

Clinical Experience With the Surgical Family of Absorbable Hemostats (Oxidized Regenerated Cellulose) in Neurosurgical Applications

A Review

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Abstract and Introduction

Abstract

Introduction. Oxidized regenerated cellulose has a long history of safe and effective use in the surgical setting. Surgicel Original, Fibrillar and Nu-Knit absorbable hemostats are composed of oxidized regenerated cellulose and are sterile, absorbable knitted fabrics that are flexible and adhere readily to bleeding surfaces. The purpose of this paper is to discuss neurosurgical applications for these absorbable hemostatic agents.

Methods. The authors reviewed the literature and described their clinical experience with Surgicel hemostatic products.

Results. Neurosurgical applications of the hemostatic products include the management of diffuse capillary oozing following bipolar cautery in brain tumor resection beds and the control of epidural oozing during spinal surgery. As an adjunct to standard hemostatic procedures, these products facilitate rapid hemostasis and have bactericidal activity that extend to antibiotic-resistant organisms such as methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus pneumoniae*, as well as *Pseudomonas aeruginosa*. Although generally safe and well-tolerated, these hemostatic agents should be removed when used around, in, or in proximity to, foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve or chiasm because it may otherwise swell and cause unwanted pressure.

Conclusion. The physical, hemostatic, and bactericidal characteristics of this material makes it a useful adjunct for conventional hemostatic and controlling capillary, venous, and small arterial hemorrhage during neurosurgery.

Introduction

Oxidized regenerated cellulose has a long history of safe and effective use for the control of bleeding during surgical procedures. Surgicel Original Absorbable Hemostat (Johnson & Johnson Wound Management, a Division of Ethicon, Inc, Somerville, NJ), (Figure 1) was approved for use in the United States in 1960.^[1] Since that time, 2 similar products (Fibrillar and Nu-Knit) have been developed by the same company. Other companies have released similar products, with all indicated for adjunctive use in surgical procedures to assist in the control of capillary, venous, and small arterial hemorrhage when ligation or conventional methods to control bleeding are impractical or ineffective.^[2] The purpose of this review is to discuss the neurosurgical applications of Original Surgicel (Product A) and Fibrillar Surgicel (Product B).

