# UNOPERATED EYES WITH PERSISTENT FETAL VASCULATURE

BY *Nishi Gulati*, **Ralph C. Eagle Jr MD**, AND **William Tasman, MD***

## ABSTRACT

*Purpose:* To present a follow-up on children with persistent fetal vasculature (PFV) when surgery was not performed.

*Methods:* From January 1992 through June 2001, 31 infants (31 eyes) with PFV were evaluated to document the number of eyes operated on versus eyes not operated on to determine whether the latter group remained stationary or became worse.

*Results:* Seventeen of the 31 eyes underwent surgery. Of the 14 eyes not undergoing surgery, 7 were judged to be inoperable. The remaining 7 eyes were not operated on because the fundus could be visualized through an undilated pupil. Follow-up on 5 of the 7 eyes ranged from 18 months to 9.5 years. None showed progression of the lens opacity or development of retinal detachment. The eyes were amblyopic but functional.

*Conclusions:* In this limited series of eyes with PFV where the plaque was not large enough to fill the pupil, the eyes followed up were amblyopic, but useful vision was retained and the lens opacity did not enlarge.

## INTRODUCTION

Persistent fetal vasculature (PFV) or persistent hyperplastic primary vitreous (PHPV) is a condition that presents during infancy. As reported by Cloquet in 1818,[1] it occurs because of a failure of the primary vitreous and the hyaloid vascular system to regress (Figure 1). His treatise, interestingly, shows a persistent tunica vasculosa lentis very similar to that documented in a recently seen 26-week-old premature infant (Figures 2, 3).

The clinical manifestations of PFV typically include unilaterality, persistence of the hyaloid system in Cloquet's canal, microphthalmos, cataract, retinal traction or dysplasia, and elongation of the ciliary processes (Figures 4 and 5).[2-4]

Management of PFV may be either surgical or by observation. Surgical intervention aims to provide the patient with useful vision and to prevent the onset of angle-closure glaucoma and/or phthisis bulbi in the PFV eye.[5] The possible benefits of surgical treatment for PFV include improvement in visual acuity and prevention or delay in the development of ocular complications, such as glaucoma, hemorrhage, and enucleation. The decision to perform surgery may be based on the severity of the PFV and whether or not the fundus can be visualized through

an undilated pupil, the presence or absence of retinal detachment, and the degree of cataract.

Clinical opinion may favor surgery because of the observation made by Reese[2] in the Jackson Memorial Lecture of 1955: "I have not been able to discover a single recognizable case in an adult" (Figure 6). But in the next sentence, Reese indicated that "mild lesions of this type may run an uncomplicated course and can be seen occasionally in adult eyes."

A number of studies reporting surgical results[5-7] relate to anterior PFV, although other studies[8-10] have reported beneficial effects of surgical treatment for posterior PFV as well as combined anterior and posterior PFV. Despite the fact that many studies provide support for surgical treatment for PFV, it may not be the best option for every patient, particularly when the fellow eye is unaffected, as is usually the case, because PFV eyes are smaller and may have macular hypoplasia (Figures 7 and 8).

In this report, we present the results of a retrospective study of PFV, with an emphasis on eyes that were observed. The number of eyes is small, and no statistically valid results can therefore be provided.

## METHODS

From January 1992 through June 2001, 31 infants (31 eyes) with PFV were evaluated at Wills Eye Hospital after institutional review board (IRB) approval was obtained. A retrospective review of all charts was conducted, and data on the best visual acuity, state of lens opacity, state of the

