) (Table 2).

The mean amount of Nd:YAG energy used in producing the initial gush was  $40.81 \pm 57.96$  mJ in the Nd:YAG group and  $33.45 \pm 35.89$  mJ in the sequential group (Table 2). There was no statistically significant difference between the two treatment groups ( $p = 0.64$ ).

The number of Nd:YAG laser shots needed to enlarge the iridotomy was significantly fewer in the sequential group with a mean of  $24.56 \pm 13.61$  compared with  $52.74 \pm 56.96$  in the Nd:YAG only group ( $p = 0.05$ ).

The mean total energy used to enlarge the iridotomy was  $222.61 \pm 183.65$  mJ in the Nd:YAG group and  $431.01 \pm 183.65$  mJ in the sequential group; the difference was statistically significant ( $p = 0.003$ ).

There was a statistically significant difference in the iridotomy sizes between the two groups ( $p = 0.05$ ) with a mean of  $2.51 \pm 0.90$  mm in the Nd:YAG group and  $2.65 \pm 0.97$  mm for the sequential group.

Segmental analysis of different parameters on follow-up was done. Regardless of treatment, there was no significant difference in visual acuity across follow-up periods ( $p = 0.72$ ). Furthermore, there was no difference between

Table 1. Baseline characteristics and treatment parameters.

	Nd:YAG (n=23)	Sequential (n=18)
<b>Age (years)<sup>1</sup></b>		
Mean +/- SD	64 ± 9	60 ± 12
Median	65	62
Range	45-82	42-86
<b>Gender<sup>2</sup></b>		
Male	5	3
Female	18	15
<b>Angles<sup>3</sup></b>		
360 open occludable	20	11
1-6 clock-hours closed	3	6
360 closed	0	1
<b>Mean Baseline Parameters</b>		
Visual Acuity <sup>4</sup>	0.80 ± 0.27	0.77 ± 0.29
Intraocular Pressure <sup>5</sup> (mm Hg)	16.00 ± 2.03	17.33 ± 3.24
Pupil Size <sup>6</sup> (mm)	2.11 ± 0.94	2.11 ± 0.93

<sup>1</sup>p = 0.25; <sup>2</sup>p = 0.50; <sup>3</sup>p = 0.13; <sup>4</sup>p = 0.66; <sup>5</sup>p = 0.33; <sup>6</sup>p = 0.83  
<sup>\*</sup>converted into decimal units: 1=20/20, 0.5=20/40, 0.25=20/80 and so on

Table 3. Visual acuity between treatment groups at follow-up.

Follow-up Time	Mean Visual Acuity (Decimal Units)		p
	Nd:YAG	Sequential	
After 24 hours (n=29)	0.76 ± 0.25	0.86 ± 0.20	0.31 <sup>*</sup>
One week (n=28)	0.76 ± 0.30	0.78 ± 0.24	0.81 <sup>*</sup>
One month (n=20)	0.93 ± 0.12	0.79 ± 0.22	0.09 <sup>*</sup>
Three months (n=5)	0.65 ± 0.21	1.00 ± 0	0.05

<sup>\*</sup>Not statistically significant.

Table 4. Intraocular pressure within treatment groups at follow-up.

Follow-up Time	Mean IOP	
	Nd: YAG <sup>1</sup>	Sequential <sup>2</sup>
Baseline (prelaser)	12.96 ± 3.94	12.00 ± 5.52
24 hrs	11.96 ± 4.37	12.13 ± 3.56
1 week	12.87 ± 2.95	14.47 ± 5.10
1 month	12.00 ± 2.87	17.64 ± 14.48
3 months	16.00 ± 5.66	17.33 ± 1.16
6 months	12.67 ± 3.06	15.50 ± 3.54

<sup>1</sup>p = 0.75; <sup>2</sup>p = 0.35.

Table 2. Comparison of Nd:YAG laser shots between treatment groups.

Parameters	Mean Number of Shots			Mean energy (mJ)		
	Nd:YAG	Sequential	p	Nd:YAG	Sequential	p
Iris perforation (initial gush)	14.52 ± 19.35	14.33 ± 14.76	0.97	40.81 ± 57.96	33.45 ± 35.89	0.64
Enlarge iridotomy	52.74 ± 56.96	24.56 ± 13.61	0.05	222.61 ± 183.65	431.01 ± 183.65	0.003

treatment groups over time (Table 3). There was also no difference in IOP between treatment groups ( $p = 0.33$ ) (Table 4) and angles over time ( $p = 0.36$ ).

There was a positive correlation between pupil size and number of Nd:YAG shots to perforate ( $r = 0.30$ ;  $p = 0.06$ ) and between iridotomy size and amount of Nd:YAG energy to enlarge ( $r = 0.38$ ;  $p = 0.01$ ). Weaker correlation between iridotomy size and total energy was found ( $r = 0.28$ ;  $p = 0.08$ ).

No significant interoperator difference was found in the number of Nd:YAG laser shots to perforate ( $p = 0.22$ ), shots to enlarge ( $p = 0.17$ ) and total energy used ( $p = 0.14$ ).

Complications seen were transient intraoperative bleeding at the site of iridotomy in 4 eyes (17.4%) in the YAG group and 4 eyes (22.2%) in the sequential group ( $p = 0.71$ ). Endothelial burn was observed in 2 eyes (8.7%) in the YAG group, none in the sequential group ( $p = 0.50$ ). Stratified analysis of anterior-chamber reaction showed no difference between treatments ( $p = 0.22$ ). Closure of iridotomies was not observed.

## DISCUSSION

The outcome of laser iridotomy is determined by several patient and treatment factors. This study gave particular attention to thick and densely pigmented irides in Filipino eyes and the effect of such on the outcomes of sequential argon-YAG laser and YAG laser only in the treatment of

angle-closure glaucoma. Other patient factors such as pupil size, chronicity of disease, and IOP were likewise taken into consideration as these affect treatment outcomes as well.

Several studies have suggested that sequential iridotomy was safe and effective especially in dark irides. Ho and Fan<sup>10</sup> conducted sequential iridotomies in 20 eyes of 13 patients, with a mean total energy delivered per eye of 3.6 J by the argon and 0.0094 J by the Nd:YAG laser. These were one-third of corresponding values reported by Robin and Pollack<sup>19</sup> for pure argon ( $12 \pm 11$  J) and pure Nd:YAG ( $0.033 \pm 0.25$  J) iridotomies. Thus, there were advantages in combining the two types of laser.

The mean energy of 0.03345 J administered in the YAG part of this study was comparable to the 0.033 J in the Robin and Pollack study.<sup>19</sup> There was no statistically significant difference between the two groups in the number of shots of Nd:YAG laser delivered to perforate the iris and in the amount of Nd:YAG energy used. However, the total energy used in the sequential technique was significantly higher since the amount of energy to enlarge the iridotomy was higher and the argon laser per se used more energy at 1000 mW per second. Twice the number of Nd:YAG laser shots was needed to enlarge iridotomies in the Nd:YAG only group compared to the sequential group. The thicker brown iris absorbs argon

energy well and less Nd:YAG energy and fewer shots were needed to enlarge the iridotomy in pretreated thinned out iris.

The use of two laser machines instead of one may be less cost-effective in the treatment of eyes requiring iridotomy. Although the sequential technique theoretically offers an advantage over Nd:YAG laser only in the treatment of darker irides, no such advantage was found in this study, considering the 100-percent perforation rate in both techniques and the comparable number of shots and amount of Nd:YAG laser energy delivered in both treatment groups. A study by Fleck<sup>20</sup> yielded similar results; pretreatment with argon was performed 6 weeks prior to Nd: YAG laser. No differences in visual acuity, IOP control, and angles were observed between treatment groups during the follow-up period.

