



Following hysterectomy, persistent oozing along the anterior vaginal margin, distal to the cuff and adjacent to the site of bladder mobilization, may be managed with the aid of a topical hemostatic agent—in this case, a fibrin sealant.



# Your surgical toolbox should include topical hemostatic agents—here is why

➡ When bleeding persists despite your best efforts, a selection of matrices, sealants, and other agents can extend your options for achieving hemostasis during surgery

Lisa A. dos Santos, MD, and Andrew W. Menzin, MD

Vessel-sealing devices and hemostatic adjuvants are expanding the surgical armamentarium. These products provide a spectrum of alternatives that can serve you and your surgical patient well when traditional techniques for obtaining hemostasis fail to provide a satisfactory result. (Keep in mind, however, that technology is no substitute for excellent technique!)

In this article, we highlight three common scenarios in which topical hemostatic agents may be useful during gynecologic surgery. In addition, in the sidebar on page 38, five surgeons describe the hemostatic products they rely on most often—and tell why.



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*Dr. dos Santos reports no financial relationships relevant to this article. Dr. Menzin reports that he is a consultant to Ethicon Biosurgery.*

## When the site of bleeding is difficult to reach

### CASE 1 Oozing at the site of bladder mobilization

You perform total hysterectomy in a 44-year-old woman who has uterine fibroids. After the procedure, you notice persistent oozing along the anterior vaginal margin, distal to the cuff and adjacent to where the bladder was mobilized.

How do you manage the oozing?

Wide mobilization of the bladder is a vital step in the safe performance of hysterectomy. Adhesions may complicate the process if the patient has had previous abdominal surgery, infection, or inflammation. Following mobilization of the bladder and removal of the uterus, bleeding may be visible along the adventitia of the posterior bladder wall or along the anterior surface of the vagina, distal to the cuff, as it is in this case (see the illustration on page 34).

Judicious application of an energy source is an option, but thermal injury to the bladder is a concern. A good alternative is proper placement of a hemostatic suture, but it can sometimes be difficult to avoid incorporating the bladder or injuring or obstructing the nearby ureter.

In this case, the location of the bleeding deep in the operative field poses a challenge, because of limited exposure and the

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proximity of the bladder and ureters. Virtually any hemostatic agent would work well in this circumstance (TABLE, page 40). For example, a flowable agent or fibrin sealant could be thoroughly applied to the area during a minimally invasive or open procedure and would naturally conform to the irregularities in the tissue, particularly the junction between the vagina and bladder flap.

A pliable product such as Surgicel Nu-Knit or Fibrillar would also work well in these circumstances, although successful application during laparoscopy may depend on the size of the trocar. For example, Nu-Knit would require trimming to a size suitable for passage through a trocar, made easier by moistening with saline. The weave of Fibrillar makes it more challenging to pass, intact, through a trocar; rolling the material into a cylindrical shape may reduce its diameter and allow it to pass more easily.

**CASE 1 Resolved**

You apply a fibrin sealant to the site of bleeding, and the oozing abates. Once complete hemostasis is ensured, you conclude the surgery and transfer the patient to recovery, where she does well.

**Controlling bleeding without injuring underlying tissue**

**CASE 2 After adhesiolysis, bleeding at multiple sites**

You perform adnexectomy on a 47-year-old woman who has a large (7 to 8 cm), benign ovarian mass. As you operate, you discover that the lesion is adherent to the sigmoid mesentery and the posterior aspect of the uterus; it is also adherent to the pelvic sidewall, directly along the course of the ureter. Although you are able to release the various adhesive attachments, persistent bleeding is noted at multiple pinpoint areas along the mesentery, uterine serosa, and pelvic sidewall, even after the application of direct pressure.

What do you do next?

Although cautery can be used liberally on the uterus, its application to mesentery

carries a risk of injury to the mesenteric vessels and bowel wall. Caution is advised when you are attempting to control bleeding on the peritoneum overlying the ureter, whether you are using suture ligation or an energy source. Ideally, you should identify the ureter using a retroperitoneal approach and mobilize it laterally before employing any of these techniques.

There are several potential approaches to the bleeding described in Case 2, all of them involving hemostatic adjuvants. The first decision you need to make, however, is whether to address each region separately or all sites in unison. If you opt to address them together—either during an open procedure or laparoscopy—a fibrin sealant (e.g., Evicel, Tisseel) is one option. It can be applied using a dripping technique or aerosolization, either of which allows for broad application of a thin film of the agent. The limitation of this approach is the volume of agent required to resolve the bleeding, with a potential need for multiple doses to completely coat the area.

