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# Retinal separation, retinotomy, and macular relocation: II. A surgical approach for age-related macular degeneration?

**Robert Machemer**[1], **Ulrich H. Steinhorst**[2]

[1] Department of Ophthalmology, Duke University Medical Center, P.O. Box 3802, Durham, NC 27710, USA
[2] Department of Ophthalmology, University of Berne, Inselspital, Berne, Switzerland

**Abstract.** Three cases of age-related maculopathy with severe and recent massive submacular hemorrhage were treated by performing complete vitrectomy. A total retinal detachment was created by infusion of fluid underneath the retina, followed by a peripheral circumferential retinotomy. This allowed access to the subretinal space for removal of blood and membranes and, more importantly, permitted rotation of the retina with relocation of the fovea. Rotations between 30° and 80° were achieved. One patient with 5 months' follow-up had a visual improvement from 1/200 to 20/80 and excyclorotation of images. The other two patients developed proliferative vitreoretinopathy after initially successful rotation. Their retinas were reattached after surgical removal of the membranes and silicone oil tamponade, but visual function remained low. The rationale for this treatment is that relocating the fovea to an area where pigment epithelium is less diseased than in the central area may allow for recovery of some useful vision.

## Introduction

With average age of the population increasing, age-related maculopathy has become one of the most threatening diseases of the eye [10]. No therapy is available for the atrophic form, and very limited therapy can be offered for the exudative, neovascular form. The causes of both the atrophic and the exudative forms are unknown. As the pathology is usually limited to the macular area, one may conclude that (a) the pigment epithelium in this area is no longer fully functional, (b) Bruch's membrane may be too thick to allow passagge of nutrients from the choroid to the pigment epithelium or metabolic products from the pigment epithelium to the choroid, and (c) the choriocapillaris may have altered.

Photocoagulation is aimed at eliminating the exudation and neovascularization. Studies have shown that neovascularization in the vicinity of the fovea can be effectively destroyed [16, 17]. Subfoveal neovascular membranes can also be destroyed, but at the price of eliminating central vision [19]. Recurrences are not infrequent. Recently, surgical attempts have been made to remove subfoveal membranes and blood, also with limited success in terms of vision [1, 4, 11, 22]. It has also been speculated that replacement of the nonfunctional pigment epithelium might be an avenue to preserve or even restore some vision, and experimental work is underway to implant pigment epithelium subretinally [6, 14, 21].

We have pursued another train of thought. If one or all of the centrally located components of the complex of pigment epithelium – Bruch's membrane – choroid are worn out, we wondered whether it might not be possible to establish a new locus of useful function at a point where these same tissues appear healthy. Such possible sites can be found above and below the fovea, perhaps as far away as the arcades. In other words, we determined to attempt relocation of the fovea to such a position. The idea of macular relocation is not new [13, 23]. However, the proposed approaches have not previously been pursued.

In the previous paper [15] we showed that the retina can be rotated in rabbit eyes. In this paper we present preliminary results of a surgical approach allowing for rotation of the retina and relocation of the fovea in three patients with severe age-related maculopathy. The purposes of this paper are to demonstrate that this therapy is possible in principle and to stimulate critical evaluation.

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*Correspondence to:* R. Machemer

## Materials and methods

### *Surgical technique*

The surgery aims at mobilizing the retina by creating a 360° giant tear, after which subretinal blood and membranes can be removed. The retina is then rotated, the foveal area is relocated, and the retina is finally stabilized in its new position. The operation consists of five steps: (1) vitrectomy with lentectomy, (2) creation of a total retinal separation, (3) cutting of a 360° retinotomy, (4) removal of subretinal blood and membranes, and (5) retinal reattachment with rotation of the retina.

*Surgery.* The surgery is performed under general anesthesia as it may take a considerable time (presently 5–6 h). After circumferential incision of the conjunctiva, traction sutures are placed under all rectus muscles, in order to provide greater mobility of the eyeball during subsequent maneuvers. An intravitreal infusion line with lactated Ringer's solution or BSS PLUS (Alcon) is introduced through the pars plana at 5 o'clock. Two additional sclerotomies are created, one at 10 o'clock and the other at 2 o'clock. Since the most peripheral retina must be well visible and easily accessible, it is advisable to have maximum dilation of the pupil, best achieved by using iris retractors [3]. A lentectomy follows. In the presence of a pseudophakos, careful removal of capsular opacities or even removal of the lens is advisable. A vitrectomy follows with special attention paid to complete removal of the vitreous base. This is done more easily when the eye wall is indented.

