

Overview of Vascular Closure

The *Endovascular Today* annual review.

BY ZOLTAN G. TURI, MD

This is the 5th year that I have had the privilege of writing a review of the vascular closure world for *Endovascular Today*. During this period, the total volume of vascular closure device (VCD) use has nearly doubled, with a market value that has passed a half billion dollars. The estimates vary widely, but the market has become important enough that, for the first time, all of the major endovascular device manufacturers are now invested in VCDs, either incorporating them in their product lines, or with significant investments in devices under development. At the same time, a number of forces may be flattening the growth curve and, for the first time, at least two major devices have essentially bowed out of the market.

Two years ago, I introduced a classification system for closure devices in *Endovascular Today*, in part to allow a rational approach to examining and comparing the various types of VCDs (Figure 1). That classification system continues to be applicable in evaluating the clinical profiles as well as the market position of the devices already available and those under development. Each year, I have lamented the absence of a decent evidence base to justify the use of VCDs as an alternative to manual compression, to compare the efficacy and safety of the VCDs, and to identify the patient subsets with the best risk/benefit ratio. Unfortunately, this year brings no significant relief from this void in the invasive literature.

I will review the status of VCDs already marketed and those in various stages of clinical testing. I will introduce an area of current investigation in my laboratory: the “safe zone,” a concept designed to enhance the safety of our vascular access techniques. Vascular access remains the single most important determiner of vascular closure outcomes. I will comment on the relationship between access technique and various complications of VCDs. Finally, I will comment on a few of the more important articles in the past year’s medical literature relevant to VCDs.

THE CLOSURE DEVICE MARKET

Belts, Suspenders, Belts and Suspenders, and Neither

Although VCD use continues to grow, they are dominant only in the US, where approximately 40% of femoral artery punctures are closed with VCDs. Use in Europe is perhaps half as frequent, both because the radial/brachial approach is much more prevalent and because lack of reimbursement appears to significantly impact the decision algorithm of both hospitals and physicians. In addition, the pattern of interventional versus diagnostic use is geographically variable; in the US, VCDs are more commonly used in diagnostic catheterizations, whereas in Europe, they are primarily deployed after intervention. The percentage use of VCDs in the rest of the world appears to remain in the single digits.

To understand the distribution of VCD use by device types, reference to the VCD Classification System is helpful (Figure 1). One could consider active approximation as the “belt,” and a thrombosing agent or a sealant in the tissue track as “suspenders.” I do not believe it is a coincidence that the two companies that dominate the VCD landscape both market devices that fall in the active approximation category. Angio-Seal (St. Jude Medical, St. Paul, MN), which continues to lead the market with approximately two-thirds share, creates an “arteriotomy sandwich”: a bioabsorbable anchor inside the artery and a collagen plug on the outside, tethered tightly together with resorbable suture. Using our analogy, Angio-Seal is the only marketed device that employs a “belts and suspenders” approach. Along with a short learning curve and high success rate, Angio-Seal upsizes the tissue track and arteriotomy only modestly. Both the VIP and 8-F versions of the device now allow use of a .035-inch guidewire, providing sufficient support for deployment in some relatively fibrosed tissue tracks. St. Jude has made regular, incremental improvements on this flagship VCD, although the platform did not change in 2006. Perclose and StarClose (both from Abbott Vascular Devices, Redwood City, CA)

also provide active approximation of the arteriotomy with suture or nitinol respectively, also use .035-inch guidewires, and provide the strongest competition to Angio-Seal. The latter has enjoyed a dominant market position over Perclose for three reasons. First, Perclose (like StarClose) approximates the vessel edges but does not incorporate a thrombosing agent (collagen) in the tissue track (a “belt without suspenders”); this may account for nonrandomized data comparisons suggesting a few percent higher hemostasis success rate for Angio-Seal. Second, there is a higher postprocedure oozing incidence with Perclose, again because of lack of a hemostatic agent in the tissue track. Third, the learning curve for Perclose is somewhat longer than for Angio-Seal. Nevertheless, high-volume Perclose users generally prefer suture closure or prefer to avoid deploying a wad of collagen, although higher infection rates or vascular occlusion rates with Angio-Seal have not been shown.