Patency of laser iridotomy over time requires an opening in the iris of at least 100 spot size; the larger the opening, the less likely it will close. In this study, there was a positive correlation between iridotomy size and amount of Nd:YAG energy to enlarge, indicating that more energy was required to obtain a larger opening. The mean iridotomy size in the sequential group was significantly larger and correlated with the higher total energy used in this group. The thick brown iris absorbs argon energy well, making subsequent perforation and enlargement of the iris opening easier. Longer-term studies are needed to determine the correlation between size of opening and patency over time.

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ORIGINAL ARTICLE

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# Epidemiological pattern of retinoblastoma at the Philippine General Hospital

## ABSTRACT

### Objective

To evaluate the epidemiological and clinical patterns of retinoblastoma in a tertiary government hospital.

### Methods

This is a retrospective case series of new retinoblastoma patients seen at the University of the Philippines-Philippine General Hospital (UP-PGH) in three periods: 1967 to 1977, 1985 to 1995, and 1997 to 2001. The demographic and clinical characteristics of retinoblastoma over the three periods were compared.

### Results

The incidence of retinoblastoma increased from 40/100,000 new cases in 1967 to 1977 to 237/100,000 new cases in 1997 to 2001. The average age at onset did not change over time but the age at consultation decreased from 1.5 years to 1 year. The most common initial ocular manifestation at onset was cat's eye reflex (77 to 79%) with findings of leukocoria (67 to 77%). Extraocular findings of proptosis and orbital mass declined through the years. Bilateral retinoblastoma comprised 30% in this series and showed no change in distribution over the years.

### Conclusion

The epidemiological and clinical patterns of retinoblastoma cases at the Philippine General Hospital may be changing over time and requires continuous monitoring of incidence and characteristics.

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Presented at the Annual Meeting of the Philippine Academy of Ophthalmology, November 2002.

The authors have no proprietary or financial interest in any product used or cited in this study.

**Key words:** Retinoblastoma, Tumor, Epidemiology

PHILIPP J OPHTHALMOL 2004; 29(3): 136-139.

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RETINOBLASTOMA is the most common primary ocular tumor in the Philippines. This paper analyzes the demographic and clinical characteristics of retinoblastoma patients over three periods:

- Series I : 1967 - 1977<sup>1</sup>
- Series II : 1985 - 1995<sup>2</sup>
- Series III : 1997 - 2001 (unpublished data)

These three series can be considered comparable because they:

- were conducted in the same location (UP-PGH) with the same catchment area,
- were performed by the same senior author using the same screening procedures, and
- compared only new retinoblastoma patients referred to the UP-PGH eye department.

### METHODOLOGY

All suspected retinoblastoma cases referred to the Retina-Oncology Service from 1967 to 1977, from 1985 to 1995, and from 1997 to 2001 were included in the study. A detailed medical and family history was obtained. All patients underwent comprehensive eye examination, which included anterior segment evaluation, dilated fundus exam with the indirect ophthalmoscope, and when necessary, B scan, computed tomography (CT), magnetic resonance imaging (MRI), spinal fluid exam, or bone-marrow evaluation. Results were classified according to a system described in a previous study<sup>3</sup> as follows:

Stage 1: *Intraocular stage*. Tumor is confined within the retina.

Stage 1a: Early intraocular (tumor less than half of the retinal surface)

- a1 – tumor size < 4DD\*
- a2 – tumor size 4 DD to 10 DD
- a3 – tumor size >10DD to 15 DD

Stage 1b: Late intraocular (tumor more than half of the retinal surface or >15 DD).

Stage 2: *Intraocular far advanced stage*. Tumor and/or pathologic changes have spread to other ocular structures.

Stage 3: *Intraorbital and/or metastatic spread*. Tumor has extended out of the eyeball into the orbit (intraorbital) or to distant tissues (metastatic).

Statistical analysis was performed using MS Excel (Microsoft Corporation, Redmond, WA, USA).

### RESULTS

#### Incidence

The average number of new cases per year increased from 5 in 1967-1977 to 16 in 1985-1995 and 33 in 1997-

2001. To adjust for the increase in population growth, the figures were converted to new cases per 100,000 new eye cases seen during the period. This yielded an incidence of 40/100,000 new cases for 1967 to 1977, 80 for 1985 to 1995, and 237 for 1997 to 2001.

#### Age of onset

The average age of onset is the approximate age when the symptoms first appeared, a better index than the age at consultation which may be affected by nonmedical factors such as accessibility of health care. The age at onset did not significantly change over time: 12 months for 1967 to 1977, 18 months for 1985 to 1995, and 14 months for 1997 to 2001.

Analysis of the data on age at consultation revealed a decrease in the average delay of consultation from 1.5 years to 1 year. The delay was 19 months for 1967 to 1977, 11 months for 1985 to 1995, and 13 months for 1997 to 2001. This means that the onset of the disease has not changed through the years but the patients are now being brought earlier for consultation.

#### Gender Distribution

For the period 1967 to 1977, the ratio of male to female cases was 1.7:1. The ratio dropped to 1.3:1 in 1985 to 1995 and 1.2:1 in 1996 to 2001, closer to the international ratio of 1:1.

#### Tumor stage at consultation

From 1967 to 1977, the number of cases seen in all three stages were similar (Table 1). From 1985 to 1995, almost half of the cases were in stage 3 at consultation. From 1996 to 2001, however, 45 percent were seen at stage 1 indicating that more cases were seen earlier during the period.

#### Ocular manifestation at onset

The most common initial eye complaint was cat's eye reflex (77 to 79%), followed by strabismus (11 to 14%). These did not change over the years. Other symptoms included proptosis, orbital mass, and ocular redness (Table 2).

#### Ocular manifestation at consultation

From 1967 to 1977, there were no cases of strabismus at first consultation (Table 3). Most Stage 1 cases consisted of partial leukocoria (tumor size less than 1/2 of retinal surface), which still required enucleation. From 1985 to 1995, strabismus as initial presentation on consultation appeared with more cases of partial leukocoria. Extraocular findings such as proptosis declined from 16% in 1967-1977 to 6% in 1985-1995 and 3% in 1997-2001, while findings of orbital mass dropped from 27% to 11% to 3% respectively (Table 3).

\*disc diameter

Table 1. Tumor stage at consultation.

Stage	Number of New Cases (Percent)		
	1967-1977	1985-1995	1997-2001
Stage 1	19 (34)	58 (35)	76.0 (45)
Stage 2	16 (29)	29 (17)	29.0 (17)
Stage 3	21 (37)	80 (48)	64.0 (38)

Table 2. Ocular manifestation at onset.

Signs & Symptoms	Number of Cases (Percent)		
	1967-1977	1985-1995	1997-2001
Cat's eye	44 (79)	130 (78)	130 (77)
Strabismus	8 (14)	23 (14)	19 (11)
Others*	4 (7)	14 (8)	19 (12)

\* Proptosis, Orbital Mass, Redness

Table 3. Ocular manifestation at consultation.

Signs & Symptoms	Number of Cases (Percent)		
	1967-1977	1985-1995	1997-2001
Leukocoria	15 (27)	112 (67)	130 (77)
Strabismus	-	10 (6)	19 (11)
Orbital Mass	15 (27)	19 (11)	5 (3)
Redness/Swelling	9 (16)	8 (5)	5 (3)
Proptosis	9 (16)	10 (6)	5 (3)
Buphthalmos	5 (9)	-	-
Others	3 (5)	8 (5)	5 (3)
<b>Total</b>	<b>56 (100)</b>	<b>167 (100)</b>	<b>169 (100)</b>

Table 4. Familial Incidence.

Pedigree	Number of Cases (Percent)		
	1985-1995	1996-2001	Percent Change
None	154 (92)	157 (93)	no change
Parents	3 (2)	7 (4)	} 7-8
Siblings	8 (5)	3 (2)	
Others	2 (1)	2 (1)	
<b>Total</b>	<b>167 (100)</b>	<b>169 (100)</b>	

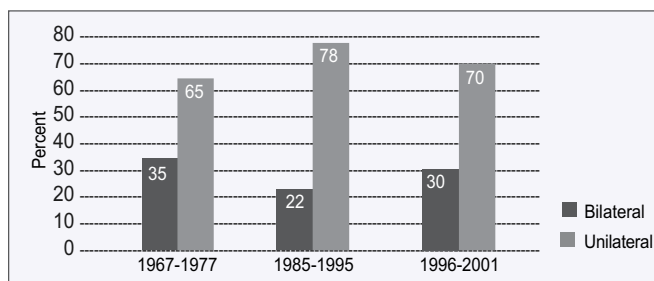


Figure 1. Distribution of cases by laterality.

