The most common treatment for both congenital and acquired hydrocephalus is the placement of a CSF shunt that diverts excess CSF from the ventricles to a part of the body in which it can be readily absorbed. While effective, newly placed shunts require on average 2 to 4 revision surgeries within the first 10 years after implantation. A large percentage of these revisions occur within the 1st year after placement, and most are required within the first 2 years. Ventricular catheter (VC) obstruction is the cause of nearly one-third of shunt failures (Fig. 1), making it the most common reason for revision surgery.

Reducing shunt failure rates remains a major goal of shunt development, and improving VC performance would constitute a major step in that direction. Although several reviews have addressed the historical development of the shunt system as a whole, none to date have focused specifically on the VC. The object of this paper is to highlight the evolution of VCs in order to inform modern efforts at improving their effectiveness and reliability.

**Historical Overview of the Pre-Shunt Era**

Following Joseph Lister’s discovery of the benefits of aseptic surgery in the 1860s, methods involving cannulation of the ventricles became feasible and were attempted with varying degrees of success. The first sterile ventricular puncture and external ventricular drain (EVD) insertion was performed in 1881 by Carl Wernicke. External drainage via catheter-like devices, including horsehair, silk, and catgut wicks, became quite popular during the late 19th century. However, in response to the risks posed by open drainage, attempts were made at the beginning of the 20th century to introduce mechanisms for internal CSF diversion. Rerouting CSF from the ventricles to the subdural space was first accomplished in 1893 by the Polish-Austrian surgeon Jan Mikulicz-Radecki, who inserted a mass of glass wool in the shape of a nail into the ventricles of a child. The child not only survived the procedure, but progression of the hydrocephalus in this case was effectively stopped. In the latter part of the 1890s, gold...
tubes and bundled strands of catgut were also used for such “ventriculocaudal” shunts. In 1903, Nicholas Senn performed the first recorded surgery using a perforated rubber tube, a crude predecessor of the modern VC, for subcutaneous drainage of CSF (Fig. 2). Most of these early attempts ended badly, however, as patients developed fatal infections in addition to the already identified danger of mechanical obstruction. As early as 1899, Adolf Dehler reported failure of an implanted gold tube due to “stoppage.” These challenges were not easily addressed by the medicine of the times, and a lack of effective antibiotics made it difficult to combat infections once they were identified. Nevertheless, surgeons practicing between 1908 and 1926 pursued many variations on this type of ventricular drainage including the use of glass tubes, split-ended silver tubes sewn to the pericranium, and even strips of omentum (peritoneal tissue). In 1917 the neurological surgeon William Sharpe reported some success with the use of linen threads. Of the 41 patients in Sharpe’s clinical study, 28 survived the procedure, and 22 of these showed marked improvement. Transplanted human or calf blood vessels were also implanted in various experiments and routed to the superior sagittal sinus, the jugular vein, or the common facial veins. In this case, the valves in the veins were used to prevent backflow and direct the CSF out of the ventricles. These early decades of the 20th century also saw many other innovations in the treatment of hydrocephalus, including the first descriptions of Kocher’s point and Frazier’s point, the optimal cranial sites for catheter insertion that are still used today. Although these early attempts created the foundation for the modern VC, the mid-20th century would see the first truly successful breakthroughs in its implementation.

**Beginnings of Modern VC Development (1950–1980)**

Arne Torkildsen developed the most notable precursor to the modern internalized shunt. The Torkildsen shunt furthered the widespread use of implanted catheters during the 1940s and 1950s and, until the introduction of ventriculoatrial and ventriculoperitoneal shunts, was the most widely used means of CSF diversion. Introduced in 1939, it consisted of a rubber catheter used to cannulate the lateral ventricle and divert CSF to the cisterna magna in cases of noncommunicating hydrocephalus. Because the Torkildsen shunt used a catheter to simply bridge 2 CSF-filled cavities, one favorable outcome was a very low incidence of catheter obstruction, which would come to be a serious issue in more complex shunt systems.}

The advent of the modern, fully internalized shunt system is generally credited to the innovations of Frank Nulsen and Eugene Spitz. In their landmark 1951 paper, they described the first successful attempt to treat hydrocephalus by means of a ventriculojugular shunt. Although this paper is commonly credited with introducing the first 1-way flow-regulating device in a ventriculojugular shunt, it also describes the use of a specific 12-Fr soft rubber catheter inserted into the ventricle.