The major entry into the vascular closure market in 2006 was StarClose. Available in Europe since 2004, it appears to have increased the total portion of the vascular closure market belonging to Abbott, although in my observation, some StarClose use has been at the expense of Perclose. This is the first of the clip/staple devices to become generally available. Perclose users might gravitate to StarClose because the two devices share VCD Classification: both are active approximators without a thrombosing or sealing agent (and both leave behind a permanent foreign body). The key differences between StarClose and Perclose include lack of an intraluminal foreign body in the case of the former, because the tines are designed

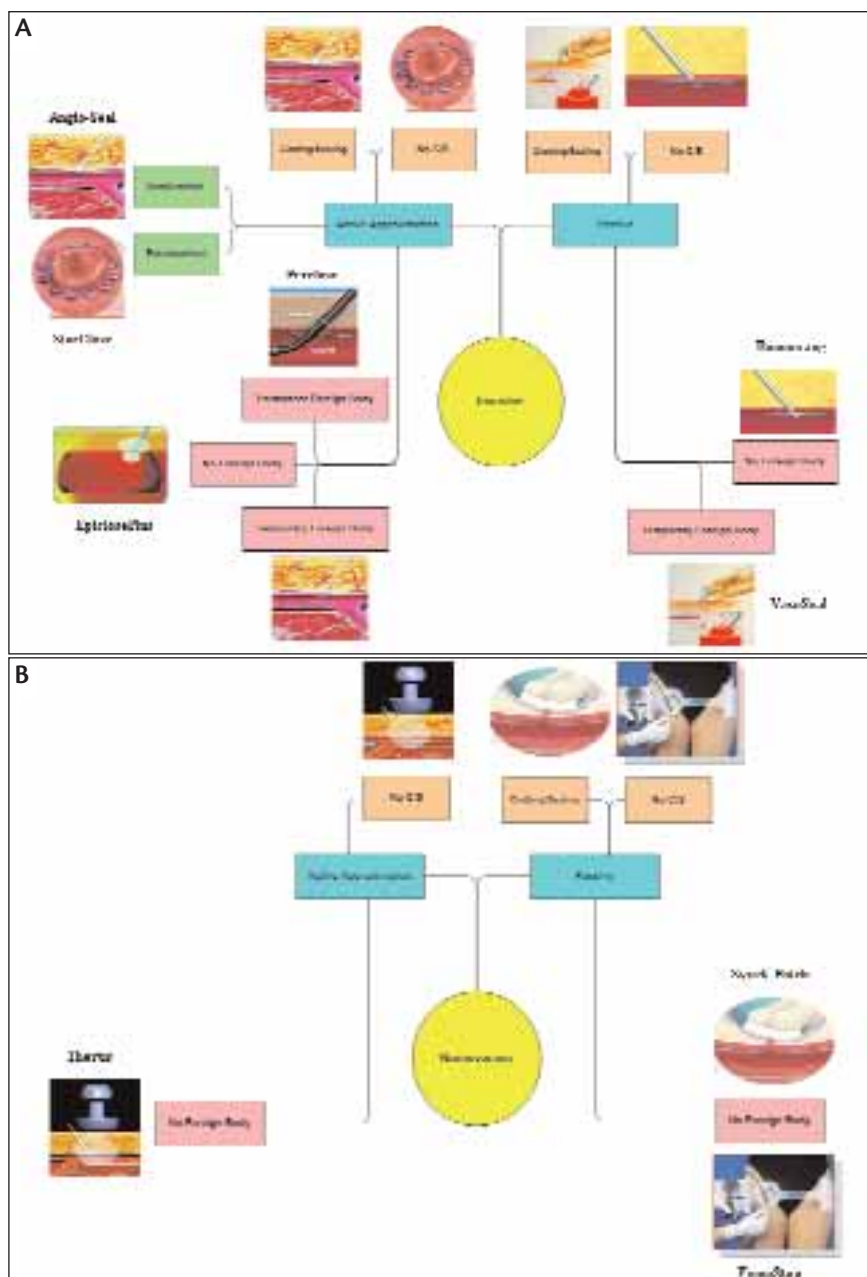


Figure 1. Classification system for invasively placed closure devices with representative FDA-approved examples of each class (EpiclosePlus [Cardiodex, Tirat-Hacarmel, Israel] is an experimental device). No C/S=no clotting or sealing agent (A). Classification system for noninvasively placed closure devices with representative FDA-approved examples of each class (Therav [Seattle, WA] is an experimental device) (B).