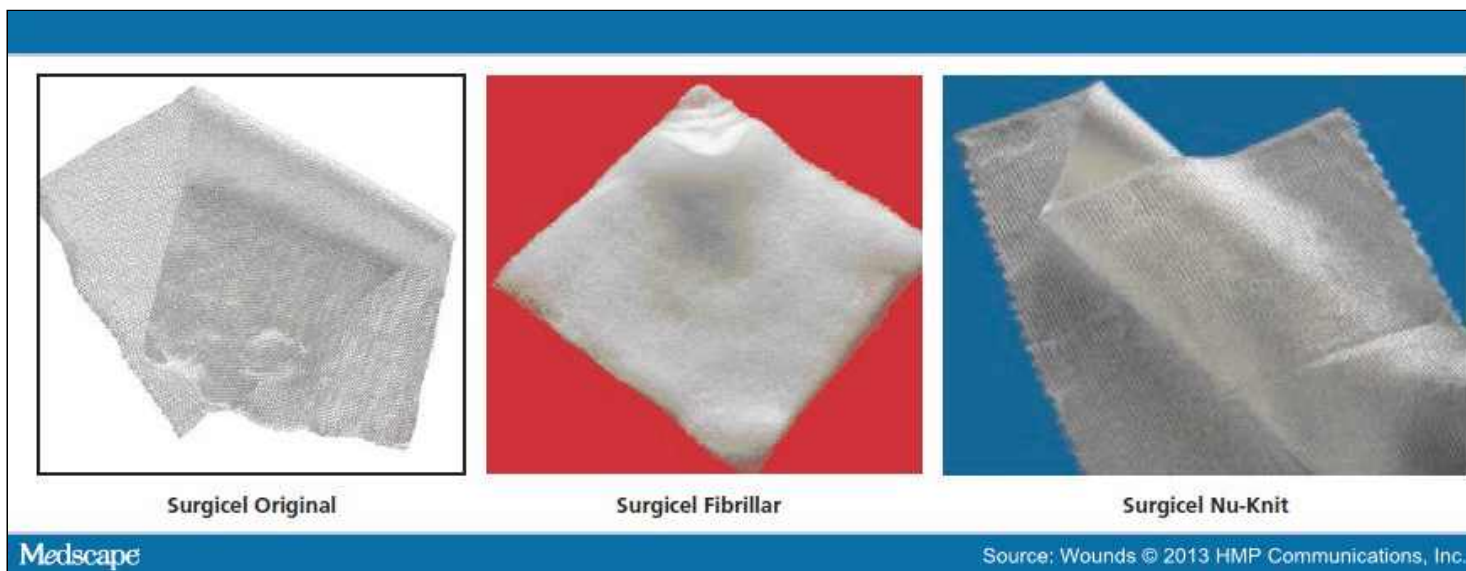


Figure 1.

The Surgicel Family of Absorbable Hemostats

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Methods

The authors undertook a literature review in PubMed using the search string (oxidized[Title/Abstract] AND cellulose[Title/Abstract] AND surgery[Title/Abstract]) AND ("humans"[MeSH Terms] AND English[lang]), which yielded 83 articles. These articles and their references were screened for relevance. Additionally, articles previously published by the authors deemed relevant were included. Textbooks which were particularly relevant are referenced.

Results

Product characteristics. Product A is a flexible, sheer-weave fabric prepared by the controlled oxidation of regenerated cellulose.^[3] Because it is flexible, it conforms to irregular surfaces, making it ideal for use during a wide variety of surgical procedures. The sheer weave also allows visualization of the bleeding site. It can be cut or folded to fit the bleeding site and can be removed with gentle irrigation after hemostasis is achieved.

Product B is also oxidized regenerated cellulose; however, the fabric is very loosely woven, having a consistency and adherence properties similar to those of cotton.^[1,3] It has a lightweight fibril structure that conforms to irregular surfaces and hard-to-reach areas, and layers can be peeled off in desired amounts to fit the wound surface. A significant benefit of both Products A and B are their ability to coagulate even when saturated with blood. Caution and suction can be performed directly through the material. This is especially helpful in cases of venous or cortical oozing, or when used to help identify a bleeding point where coagulation can be achieved with Product B held in place with a Fukushima-type sucker. Product B is ideal for controlling venous bleeding and oozing from cortical surfaces after lobectomies or tumor resection.^[1]

Hemostatic Activity of Oxidized Regenerated Cellulose

Careful dissection with an exceptional knowledge of neural and vascular anatomy is the best strategy to not only prevent hemorrhage but also to avoid injury to the neural elements. As noted by Yasargil,^[4] neurosurgeons must be well-acquainted with the concept and skills of electrocautery. Diligent and

meticulous bipolar electrocautery plays a significant role in accomplishing hemostasis, and good electrocautery technique can minimize the necessity of a hemostatic agent. But inevitably bleeding does take place and electrocautery is not always the best choice, or even possible. The mechanisms by which oxidized regenerated cellulose facilitate hemostasis are not completely understood; however, it is likely that activation of the intrinsic coagulation pathway plays a role.^[5] Additional proposed mechanisms include the formation of a gel-like layer (matrix) that holds clots in place and vasoconstriction triggered by the low pH of the product.^[5,6] Effective hemostasis is typically achieved between 2 minutes and 8 minutes following application. (Data on file, Johnson & Johnson Wound Management, a division of Ethicon, Inc, Somerville, NJ.)