From the Department of Ophthalmology, Jefferson Medical College, Philadelphia, Pennsylvania.
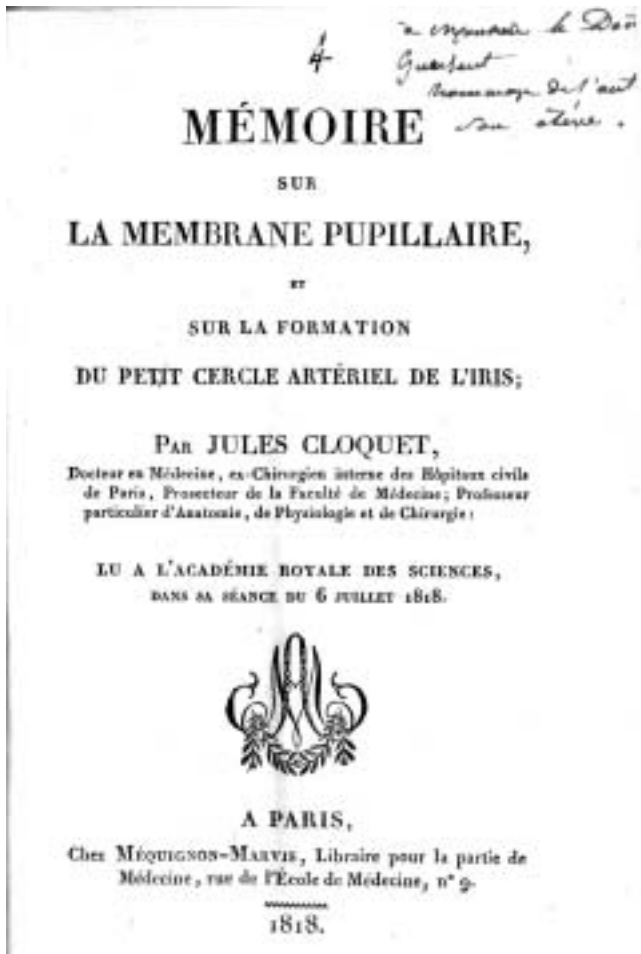*Presenter.
Bold type indicates AOS member.

FIGURE 1
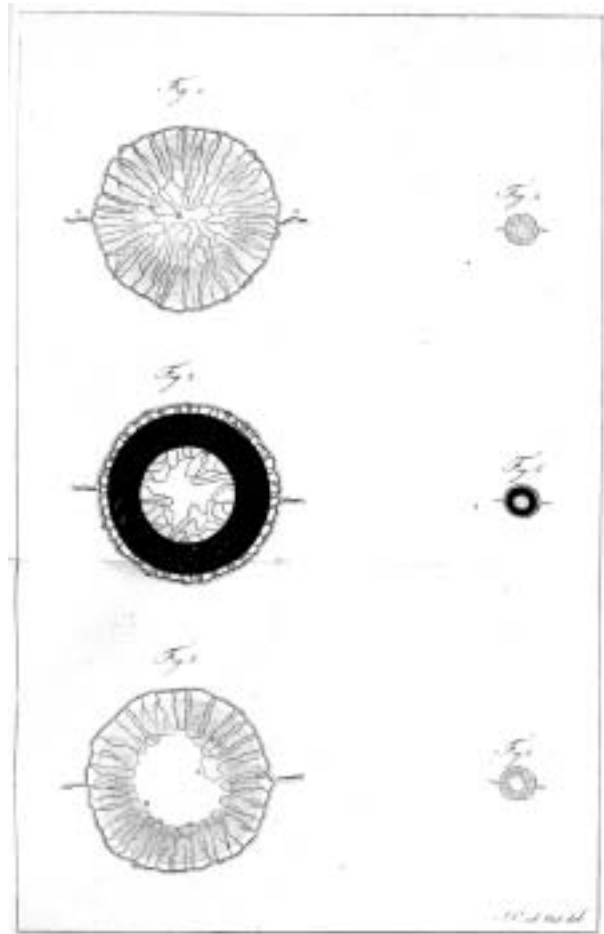Title page from Cloquet's treatise published in 1818.



