Retinal Detachment Surgery and Proliferative Vitreoretinopathy

From Scleral Buckling to Small Gauge Vitrectomy

Ulrich Spandau
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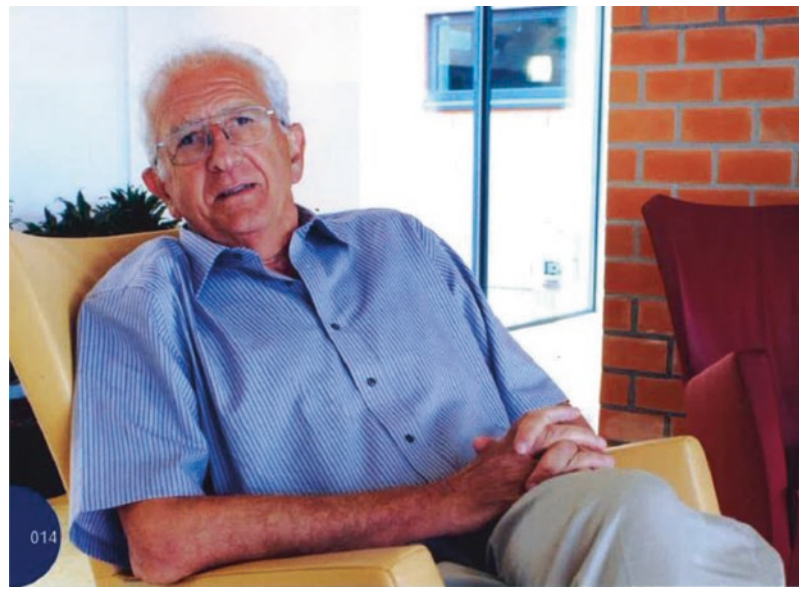
This book is dedicated to Dr. Živojnović. Relja Živojnović is one of the fathers of modern vitreoretinal surgery that put together all its puzzles: vitrectomy (invented by Robert Machemer), membrane dissection (developed by John D. Scott) and silicone oil injection (introduced by Paul A. Cibis).
He worked at the Eye Hospital Rotterdam and Middelheim Hospital Antwerp.



Dr. Živojnović (Photo courtesy DORC)

Preface

The retinal detachment is the most important surgery for a vitreoretinal surgeon. Its broad pathological spectrum presents a never ending challenge.

Ophthalmology is a specialized handcraft. But in contrast to a handyman we do not work with dead objects but with a living organ, which wants to be treated like a raw egg.

The best situation for an ocular surgeon would be to operate one eye as an exercise and the second eye for real. Especially in PVR detachment such a situation would be a dream. The pathology is extremely difficult and we have a broad choice of surgical options: vitrectomy, episcleral buckling, different gases, light and heavy silicone oils.

If you want to become a good VR surgeon you need:

1. Practical knowledge of many different *surgical techniques* (binocular ophthalmoscopy, scleral buckling, vitrectomy, retinectomy, phacoemulsification, secondary IOL implantation). A surgeon needs many different weapons to succeed against retinal pathologies.
2. *Experience*, because experience results in correct assessment. An important part of experience is a tight and complete follow-up of your patients which results in a valuable feedback about your surgery.
3. *Visit* other vitreoretinal clinics in order to learn tips and tricks and to be able to assess the quality of your surgery within the surgical world.
4. Modern *equipment* and qualified *staff*. A microscope with a good viewing system is essential for successful surgery. Vitreoretinal surgery requires well-educated staff.
5. And finally last but not least and maybe the most important point: *Motivation* and *passion* for ophthalmology and surgery.

Retinal detachment surgery requires theoretical and practical knowledge. Easy retinal detachments can be learned within 1 year but complicated retinal detachments require 5 years of training. Avoid being ideological about the best method to attach the retina. Be pragmatic. The simplest method which reattaches the retina is the best. And the best method for one eye may not be the best method for another eye.

What is the difference between theory and praxis? Theory means that you know everything, but nothing works. Praxis means that everything works, but you do not know why. So try to acquire as a vitreoretinal surgeon a good mixture of practical and theoretical knowledge.