*Retinal detachment.* Next, a total retinal detachment is created by means of infusion of fluid into the subretinal space. Animal experiments have shown us that this is best done via an exterior approach [15]. We used a sharp, short-beveled 27–G needle connected to a separate infusion bottle filled with lactated Ringer's solution or BSS PLUS. The needle is used to perforate the sclera and choroid and is then guided into the subretinal space. Under microscopic observation, a site on the temporal or nasal superior retina in the vicinity of the equator is selected. Initially we made a sclerotomy such as one might use for drainage of subretinal fluid; later we simply perforated the sclera using slight rotating movements of the needle. The intraocular pressure should be high during this maneuver, in order to keep choroidal hemorrhages to a minimum. Perforation of the retina should be avoided, although getting the needle into the subretinal space without causing perforation is difficult. Bruch's membrane gives so much resistance that the retina is often perforated that way as well. If perforation does occur, the retinal hole should be kept as small as possible. The needle should be retracted slowly to the choroidal level, then tilted tangentially to the eye and slowly pushed beneath the retina. Infusion is now started into the subretinal space. By raising and lowering the respective infusion bottles, infusion pressure is increased subretinally while simultaneously decreased in the vitreous cavity. The needle is then pushed further underneath the retina. The detachment increases and eventually becomes essentially complete.

If a subretinal blood clot must be dissolved, tissue plasminogen activator (tPA) can be injected into the subretinal space by the same route [12, 21, 25]. We have used 40 µg. A waiting period of 30 min follows to allow the tPA to dissolve the clot.

*Retinotomy.* The next step is the creation of a 360° retinotomy. The retina should be cut as peripherally as possible. Not only does this preserve functional retina but one also avoids retinal vessels and hemorrhages. All subretinal fluid must first be drained so that the retina flattens out again. If a drainage-type sclerotomy was made, this site can be used to let the fluid escape. One can also try to aspirate fluid internally through a retinal perforation site anywhere in the upper part of the fundus. With the periphery of the eye indented, the vitreous cutter is used to carry out the retinotomy. The cutting port is directed toward the retina and, with gentle suction, the retina is lifted from the pigment epithelium before being cut. The retina is now fully mobilized. Remaining small adhesions to the pigment epithelium are lysed by pulling on the edge of the peripheral retina posteriorly with a soft-tipped suction needle. If later silicone-oil tamponade is anticipated, an inferior peripheral iridectomy can be performed at this point.

*Removal of subretinal blood and membranes.* The subretinal space is now fully accessible for removal of any blood or tissue. Despite previous use of tPA any large fresh blood clot is usually still adherent to the retina. Careful stroking movements with the shaft of the vitreous cutter or dissection using a blunt pick will separate it little by little. Frequent irrigation is needed to clear blood stirred up from the medium. Tissue is removed with forceps and usually adheres only slightly to pigment epithelium. If bleeding should occur, the intraocular pressure is temporarily raised. Care is taken throughout not to damage the pigment epithelium.

*Reattachment.* The final step is rotation and reattachment of the retina with resultant relocation of the fovea. The retina is treated basically with the techniques used for giant tears. At first the retina is completely unfolded. This can be done under perfluorocarbon, later replaced by gas or siliconeoil. We use a soft-tipped needle to aspirate the fluid and to stroke or suck the retina into its normal position. The retina is then rotated by one hour by application of suction to its periphery and by pulling it either clockwise or counterclockwise. Immediately a long fold between disk and periphery appears. By continuing this maneuver along the entire peripheral circumference we can rotate the retina about 30°. Additional rotation can be achieved by repetition of the process. Additional adjustments must be made to stretch the retina towards the periphery as well. To avoid later slippage of the retina the subretinal fluid is removed by repeated aspiration, as it appears at the retinal edge through capillary action. We can thus change the position of the fovea by between 30° and 80°. The result will be a smoothly attached retina with three or four swirling folds at the disk. If a fold should occur at the foveal area, it must be moved by careful stroking and pulling maneuvers. It is also important to make sure that the fovea comes to rest over intact pigment epithelium. Finally, the peripheral retina is photocoagulated. The instruments are now retracted and the sclerotomy sites are closed with 7–0 Vicryl sutures.