FIGURE 2
Illustration of persistent tunica vasculosa lentis from Cloquet's treatise.

retina, and the presence or absence of ocular complications recorded during the follow-up visits in a period ranging from 18 months to 9.5 years were recorded. Measurable vision was equated with the ability to count fingers or better. The final analysis rested upon the status of the nonoperated eyes at the end of the follow-up period and a comparison of the ocular complications noted in each group (unoperated versus operated eyes).

## RESULTS

Thirty-one patients with PFV were reviewed. Nineteen were male and 12 were female. Seventeen (55%) of 31 eyes underwent surgery. Of the remaining 14 eyes, seven (23%) were judged to be inoperable. The remaining seven eyes (23%) were not operated on because the fundus could be well visualized (Figure 9). The range of follow-up for this group was 3 to 10 years, with an average and median of 6 years. Follow-up of the operated eyes ranged from 4 to 10 years, with an average of 8 years and a median of 10 years. Ultrasound and, in certain cases,

computerized tomography (CT) were helpful diagnostic tools (Figures 10 and 11). Four affected eyes that underwent surgery had measurement of their axial length as well. These ranged from 13.37 mm to 17.47 mm. When compared with the fellow eyes, the PFV eyes were 0.9 mm to 3.2 mm shorter.

The data on the best visual acuity, state of the retina, state of lens opacity, and other ocular complications obtained during the stated follow-up period for each of the unoperated PFV eyes is presented in Table I. Best visual acuity results ranged from "fix and follow" to 20/100. The condition of the lens and retina remained stable, and each unoperated eye remained amblyopic. In addition, one eye developed a macular scar. The latter patient was seen within 2 weeks of birth. The right eye was microphthalmic and nonfunctional. The left had a persistent hyaloid artery with a branch to the macula causing a traction retinal detachment with a pigmented demarcation line (Figure 12). A lens-sparing vitrectomy had been considered, but because the detachment occurred in utero and was long-standing, observation was

**FIGURE 3**

Persistent tunica vasculosa lentis and persistent hyaloid artery in 26-week-old preemie.
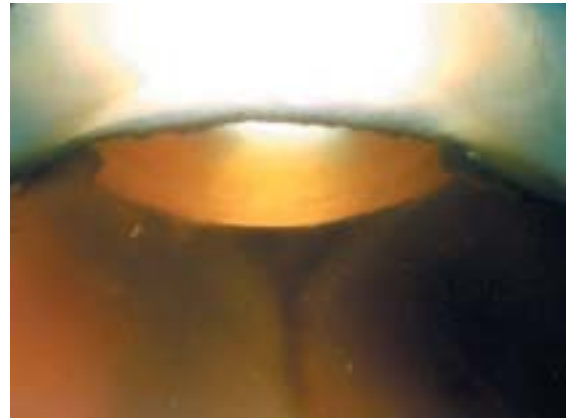


**FIGURE 4**

Cloquet's canal.



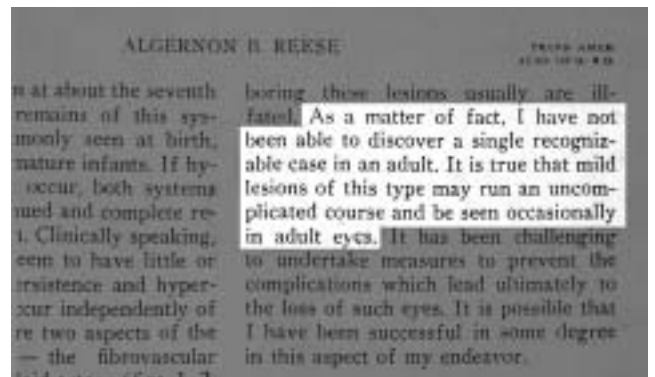**FIGURE 5**

Persistent fetal vasculature in hyaloid canal.



**FIGURE 6**

Excerpt from Reese's 1955 Jackson Lecture.



**FIGURE 8**

Absence of foveal reflex due to macular hypoplasia in affected left eye.



