

Management of Complicated Vitreoretinal Cases in Children

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Eric Nudleman and Antonio Capone Jr.

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2.1 Introduction

Pediatric vitreoretinopathies pose unique challenges to the retinal surgeon because of the distinct anatomic and physiological differences from adult retinal diseases. The pars plana, through which the vitreoretinal instrumentation may be safely introduced, is not fully formed until approximately the age of 8 or 9 months, thereby necessitating entry through the pars plicata when a posterior approach is desired in the newborn eye [17]. The vitreous gel, which is well formed and firm in normal newborn eyes, may be optically empty or abnormally synergetic in various pediatric diseases. The vitreoretinal adhesion is stronger in children than in adults, making the surgical induction of posterior vitreous detachment relatively difficult [19, 44]. The biochemistry of the newborn eye is influx, with rising and falling levels of vascular endothelial growth factor (VEGF), insulin-like growth factor 1, tumor growth factor-b, and other cytokines, which may affect the progression or stabilization of pediatric vitreoretinopathies [10, 47, 54]. To operate safely, the pediatric vitreoretinal surgeon must understand the characteristics that define diseases, such as retinopathy

E. Nudleman, MD, PhD
Department of Ophthalmology,
Shiley Eye Center and Jacobs Retina Center,
University of California, San Diego,
CA, USA
e-mail: enudleman@ucsd.edu,
eric.nudleman@gmail.com

A. Capone, Jr., MD (✉)
Department of Ophthalmology, Oakland University
William Beaumont School of Medicine, Associated
Retinal Consultants, Royal Oak, MI, USA
e-mail: acaponejr@arpc.net, acaponejr@yahoo.com

of prematurity (ROP), familial exudative vitreoretinopathy (FEVR), persistent fetal vasculature syndrome (PFVS), congenital x-linked retinoschisis (CXLRS), and Coats disease. Here we discuss key features of the surgical approach to complicated pediatric vitreoretinopathies.

2.2 Retinal Detachment in Retinopathy of Prematurity

The international classification of ROP is well established [22]. A stage 4A detachment is subtotal and spares the macula, whereas a stage 4B detachment is subtotal and involves the macula. A stage 5 detachment is a total retinal detachment. In the Early Treatment for Retinopathy of Prematurity (ETROP) study, 9.1 % of eyes progressed to retinal detachment following laser photocoagulation at 2 years [14]. ROP retinal detachments may have varying degrees of hyaloidal organization and preretinal proliferation, but most lie on a spectrum from primarily exudative to primarily tractional in etiology.

The international classification system of ROP was designed to characterize untreated eyes. Once peripheral laser ablation has been performed, anatomic permutations may defy simple categorization. After peripheral laser scars have formed, a true stage 5 retinal detachment cannot occur because the far peripheral retina remains attached. However, the retina may appear totally detached on clinical examination if the space between the attached peripheral retina and the more central proliferative tissue is not readily visible. We describe such retinal detachments as “stage 4b/5” because they are technically stage 4b detachments but are clinically indistinguishable from stage 5 detachments without the knowledge of earlier laser treatment.

Predominantly exudative retinal detachments are believed to occur as a consequence of vascular leakage into the subretinal space [19]. Exudative detachments in ROP have been reported following both cryotherapy [53] and laser photocoagulation [34–36]. The appearance of a predominantly exudative detachment differs from a predominantly tractional detachment due to the presence

