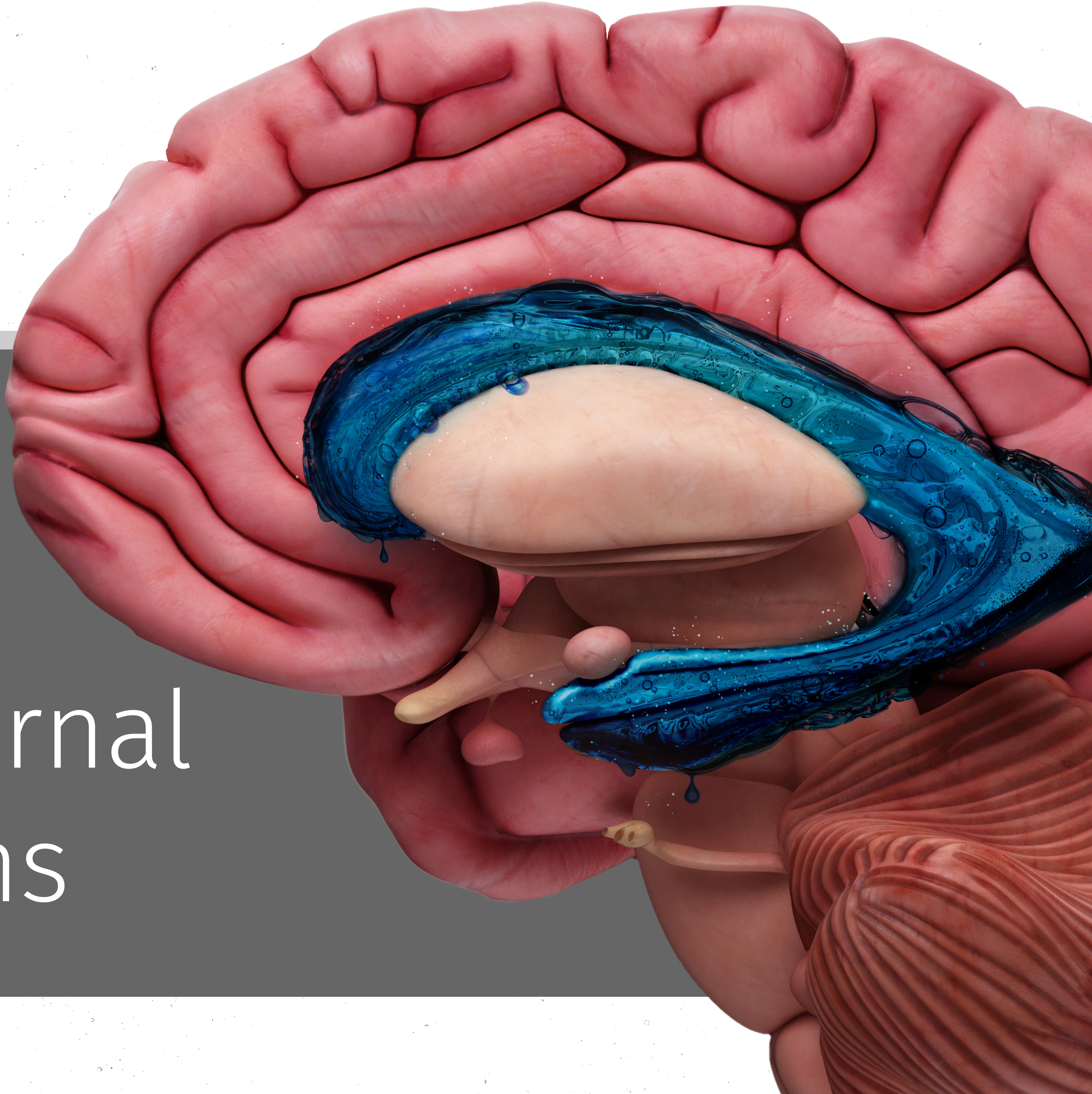
Finally, Advances in the Standard of External Ventricular Drains



Two hundred years ago, doctors discovered the lifesaving potential of inserting horsehairs in the brains of children with hydrocephalus. It took more than a hundred years of medical advancements to arrive at the ventriculostomy catheters, also known as external ventricular drains (EVD), that can successfully and safely drain excess cerebrospinal fluid (CSF) from the lateral ventricles of the brain.

IN FACT, EVD PLACEMENT IS CURRENTLY ONE OF THE MOST COMMONLY PERFORMED CRANIAL NEUROSURGICAL PROCEDURES.