**FIGURE 7**

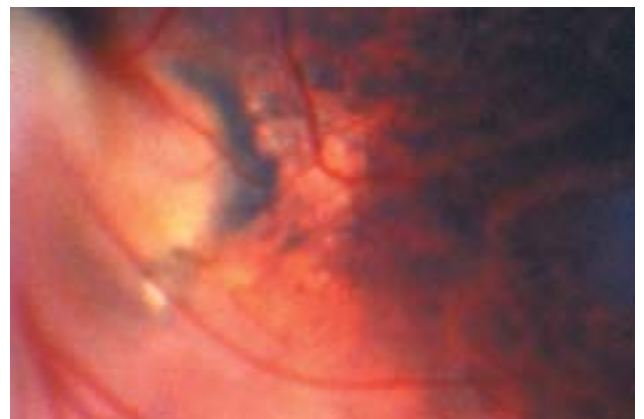Fellow normal right eye of patient with persistent fetal vasculature OS showing good foveal reflex.



**FIGURE 9**

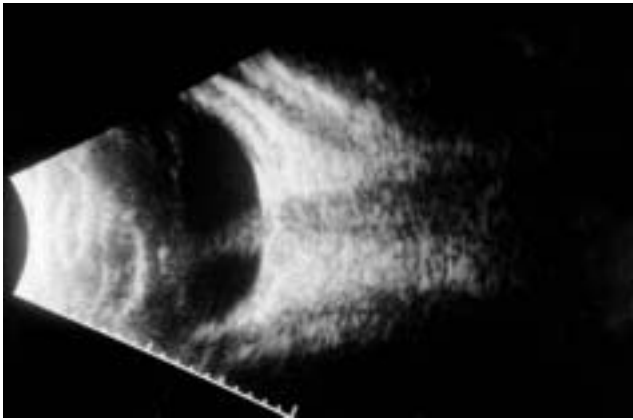Mild persistent fetal vasculature with fundus visible.

**FIGURE 10**
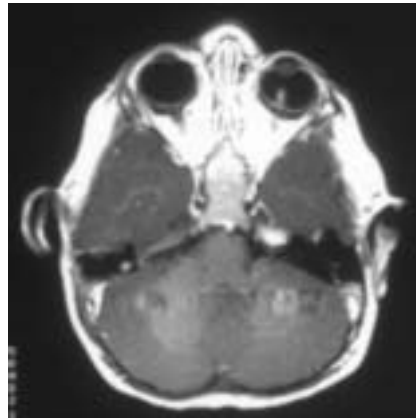B-scan showing persistent fetal vasculature.



**FIGURE 11**
Computed tomography showing persistent fetal vasculature.
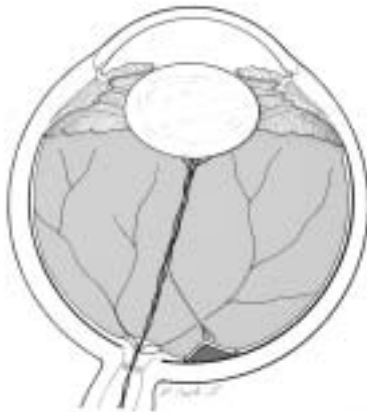


**FIGURE 12**
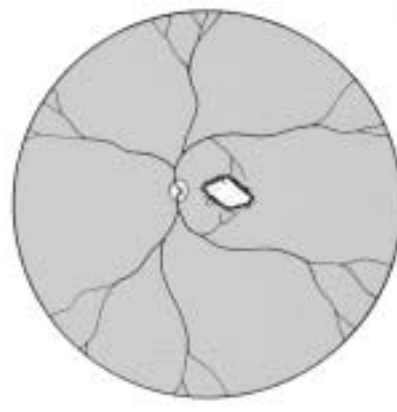Persistent fetal vasculature causing macular detachment.



**FIGURE 13**
Several months later, an atrophic scar is present after spontaneous release of persistent fetal vasculature seen in Figure 12.