In the meantime, the search for improved biomaterials continued. Franc D. Ingraham, a pioneer in pediatric neurosurgery, published a report in 1947 on the use of polyethylene as a new synthetic plastic for use in neurosurgery, suggesting that it could be safely implanted into the tissues of the ventricular system. Until this period, rubber tubing had been the standard material used in the Torkildsen shunt and in the first Nulsen-Spitz shunt. Ingraham’s findings led to the choice of polyethylene as the material for a new generation of VCs. Polyethylene, however, ultimately proved to be an unsatisfactory shunt material due to complications at the distal end of the device, thus prompting a search for a better polymer. This search led to polydimethylsiloxane (PDMS), or silicone rubber. Originally investigated as an insulation material for electric motors and generators, PDMS was studied as a potential biomaterial throughout the 1940s due to its elasticity, thermal stability, and bio-inertness.

In 1948, the first successful replacement of a male urethra by a narrow silicone catheter was accomplished, leading to the consideration of other clinical applications for silicone catheters. In 1957, Robert Pudenz reported on the successful use of a ventriculoatrial shunt made completely of silicone rubber. The first silicone ventriculoperitoneal shunt was implanted in 1958 by Richard Ames, and 9 years later he reported promising results after per-
forming 120 additional procedures using silicone tubing. This period marked an increase in the popularity of silicons, in part due to their prominent use in the Apollo space program, and there was a significant transition to the almost exclusive use of medical-grade silicone (marketed as Silastic by the Dow-Corning Corporation) tubing in shunts, and specifically in VCs (Fig. 3).

With this successful shift in materials, engineers began to focus on how to solve the other problems inherent in shunts, particularly that of VC obstruction. In his 1969 report on the nature of VC hole occlusion, Salomon Hakim identified the main cause of obstruction as the invasion of choroid plexus via the catheter holes. Hakim, as well as other neurosurgeons, attempted to remedy this problem by modifying VC architecture. He introduced the “shepherd crook” or J-shaped catheter, the tip of which was curved, with holes on the inside of the curve so as to distance them from invasive fronds of choroid plexus. Despite some early recorded success with this design, the experience with this particular catheter was disappointing overall, as elongated filaments of choroid plexus were still able to reach the catheter tip, obstructing the orifices.

Another design was the Portnoy flanged catheter, introduced in 1971. Although seriously flawed, this design has seen relatively prolonged use in the neurosurgical community. The original design included several soft silicone rubber “umbrella” flanges positioned between the catheter holes (Fig. 4); these were intended to protect the holes from brain parenchyma during insertion and from invasion of choroid plexus in the ventricles. The flanges folded back over the holes during insertion and opened once the catheter tip was inside the ventricle. Although there was some early clinical evidence that this design reduced catheter occlusion, and therefore the need for shunt revision, this initial conclusion was later reexamined in a report that found evidence of a higher risk of proximal occlusion with long-term use of the flanged design. Moreover, the presence of the flanges was detrimental to those patients who did require revision, in that the flanges made catheter removal extremely dangerous by creating a risk of hemorrhage and permanent damage to surrounding brain tissue.

**Fig. 3.** Photograph of a Silastic shunt system with various components labeled. Reprinted with permission from Ames: J Neurosurg 27:525–529, 1967.

**Maturing of the Modern VC (1980–2005)**

Root cause investigation of VC failures during the 1980s offered new insights into the mechanisms of shunt failure, particularly occlusion, and new countermeasures to circumvent problems were devised. In 1981 Go et al. histologically examined explanted catheters and identified obstructions related to dead cells that developed within 1 month of implant and choroid plexus invasion occurring within 3–6 months. In 1982, Sekhar et al. identified adsorbed tissue types including connective, inflammatory, granulomatous, glial, and choroid plexus as sources of occlusion. Characterization of obstructions and obstructed flow through VCs was also studied via mathematical models and shunt reservoir taps, and a number of investigations of materials and methods to circumvent this problem were subsequently undertaken. A 1982 design included a floating catheter that included an air cell integrated into
the catheter. This was intended to provide some distance between the ventricle walls and the center of the ventricle in order to avoid significant choroid plexus contact and invasion. Other patented approaches similarly attempted to protect the catheter holes from occlusion (Fig. 5).