to deploy in the vessel wall media, and simpler and more-intuitive device deployment. These are both advantages, although the expansion of the tissue track to 12 F increases the likelihood of postprocedural oozing, in my opinion, although this has not been an issue after diagnostic catheterizations in our laboratory. At

the same time, unlike most VCDs, StarClose does not upsize the arteriotomy itself. An advantage of Perclose not replicated by StarClose is the ability to leave a guidewire (a “safety wire”) in the vessel during suturing, allowing reaccess or repeat suture deployment if the initial deployment is unsuccessful, a feature predominantly useful in interventional cases. StarClose was recently approved by the FDA for interventional cases as well.

REST IN PEACE, VASOSEAL AND THE DUETT

I feel some sentimental regret that VasoSeal (Datascope, Montvale, NJ) exited the VCD scene in 2006; they were the pioneers in this arena. Although still available by order from the manufacturer (as is the Duett from Vascular Solutions, Minneapolis, MN), active marketing of this product has ended. VasoSeal was a revolutionary product when it was introduced in 1995, and for several years it dominated the VCD world. Although failure to significantly improve the platform hurt this product and eventually resulted in a decline to single-digit percentages of overall VCD use, I believe the most important limitation of VasoSeal was the lack of active approximation. An improved collagen sponge and a better-designed delivery platform were incorporated into the OnSite device, but my experience with the latter suggested that the failure rate may have been generic to the “suspenders only” classification inherent in this approach. The fact is that both of the first four major devices that have failed, VasoSeal/OnSite and the Duett, fall into the same passive approximation category. Like many early adopters of VasoSeal, I eventually grew disenchanted with its failure rate, particularly in interventional cases. In fairness to the product, much of the VasoSeal literature is from the early to mid 1990s, an era when much larger sheaths and higher levels of anticoagulation were used, postprocedure heparin was commonly given, and operators were in their learning curve on VCD use overall. Unfortunately, the evidence continues to suggest that complication rates were higher with VasoSeal, including the most recent analysis of the ACC-NCDR database in 2005 by Tavris et al.¹

Several devices on the market account for low single-digit percentages of VCD use. In the active approximation category, SuperStitch (Sutura, Fountain Valley, CA) is a suture device available in 6-F and 8-F versions, with a 12-F model under development. The SuperStitch GW, a “preclose” version of theoretical benefit for larger arteriotomies when deployed prior to placement of the larger sheaths, has been FDA approved but not released. Potential benefits of SuperStitch include its

deployment through the original sheath, avoiding upsizing of the tissue track or arteriotomy. Like Perclose, this is an active approximator only, but unlike Perclose, it does not provide a means to place a “safety wire.” A radically different device is the Boomerang Wire (Cardiva Medical, Mountain View, CA). This device falls in the no-footprint category; it leaves behind no intravascular foreign body. Deploying a disk inside the artery, tension applied to the device provides temporary mechanical closure and theoretically allows the arteriotomy to recoil. Once hemostasis has occurred, the disk is collapsed and removed from inside the vessel. Because pulling out the wire disrupts the clot, albeit creating a relatively small 4-F hole, it requires additional compression.

Several devices are FDA approved but not generally available. These include the AngioLink (Medtronic, Santa Rosa, CA). It is a staple device that shares some features in common with the StarClose (both are percutaneous metallic arterial closure devices or PMACs), including its classification as an active approximator that does not leave an intraluminal foreign body behind. Unlike StarClose, which upsizes the tissue track but not the arteriotomy, AngioLink upsizes the hole in the artery to 10 F; a number of other VCDs upsize the arteriotomy in a similar fashion. Also, unlike StarClose, the original device developers obtained FDA approval for use in arteries with peripheral vascular disease and in locations outside the common femoral artery (CFA). The evidence base for these additional indications is, in my opinion, extremely thin, and I believe strongly that the routine use of any closure device outside the CFA or in the presence of significant peripheral vascular disease is ill-advised until a suitable series of studies are performed. This is particularly true for “high sticks,” as discussed subsequently, in which retroperitoneal bleeding and/or death may be a significant risk. X-Site, never marketed in the US, is a suture device that was part of Datascope’s family of VCDs. It is being redesigned to meet the “belts and suspenders” concept—incorporating a collagen plug for the tissue track along with a suture anchor. AccessClosure (Mountain View, CA) is awaiting FDA approval for a device (final name not yet chosen) that contains a resorbable polyethylene glycol hydrogel wafer. Delivered through the existing vascular sheath, it has a streamlined delivery system with which I have favorable animal experience. It is a passive closure device—unlike the Duett and VasoSeal/OnSite, it does not incorporate collagen but rather a sealant—with a theoretically lower risk of vascular obstruction. It is likely to be available during the coming year, indicated for diagnostic and interventional use.