| CASE | BEST VISUAL RESULTS | STATE OF RETINA | OTHER OCULAR LENS OPACITY | COMPLICATIONS |
|---|---|---|---|---|
| 1 | Fix and follow | Attached | Lens is quiet and stable; no progression | Amblyopia |
| 2 | Counting fingers | Attached | Lens is quiet and stable; no progression | Amblyopia |
| 3 | Counting fingers | Attached | Lens opacity remains small; no progression | Amblyopia |
| 4 | Counting fingers | Attached | Lens is quiet and stable; no progression | Amblyopia |
| 5 | Counting fingers | Attached | Lens remains clear; no progression | Amblyopia |
| 6 | Counting fingers | Attached | Lens remains clear; no progression | Scar in macula, amblyopia |
| 7 | 20/100 | Attached | Lens is quiet and stable; no progression | Amblyopia |

**TABLE I: STATUS OF UNOPERATED EYES DURING THE FOLLOW-UP PERIOD**

recommended. Over the next several months, the PFV spontaneously released, leaving a scar in the macula (Figure 13). Eight years later the patient has count fingers vision in this only seeing eye and gets around quite well.

Ocular complications that resulted in a lack of measurable vision in the operated eyes within the follow-up period are recorded in Table II. Complications included retinal detachment in four eyes. Three were successfully repaired, but one eye ultimately required enucleation. Another eye became phthisical and was later removed.

## DISCUSSION

Our study reviewed 7 of 31 eyes with PFV who were managed conservatively by observation only. While only one of these eyes achieved a vision of 20/100, all 7 had the ability to at least fix and follow. Six eyes were able to count fingers. During the follow-up period (Table I), none of the eyes being followed developed retinal detachment or progression of the lens opacity. In each case, either the lens was clear and quiet or the plaque was

**TABLE II: OCULAR COMPLICATIONS IN THOSE TREATED SURGICALLY**

| CASE | OCULAR COMPLICATIONS |
| --- | --- |
| 1 | No complications |
| 2 | No complications |
| 3 | Enucleation (phthisis) |
| 4 | No complications |
| 5 | No complications |
| 6 | Enucleation (after retinal detachment) |
| 7 | No complications |
| 8 | Retinal detachment (repaired) |
| 9 | No complications |
| 10 | No complications |
| 11 | No complications |
| 12 | No complications |
| 13 | No complications |
| 14 | Retinal detachment (repaired) |
| 15 | No complications |
| 16 | No complications |
| 17 | Retinal detachment (repaired) |

stable and did not enlarge. Other ocular sequelae included amblyopia and, as previously described, a macular scar in the only seeing eye.

Amblyopia was treated by patching the better eye. Without patching, the visual acuity in the PFV eye neither improved nor significantly worsened. In the eye with a macular scar, any hope of "reading visual acuity" was eliminated, and even though it was the only seeing eye, the patient was able to navigate well. Since none of the eyes managed in a conservative manner deteriorated over the follow-up period, it can be inferred that this method, although not one that is likely to improve visual acuity, allows for maintenance of eye stability and some functional vision.

When the ocular complications occurring in the nonsurgically managed group (Table I) were compared with those occurring in the surgically treated group (Table II), it became apparent that more serious changes occurred in the latter group. Specifically, four eyes developed a retinal detachment and two eyes were enucleated. However, surgery may be the only option in severer forms of PFV to salvage the eye and to improve visual acuity.

Although based on a limited number of cases, our findings are in agreement, at least in part, with those of Anteby and colleagues.[11] In their study of 89 children with PFV in one eye, 61 of whom were surgically treated and 28 of whom were managed conservatively, they found that nonsurgical treatment provided for a stable PFV eye with relatively fewer ocular complications than surgical treatment. They reported that the nonsurgical group of patients had a slightly lower incidence of increased intraocular pressure and glaucomatous changes (11.8%) than the surgically treated patients (average of the aphakic and psuedophakic group, 15.5%) and that the percentage of conservatively handled patients requiring a prosthesis or shell was only 7% (2 of 28)

compared to 13% (8 of 61) in the surgically treated group.