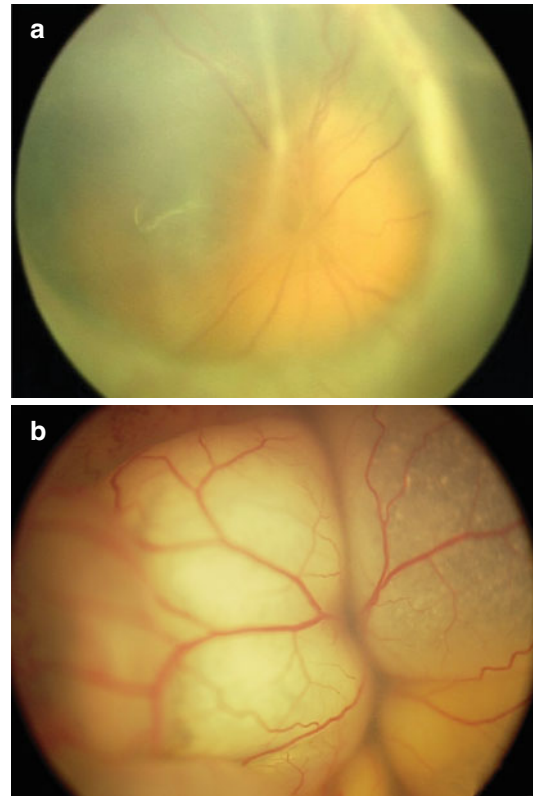


Fig. 2.1 Tractional versus exudative retinal detachment in advanced ROP. **(a)** RetCam photogram of stage V tractional retinal detachment with open funnel configuration, demonstrating anterior fibrous ring. **(b)** Exudative retinal detachment demonstrating smooth contour with subretinal lipid and absence of cicatricial fibers

of copious subretinal lipid and the absence of preretinal cicatricial fibers (Fig. 2.1). Effusive detachments can be safely managed medically with aggressive steroid therapy and cycloplegia.

Predominantly tractional retinal detachments in ROP occur due to formation of fibrous proliferation along the ridge tissue and extending into the overlying vitreous. The vitreous sheets act as scaffolds for the extension of the fibrotic tissue. Contraction occurs along various vectors, most commonly toward the center of the eye, as well as posterior toward the optic nerve or anterior toward the lens. The tractional vectors can be summarized as (1) intrinsic to the retina, (2) ridge to lens, (3) ridge to ridge, (4) ridge to ciliary body, (5) ridge to retina, and (6) persistent stalk tissue (Fig. 2.2).

Knowledge of the tractional vectors present in ROP is critical to surgical success. The primary

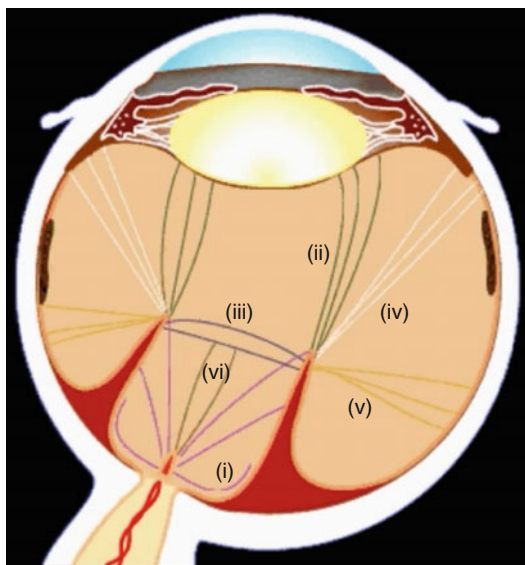


Fig. 2.2 Schematic demonstrating the tractional vectors in advanced retinopathy of prematurity, including (i) intrinsic to the retina, (ii) ridge to lens, (iii) ridge to ridge, (iv) ridge to ciliary body, (v) ridge to retina, and (vi) persistent stalk tissue

surgical goal in ROP detachments is interrupting the traction resulting from fibrous proliferation. Successful efforts can prevent the progression from stage 4A to stage 4B or from stage 4B to stage 5, reduce dragging of the macula, and spare visual function. Successful reattachment has been reported in 74–91 % of stage 4A detachments [4, 6, 21, 26, 34, 46], 62–92 % of stage 4B detachments [8, 21, 26, 41, 46, 58], and 22–48 % of stage 5 detachments [9, 15, 27, 49, 50]. In stage 5 detachments, partial residual retinal detachment is common, but the goal is to remove the traction so as to reattach as much of the retina as possible and provide a stable anatomic result. Visual outcomes in successful repair of stage 4A detachment can be expected to be 20/80 or better [21, 28, 39], ambulatory vision following stage 4B repair [41], and form vision following stage 5 repair [33, 51].