Yet despite how routine the procedure is, there are real concerns over the rate of complications such as infection, malposition, hemorrhage, and occlusion associated with EVD management, despite progress in devices and procedures.

Complications and impact on patient morbidity and healthcare cost are more than just a small clinical problem. A 2016 study by Fargen et al. tracked EVD outcomes in 101 patients receiving bedside EVD in a neurosurgical ICU, where the vast majority of patients' elevated intracranial pressure (ICP) was due to subarachnoid hemorrhage (SAH). Forty-one percent of those patients developed at least one temporary obstruction, leading to an average of 2.4 irrigations per patient, and 19% developed permanent EVD catheter occlusions, requiring at least one catheter replacement.[1]

After the first EVD placement, 28% experienced a secondary intracranial hemorrhage. When catheters were replaced, intracranial hemorrhage occurred in 62% of patients. While various studies offer a range of cause-and-effect factors, each time a catheter is manipulated or replaced, risk of poor patient outcome increases as does the burden of care on hospital staff.

EVD management that addresses complications of infection, occlusion and hemorrhage may also lead to significant costs between $1,300 and $3,200 per replacement, according to a 2020 study by Aten et al. If the patient acquires an EVD-associated infection because of the replacement, the cost could spike to anywhere from $24,995 to $62,265.[2]

Centuries of Innovation

The lifesaving power of the procedure is based on fundamental fluid dynamics that have been used for more than two centuries. In 1744, French surgeon Claude-Nicolas Le Cat placed a wick into the lateral ventricle of a newborn boy with hydrocephalus, successfully decompressing his ICP but unable to save the child's life. Over a hundred years later, Carl Wernicke performed the inaugural sterile ventricular puncture and EVD in 1881.

In these early days, catgut wicks, silk, and horsehair were used as catheter-like devices typically for congenital pediatric hydrocephalus. Major advancements in the procedure include the development of a closed drainage system in 1941, the introduction of the flexible Silastic catheter in 1969 and the use of subcutaneous tunneling, introduced in 1979.

As research led to more sophisticated catheters and more ideal insertion techniques, EVDs were expanded for use in cases of excess CSF caused by SAH, intraventricular hemorrhage (IVH), intraparenchymal hemorrhage, infection, brain tumors, shunt failure, and traumatic brain injury.

Despite the development, refinement, and application of this very common procedure over the last 200-plus years, risks of infection, hemorrhage, and occlusion persist. In order to offer guidance to neurosurgeons addressing the myriad of risks, the Neurocritical Care Society (NCS) published an evidence-based Consensus Statement regarding best practices for EVD management in 2016.[3]

TIMELINE

MAJOR ADVANCEMENTS IN EVD

BASED ON J NEUROSURG ARTICLE, THE HISTORY OF EXTERNAL VENTRICULAR DRAINAGE.

- **1744** Le Cat placed horsehair into the lateral ventricle of a newborn boy with hydrocephalus
- **1881** Wernicke performed the inaugural sterile ventricular puncture and EVD
- **1941** Ingraham and Campbell standardized closed drainage system
- **1969** Silastic catheters developed
- **1972** Antibiotic prophylaxis used
- **1980** Tunneling standardized
- **1991** Findlay uses tPA in EVD to dissolve clots
- **2002** Antibiotic-impregnated catheters developed
- **2017** CerebroFlo with Endexo technology introduced
- **2019** Dual-lumen catheters engineered to both aspirate and irrigate

Risk of Infection

Complications of EVD placement include skin and soft tissue infections, ventriculitis, meningitis, subdural empyemas, osteomyelitis, sepsis, endocarditis, and both intracranial and intra-abdominal abscesses.[4]

Thanks to sterile techniques, intravenous antibiotics, and antimicrobial catheters, infection control has come a long way since 18th-century doctors placed horsehairs directly into patients' ventricles and let the CSF flow out onto the bedding. Even still, reported infection rates can be as high as 32% even with modern-day medicine,[5] though more typically, infection rates fall at 10% or less, according to NCS. In its Consensus Statement, the NCS lists possible risk factors for catheter-associated infection as systemic infection, depressed skull fracture, lack of tunneling of EVD catheter, site leak, catheter irrigation, frequency of CSF sampling and duration of EVD placement.