Studies by Scott and associates[7,12] also support our findings. More than half of their subjects, 25 of 48 (52%), were managed nonsurgically, yet only 2 of the 25 (8%) ultimately required enucleation. Thus, although this group of patients had poor visual results, they remained stable without surgical intervention.

Our findings, along with those of Anteby and colleagues[11] and Scott and associates,[7,12] also support the observations made by Goldberg in the 55th Jackson Memorial Lecture, in which he reviewed and summarized the observations of other investigators, along with his own.[3] Goldberg indicated that many minimally affected eyes, such as those with either normal visual function or lack of progressive anatomic changes, do not develop secondary complications and remain stable without surgical treatment. According to Goldberg, a number of such minimally affected eyes remain glaucoma-free.

In contrast to our findings and those of Anteby and colleagues[11] and Scott and associates,[7,12] Alexandrakis[13] has reported a relatively greater incidence of complications in the nonsurgical group as compared to the surgical group. Of the 42 patients with PFV evaluated by Alexandrakis (30 treated surgically and 12 managed nonsurgically), 5 (20%) of 30 in the surgical group and 4 (33%) of 12 in the nonsurgical group developed ocular complications. However, Alexandris points out that "some patients may not be candidates for surgery because of either minimal changes or advanced disease that limit the potential of visual improvement."

Yet another study, although based on a limited number of cases, found results differing from ours. Federman and coworkers,[14] through follow-up of 9 of 16 patients managed nonsurgically, observed progressive deterioration of the PFV eye over the course of 1 to 4 years in 8 of 9 eyes (90%). However, 6 eyes in this series were considered inoperable and the remaining families declined surgery.

## CONCLUSION

Conservative management of PFV is undertaken less often than surgical treatment because, typically, surgery offers a greater chance of obtaining better visual acuity, although even these eyes are predominantly amblyopic. Visual improvement is not an expectation of nonsurgical management, but our data suggest that conservative therapy in appropriately selected eyes can allow for the maintenance of an amblyopic stable eye in children with PFV.

## REFERENCES

1.    Cloquet, Jules. *Mémoire sur la membrane pupillaire, et sur la formation du petit cercle artérial de l'iris.* Paris, 1818.

2.  Reese AB. Persistent hyperplastic primary vitreous. The Jackson Memorial Lecture. *Am J Ophthalmol* 1955;40:317-331.

3.  Goldberg M. Persistent fetal vasculature: an integrated interpretation of signs and symptoms associated with persistent hyperplastic primary vitreous. *Am J Ophthalmol* 1997;124:587-626.

4.  Tawansky, K. Macular features of pediatric surgical vitreoretinal diseases. *Ophthalmol Clin North Am* 2002;15:503-516.

5.  Pollard, ZF. Persistent hyperplastic primary vitreous: diagnosis, treatment, and results. *Trans Am Ophthalmol Soc* 1997;95:487-549.

6.  Roussat B, Barbat V, Cantaloube C, et al. Persistent hyperplastic primary vitreous syndrome: clinical and therapeutic aspects. *J Fr Ophthalmol* 1998;21(7):501-507.

7.  Karr DJ, Scott WE. Visual acuity results following treatment of persistent hyperplastic primary vitreous. *Arch Ophthalmol* 1986;104(5):662-667.

8.  Mittra RA, Huynh LT, Ruttum MS, et al. Visual outcomes following lensectomy and vitrectomy for combined anterior and posterior persistent hyperplastic primary vitreous. *Arch Ophthalmol* 1998;116(9):1190-1194.

9.  Dass AB, Trese MT. Surgical results of persistent hyperplastic primary vitreous, *Ophthalmology* 1999;106(2):280-284.