2.3 The Timing of Surgical Intervention in Retinopathy of Prematurity

ROP is characterized by a relatively predictable timeline of progression. Initial manifestations of

the disease are usually seen approximately 32 weeks postmenstrual age (PMA), and the threshold for laser ablation is reached at a mean of 37 weeks PMA [37, 43]. Retinal detachment after appropriate laser ablation occurs at a mean of 41 weeks PMA [42]. The most dramatic exception to this timeline is aggressive posterior ROP that is characterized by rapid progression of zone 1 or posterior zone 2 plus disease and ill-defined retinal neovascularization to retinal detachment [22].

The rapidity of disease progression correlates to some degree with the level of retinal vascular activity at the time of retinal detachment. Surgery for stage 4A ROP targets interruption of transvitreal proliferative condensations. For this reason, vascular activity is rarely a reason to defer surgical intervention. In general, once surgical intervention is necessary for stage 4A ROP, the earlier the procedure is performed, the better to minimize the extent of the detachment.

Surgery for stages 4B and 5 ROP typically entails the mechanical removal of preretinal proliferation. An eye with a high degree of vascular activity, as represented by plus disease, florid retinal neovascularization, and rubeosis iridis, is likely to encounter significant intraoperative bleeding. In eyes with stage 4B or stage 5 detachments in the setting of significant vascularity, it is usually necessary to wait until 48–52 weeks PMA for vascular activity to decrease to intervene [18].

2.4 Lens-Sparing Vitrectomy

In most stage 4A and many stage 4B ROP detachments, it is possible to relieve traction with a lens-sparing vitrectomy (LSV). The eye is entered at the pars plicata, approximately 0.5 mm posterior to the limbus. A two-port approach using an infusing light pipe or pic and three-port approach using a separate infusion line have both been reported with similar success rates [6, 21, 26, 31]. A core vitrectomy is carefully performed with attention to the vectors of traction. Specifically, an effort should be made to address the transvitreal ridge to ridge tissue, ridge to periphery, ridge to lens, and optic nerve head to the ridge (Fig. 2.2). In many cases, successful release of