In this book all surgical techniques to reattach the retina are demonstrated in detail. The surgery is described like in a cookbook: First the instruments and material and then the surgery step-by-step. This surgery is illustrated with pictures, drawings and many videos.

Additional videos can be viewed on the YouTube channel of Ulrich Spandau and of Diego Ruiz-Casas.

Uppsala, Sweden — Ulrich Spandau
Madrid, Spain — Diego Ruiz-Casas
Belgrade, Serbia — Zoran Tomic

Acknowledgements

I want to thank my wife, Katrin, for her non-ending patience regarding her book-writing husband and I want to thank my children, Maximilian, Moritz and Oskar, for showing me that there is a world outside my beloved ophthalmology.

Ulrich Spandau

I want to thank to my wife Bojana and our daughter Petra for all the love they gave me and the inspiration to continue with my work.

Zoran Tomic

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Part I

Proliferative Vitreoretinopathy (PVR). Introduction

1 Surgery of Vitreoretinal Disorders: Past, Present, and Future

Relja Živojnović

Pre-Gonin era: Retinal detachment has always been a dramatic and terrifying experience for the patient and for the surgeon a source of frustration for a long time. Practical knowledge in the nineteenth century was based on pathoanatomical observations, and the therapy consisted of drainage and bed rest. Invention and introduction of ophthalmoscopy by Helmholtz in 1851, enabling fundus visualization in vivo for the first time, marked the decisive step in understanding and treatment of retinal detachment. Nevertheless, it took 70 long years to totally comprehend the course and dynamics of the pathological process. The main components of this process—traction, fluid, current in the eye, as well as the hole in the retina—were observed separately but were not causally connected. The importance of particular components of the pathological process was either over- or underestimated, while the therapy itself relied on the surgeon's assumptions. Cutting of the "vitreous strands" (Deutschmann and Graefe); intraocular injection of various substitutes with or without drainage of subretinal fluid; extensive diathermy (Lagrange); and shortening of the eyeball (Müller), combined with strict bed rest and positioning are some of many futile attempts whose rare positive results were at the most only temporary.

R. Živojnović
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1.1 The Beginning of Retinal Surgery: Jules Gonin

In the early twentieth century, after extensive studies of pathological specimens, ophthalmoscopic observation of the dynamics of pathological process and looking for holes in the retina, and trying all the hitherto applied surgical methods in treatment of retinal detachment, Jules Gonin, Lausanne, Switzerland, came to the epochal conclusion that a hole in the retina is the cause of detachment. Using Paquelin's thermocautery to perforate the eyeball on the spot of defect and incarcerating its edges by withdrawal of the needle, he achieved retinal reattachment. Using this method he successfully reattached the retina in 40–50% of cases. After long years of disbelief and dismissal, he finally got recognition for his work at the international congress in Amsterdam in 1929. His enthusiastic followers were Arruga in Spain, Amsler in Switzerland, and Wewe in the Netherlands. However, in spite of the 40–50% success rate in the previously inoperable cases, a large number of patients still could not be treated successfully. The reason was that the treatment did not comprise the other two components of the pathological process, vitreoretinal traction and fluid current in the eye. Shortening of the eyeball to reduce its volume as introduced by Lindner and later by Wewe, based on earlier attempts by Müller, resulted in certain improvement.

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Ophthalmoscopy. As it was said before, in 1850, Helmholtz introduced ophthalmoscopy, which technically consisted of a strong source of light near the patient's head and concave mirror with a hole in the middle through which the surgeon—by means of reflected light via convex lens—could see the lightened fundus. In the 1950s that system was developed into a sophisticated ophthalmoscope with light and a system of lenses, which was used as both direct and indirect ophthalmoscope. Development of visualization was of crucial importance for the development of vitreoretinal surgery and had a curious course. In the early 1950s, Schepens, Boston, USA, and the Fison in London, UK, designed the binocular indirect ophthalmoscope, which was accepted and used in these countries at the time. In Germany the Zeiss ophthalmoscope for direct and indirect ophthalmoscopy came into use very early. In the 1960s, it was replaced by the bonoscope, an indirect monocular ophthalmoscope with extra strong light. In France, indirect ophthalmoscopy was as good as unknown, and direct ophthalmoscope was used in surgery, which culminated in the use of Goldmann's three-mirror glass under the microscope. Superiority of the binocular indirect ophthalmoscope with the possibility of indentation of the periphery was obvious, so that in the 1980s it was eventually generally accepted. For diagnostic purposes, besides the ophthalmoscope, Goldmann's three-mirror glass and panfundoscope for its panoramic picture were used. In the 1990s they were all replaced by 90D lens.

