In Vitro and In Vivo Flow Characteristics of Glaucoma Drainage Implants

João Antonio Prata, Jr., MD,[1,2] Andre Mérmoud, MD,[1] Laurie LaBree, MS,[1] Don S. Minckler, MD[1]

Purpose: To determine pressure-flow characteristics at physiologic flow rates in vitro and in vivo in rabbits for Ahmed, Baerveldt, Krupin disk, and OptiMed glaucoma implants. The Molteno dual-chamber implant also was evaluated in vivo only.

Methods: Five samples of each glaucoma implant were studied. Baerveldt implants were ligated partially for in vitro testing. Opening and closing pressures in air or after immersion in balanced salt solution or plasma were evaluated for the valved devices (Ahmed and Krupin). Pressures were measured in vitro and in vivo in normal rabbits at flow rates preset at between 2 and 25 μl/minute after the tubes were connected to a closed manometric system. In vivo measurements were made 24 hours after implantation. Resistance to flow was calculated using Poiseuille's equation after at least three separate flow rate readings.

Results: In air, the Ahmed and Krupin valves had opening pressures of 9.2 ± 3.4 and 7.2 ± 0.6 mmHg and closing pressures of 5.2 ± 0.9 and 3.9 ± 1 mmHg, respectively. Neither opening nor closing pressures could be determined when Ahmed and Krupin valves were immersed. In vitro, the Ahmed and OptiMed devices had higher pressures than did other devices at a 2-μl/minute flow rate of balanced salt solution. During perfusion with plasma, only the OptiMed device maintained higher pressures than with balanced salt. With all devices, pressures fell rapidly to zero after flow was stopped. The OptiMed device demonstrated the highest resistance values. In vivo, the Ahmed device provided pressures of 7.5 ± 0.8 mmHg and the OptiMed device gave pressures of 19.6 ± 5.6 mmHg at a 2-μl/minute flow rate. After 15 minutes of flow shutdown, the OptiMed implant maintained pressures of 7.1 ± 1.1 mmHg. The Baerveldt (nonligatured), Krupin, and Molteno dual-chamber implants had similar resistances and pressures in vivo. Pressures with all devices in vivo fell rapidly to zero after conjunctival wound disruption.

Conclusion: Neither the Ahmed nor Krupin devices had demonstrable opening or closing pressures when tested in vitro immersed in balanced salt solution or plasma. With all devices, pressures were higher in vivo than in vitro due to tissue-induced resistance around the explant. Both Ahmed and Krupin valves functioned as flow-restricting devices at the flow rates studied, but did not close after initial perfusion with fluid.

Ophthalmology 1995;102:894–904

Originally received: July 5, 1994.
Revision accepted: December 31, 1994.

[1] Department of Ophthalmology, University of Southern California School of Medicine and the Doheny Eye Institute, Los Angeles.

[2] Escola Paulista de Medicina, Department of Ophthalmology, São Paulo, Brazil.

Presented in part at the Association for Research in Vision and Ophthalmology Annual Meeting, Sarasota, May 1994.

Supported in part by the L. K. Whittier Foundation, South Pasadena, California; core grant EY 03040, National Institutes of Health, Bethesda, Maryland; an unrestricted grant to the Department of Ophthalmology from Research to Prevent Blindness, Inc, New York, New York; and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Brasília, Brazil.

The authors have no proprietary interest in any instrument, device, or technique described in this article.

Reprints request to Don S. Minckler, MD, Doheny Eye Institute, 1450 San Pablo St, Los Angeles, CA 90033.

Glaucoma drainage devices are used widely to control intraocular pressure (IOP) in complicated glaucomas.[1-9] Currently available devices share many characteristics generally modified from the Molteno implant, which remains the world's clinical "gold standard." [1-3] Common denominators of many available implants include a flexible silicone rubber drainage tube and an equatorial explant constructed from materials (polymethylmethacrylate, polypropylene, silicone-rubber) to which fibroblasts cannot adhere firmly.[1,10,11] Differences among currently available devices include unique flow regulators, advertised as valves. They also have large variations in explant surface area, shape, thickness, and flexibility (Table 1).[1,10,11] The pathophysiology of all of these devices is presumed to include the development of an aqueous pool bounded by a fibrous capsule (bleb) around the explant.[1-3,10,11] Over many days after implantation, the bleb capsule becomes the primary resistance to passive diffusion of aqueous into periocular intercellular spaces, capillaries, and lymphatics.[3,11]

Installation of glaucoma drainage implants has always been associated with risk of hypotony (overfiltration) and its attendant complications, including corneal damage, choroidal effusion, and choroidal hemorrhage.[1,10,12-14] Nonvalved devices such as the Molteno and Baerveldt implants generally have been installed in two stages, or temporarily or partially ligated for many days to permit the fibrous capsule to develop before full aqueous flow is begun.[15-18] The presence of valves or flow regulators in glaucoma drainage implants should permit installation in one stage and eliminate the need for temporary ligatures to prevent immediate postoperative hypotony.[19-22]

The Ahmed implant (New World Medical, Inc, Rancho Cucamonga, CA) is fitted with a protected silicone sleeve valve that is calibrated in air and advertised to provide opening pressures between 8 and 10 mmHg. The surface area (1 side of the plate) is 184 mm^2.

The Krupin Eye Disk (Hood Laboratories, Pembroke, MA) includes a slit-valve that protrudes onto the surface of the explant inside the boundary ridge. The advertised opening and closing pressures in air are 11 and 9 mmHg, respectively. The silicone plate of this device has a surface area (1 side) of 180 mm^2.

The OptiMed implant (OptiMed, Inc, Santa Barbara, CA) contains a "flow restricting" unit that provides continuous resistance to outflow. The explant portion of the device includes a $3 \times 2 \times 2$-mm polymethylmethacrylate box that contains 180 to 200 microtubules (inside diameter, 0.06 mm) through which aqueous humor escapes into the periocular space. The box base has two lateral extensions for suture fixation and a top surface area of 18 mm^2.

The dual-chamber Molteno implant (IOP, Inc, Costa Mesa, CA) includes a V-shaped ridge on the explant adjacent to the tube–plate junction that subdivides the available space inside the explant ridge into a small antechamber and larger main chamber.[23] The volume of the small antechamber is approximately 15 μl. After flow sufficient to fill the antechamber, aqueous must percolate between overlying Tenon capsule and the ridge to fill the larger main chamber of the plate. The surface area (1 side) is 134 mm^2.

The Baerveldt implant (Iovision, Irvine, CA) is nonvalved and is implanted in two stages or with a temporary ligature to close or restrict the tube lumen, as has been recent custom with standard Molteno implants.[15-18] Although previously available in 200- and 500-mm^2 versions, it is currently available only in surface areas of 250, 350, and 425 mm^2.

