Intraoperative Perfluorocarbon Liquids in the Management of Proliferative Vitreoretinopathy

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Three low-viscosity perfluorocarbon liquids were used intraoperatively for hydrokinetic manipulation of the retina during vitreous surgery for retinal detachment with advanced proliferative vitreoretinopathy. All 23 patients had massive proliferative vitreoretinopathy (Grade D, Retina Society classification), and 16 (69.6%) had Grade D-3 with a closed-funnel configuration. In 21 eyes the retina could be flattened intraoperatively by perfluorocarbon liquids without requiring posterior retinotomy for internal drainage of subretinal fluid. The temporary mechanical fixation of the retina provided by this tool facilitated the removal of epiretinal membranes and release of traction. Fifteen eyes (65.2%) maintained long-term retinal reattachment with follow-up of six months or more. These liquids are useful adjuncts in the management of retinal detachment with severe proliferative vitreoretinopathy.

THE DEVELOPMENT of new techniques for the management of retinal detachment with severe proliferative vitreoretinopathy has resulted in improved rates of retinal reattachment. Retinotomy has allowed release of forces exerted by intractable membranes.[1,2] Retinal tacks provide temporary or permanent mechanical fixation of the retina.[3-6] Intraoperative hydrokinetic manipulation of the retina with silicone oil or gas has assisted in the removal of epiretinal membranes.[1,7] Low-viscosity perfluorocarbon liquids are a class of compounds with physical properties that offer potential as an intraoperative tool during vitrectomy for proliferative vitreoretinopathy. In a preliminary report, low-viscosity perfluorocarbons were used in two patients with severe proliferative vitreoretinopathy.[8] The high specific gravity of perfluorotributylamine flattened the retina and displaced the subretinal fluid without posterior retinotomy. This report summarizes the techniques, clinical results, and complications of 23 consecutive patients with retinal detachment and severe proliferative vitreoretinopathy managed intraoperatively with low-viscosity perfluorocarbons.

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Material and Methods

Twenty-four consecutive patients were managed with intraoperative perfluorocarbon liquids for retinal detachment with advanced proliferative vitreoretinopathy from May 1986 to September 1987. In all patients the severity of proliferative vitreoretinopathy was massive (Grade D, Retina Society classification[9]). The patients were observed for a minimum of six months. One patient was lost to follow-up after one month. This patient's retina had been reattached under silicone oil. Of the 23 patients included in the study, ten were male and 13 female. The mean age was 45.8 years (range, 10 to 87 years). Eight patients had a previous history of ocular trauma ranging from 1.5 to 8 months previously (mean, 3.8 months). Four patients had had penetrating wounds of the anterior segment involving the lens and vitreous. In two of these patients, retinal detachment was associated with proliferation from a posterior retinal impact site by a metallic intraocular foreign body. Two eyes had posterior scleral ruptures following blunt nonpenetrating injuries. A history of blunt trauma was obtained in two patients without evidence of ocular penetration. In three patients, retinal detachment with proliferative vitreoretinopathy developed following expulsive choroidal hemorrhage during cataract surgery. Preoperatively, 11 patients were phakic, nine patients aphakic, and three pseudophakic with anterior chamber lenses. Seven patients had no previous history of retinal surgery. Sixteen patients had had at least one previous scleral buckle procedure and six of these had had several. Ten patients had had a previous vitrectomy. Four patients had had fluid-gas exchange with photocoagulation after vitreous surgery.

Vitreous surgery was performed by means of the standard 20-gauge, three-port, pars plana approach. In phakic eyes, lenses were removed by phacofragmentation. An anterior chamber lens implant was removed in one eye because of partial dislocation.

The decision to use a perfluorocarbon liquid was made intraoperatively when either the retinal detachment had a narrow-funnel (Stage D-2) or closed-funnel (Stage D-3) configuration and large folds obscured visualization of residual epiretinal membranes. They were also used after removal of posterior membranes when there was extensive anterior peripheral proliferation that could not be released without risk of iatrogenic retinal tears. The perfluorocarbon liquids could not be used when large posterior retinal breaks were present.

