

TOPICAL HEMOSTATS IN NEUROSURGERY

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Hemostasis in neurosurgery

- One of the most important aspects of surgery.
- Control of bleeding without ligature unlike in abdominal and other surgeries ligatures and packs rarely useful.
- Many hours lost in bleeding control



Topical hemostats

- Agents that help in controlling bleeding.
- Ideal topical hemostat:
 - safety,
 - efficacy,
 - usability,
 - cost, and
 - Approvability



Sources of bleeding

- Scalp/muscles
- Bone
- Dura and sinuses
- Brain: capillary/venous/arterial



Muscle

- 1st used by Sir Harvey Cushing
- Mechanism : mechanical plus as a source of tissue thromboplastin.

Cotton Balls and Cotton Patties

- Mainly mechanical by applying gentle pressure.



Gelatin sponge (Gelfoam)

- Introduced in the 1940s for neurosurgical procedures.
- Derived from purified pork skin gelatin.
- Mechanical barriers to bleeding by forming a matrix.
- Absorbs approximately 45 times its weight in blood and can expand to approximately 200% of its initial volume.
- Not to be used in combination with blood salvage equipments as their fibres can pass through the 40 mm filters of salvage systems.
- Can be used dry or saline soaked, better when excess saline is removed as compare to supersaturated.




Microfibrillar collagen (Avitene)


- Collagen which is derived from bovine skin binds tightly to blood surfaces.
- Causes minimal swelling especially when compared to Gelfoam .
- serving as a matrix for clot formation and enhancing platelet aggregation, degranulation, and release of clotting factors which then combine with plasma factors to produce fibrin clot
- May reduce the number of free platelets in normal individuals .
- Loses effectiveness in thrombocytopenia(<10,000).
- It is absorbed in 3 months and needs to be applied dry.



Oxidised regenerated cellulose (Surgicel)

- Introduced in 1940s.
- Surgicel (Ethicon) is an oxidized cellulose polymer (the functional unit is poly anhydroglucuronic acid) formed by dissolving pure α -cellulose (plant derived) in an alkaline solution.
- It is then regenerated into continuous fiber, knitted into gauze, and oxidized.
- Applied dry, absorbs within 4 to 8 weeks.
- Forms a brownish or black gelatinous mass in contact with blood.


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- Acts as a physical matrix to which platelets can adhere which, in turn, aids in clot formation
 - Additional pressure of the mass also contributes to the haemostatic process.
 - They create an acidic environment and are bactericidal.
 - Cellulosic acid facilitates hemostasis by denaturing blood proteins.
 - Needs to be applied dry.
 - They can be best removed by gentle irrigation with saline.


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- Oxycel (Becton Dickinson) is another oxidized cellulose polymer product that is similar.
 - Surgicel is composed of solid fibers with irregular contours on cross-section, whereas Oxycel is composed of hollow “twisted tubule” fibers.



SURGICEL Fibrillar

- Oxidized regenerated cellulose(1969)
- Layers can be peeled off in desired amounts.
- conforms to irregular surfaces, even hard-to-reach areas
- surgical visualisation is improved by ability to cauterise directly through it
- fully absorbed within 14 days

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- **Oxidised regenerated cellulose as a cause of paraplegia after thoracotomy: case report and review of the literature.** Spinal Cord. 2005 Jul;43(7):445-7.


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- Rapid closure technique in decompressive craniectomy. [Güresir E](#), [Vatter H](#), [Schuss P](#), [Oszwald A](#), [Raabe A](#), [Seifert V](#), [Beck J.](#) J Neurosurg. 2011 Apr;114(4):954-60. Epub 2010 Jan 29. Total of 314 patients. The surgical time is significantly shorter without increased complication rates or additional complications. Cranioplasty after a RCDC procedure was also feasible, fast, safe and not impaired by the RCDC technique.



Active

Thrombin

- Thrombin is marketed as bovine (Thrombin-JMI, King Pharmaceuticals, Bristol, TN), human pooled plasma (Evithrom, J&J), and recombinant (Recothrom, Zymogenetics, Seattle, WA).
- Thrombin directly activates fibrinogen and converts it into fibrin monomers.
- Can be used directly or combined with gelatin sponge
- Bovine thrombin is antigenic.
- If injected into large vessels can lead to thrombosis and complications.

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- The three commercially available thrombins are functionally equivalent in terms of efficacy with 95 percent or greater of patients achieving hemostasis within 10 minutes of application and approximately two-thirds of patients achieving hemostasis within 3 minutes. *Chapman WC, Singla N, Genyk Y, McNeil JW, Renkens KL Jr, Reynolds TC, Murphy A, Weaver FA. A phase 3, randomized, double-blind comparative study of the efficacy and safety of topical recombinant human thrombin and bovine thrombin in surgical hemostasis. J Am Coll Surg 2007;205: 256-65*

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- The human antibodies to bovine FII and FV have been linked to coagulopathy and potentially fatal complications.