Several modifications in material were also experimentally evaluated during this period. One of the most notable investigations included the testing of what eventually developed into Codman’s Bactiseal antimicrobial catheter. In 1981, Bayston and Milner evaluated the addition of various antibiotics to silicone catheters as a means of reducing obstruction due to microorganism colonization, which was believed to develop from skin bacteria (e.g., Staphylococcus albus) proximal to catheter incision sites. This study evaluated various antibiotics introduced at 4 different process steps of silicone vulcanization. Other patents issued in the 1980s used meshlike porous materials, formed by processes such as ion beam sputter-etching, to promote a more favorable biological response. A further investigation presented by Medow also suggested that such a catheter material, which is permeable to most components of CSF but not to prokaryotic or eukaryotic cells, could help prevent catheter obstruction.

In contrast to the silicone (PDMS) catheters that were widely used during the 1980s, Wong et al., in a 1991 publication, evaluated construction of catheters from polyhydroxyethylmethacrylate (pHEMA), a semi-wettatable polymer that is essentially a gel-like material in water. pHEMA materials, which began to be studied for biocompatibility in the 1960s, reportedly hinder protein adsorption and cell binding by offering a strongly hydrophilic surface composition. Although Wong’s study showed intriguing promise for pHEMA construction, the device design used in the study consisted of a subdural shunt configuration, in which fibrous subdural catheter encapsulation developed. Consequently, the evaluation was inconclusive and the possible benefits of pHEMA as an antifouling catheter material were obscured. In 1992, Gower et al. evaluated expanded polytetrafluoroethylene (e-PTFE) as another alternative to silicone. Commonly known as Gore-Tex, this material is currently used as a long-term implant in vocal cord treatments, arterial grafts, orthopedic joint implants, and facial plastic surgery because it is associated with minimal adverse tissue reactions. However, Gower found that, although e-PTFE is successful in other applications and is safe as a cerebral implant, the porosity of the material, which is on the order of only 5 µm, unfortunately permitted tissue ingrowth and catheter obstruction.

An additional material modification included a VC coated with polyvinylpyrrolidone (PVP) for surface functionalization. Introduced in 1995 by Medtronic under the brand name BioGlide, PVP is a hydrophilic substance that can covalently bond to the surface of silicone as a hydrogel, providing a “water jacket” by virtue of water absorption and thereby creating a slippery surface. A 2004 study showed that such functionalization indeed provides some resistance to bacterial colonization. However, the BioGlide’s surface was so slippery that the catheter lumen would sometimes slip out of the connectors attaching it to the valve in the shunt system, a problem that caused it to be removed from the market in 2010.

At the turn of the millennium, new advances in VCs were introduced by commercial conglomerates, including Johnson & Johnson and Medtronic. Codman (J&J) investigated the antimicrobial-impregnated lumens previously researched by Bayston and Milner, and the resulting catheter, branded Bactiseal, was approved by the FDA in 2001. The catheter featured impregnation of 2 antimicrobials, Rifampicin and Clindamycin HCL, into the silicone matrix. A few years later in 2008, Medtronic introduced extracted silicone catheters, having unpolymerized oligomers removed for treatment in silicone-sensitive patients.

On the design front, a wide variety of proposed catheter geometries were patented during this time, although few were actually adopted for clinical use. Lin et al. published a landmark study in 2003 that demonstrated, through computational fluid dynamics and experimental validation, that the commonly used 12- to 32-hole perforation patterns in VCs make them highly prone to the type of obstructions that cause shunt failure. The study showed that only the most proximal hole sets (those furthest from the catheter tip) actually experience significant flow rates (50%–75% of the entire flow volume) during CSF drainage, while the distal holes (those nearest to the tip) have substantially lower flow rates in comparison (Fig. 6). The study suggested that a more uniform flow distribution among the catheter holes could help prevent shunt failure by decreasing the probability of occlusion of the proximal hole sets and that, in the case of a distal hole occlusion, at least some of the functionality of the catheter would be preserved. The resulting improvement was later approved by the FDA and introduced to the market in 2007 as Medtronic’s Rivulet catheter. This device uti-
lizes a configuration of 4 parallel rows comprising holes of decreasing size, with the distal hole set being the largest. The uniformity of flow distribution of this design was verified again more recently in computational simulations by Galarza et al.\textsuperscript{22,23}

### Contemporary Ventricular Catheters (2005–2015)

The last decade of shunt development has seen a renewed interest in VC design, as well as the incorporation of new materials and coatings. Today, most VCs are made of silicone polymer tubing and are available in straight configurations, which may be cut to the appropriate length intraoperatively, or angled configurations, which have a set length. Inner diameters of the tubing range between 1.0 mm and 1.6 mm and outer diameters between 2.1 mm and 3.2 mm.\textsuperscript{19} Holes are usually arranged in 3 or 4 rows, equally spaced around the catheter diameter in the 1.0–1.5 cm nearest the catheter tip, with rows arranged either in parallel or staggered configurations, generally with 4–8 holes in each row. Holes within a row may be the same size, typically measuring between 0.25 mm and 0.5 mm at the outer catheter surface, or may change along the length of the row. Many holes feature a conical shape, slightly tapering toward the inner surface. Hole number, size, shape, and spacing vary among the different manufacturers.\textsuperscript{19,22,23}