Postoperative hypotony continues to be a clinical problem with glaucoma implants, despite the presence of valves or flow regulators.[22-28] Possible causes of hypotony include valve or ligature failure, leakage around the tube, or a decrease in aqueous production.[22] Differences in device function in air and after immersion in fluid, or alterations of function in vivo, also may explain postoperative hypotony.[22-28]

Several innovative methods to provide temporary or partial closure of drain tubes have been reported.[15-18,24,25] All of the devices studied here use an identical silicone-rubber tube, except the OptiMed implant which has its own molded tube.

The purpose of this study is to compare pressure flow characteristics in vitro and in vivo of several currently available glaucoma drainage devices at physiologic flow rates under controlled conditions.

Materials and Methods

Several examples of each of five kinds of glaucoma drainage implants kindly were provided for this study by the respective manufacturers (Fig 1); Table 1 lists the features of these implants. The study protocol (#8416) was approved by the Institutional Animal Care and Use Committee of the University of Southern California, and all procedures were conducted in accordance with the Association for Research in Vision and Ophthalmology Resolution on the Use of Animals in Research.

Tests were done to determine (1) the opening and closing pressures of valved implants when in air or when immersed; (2) the resistance to fluid flow (balanced salt solution or plasma) afforded by the valves or flow regulators; and (3) the pressure maintained at various flow rates (2–25 μl/minute). We chose to use a flow rate of 2 μl/minute as our "standard" for comparison among and between various devices as a reasonable approximation of physiologic aqueous flow rates in human eyes.[29] Measurements were done in vitro (bench tests) and in vivo (rabbits). All measurements were made using the same micromanometric apparatus, which consisted of a pressure transducer (Model P23XL, Spectramed, Inc, Oxnard, CA) connected to a pressure monitor and recorder (Models SP1400 and SP2006, Gould, Inc, Oxnard, CA). A mercury manometer and an adjustable electronic syringe pump (Model SP200i, World Precision Instruments, Sarasota, FL) and a 250-μl glass microsyringe (Hamilton Co, Reno, NV) also were used (Fig 2). The microsyringe at the electronic syringe pump (a) was connected to a 27-gauge cannula (b) via polyethylene tubing. The cannula was inserted into the

Table 1. Glaucoma Drainage Device Characteristics

	Ahmed Valve	Baerveldt Implant	Krupin Eye Disk	OptiMed Restrictor	Molteno Dual Chamber
Plate shape	Oval	Oval	Oval	Rectangular	Circular
Plate length (mm)*	16	13	14	3	13
Plate width (mm)*	13	20	18	6	13
Plate area (mm^2)†	184	200	180	18	134
Height (mm)‡	2.0	0.84	2.2	2	2.2
Valve or flow regulating device§	Silicone elastomer sleeve valve	None	Silicone slit valve	Flow restricted by 180–200 microtubes; ID = 0.06 mm§	V-shaped ridge
Opening pressure in air (mmHg)	8–10	—	11	Starts flow above 10 mmHg	—
Closing pressure in air (mmHg)§	5–6	—	9	—	—
Plate material§	Polypropylene	Silicone	Silicone	Polymethylmethacrylate	Polypropylene
Manufacturer	New World Medical, Inc	Iovision, Inc	Hood Laboratories	OptiMed, Inc	IOP, Inc

ID = internal diameter.

* Anterior–posterior length/circumferential width on eye (mm).

† One side flat surface area (provided by manufacturer).

‡ Maximal height above scleral surface.

§ Information provided by the manufacturer.

anterior end of the implant tube. The pressure transducer (c) and the recorder were placed between the microsyringe and the cannula. The mercury manometer (e) and the fluid reservoir (f) were connected to the system by a "T" connection and stopcock (d). A stopcock also was positioned between the fluid reservoir and the stopcock (d) to permit isolation of the fluid reservoir. To preclude the entrance of air into the system, the mercury transducer was connected to a sealed vacuum bottle partially filled with fluid. A valved rubber bulb with valve connected to the lateral opening of the vacuum flask allowed presetting with increase or decrease of pressure in the system.

After the system was filled with fluid and air bubbles had been flushed, the pressure monitor and recorder were calibrated with the mercury manometer. For many measurements, a desired pressure was established in the system and the stopcock (d) closed. The infusion rate was set at the syringe pump and the pump then was started. During measurements, only the syringe pump, the pressure transducer, and the implant were active. Infusion rates as low as 0.03 μl/minute could be set on the syringe pump with a 250-μl microsyringe. The sensitivity of the pressure transducer and strip recorder permitted identification and recording of pressure alterations as low as 0.1 mmHg,

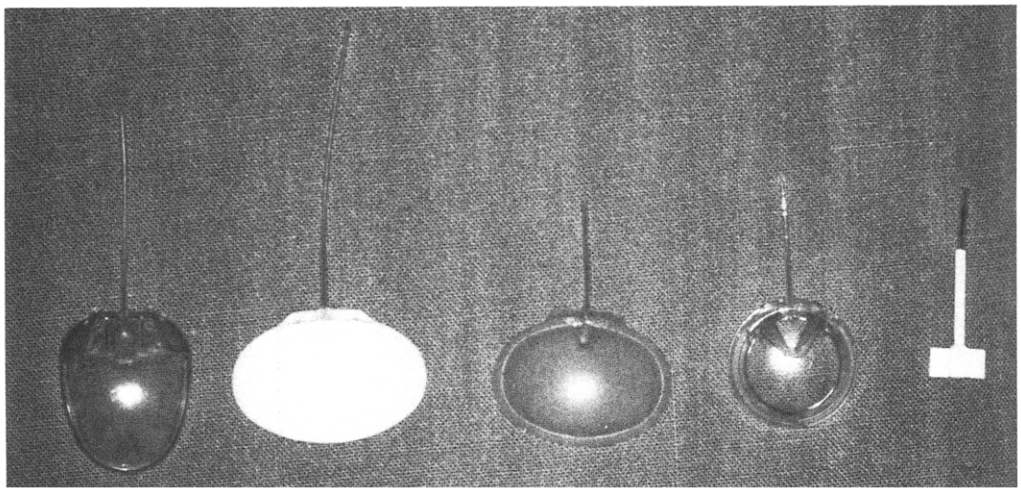


Figure 1. Glaucoma drainage devices. From left to right: Ahmed valve (New World Medical, Inc, Rancho Cucamonga, CA); 200-mm^2 Baerveldt implant (Iovision, Irvine, CA); Krupin eye disk (Hood Laboratories, Pembroke, MA); Molteno dual-chamber implant (IOP, Inc, Costa Mesa, CA); and OptiMed pressure regulator (OptiMed, Inc, Santa Barbara, CA).