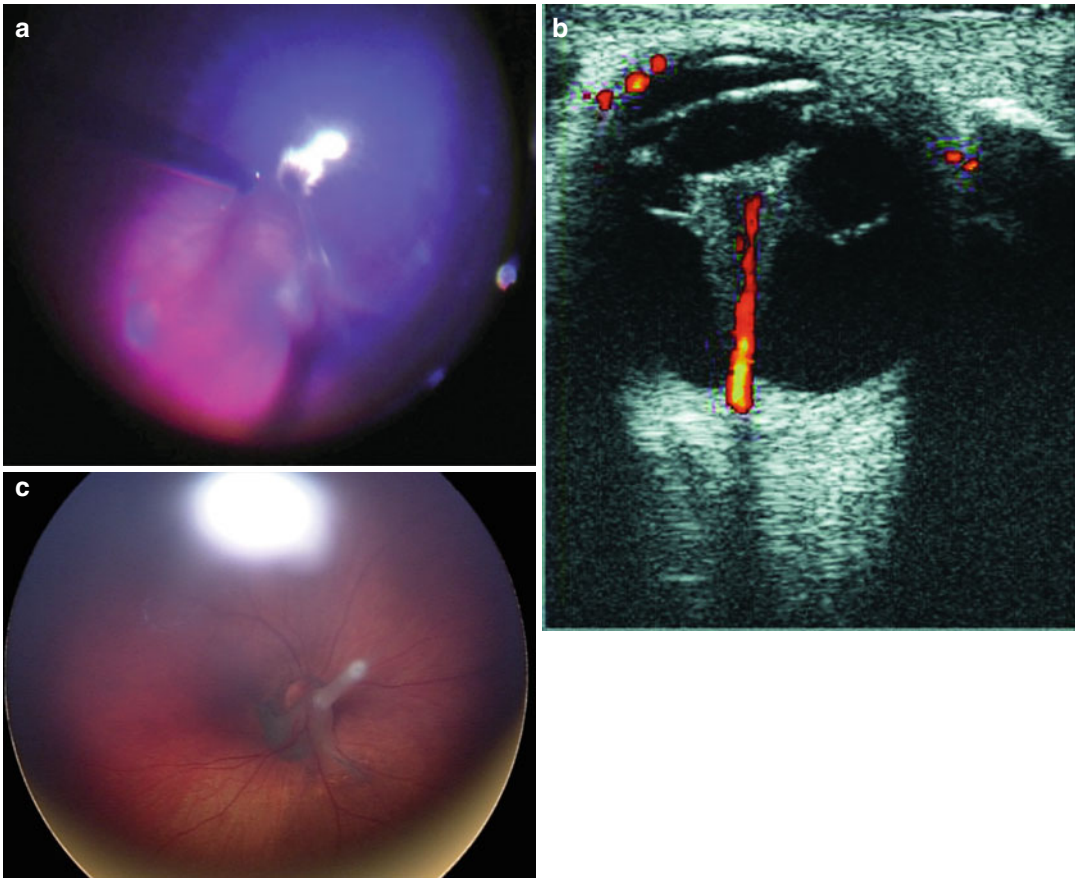


Fig. 2.3 Stalk tissue in persistent fetal vascular syndrome. (a) Intraoperative photograph demonstrating traction on the retinal tissue with dragging of retinal vessels into the stalk. (b) Doppler ultrasound showing vessels

within the stalk approaching the posterior lens capsule. (c) One month postoperative photograph following transection of the anterior stalk with retraction of the stalk tissue

traction is evident during the case with relaxation of the tented retina. When the dissection is complete, a fluid-air exchange is performed, and the sclerotomies are sutured. Persistent subretinal fluid is expected at the conclusion of the case and will reabsorb over the course of weeks to months. Similarly, this approach is effective in treating the tractional component of stage 3B and stage 4B FEVR detachments [38].

In some cases of stage 4 ROP-related retinal detachments, anterior ridge to ciliary body tissue cannot be safely dissected by a transvitreal approach without damaging the crystalline lens. In such instances, the surgeon can cleave these anterior bands at the time of entry into the eye by placing the MVR blade through the sheet of tis-

sue and drawing back, an approach described as an *ab interno* incision [20]. The tissue can be incised parallel to the lens capsule once the blade has entered into view; however, care must be taken to avoid the lens equator on entry. Safe entry is accomplished by pointing the instrument posteriorly, parallel to the visual axis. If the anterior bridging tissue between the retina and the lens-ciliary body diaphragm cannot be safely separated through the pars plicata incisions, then a lensectomy and an anterior approach may be necessary to safely relieve vitreoretinal traction and allow for retinal relaxation.

In some cases of PFVS, the stalk tissue is attached eccentric to the visual axis and extends posteriorly. Traction is exerted on the posterior

lens surface and on the posterior pole. To address this traction, a lens-sparing technique with entry similar to a stage 4 ROP-related detachment can be performed. In contrast to the approach to ROP-related retinal detachment, the first step is to divide the stalk anteriorly without vitrectomy [45]. This is accomplished with an MPC type scissor, with careful attention to avoid manipulating the stalk, which can result in damage to the posterior lens capsule. Once the stalk has been divided, the anterior remnant is not manipulated. This is to avoid damage to the intrinsic retinal vessels and folds of retinal tissue, which may be dragged into the stalk as far as two-thirds the distance toward the lens (Fig. 2.3). The posterior stalk often retracts several millimeters immediately following transection, demonstrating the effect of the traction (Fig. 2.3). A limited core vitrectomy is then performed and the sclerotomies are closed. This approach has been demonstrated to improve function with resolution of strabismus without muscle surgery in the majority of children with this presentation [45].

2.5 Limbal Approach for Lensectomy and Vitrectomy

In cases of advanced retinal detachment or a poor view posterior to the lens, including stage 5 ROP, stage 5 FEVR, and PFVS cases with diffuse retrolental plaques, the risk of creating an iatrogenic retinal break may outweigh the benefits of performing lens-sparing surgery, and an anterior (translimbal) approach to lensectomy and vitrectomy may be preferable. When an anterior approach is desired, an inferotemporal or inferior infusion cannula is placed at the limbus to stabilize the anterior chamber initially and the unicameral anterior-posterior chamber subsequently. Limbal incisions are then made superonasally and superotemporally. The pediatric crystalline lens is aspirated with a vitrector once the anterior lens capsule has been opened. Importantly, the goals of lensectomy in such a situation differ from those of the removal of an uncomplicated congenital cataract. The benefits of preserving capsu-