10. Sibert M. Persistent hyperplastic primary vitreous. *Clin Eye Vis Care* 2000;12(3-4):131-137.

11. Anteby I, Cohen E, Karshai I, et al. Unilateral persistent hyperplastic primary vitreous: course and outcome. *J AAPOS* 2002;6(2):92-99.

12. Scott WE, Drummond GT, Keech RV, et al. Management and visual acuity results of monocular congenital cataracts and persistent hyperplastic primary vitreous. *Aust N Z J Ophthalmol* 1989;17:143-152.

13. Alexandrakis G. Visual acuity outcomes with and without surgery in patients with persistent hyperplastic primary vitreous. *Ophthalmology* 2000;107(6):1068-1072.

14. Federman JL, Shields JA, Altman B, et al. The surgical and nonsurgical management of persistent hyperplastic primary vitreous. *Ophthalmology* 1982;89(1):20-24.

## DISCUSSION

DR PAUL E. TORNAMBE. I had the opportunity to hear this presentation at the recent Macula Society meeting and Dr Morton Goldberg's comments, which helped in the preparation of this review. This paper by Gulati, Eagle, and Tasman retrospectively asks the question 'what happens to salvageable eyes with PFV that are managed conservatively?' How does this compare with surgical intervention?

The cohort was selected from a retrospective chart review of all eyes encountered between 1992 and 2001. A total of seven eyes were for conservative management because the retrolental opacity was small enough to permit visualization of the fundus through an undilated pupil revealing 'mild' PFV. The outcome was compared with 17 eyes treated with surgery. All observed salvageable eyes showed no progression of lens opacification, no progression of retinal traction, none required enucleation, and all were amblyopic. One eye attained 20/100 vision. Follow up was 1.5 to 9.5 years. Fewer complications were noted than occurred in the surgically treated group. The authors concluded that selected eyes with mild PFV do well without surgery.

Knowledge of the natural history of a disease process is required for a surgeon to make the decision not to operate, rather than to recommend surgery. Only prospective randomized trials give us that information. The doctor assumes an awesome responsibility, and shows courage, and self-confidence to look at these infants' parents straight in the eye and make a conservative decision, which will have a tremendous impact on their child's life for perhaps the next 80 years. People, and particularly well-intentioned surgeons, have a tendency to want to do something about an uncomfortable situation, rather than do nothing. It is therefore extremely important that studies such as this ask the question, what happens if we manage these eyes with observation? There is truly no disease in the human body that cannot be made worse by a doctor!

This is a retrospective study, and as with all retrospective studies there may be selection bias. In this paper the decision not to operate was decided either because the eye was not deemed salvageable, or, the view in was good enough through an undilated pupil to determine that the disease was 'mild'. I am not a pediatric retina surgeon, and unfortunately after reviewing this paper, I am not comfortable deciding which patients with PFV should be managed conservatively and which should be operated upon. As Goldberg notes,[1] 'the spectrum of clinical severity extends broadly in PFV' and in this study the criteria for surgery and observation are not precisely defined. In the manuscript, the legend for figure 7 broadly refers to mild PFV. This reader would like to know exactly why an eye is considered not salvageable, or salvageable managed conservatively, or salvageable when managed with surgery.

Goldberg[1] suggests indications to operate include severe, recurrent vitreous hemorrhaging, angle shallowing and closure, and retinal detachment. The authors did not define the specific criteria they used to select patients for surgery.

Although one eye in this series attained 20/100 vision, in most cases, the goal is to maintain the globe. Clearing the visual axis may not improve vision due to anomalies of the optic nerve and macula. Surgery should always be considered for secondary complications such as severe or recurrent vitreous hemorrhaging, retinal detachment or angle closure. Goldberg[1] considered a clear visual axis, non-progressive anatomic anomalies and a stable angle as indications for conservative management. Surgical indica-

tions will likely change in the future with new instruments or pharmacological therapies to control or address scar tissue formation. Even amblyopia might be treatable in the future.