Because fibrin sealants function independently of the patient's coagulation cascade, they are particularly useful in the presence of disseminated intravascular coagulation (DIC) and other coagulopathies that might limit the effectiveness of preparations that require the patient's own serum.

An alternative approach to Case 2 is to apply an oxidized regenerated cellulose (ORC) derivative directly to the affected areas. Various forms are available (e.g., Surgicel Fibrillar, Surgicel Nu-Knit). These ORC products can be cut and customized to the area in need of hemostasis, allowing each site to be addressed individually. These agents typically remain adherent after they are applied due to the nature of the interaction between the product, blood, and tissue.

A liquid or foam hemostatic agent (e.g., Surgiflo, Floseal, topical thrombin) could also be employed in this case, but application can be a challenge on a large area with a heterogeneous topography because of the tendency of such agents to migrate under the force of gravity, pooling away from the source of bleeding.



**Fibrin sealants are particularly useful in the presence of DIC and other coagulopathies**

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## Choosing a topical agent? First, consider surgical technique.

**C**urious to discover the preferences and practices of surgeons likely to utilize topical hemostatic agents, OBG MANAGEMENT polled several experienced and expert surgeons, including members of the journal's Board of Editors and Virtual Board of Editors. Their diverse responses offer a snapshot of gynecologic surgical practice in 2012—but all agree that hemostatic products are no substitute for sound surgical technique.

>> JANELLE YATES, SENIOR EDITOR

### Know and employ microsurgical principles



**Joseph S. Sanfilippo, MD, MBA**  
University of Pittsburgh and  
Magee-Women's Hospital,  
Pittsburgh, Pa.

There is no substitute for microsurgical principles in the OR. These principles include gentle tissue handling and excellent primary hemostasis.

That said, sometimes secondary hemostatic agents are necessary. My armamentarium includes collagen, cellulose, and gelatin products and thrombins—all good agents. Fibrin sealants and synthetic glues are helpful tools as well.

Cost is an important variable. Consider Gelfoam and Floseal, which range in price from \$131 for Gelfoam (box of 6) to \$2,064 for Floseal (10 mL) (box of 6). Compare, too, the cost of Avitene (1 g), which is \$530 (box of 6), and thrombin (20,000 U) (with kit), which is \$253. I look for the most cost-effective approach, based on the location of the bleeding.

Another option: the original topical agent—cotton (i.e., the gauze sponge). Sometimes pressure with gauze is the best and cheapest approach!

### Liquid-based products are well suited to laparoscopy



**Cheryl Iglesia, MD**  
Georgetown University  
School of Medicine and  
Washington Hospital Center,  
Washington, DC.

I'm happy to report that I rarely encounter a lot of bleeding! But when arterial bleeding does occur during laparoscopic or robotic sacrocolpopexy, my first-line agent is Surgiflo. It's a good tool for stubborn bleeding in the presacral space (there are lots of arteries and arterioles off the middle sacral vessels and plexus).

We have to call for Surgiflo; it's in the room and a nurse mixes it in a sterile cup. She (or he) then connects the syringe for me to inject through the trocar to the area involved.

One drawback is the expense. Our hospital value-analysis team examined pricing for hemostatic products. Working with surgeons across specialties, our nine-hospital system negotiated more favorable pricing with the manufacturer for the products we use most often.

Another option is Evicel, but it's a little more of a hassle because it has to be refrigerated and brought from the pharmacy. If it is left out of the refrigerator and not used, it is wasted. Our nurses find this product slightly more cumbersome than Surgiflo.

Both products are good for laparoscopic procedures because they are liquid-based. Sponges, such as Gelfoam, and powders, such as Avitene, are harder to introduce laparoscopically, in my opinion.

One caveat: Know which products are human in composition because some patients (Jehovah's Witnesses, for example) will refuse them (Evicel is human). Other patients may have religious reasons for avoiding porcine- and bovine-derived products.

#### FAST TRACK

The liquid-based agents Surgiflo and Evicel are well-suited to laparoscopic procedures

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## Robotic surgery enhances hemostasis



**Robert delRosario, MD**  
Partners in Women's Healthcare,  
Lemoine, Pa, and  
Pinnacle Health,  
Harrisburg, Pa.

The meticulous dissection afforded by robotic surgery offers me the best hemostatic mechanism by providing more acute, direct visualization of each blood vessel. I find that my ability to access the retroperitoneum during hysterectomy and sacrocolpopexy, in particular, allows me to cauterize or ligate individual vessels rather than pedicles.