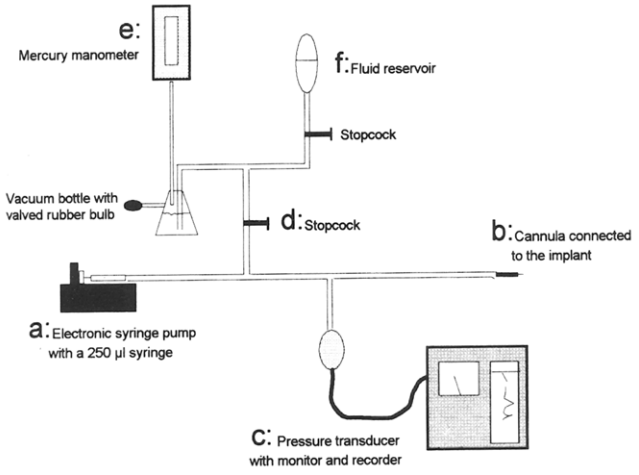


Figure 2. Closed manometric apparatus.

with flow changes as small as 0.03 µl/minute. The closed system was demonstrated to be leak proof at pressures between 0 and 100 mmHg.

Bench tests were done either with the device in air (valved implants) or while immersed in 1 cm of fluid (all devices). Balanced salt solution and fresh human plasma were used as perfusants in separate measurements. Fluorescein was added to the perfusant during attempts to measure opening pressures while immersed. Human plasma was intended to mimic protein-rich secondary aqueous humor. For in vitro experiments, the Baerveldt implants were ligated partially with a 5–0 nylon suture inside the tube lumen; an 8–0 polyglactin suture was tied around the tube before the nylon suture was removed. Implants of all types were irrigated with balanced salt solution before being tested in air or while immersed in fluid in vitro or implanted surgically, as suggested by all of the manufacturers.

For in vivo studies, the devices were sterilized with gas before implantation in normal adult New Zealand albino rabbits that weighed 2.2 to 2.7 kg. All surgeries were performed by the same surgeon, under microscopic view, and under sterile conditions. All surgical procedures and the flow–pressure measurements were performed with the animals under general anesthesia induced by an intramuscular injection of ketamine (35 mg/kg) and xylazine (5 mg/kg).

Implants were secured to the sclera 5 to 6 mm superotemporal from the limbus through a fornix-based conjunctival flap. The tubes were inserted into the anterior chamber via a 23-gauge needle track. Balanced salt solution was used to reform the anterior chamber. The conjunctiva was closed at the limbus with multiple interrupted 10–0 nylon sutures to ensure a water-tight closure. The suture line was checked for leaks by topical application of fluorescein (Seidel test). At the conclusion of surgery, all animals received a subconjunctival injection of gentamicin (0.1 ml of 50 mg/ml), 180° from the surgical site.

Flow tests in vivo were conducted using balanced salt solution 24 hours after implantation. The anterior chamber tubes had been left intentionally long in the anterior chambers. Cannulation of these drain tubes in the anterior chamber was done easily 24 hours after surgery through a large paracentral corneal incision which permitted direct grasping of the tube by forceps and insertion of the connecting cannula. The animals were examined preoperatively and postoperatively with a hand-held slit lamp. The IOP in each eye was measured at the same time of the day using the Tono-Pen 2 (Bio-Rad, Anaheim, CA). Verification of the accuracy of the Tono-Pen 2 for measuring the IOP in rabbit eyes had been accomplished at our institution in a previous, as yet unpublished study. Flow–pressure measurements were done in vivo using methodology identical to that for in vitro tests. After testing, the animals were killed with an overdose of sodium pentobarbital administered intramuscularly.

The resistance to flow (R) offered by all devices was determined using the same methodology. For three different variable flow rates (2–25 µl/minute) set at the syringe pump, the corresponding stabilized pressures were recorded. For each device, a flow–pressure line was plotted. Resistance to flow (R) was calculated using a simplified version of Poiseuille's equation applicable to noncollapsible tubes.[30,31] According to Poiseuille's equation, the flow rate of fluid through a tube (Q) = $\pi pr^4/8\ l\eta$, where p is the pressure difference between the ends of the tube; r is the tube radius; l is the tube length; and η is the viscosity of the perfusant fluid.

Simplified: Q = (P input − P output/R (viscous resistance of tube)[31] or resistance (R) = change in pressure (mmHg)/change in flow (µl/minute).

For all devices, the determination of pressures at a "standard" flow rate of 2 µl/minute was done by starting the pump with zero pressure in the system and waiting for stabilization to occur.

Statistical analyses included the Student's t test and one-way analysis of variance (ANOVA) when appropriate. When multiple comparisons were made, the significance level ($P = 0.05$) was adjusted.

Results

In Vitro Tests

In vitro tests were performed with the Ahmed, Baerveldt (partially ligated), Krupin, and OptiMed devices. No in

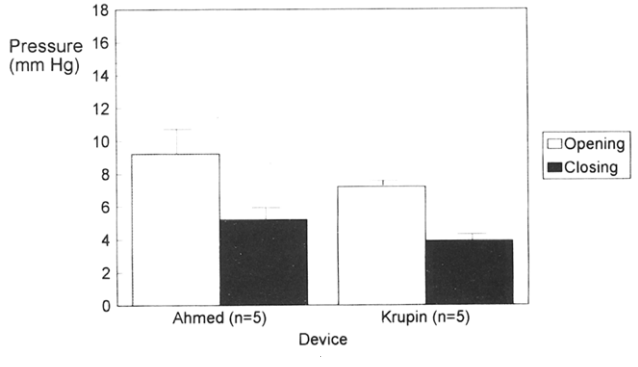


Figure 3. Opening and closing pressures in air.

Table 2. In Vitro Tests

Parameter	Ahmed (n = 5) Mean ± SD	Baerveldt* (n = 5) Mean ± SD	Krupin (n = 5) Mean ± SD	OptiMed (n = 5) Mean ± SD	P†
Resistance‡ (mmHg/μl/min)					
Balanced salt	0.32 ± 0.03	0.05 ± 0.008	0.08 ± 0.01	0.9 ± 0.4	<0.0001
Plasma	0.33 ± 0.03	0.08 ± 0.007	0.17 ± 0.05	2.1 ± 0.4	<0.0001
P§	0.3	0.007	0.02	0.02	
Pressure at a 2 μl/min flow (mmHg)					
Balanced salt	2.7 ± 0.8	0.2 ± 0.1	0.4 ± 0.2	1.8 ± 0.9	<0.0001
Plasma	2.6 ± 0.3	0.3 ± 0.08	0.6 ± 0.2	3.9 ± 0.8	<0.0001
P§	0.9	0.18	0.06	0.05	

SD = standard deviation.

* Baerveldt Implant partially ligated.

† One-way analysis of variance. Comparison among all devices.

‡ Resistance (R) = change in pressure (mmHg)/change in flow (μl/min).

§ Paired Student's *t* test. Comparison between balanced salt solution and plasma.

vitro testing was done with the Molteno dual-chamber device, because we had no reason to expect its performance to differ from that of the Baerveldt implant in bench tests.