### Material Considerations

Limiting the adhesion of proteins and cells that can cause catheter obstruction or infection has been a primary focus of VC research. Surprisingly, it has been found that high CSF protein concentrations may actually inhibit bacterial adhesion by rendering the generally hydrophobic silicone more hydrophilic.\textsuperscript{8} Protein adsorption alone has not been shown to cause accumulations in large enough amounts to generate occlusion, and the thin albumin film that most often forms may actually serve to improve the biocompatibility of the catheter.\textsuperscript{8} A 2010 report showing that astrocyte adhesion was positively correlated with fluid flow through VCs\textsuperscript{19} may explain the favorable initial results of experiments evaluating the cell growth characteristics of electrospun polyurethane catheters, which are microporous in nature and would have inherently lower flow rates than most catheters.\textsuperscript{70} Another approach to reducing obstruction is to limit contact of the VC holes with brain tissues during ventricular puncture, so as to avoid the ingestion of parenchymal cells by the catheter. A peel-away sheath technique has been implemented by some neurosurgeons to protect the VC holes from brain debris during insertion. However, a randomized study, performed in 2012 by Kehler et al.\textsuperscript{41} in 177 patients with ventriculoperitoneal shunts, showed no statistically significant difference in the number of obstructions among patients in which a peel-away sheath insertion technique was used.

A focus on catheter surface properties and coatings has also led to recent advances. In 2007, a National Institutes of Health–sponsored workshop on the priorities for hydrocephalus research indicated the need for more in-depth research into the possible benefits of antibiotic-impregnated catheters.\textsuperscript{31} In vitro and preclinical studies have shown that various forms of polyethylene glycol, a nondegradable hydrophilic polymer, may reduce protein adsorption and macrophage and astrocyte attachment when used as a catheter coating.\textsuperscript{32,34} The addition of silver nanoparticles to such coated catheters also produced a notable drop in catheter-related infections.\textsuperscript{34} Another suggested improvement is diamond-like carbon coatings that are produced by plasma-assisted chemical vapor deposition.\textsuperscript{6} By acting as an effective ion diffusion barrier, such coatings can protect the patient from ions released from the catheter while at the same time protecting the catheter from the harsh biological environment. The incorporation of other surface-modifying coatings and additives, including surfaces that mimic native extracellular matrix or endothelial cell layers, incorporation of pharmaceuticals, bioactive agents, self-locating fluoro-oligomeric additives, and antithrombogenic agents, show promise for further investigation.\textsuperscript{31}

### Design Considerations

Along with material and surface improvements, inlet hole design may also be a key to improved VC functionality. It has recently been shown that macrophage and astrocyte adhesion to catheters is greater in flowing fluid conditions than in static fluid conditions, making flow rate through each of the holes an important parameter to consider.\textsuperscript{31} In addition to flow rate, the number and size of holes may also affect the rate of cell adhesion. Decreasing the number of inlet holes or the hole diameters causes fluid wall shear stress at the hole surface to increase, and increased shear stress has been linked to increases in cell adhesion (although at the other extreme, very low shear stress may increase cell adhesion as well).\textsuperscript{30} Further investigations into the influence of these factors on obstructions resulting from cell adhesion and inflammatory response are necessary, but changing hole configurations may be an inexpensive way to make meaningful advancements in VC design. The fabrication of these inlet hole configur-
tions is also of interest since the techniques currently used sometimes result in the creation of inherently rough hole surfaces. Improving these techniques and/or adding secondary manufacturing steps to smooth the hole surfaces, after hole punching processes for example, may help to reduce cell adhesion to these surfaces as well as decrease the incidence of thrombogenesis at the inlet holes.\textsuperscript{30,31}

Optimizing hole design and configurations has also been investigated as a means to reduce catheter obstruction. Along with the computational fluid simulations done by Galarza et al.\textsuperscript{22,23} on different catheter configurations, an experimental study published in 2010 by Thomale et al.\textsuperscript{24} examined VCs with substantially fewer perforations. These experimental catheters were designed with a total number of either 4 or 6 holes (as opposed to the more common 12–32 holes) located closer to the catheter tip, thereby reducing the length of the perforated catheter segment. The study was conducted in response to the hypothesis that proximal holes in the catheter may, on occasion, be positioned outside the ventricle, thereby increasing the risk of obstruction, especially in cases of slit-like ventricles. It was demonstrated clinically that catheters with fewer perforation holes, when correctly positioned within the ventricles, are sufficient to maintain shunt function and flow capacities. This finding confirms an earlier study,\textsuperscript{25} which argued that the same pressure-flow correlations may be observed in catheters bearing as few as 2 holes as well as those with the standard 32 holes. Both studies suggest that designs utilizing more than 2 holes do not necessarily correlate with improved drainage through the catheter.