Nevertheless, when the hemostatic going gets tough, I find Floseal to be a savior. The major downside: It's expensive [see *Dr. Sanfilippo's comments, above—the Editors*].

Another matter worth noting: I have attended conferences where surgeons have anecdotally observed that they inject Floseal into a dissected space when they are concerned about *future* bleeding. This is the exact circumstance in which a hypercoagulable incident can befall the patient. By its mechanism of action, Floseal is designed for use in a site of *active* bleeding. These surgeons may sleep better at night, thinking they have prevented bleeding—but they should be up worrying about a clotting event instead!

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## Cream agents reach hard-to-access areas



**Kurian Thott, MD**  
Women's Health and Surgery  
Center and Stafford Hospital,  
Stafford, Va.

For laparoscopic use, I prefer Floseal or Surgiflo to manage annoying peritoneal bleeds.

I also like them for hard-to-reach areas because they are dispensed as a cream, which offers broad distribution.

In my practice, we like to be as cost-effective as possible, and there is a price differential between these two products. (Our hospitals' supply chain usually manages expense.) There is also a volume differential—a unit of Surgiflo contains more product than a unit of Floseal.

One concern that has been raised in regard to topical hemostatic agents is whether they cause more adhesions. Regrettably, the answer to this question is not yet known.

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## Tips on using Floseal



**Devin Namaky, MD**  
TriHealth,  
Cincinnati, Ohio.

I use topical hemostatic agents when good technique alone fails to achieve hemostasis. Many physicians believe that Floseal should be applied within a very short window after it is mixed, but, in reality, it can be used as long as 2 hours after preparation. For maximal effectiveness, Floseal should be pressed against the surface to which it is applied using a saline-moistened sponge.

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*Dr. Sanfilippo reports that he is a consultant to Bayer. The other commentators report no financial relationships relevant to their recommendations.*

### >> WE WANT TO HEAR FROM YOU!

What are your pearls for using topical hemostatic agents?

Send your pearl to [obg@qhc.com](mailto:obg@qhc.com), with your name and practice city and state. We'll consider publishing it in an upcoming issue of OBG MANAGEMENT.



**Floseal is designed for use in a site of active bleeding—not to avert potential bleeding**

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**Profiles in hemostasis: Strengths and weaknesses of topical agents**

<b>Agent (brands)</b>	<b>Composition</b>	<b>Forms available</b>	<b>Mechanism of action</b>	<b>Advantages</b>	<b>Caveats</b>	<b>Duration</b>	<b>Relative cost*</b>
<b>Physical agents</b>							
<b>Gelatin matrix</b> (Gelfoam, Gelfilm, Surgifoam)	Porcine-derived collagen	Sponge, film, powder	Provides physical matrix for clot formation	Non-antigenic; neutral pH; may be used with thrombin	Material expansion may cause compression; Not for use in closed spaces or near nerve structures	4–6 weeks	\$
<b>Oxidized regenerated cellulose</b> (Surgicel Fibrillar, Surgicel Nu-Knit)	Wood pulp	Mesh or packed fibers	Provides physical matrix for clot formation; acidic pH causes hemolysis and local clot formation	Pliable, easy to place through laparoscope; acidic pH has antimicrobial effect	Works best in a dry field. Acidic pH inactivates biologic agents, such as thrombin, and may increase inflammation. Avoid using excess material.	2–4 weeks	\$
<b>Microfibrillar collagen</b> (Avitene, Instat, Helitene Helistat)	Bovine-derived collagen	Powder, non-woven sheet, sponge	Absorbable acid salt. Provides physical scaffold for platelet activation and clot initiation.	Sheet form may be passed through laparoscope; minimal expansion	Rare allergic reactions reported; may contribute to granuloma formation	8–12 weeks	\$\$
<b>Biologically active agents</b>							
<b>Topical thrombin</b> (Thrombin-JMI, Re-cothrom, Evithrom, rh Thrombin)	Bovine, human, or recombinant	Liquid	Promotes conversion of fibrinogen to fibrin	May be combined effectively with physical agents of neutral pH; recombinant human thrombin will be available in the near future	Risk of blood-borne infection with non-recombinant human thrombin; risk of anaphylaxis and antibody formation with bovine thrombin	N/A	\$\$
<b>Hemostatic matrix</b> (Flo seal, Surgiflo)	Thrombin plus gelatin	Foam	Gelatin granules provide expansion and compression while thrombin initiates clot formation	May be used in areas of small arterial bleeding	Requires contact with blood	6–8 weeks	\$\$\$
<b>Fibrin sealants</b> (Evicel, Tisseel, Crosseal)	Human	Liquid	Combination of fibrinogen and thrombin causes cleavage of fibrinogen to fibrin and resultant clot initiation	Fast-acting; hemostatic and adhesive properties; works well for diffusely oozing surfaces	Contraindicated in patients who have a history of anaphylactic reaction to serum-derived products or IgA deficiency	10–14 days	\$\$\$