(Sarfati MR , Dilorenzo DJ, Kraiss LW, Galt SW. Severe coagulopathy following Intraoperative use of topical thrombin. Ann Vasc Surg 2004;18:349-51.)



Complications

- Nidus of infection
- Inflammatory reaction (esp. avitene)
- Antigenicity (animal products)
- Mass effect (esp. gelatin)
- Gossipiboma



Bone wax

- Pioneered by Sir Victor Horsley(1892).Horsley's wax: bees wax, 7 parts; almond oil, 1 part; salicylic acid, 1 part.
- Modern wax: 88% refined beeswax and 12% isopropyl palmitate (softening agent).
- Effective in controlling bleeding from bone
- Once smeared across the bleeding edge, immediate hemostasis occurs.



Complications

- Bone wax inhibits osteogenesis.
- Increases infection rates (the number of bacteria needed to produce osteomyelitis is reduced by a factor of 10,000).
- Remains as a foreign body for many years.




Ostene

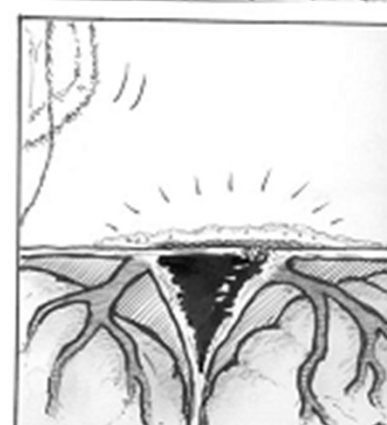
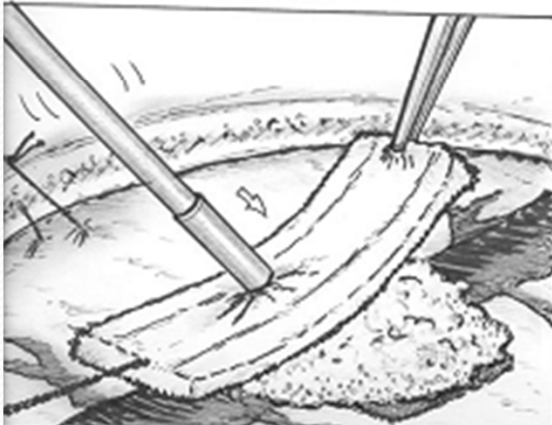
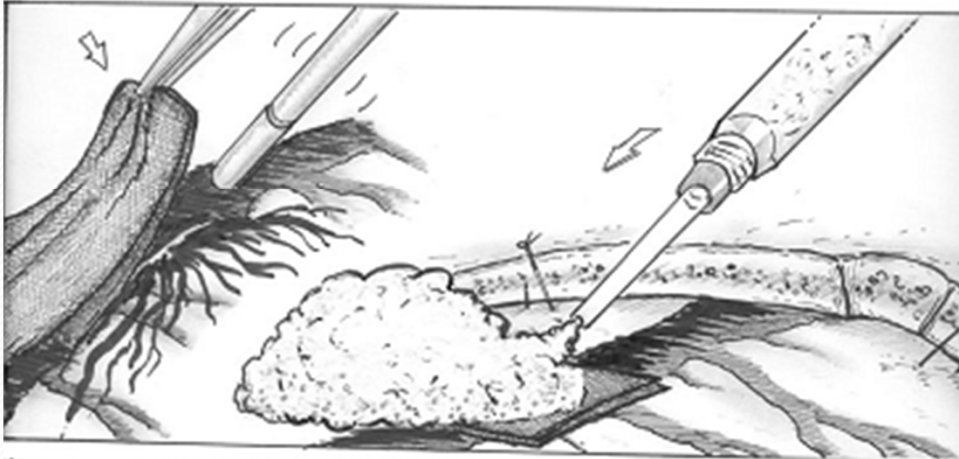
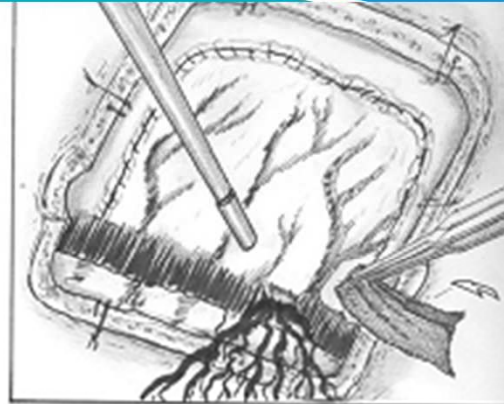
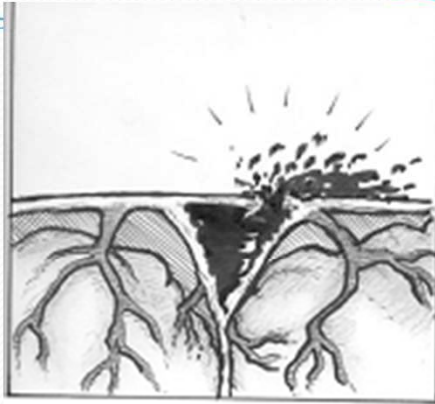
- Sterile mixture of water-soluble alkylene oxide copolymers.
- Inert artificial material feels and works like wax.
- Does not increase infection rates, does not interfere with bone healing, and is non-inflammatory.