### *Case reports*

*Case 1.* A 77-year-old man suffered from severe age-related maculopathy in his right eye with vision of 2/200 for 6 years. Although macular changes had been noticed in the left eye, he could still read the newspaper until he noticed a sudden major decrease in vision in this eye. Two days later visual acuity was found to be 1/200. Except for 2 to 3+ nuclear sclerosis, the anterior segment was normal. A massive subretinal hemorrhage was found to underly the entire macular area, including the arcades and extending temporally inferiorly (Fig. 1). By ultrasound its elevation was measured at 2.6 mm. Because of the thick blood barrier, fluorescein angiography could not reveal any neovascularization.

The chronic low vision in the right eye and recent onset of acute visual loss in the left eye led us to plan an evacuation of the subretinal hemorrhage with relocation of the fovea. After lentectomy, a complete vitrectomy including the vitreous base was carried out. The subretinal space was then infused with BSS PLUS solution. Only the temporal half of the retina could be detached, as a small retinal hole at the subretinal infusion entry site enlarged under the pressure of the subretinal fluid. The retina was then cut 360° along the ora serrata and the temporal retina was folded over to the nasal side. Subretinal blood clots intimately adherent to the retina had to be lysed mechanically from the under-surface, a difficult maneuver. In the foveal area a fibrous membrane adhering to the choroid was removed, leaving a pigment epithelial defect. The nasal retina was then lysed from the pigment epithelium by suction-pulling periph-

eral retina towards the disk. After filling the vitreous cavity with silicone oil and reattaching the retina, an 45° counterclockwise rotation of the unfolded retina was performed. The periphery was photocoagulated.

*Case 2.* A 72-year-old woman was known to have macular degeneration in her right eye for 20 years with a vision of 3/300, although with her left eye she could read the newspaper. Two days before she was seen she noticed a sudden major decrease in vision. She was found on examination to have a visual acuity of 2/200. Aside from 2+ nuclear sclerosis, the anterior segment was normal. The fundus showed huge amounts of fresh subretinal blood causing a retinal bulge (4.9 mm by ultrasound) above and below the fovea. Fluorescein angiography showed a subretinal neovascular lesion temporal to the fovea (Fig. 2a, b).

Because of the longstanding low vision in the right eye and the very recent acute deterioration of vision in the left eye, we undertook evacuation of the subretinal space and a macular relocation procedure. After lentectomy and complete vitrectomy the retina was completely detached using a subretinal infusion of lactated Ringer's solution with added glucose. A 360° retinotomy was performed near the ora serrata. Huge amounts of clotted blood were found beneath and intimately adherent to the retina. These clots had to be mechanically lysed from the retina. During manipulations near the fovea, fresh bleeding occurred, presumably after lysis of the neovascular membrane from the choroid. To avoid further hemorrhage a small clot was left in this area. The retina was then unfolded under silicone oil and rotated counterclockwise about 50° to move the foveal region away from its previous location. Three small flat spiral folds appeared at the disk. The rest of the retina was flattened out. The peripheral edge of the retina was photocoagulated.

*Case 3.* An 84-year-old man had lost vision in the right eye 2 years before examination. His visual acuity was limited to finger counting at 6 in. (15 cm) centrally on account of a large old macular scar resulting from massive subretinal hemorrhage. In his left (better) pseudophakic eye he had noted a decrease in vision 2 months previously. The fundus at the time had shown a major hemorrhage above and below the fovea, and fluorescein angiography demonstrated a subfoveal neovascular membrane (Fig. 3a, b). One week before the patient was seen again, a major additional decrease in visual acuity to 2/200 had occurred. Through hazy vitreous one could see a massive subretinal macular hemorrhage extending around the disk to the nasal side. By ultrasound the hemorrhage was 1.7 mm high. Given the low vision in the right eye and the 1-week history of additional visual loss, we decided to attempt removal of the subretinal blood and consider a retinal rotation. By doing this we hoped to avoid further deterioration of vision, should neovascular tissue regrow after being removed.

After careful complete vitrectomy the retina was detached by subretinal infusion of lactated Ringer's solution with added glucose and 40 µg tPA. Thirty minutes later a 360° retinotomy was carried out near the ora serrata. Blood was then washed out from the subretinal space, and huge fibrinous hemorrhagic clots were removed together with fibrous tissue. Thin remnants of blood were left after gentle washing of the pigment epithelium to avoid damage of this layer. The retina was then reattached by unfolding it under silicone oil. Counterclockwise rotation of 50° was performed to place the fovea above its previous location. The periphery of the retina was photocoagulated.