Bactericidal Activity of Oxidized Regenerated Cellulose

Product A has demonstrated broad spectrum bactericidal activity that may reduce the incidence of postoperative infection.^[3,7-10] In one early comparative study from 1976^[7] conducted in guinea pigs, relative rates of sepsis were lower following the application of Product A (1/30) vs an absorbable gelatin sponge (29/30) to experimentally contaminated wounds. In a separate animal study^[8] in which various hemostatic agents were implanted in infected spleens, survival beyond 5 days was approximately 90% in the Product A group vs 0% in the control, absorbable gelatin sponge, and microfibrillar collagen groups (n = 35 animals per group). The bactericidal effects of Product A absorbable hemostats are mediated by the low pH of the product, making it effective against antibiotic-resistant organisms (such as methicillin-resistant *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Staphylococcus epidermidis*, and *Pseudomonas aeruginosa*).^[11]

Use of Oxidized Regenerated Cellulose Following Operative Intervention Into the Cerebrum

Product A has been commercially available in the United States for nearly 5 decades.^[2] Although oxidized regenerated cellulose products are not appropriate for arteriolar bleeding encountered during surgery, they quickly aid in the hemostasis of slow venous and capillary ooze frequently associated with the excision of intrinsic tumors, lobectomy, or the removal of an intracerebral hemorrhage. Product A is frequently used to decrease oozing from the epidural space and to slow epidural hematoma formation during intracranial surgery (via application to the interface between the dura and the margins of the craniotomy defect).^[3] The authors recommend the use of loosely woven cellulose, such as Product B, for these procedures as it allows placement around the resection cavity with rapid adherence to the cavity wall. In 2004, Bakshi and colleagues^[12] reported the use of Product A hemostats to facilitate hemostasis in all 3 patients who required bipolar instrumentation for persistent capillary ooze following the neuroendoscopic removal of large intracranial hematomas. In the other cases (n = 10), hemostasis was achieved with gentle irrigation. This procedure has long posed a formidable challenge because of the need to control bleeding deep within the brain.

In contrast to thrombin-soaked gel sponges, which commonly stick to the surgical instruments and do not form tight bonds with the tissue, Products A and B handle easily, stick to the tissue, and provide reliable hemostasis. Product B may be particularly useful in this setting, as suctioning can be directly applied in the absence of a bulky, cotton sponge overlay that could obstruct the surgeon's view, and it is associated with a faster time to hemostasis than the thrombin-soaked gel sponges.^[6,13]

Following placement, if slow ooze or bleeding continues, electrocoagulation of the saturated oxidized regenerated cellulose can stop further bleeding. Moyamoya-type vessels or the abnormal arterioles associated with arteriovenous malformations need to be electrocoagulated and sectioned to achieve hemostasis. Use of an oxidized regenerated cellulose product in the case of bleeding vessels of this type is not appropriate.

Use of Oxidized Regenerated Cellulose in the Ventricular System

Following resection of posterior fossa tumors, the authors use oxidized regenerated cellulose products with caution in the hemostasis of denuded areas in the posterior fossa in direct contact with the fourth ventricular chamber or for lesions directly involving the lateral ventricles. Product A is used in conjunction with the use of bipolar electrocoagulation and surgical sponges with variable action suckers

to promote hemostasis. Following their use, the oxidized regenerated cellulose is irrigated free from the surface. In instances where oxidized regenerated cellulose has been left following interventions into the fourth ventricular chamber, the authors have not noted postoperative hydrocephalus or pseudomeningocele formation in children. So far there have been no documented cases of hydrocephalus caused by leaving oxidized regenerated cellulose in the fourth ventricle. The authors have utilized Product A in conjunction with tissue glue to seal the ventricle, and potentially avoid the complication of subdural hygroma following transcortical approaches.

Use of Oxidized Regenerated Cellulose in Spinal Surgery

Oxidized regenerated cellulose has been found to be useful in stopping epidural oozing during spinal surgery, a situation in which bipolar cautery is often avoided, as it can induce thermal injury to adjacent nerve roots.^[14] Intraosseous implantation of oxidized regenerated cellulose can help to control bleeding and may additionally benefit patients by promoting lamellar bone formation. In 1 animal study,^[15] the intraosseous implantation of oxidized regenerated cellulose promoted lamellar bone formation of the same rate and quality as collagen-based implants. Bone wax has been traditionally used to stop bleeding from the bone in procedures (such as iliac crest bone graft harvesting), but it impedes the formation of new bone, and has been shown to promote the development of *Staphylococcus aureus* osteomyelitis in animal studies.^[9,16] Novel pluronic waxes have been developed which have hemostatic and bacteriostatic properties while being reabsorbed over a 4-week period so as not to interfere with bone growth.