1.2 Scleral Indentation

Introduction of scleral indentation was a capital contribution in this surgery, as it simultaneously treated all three components of the pathological process: vitreoretinal traction, fluid current, and their consequence—the retinal hole. The first attempt at indentation—"buckle"—was reported in 1937, when Jess sutured a gauze tampon under Tenon's capsule. Although basically logical, this attempt did not find followers. The father of the "buckle" surgery was undoubtedly Ernst Custodis, Dusseldorf, Germany, who used a plastic "egzoplant" sutured on the sclera. This technique was soon accepted and increased positive results in surgery to 80%. However, frequent complications of globe perforation due to hardness of the plastic material, combined with surface diathermy, inspired surgeons in many countries to look for other solutions. For detachments with multiple holes in the periphery, Arruga introduced *cerclage equatorial*—circumferential buckle—by suturing a nylon thread through the sclera on the equator of the eyeball. The logic and simple use of this method was appealing. Perhaps that is why perforation of the globe during surgery and ischemia of the anterior segment postoperatively were rather frequent complications. The idea itself was perfected by Schepens, Boston, USA, who used softer material, i.e., silicone. An encircling band with or without a radial buckle, combined with diathermy, replaced finally Arruga's cerclage. Complications with plastic material inspired Pofique and Spira, Lyon, France, to use a biological material—the human sclera. Lamellar scleral pocket—*poche scleral*—filled with pieces of the human sclera or sutured upon the sclera, and *poche apportee*, filled with the same material, were frequently used in the 1960s. At the same time Kloeti, Zurich, Switzerland, propagated the use of fascia lata as cerclage material. Naturally, biological materials did not cause any complications, but the effect of indentation was short-lived and in some cases caused redetachment. Looking for new materials more or less ended, when Lincoff, New York, USA, introduced Silastic sponge and replaced diathermy by cryocoagulation. In the early 1970s, this became the method of choice in treatment of detachment and has been sustained as such up to the present time. Recently hydrogel as the material for indentation has not brought much change.

Retinopexy: The purpose of retinopexy is to create a chorioretinal scar, and it has no impact on vitreoretinal traction. After the use of thermocautery in Gonin's time, surgery moved on to non-perforative diathermy as introduced by Pischel. Diathermocoagulation, technically improved by Wewe, was applied for many years.

In the 1970s, Lincoff, following Bietti's (Rome, Italy) experience, combined the Silastic buckle with cryocoagulation, which, properly used, did not damage the sclera. It should be mentioned that extensive use of diathermy and also of cryocoagulation may have very serious consequences and provoke proliferative process in the eye. At the beginning of the 1960s, Meyer-Schwickerath, Essen, Germany, introduced xenon photocoagulation opening a new chapter in retinopexy. Laser coagulation based on the same principle and introduced by Zweng and Little, USA, was technically much easier to use and replaced completely xenon photocoagulation. In this way the chapter of retinopexy has been completed.

1.3 Intraocular Tamponade

Owing to his attempt in 1911 to treat retinal detachment by means of intravitreal air injection, Ohm can be regarded as the forerunner of tamponade. With much more understanding of the pathological process, Rosengren, Gothenburg, Sweden, used the air for tamponade in 1938. In the early 1970s, Norton, Miami, USA, introduced SF6, and in the early 1980s, Lincoff pioneered long-lasting gases, which have the advantage of long-lasting tamponade and disadvantage of expansion under low pressure.