Methods of response to VC obstruction have also been improved in recent years. Invasive techniques of catheter recanalization, which require surgical exposure of the catheter, have been investigated over the past 2 decades. These techniques include pulsed laser energy delivered via a flexible optical fiber,\textsuperscript{12} ultrasound waves transmitted over a fine wire,\textsuperscript{24} and percutaneous endoscopic recanalization via electrocautery.\textsuperscript{56} However, focus has more recently turned to finding noninvasive treatments. When an occlusion is suspected, a new noninvasive imaging method combining pulsed laser light and ultrasound techniques has been proposed to allow surgeons to view the occluded catheter through the skull.\textsuperscript{17} Once an occlusion has been identified, another recent study reports that transcutaneous vibration in the 50- to 60-Hz range, applied in short intervals, has been shown to maintain in vitro catheter performance and clear blocked holes. These microactuators may prove advantageous, as they can be controlled noninvasively and require no integrated circuits or power sources.\textsuperscript{37}

Some of the recently patented design improvements to VCs have shown more of this novel thinking. One design features a rounded transparent tip that allows the concurrent insertion of an endoscope through the catheter during surgery (Fig. 7 left).\textsuperscript{18} This design can provide continuous visualization for intraoperative navigation of the catheter tip while in the fluid-filled ventricle. The tip’s round shape is specifically designed to minimize contact with tissues that could potentially obstruct the view of the implant site. Another configuration features a biocompatible housing made of several components (Fig. 7 right). This housing may be fitted onto a standard catheter to specifically combat the potential for occlusions, particularly those initiated by an inflammatory response.\textsuperscript{51}

### Future Directions

Overall, shunt development could benefit from a more holistic approach to VC engineering, taking into consideration the component’s biocompatibility, surface properties, surroundings, lifespan, and mechano-fluid dynamics. Evaluating the effectiveness of antimicrobial-impregnated catheters as well as other infection prevention mechanisms should be a priority as these technologies continue to mature. Alongside material advances, design optimization through systematic fluid flow testing of catheter hole configurations, for example, may also prove beneficial and remains a largely underexplored area for improvement.

Another particular emphasis in several recent publications\textsuperscript{30,31} has been on the role of VC placement in overall shunt success, especially in patients with smaller or abnormal ventricular anatomy. Achieving optimal positioning with the VC completely surrounded by CSF remains challenging. Radiopaque indicators, typically utilizing barium sulfate or tantalum and incorporated into the VC polymer, are included in most commercially available catheters today and aid in verifying VC positioning. Still, the push for more accurate VC placement processes has certainly had an effect on surgical technology\textsuperscript{36,39,45,75} and may have future effects on VC design.

### Conclusions

Advances in the fields of biomaterials and biomedical engineering have made significant contributions to the
ability of implanted CSF shunts to allow many patients to lead relatively normal lives. Unfortunately, VC development has been disappointingly slow, and this component remains plagued by both mechanical and bio-adaptability issues. Additionally, the environment into which VCs are implanted is unique and complex, making it difficult to attain a comprehensive understanding of their in vivo functionality. Detailed imaging of operational VCs in action is not available, and in vitro experiments cannot accurately mimic what a VC would encounter over the course of its implanted lifetime. The solution to catheter obstruction continues to elude engineers and neurosurgeons alike, due to the many variables that influence obstruction rates. These include location of the catheter tip, varying CSF composition and flow characteristics among patients, and differences in catheter geometry among the many competing commercial designs available today. By gaining an improved understanding of each of these mechanisms and their interactive effects, the scientific community can optimize VC design to resist or prevent obstructions, thereby reducing emergency interventions, revision surgeries, and their associated risks to the patient.

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References


84. Zemack G, Rommer B: Seven years of clinical experience with the programmable Codman Hakim valve: a retrospective study of 583 patients. *J Neurosurg* 92:941–948, 2000

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