Bactericidal activity of Product A and related materials against several of the organisms commonly implicated in osteomyelitis infections can be useful in these procedures.^[10] There are also reports of the use of Gelfoam powder (Product C) (Pfizer, New York, NY) to stop bone oozing during both skull base and spine surgery, which note it is relatively easy to apply and has minimal impact on the surgeons view.^[17]

Use of Oxidized Regenerated Cellulose in Approaches to the Skull Base

In approach to the skull base, where safe and meticulous hemostasis is challenging but paramount to adequate exposure, the authors find oxidized regenerated cellulose especially helpful. Three skull base approaches are described here in which the authors used oxidized regenerated cellulose to promote hemostasis: dissections in the region of the cavernous sinus, extreme lateral inferior transcondylar-transtubercular exposure (ELITE), and the lateral suboccipital craniotomy.

In their dissections in the region of the cavernous sinus, there are key areas where oxidized regenerated cellulose is used to control venous bleeding and obtain hemostasis. Manipulation of the dura propria for transcavernous approaches can be fraught with significant venous bleeding. It is often necessary to mobilize the dura propria to enhance the operative corridor; however, substantial venous ooze and bleeding can be encountered. Oxidized regenerated cellulose allows the surgeon to tamponade through direct packing. By layering thin layers of oxidized regenerated cellulose into this region and allowing the oxidized regenerated cellulose to become saturated with venous blood, a coagulum can form using bipolar electrocautery. The authors placed small surgical sponges over the coagulum and vacuum with variable action suckers to increase the speed with which hemostasis can be obtained. There are times in the orbitozygomatic approach for intracavernous interventions that make it necessary to extradurally remove the anterior clinoid. Keeping in mind the tip of the anterior clinoid is embedded into the siphon angle at the anteromedial triangle of the cavernous sinus, it is not uncommon to encounter significant bleeding during this stage of the exposure.

The challenge in obtaining hemostasis is there are several nearby structures which are sensitive to compression: the optic nerve and carotid lie medial to the clinoid; the 2 cavernous membranes and the oculomotor nerve are lateral; and the anterior medial cavernous sinus triangle is inferior. The goal is to obtain hemostasis safely, without causing injury to any of these critical surrounding structures. This can be accomplished by packing pieces of oxidized regenerated cellulose and then using a bipolar electrocoagulator. Generous packing of the lateral region can be completed, but compressing the

oculomotor nerve should be avoided.

To allow exposure of the posterior cavernous sinus, the authors skeletonize foramen ovale after the superior orbital fissure, foramen rotundum, and lateral loop between V-2 and V-3 are drilled, using the high-speed diamond drill with copious amounts of irrigation. The bleeding that is usually encountered in the area of the foramen ovale is the result of sphenoid emissary veins or veins that connect the lateral cavernous sinus to the pterygoid venous plexus. This bleeding can be controlled with the application of oxidized regenerated cellulose. During the dissection of the posterior cavernous region of the middle fossa, once the middle meningeal artery is electrocoagulated and sectioned, the bleeding from the surrounding venous plexus can be controlled through the use of bipolar electrocoagulation and the application of oxidized regenerated cellulose.

One of the greatest challenges with dissection in the region of the cavernous sinus is the direct entry into the cavernous sinus via the numerous triangular corridors. The authors have found that by packing each triangle with oxidized regenerated cellulose, followed by electrocoagulation of the saturated oxidized regenerated cellulose, they have been able to rapidly obtain hemostasis. Although not common in their practice, an alternative to packing Product A into the triangles of the cavernous sinus is the use of tissue glue, which may minimize the packing and any compression of cranial nerves.