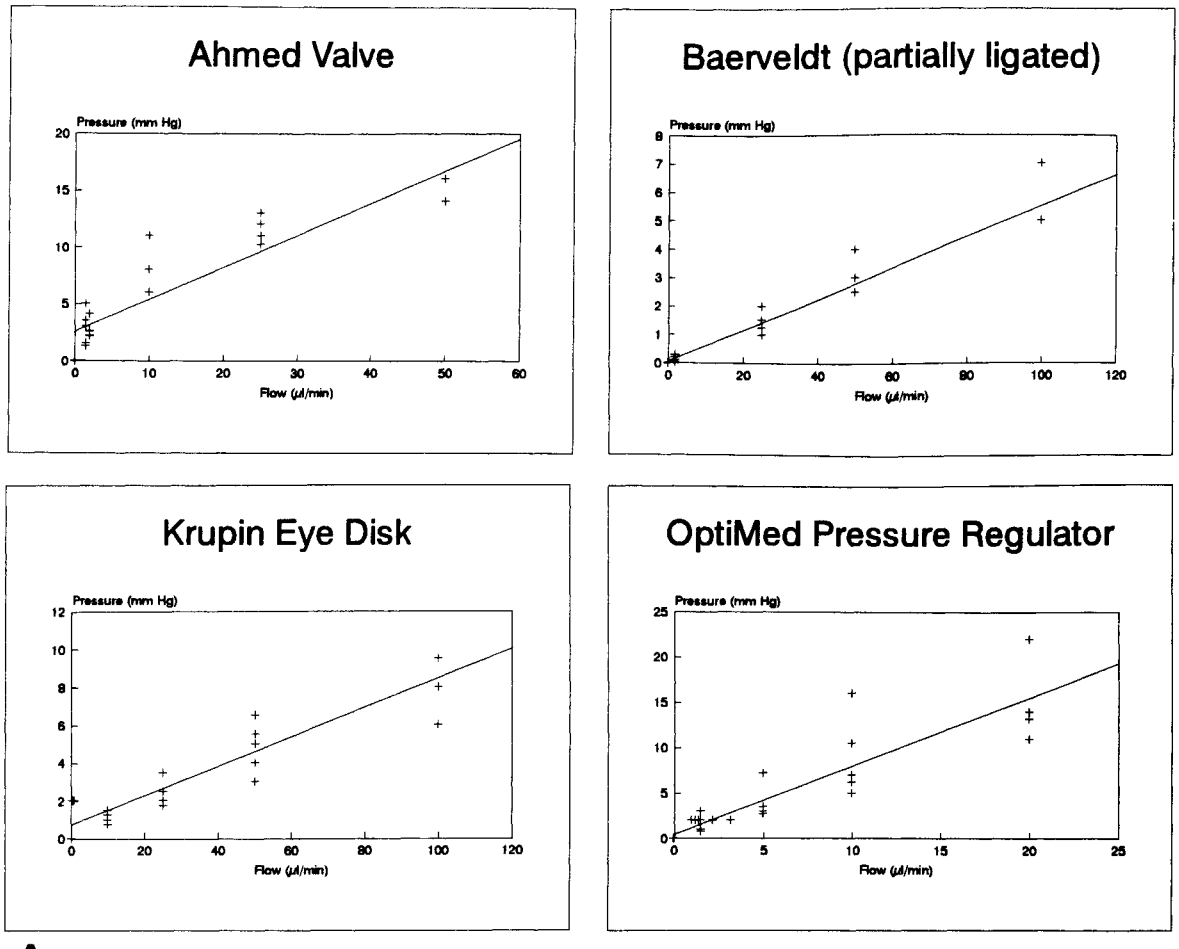
Opening and closing pressures of the valved devices (Ahmed and Krupin disk) first were determined with the valves in air. Five readings of opening and closing pressures were done for each valve. To determine opening and closing pressures in air, the pump was started at a flow rate of 2 μl/minute with zero pressure. Under microscopic view, the dry valve surface was observed until fluid was first seen to escape from the device, at which point the pressure was noted. Pressure at the first escape of fluid was considered to be the opening pressure. After opening, accumulated fluid was removed continually from the external surface of the valve using Weck-cell sponges. Closing pressures were recorded as the stabilized pressure noted when flow through the valve could no longer be detected visually after pump flow was stopped and pressure in the system was allowed to decrease. After observable flow ceased, pressure was monitored for several minutes to verify stability.

For the Ahmed and Krupin devices, opening and closing pressures were measurable only with the implant surface dry in air. Mean opening pressures of 9.2 ± 3.4 mmHg and 7.2 ± 0.6 mmHg were observed for Ahmed valves and Krupin disks, respectively (Fig 3); closing pressures were 5.2 ± 0.9 mmHg for Ahmed valves and 3.9 ± 1 mmHg for Krupin disks (Fig 3). The Student's *t* test did not show any statistically significant differences for opening or closing pressures between Ahmed valves or Krupin disks in air (*P* opening = 0.245 and *P* closing = 0.07).

To determine the effects of total immersion on valve function, the Ahmed and Krupin devices were placed under 2 cm of balanced salt solution in a dish with fluorescein added to the perfusant. The pump was started (≥2 μl/minute), and rising pressure in the system was monitored continuously until stabilized, always at low levels. Flow of perfusant, marked by fluorescein, occurred gradually and continuously through the valves while under observation with the dissecting microscope, without a clearly detectable first wave. Furthermore, no correlating alterations on the strip recorder or the pressure transducer monitor that would correspond to valve opening were ever noted. After flow was stopped, pressures with the Krupin disk fell to 0 mmHg over 10 to 15 seconds. Pressure decay to 0 mmHg with the Ahmed device was slower, taking approximately 1 minute. Reverse flow of fluid through the Krupin disk valve was noted with gentle backward aspiration by a hand-held syringe. Similar reflux could not be demonstrated with the Ahmed device.

Table 2 shows the mean values of the resistance to flow (R) observed with the four devices bench tested (Ahmed valve, Baerveldt implant, Krupin disk, and OptiMed). Figures 4 and 5 illustrate the mean pressure values and corresponding flow rates under balanced salt solution and human plasma observed with each device, respectively. These values were measured using balanced salt solution or human plasma as perfusants, with the devices under 1 cm of the same fluid. Analysis showed statistically significant differences among the groups of devices tested for the measurements made with balanced salt solution ($P < 0.0001$) and for the tests using human plasma ($P < 0.0001$). Multiple comparisons between all devices demonstrated that only the OptiMed device had statistically significant higher resistance values with both perfusants.