## Results

*Case 1.*

Postoperatively the retina was well attached. Initially one could see some flat folds radiating from the disk blurring the disk margin. Small thin patches of blood were seen subretinally. With time the folds disappeared completely and the blood resorbed. The fovea was located at the 2 o'clock meridian, rotated upwards about 45° from its original position. It was now resting over intact pigment epithelium, whereas the original foveal area showed pigment loss and small choroidal scars (Fig. 1b).

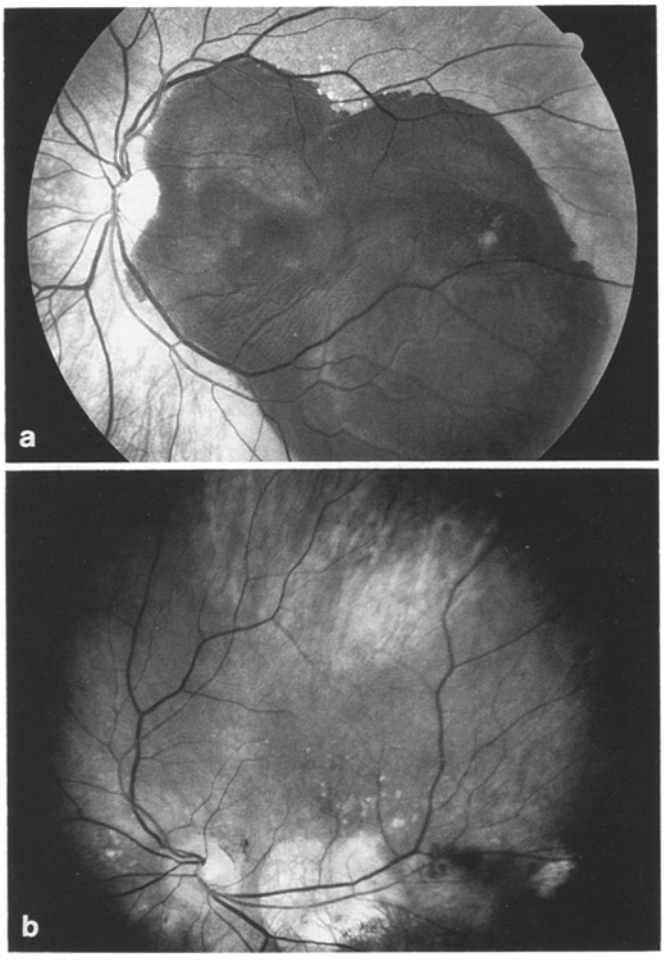


**Fig. 1. a** Fundus photo of case 1, showing a 3-day-old massive subretinal hemorrhage extending far beyond the macular area. **b** Five months after removal of subretinal blood and relocation of the macula. Note that the fovea, rotated 45° upward, is now in an area with intact pigment epithelium. The original foveal site shows considerable loss of pigment epithelium and some scarring

One month after the operation intraocular pressure was found to be elevated (43 mmHg) in consequence of a narrow chamber angle. Silicone oil was therefore removed. The pressure returned to normal. Two months after the rotation, visual acuity was found to be 20/200 (+9.00 sph). The patient reported that images were rotated; by Maddox rod examination a 50° excyclotorsion was found. Fixation was unsteady but attempted in the area of the new foveal location. Inversion of the optokinetic nystagmus was also noted, both horizontally and vertically. The visual field was constricted to 50° and the blind spot was found temporal and superior to the fixation point. There was no central scotoma. At this point the patient was provided with an appropriate corrective lens and asked to begin to use and train this eye and cover the other eye.