Another approach where the authors employ oxidized regenerated cellulose is in the ELITE. During this approach, in the dissection and identification of the vertebral artery, bleeding will frequently result from the manipulation of the vertebral venous plexus and vertebral artery within the suboccipital triangle, which is comprised of the obliquus capitis superioris and inferioris, and the semispinalis. The authors have found the use of the oxidized regenerated cellulose for control of venous plexus bleeding in conjunction with irrigation and bipolar coagulation has been extremely helpful in controlling bleeding. They also employ this technique in obtaining hemostasis during the dissection of the extradural component of the vertebral artery and the removal of the venous plexus. However, any small muscular branches of the vertebral artery that are present along this segment should be coagulated, as the use of oxidized regenerated cellulose is not appropriate for this type of bleeding.

For the lateral suboccipital approach, where exposure of the jugular bulb is necessary for cases such as glomus tumors and other jugular foramen tumors, a significant venous oozing may be encountered. After reaching the prominent posterior condylar vein and the extradural venous plexus surrounding the jugular bulb, this venous ooze can be treated efficiently by packing with oxidized regenerated cellulose and electrocoagulation. Drilling and dissection between the jugular bulb and the C-1 condyle will allow for skeletonization of the hypoglossal canal and the condylar triangle. Although this maneuver maximizes intradural exposure, it can be associated with significant venous bleeding. In these cases, oxidized regenerated cellulose is appropriate for rapid and efficient hemostasis.

Significant venous ooze and hemorrhage can be encountered in approaches to the cranial base and cavernous sinus. Surgeons need hemostatic agents that will promote safe and prompt hemostasis. Packing with Product A should have the effect of creating a hemostatic environment while avoiding excessive packing with the potential for neural compromise to the cranial nerves secondary to compression. Others have described the use of tissue glue instead to obtain hemostasis in surgeries in or around the cavernous sinus.

Use of Oxidized Regenerated Cellulose in Cerebrovascular Surgery

More current use of oxidized regenerated cellulose products is based upon the novel physical characteristics that have recently been incorporated into these products. Sundt^[18] initially described the use of micro cottonoids for manipulation of the aneurysmal dome and surrounding perforators and in enhancing the corridor for satisfactory clip placement. The new loosely woven oxidized regenerated cellulose products are also appropriate for this type of use and, in the authors' experience, have become commonplace. Additional application has been noted in relation to intraoperative rupture. If oxidized regenerated cellulose is being utilized during the dissection and rupture occurs, the authors will identify the rupture point and place it at the site of rupture, then follow with suction and copious

irrigation; this allows for inspection of the normal anatomy and the subsequent placement of a surgical sponge. Oxidized regenerated cellulose is not usually the author's first choice in this setting if appropriate surgical sponges are readily available.

Further dissection and manipulation (allowing for clip placement) can then be initiated. The ease of use of oxidized regenerated cellulose products in the manipulation of the perforating vessels and aneurysmal dome has enhanced the authors' ability to treat these lesions. Obviously, scenarios remain where the use of an oxidized regenerated cellulose product is not effective. These cases will vary depending on the experience of the surgeon. In addition, the use of oxidized regenerated cellulose products should not be used to bypass certain principles of intervention with regard to cerebrovascular abnormalities.

Obviously, the best approach to intraoperative rupture is avoidance by using an adequate craniotomy and establishing proximal control early in the case. However, if encountered, effective suctioning and a calm attitude are requisite to optimize clinical outcomes.

Safety of Oxidized Regenerated Cellulose

Although oxidized regenerated cellulose products are rapidly cleared from the implant site and are generally safe and well-tolerated, save for a few complications associated with neurosurgical use, some adverse reactions have been reported. Rare reports of granulomatous foreign-body reactions that mimic brain tumor recurrence or hematoma have been described in patients who had undergone surgical brain tumor resection.^[11,19,20] All were removed surgically with positive results, and histologically, most comprised cellulose remnants in addition to monocytes and multinuclear giant cells. Additionally, there have been reports of paralysis and nerve damage when oxidized regenerated cellulose was used around, in, or in proximity to, foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve or chiasm ().