The mean values of pressures recorded at a 2-μl/minute flow rate using balanced salt solution and human plasma also are shown in Table 2. Analysis of variance detected statistically significant differences among devices for tests conducted with balanced salt solution ($P < 0.0001$) and human plasma ($P < 0.0001$). With balanced salt solution, the Ahmed valve and the OptiMed device had statistically significantly higher pressures than did the other implants. No differences were found between the Ahmed and OptiMed devices. With human plasma, the OptiMed de-



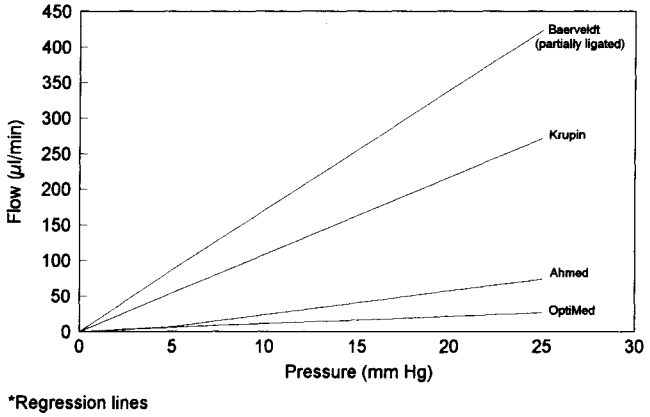
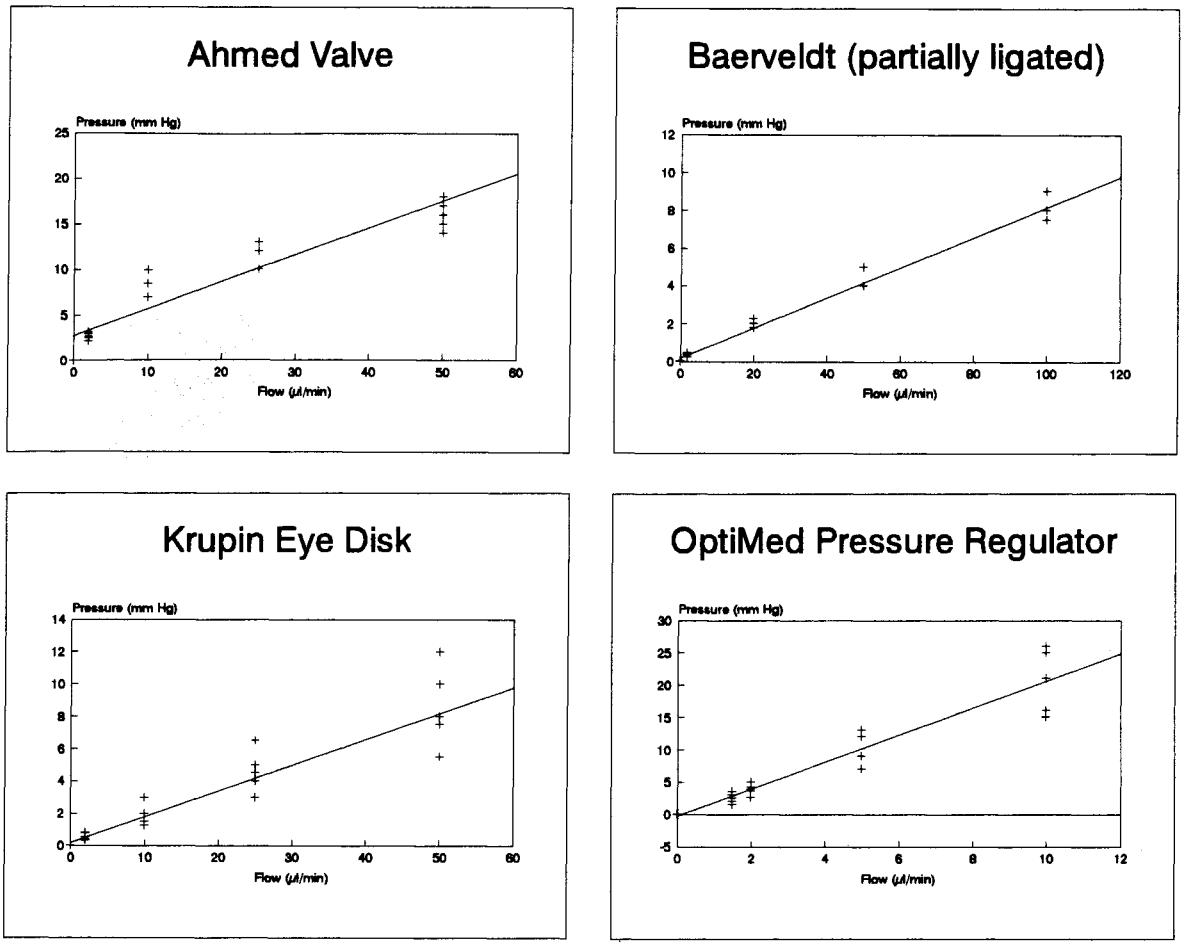
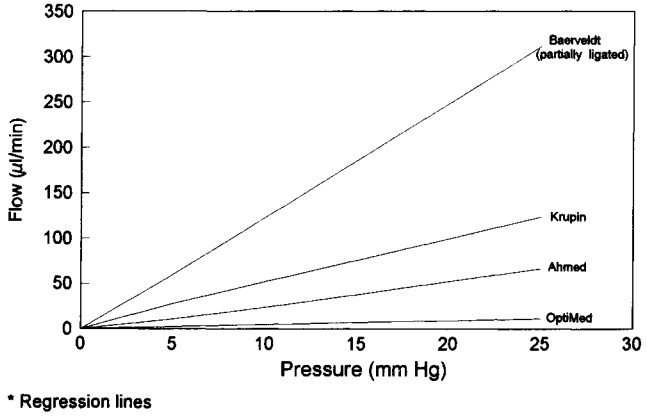


Figure 4. A, pressure versus flow in vitro (balanced salt). B, summary: pressure versus flow in vitro (balanced salt).*

vice maintained statistically significantly higher pressures than did all of the other implants tested. The differences between Ahmed valves and Krupin eye disks and Ahmed valves and Baerveldt implants also were statistically significant. No statistically significant differences were found in pressure values observed in vitro comparing partially ligated Baerveldt implants and Krupin eye disks. In vivo tests were performed with the same four devices previously bench tested (Ahmed, Baerveldt, Krupin, and OptiMed) in addition to the Molteno dual-chamber implant. Baerveldt and Molteno dual-chamber implants were tested in vivo without ligatures. Table 3 summarizes the preoperative and postoperative mean IOPs, the mean resistance to flow (R) observed, and the mean pressures detected at 2 µl/minute flow rate and at zero flow rate after at least 15 minutes of observation. Figure 6 shows the mean pressure levels observed for each device at the flow rates tested.



A



* Regression lines

B

Figure 5. **A**, pressure versus flow in vitro (plasma). **B**, summary: pressure versus flow in vitro (plasma).*

Comparison of "Rs" calculated for all groups of devices in vivo using ANOVA demonstrated statistically significant differences ($P < 0.0001$). Comparisons also indicated that the OptiMed device had statistically significantly higher values of resistance than did all other implants tested. No statistically significant differences in Rs were found in vivo between the groups of Ahmed, Baerveldt, Krupin, or Molteno dual-chamber implants.

Analysis of the pressure levels observed at a flow rate of 2 µl/minute in vivo among all devices using ANOVA also demonstrated statistically significant differences ($P < 0.0001$). Comparison between types of implants showed that the OptiMed device maintained statistically significant higher pressures than did all other devices.