In all cases perfluorocarbon liquids were purified for intraocular use. The physical characteristics of the three compounds used are listed in Table 1. Each perfluorocarbon compound was at least 98% pure with minimal residual hydrogen content. Perfluorotributylamine was used initially in ten patients, and later, perfluorooctane (seven patients) and perfluorodecalin (six patients) were randomly assigned. The liquids were sterilized through double 0.22-μm Millipore filters immediately before use.

During surgery, a broad encircling scleral buckle supporting the region of the vitreous base was added if not present from previous surgery. Epiretinal membranes were dissected and peeled with a membrane forceps or pick, and transected or delaminated with vitreous scissors. After removal of all visible posterior preretinal membranes the perfluorocarbon liquid was injected into the eye with a blunt 20- or 23-gauge needle placed over the optic disk. The funnel of the retinal detachment was spread open by the clear perfluorocarbon liquid, disclosing areas of residual traction and membranes. The perfluorocarbon interface was kept posterior to these areas and epiretinal membranes were removed from a posterior to anterior direction. As traction was released, the retina flattened posteriorly, and more perfluorocarbon liquid was added. By keeping the tip of the needle in the initial bubble, dispersion was minimized. The final level of the perfluorocarbon liquid was kept posterior to any large retinal breaks. Using scleral depression, anterior peripheral proliferation near the vitreous base was dissected (Fig. 1). When adherent membranes could not be removed, circumferential relaxing retinotomies were made anterior to the level of perfluorocarbon liquid. Subretinal membranes were extracted through retinotomies only if the traction was thought to prevent retinal reattachment. A partial fluid-air exchange with internal drainage of subretinal fluid flattened the anterior retina and breaks against the buckle. Argon laser endophotocoagulation was applied 360 degrees on the scleral buckle and surrounding all retinal breaks posterior to the buckle. The air bubble replaced the infusion solution above the perfluorocarbon liquid that kept the posterior retina in place. After completion of laser, the remaining perfluorocarbon liquid was removed with a 20-gauge flute needle. The air-filled vitreous was replaced with an air-perfluorocarbon gas

TABLE 1
PHYSICAL PROPERTIES OF PERFLUOROCARBON LIQUIDS

	PERFLUOROTRIBUTYLAMINE	PERFLUOROOCTANE	PERFLUORODECALIN
Chemical formula	$C_{12}F_{27}N$	C_8F_{18}	$C_{10}F_{18}$
Molecular weight	671	438	462
Specific gravity	1.89	1.76	1.94
Surface tension (dynes/cm, 25 C)	16	14	16
Refractive index	1.29	1.27	1.31
Viscosity (centistoke, 25 C)	2.6	0.8	2.7

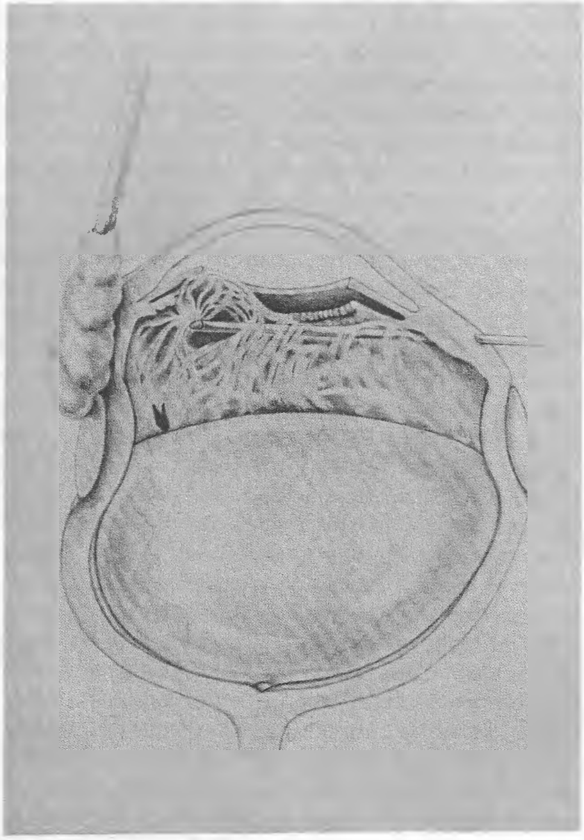

Fig. 1 (Chang, Ozmert, and Zimmerman). Perfluorocarbon liquids flatten the posterior retina and provide temporary mechanical fixation of the peripheral retina during removal of anterior proliferation.