Antimicrobial EVD catheters reduce the potential for gram positive bacterial colonization on the tubing surface. An ionized silver particle coated EVD catheter such as VentriGuard incorporates minimal amounts of antimicrobial silver in a non-metallic porous molecular structure. Likewise, an antimicrobial impregnated catheter like Bactiseal® resists colonization of organisms on the device for up to 28 days through the slow release of two antibiotics. A 2015 study by Cui et al. of 4,399 patients found that use of such antimicrobial EVDs resulted in a risk reduction of 62% for catheter-related infections.[6]

Occlusion Risks

While standard of care has been able to greatly diminish the risk of infection, the risk of EVD catheter occlusion remains more pronounced. As Fargen et al. found, the risk of occlusion is upwards of 20%, leading to irrigation and replacement, which can result in higher incidences of infection and secondary hemorrhage.

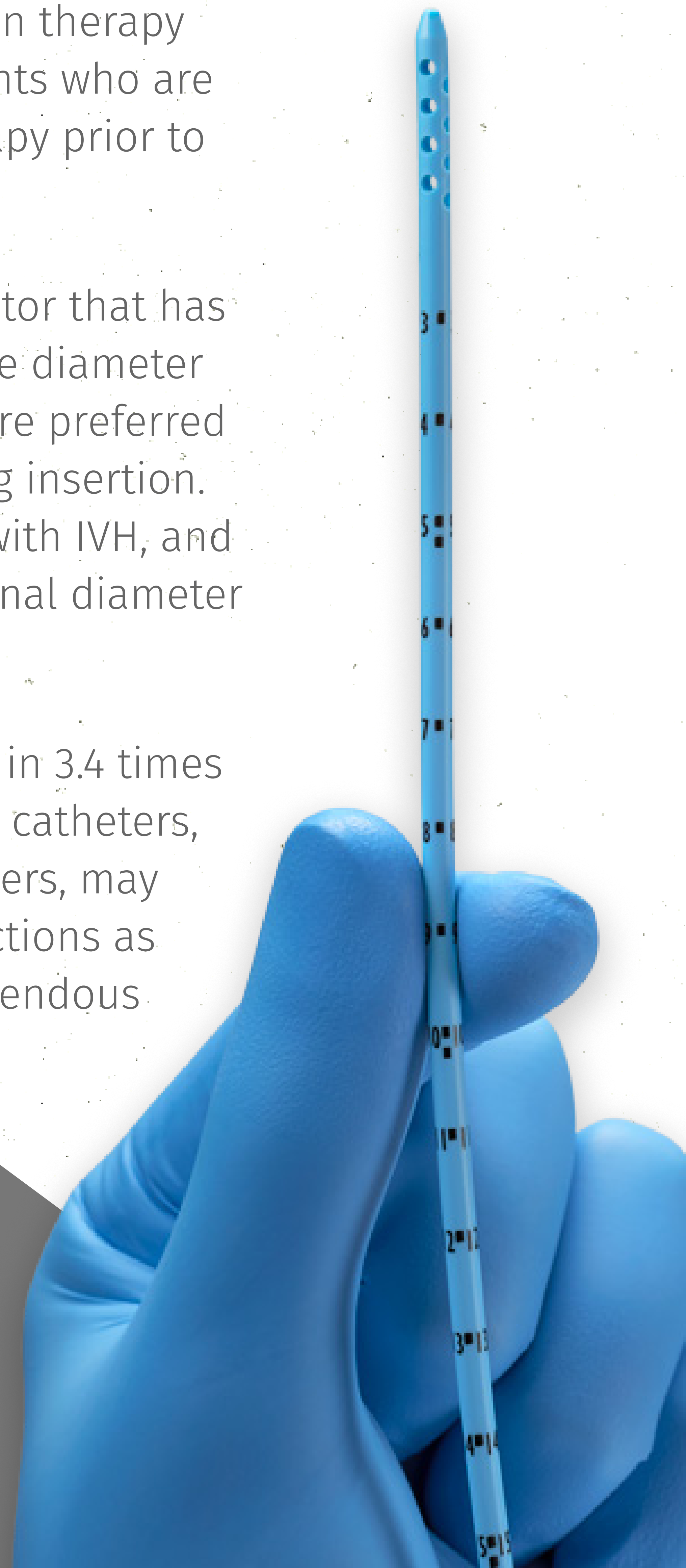
EVD catheters can occlude due to cellular debris such as blood clots and tissue fragments. Patients with bloody CSF at the time of procedure have a known risk for developing catheter obstructions as the catheter surface can become coated with plasma and CSF proteins, promoting platelet adhesion and activation. One study found that 25% of patients with SAH develop secondary IVH, as did 30% to 45% of patients with ICH.[7]

Even if bloody CSF is not present at the time of catheterization, all patients receiving EVD may experience new hemorrhages due to the invasive nature of the procedure and risk blood accumulation in their catheters. Multiple studies have investigated hemorrhage related to EVD placement, with rates varying from 0% to 42%. A 2017 study of 482 EVDs placed in 380 patients by Miller and Tummala found that hemorrhage also occurred in 22.5% of patients after EVD removal.[8]

Furthermore, patients receiving therapeutic anticoagulation therapy are 6.7 times more likely to develop occlusions than patients who are not anticoagulated.[9] Such patients are given reversal therapy prior to EVD placement to minimize such risk.