Tamponade is fully effective only when combined with indentation. Without indentation, propagated as fast and cheap surgery, it only has a temporary effect because of persistence of vitreoretinal traction. From the early 1970s, the "buckle" surgery combined with cryocoagulation, drainage if necessary, with or without tamponade has become the method of choice in treatment of retinal detachment, and it is successful in 90–95% of detachments with the mobile retina. But it failed with detachments complicated by multiple equatorial ruptures, with giant tears, and detachments caused by proliferative process.

Introduction of silicone oil. In the 1970s, Paul Cibis, Saint Louis, USA, introduced silicone oil in retinal detachment surgery (Fig. 1.1). Under control of binocular ophthalmoscope in reversed picture, using surface tension of silicone oil and expansion of the silicone bubble, he tried to separate the detached retina from the changed vitreous and fibrotic membranes. At the same time, he tried to attach the retina by evacuating intraocular fluid. With successful result, he left silicone oil in the eye as permanent tamponade. By this extremely difficult technique, he achieved surprisingly good results in some cases that used to be inoperable. Probably owing to its difficult application, this technique had only few followers in the USA (Okun, Watzke). In the mid-1960s, attempts to establish this technique in some European countries were published—Moreau in France, Dufour in Switzerland, Liesenhof, Lund in Germany. Cibis' early death and legal problems concerning the use of silicone oil being an industrial product not registered by FDA resulted in restricted spread of this method. In Europe surgeons did not use binocular ophthalmoscope and were not very familiar with dynamics and consequences of pathological processes in the eye, which resulted in poor outcome and discontinuation of the use of silicone oil in Europe in the late 1960s.

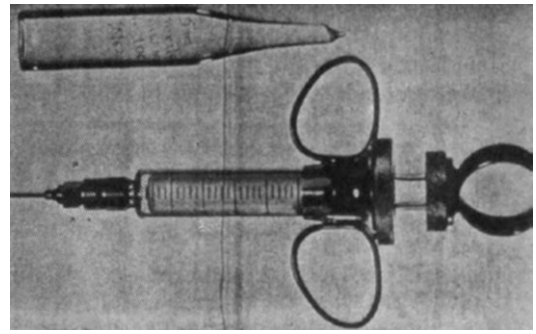

Fig. 1.1 Cibis syringe for injection of silicone oil

Modern times. In the early 1970s, John Scott, Cambridge, UK, impressed by Cibis' results with silicone oil, attempted the treatment of complex cases in which conventional technique was unsuccessful. Trying to separate fibrotic membranes and the changed vitreous body from the contracted retina by means of expansion of the silicone bubble, he also used intraocular instruments. He used the bent pick needle to lift membranes, the blunt flute needle for fluid evacuation, and scissors. The surgery was performed under control of binocular ophthalmoscope in reversed picture. With positive outcome the central retina could be reattached and

the fibrotic tissue and membranes pushed to the periphery. Silicone oil would stay as permanent tamponade preventing recontraction of fibrotic tissue. With his skill, insight in the course of pathological process, as well as by his enormous persistence, John Scott achieved remarkable results. Owing to difficulty of the procedure itself and his good results, only a small number of surgeons could be compared to him, so that Cambridge was the place of reference for patients from all over the world. With this method John Scott made a huge step forward in the treatment of difficult cases, but even this method had its limitations. Giant tears with PVR, traumatic detachments with the incarcerated retina, diabetic tractional detachment, and others could not be treated successfully in this way. Permanent tamponade with silicone oil also caused complications in the long run.