mixture (17% to 20% perfluoropropane in 21 eyes, 20% to 25% perfluoroethane in one eye) or silicone oil of 1,000 centistokes (one eye) for long-term retinal tamponade. The patients were followed up weekly for the first six weeks postoperatively at which time visual acuity, intraocular pressure, slit-lamp, and ophthalmoscopic findings were noted. Reoperations were done if retinal detachment occurred secondary to recurrent proliferation. The retina was considered reattached if the retina posterior to the encircling buckle and line of photocoagulation was flat. Cases were considered failures if the retina redetached posterior to the scleral buckle.

Results

The perfluorocarbon liquids were effective in flattening the retinas of 21 of 23 patients intraoperatively. Subretinal fluid was displaced anteriorly through retinal breaks and into the vitreous space. Frequently during injection the subretinal fluid entering the vitreous exhibited a schlieren effect observed when fluids with differing refractive indices are mixed. In two patients with D-3 proliferative vitreoretinopathy the closed funnel of retina could not be opened. Both patients had retinal detachments following expulsive choroidal hemorrhages that developed during cataract surgery. One patient was operated on two weeks after cataract surgery and the other at 15 months.

During surgery iatrogenic retinal breaks developed in five eyes. In three eyes, the retina was adherent to the posterior iris surface and the tears were made as the instruments were passed through the sclerotomy sites. In the other two eyes, retinal breaks developed during membrane dissection. In five patients, a portion of the perfluorocarbon bubble was expressed through a tear and into the subretinal space during extensive pulling on adherent epiretinal membranes. The perfluorocarbon was easily aspirated from the subretinal space using the flute needle.

Nine eyes (39%) underwent vitrectomy revision, seven for recurrent retinal detachment and two for macular pucker. Perfluorocarbon liquid was used a second time in one patient for recurrent retinal detachment. In all seven patients reoperated on for retinal detachment, the retina was flattened intraoperatively. In this group, iatrogenic retinal breaks developed in two patients during membrane peeling. Perfluoropropane gas was used for long-term tamponade in five eyes, and silicone oil in two eyes. Two eyes achieved long-term retinal reattachment, both with perfluoropropane gas. In both eyes that underwent reoperation for extensive macular pucker, the retina remained attached.

Overall, the retina was finally reattached in 15 of 23 eyes (65.2%). The reattachment rate for each grade of proliferative vitreoretinopathy is listed in Table 2. The follow-up period ranged from six to 20 months with a mean of 10.4 months. The number of retinas reattached using each of the three perfluorocarbon compounds is listed in Table 3. The postoperative visual acuities of 13 patients with successful retinal reattachment are listed in Table 4. Nine patients regained vision of 20/400 or better. In two patients the visual acuity could not be measured because of mental retardation but the retinas were reattached in both patients in their

TABLE 2
PROLIFERATIVE VITREORETINOPATHY

GRADE	NO. OF PATIENTS	REATTACHMENTS NO.	(%)
D1, Wide funnel	3	2	(66.7)
D2, Narrow funnel	4	3	(75.0)
D3, Closed funnel	16	10	(62.5)
Total	23	15	(65.2)

TABLE 3
COMPARISON OF PERFLUOROCARBON LIQUIDS USED

PERFLUOROCARBON LIQUID	NO. OF PATIENTS	NO. OF REATTACHMENTS
Perfluorotributylamine	10	5
Perfluorooctane	7	6
Perfluorodecalin	6	4

only eye and they became ambulatory without help.