In addition to the presence of bloody CSF, another EVD factor that has been associated with a higher incidence of occlusion is the diameter of the catheter. In the past, smaller diameter catheters were preferred in order to lessen the chance of parenchymal injury during insertion. Yet, Gilard et al. measured catheter occlusion in patients with IVH, and found a permanent obstruction rate of 54% for small internal diameter catheters (1.5-mm) and 25% in large catheters.[10]

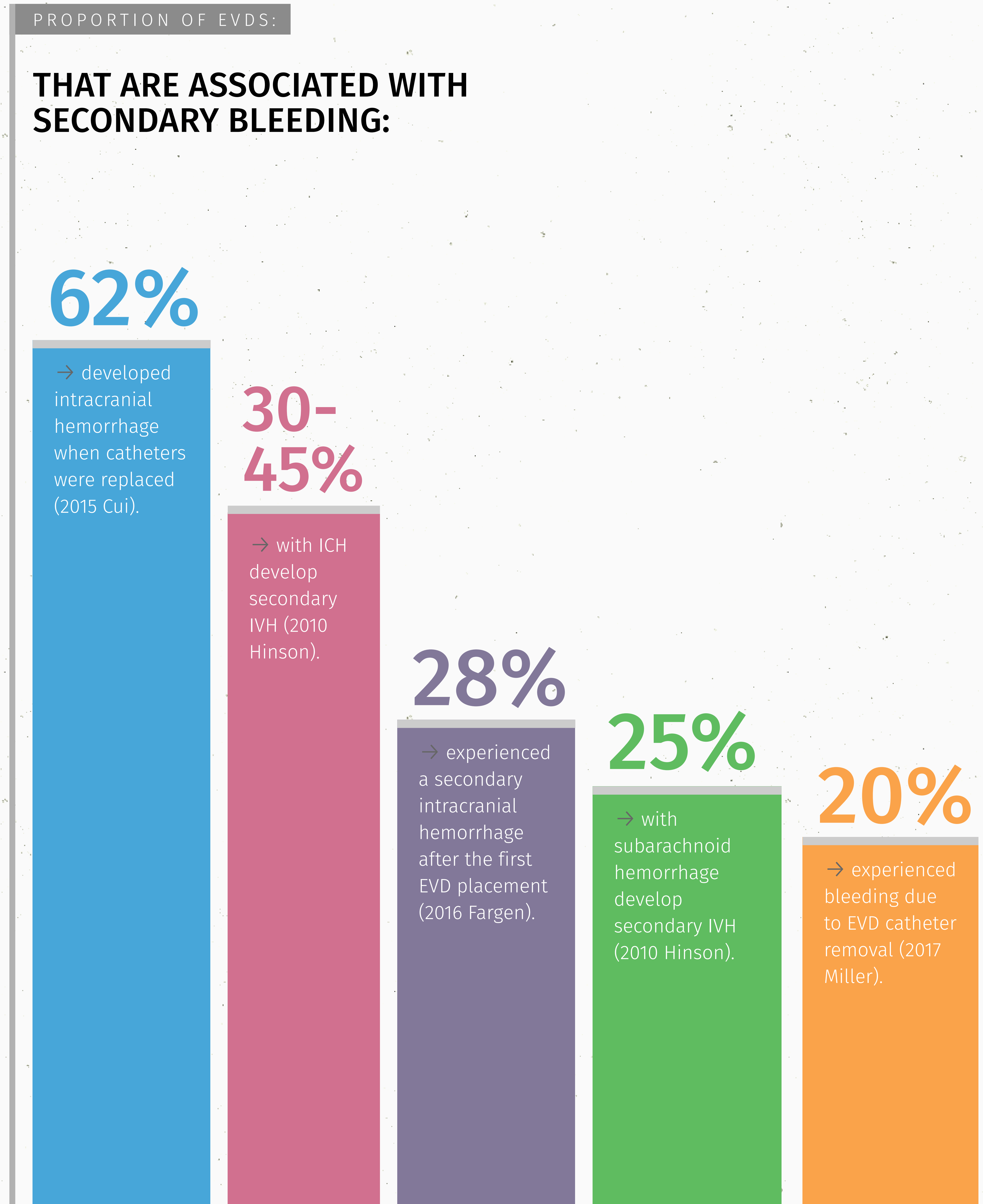
Similarly, Fargen et al. found that small catheters resulted in 3.4 times higher incidence of occlusion than larger ones. "The small catheters, with only 79% of the internal diameter of the larger catheters, may have greater resistance to flow and more frequent obstructions as suggested by Poiseuille's law, where the radius has a tremendous effect on the pressure of a fluid column."[11]