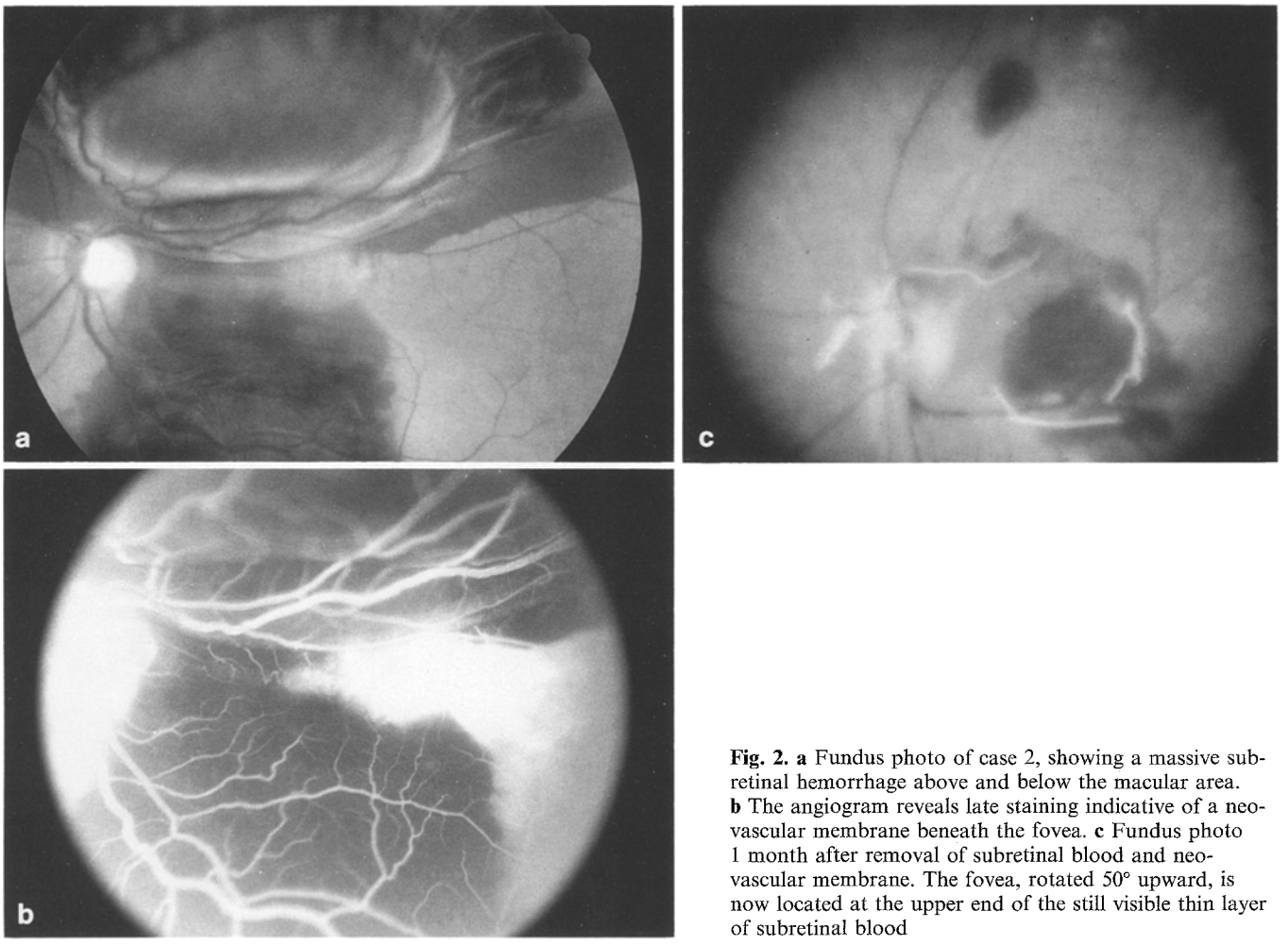


**Fig. 2. a** Fundus photo of case 2, showing a massive subretinal hemorrhage above and below the macular area. **b** The angiogram reveals late staining indicative of a neovascular membrane beneath the fovea. **c** Fundus photo 1 month after removal of subretinal blood and neovascular membrane. The fovea, rotated 50° upward, is now located at the upper end of the still visible thin layer of subretinal blood

Five months after the operation the corrected visual acuity had improved to 20/80 and near vision to 20/60. Excylotorsion by Maddox rod measurement was 15°–30° from the horizontal plane. Fixation was steady in the new foveal area. The patient had difficulty with a tilted image and tended to use the other eye, which had an improved corrected visual acuity of 20/160. We are now considering a counter-rotation of the eyeball by means of muscle surgery.