Postoperatively, small droplets of residual perfluorocarbon liquid were observed in four patients when all perfluorocarbon liquid was thought to have been removed during surgery. In three patients one or two small droplets were freely mobile on the retina and rolled posteriorly as the patient was reclined. In two patients the mobile residual perfluorocarbon droplets were removed during a reoperation. There was no inflammatory reaction around the perfluorocarbon in the third patient followed up for eight months. In one patient, two preretinal droplets were seen encapsulated on the buckle shortly after surgery and have remained unchanged for 15 months.

After retinal reattachment, two patients underwent penetrating keratoplasty. Both patients had preexisting corneal disease (one had a corneal laceration, the other a previous penetrating keratoplasty for aphakic bullous keratopathy). The visual acuity improved in both patients after surgery.

Discussion

Perfluorocarbon liquids are useful for hydrokinetic retinal manipulation during vitreous surgery for retinal detachment with severe proliferative vitreoretinopathy. These liquids have unique physical characteristics which are ideal for temporary tamponade and mechanical fixation of the retina. The high specific gravity (approximately 1.9) exerts a flattening force on the retina, which is over three times greater than that exerted by the same volume of fluorosilicone oil. The low viscosity of liquid perfluorocarbons facilitates easy introduction and aspiration from the eye by means of vitreous microsurgical instrumentation. While others have suggested the use of fluorosilicone oil as an intraoperative tool,[10,11] the physical properties of perfluorocarbon liquids are preferable.

There are advantages of the perfluorocarbon liquids in the intraoperative management of proliferative vitreoretinopathy. The liquid perfluorocarbon flattens the retina, exposing residual membranes within the folds around the optic disk. Posterior flattening of the retina by perfluorocarbon liquid also displays tractional relationships on remaining areas of detached retina. Circumferential traction with radial folds can be differentiated from anteroposterior shortening of the retina. As these relationships are recognized, the progressive release of traction by membrane dissection allows the retina to flatten more completely. During membrane dissection, the high specific gravity of the perfluorocarbon liquids provides temporary mechanical fixation by stabilizing the retina and providing countertraction during dissection of epiretinal membranes. The perfluorocarbon liquid assists in separating radial folds as membranes causing circumferential traction are cut. During removal of residual vitreous in the region of the pars plana and ciliary body the retina is immobilized by the perfluorocarbon bubble and cannot be as easily aspirated into the cutting port of the vitrectomy instrument. Thus the potential for iatrogenic retinal tears during membrane dissection is reduced.

If a circumferential relaxing retinotomy is

TABLE 4
POSTOPERATIVE VISUAL ACUITY IN PATIENTS WITH RETINAL REATTACHMENT

VISUAL ACUITY	NO. OF PATIENTS
Hand motions	1
3/200	1
6/200	2
20/400	4
20/200	1
20/100-20/40	4

necessary it should be done anterior to the perfluorocarbon bubble. The extent of the retinotomy can be determined by observing the degree of retinal flattening as the retinotomy is performed. Retinal tacks, for permanent mechanical fixation of the retina, can also be inserted through the perfluorocarbon liquid.

A posterior retinotomy for internal drainage of subretinal fluid was not required because the perfluorocarbon liquid displaced subretinal fluid anteriorly through existing retinal breaks. In one patient a subretinal membrane tightly encircled the retinal detachment and was extracted through a posterior retinotomy (Fig. 2). The perfluorocarbon liquid was removed before making the retinotomy. By reducing the need for internal drainage of subretinal fluid via posterior retinotomy, potential complications such as bleeding and reproliferation occurring at the site of the retinotomy are reduced.[2]

Intraoperatively the interface of the perfluorocarbon liquid was always visible. The refractive index is slightly dissimilar to saline and it did not alter the refractive error of the eye allowing conventional contact lenses to be used throughout surgery. Membrane dissection usually proceeds anterior to the perfluorocarbon interface under balanced saline for optimal visibility.

The differences in physical characteristics between these three perfluorocarbon liquids were not clinically significant. Perfluorodecalin had a slightly greater tendency to disperse during injection and the interface was not as easily seen because its refractive index is more similar to that of saline. Perfluorotributylamine and perfluorodecalin have higher viscosity than perfluorooctane but each could be aspirated easily. The mechanical effects desired for intraoperative retinal manipulation were achieved with each of the perfluorocarbon compounds. The lower long-term retinal reattachment rate when perfluorotributylamine was used may have been a result of early experience when the surgical technique was evolving. Initial patient selection was limited to eyes which we believed were hopeless because of inability to visualize epiretinal membranes.