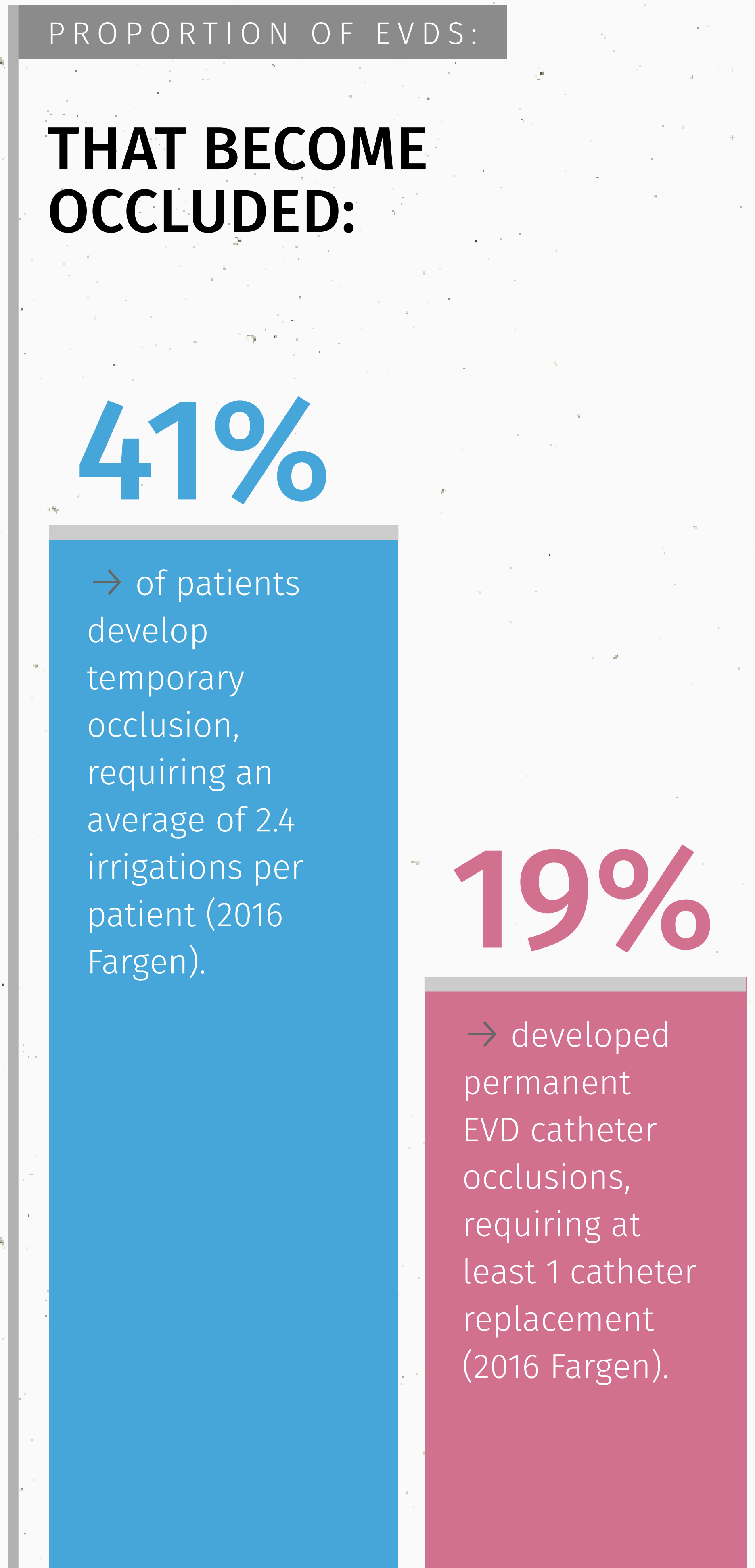


"Large catheters tend to not clot as much," says Dr. Timothy O'Connor at University of Buffalo Neurosurgery, "so if you are putting it inside a ventricle that has blood in it, I've used the large one. If you're putting it inside a ventricle that's very small, as with traumatic brain injury, then a smaller one would be a little bit better."

