

Managing a Failing Filtering Bleb

An understanding of wound healing and predisposing risk factors will help surgeons in their rescue efforts.

BY NILS A. LOEWEN, MD, PhD, AND JAMES C. TSAI, MD

Despite the introduction of potent inhibitors of fibroblastic proliferation nearly 2 decades ago,¹⁻³ the single most common cause of the filtering bleb's failure in trabeculectomies remains fibroplasia, the proliferation of fibroblasts in the Tenon's capsule⁴⁻⁷ resulting in scarring and shrinkage of the filtering bleb. Early recognition is key to adjusting treatment.

In order to choose the right interventions for a failing bleb, it is helpful to recall the phases of wound healing (Figure 1). Fibroblastic proliferation and subsequent differentiation into contracting myofibroblasts are a part of an intricate process that encompasses the phases of inflammation, proliferation, and maturation. Because these depend upon each other and overlap significantly, the control of fibroblasts' growth begins in the OR.

WOUND HEALING

Inflammatory Phase

Hemostasis is an intimate part of the inflammatory phase (Figure 1B). It involves clotting, platelet aggregation, and changes in the diameter and permeability of the conjunctival and episcleral vessels. During surgery, chemotaxins are released that recruit polymorphonuclear neutrophils (Figure 1C) and macrophages (Figure 1D). The intense use of glucocorticosteroids immediately after surgery in the form of subconjunctival dexamethasone in the OR and prednisolone acetate drops every hour subsequently helps to control both inflammation and the ensuing proliferation.⁸ Fibroblasts are stimulated primarily by the secretion of transforming growth factor beta (TGF- β), vascular endothelial growth factor (VEGF), fibroblast

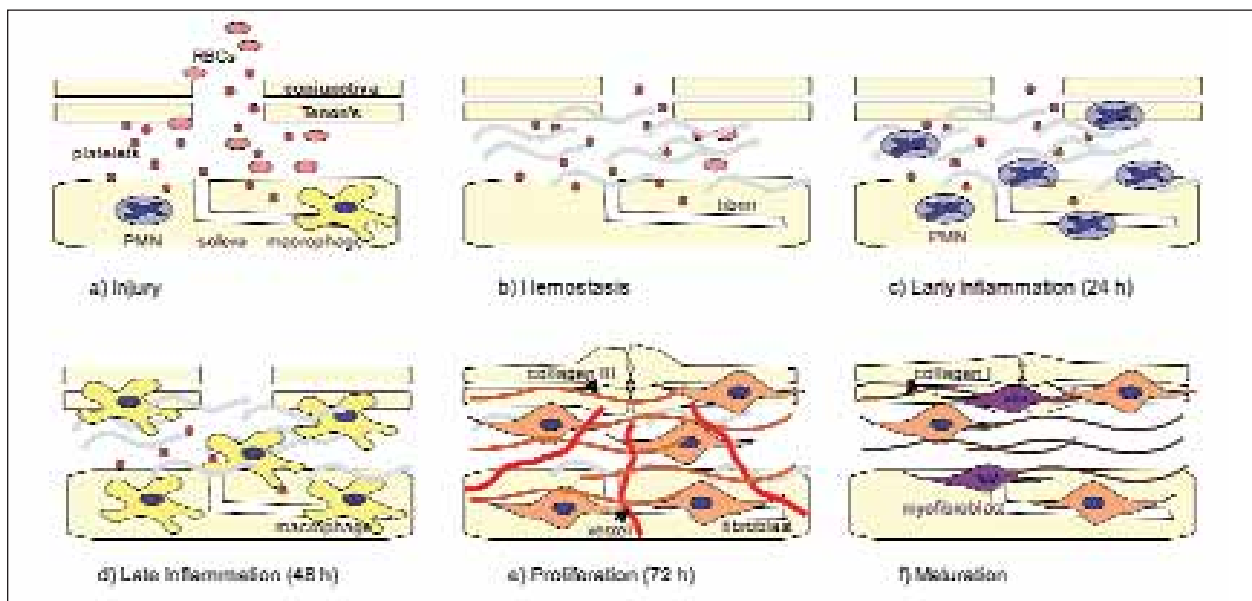


Figure 1. The phases of wound healing. No bleb is formed.

TABLE 1. THE SIGNS OF BLEB FAILURE

Approximate Time	Signs	Predisposing Factors
	• Hyperemia • Excessive vascularization • Increased IOP during first month • Small bleb • Encapsulated bleb • Ring of steel • Small, avascular, cystic bleb • Flat bleb	• Maximum eye drops • Neovascular glaucoma • Uveitis • Aphakia • Prior surgery • Iridocorneal endothelial syndromes

growth factor-2 (FGF-2), platelet-derived growth factor (PDGF), and epidermal growth factor (EGF).