Neither opening nor closing of the valved implants could be detected by our recording devices in vivo, presumably because the valves had remained open after in-

Table 3. In Vivo Tests (balanced salt solution)

	Ahmed (n = 5)	Baerveldt* (n = 5)	Krupin (n = 5)	Molteno† (n = 5)	OptiMed (n = 5)	
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*P*‡
Preoperative IOP	13.6 ± 1.1	13.2 ± 0.8	12.8 ± 1.3	12.2 ± 1.1	13.8 ± 0.8	0.16
Postoperative IOP 24 hrs (mmHg§)	12.4 ± 1.8	11.4 ± 1.1	12.6 ± 3.2	9.2 ± 1.3	11.2 ± 1.3	0.075
Resistance (mmHg/μl/min)	0.7 ± 0.1	0.2 ± 0.1	0.4 ± 0.1	0.1 ± 0.1	8.2 ± 3.1	<0.0001
Pressure at 2 μl/min (mmHg)	7.5 ± 0.8	4.6 ± 1.5	3.8 ± 1.4	3.6 ± 1.5	19.6 ± 5.6	<0.0001
Pressure zero flow (mmHg)‖	3.8 ± 1.1	3.3 ± 1.1	2.0 ± 0.9	2.6 ± 1.3	7.1 ± 1.1	<0.0001

SD = standard deviation; IOP = intraocular pressure.

* 200 mm^2 Baerveldt partially ligated.

† Dual-chamber Molteno implant.

‡ One-way analysis of variance. Comparison among all devices.

§ Intraocular pressure measured between 9:00 and 9:30 AM.

‖ Stable pressure after at least 15 minutes of flow shut-down.

stallation. After flow was stopped, pressures with all devices slowly decreased to lower levels and remained stabilized for at least 15 minutes (Table 3). The OptiMed device had statistically significant higher residual pressure levels after 15 minutes of pump shut-down than did all other implants. After conjunctival wound rupture and device exposure, pressure decreased rapidly to 0 mmHg with all devices.

Results of preoperative biomicroscopic examinations of all eyes were normal. Postoperatively, results of biomicroscopic examination performed just before the 24-hour experiments did not show shallow or flat anterior chambers in any eyes. In all animals, the tube was well positioned inside the anterior chamber, and no external wound leaks were detected. Fibrin was observed inside the anterior chambers of all surgical eyes. Comparison of preoperative IOPs using ANOVA did not demonstrate any statistically significant differences ($P = 0.16$) (Table 3). At 24 hours, IOP analysis showed only marginally significant differences among the groups ($P = 0.075$) (Table 3). Multiple comparisons between groups of devices did not show any statistically significant differences in IOP.

Comparison of R values in vitro and in vivo for each device, using ANOVA, showed that the resistance in vivo was statistically significantly higher for all devices (Ahmed, $P < 0.0001$; Baerveldt, $P = 0.0004$; Krupin, $P = 0.0003$; and OptiMed, $P < 0.0001$) (Table 4). The same analysis performed for the pressure values at the 2-μl/minute flow rate indicated that pressures also were statistically significantly higher in vivo than they had been in vitro (Ahmed, Baerveldt, Krupin, and OptiMed: $P < 0.0001$) (Table 4).

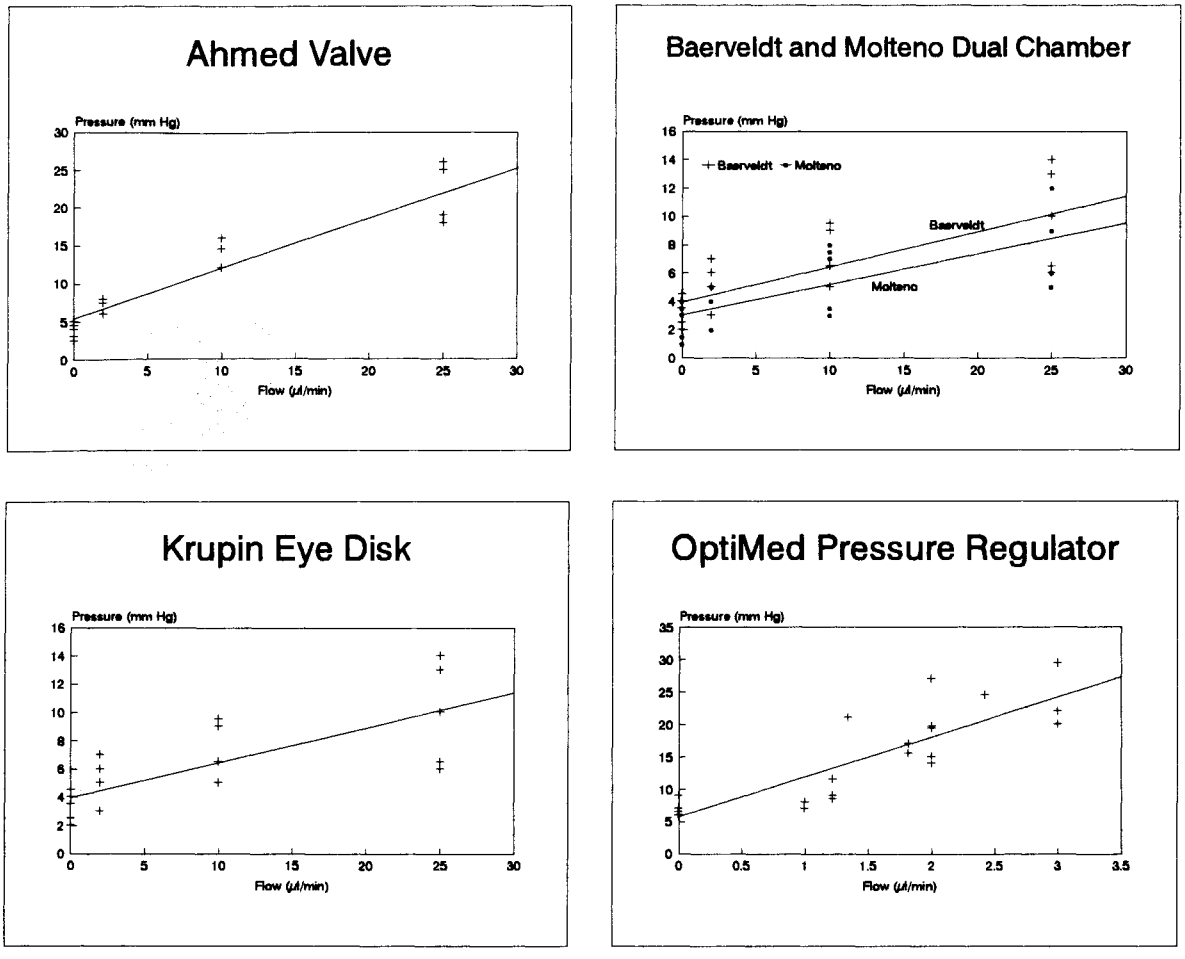
Discussion

Our in vitro bench tests indicate that valved implants behave differently when tested in air than when tested under fluid. In air, the valved devices had detectable opening and closing pressures; when immersed, opening and closing pressures could not be detected with our apparatus. Saravitz et al (unpublished data; presented at the 1992 ARVO Annual Meeting) also reported significant differences between opening and closing pressures in air and after immersion with the Krupin–Denver valve, using a gravity perfusion system with much higher flow rates than in our experiments.