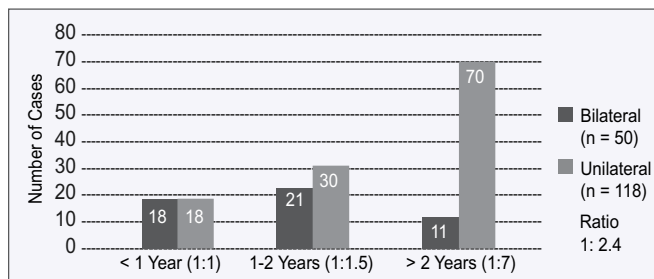


Figure 2. Age of onset of bilateral and unilateral cases (1996-2001 series).

### Familial incidence

Familial incidence remained at 7 to 8%, the same as the international rate (Table 4).

### Laterality

Bilateral cases comprised 30% of the series, which showed no change in distribution over the years (Figure 1). This is important as all bilateral cases are considered hereditary.<sup>5</sup> In our series, most of the bilateral cases presented early, before 2 years of age (Figure 2). Below the age of 1 year, the ratio of bilateral to unilateral cases was equal (1:1). At 1 to 2 years, the ratio was 1:1.5. After 2 years, the ratio decreased to 1:7.

## DISCUSSION

In contrast to the usual epidemiologic surveys that cover short duration, this study has a long observation period. Prolonged follow-up data are available, and changes and variations in trend can be detected.

One of the significant findings is the five-fold increase in incidence of retinoblastoma over the periods covered. This may be attributed to advances in disease evaluation and therapy, allowing more survivors to reach child-bearing age. Gene mutations, which comprise 40% of all new cases, continue to add to the genetic pool. This may explain the higher incidence despite advances in medical technology.

The male-female ratio declined from 1.7:1 to 1.2:1, which is closer to current international data. There is no reported gender bias in retinoblastoma.

The average age of onset, clinical course and frequency of ocular manifestations remain unchanged. However, the average delay in consultation had been shortened by 6 months from 1.5 years to 1 year of age. This may be a result of greater public awareness, better communication systems, and improved public-health programs. These translated to early consultation and detection of cases and corresponding decline of advanced cases. More cases of partial leukocoria (tumor less than 1/2 of retina) were seen, allowing vision to be saved in some cases. Ocular findings of strabismus, previously noted only in the family history, were present at the time of consultation in the last two series, indicating that earlier cases of retinoblastoma were seen. The percentage of ocular proptosis and intraorbital mass, which were late manifestations, also decreased. All these will lead to better rate of therapeutic success.

The familial incidence remained the same in these series. However, with the increase in survivors for the past 10 to 15 years, an increase in familial incidence is predicted in the coming years as more of these survivors reach childbearing age.

The data on laterality showed no change over the years

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studied and showed that bilateral cases have earlier age of onset. Other studies also showed a more rapid course and a greater tendency for secondary tumors in the later years of life especially if the patients were subjected to radiotherapy or radiomimetic chemotherapeutic agents.<sup>5</sup>

In summary, a 35-year longitudinal study of retinoblastoma incidence in the Philippines showed the following trends:

1. A fivefold steady increase in incidence from 48/100,000 eye cases to 237/100,000 eye cases.
2. A decreasing male preponderance from male-female ratio of 1.7:1 to an almost equal 1.2:1.
3. No change in average age of onset, clinical course, clinical manifestations, and familial incidence.

4. Decrease in the average delay in consultation by six months from 1.5 years to 1 year.

5. More cases of early detection and fewer cases of late presentation.

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ORIGINAL ARTICLE

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# Profile of childhood cataract cases at the Philippine General Hospital

## ABSTRACT

### Objective

The study determined the major causes of childhood cataract among patients seen at the pediatric ophthalmology clinic of the University of the Philippines-Philippine General Hospital (UP-PGH).

### Methods

Case records of all patients seen at the pediatric ophthalmology clinic of UP-PGH from January 1, 2000 to August 31, 2003 were reviewed. Included were patients less than 21 years old diagnosed with cataract not associated with trauma. Cases were classified as to presumptive etiology: idiopathic, familial, or secondary to a systemic or an ocular disorder.

### Results

The cause of cataract was identified in 37.6% of the 218 cases reviewed. Rubella was the leading cause (20.5%), followed by suspected rubella infection (8.2%). There were 2 cases of varicella and 1 case of cytomegalovirus (CMV) infections. Down syndrome and Lowe syndrome had one case each. Three cases (1.4%) were familial. Cataract was idiopathic in 133 cases (61.0%).

### Conclusion

The pattern of childhood cataract in this study is typical of a developing country where rubella infection is the major cause.

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**Key words:** *Cataract, Congenital, Blindness, Rubella*

The authors have no proprietary or financial interest in any product used or cited in this study.

PHILIPP J OPHTHALMOL 2004; 29(3): 140-143

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CATARACT in infancy is a significant cause of visual handicap worldwide.<sup>1</sup> The loss of vision is mainly caused by amblyopia.<sup>2</sup> About 1.5 million children throughout the world are blind, one million of them in Asia.<sup>3</sup> Recent surveys in developing countries have shown that 10 to 40% of childhood blindness is due to cataract (Figure 1).<sup>4,8</sup> Approximately 75% of childhood blindness in developing countries is associated with an infectious agent that is preventable or curable.<sup>3</sup> Rubella is the major infectious agent associated with childhood cataract.

In the Philippines, the Third National Survey on Blindness<sup>9</sup> placed the incidence of childhood blindness at 0.44%. Cataract is one of the primary causes.

Table 1. Age and sex distribution of patients at the time of cataract presentation.

Age (months)	Female	Male
0 - 6	63	62
7 - 36	20	25
37 - 60	11	9
> 60	15	13
<b>Total</b>	<b>109</b>	<b>109</b>

Table 2. Age distribution of patients at consultation per type of cataract.

Age (months)	Idiopathic	Secondary	Familial	Total
0 - 6	22	32	-	54
7 - 36	35	33	-	68
37 - 60	19	5	1	25
> 60	57	12	2	71
<b>Total</b>	<b>133</b>	<b>82</b>	<b>3</b>	<b>218</b>

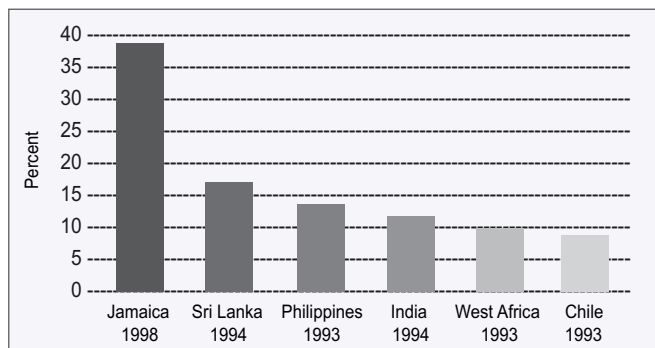


Figure 1. Childhood blindness caused by cataract in developing countries.

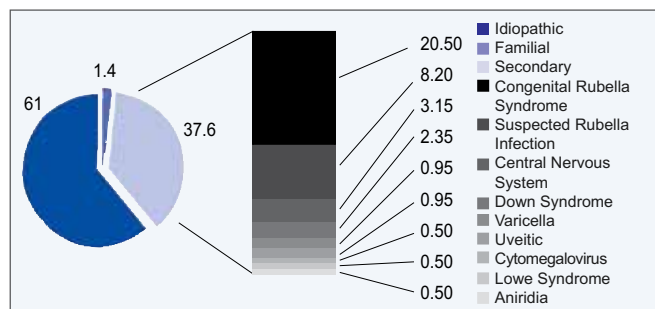


Figure 2. Profile of childhood cataract (%)

In the developed world, about half of all congenital cataract cases are idiopathic.<sup>10</sup> In an Australian study, one-fifth had familial cataract.<sup>11</sup> Of those with an identified etiology, the most common is Down syndrome.