At the end of the 1960s, David Kasner, Miami, USA, tried a new treatment of prolapse of the vitreous body during cataract surgery and trauma of the eye and called it open sky vitrectomy. Using cellulose sponges and scissors, he removed the prolapsed vitreous body. By successful surgery he proved that the vitreous body was not of vital importance to the eye. In 1970 the new technique inspired Robert Machemer, Miami, USA, with technical assistance of J.M. Parel, to design an instrument which enabled entering the vitreous space through a relatively small opening and under the microscope to remove the blurred vitreous body. The multifunctional instrument called vitreous infusion suction cutter was a revolutionary step in the history of vitreoretinal surgery. Short time after that, O'Malley introduced a bimanual system with a separate source of light and standardized system of 20-gauge instruments. Pars plana vitrectomy opened new possibilities in the vitreous body surgery, but it was not aimed at the treatment of retinal detachment. Even more the fear of injuring the retina during surgery was great and comparable to the fear of loss of the vitreous body in earlier cataract surgery. In the USA, the standard procedure for the treatment of retinal detachment for more than 10 years was the Silastic buckle with cryopexy and possible gas tamponade. Complex cases of detachment with proliferative process usually were not operated on. The only kind of detachment in which vitrectomy was implemented was detachment caused by a hole in the macula, which due to its location used to present a problem. In the past, indentation techniques were applied with modest success, such as the silver ring of Rosengren, the silver plomb of Gloor (Zurich, Switzerland), and others. For this kind of detachments, pars plana vitrectomy with removal of epiretinal membranes, gas tamponade, and positioning was the method of choice then and has remained so ever since. Recently, relocation of the macula as introduced by Machemer in the 1990s is one more indication for implementation of vitrectomy.

Pars plana vitrectomy has opened new possibilities for research of proliferative processes which now can also be followed in pathological specimens of the ocular tissue. In the late 1970s, Machemer described proliferative process in the eye on the basis of acquired specimens and clinical experience and introduced the familiar name proliferative vitreoretinopathy (PVR), instead of MVR (massive vitreous retraction).

Pars plana vitrectomy was rather hesitantly accepted in Europe by way of pioneers in particular countries: Kloeti in Switzerland, Laqua and Heimann in Germany, and Leaver in the UK. In the 1970s, Jean Haut, Paris, France, was the first to combine vitrectomy with silicone oil.

1.4 The New Concept

In the early 1970s, practicing retinal surgery in Rotterdam, the Netherlands, I was dissatisfied with my results. Visiting other centers in Europe—Zurich, Bonn, and Paris—and comparing my work with that of the others, I did not notice major differences in results. After several visits to John Scott, I was convinced that his technique and approach were absolutely superior to anything I had seen before. In the late 1980s, I implemented his technique in surgery of a considerable number of patients and achieved results satisfying for that time. After a year, together with Diane Mertens, I abandoned binocular ophthalmoscopy. I switched to the surgical microscope with contact lens (Fig. 1.2). Now I had a free hand and a direct image as in reality. For me the surgical microscope is part of vitrectomy as surgical technique.

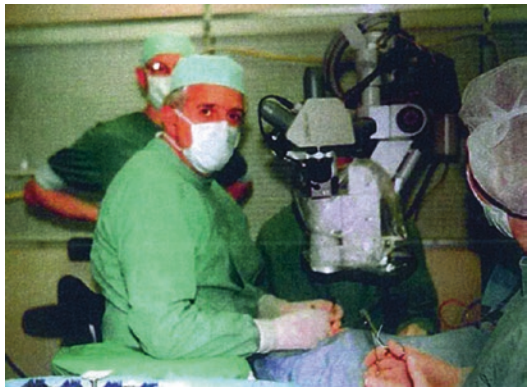

Fig. 1.2 The surgical microscope is an essential part of vitrectomy

I also abandoned combined vitrectomy with silicone oil, using it only as temporary tamponade. As the admitted patients were increasingly complex, it was soon obvious that this technique also had its limitations. In complex cases, when due to proliferative process the retina was contracted, incarcerated, or shortened, removal of all membranes and scarred tissue was not sufficient to produce results we aspired to. The only solution for these cases appeared to be surgical intervention—retinotomy and retinectomy. Initially only one-eyed patients in a desperate situation were treated in this manner. Nevertheless, I very soon managed to operate a considerable number of the most difficult, previously inoperable cases with favorable results.

I therefore established a new concept of treatment, which consisted of vitrectomy, meticulous removal of all epi- and subretinal membranes, retinal surgery, retinotomy, and retinectomy—if necessary, laser coagulation and temporary tamponade with silicone oil. After the first publications and frequent presentations at meetings, the introduction of retinal surgery in the arsenal of surgical measures was soon accepted and adopted.