In other published studies, eyes treated conservatively did rather well. Scott[2] reported only 8% of eyes required enucleation. However, even a decade of follow up is relatively short. Will these eyes survive in 50 or 60 years when the aging eye begins to develop nuclear sclerotic cataract, vitreous syneresis and vitreous detachment? The authors might consider re-reviewing these cases to determine which specific characteristics are most important to advise conservative management. Such information might provide a springboard for a multi-center prospective clinical trial.

I agree with the author's conclusions that conservative management is reasonable for selected cases. The challenge now addresses case selection.

## REFERENCES

1. Goldberg M. Persistent Fetal Vasculature: An Integrated Interpretation of Signs and Symptoms Associated with Persistent Hyperplastic Primary Vitreous. *Am J Ophthalmol*, 1997;124:587-626.
2. Scott WE, Drummond GT, Keech RV, et al. Management and Visual Acuity Results of Monocular Congenital Cataracts and Persistent Hyperplastic Primary Vitreous. *Aust N Z J Ophthalmol*, 1989;17:143-152.

DR THOMAS D. FRANCE. My experience has been that if you see the child early enough, then the likelihood of a good visual response is good. Dr Jack Crawford pointed out years ago that any difference between two eyes, even the smallest cataract in one eye versus a normal other eye, leads to a deprivation-type amblyopia. I would wonder why these patients were not being operated upon if there was a likelihood of anterior segment improvement without posterior segment abnormalities. Was it an age-factor or was it something else?

DR DAVID R. STAGER. Dr Eileen Burch and I have been doing studies on unilateral cataracts. If you have an opportunity to treat them early (and that is 2-4 weeks of age), fit them with a contact lens, and patch them half-time, then you can get good visual results on these patients. We've had results of 20/20 and a stereoscopic binocular vision if you allow them to use their eyes together at least half of the time.

DR RICHARD A. LEWIS. Please amplify your comment about the foveal or macular hypoplasia in the children whom you have followed long-term. When they were old enough, have you been able to do either fluorescein angiography or multifocal ERG on their eyes to compare one eye to the other and to determine if there are any anatomic correlates?

DR WILLIAM TASMAN. Dr Tornambe raises the key point that this is a retrospective, not a prospective, study. While I endorse a prospective trial I believe that would be difficult because PHPV is fortunately not a widespread condition. My selection bias was obviously reflected in the study. Those eyes not operated were considered unsalvageable, because they had a total retinal detachment, often with a closed funnel, and sometimes associated vitreous hemorrhage as well.

There were no cases of shallowed anterior chamber, and the fellow eye was normal. The follow-up indeed is short at six years in light of the fact that many PHPV eyes later are reported to develop glaucoma. The main indication that I used for observation was the ability to visualize the fundus through an undilated pupil. Being able to retinoscope through an undilated pupil was an additional reason to observe, and finally evidence of no retinal detachment was essential in order for eyes to be followed.

Dr France raised the question regarding the age of the patients when operated. They were all done within the first two months of life. He also mentioned that congenital cataracts do well if done within the first two to four weeks. However, I am not sure that we are not mixing apples and oranges here, because congenital cataracts are usually in eyes that are of normal size. PHPV eyes are microphthalmic, often have macular hypoplasia and should not be compared to a normal eye. There is a difference as well in that vitreous surgery is involved.

Dr Stager also stated that when you operate congenital cataracts at 2-4 weeks good visual results occur, and I would agree with that. But my answer here is the same as to Dr France.

Dr Lewis asked about whether multifocal ERGs or fluorescein angiography (IVF) had been done to verify macular hypoplasia. So far we have not done either. Most of these youngsters are still 10 or younger, and if the IVF is not going to influence the management, I prefer not to do invasive testing. Some 10-year-olds can cooperate for an ERG and this is a test that could be helpful. We have attempted ocular computerized tomography (OCT) on one 6-year-old boy postoperatively, but he was not cooperative enough to get a good picture.