lar support for potential secondary intraocular lens implantation in the future are outweighed by the likelihood of residual capsule serving as a scaffold for preretinal proliferation and circumferential vitreoretinal contraction. Once the residual capsule and the ciliary body are drawn into a contractile anterior ring, the ensuing hypotony may be difficult to treat both because the anterior contractile ring is difficult to visualize and safely dissect and because the ciliary body sustains permanent injury. Even in cases of chronic total retinal detachment with lenticuloretinal apposition, capsular material can generally be stripped away from the retina without causing retinal breaks. The surgeon may then proceed with anterior dissection of preretinal proliferative tissue, hyaloidal organization, or anterior stalk tissue.

2.6 Minimal Intervention to Achieve Surgical Goals

As in adult vitreoretinal surgery, the goals of pediatric vitreoretinal surgery are generally evident at the outset of the procedure: removal of significant media opacities, relieving of the transvitreal or vitreoretinal traction, peeling, and removal of the proliferative tissue. However, the risks of operating in an aggressive manner are far greater in children than in adults. Simply put, perfection is expensive in terms of risk of complications. In particular, the consequences of creating an iatrogenic retinal break can be devastating in children because of the massive proliferative response that often ensues [19]. As the pediatric vitreous is relatively well formed and is adherent to the retinal surface, the surgeon may be tempted to shave close to the retina with the vitreous cutter to remove the preretinal vitreous cortex. Such a maneuver is useful only rarely in pediatric cases and should be avoided in the absence of very specific relevant surgical goals. Performing a vitrectomy without complete removal of the posterior hyaloid in a child may lead to posterior hyaloidal contraction syndrome and retinal detachment, but in our experience this rare sequela does not warrant aggressive removal of adherent vitreous cortex on a routine basis [23].

2.7 Enzymatic Targeting of the Vitreoretinal Junction

The vitreoretinal adhesion is mediated in part by laminin and fibronectin [25]. Plasmin enzyme, either the intact protein procured from blood obtained from the patient (autologous) or a parent (heterologous) or the recombinant fragment ocriplasmin (Jetrea), can be administered to cleave laminin and fibronectin and facilitate posterior vitreous detachment [12, 30]. In adult cases with unusually strong vitreoretinal adhesions, such as in proliferative diabetic retinopathy, plasmin facilitates the surgical induction of posterior vitreous detachment [3, 52]. Ocriplasmin has also been evaluated for the treatment of vitreomacular adhesion in two randomized controlled studies and was shown to induce a posterior vitreous detachment in 30 % of patients [48].

A subset of pediatric vitreoretinal surgery requires successful peeling of preretinal membranes or the posterior hyaloid to achieve primary surgical goals, and plasmin may be useful in these situations. The posterior hyaloidal contraction syndrome is perhaps the most direct example, as a persistent vitreoretinal adhesion combined with hyaloidal contraction is relieved by successful vitreoretinal separation [23]. Preretinal proliferative membranes are also central components to the pathology of advanced cases of ROP, FEVR, CXLRs, and PVR-associated retinal detachments. The use of plasmin enzyme or ocriplasmin may facilitate the removal of such membranes and reduce the risk of creating an iatrogenic retinal break during membrane peeling (for review, see [55]). In young children who cannot tolerate an intravitreal injection in the clinic, plasmin is injected into the vitreous cavity following induction of general anesthesia, and surgery initiated approximately 30 min thereafter.

2.8 Retinal Folds Versus Stalks

Stalk tissue extending from the disk toward the posterior aspect of the crystalline lens is characteristic of PFVS [16]. The stalk tissue represents residual hyaloidal vasculature, which may include

elements within the vitreous cavity, as well as remnants of the tunica vasculosa lentis, which surrounds the lens. The hyaloid system normally begins to regress by 12 weeks' gestation and is completely regressed by 35–36 weeks' gestation [59]. The main hyaloid trunk is the last element to undergo regression. As a result, persistent fetal vasculature is often present in pediatric vitreoretinopathies where the normal development program failed, and the surgeon must differentiate persistent stalk tissue from a retinal fold to identify and address the pathology.