Other studies have found that the risk of obstruction increases if the EVD catheter tip is misplaced or migrates into the parenchyma, leading to accumulation of blood clots and cellular debris. Instead of a freehand insertion with a straightforward trajectory using anatomical landmarks, some neurosurgeons have begun using technological adjuncts such as CT guidance, stereotactic navigation, intraoperative ultrasound guidance, and electromagnetic navigation to improve EVD insertion accuracy.

Navigation or image-guided EVD insertion requires both the technology to be available bedside or in the operating room. "It also takes about 10 to 15 minutes to set up, but if you're waiting for a patient to get reversed for anticoagulation, then you can register the brain to a scan and see on the screen exactly where it is within the brain," says Dr. O'Connor. "But because the procedure is typically an emergency, placing an external ventricular drain with navigation isn't common."





The Complexities of Managing Occlusion

Despite mitigating factors such as bleeding, catheter diameter and placement, a fifth of EVD catheters could get occluded. When the catheter is clogged, within as little as 27 minutes patients' ICP could rise to levels that could lead to poor clinical outcomes.[12] The first approach is to clear the obstruction by flushing and irrigating the catheter with saline.

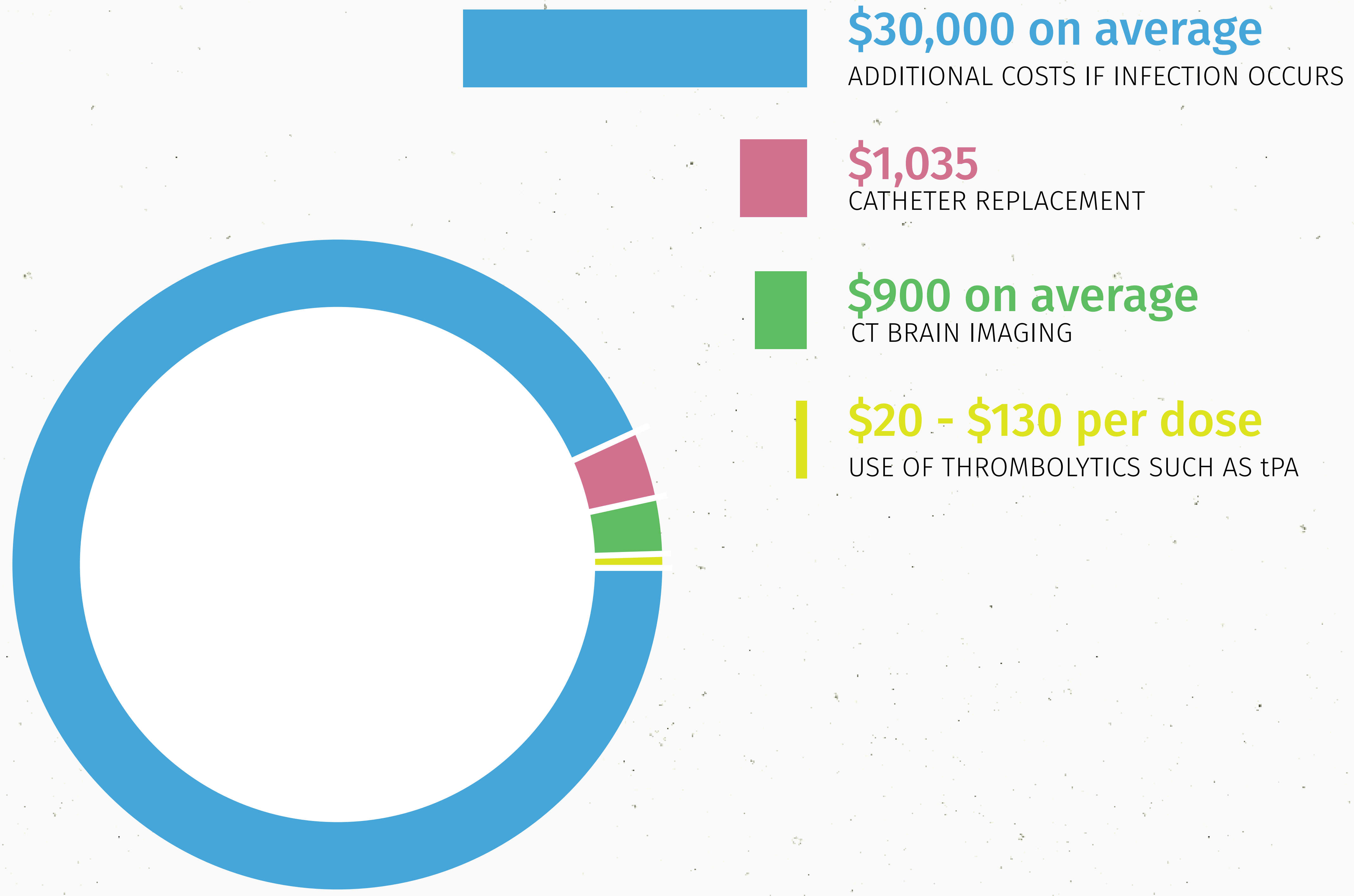
If that doesn't clear the clot, a recent approach is to use the EVD catheter to administer fibrinolytics such as tissue plasminogen activator (tPA). "We put in tPA and let it sit there for about an hour so it can break up that clot," says Dr. O'Connor. While placing tPA is not thought to increase a patient's ICP to dangerous levels, studies are ongoing to gauge its effect on secondary hemorrhage and ventriculitis.