The noninvasive patches are worth mentioning again. These appear to be continuing a steady growth, and occupying perhaps one-fifth of the overall vascular closure market in terms of procedures. The Syvek patch (Marine Polymer Technologies, Tewksbury, MA) has been released in an additional form incorporating a larger amount of active agent, the Syvek Excel. D-Stat (Vascular Solutions) has released several devices coated with thrombin, including one for radial artery application and one for use with compression devices, similar to a combination of the FemoStop with a topical patch of oxidized cellulose that accelerates clotting, the FemoStop HD (Radi Medical Systems, Wilmington, MA). There are now a large number of topical agents available. These do lend themselves to carefully designed, randomized, placebo-controlled trials, much more so than the invasive devices. No manuscript to date has surfaced, although I believe at least one such trial has been performed.

TECHNOLOGY IN THE WORKS

Therus once again retains the distinction of the most original and, in my opinion, revolutionary concept in vascular closure. In pilot phase clinical trials of its revamped ultrasound heating approach, a locator system akin to GPS identifies the arteriotomy site using a catheter placed inside the sheath. As described last year, several questions remain to be answered before the effectiveness of this technology is known. It falls into a distinctive category of noninvasive, active approximation, with no foreign body left behind. It is distinct from EpiclosePlus, which uses a double balloon combination to locate the arteriotomy, tamponade it, and deliver heat energy to the arterial puncture site after the intraluminal balloon is deflated. This device is also in early clinical trials. The accuracy of this targeting scheme (as well as that of the Therus device), the effectiveness of the seal provided, and patient tolerance of heat will be important determinants of the future of these approaches.

Similar in classification to VasoSeal and the AccessClosure device is the Eclipse (Ensure Medical, Sunnyvale, CA), which was recently purchased by Cordis Corporation (a Johnson & Johnson company, Miami Lakes, FL). The device is designed to be deployed on the surface of the arteriotomy through the procedural sheath and incorporates a bioabsorbable polymer plug. A pivotal trial of patients undergoing 6-F diagnostic or interventional catheterization is set to begin this year.

VASCULAR ACCESS—THE SAFE ZONE

This year, I would like to introduce the concept of the "safe zone" for vascular access and closure. A series

of studies have demonstrated that retroperitoneal hemorrhage (RPH) in interventional cases has increased over the past decade from 0.2% to 0.5% to roughly 0.9% of cases. Some of this increase appears to be related to VCD use; the literature shows RPH in interventional cases in the 0.1% to 0.2% range when manual compression was used, with up to a 10-fold increase with closure devices.² In my opinion, this was largely related to the higher ACT levels when VCDs were deployed. Femoral angiography was not routinely performed in those cases, and I suspect a significant number of the RPHs were associated with high sticks. The association with high sticks (odds ratio 5.3:1) was demonstrated by Farouque et al.³ Importantly, they could not show an association with VCD use, likely because unlike the former trial, routine femoral angiography was performed and influenced case selection for VCD deployment.

How high is a high stick? This issue was addressed in the smaller study by Sherev et al.,⁴ who used the inferior excursion of the inferior epigastric artery (IEA) to localize the bottom of the inguinal ligament. Retroperitoneal bleeding, in a study too small for statistical significance of this single parameter, occurred only in the patients in whom entry was above the inferior-most portion of the IEA. Similarly, a recent second study from the Cleveland Clinic by Ellis et al.,⁵ in which approximately 80% of patients with RPH received femoral angiograms, found an odds ratio of 17:1 for RPH when the puncture was above the inferior-most portion of the IEA. They also observed a 2.8:1 odds ratio for RPH with Angio-Seal, though it is not clear what percentage of these were high sticks. The investigators postulated a mechanism: failure of the collagen sponge to penetrate the transverse abdominis muscle when the puncture was above the inguinal ligament, resulting in a gap between the plug and the arteriotomy. Because their use of other closure devices was small, there is no way to ascertain whether this observation is generic to all VCDs. Regardless, the mortality rate associated with RPH was >10%, with approximately one-third appearing to be directly attributable to the RPH.