The stalk tissue may be fibrous or contain patent vessels. In ROP, the stalk tissue can be adherent to the detached retina, complicating the surgical dissection [11]. FEVR is a disease characterized by radial retinal folds, which may be pulled anteriorly by transvitreal traction toward the lens-ciliary body diaphragm. Persistent fetal vasculature may be found along the edge of the fold, and the fold itself may be difficult to identify clinically when viewed on end (Fig. 2.4). In such a case, if a

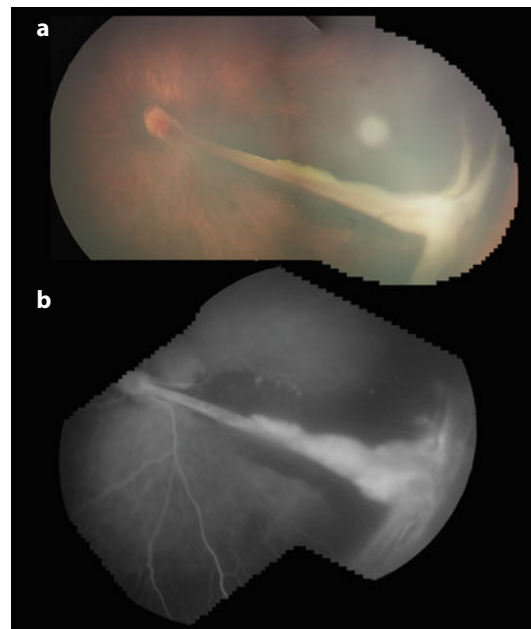


Fig. 2.4 Radial retinal fold in FEVR. (a) Montage color photograph of the left eye demonstrating knifelike radial fold extending through the macula to the anterior periphery and posterior lens capsule. (b) Montage fluorescein angiogram of same eye demonstrating retinal vessels drawn into fold with vasculature extending to the far periphery

knifelike fold is mistakenly identified as a stalk, the diagnosis of FEVR may be missed entirely [40]. A limited clinical examination in an uncooperative child may limit the physician's ability to distinguish between a fold and a stalk, and examination under anesthesia may be necessary.

2.9 Fluorescein Angiography for the Detection of Subclinical Avascularity

Primary avascularity of the peripheral retina is a key feature of several pediatric vitreoretinopathies [5, 22]. In ROP, the staging system depends on the ability of the clinician to identify the line (stage 1) or ridge (stage 2) separating vascular and avascular retina and any neovascularization that may extend from the ridge (stage 3). VEGF is produced by the avascular peripheral retina, thereby fostering retinal neovascularization and intraretinal vascular changes [57]. Peripheral avascularity is also seen in FEVR, Coats disease, CXLRS, and incontinentia pigmenti, although the relationship between disease activity and VEGF produced by an avascular peripheral retina is less clear in these conditions. Areas of avascu-

larity may escape detection on clinical examination when they are not bounded clearly by a demarcation line or a ridge. FEVR, in particular, is characterized by crescents of peripheral retinal nonperfusion, which may be difficult to identify without angiography [24]. In Coats disease, patches of nonperfused retina may be seen anteriorly or adjacent to characteristic vascular changes. In CXLRS, retinal nonperfusion may occasionally be seen within areas of retinoschisis. The standard of care for the treatment of ROP does not require fluorescein angiography, but angiography may be appropriate when an inadequate clinical response is seen after standard-of-care peripheral laser ablation, as angiography may identify islands of retinal nonperfusion posterior to the clinically identifiable ridge, which usually demarcates vascular and avascular retina. Fluorescein angiography is also invaluable in the detection of posterior avascular islands in FEVR, Coats disease, and incontinentia pigmenti (Fig. 2.5). The treating surgeon may then apply ablative laser to the avascular retina, although the efficacy of such treatment remains to be confirmed in a large case series or in a prospective study [56]. Broad areas of clinically inapparent avascular retina may also be present in conditions