At the very beginning of the development of this demanding technique, I was confronted with absence of adequate instruments for this new kind of surgery. Presence of Ger Vijfvinkel, a technician in our hospital, was crucial for the development of new instruments (Fig. 1.3).

His frequent presence in the operating theater and observation of surgery resulted in prompt design and construction of adequate instruments.

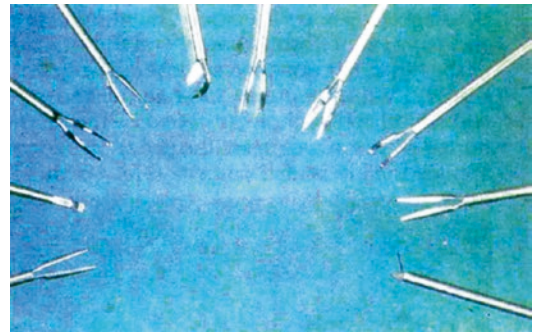

Fig. 1.3 Scissors and forceps

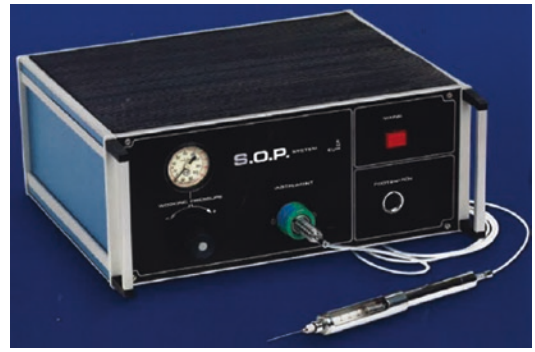

Fig. 1.4 Air-driven silicone oil pump

Fig. 1.5 Back-flush needle with silicone tip

Besides numerous small instruments, we developed together the foot-driven silicone pump (Fig 1.4), the back-flush needle with silicone tip (Fig 1.5), 4-port system, 25-gauge vitreous cutter and instruments, replaced Ando's plastic tacks with steel ones for preoperative use, etc. Ger Vijfvinkel with his inventiveness contributed considerably to the development of vitreoretinal surgery.

This new, more aggressive concept of vitreoretinal surgery was not associated with many postoperative complications. After the introduction of 6 o'clock iridectomy (Ando, Japan, 1986), the problem of pupillary block was solved. Other complications could be ascribed to inadequate surgical technique or to continuation of prolifera-

tive process which had required frequent reoperations. This proliferative process was also often provoked by careless surgery. It should be mentioned that the pathological basis of all complex cases was the biological process and that surgical therapy is only adequate and indicated in absence of a better and more appropriate treatment.

In the last 20 years, no radical changes in therapy have taken place. Introducing PFCL (heavy liquid), Stanley Chang greatly simplified the surgical process. Double filling silicone with PFCL as used by Peperkamp, Rotterdam, the Netherlands, in prevention of inferior detachment gave positive results. Improved visualization of membranes by the use of colors—trypan blue—as well as triamcinolone acetonide for better visualization of vitreous cortex made the surgical process easier and safer. The use of finer instruments, thinner vitreous cutters, as well as sutureless vitrectomy simplified the course of surgery. Even with all this technical progress, meticulous removal of complete proliferative tissue before retinal surgery and injection of silicone oil remain an absolute must for success of the operation.

A correctly performed "buckle" surgery with binocular ophthalmoscope and its success rate of 90–95%, with the mobile retina, is practically complication-free. (Choroidal bleeding at drainage is the complication most frequently mentioned, which we practically reduced to zero by using the blunt lacrimal probe for penetration of the choroid after incision of the sclera.) This conventional surgery is much cheaper than vitrectomy in terms of both personnel and instruments. Pars plana vitrectomy in itself is an invasive method with more possible complications such as endophthalmitis, cataract, etc. However, nowadays, there are a few people ready to master indirect ophthalmoscopy, and I am afraid that in the future conventional surgery will lose battle with 90D lens, wide-angle microscope and vitrectomy.