*Case 2.*

The retina attached nicely after the surgery. The fovea was found to be 60° above its normal position. Two small folds extending from the disk initially became flatter with time and ultimately disappeared. In the former foveal area a small mound of blood persisted, the result of a slight rebleed following removal of vasoproliferative tissue. The pigment epithelium under the new location of the fovea appeared normal (Fig. 2c).

Four weeks after the operation vision had improved to 10/200. With Maddox rods an excyclorotation of 60° was found. Intraocular pressure was 5 mmHg. The visual field was constricted to between 30° and 50°. It was decided to remove the oil.

When we saw the patient 6 weeks later she had observed no change in her vision, which was now 9/200. The retina was shallowly detached on account of preretinal proliferation over the disk and macula. Revision of the vitrectomy was performed and the eye was filled with silicone oil.

Five and one half months after the initial operation the corrected visual acuity was 20/400 and applanation pressure was 16 mmHg. The cornea was slightly swollen with Descemet's folds. The vitreous cavity was filled with silicone oil and the retina was attached. There was unsteady fixation and the Maddox rod test shows 50°–60° excylotorsion from the horizontal plane.

*Case 3.*

The retina of this patient attached very well, although 1 month after the operation visual acuity was found to be low (0.5/200). The intraocular pressure was 6 mmHG. The cornea had a diffuse slight haze, and an oil bubble was found in the upper part of the anterior chamber. Radiating folds at the disc seen immediately after surgery had disappeared. Initially remaining subretinal blood had also nearly disappeared. The fovea was located in the meridian halfway between 1 o'clock and 2 o'clock, just