In vitro, the comparisons of resistance values obtained with balanced salt solution were statistically significantly lower than those obtained with human plasma for most devices. However, when tested using flow rates of 2 μl/minute, the pressure levels maintained in vitro were relatively low with all devices with either purfusant (Table 2).

In vivo tests demonstrated higher values of R and pressures at 2-μl/minute flow rates than did in vitro tests with all devices. The highest pressures and Rs were observed with the OptiMed device and with the Ahmed valve (Table 3). However, the Ahmed valve did not provide statistically significantly more resistance in vivo than did the other devices. In vivo, all devices maintained a stable residual pressure after at least 15 minutes after syringe pump shut-down. With conjunctival wound opening, pressures fell rapidly to 0 mmHg with all devices. These observations suggest that the differences observed between in vitro and in vivo tests with specific devices were due to tissue effects around the explants. If we assume that virtually no resistance is contributed by the nonrestricted tubes in Baerveldt implants, the measured resistance R and pressure at a 2-μl/minute flow in vivo with the Baerveldt device would be due entirely to tissue influences around the explant. Considering the apparent magnitude of conjunctival tissue contributions to resistance, our results suggest that no additional resistance was added by the valve in the Krupin disk or extra ridge in the Molteno dual-chamber implants.

The measured Rs of the various devices tested in vivo 24 hours after installation bore no consistent relation to



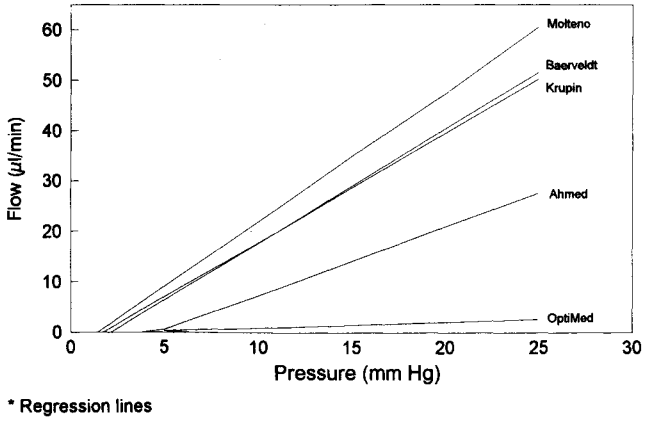


Figure 6. **A**, pressure versus flow in vivo (balanced salt). **B**, summary: pressure versus flow in vivo (balanced salt).*

their surface areas (Table 4). We can speculate that the surface area of drainage implants without flow regulators should at least transiently correlate inversely with tissue resistance after surgical installation, because the larger the explant, the larger the potential space available into which fluid can flow. In the rabbit eye, which characteristically produces large amounts of fibrin immediately after surgical manipulation, the explant plate is presumed to be rapidly covered by coagulation products, perhaps accounting for the lack of shallow or flat chambers 24 hours after installation.[32] In any case, variability of fibrin sequestration or hemorrhage around the explant may have confounded measurement of Rs 24 hours after surgery. Previous experimental and clinical studies have indicated

Table 4. In Vitro Versus In Vivo Tests

	Balanced Salt Solution (in vitro)	Plasma (in vitro)	Balanced Salt Solution (in vivo)	
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	*P**
Resistance to flow (mmHg/μl/min)				
Ahmed (n = 5) (184 mm²)	0.32 ± 0.03	0.33 ± 0.03	0.7 ± 0.1	<0.0001
Baerveldt (n = 5)† (200 mm²)	0.05 ± 0.008	0.08 ± 0.007	0.2 ± 0.1	00.0004
Krupin (n = 5) (180 mm²)	0.08 ± 0.01	0.17 ± 0.05	0.4 ± 0.1	00.0003
Molteno D (n = 5) (134 mm²)	—	—	0.1 ± 0.1	—
OptiMed (n = 5) (18 mm²)	0.9 ± 0.4	2.1 ± 0.4	8.2 ± 3.1	<0.0001
Pressure at a 2-μl/min flow (mmHg)				
Ahmed	2.7 ± 0.8	2.6 ± 0.3	7.5 ± 0.8	<0.0001
Baerveldt†	0.2 ± 0.1	0.3 ± 0.08	4.6 ± 1.5	<0.0001
Krupin	0.4 ± 0.2	0.6 ± 0.2	3.8 ± 1.4	<0.0001
Molteno D	—	—	3.6 ± 1.5	—
OptiMed	1.8 ± 0.9	3.9 ± 0.8	19.6 ± 5.6	<0.0001

SD = standard deviation.

* One-way analysis of variance. Comparison among all readings.

† Baerveldt (200 mm²) partially ligated for in vitro testing.

that with maturation of the capsule around the explant over time, there is a correlation between explant surface area and flow.[3,9] Explant surface area would at least be one plausible common denominator of differences in measured resistance between various devices in vivo at 24 hours, considering that the "valves" studied in these experiments behaved only as flow restriction devices and that there was clearly a conjunctival tissue contribution to resistance to flow.

The technique used to partially ligate the Baerveldt implants during in vitro experiments provided relatively low resistance and pressure values (Tables 2 and 4). The application of a partial ligature, as described, would be expected to provide variable occlusion of the tube, so we were surprised at the relatively small standard deviation noted (Table 2). Neither Baerveldt implants nor dual-chamber Molteno implants were ligated in vivo so as not to confuse the analysis of conjunctival tissue influence on device function.