Finally I would like to add a few comments. Development of the surgery has confirmed an old truth again: Not a single, even the most important step in development can exist alone but only builds on earlier achievements of its predecessors. Still, the development of vitreoretinal surgery was many times slowed down for seemingly incomprehensible reasons. For instance, it took many years before absolutely superior binocular ophthalmoscopy was generally accepted in Europe. Further, more than 10 years after the epochal invention of pars plana vitrectomy, the complex pathology was not treated in the USA, while at the same time, such cases were successfully treated in Cambridge. How to explain it? Was it complacency, vanity, conservatism, or arrogance? Perhaps some of it all, but the main reason was poor flow of information. For a long time retinal surgeons were perceived as curious people, almost hobbyists, and were isolated. Results of both successful and unsuccessful operations were considered inadequate. For quite a while, the prestigious biannual Gonin club meeting was almost the only place for exchange of ideas and experiences. The presentation technique was weak and unconvincing. Mutual visits were not frequent or common, and learning and transfer of knowledge were not formalized, at least not in Europe.

This situation dramatically changed in the early 1980s. With introduction of new surgical methods, new technology, and better results, interest in the new surgery was on the rise. At numerous meetings the new surgery was presented by new visual means: film, video, and live surgery, in an attractive, instructive, and impressive way. Initially, that advancement was limited to the developed countries, but now it has covered most countries that can afford it. Vitreoretinal surgery is not restricted to a small number of places. Instead, the number of centers as well as the number of vitreoretinal surgeons has multiplied.

However, this very optimistic and stimulating development is followed by another, much less positive one. For years the existing management in healthcare service has applied the system of general cost-effectiveness and control in order to reduce expenses. This system, which has savings of both money and time as its main aim, is undoubtedly useful in many aspects, but it often neglects interests of the patient. In its aspiration to maximize results in the shortest possible

time—calling the operation a product and the patient a client—this system is focused on routine surgery. A patient with complex pathology demanding long operations is not a welcome guest. Working in such circumstances, pressurized by the hospital, insurance company, and a lawyer in front of the operating theater, the surgeon is less and less stimulated to treat difficult cases with uncertain outcome and prospect of reoperations. Moreover, the challenge and attractiveness of this surgery in the pioneering time are no longer present, and there is no financial incentive. Accordingly, negative selection of difficult cases becomes understandable and increasingly frequent. Besides the fact that not operating such cases is an ethical offense, it also has other far-reaching consequences. Frequent selection and exclusion of these cases becomes a common practice. The decreased number of such operations, the pathology being rare anyway, and its distribution on a great number of centers and surgeons question the possibility of surgical experience building and, consequently, the quality of surgical work. Under the circumstances, transfer of experience in this atypical surgery to our younger colleagues also becomes an issue. A solution of this unfavorable situation, which tends to worsen with time, lies in triage of difficult, complex cases and concentration of their treatment in corresponding centers. There, experienced surgeons, working without pressure and limitations, would provide appropriate treatment to such patients. Young surgeons would get an opportunity to acquire knowledge and experience in these centers.

Institutions in charge of health expenses, which disparagingly criticize modest result of this demanding surgery and consequently do not stimulate its development, have to remember that an operated patient with the final visual result, even only light projection or hand movement, demands much less money from the society than a totally blind person.

2 Pathogenesis, Histopathology, and Classification

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2.1 PVR

2.1.1 Overview of the Disease: Pathogenesis

Proliferative vitreoretinopathy, or PVR, is a term adopted in 1983 for describing a complication occurring after some retinal detachments (RD) [1]. PVR develops in 5–10% of RD, and although it can occur spontaneously, before surgery, it is commonest after it [2]. Pathogenesis, in the original description, was focused on the formation of membranes in both surfaces of the retina, but more recently, the existence of intraretinal changes have been added as the more severe form of PVR [3].