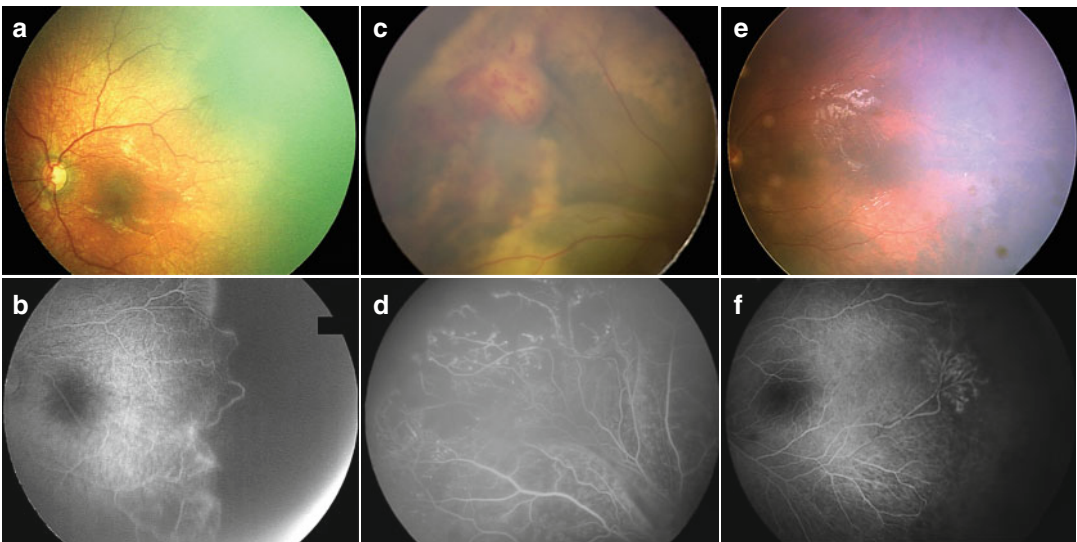


Fig. 2.5 Fluorescein angiography of peripheral retina. (a) RetCam color photograph and (b) FA of patient with incontinentia pigmenti demonstrating peripheral avascu-

larity. (c, d) Peripheral avascular islands in Coats disease. (e, f) FEVR with peripheral avascularity and frond of neovascularization at the vascularized border

not usually thought to be associated with retinal nonperfusion. Shaken baby syndrome is characterized clinically by intraretinal hemorrhages extending to the ora serrata and occasionally preretinal or subhyaloid hemorrhages [1, 32]. Retinal nonperfusion is often apparent on fluorescein angiography [13]. The implications and management of such nonperfusion are unclear, but these findings likely warrant close follow-up for signs of neovascular sequelae secondary to ischemia.

2.10 Complications of Syndromic Myopia in Infants and Children

The syndromic conditions associated with myopia in infants and children, such as Stickler and Marfan syndrome, have unique vitreoretinal features predisposing them to retinal tears and detachments. These children often present with chronic macula-off retinal detachments associated with PVR. Although such eyes may be repaired successfully employing contemporary vitreoretinal surgical techniques, they frequently require multiple surgical procedures, and visual results can be disappointing due to amblyopia. The high emotional and financial cost, in addition to the high rate of bilaterality of retinal detachment, justifies consideration of prophylactic retinopexy of the fellow eye in these patients. Both cryotherapy and laser photocoagulation applied contiguously 360° and posterior to the vitreous base have reduced rates of detachments in the fellow eyes of patients with Stickler syndrome [2, 7, 29]. Peripheral retinopexy for such eyes is not a panacea: failure ranges from approximately 6 to 10 %. With the advanced presenting pathology of many of these patients, prophylactic retinopexy of the fellow eye may be the most important procedure performed.

Conclusions

Surgical management of pediatric vitreoretinopathies can be complex. Successful intervention in these diseases requires an understanding of the relevant anatomy and biochemistry. Examination under anesthesia

with careful attention to detail and fluorescein angiography or ultrasonography when appropriate can provide the pediatric vitreoretinal surgeon with crucial information before surgery. Overly aggressive surgical techniques, failure to recognize anterior or posterior retinal folds, or inadvertent intraoperative traction on vitreoretinal adhesions may result in iatrogenic retinal breaks with catastrophic consequences. A careful and conservative surgical approach is therefore particularly important when performing surgery in eyes with pediatric vitreoretinopathies.

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