Table 1. Complications associated with use of Product A and Product B.

Region	Complication	References
Brain	Intracranial mass	11, 19, 20
Thorax	Paraplegia	21, 30, 31, 32
Lumbar spine	Nerve root compression	33, 34

In cases of swelling of the oxidized regenerated cellulose, nerve compression and damage was only partially reversible upon reoperation and removal. Therefore, it is recommended that Product A be removed whenever possible after hemostasis is achieved. This is particularly true when the product is applied in confined areas^[21,29] ().

Table 1. Complications associated with use of Product A and Product B.

Region	Complication	References
Brain	Intracranial mass	11, 19, 20
Thorax	Paraplegia	21, 30, 31, 32
Lumbar spine	Nerve root compression	33, 34

In accordance with its labeled indications, the Product A family of hemostats should not be used to control hemorrhage from large arteries. Rather, it should be used as an adjunct to ligation or other conventional methods to control capillary, venous, and small arterial hemorrhage. To avoid complications, it should not be closed in a contaminated wound without drainage. One of the advantages of oxidized regenerated cellulose is that it is plant-derived, and thus contains no human components.^[21] Therefore, there is no risk of viral disease (eg, human immunodeficiency virus)

transmission.

Comparison to Other Hemostatic Agents

Multiple hemostatic agents have proven fast, safe, and effective. In addition to the Product A line, there are a number of other hemostatic agents widely used in neurosurgery.

One of the most widely used hemostatic products is Product C, which is made of purified porcine skin gelatin. For both Products C and A, the mechanism of action is to provide a mechanical matrix that facilitates clotting by release of thromboplastin. Compared to Product A (Oxidized regenerated cellulose), Product C has an excellent total fluid and blood absorption capacity. However, Product C's resorption after implantation tends to be slower (4–6 weeks) compared to Product A.

Product C is most commonly used in combination with thrombin, although this is not the manufacturer's recommendation. The concern is not only that thrombin adds to the cost but also that it may potentially cause allergic reactions and anaphylaxis, especially when the product is prepared with bovine thrombin. However, this preparation is popular among surgeons, because when combined with thrombin, the hemostatic properties of Product C are greatly enhanced.

Indications for applications of Products A and C are similar. Also similar are the precautions which include removal after laminectomy or placement near nerve root foramina to prevent nerve compression,^[22] and after intracranial implantation to prevent brain granuloma formation.^[11,19,20,23] One significant difference is that Product C does not adhere to the tissue as aggressively as Product A, a property which serves as both a strength and weakness, depending on what the surgeon is trying to accomplish. According to the manufacturer, Product C should not be used in combination with methyl methacrylate, which will further reduce its adherence to the tissues. Another very significant difference is Product C is contraindicated to be implanted in the case of infection because it can increase bacterial growth; whereas Product A has bactericidal activity that extends to antibiotic-resistant organisms such as methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus pneumoniae*, as well as *Pseudomonas aeruginosa*.

FloSeal (Product D) (Baxter Fremont, California, US) is a gelatin-thrombin matrix hemostatic agent that is gaining wide use. It contains human thrombin and cross-linked, bovine-derived gelatin granules. FloSeal has a convenient syringe-type delivery system and a hydrophilic property which allows it to easily conform to wet surfaces. In the authors' experience, it is efficient in controlling epidural bleeding during spinal surgery and craniotomy. There have been multiple reports of its safety for intracranial use during craniotomy and transsphenoidal pituitary surgery.^[24,25] However, 1 animal study raised concerns that, in contrast to Product A (Oxidized regenerated cellulose), leaving Product D in the cranium may lead to granuloma formation.^[26] Although this product uses human thrombin, it still carries a risk of allergic reactions and possible infection transmission risk of Creutzfeldt-Jacob disease since it contains gelatin of bovine origin. One limitation of Product D is it does not allow simultaneous electrocautery and provides little in the way of tamponade. Although when used in conjunction with the minimal tamponade provided by an overlying cottonoid sponge, Product D can provide hemostasis with low pressure venous or capillary ooze.