Flowables


- Human plasma thrombin with bovine gelatin matrix. (**Floseal**, Baxter, Fremont, CA)
- Create a granular hemostat that employs both active and mechanical components to achieve hemostasis.
- It is applied as a paste to which it is recommended that gentle pressure be applied with a moist saline sponge for 2 minutes to achieve hemostasis.


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- Hemostatic matrix sealant in neurosurgery: a clinical and imaging study. Roberto Gazzeri & Marcelo Galarza & Massimiliano Neroni & Alex Alfieri & Marco Giordano. *Acta Neurochir* (2011) 153:148–155. Effective hemostasis, defined as cessation of bleeding, was achieved no later than 3 min after topical agent application in all patients except in 11 cases out of 214 cases it was used.





Complication	Number of patients (%)	Pathology
Rebleeding	4 (1.8)	2 malignant gliomas, 1 spontaneous ICH, 1 traumatic ICH
Abscess	1 (0.4)	1 malignant glioma
Status epilepticus	1 (0.4)	1 extra-axial hematoma


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- The role of FloSeal in reducing epidural fibrosis in a rat laminectomy model.. [Dogulu F, Durdag E, Cemil B, Kurt G, Ozgun G](#) *Neurol Neurochir Pol.* 2009 Jul-Aug;43(4):346-51. Application of FloSeal at a laminectomy site may be useful to decrease adhesion at the interface between the dura mater and epidural fibrosis.

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- A study in cardiac, vascular, and spinal or orthopedic patients designed to show equivalence between bovine thrombin gelatin matrix and bovine thrombin with porcine gelatin sponge demonstrated statistically significant ($p < 0.001$) superiority of the flowable matrix product for percent of patients with hemostasis at 10 minutes, 96 percent (149/156) versus 77 percent (118/153). *Package Insert. Floseal, Baxter. 2005.*



Fibrin sealent

- Human plasma derived fibrin sealent
- **Fibrin glue**(Tisseel/evicel)
- Commercially available/autologous.
- 2 components:
 - a)fibrinogen, factor13, fibronectin, aprotinin, plasminogen, cryoprecipitate
 - b)thrombin and calcium
- After mixing, fibrinogen is converted to fibrin
- Aprotinin inhibits premature fibrin degradation

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- Supply a source of fibrinogen to the site of injury and do not need active bleeding or blood-derived fibrinogen to polymerize.




Use


- For hemostasis and tissue sealing
- To reinforce dural closure and prevent CSF leak.
- In anastomosis of nerves and nerve grafts
(Micro neural anastomosis with fibrin glue : an experimental study. Suri A, Mehta VS, Sarkar C .Neurology India.2002)
- Fixation of bone fragments to repair skull defects.




Hydrogen peroxide

- 3% solution is used in neurosurgery
- Use is very controversial
- Mechanism : mechanical obstruction of the microvasculature, mechanical removal of tissue debris, and vasoconstriction. Exact mechanism is not known.
- Primarily used to achieve hemostasis after complete tumor removal of the surrounding arachnoidal surface of the brain.

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- Recent evidence suggest significant tissue damage in surrounding functional brain.
 - *INTRATUMORAL HYDROGEN PEROXIDE INJECTION DURING MENINGIOMA RESECTION*. Roger Lichtenbaum, M.D. Neurosurgery 59[ONS Suppl 4.]:ONS-470–ONS-473, 2006.
 - *Hydrogen peroxide–induced stroke: elucidation of the mechanism in vivo*. Melike Mut, M.D., Ph.D J Neurosurg 110:94–100, 2009

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- Comparative safety and efficacy of topical hemostatic agents in a rat neurosurgical model Neurosurgery. 2008 Oct;63(4 Suppl 2):369-72.
 - Avitene, FloSeal, and Surgicel performed better (defined as complete hemostasis within 1 minute) than control (no treatment). Residual material was not present at any time with Arista, markedly contrasting with the presence of residual material in 100% of lesions in the Avitene, FloSeal, and Surgicel groups on Day 14. Avitene and FloSeal also demonstrated a propensity for causing granuloma formation, whereas Arista and Surgicel showed no such evidence

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- **The use of local agents: Surgicel and Surgifoam.**
Eur Spine J (2004) 13 (Suppl. 1) : S97–S10.
 - The use of absorbable porcine gelatine and regenerated, oxidised cellulose as haemostats in intraspinal surgery must be considered safe and beneficial. However, the appropriate use of haemostats requires a certain understanding of their advantages, limitations and the nature of complications associated with their application



Conclusion

- Proper surgical principle remains the key.
- Judicious use of hemostatic agents is advised.