In contrast, an increasing percentage of childhood cataract in India had been traced to congenital rubella syndrome.<sup>12</sup> No data were given on the association of cataract with galactosemia.

In the Philippines, aggressive newborn screening in 2001 reported the incidence of galactosemia at 1:71,593.<sup>13</sup> Cataract was not present in the patient that had galactosemia.

Childhood cataract must be diagnosed and managed early to avoid blindness and other serious complications. Long-term rehabilitation, visual assistance, and lost productivity are serious concerns.

This study determined the major causes of childhood cataract among patients seen at the pediatric ophthalmology clinic of the University of the Philippines-Philippine General Hospital (UP-PGH). The data obtained would serve as basis for formulating policy recommendations for prevention, diagnosis, and management of the disease.

## METHODOLOGY

A review of all available case records of patients seen at the pediatric ophthalmology clinic of the UP-PGH from January 1, 2000 to August 31, 2003 was done. Patients less than 21 years old diagnosed with cataract by ocular examination and not associated with trauma were included in the study. The following parameters were recorded: demographic information, onset of cataract by history, maternal illness during pregnancy, maternal drug ingestion, history of cataract in the family, associated clinical findings and associated syndromes, and result of galactosemia screening. Cases were classified as to presumptive etiology (whether idiopathic, familial or secondary to a systemic or an ocular disorder). The age range and median at the time of consultation were also computed.

## RESULTS

Over 4 years, 218 index cases of childhood cataract were identified and included in the study. Fifty percent were male. The youngest patient was 1 month old and the oldest was 20 years old. The median age at the time of consultation was 24.5 months (Table 1). The cataract was bilateral in 70% of cases.

There was no presumptive etiology in 133 cases. Eighty-two were secondary to a systemic or ocular disorder and 3 were familial in nature (Table 2).

### Familial Cataract

The cataract was deemed familial when one of the parents was shown to have childhood-onset cataract on clinical history or examination, or was aphakic from

surgery performed during childhood. There were three (1.4%) cases of familial cataract involving siblings. All were bilateral.

### Secondary Cataract

Among secondary cataract cases, rubella was the most common identifiable cause in 45 cases of congenital rubella syndrome (Figure 2). Clinical findings of congenital heart defects and history of maternal rubella were present in these cases. Eighteen cases (8.2%), however, were classified as suspected rubella infection where there was unconfirmed history of maternal rubella illness during the first trimester of pregnancy.

Other causes included 7 cases (3.15 %) with central nervous system (CNS) abnormalities manifesting as delayed development, cerebral palsy or epilepsy, 5 cases (2.85%) with Down syndrome, 2 cases with uveitis, and one each with Lowe syndrome and aniridia.

### Idiopathic Cataract

The cause could not be ascertained in 133 cases (61%).

## DISCUSSION

Studies in other countries have shown that the etiology of childhood cataract was determined in only 35 to 40% of cases.<sup>11-12</sup> Heredity, ocular and systemic disorders were the most common causes in developed countries. Rubella, an infectious but preventable etiology,<sup>2</sup> was the most common cause in developing countries (Figure 3).

Congenital rubella was the most common cause of secondary cataract in this study, similar to results reported in India.<sup>12</sup> Other causative agents were varicella (0.95%) and cytomegalovirus (0.5%). The low incidence rate of these two factors was consistent with the findings in other studies.<sup>14</sup>

Down syndrome was the cause in only 2.35% of cases, lower than those found in Brazil (13%) and Australia (6%),<sup>11</sup> but similar to that in China (2.7 %).<sup>15</sup> This low figure may be attributed to several factors. Many parents may not bring their children with Down Syndrome for

early eye consultation because of the stigma associated with the condition. Cataract in Down syndrome may present as arcuate opacities along the equator of the lens nucleus visible only on slit-lamp examination.<sup>15</sup> Thus, subjective complaints may go unnoticed.

The lone case of cataract attributed to Lowe syndrome, an X-linked recessive disorder, presented with bilateral lens opacification associated with a typical facie and frontal bossing.

Three cases (1.4 %) were documented as familial. In other series, 8 to 23% of reported cases were hereditary.<sup>2</sup> Under-reporting of familial cases may occur when there is no opportunity to examine parents and siblings.

Idiopathic cases or those not associated with any ocular pathology, systemic disorders, or syndromes accounted for almost two-thirds of cases in this study. In these cases, there was no family history and heart findings were normal. Galactosemia screening was negative.

Several problems were encountered by the investigators in the conduct of this study. There was difficulty in the retrieval of some case records and information was lacking in others.

The need for a more thorough evaluation of childhood cataract by the appropriate specialty is apparent. The character and location of the lens opacity must be described or documented by photographs or drawings since some forms of cataract are peculiar to certain disease entities.

The initial investigation of any pediatric cataract should include exploring possible familial or hereditary diseases (Figure 4). The presence of cataract in a family member should alert the clinician to a possible familial cause. A detailed family history should be elicited with examination of the parents and siblings. The birth and maternal history may yield important information as to the etiology if infection was suspected as a cause. Children who present with heart disease should prompt the ophthalmologist to investigate the possibility of rubella infection. Congenital rubella syndrome is often diagnosed based on systemic findings. Expensive confirmatory tests are reserved for

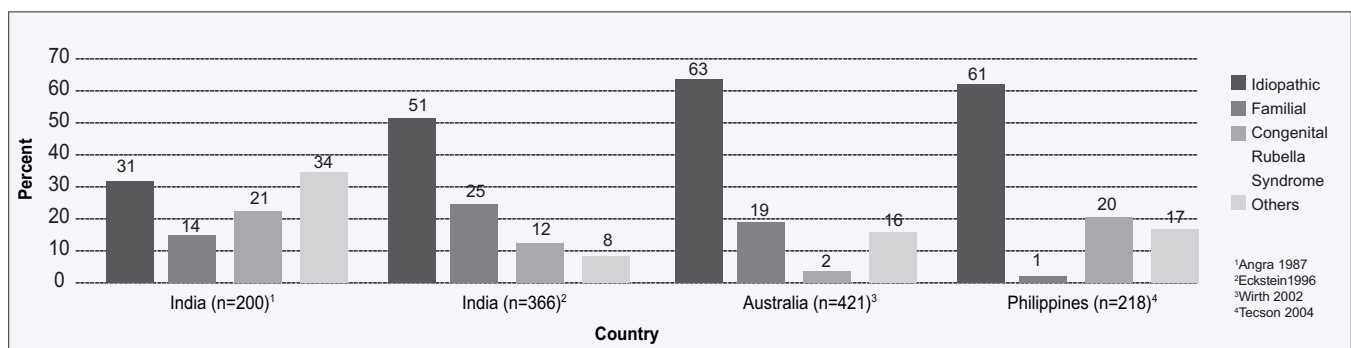


Figure 3. Causes of childhood cataract in different studies.