Fibrin glue is a 2-component system containing liquid fibrinogen and fibrin in 2 separate syringes that, when combined, create fibrin coagulum. This is a rapid system that results in fibrin clot formation in approximately 10 seconds. Fibrin glue is primarily used for large, oozing surface areas that can be quickly covered by spraying the area with the mixture while providing the surgeon with a clear and clean view of the operative field. It is particularly useful in hemostasis for patients with hemophilia. Many use fibrin glue over durotomies after a cerebrospinal fluid (CSF) leak repair or for CSF leak prevention, occasionally in combination with Product A. In preventing CSF leak, Product A acts as a scaffold for fibrin glue coagulum. Symon and Pell^[27] report that use of these 2 products combined for closing of open mastoid air cells after acoustic neuroma surgery reduced incidence of CSF rhinorrhea from 16% to 5%. Significant limitations to its use include its inability to allow continual bipolar electrocautery or

tamponade, and its significant cost. There are also concerns that fibrin glue is associated with potential infectious risk because its components are made from pooled human plasma.^[28] Using fibrin glue could expose patients to Hepatitis virus,^[28] Parvovirus B19,^[6,16] and possible allergic or anaphylactic reactions.

Conclusions

Products A and B have multiple neurosurgical applications. As an adjunct to standard hemostatic procedures, they facilitate rapid hemostasis and have bactericidal activity that extends to antibiotic-resistant organisms such as methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus pneumoniae*, as well as *Pseudomonas aeruginosa*. Risks can be minimized with appropriate use, including product removal following hemostasis whenever possible, and removal at all times when the product is applied in, around, or in proximity to, foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve. Both products are effective in controlling venous oozing during approaches to the skull base where safe, precise, and rapid hemostasis is critical. The authors recommend the use of oxidized regenerated cellulose for interventions in the cerebrum for rapid hemostasis of capillary or post-resection ooze. Whether to help with manipulation of the aneurysmal dome or to aid in the rapid identification of the rupture point during an intraoperative rupture, the use of oxidized regenerated cellulose is not uncommon in practice and approach to cerebrovascular disease.

Sidebar

Keypoints

- The purpose of this review is to discuss the neurosurgical applications of Original Surgicel (Product A) and Fibrillar Surgicel (Product B).
- Product A is a flexible, sheer-weave fabric prepared by the controlled oxidation of regenerated cellulose.³ It conforms to irregular surfaces, making it ideal for use during a wide variety of surgical procedures.
- Product B is also oxidized regenerated cellulose; however, the fabric is loosely woven, having a consistency and adherence properties similar to those of cotton.^{1,3} It has a lightweight fibril structure that conforms to irregular surfaces and hard-to-reach areas.
- Oxidized regenerated cellulose has been found to be useful in stopping epidural oozing during spinal surgery, a situation in which bipolar cautery is often avoided, as it can induce thermal injury to adjacent nerve roots.¹⁴
- Intraosseous implantation of oxidized regenerated cellulose can help to control bleeding and may additionally benefit patients by promoting lamellar bone formation.
- The authors also employ oxidized regenerated cellulose in the extreme lateral inferior transcondylar transtuberular exposure.
- In the dissection and identification of the vertebral artery, bleeding will frequently result from the manipulation of the vertebral venous plexus and vertebral artery within the suboccipital triangles
- The authors have found using oxidized regenerated cellulose for control of venous plexus bleeding in conjunction with irrigation and bipolar coagulation has been extremely helpful in controlling bleeding.
- In cases of swelling of the oxidized regenerated cellulose, nerve compression and damage was only partially reversible upon reoperation and removal. Therefore, it is recommended that Product A be removed whenever possible after hemostasis is achieved.

- One of the advantages of oxidized regenerated cellulose is that it is plant-derived, and thus contains no human components.²¹ Therefore, there is no risk of viral disease (eg, human immunodeficiency virus) transmission.

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