Minimizing trauma using a small (2- to 3-mm) perilimbal conjunctival incision, careful sub-Tenon's dissection with a blunt instrument (eg, the Blumenthal dissector [No. K3-1124; Katena Products, Inc., Denville, NJ]), and careful cauterization help to optimize hemostasis and minimize the damage to tissue.

Proliferative Phase

The proliferative phase (Figure 1E) is dominated by angiogenesis, fibroplasia, granulation tissue formation, and contraction. After initial proliferation, fibroblasts start to deposit type 3 collagen on the third day, a process that peaks by 1 to 3 weeks. It can be blunted by the intraoperative use of mitomycin C (MMC) or 5-fluorouracil (5-FU). MMC is an alkylating agent that cross-links DNA, thus allowing it to interfere with any phase of the cell cycle and to affect DNA replication, mitosis, and protein synthesis. MMC also induces apoptosis of fibroblasts,⁹ thereby contributing to its increased potency compared with 5-FU.¹⁰ In contrast, 5-FU is an antimetabolite that specifically antagonizes pyrimidine affecting DNA assembly (S phase of the cell cycle) and, after incorporation into RNA in its ribosylphosphate form, protein synthesis (G2 phase).

Maturation Phase

The maturation phase (Figure 1F) is characterized by a more balanced production and degradation of the extracellular matrix, with increasing tensile tissue strength. Collagen production is switched to the stronger type I collagen. Hyperemia disappears as unneeded blood vessels undergo apoptosis. The long-term daily use of prednisolone eye drops may prevent the excessive deposition of collagen.

THE SIGNS OF A BLEB'S FAILURE

Blebs can fail at any time due to unsuccessfully inhibited wound healing. The most common early signs are

local conjunctival hyperemia and excessive vascularization, followed by an increase in IOP during the first month and a small, encapsulated, or flat bleb later. Surgical technique can also induce failure. For instance, older techniques that involve a limbus-based conjunctival flap often result in a suture granuloma that compresses the bleb. The construction of the scleral flap is equally important and must avoid features that make the incision self-sealing (eg, inverse curving, no dissection of the flap's sides, great length, shelved architecture).

To determine if a bleb has failed, the surgeon first must gonioscopically confirm a patent sclerectomy. Next, he or she evaluates the bleb's function and remaining potential by applying pressure 180° away while observing through the slit lamp. This test can be performed somewhat forcefully if no bleb forms with light massage. Alternatively, the Carlo E. Traverso maneuver involves pushing directly adjacent to the side of the scleral flap with a blunt object such as a scleral depressor or through the upper eyelid with a finger or cotton swab.

PREDISPOSING FACTORS TO FAILURE

Preexisting factors that make a filtering bleb more likely to fail reflect actual phases of wound healing (Table 1). Hyperemia (eg, from the chronic use of topical antiglaucoma agents) causes growth factors and chemotaxins to leak through dilated, permeable vessels and thus primes conjunctival and Tenon's fibroblasts.¹¹ Neovascular glaucoma is the result of increased angiogenic substances, some of which are also fibroblastic growth factors. Inflammation in uveitis triggers fibrosis and can markedly reduce the longevity of a bleb.¹² Aphakia is another risk factor for the bleb's failure, possibly because of preexisting scarring,¹³ the stimulation of fibroblastic proliferation due to unknown factors released by the vitreous,¹⁴ or rapid wound healing in certain patients.¹⁵ Prior violation of the superior conjunctiva (eg, trabeculectomy, canaloplasty, cataract surgery with access through the superior

TABLE 2. INTERVENTIONS FOR BLEB FAILURE

Status	Characteristics	Primary Intervention	Secondary/Novel Intervention
Surgery	Trauma, bleeding	Small limbal incision, blunt dissection, hemostasis, subconjunctival steroids	Decanted intrableb triamcinolone
Active wound healing early 	Inflammation	Prednisolone acetate drops q1h	Topical NSAIDs, subconjunctival triamcinolone, oral triple therapy (steroids, colchicine, diclofenac)
	Proliferation	Suture lysis, prednisolone acetate drops q1h, 5-FU, subconjunctival triamcinolone for 1 week, digital massage	As above and anti-TGF- β
	Maturation	5-FU needling, digital massage	
Failed bleb	Inactive scar tissue	MMC needling; dissection + internal revision in OR, MMC	Second trabeculectomy, tube shunt, cyclodestruction
Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; 5-FU, 5-fluorouracil; TGF- β , transforming growth factor beta; MMC, mitomycin C.			