There were several reasons for changing from perfluorotributylamine to perfluorodecalin and perfluorooctane during this study. Theoretically, compounds consisting solely of fluorine and carbon atoms are more likely to be biologically inert. Perfluorotributylamine contains a nitrogen heteroatom. In artificial blood substitution application, the systemic retention times of perfluorooctane and perfluorodecalin were found to be much lower than perfluorotributylamine.[12] Thus, any residual droplets of these two compounds would be likely to disappear more rapidly.

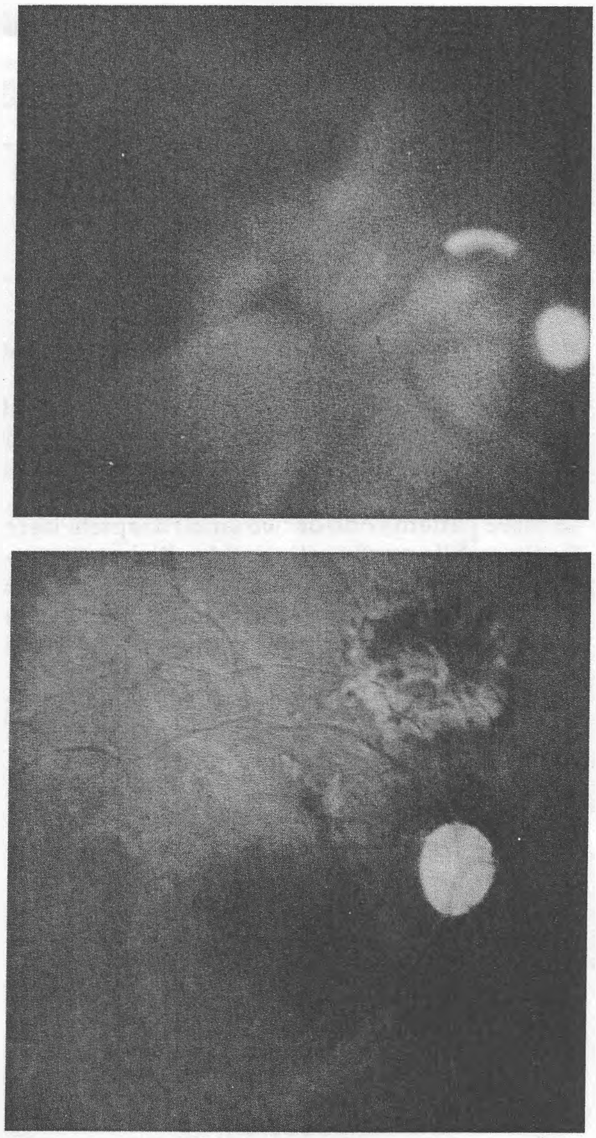

Fig. 2 (Chang, Ozmert, and Zimmerman). Top, Intraoperative photograph of a subretinal membrane that encircled the retina. It could only be seen after perfluorocarbon liquids were used. Bottom, Postoperative photograph with posterior retinotomy site above the optic disk. The visual acuity was 20/200.

The potential complications resulting from the use of perfluorocarbon liquids appear to be minimal. In some cases, as the liquid was injected dispersion occurred with small droplets of perfluorocarbon around the edge of the large bubble. Upon contact, small droplets tended to coalesce with the large bubble but remaining