\* Median cost for use in one case

Key: \$ = inexpensive; \$\$ = moderately expensive; \$\$\$ = expensive



### Is combining agents a good idea?

Although they are not typically approved for use in combination, sequential application of hemostatic agents may be considered when bleeding persists.

All hemostatic agents work best in combination with the application of pressure. It usually is advisable to use moist gauze for this purpose because it can be lifted away without significant adherence to the underlying hemostatic complex, avoiding clot disruption.

#### **CASE 2** Resolved

You opt to use an ORC product, customizing it to fit each bleeding site, and apply direct pressure. When hemostasis has been achieved at all sites, you complete the operation. The patient has an uneventful postoperative course.

### Protect structures along the pelvic sidewall

#### **CASE 3** When the application of pressure isn't enough

While performing a left salpingo-oophorectomy for a 12-cm ovarian lesion, you use a retroperitoneal approach to identify the structures along the pelvic sidewall. During identification of the ureter, you encounter bleeding from a small vessel in the adjacent fatty areolar tissue. After a period of observation, during which you apply pressure to the area of concern, bleeding persists.

What hemostatic agent do you employ to stop it?

The careful application of steady pressure is often enough to safely control bleeding in the area of the pelvic sidewall. In the event that pressure alone fails to resolve the bleeding, however, it is critical to choose a remedy that avoids injuring the ureter, iliac vessels, and infundibulopelvic ligament. Wide exposure of the space may allow for direct identification of the point of bleeding and precise application of cautery, a hemoclip, or a tie. When this approach is not feasible, other solutions must be sought.

When traditional hemostatic techniques fail in delicate anatomic sites, such as the periureteral area, hemostatic agents are an effective option that can minimize the risk of injury to surrounding vital structures. The contour of the space calls for a product that can intercalate, such as a foam, sealant, or Surgicel Fibrillar. Direct, precise application to the point of bleeding is critical, and the “bunching up” of a more rigid and bulky agent may limit its application to the area of concern. Use of a moist gauze to apply direct pressure after application of the agent will increase the likelihood of success.

#### **CASE 3** Resolved

You decide to apply a foam hemostatic agent because of its ability to conform to the irregular space. You also continue to apply gentle pressure to the point of bleeding, using a moist gauze. Within

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minutes, hemostasis is achieved. You are then able to finish the operation.

### Other variables to consider

As these three cases illustrate, the use of hemostatic agents to control surgical bleeding requires an individualized approach. The site and amount of bleeding, as well as the patient's hemodynamic and coagulation status, are key variables to be considered when selecting an agent.

For instance, because of their components, fibrin sealants can function independently of the patient's coagulation status. ORC products provide a matrix that facilitates platelet aggregation and may be less effective when anti-platelet agents have been used.

It is also appropriate for the surgeon to be familiar with the relative cost of the agents available at his or her institution. In particular, when several agents may be equally effective in a particular set of circumstances, cost may be the determining factor.

Availability of these agents varies from one institution to the next; as a result, it can be challenging to maintain familiarity with all of the products in the marketplace. Having access to a diverse, readily available set of "go to" agents is critical to ensure rapid application in a clinical setting.

The surgeon's preference also is important,

particularly in regard to the ease of preparation and handling. Some agents may not be as suitable for minimally invasive procedures (see **TABLE**, page 40). For others, special laparoscopic applicators are available.

When using a hemostatic agent, it pays to consider the duration of its effect in the surgical site. Both the quantity of the agent that is applied and characteristics of the local operative site influence how quickly the agent degrades. Keep this in mind when imaging studies are planned for the early postoperative period. An ORC preparation, for example, may appear with small pockets of air that resemble an abscess. Effective communication with the radiology team is critical to avoid the misinterpretation of findings. 🚫

#### Recommended reading

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