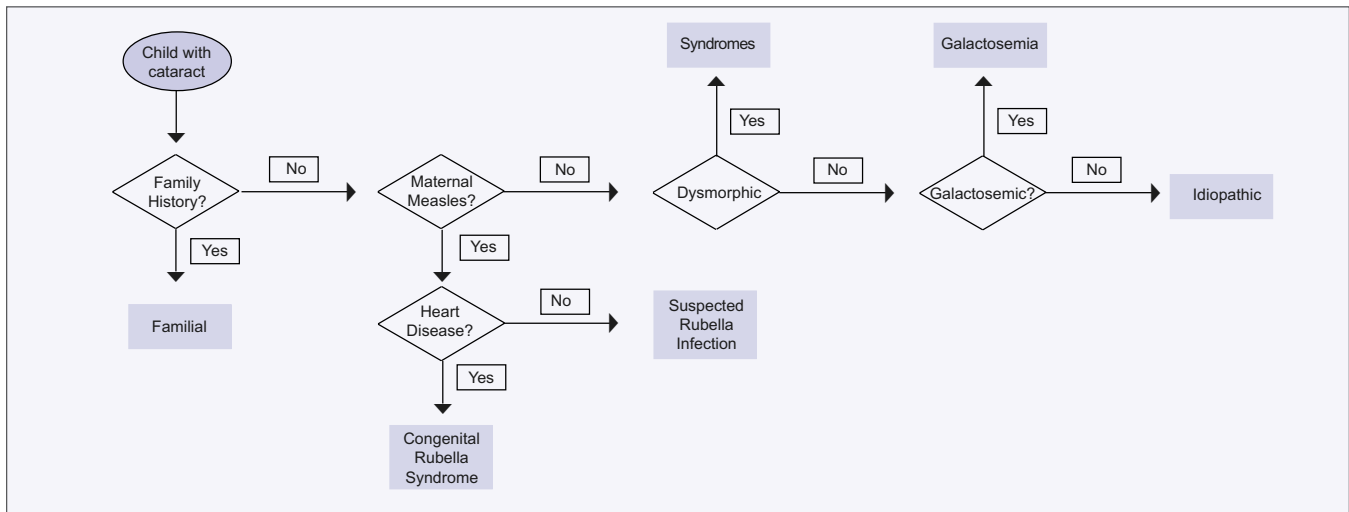


Figure 4. Flowchart of diagnostic work-up for childhood cataract.

those with atypical presentations. If the child is dysmorphic or developmentally delayed, the possibility of a genetic syndrome is considered, and referral to a geneticist for work-up is beneficial.

Newborn screening can help identify infants who have galactosemia and stand to benefit from diet modification to prevent the development and worsening of lens opacity or to reverse its course.

In children who are otherwise well with an isolated diagnosis of cataract, the benefit of an exhaustive laboratory work up is inconclusive. These patients should be comanaged with a pediatrician. Work-up for other disorders may be done when there are suspected findings.

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**CASE REPORT**

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# The hidden eye

## A case of cryptophthalmos

### ABSTRACT

#### Objective

To report a case of cryptophthalmos.

#### Methods

This is a report of a case of cryptophthalmos seen at the University of the Philippines-Philippine General Hospital (UP-PGH). Differential diagnosis and management options are discussed.

#### Results

A 12-day old boy presented with no right palpebral fissure, eyelashes, or eyebrow. The skin overlying the right orbit was continuous from the forehead to the cheek. Under this skin was a 17 mm x 15 mm soft, round, movable mass anterior to the globe. The left upper lid was colobomatous with no eyebrow and fornix. The left cornea measured 9 mm x 6 mm with exposure keratitis and large ulcer. Ultrasound of the right orbit identified the presence of the right globe with normal posterior segment. Cranial computed tomography (CT) showed a cystic mass anterior to the right globe with absent lens. Visual-evoked response of the left eye established nonspecific severe optic-nerve damage, delayed visual-pathway maturation and visual-pathway affectation.

#### Conclusion

Management of complete cryptophthalmos is difficult and requires separation of the lids and placement of mucous membrane grafts to allow for fitting of prosthesis. Reconstruction of the lid coloboma is necessary to prevent exposure keratitis. Genetic counseling is also important in the management of cryptophthalmos.

**Key words:** *Cryptophthalmos, Palpebral fissure, Coloboma, Symblepharon, Congenital*

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The authors have no proprietary or financial interest in any product used or cited in this study.

CRYPTOPHTHALMOS is a rare congenital eye defect in which the lid folds fail to separate in the embryo, resulting in a continuous sheet of skin from the forehead to the cheeks covering the eyes.<sup>1</sup> The skin over the eye is blended with the cornea, which is usually malformed. Also known as ablepharon or complete congenital symblepharon, cryptophthalmos may be unilateral or bilateral.

Its mode of genetic transmission is usually autosomal recessive, present in 15% of cases particularly in consanguineous marriages. It usually affects siblings, and lacks vertical transmission. It affects both genders and has no known chromosomal abnormality.<sup>2</sup>

In this article we describe the second case of cryptophthalmos seen in the Philippines. The first case was reported in 1978 involving an 8-month old male.<sup>3</sup>

### CASE HISTORY

A 12-day old baby boy was referred to the UP-PGH because of absent palpebral fissure. Born full-term (3 kg) via spontaneous vaginal delivery to a 28-year-old G3P2, the infant had a right eye noted by the pediatrician to be "hidden" and a left eye that would not close. Maternal history was negative except for a congenital left upper lid coloboma that was repaired in 1980. The mother's paternal half-sister, paternal first-degree cousin, and maternal aunt had eyelid coloboma. The other siblings have no congenital deformities.

Gross examination of the right eye showed no palpebral fissure, eyelashes, or eyebrow. The skin overlying the right orbit was continuous from the forehead to the cheek, with a 17 mm x 15 mm soft, round, freely movable mass underneath. Examination of the left eye revealed coloboma of the left upper lid with no eyebrow and fornix. The bulbar conjunctiva was hyperemic with yellowish discharge. Cornea was 9 mm x 6 mm vertically with a 6 mm x 4 mm ulcer at the inferior area. The rest of the anterior and posterior segment were not seen due to the corneal ulcer. Dazzle reflex to bright light was present.

Systemic workup was negative. Slide smear of the left eye discharge showed gram-positive cocci confirmed on cultures to be *Staphylococcus epidermidis*. Ocular ultrasound of the right eye showed attached retina, clear vitreous, and no intraocular mass. Visual-evoked response of the left eye showed findings consistent with nonspecific severe optic-nerve damage, delayed visual-pathway maturation and visual-pathway affection. Cranial computed tomography (CT) showed a 1.6 cm x 5.0 cm x 1.6 cm enhancing cystic mass anterior to the right globe with absent lens (Figure 1).

Emergent tarsorrhaphy was performed for the exposure keratitis in the left eye supplemented with intensive antibiotic eyedrops and ointment. A small incision was made on the skin overlying the right orbit; sample tissues obtained revealed disorganized ocular tissue on histopath.

### DISCUSSION

Differential diagnosis of cryptophthalmos are anophthalmos and microphthalmos. Both are also rare conditions, arising from abnormal development of the optic vesicle and better differentiated histologically by orbital sections.

In anophthalmos, ocular tissues are completely absent while in microphthalmos some ocular tissues are present but usually not functional. These disorders are frequently associated with reduced orbital volume and eyelid deformities. In those associated with ankyloblepharon, the lid margins are fused together, producing shortening of palpebral fissure with normal conjunctival fornices and cornea.<sup>4</sup> In anophthalmos, ankyloblepharon may be an expression of developmental arrest due to lack of mechanical stimulus for full differentiation. In normal eyes, it may represent a primary aberration of growth dating from the commencement of development of the lid folds.<sup>1</sup>

In cryptophthalmos, the eyeball is usually present but disorganized. The lid muscles, extraocular muscles, and nerve elements in the brain controlling ocular movement are developed.<sup>5</sup> Findings in this patient consistent with these clinical manifestations were the presence of a normal posterior segment confirmed by ocular ultrasound, a normally attached retina with clear vitreous, and no mass. The CT showed the presence of the right globe and histopath revealed disorganized anterior segment.