Ultimately, if the clot can't be cleared, the catheter must be replaced, a step which carries yet more risks. Recent imaging studies have shown that EVD catheter removal can lead to bleeding in 20% of patients, and placement can result in new hemorrhage in approximately 17% to 41% of patients.[13]

Another approach is to use a dual-lumen catheter called IRRAflow®, which actively irrigates with saline as it drains CSF via a fluid exchange system and proprietary software to monitor the exchange. It's critical that catheter obstructions are cleared quickly and effectively, yet most available management options introduce new costs, complex systems and potential risks.

GRAPH

COST OF OCCLUSION BREAKDOWN



A Simple Solution

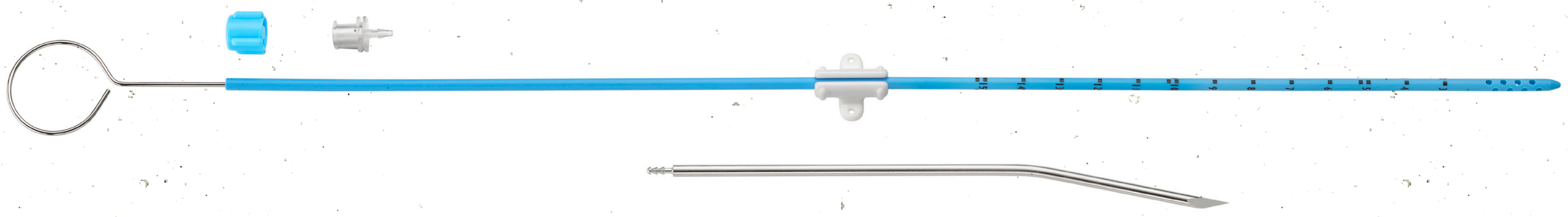
Once occlusion happens, as in the case of upwards of 19% to 40% of patients, addressing clots requires complex care that may introduce unintended new risks of secondary bleeding and infection.

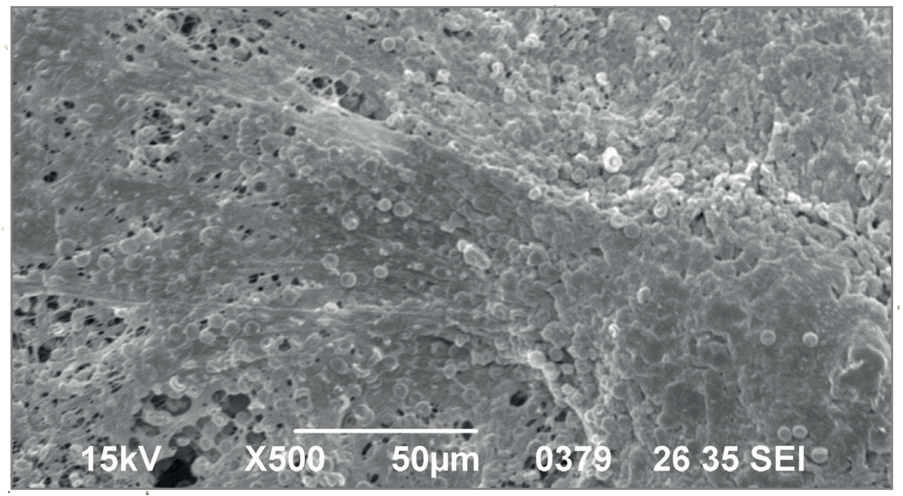
Yet, recent advances in EVD catheters include the ability to passively prevent adhesion in the first place without using a complex system of pumps or the need to place saline or fibrinolytics into a healing brain. For instance, catheters such as CerebroFlo® are designed with Endexo® technology that reduces adhesion of protein, platelets and blood cells on all catheter surfaces. Endexo, an anti-thrombogenic additive, is dispersed throughout the catheter material, creating a passive surface modification that lessens the chance of thrombus formation.