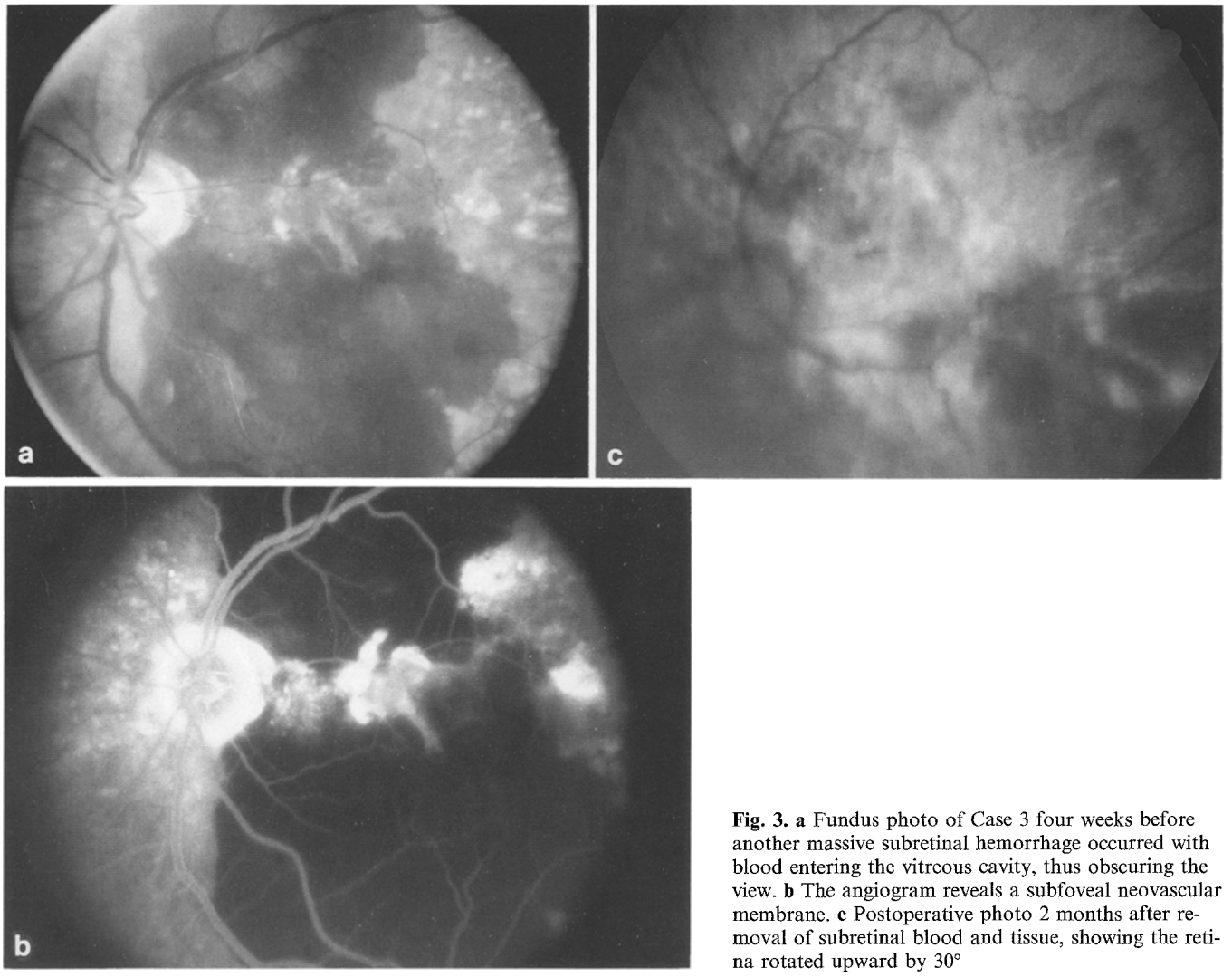


**Fig. 3.** **a** Fundus photo of Case 3 four weeks before another massive subretinal hemorrhage occurred with blood entering the vitreous cavity, thus obscuring the view. **b** The angiogram reveals a subfoveal neovascular membrane. **c** Postoperative photo 2 months after removal of subretinal blood and tissue, showing the retina rotated upward by 30°

at the edge of atrophic pigment epithelium of the former macular area. It was decided to remove the oil (Fig. 3c).

Six weeks later an intraocular hemorrhage had occurred with a decrease in vision to hand motion at 1 foot (30 cm) temporally. The eye was hypotonous (1 mmHg), with blood in the anterior chamber and vitreous cavity. Retinal detachment was found by ultrasonography. Revision of the vitrectomy revealed a total retinal detachment with epiretinal membranes over the macula extending temporally. The retina was reattached after membrane peeling, retinotomy and oil tamponade.

Four months after initial surgery visual acuity was measured to be 3.5/200. The intraocular pressure was very low. The retina was well attached with oil still in the eye. Maddox rod testing revealed an excylotorsion of 30° from the horizontal plane and distortion.

## Discussion

While photocoagulation is clearly destructive to both the pigment epithelium and the outer retina [19], recent reports have demonstrated the feasibility of surgical removal of submacular hemorrhages and neovascular membranes [1, 4, 11, 22], provided the overlying retina remains reasonably intact. Visual results, especially in the treatment of age-related maculopathy, have been disappointing, less so in the cases of presumed ocular histoplasmosis [1, 22].

There seem to be several important parameters that determine visual success. Duration of the disease and concomitant degeneration of the overlying retina are obvious factors. Probably more important is the lack or nonfunctioning of underlying pigment epithelium [1, 22]. Although in an artificially created pigment epithelial defect, adjacent pigment cells have been seen to migrate into the defect [9, 14], by clinical observation the retinal function does not improve [1]. Furthermore, recurrences of neovascular membranes are quite frequent and necessitate either additional surgery or destructive photocoagulation [18, 20]. Finally attempts have been made to transplant healthy pigment epithelium into the subretinal space [6, 14, 21] or to achieve atrophy of the neovascularization through the use of interferon [7]. These studies are at such an early stage that evaluation is not yet possible.

For all these reasons, we believe there is a strong rationale for pursuing relocation of the macula. Such a relocation would allow us to make use of a healthier pigment epithelium – Bruch's membrane – choriocapillaris complex and place the fovea away from areas of impaired function. The fact that a fovea is in an abnormal position does not necessarily presuppose decreased vision. An example would be eyes with slight forms of retinopathy of prematurity with either temporally or even superiorly and inferiorly dragged foveas. We are also aware of a successfully treated 360° giant tear with the fovea transposed 45° inferiorly and resultant vision of 20/60 [2].

The surgical technique was worked out in an animal model first, and appropriate structural evidence was available before such surgery was undertaken in the human eye [15]. Having had this supportive experience, we were able at the first attempt to achieve our goal of relocating the fovea by rotation of the retina, after creating a total retinal separation with a 360° peripheral tear. In our experience the fovea can be moved either upward or downward by as much as 60°. Remaining shallow folds in the vicinity of the optic nerve head smooth out over time.