Ehlers in 1966 reported that one out of five cases of cryptophthalmos was associated with microphthalmos and colobomatous cyst. These presented clinically as bilobular masses beneath the cryptophthalmic skin. The large cyst

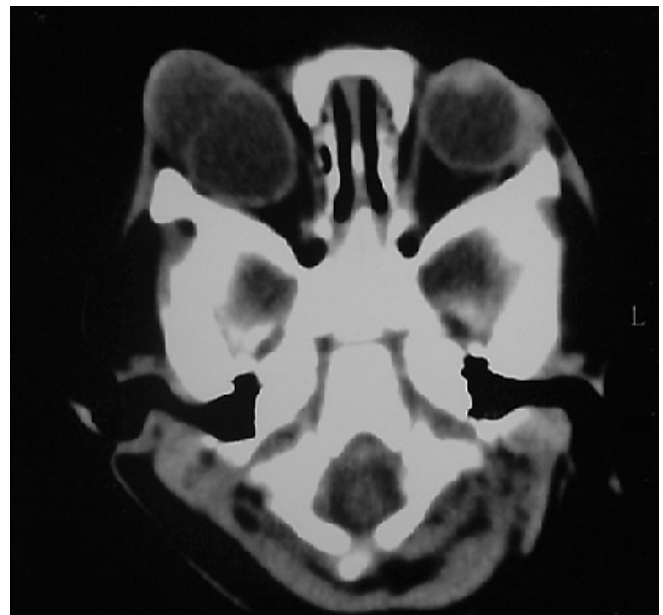


Figure 1. Cranial CT (axial cut) showing a cystic mass anterior to the right globe with no lens. The rest of the structures was normal.

may arise from the small globe, the optic nerve or a noncystic colobomatous malformation of the retina and optic nerve,<sup>6</sup> which was present in the first reported case in the Philippines. When the eyeball was exposed, the thin-walled, fluctuant, and opaque cyst was composed of uveal tissue.<sup>3</sup> In this patient, coronal and axial views of cranial CT showed a 1.6 cm x 5.0 cm x 1.6 cm peripherally enhancing hypodense mass anterior but separate from the right globe, suggesting the presence of a cystic mass.

Some studies have noted through histologic examination that the skin over the globe represented metaplastic change from corneal epithelium rather than a true skin where accessory skin appendages are present. The orbicularis oculi and levator palpebrae superioris muscles are generally present but the other eyelid structures including tarsal plates are rarely evident. The anterior segment of the eye is disorganized,<sup>7</sup> findings consistent with the biopsy of the right orbit of this patient.

In unilateral cryptophthalmos, associated anomalies have been described, including syndactyly of the fingers and toes, genital anomalies, dyscephalies, and ocular anomalies in the other eye such as dermoids, coloboma of upper lids, and microphthalmia.<sup>8</sup> When associated with multiple organ system anomalies, the condition is known as Fraser syndrome.<sup>9</sup> This syndrome should be considered in the differential diagnosis if prenatal echographic examination revealed oligohydramnios with contrastingly voluminous, hyperechogenic lungs.<sup>10</sup> However, ancillary examinations in this patient revealed no other anomalies.

Congenital coloboma of the eyelids can be associated with cryptophthalmos. A defect of the lid margin, one or all four lids may be involved. The defect may vary from a small indentation of the lid border to complete absence of the lid. The entire thickness is usually absent and the edges of the defect are rounded and covered with conjunctiva that unites the lid to bulbar conjunctiva. With large defect, such as in the left eye of this patient, corneal exposure and ulceration can occur. The coloboma is thought to be the result of trauma from amniotic bands or of a localized failure of fusion of the processes of embryonic lid folds.<sup>4</sup> Heredity played little role.

Three theories have been proposed to explain the pathogenesis of cryptophthalmos:

- Failure of mesodermal and ectodermal differentiation resulting in the absence of eyelid folds.
- Intrauterine inflammation resulting in the fusion of the eyelids to the globe.
- Amniotic bands exerting pressure on developing eyelids, causing colobomas with maldifferentiation of the conjunctiva resulting in symblepharon.<sup>11</sup>

Duke-Elder and Ida Mann described two types of this

condition: one arising from an initial failure of the lids to form, and the other from a subsequent destruction or absorption of the conjunctivae.<sup>12</sup> Other authors explained the condition on the basis of ankyloblepharon by ankylosis. Currently, many believed that the primary cause is failure of the lids to form or an arrest of development.<sup>13</sup>

Three different forms of cryptophthalmos have been described:

- Complete, as seen in this patient, is the most common. The skin replaces the eyelids, covers the orbit, and connects to the globe so that ocular movement can be seen beneath it.<sup>11</sup>
- Partial or hemicyptophthalmos is seen in about 20% of cases. The lateral portion of the eyelid is normal with fusion of the facial skin to the cornea medially.<sup>11</sup>
- Congenital symblepharon, where the upper eyelid fuses with the globe and the superior cornea is covered by keratinized stratified squamous epithelium.<sup>11</sup>

Management of complete cryptophthalmos is difficult. Extensive reconstructive surgery is involved, including separation of the lids and placement of mucous membrane grafts to allow a conformer or prosthesis to be fitted. Reconstruction of the left eyelid coloboma involves several stages and the use of ear cartilage graft under the skin membrane over the globe to increase mass and act as tarsal plate or the use of mucosal graft to cover the raw surface of the inner side of the upper lid and globe area.

In this patient, the tarsorrhaphy failed on the third week. Repair of the upper lid coloboma by pedicle rotation graft and separation of the skin of the right orbit with placement of mucous membrane grafts were considered.

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**BRIEF REPORTS**

## Malignant Melanoma of the Conjunctiva

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### ABSTRACT

#### Objective

*To report a case of malignant melanoma of the conjunctiva.*

#### Methods

*This is a case report of a malignant melanoma of the conjunctiva seen at the University of the Philippines-Philippine General Hospital (UP-PGH).*

#### Results

*A 42-year-old male presented with an enlarging, bleeding mass on the left upper lid. There was dark, diffused pigmentation of the caruncle and the bulbar conjunctivae. A section biopsy revealed findings consistent with malignant melanoma. An orbital exenteration was performed.*

#### Conclusion

*The management of malignant melanoma of the conjunctiva should involve removal of the tumor, prevention of local recurrence, and prevention of metastasis and death.*

Malignant melanoma of the conjunctiva is a rare unilateral disease occurring most frequently in patients 50 years or older.<sup>1</sup> Although its natural history has not been clearly established, it is potentially life-threatening.<sup>2</sup> This paper presents the history and management of a case of malignant melanoma of the conjunctiva seen at the UP-PGH.

A 42-year-old male sought medical attention for an enlarged mass on the inner portion of the left upper lid. Two darkly pigmented lesions, one measuring 1 mm x 1 mm over the bulbar conjunctiva at the medial canthus, the other measuring 3 mm x 1 mm on the inner portion of the left upper eyelid, had been present since age 10.

Visual acuity was 6/6 (20/20) in the right eye and 6/15 (20/50) pinhole to 6/6 (20/20) in the left eye. Gross examination showed a reddish-black, nodular, vascularized, and bleeding mass measuring 2 cm x 3 cm x 3 cm on the left upper palpebral conjunctiva. There was diffuse pigmentation of the caruncle and bulbar conjunctiva. The rest of the eye findings were normal.

Systemic work-up were negative. Cranial computed tomography (CT) showed a homogenous, slightly hyperdense soft-tissue mass on the left eyelid, measuring 1.5 cm x 2.2 cm x 0.8 cm and without osseous involvement. The left globe was intact.

Differential diagnosis for the pigmented lesions include a large nevus, ciliary body melanoma with extraocular extension, a pigmented conjunctival carcinoma, and melanocytoma. Grossly, these disease entities are similar; only a histological examination can differentiate them from true malignant melanoma.

A section biopsy of the mass was done showing epithelial configuration of spindle cells also seen in samples taken from the medial and lateral canthal areas.

Two principal cell types are found in malignant melanoma: the fascicular type where spindle cells are arranged in rows and the epithelioid configuration consisting of larger polygonal cells with distinct boundaries.