Low sticks into the femoral bifurcation vessels remain problematic as well. Although some interventionists comfort themselves with the notion that low sticks are not likely to cause RPH and mortality, they are associated with a substantially higher risk of vessel occlusion, pseudoaneurysm, and hematoma. The proximate causes are the smaller caliber of these vessels and the lack of bony structure against which to apply compression, as well as a higher incidence of vascular disease in the superficial femoral artery in particular and

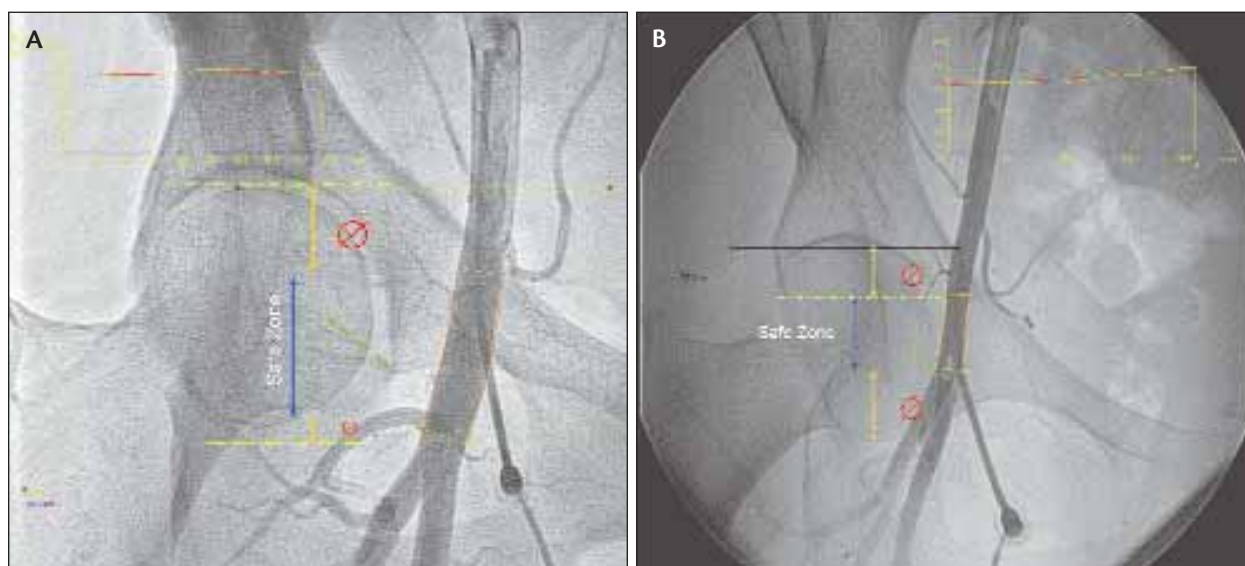


Figure 2. Type 1 safe zone: The femoral artery bifurcation is at or below the inferior border of the femoral head. With this anatomy, the safe zone extends from the bottom of the femoral head to the bottom of the IEA. Because the location of the IEA is not known before puncture, we recommend puncture at a point near the top of the bottom half of the femoral head, as indicated by the green arrow. The image is in the right anterior oblique view for clarity; the common femoral courses over the medial half of the femoral head (A). Type 2: The femoral artery bifurcation is above the inferior border of the femoral head. With this anatomy, the safe zone extends from the bifurcation to the bottom of the IEA. Again, we recommend puncture at a point near the top of the bottom half of the femoral head, as indicated by the green arrow. The safe zone is typically much narrower in type 2 anatomies. The image is in the right anterior oblique view for clarity; the common femoral artery courses over the medial half of the femoral head (B).

the dire consequences of inadvertent occlusion of the profunda femoris when it serves as the source of collaterals to an already occluded superficial femoral artery. There is also greater frequency of arteriovenous fistulae because of the course of the superficial femoral vein, and potential complications associated with VCD use at or below the level of the bifurcation. Most devices have intra-arterial locators capable of snagging on the femoral bifurcation or in the smaller confines of the bifurcation vessels with what appears from case reports to be more common occlusion of these vessels when VCDs are used.