Anecdotal and published clinical studies continue to report significant postoperative hypotony, even with valved devices.[22] In addition to possible improper function of a valve or ligature in glaucoma drainage devices, leakage of aqueous around the tube at the anterior chamber or pars plana insertion site can occur. Additionally, ciliary body function may fail or decrease after surgery in the complicated cases in which such devices are used commonly.[22]

These studies did not include a "pulse" generator in the manometric system, and all tests were conducted at room temperature. Furthermore, we did not attempt to measure "endurance" of the flow restrictor or valves over time. Previous studies of hydrocephalus shunt valves, which generally function at much higher flow rates and with much larger pressure fluctuations than expected in eyes, have noted the importance of pulsatile flow, temperature, and time-in-service for valve performance.[33,34]

Our results demonstrated that none of the implants tested maintained advertised pressure levels during in vitro tests while immersed and while being perfused at flow rates close to those expected in normal human eyes. The valves in the Ahmed and Krupin implants functioned as flow restriction devices or regulators rather than as valves that truly open and close in response to pressure change after immersion in fluid. We are skeptical that the valves in the Ahmed and Krupin devices ever close once perfused and maintained in a fluid environment. In vivo, our results indicate that the conjunctival tissue reaction surrounding the explant portion of the devices contributes substantially to the measurable resistance to flow. Because of obvious differences in the typical postoperative reaction between human and rabbit eyes, we cannot directly extrapolate this information to the use of these devices clinically in humans. Specifically, this study provides no basis for choosing "valved" over "nonvalved" glaucoma drainage devices currently available for clinical use. We encourage the development of uniform standards for the manufacture and testing of glaucoma drainage devices, and hope these experiments will stimulate continued innovation and evolution of their applications to glaucoma therapy. Prospective clinical studies are necessary to evaluate the proper clinical roles and efficacy of valved and nonvalved glaucoma drainage systems.[10,28]

References

1. Lieberman MF, Ewing RH. Drainage implant surgery for refractory glaucoma. Int Ophthalmol Clin 1990;30:198–208.
2. Melamed S, Fiore PM. Molteno implant surgery in refractory glaucoma. Surv Ophthalmol 1990;34:441–8.
3. Minckler DS, Shammas A, Wilcox M, Ogden TE. Experimental studies of aqueous filtration using the Molteno implant. Trans Am Ophthalmol Soc 1987;85:368–92.

4. Wilcox M, Minckler DS, Ogden TE. Pathophysiology of artificial aqueous drainage in primate eyes with Molteno implants. Glaucoma 1994;3:140–51.
5. Lloyd MA, Sedlak T, Heuer DK, et al. Clinical experience with the single-plate Molteno implant in complicated glaucomas. Update of a pilot study. Ophthalmology 1992;99: 679–87.
6. Omi CA, deAlmeida GV, Cohen R, et al. Modified Schocket implant for refractory glaucoma. Experience of 55 cases. Ophthalmology 1991;98:211–4.
7. Hill RA, Heuer DK, Baerveldt G, et al. Molteno implantation for glaucoma in young patients. Ophthalmology 1991;98:1042–6.
8. Munoz M, Tomey KF, Traverso C, et al. Clinical experience with the Molteno implant in advanced infantile glaucoma. J Pediatr Ophthalmol Strabismus 1991;28:68–72.
9. Minckler DS, Heuer DK, Hasty B, et al. Clinical experience with the single-plate Molteno implant in complicated glaucomas. Ophthalmology 1988;95:1181–8.
10. Heuer DK, Lloyd MA, Abrams DA, et al. Which is better? One or two? A randomized clinical trial of single-plate versus double-plate Molteno implantation for glaucomas in aphakia and pseuodphakia. Ophthalmology 1992;99:1512–19.
11. Katz LJ. Tube shunts for refractory glaucomas. In: Tasman W, Jaeger EA, eds. Duane's Clinical Ophthalmology, rev ed. Philadelphia: JB Lippincott, 1993; vol. 6, chap. 17.
12. Minckler DS. Pathophysiology of artificial drainage devices. In: Minckler DS, Van Burskirk EM, eds. Color Atlas of Ophthalmic Surgery: Glaucoma. Philadelphia: JB Lippincott, 1992; chap. 14.
13. Drake M. Complications of glaucoma filtration surgery. Int Ophthalmol Clin 1992;32(4):115–30.
14. Melamed S, Cahane M, Gutman I, Blumenthal M. Postoperative complications after Molteno implant surgery. Am J Ophthalmol 1991;111:319–22.
15. Freedman J. The use of the single stage Molteno long tube seton in treating resistant cases of glaucoma. Ophthalmic Surg 1985;16:480–3.
16. Sherwood MB, Smith MF. Prevention of early hypotony associated with Molteno implants by a new occluding stent technique. Ophthalmology 1993;100:85–90.
17. Hoare Nairne JEA, Sherwood D, Jacob JSH, Rich WJCC. Single stage insertion of the Molteno tube for glaucoma and modifications to reduce postoperative hypotony. Br J Ophthalmol 1988;72:846–51.
18. Molteno ACB, Polkinghorne PJ, Bowbyes JA. The vicryl tie technique for inserting a draining implant in the treatment of secondary glaucomas. Aust N Z J Ophthalmol 1986;14:343–54.
19. Molteno ACB, Van Biljon G, Ancker E. Two-stage insertion of glaucoma drainage implants. Trans Ophthalmol Soc N Z 1979;31:17–26.
20. Krupin T, Podos SM, Becker B. Valve implants in filtering surgery. Am J Ophthalmol 1976;81:232–5.
21. Forestier F, Salvanet-Bouccara A. An evaluation of the Krupin-Denver valve implant in glaucoma. Glaucoma 1986;8:92–9.
22. Krupin T, Ritch R, Camras CB, et al. A long Krupin-Denver valve implant attached to a 180° scleral explant for glaucoma surgery. Ophthalmology 1988;95:1174–80.
23. Fellenbaum PS, Almeida AR, Minckler DS, et al. Krupin disk implantation for complicated glaucomas. Ophthalmology 1994;101:1178–82.
24. Molteno ACB. The dual chamber single plate implant—its use in neovascular glaucoma. Aust N Z J Ophthalmol 1990;18:431–6.
25. Susanna R Jr. Modifications of the Molteno implant and implant procedure. Ophthalmic Surg 1991;22:611–13.
26. Kooner KS, Goode SM. Removable ligature during Molteno implant procedure [letter]. Am J Ophthalmol 1992;114:102–3.
27. Krupin T, Feitl ME. The long Krupin-Denver glaucoma valve implant attached to a 180° scleral explant. In: Minckler DS, Van Buskirk EM, eds. Color Atlas of Ophthalmic Surgery: Glaucoma. Philadelphia: JB Lippincott, 1992; chap. 17.
28. The Krupin Eye Valve Filtering Surgery Study Group. Krupin eye valve with disk for filtration surgery. Ophthalmology 1994;101:651–8.
29. Brubaker RF. Flow of aqueous humor in humans. [The Friedenwald Lecture]. Invest Ophthalmol Vis Sci 1991;32: 3145–66.
30. Isaacs A, ed. A Concise Dictionary of Physics, 2nd ed. New York: Oxford University Press, 1992;215.
31. Seymour RS, Hargens AR, Pedley TJ. The heart works against gravity. Am J Physiol 1993;265 (Regulatory integrative comp physiology 34):R715–20.
32. Miller MH, Joseph NH, Ennis KW, et al. An animal model of filtration surgery. Trans Ophthalmol Soc U K 1985;104: 893–7.
33. Keith HD, Watts C. Testing of cerebrospinal fluid shunt systems under dynamic flow conditions. Med Instrum 1983;17:297–302.
34. DiNovo JA, Tylka CR, March E. Testing of central nervous system shunt devices. J Clin Eng 1991;16:215–22.