Malignant melanoma starts as an extraepithelial proliferation of atypical melanocytes that can spread radially (superficial spread or pagetoid growth) within the epithelium for prolonged periods and produce flat, golden brown pigmentation that may have a waxing and waning course. A vertical, invasive phase occurs later, which extends into the substantia propria. If the radial phase is short, a localized invasive nodule may become present.<sup>3</sup> Malignant melanomas have no known association with solar exposure, but host factors play an important role in its development.<sup>2</sup>

Almost all conjunctival melanomas develop in a preexisting pigmented conjunctival lesion. Eighteen percent arise in a conjunctival nevus and can occur as a solitary circumscribed lesion, which never recurs after local excision. About 57% present as a diffuse lesion or multiple lesions associated with or arising from primary acquired melanosis (PAM) of the conjunctiva.<sup>2, 3</sup> PAM usually presents in middle age with flat, granular, intraepithelial reddish-brown pigmentary change, initially noted in the bulbar conjunctiva. Clues to malignant transformation of PAM include increased thickness, a change in pigmentation, the appearance of prominent blood vessels feeding a tumor, and tethering of the

conjunctiva to the underlying sclera, where it is usually mobile.<sup>3</sup> In this patient, the lesion behaved like it arose from a PAM by spreading to contiguous areas, developing blood vessels that fed the tumor, and increasing in thickness and size over the years.

When the melanocytes remain in the epithelium, there is no possibility for metastasis. However, once intraepithelial pagetoid tumors involve 50% to 100% of the bulbar and palpebral conjunctiva, the chance for metastasis is larger.<sup>1,2</sup> Advanced melanomas ultimately invade lymphatics and spread to preauricular, submandibular, and cervical nodes before disseminating to the parotid gland, liver, subcutaneous tissues, and brain.

Management of malignant melanoma of the conjunctiva is difficult and the subject of many controversies. Complete excision of the tumor and prevention of local recurrence, metastasis, and death are the goals.<sup>2</sup> Options include a wide excision of the melanoma with cryotherapy of the margins,<sup>5</sup> wide excision with topical chemotherapy such as mitomycin-C,<sup>4</sup> (Mitomycin C, Kyowa, Tokyo, Japan), wide excision with radiotherapy, and orbital exenteration. For small circumscribed melanomas, beta-irradiation with strontium-90 surface applicators, proton-beam therapy, gamma emissions from cobalt-60 or cobalt plaques have been found effective.<sup>4</sup>

Due to the extensive involvement of the conjunctivae, including the caruncle and upper lid, an orbital exenteration was done in this patient. Histopath results showed largely epithelioid configuration of spindle cells. The eyeball, optic nerve, lacrimal gland, and all surgical margins were negative for tumor.

Malignant melanoma is the most serious of the conjunctival malignancies. Nearly 50% of patients have recurrence after resection, while 26% develop metastasis after 10 years.<sup>1</sup> Prognosis is often poor for patients with malignant melanoma in the palpebral conjunctiva, fornices, plica, caruncle, or eyelid margin. Among these patients, mortality is 2.2 times higher.<sup>2</sup> Prognosis improves for patients with lesions found in the bulbar conjunctiva.<sup>1</sup>

Proximity to the lymphatic system may explain why some locations are less favorable than others.<sup>2</sup> Survival rates are worse for the following: lesions arising from PAM, those with an initial thickness of more than 4 mm, lesions arising from an unfavorable site, multifocal disease in favorable sites, mixed spindle and pure epithelioid cells with lymphatic invasion, high mitotic index, and lesions that grow vertically.<sup>1,2</sup>

In this patient, prognosis was considered poor because the tumor involved the palpebral conjunctiva, fornices, and caruncle, and the lesions arose from a PAM. Whether orbital exenteration can prevent metastasis is uncertain. Some studies have reported that the procedure did not lead to increased survival rate.<sup>4</sup>

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## Retinal Dysplasia\*

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### ABSTRACT

#### Objective

To report a case of retinal dysplasia.

#### Method

This is a case report of retinal dysplasia, the first documented case seen at the University of the Philippines-Philippine General Hospital (UP-PGH).

#### Results

A three-month-old female presented with bilateral leukocoria and an intraocular mass in the right eye. The right eyeball was enucleated and histopathology results revealed retinal dysplasia.

#### Conclusion

Ocular ultrasonographic and cranial computerized tomography are helpful in the diagnosis of suspected retinal dysplasia.

Retinal dysplasia consists of an abnormal proliferation of developing retina, producing tubular structures with a rosette-like appearance in cross section.<sup>1</sup> It appears to be associated with a single pathogenetic basis: the separation of the retina during a critical stage of its differentiation from its underlying pigment epithelium.<sup>2</sup>

We are presenting the first reported case of retinal dysplasia seen at the UP-PGH.

A three-month-old female, the second of twins, born preterm at 7 months (1,400 grams) via Caesarean section,

\*Presented at the Annual Meeting of the Philippine Academy of Ophthalmology, November 2003

presented with bilateral leukocoria at 2 months of age. Supplemental oxygen was given for 7 days. Her development was at par with other infants her age. The patient's twin sister had retinopathy of prematurity in both eyes (OU).

Ophthalmologic examination revealed negative dazzle in OU. The right cornea measured 8 mm x 8 mm while the left cornea measured 10 mm x 10 mm. Pupils were 3 mm, slowly reactive to light with no afferent pupillary defect. Full range of ocular movements were present in OU. Intraocular pressure (IOP) was less than 4 mm Hg in the right eye (OD) and 7 in the left eye (OS). The anterior chambers in OU were shallow with posterior synechiae. A whitish mass was noted in OU with retinal vessels and hemorrhages. Gonioscopy revealed primarily open angles in OU with peripheral anterior synechiae interspersed inferiorly in OS.

The rest of the organ systems were normal. Cranial computerized tomography (CT) showed no intracranial lesions.

Ocular ultrasonography showed a right eyeball measuring 1.6 cm in anteroposterior diameter. The anterior half of the vitreous showed granular density with high narrow spikes and a midline irregular membranous density indicating detached retina. Behind the membrane was an irregularly shaped mass with spikes 50 to 70% of the anteriorly located densities. The choroid was markedly thickened (Figure 1). The left eyeball was 1.8 cm in length with findings of retinal detachment and thickened choroid.

CT showed a small right globe with calcifications in the posterior globe and enlarged optic nerve, and a larger left globe with irregular thickening and increased attenuation of the inferoposterior aspect accompanied by calcifications.

Differential diagnoses for leukocoria in infancy include retinopathy of prematurity (ROP), persistent hyperplastic primary vitreous (PHPV), Coats' disease, and retinoblastoma.

ROP is a proliferative retinopathy seen in premature infants weighing less than 1,500 g at birth. The younger the gestational age and the lower the birth weight, the more severe is the case. Administration of supplemental oxygen to the newborn has been implicated as a cause. It is typically a bilateral disease that affects the vitreous and peripheral retina. Even though the patient was born preterm with low birth weight, the presence of an intraocular mass and calcification ruled out this condition.

PHPV is a congenital, nonhereditary malformation of the eye that is usually unilateral and not associated with systemic defects. Severe cases may present with microphthalmic eyes with shallowing of the anterior chamber and retinal detachment. The bilateral involvement in this patient and the presence of calcifications make this condition unlikely. In less severe PHPV, a

membranous band extending from the posterior lens capsule to the optic disc may be present.

Coats' disease is an idiopathic condition characterized by telangiectatic and aneurysmal retinal vessels with intraretinal and subretinal exudates. It is unilateral in 80% or more of cases,<sup>3</sup> affecting more males (3:1 ratio). Gradual progression with increasing exudation occurs over time. Massive exudative retinal detachment can occur with cholesterol crystals producing characteristic echograms that were not seen in this patient.

Retinoblastoma is a neuroblastic tumor that is the most common primary intraocular malignancy of childhood. The most common initial sign is leukocoria. Exophytic tumors are usually yellow-white and occur in the subretinal space with subretinal fluid accumulation and exudative retinal detachment. Calcification is a common finding in areas of necrosis of tumor cells producing echograms of extremely high reflectivity on A-scan and very bright signals on B-scan.<sup>4</sup> Retinoblastoma was considered in this patient because of the early presentation of bilateral leukocoria and findings on ultrasonography confirmed by CT.