So where is the safe zone? I suggest that the bottom of the safe zone is at the bottom of the femoral head when the bifurcation is at or below the femoral head (type 1, Figure 2A) and at the top of the bifurcation when it occurs above the bottom of the femoral head (type 2, Figure 2B). Based on our data, type-2 bifurcations occur in about 25% of femoral artery anatomies.⁶ We define the bottom of the safe zone in type-1 anatomy as the bottom of the femoral head and not the level of the bifurcation. This is because puncture into the CFA below the femoral head results in inadequate support for manual compression because the compression occurs against soft tissue rather than the anvil provided by the femoral head. This is a problem whether

manual compression alone is being used or supplemental compression is applied when VCDs are used and device failure occurs. In addition, we advocate at least gentle manual compression after VCD use regardless of successful deployment.

The ideal way to reach the safe zone with every puncture is routine use of fluoroscopy before femoral puncture to identify the bony landmarks and during the puncture as well. "During" requires penetration of the skin with the needle and advancement to a point just short of actually entering the artery, withdrawing the operator's hands for radiation safety, and fluoroscopy to make sure that the needle entry is above the bottom of the femoral head and below the center line, the femoral head "equator." The inferior sweep of the IEA rarely extends below this line. Figure 3 shows a needle placed in what we consider the ideal location the moment before it enters the arterial wall.

LITERATURE

I try to restrict this section to the major literature in the past year that has a broad impact on the field of vascular closure. Thus, although each year brings descriptive series that are the outgrowth of pilot or pivotal trials of various devices, small series of complica-



Figure 3. Fluoroscopic image after needle penetration to the surface of the femoral artery but just before entering the vessel. The location of the needle tip, just below the "equator" (dashed red line) over the lower inner quadrant gives the best chance to avoid the femoral bifurcation but remain low enough to minimize risk of retroperitoneal hemorrhage.

tion reports, or nonrandomized between device comparisons, I am mentioning only two studies that the reader may find compelling. First, Sohail et al,⁷ from the Mayo Clinic, reviewed 52 cases of VCD-related infections in the literature, including five cases from their own institution; these five occurred in a total population of 1,877 VCD deployments. Important observations, besides incidence <0.3%, were a median incubation time of 8 days and typical presentation features of pain, erythema, swelling, and drainage in decreasing order of frequency, along with fever in approximately one-third of patients. Mycotic pseudoaneurysm was the most common complication (42%); in my experience, this always needs to be ruled out. *Staphylococcus aureus* was the predominant organism. Mortality rate in the combined Mayo and medical literature experience was 6% due to sepsis and multiorgan failure. A high index of suspicion is essential if any of these symptoms are noted or if fever occurs. Aggressive efforts at diagnosis including blood cultures (positive in 86%) and femoral ultrasound are important, and adequate antibiotic therapy as well as surgical intervention when mycotic pseudoaneurysm is noted are all part of treating what is a particularly distressing complication of VCD use. Preventing the infection in the first place is a function of proper preparation of the groin, meticulous techniques to maintain sterility during the case, and avoiding deployment in cases when there is a concern regard-

ing breaking of sterility. We reprep the puncture area and use fresh gloves for device deployment. Use of prophylactic antibiotics, while common in some institutions is of unproven benefit in most settings, and is associated with a variety of infection control concerns. Besides vascular obstruction, no other complication is such a pervasive concern to most VCD users, including myself.

In another study, Applegate et al report a propensity analysis of vascular complications comparing VCDs and manual compression in more than 21,000 patients undergoing diagnostic or interventional procedures.⁸ The unadjusted incidence of vascular complications was 1.3% for VCD use and 1.4% for manual compression with a propensity score-adjusted odds ratio of 0.86 (straddling the null hypothesis) for VCD-related complications. This study contributes both size and elegance, and a single-center cohort controls for some demographic and operator variables. Ultimately, although the results are heartening, propensity analysis and logistic regression in observational studies do not substitute for prospective randomized trials. This excellent study comes as close as we are likely to see in the near future to a solid, evidence-based comparison.

Finally, I occasionally receive e-mail from the readers of *Endovascular Today* about unique experiences, good and bad, with VCDs. I would be grateful for any observations that readers wish to share that may enhance the effectiveness, or more importantly, the safety of VCD use. ■

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