limbus, vitrectomy) means that the tissue has already entered the proliferative or maturation phases in an uncontrolled fashion. Iridocorneal endothelial cells in the iridocorneal endothelial syndromes can proliferate into or over the sclerectomy site¹⁶ in addition to increasing inflammation.¹⁷

INTERVENTIONS

Primary

Early

Early inflammation and hyperemia are best treated with the aggressive hourly use of prednisolone acetate eye drops and coadministration of sub-Tenon's 5-FU 50 mg/mL adjacent to or even 180° away from the bleb after the administration of a topical anesthetic^{18,19} (Table 2). Because this is not an intraocular procedure, disinfection with beta-iodine and draping or subsequent antibiotics are not necessary. Postoperative injections of 5-FU should be increased from four during the first 3 months to weekly until improvement is seen. Both 5-FU and MMC also have considerable bactericidal properties that can be measured at concentrations 25,000 times²⁰ and 80 times^{21,22} lower, respectively, than the concentrations used to manage the bleb.

If the bleb forms only reluctantly with digital massage during the first 1 to 2 postoperative weeks, flow through the sclerectomy must be improved by laser suture lysis, ideally accompanied by a 5-FU injection, because a re-

duction in flow not observed in the OR is most likely due to wound healing. Digital ocular massage during office visits, although uncomfortable, flushes out a matrix of fibrin and blood clots from the scleral flap interface and breaks bleb adhesions early. A small bleb experiences a greater inward force than a large one, so the former is progressively more likely to fail (law of Laplace). Most patients readily learn how to perform ocular massage on their own and should use the procedure several times a day while undergoing treatment for bleb failure.

Late

Once the bleb has reached the late proliferative phase or entered the maturation phase, interventions become more invasive. For a flat or small bleb, it is worth attempting to increase flow by laser suture lysis, even several months postoperatively if MMC was used. The bleb area can be increased, and adhesions can be broken months after surgery with bleb needling using 5-FU, a more involved process if the conjunctiva is still mobile. If ring-shaped fibrosis has formed that encases the bleb (the ring of steel²³), MMC should be selected in combination with a stiffer, larger gauge or dedicated bleb needle that has a blade (eg, Lederer glaucoma revision pick [Nos. 585133 and 585135; BD, Franklin Lakes, NJ]). MMC has more endothelial toxicity that may result in corneal edema, whereas 5-FU has higher epithelial toxicity and can cause

severe punctate-to-confluent epithelial erosions during intensified treatment.

The surgeon can perform needling at the slit lamp with wide illumination and low magnification²⁴ or in a minor room with an operating microscope. Slit-lamp needling has the advantage of being less intimidating than a minor room procedure. Needling is technically an intraocular procedure and should be performed using sterile techniques including beta-iodine. Because larger studies of needling outcomes have not reported intraocular infection, perhaps partially due to the antibiotic activity of 5-FU and MMC, some surgeons feel that using fourth-generation fluoroquinolones alone is sufficient. The technique is similar to the OR procedure described later in this article, but it uses a 27-gauge needle instead of a knife. Lidocaine can be mixed in to make the procedure more comfortable.²⁴

Manipulation in a more controlled environment with rigid instruments (eg, angled paracentesis knife, bleb knife) becomes necessary if adhesions cannot be managed at the slit lamp. Trabeculectomies performed with small limbal incisions have excellent potential, because scarring is typically limited to the incision site. Even in avascular, cystic blebs with a ring of steel, however, the filtration area can often be successfully enlarged. In this procedure, a temporal MMC veil is formed directly adjacent to the bleb. The surgeon inserts a paracentesis knife and advances it toward the bleb with sweeping movements while holding it close to the sclera. He or she should attempt to break and enlarge the entire periphery of the bleb before moving the blade under the scleral flap to dissect adhesions. After making a paracentesis, the surgeon inserts a cyclodialysis spatula across the anterior chamber through the sclerectomy into the bleb to confirm patency and to break remaining scar tissue at the scleral flap. Because the existing bleb has a mature wall, persistent hypotony is uncommon despite the bleb's enlargement.

CONCLUSION

Preventing a bleb from failing starts at the time of surgery and involves both surgical techniques and perioperative medications. Postoperatively, surgeons must promptly recognize a failing bleb to maximize the likelihood of its rescue. A failing bleb requires careful evaluation to determine the predominant cause. Intensifying existing topical treatment with steroids and 5-FU injections is the first step, and manipulation at the slit lamp can actively break early scar tissue. More aggressive physical manipulation of existing blebs is very successful, but it requires rigid instruments and is reserved for the OR. □

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