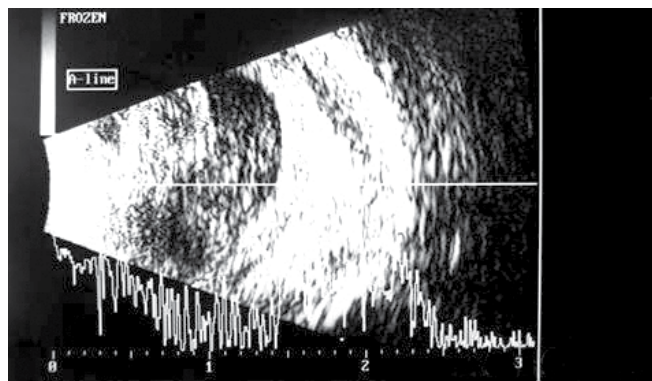


Figure 1. Ultrasound of the right eye.

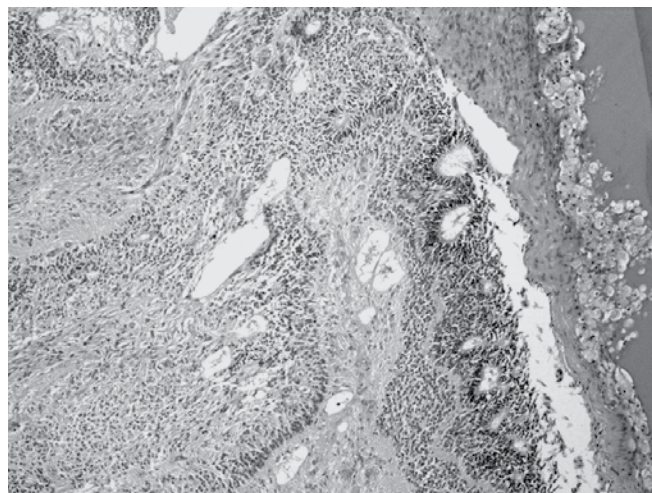


Figure 1. Rosettes of retinal dysplasia.

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The right eye was enucleated. Dissection of the globe showed a white retrolental mass occupying the anterior one half of the vitreous cavity. Microscopically, a completely dysplastic detached retina was totally separated from the choroid by eosinophilic, serous subretinal fluid and hemorrhage. There were numerous macrophages ingesting the red blood cells and cholesterol clefts in the subretinal fluid denoting an old vitreous hemorrhage. Focal retinal dysplasia includes extensive glial formation, cellular proliferation and rosette-like formation (Figure 2). The optic nerve was unremarkable.

The pathogenesis of retinal dysplasia include the following:

- resulting from hyperplastic extension of the retina into "abnormal" sites away from its pigment epithelium,
- secondary to detachment of the retina from the pigment epithelium,
- occurring in an otherwise normal location over areas devoid of pigment epithelium, and
- *in situ* dysplastic process with no evidence that the dysplastic retina has ever been separated from its underlying epithelium.<sup>5</sup>

The underlying feature of each of these processes is the absence of a presumed normal histogenetic control by the pigment epithelium on the developing retina.<sup>5</sup> Dysplastic changes appear to be intermediate between a receptor that has developed normally and one that has

followed uncontrolled, neoplastic growth. Muller fibers contribute to dysplastic rosette formation but not retinoblastoma rosette formation.

Retinal dysplasia may also be associated with congenital anomalies (13%),<sup>6</sup> or with chromosomal abnormalities<sup>7</sup> like Trisomy 13, or systemic findings such as Norrie's disease (x-linked recessive).<sup>7</sup>

Retinal dysplasia should be considered as a differential diagnosis in patients presenting with leukocoria. The ultrasonographic and tomographic findings are helpful in the diagnosis of suspected retinal dysplasia. A thorough physical examination is needed to rule out systemic abnormalities associated with the disease. Early screening will be of help in genetic counseling of the parents.

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- Study Design: Identifies the study design using a phrase such as randomized or nonrandomized clinical trial, case-control study, cross-sectional study, cohort study, case series, case report, systematic review, metaanalysis, review, experimental study, or historical manuscript. Additional modifiers may be included (e.g. consecutive, nonconsecutive, retrospective, prospective, observational, interventional).
- Setting: (e.g. multicenter, institutional, clinical practice)
- Participants, Patients, or Study Population: Number of patients/eyes, selection procedures, inclusion/exclusion criteria, randomization procedure, and masking.
- Intervention or observation procedure(s)
- Main and secondary outcome measure(s)
- Data and statistical analyses.

For clinical studies, statements regarding adherence to the Declaration of Helsinki, approval by Institutional Review Board (IRB)/Ethics Committee, and description of the informed consent process should be included. For

animal research, the Association for Research in Vision and Ophthalmology (ARVO) guidelines for animal research should be followed and adherence to the said guidelines should be stated. Previously published procedures should be identified by reference only.

*Results:* Results must be concise. Provide demographic data of the study population. Describe outcomes and measurements in an objective sequence with minimum discussion. Data should be accompanied by confidence intervals (usually at the 95% interval) and exact *p* values or other indications of statistical significance.

*Discussion:* The Discussion should be restricted to the significant findings presented. Avoid excessive generalization and undue speculation. Digressions and theorizing are not appropriate. Elucidate on (but do not reiterate) the results, provide responses to other and contradictory literature, identify limitations or qualifications of the study, and state the conclusions that are directly supported by the data. Give equal emphasis to positive and negative findings, whether and what additional study is required, and conclude with the clinical applications or implications supported by the study. The conclusion(s) is (are) incorporated into the end of the discussion and should be directly supported by the results. Authors should avoid making statements on economic benefits and costs unless their manuscript includes economic data and analyses. Avoid claiming priority of the content unless you provide the literature search protocol used.

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Because readers may infer their endorsement of the data and conclusions, all persons acknowledged must have given permission to be acknowledged and this must be confirmed in the cover letter.

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## APPENDIX

An appendix should be used very sparingly. However, it is appropriate to provide survey forms, to list the members of a study group, or explain complex formulas or information.

In studies involving a study group, the writing group authors should be listed along with the group name (e.g. Smith TT, Jones JJ on behalf of the Pediatric Amblyopia Study Group) on the title page. Other group members should be listed in an appendix. When the study group name alone is listed on the title page, the Copyright Transfer Agreement requires only the original signature of the Corresponding Author. When a series of authors is listed on the title page in conjunction with the study group name, the Copyright Transfer Agreement must include the original signatures of these authors.

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Web site references must include author (or web site owner), title of article, date article was posted, publication (if applicable), complete web site address, and date accessed.

### Examples

*Journal Article* (If four or fewer authors, list all)

Fishman GA, Alexander KR, Milam AH, Derlacki DJ. Acquired unilateral night blindness associated with a negative electroretinogram waveform. *Ophthalmology* 1996; 103: 96-104.

*Journal Article* (If five or more authors, list only the first three and add et al.)

Vail A, Gore SM, Bradley BA, et al. Clinical and surgical factors influencing corneal graft survival, visual acuity, and astigmatism. *Br J Ophthalmol* 1996; 103: 41-49.

*Chapter in a Book*

Parks MM, Mitchell PR. Cranial nerve palsies. In: Tasman W, Jaeger EA, eds. *Duane's Clinical Ophthalmology*, revised ed. Philadelphia: JB Lippincott, 1993; v. 1, chap. 19: 550-551.

*Book*

Miller NR. *Walsh and Hoyt's Clinical Neuro-Ophthalmology*, 4th ed. Vol. 4. Baltimore: Williams & Wilkins, 1991; 2102-2114

*Web site*

World Health Organization. Hospital infection control guidelines for severe acute respiratory syndrome. April 16, 2003: <http://www.who.int/csr/sars/infectioncontrol/en> (accessed April 24, 2003).

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