As it is non-eluting and integrated into the catheter's polyurethane formulation, the Endexo polymer remains over the catheter's EVD drainage course without depleting and without the potential for systemic anticoagulation.[14] CerebroFlo catheters also have a large diameter of 1.9mm and 16 large drainage holes to prevent physical clogging.

When compared to one equally-sized EVD catheter in two in vitro models of IVH drainage, CerebroFlo showed a significant decrease in thrombus formation by 99%, making it 8 times less likely to become obstructed than the non-Endexo catheter tested. The same Endexo technology has already been used in PICC lines and midline and dialysis catheters for years, reducing line obstructions.

"Our standard EVD catheter is Bactiseal," says Dr. Ramesh Grandhi at the University of Utah, "but I would consider placing CerebroFlo if a patient comes in with a high blood load in the ventricular system of their brain, maybe after a primary intraventricular hemorrhage, or with a patient with subarachnoid hemorrhage and significant blood spilled into the ventricle."

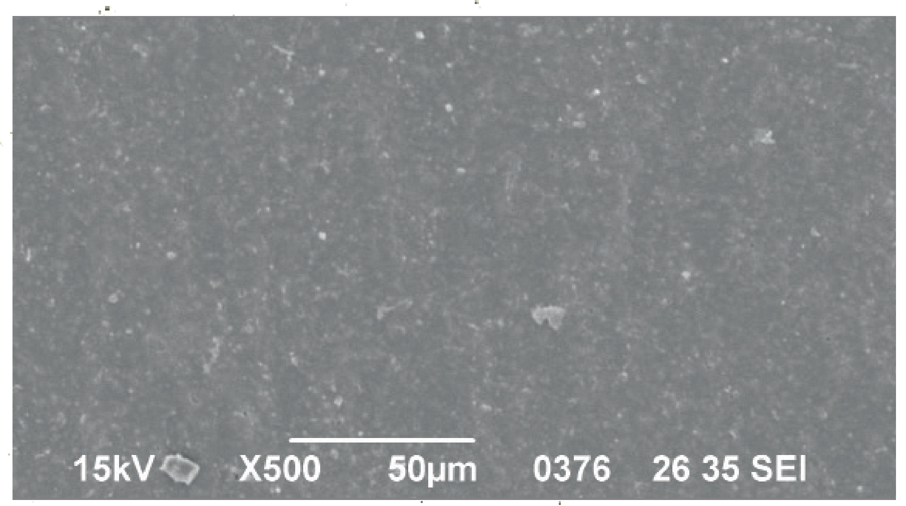




NON-ENDEXO CATHETER

SEM images at 500x magnification revealing thrombus matrix and red blood cell adhesion to catheter.

VS



CEREBROFLO® EVD CATHETER

WITH ENDEXO® TECHNOLOGY

SEM images at 500x magnification displaying a substantially clean surface.

The Way Forward

Neurosurgeons have long viewed EVD catheters as a somewhat archaic procedure of gravity-driven drainage to relieve excess CSF from the lateral ventricles of the brain in order to prevent neurological damage or death. Yet as the history of EVD shows, there have been great leaps that have drastically improved patient outcomes, expanded life-saving applications, and streamlined healthcare cost and management.

That progress had relatively stalled over recent decades, but new advents are impacting what has always been a very common but burdensome neurosurgical procedure. Insertion has been improved by image navigation, clots can be dissolved by fibrinolytics, infection risk is mitigated via antimicrobial catheters and antibiotic prophylaxis, and now there are catheters engineered to passively resist thrombus accumulation.

Just as horsehairs were replaced with sterile techniques and flexible catheters, these recent advances in EVD catheter technology have the potential to substantially improve patient outcomes while reducing management and cost burdens of this cranial neurosurgical procedure that is as common as it is challenging.

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Integra would like to thank Dr. Timothy O'Connor and Dr. Ramesh Grandhi for their insight for this article.
Disclosure: Dr. Grandhi has a general consulting agreement with Integra.

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