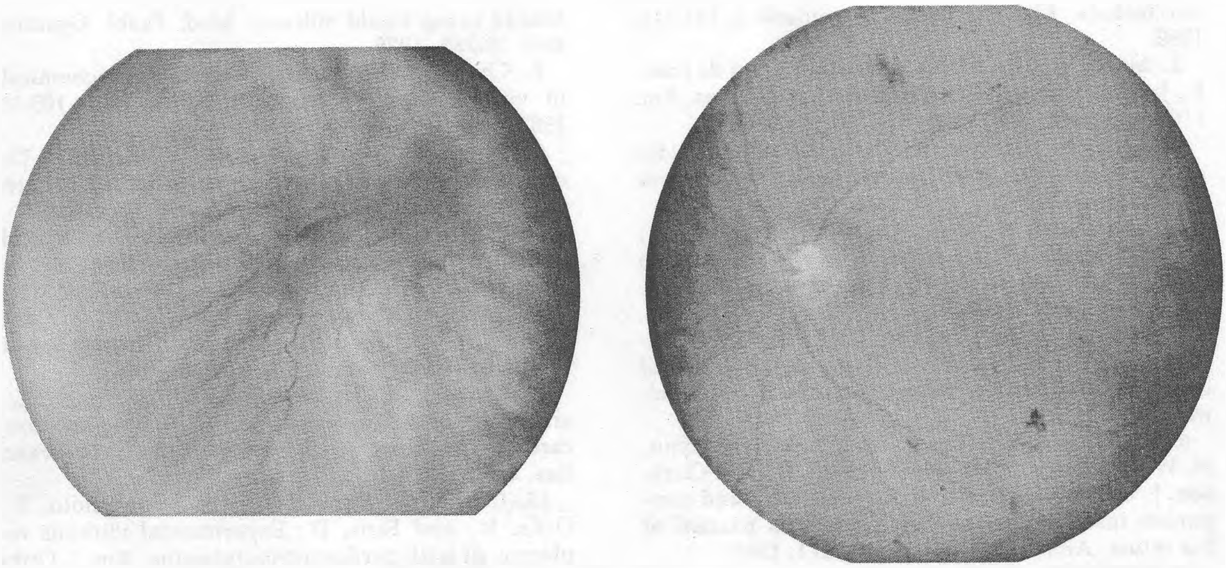

Fig. 3 (Chang, Ozmert, and Zimmerman). Left, Preoperative photograph of a patient with recurrent retinal detachment and Stage D-3 proliferative vitreoretinopathy. Right, Postoperative photograph taken six months after surgery; visual acuity was 20/40−2.

droplets could be easily aspirated with the 20-gauge flute needle. Subretinal perfluorocarbon could also be removed. As we gained experience with the use of these fluids, the likelihood that perfluorocarbon would be expressed into the subretinal space was reduced.

It was surprising to observe that a residual droplet of perfluorocarbon liquid remained in some eyes. Internal reflections during air-fluid exchange may have prevented visualization of these tiny droplets. These have not been observed to cause any deleterious effects with visual acuity in these patients who have remained stable for up to 15 months after surgery. The long-term effects of these small amounts of perfluorocarbon liquids are uncertain, and patients will be closely observed for potential adverse effects.

The three perfluorocarbon compounds used for this clinical study have been studied for retinal toxicity in rabbit, pig, and monkey eyes following vitrectomy. After the liquids have been in the vitreous for three hours, no retinal toxicity has been observed with light and electron microscopy (unpublished data). In previous reports using perfluorotributylamine, the outer segments of rabbit eyes demonstrated irregularly shaped defects which reverted to normal after perfluorocarbon removal.[13] In rabbit eyes bubble dispersion and preretinal glial membrane formation were observed at three months after replacement of two thirds of the vitreous by perfluorotributylamine. To date the human response to small residual amounts has not resulted in preretinal membrane formation.

The introduction of a new device and techniques in vitreous surgery merits the consideration of risks versus benefits of the new approach. In eyes with the most severe grades of proliferative vitreoretinopathy, the use of perfluorocarbon liquids allowed more effective removal of epiretinal membranes and release of traction forces on the retina. The mechanical stabilization of the retina provided by these liquids reduced iatrogenic complications such as retinal tears. We believe that some of these retinas could not have been reattached without the use of perfluorocarbon liquids. Effective removal of membranes, release of tractional forces caused by proliferation, and reduction of intraoperative complications will result in improved long-term success in the management of retinal detachment with severe proliferative vitreoretinopathy (Fig. 3). The encouraging results found in this study warrant the use of these materials during vitrectomy for less severe forms of proliferative vitreoretinopathy.

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