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Anyway, initial mechanisms implicated in PVR are similar to any retinal injury repair process [2]. After separation of the neuroretina, photoreceptors started to die mainly by apoptosis (and also by other cell death mechanisms) very early, but also outer layers of the retina became ischemic, because of their separation from the choriocapillaris. Ischemia obviously produces the loss of neurons but also triggers several cell and molecular processes. This loss of neurons stimulates a reaction of retinal glial cells (Müller, astrocytes, and microglia) starting a new event directed to remodeling the retina and to preserve the retinal structure [4]. Those changes lead to membrane formation, over and behind the retina, but above all, they induced intraretinal glial changes, which shorten the retina making it very difficult to reattach even by surgery, unless a retinectomy was performed [3].

Not all RD develop this severe complication, although all of them have many common facts: separation of retina layers, ischemia, breaks affecting the whole thickness of the retina, and a breakdown of the blood-retinal barriers allowing an intraocular inflammation and also facilitating the intraocular migration of cells which release more inflammatory products into the vitreous cavity [2]. Therefore, one of the current challenges is the appropriate identification of those patients with a high risk of developing this complication.

Initial approaches for detecting those patients at high risk of developing PVR were based on the identification of clinical factors [5], but since

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2006, we have been working in elucidating the role of the genetic profile of each patient [6–8]. We are now convinced that genetics plays an important role in some crucial steps of this complication. For instance, cytokine production, which is a crucial element in retinal scarring, is a gene-regulated process [9, 10].

PVR still poses some challenges to the retina specialist, because despite the efforts made over the past 40 years, we are still unable to prevent or to treat it, and continues to be the most frequent and severe complication after RD surgery [2, 11].

For almost two decades, researchers have been focused on several steps of the disease: cell migration (giving a crucial role to RPE cells in PVR pathogenesis), epi- and subretinal membrane formation, and further contraction of those membranes [11]. These events are essential parts of PVR, but currently we know that there are more players in this story and probably more relevant if our target is inhibiting this abnormal repairing process and then getting an efficient prophylaxis. One, without any doubt, is the glial reactivity and hypertrophy which is a basic repair element in the retina as well as in any other part of the central nervous system [12]. And there are some others.

The lack of an appropriate classification is also a bottleneck which has prevented an adequate comparison of the proposed treatments along decades.

This problem has not yet been solved and seems an essential point to set the appropriate framework for an efficient clinical research, since now.

In fact, in a recent review of the literature [13], we found that only 74% of the revised papers related to treatments, published between 2000 and 2014, used a standardized classification, being in the 56.3% of cases the updated Retina Society classification of 1991 and in 33.9% the original one of 1983 [1] (Fig. 2.1). But when the updated Retina Society classification was used, only 10.4% of authors used a full C grade description (Fig. 2.2). It is clear that current classifications have a very limited value in clinical practice, but for clinical research purposes, we are convinced that a new one is needed.

We have pointed out some of the critical elements, which in our opinion must be part of this new classification [2]: type of morphologic changes, extension of changes, signs of severity and progressiveness, and, for sure, some still unidentified signs.

Regarding the prophylactic measures or medical treatments, no one has been widely accepted for clinical use [2].

PVR is a complex process involving several risk factors and over the last 25 years, and besides the spectacular evolution of vitreoretinal surgery techniques, which includes small gauge instrumentation, the emphasis has been placed on having a success in the primary surgery for RD repair, ignoring some other important factors.

Retina Society Terminology Committee classification	
Grade	**Clinical signs**
A (minimal)	Vitreous haze and pigment clumps
B (moderate)	Surface retinal wrinkling, rolled edges of the retinal, retinal stiffness and vessel tortuosity
C (marked) C-1 C-2 C-3	Full thickness fixed retinal folds in: One quadrant Two quadrants Three quadrants
D (massive) D-1 D-2 D-3	Fixed retinal folds in four quadrants that result in: A wide funnel shape; A narrow funnel shape; Closed funnel without view of the optic disc

Fig. 2.1 Classification from the Retina Society Terminology Committee (1983). Modified from: The Retina Society Terminology Committee, "The classification of retinal detachment with proliferative vitreoretinopathy," Ophthalmology, vol. 90, no. 2, pp. 121–125, 1983