In the presented cases with human subjects, we faced the additional problem of having to remove large amounts of subretinal blood. It has been shown that freshly clotted blood adheres intimately to the outer retina. The acute retinal detachment and blood-clot contraction [8, 24] lead to tearing off of outer segments. To avoid this potential damage, we tried to dissolve as much of the clot as possible during retinal separation by adding tPA to the subretinal infusion fluid [12, 25]. It remains to be seen whether the dissolution can keep up with the extending detachment during continuous infusion into the subretinal space or whether a considerable slowdown of the retinal separation is necessary. The 30 min given to allow the tPA to act on the subretinal clot after the detachment was achieved would seem a long enough period for at least some of the clot to dissolve, as indicated by the large amount of blood that could be washed out of the eye, but it may not have been sufficient to allow the tPA to dissolve the clot completely. We have used 40 μg of tPA, but believe that this amount may be too small considering the dilution in the large, newly created subretinal space. Doses of up to 200 μg have been shown to be nontoxic [24]. Perhaps even larger doses are admissible and required.

Once the retinotomy is complete, the entire subretinal space is accessible. Large blood clots remain a challenge for removal as they are too soft to be grasped with forceps. They must be mechanically stripped from the retina and then removed by means of the vitreous cutter. Mechanical damage to the outer retina is very likely at this stage. Considering that two of our patients had good vision just 3 days before surgery we have to assume that such damage occurred. Better means of lysing the clot from the retina must be found if we are to avoid this damage.

We were pleasantly surprised not to find any pigment epithelium adherent to the underside of the retina as we had occasionally been in the animal experiments [15]. One can thus assume that the pigment epithelium was not damaged during the separation from the retina.

On the other hand, membranes that had small points of adhesion to the underlying choroid seemed to separate relatively easily from the retina and choroid. The problem with larger membranes is that they are difficult to remove with the vitreous cutter as they are stiff and consist mostly of collagen. One may have to remove them as one would extricate a foreign body.

As these retinas are not afflicted with pre-retinal proliferation, they unfold easily and tend to settle more smoothly in the posterior part of the eye. A posterior drainage retinotomy may not be needed, because subretinal fluid can be aspirated from the edge of the rolled-over retina or through the small retinotomy created earlier. One should not make use of the original scleral perforation for subretinal drainage. Too large an opening in the choroid-sclera can cause incarceration of the retina, making subsequent rotation of the retina impossible.

We are very conscious that this surgery necessitates major surgical steps and thus includes many risks. The proliferative vitreoretinopathy and hypotony seen in two of the three cases is a strong reminder of this fact. At present we are not able to explain this development.

Macular relocation involves not only mechanical but also psychophysical considerations. Rotation of the retina around the optic nerve head creates a situation comparable to and even more pronounced than palsy of the oblique muscles, producing vertical, horizontal, and rotatory deviation of the visual axis in the operated eye. One result is the patient's perception of tilted images. In addition, one must expect at least temporary changes in orientation of photoreceptors as well as receptive fields with distorted images. The brain can be expected to adjust to some of these changes as long as the operated eye becomes the dominant eye. In the least desirable case, suppression of the operated eye occurs, but a suppressed eye could be activated at a later time if the contralateral eye should suffer a catastrophic event. Deviations may have to be corrected by compensatory external muscle surgery. Our experience is still too limited to allow us to address these issues in any detail.

Consideration can be given to whether upward or downward movement of the fovea is better. In general, the area with the best-preserved pigment epithelium and perfusion of the choriocapillaris as assessed by fluorescein angiography should be preferred.

We would like to reemphasize that the three cases represent a very first attempt in the evolution of a possible surgical approach to sight-destructive macular lesions. While the surgical approach seems feasible, we have encountered complications and have obtained a satisfactory functional result only in one patient (case 1). Yet it is possible that recovery may occur very slowly, especially for the cones over a period of up to a year [5]. The one successful case certainly gives grounds for hope, but longer follow-up is needed.

What could be the indications for macular relocation? First of all, one should consider this very involved surgery only if the risks turn out to be acceptable. Prolifera-

tive vitreoretinopathy, as we have experienced it, is probably the most important and severe complication. How much vision can be retained or recovered is not yet known. Will patients be able to adjust to the altered images? If all this can be worked out satisfactorily, macular relocation might one day be considered for cases of subfoveal neovascular membranes with very recent hemorrhages, but also without hemorrhages and with preserved vision. The procedure may ultimately even be considered for early atrophic age-related maculopathy.

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