

# Hemostatic Dressings for the First Responder: A Review

**Guarantor:** Kelly King, MD

**Contributors:** 2nd Lt Marcus C. Neuffer, MSC USAF; ENS Jonathan McDivitt, MC USNR; 2nd Lt David Rose, MSC USAF; Kelly King, MD; COL Clifford C. Cloonan, MC USA (Ret.); Joshua S. Vayer, BA

The military is interested in finding a hemostatic dressing that is effective in controlling hemorrhage from combat wounds, relatively inexpensive, and easy to transport. The fibrin dressing has existed for decades, but the military has been reluctant to use the dressing because it is not Food and Drug Administration approved, fairly expensive, and difficult to apply on certain wounds. Newer dressings such as the microporous polysaccharide hemosphere (TraumaDEX), mineral zeolite (QuikClot), poly-*N*-acetylglucosamine (HemCon), and microporous hydrogel-forming polyacrylamide (BioHemostat) dressings have addressed these deficiencies in that they are relatively inexpensive, easy to transport, and easy to apply. However, the effectiveness of these new dressings on wounds sustained in combat is still questionable according to studies and anecdotal reports from Operation Iraqi Freedom. More research is needed to draw definite conclusions about the effectiveness of these dressings in a combat setting.

## Introduction

Uncontrolled hemorrhage is the leading cause of death during the prehospital period in both military combat and civilian trauma cases.<sup>1-3</sup> Immediate intervention by an on-scene first responder or by the wounded themselves is one of the most effective methods of limiting patient mortality.<sup>4</sup> Interestingly, the methods of controlling bleeding in the prehospital period have not changed significantly in the last 2,000 years.<sup>5</sup> Although bleeding from extremity injuries can usually be controlled by direct pressure or, if severe, by the application of a tourniquet, presently little can be done to control bleeding from complex chest, abdomen, or pelvis wounds. This was certainly the case during military operations in Somalia and Afghanistan in which penetrating wounds to the groin and pelvic regions caused significant mortality among American military personnel.<sup>6</sup> To reduce the mortality from these types of wounds as well as the time required to control severe bleeding, the U.S. Army (USA) and Marine Corp (USMC) are investigating a number of recently developed hemorrhage control technologies. The military is seeking a hemostatic device that is effective, inexpensive, easy to transport, and easy to apply. In this article, we review the hemostatic dressings and tourniquets examined and used by the USA and USMC and report on their effectiveness in both laboratory trials and field situations during Operation Iraqi Freedom.

## Fibrin

Fibrin glues, foams, and tissue-adhesive bandages are a group of products that lead to the formation of a thrombus or

clot at the site of application. These products contain extremely high concentrations of fibrinogen, thrombin, and sometimes additional components such as calcium, factor XIII, or even antifibrinolytics, all of which work to mimic the final stages of the blood coagulation cascade. Although these components are naturally present in every wound, these products supply the clotting cofactors in a much higher concentration than is available physiologically, leading to more rapid clot formation.<sup>7</sup>

The medical use of fibrin to assist in clotting is not an entirely new concept.<sup>8,9</sup> The development and application of fibrin in a military setting began in World War II:

When thrombin first became available, Lt. Edgar A. Bering, Jr., MC, USN and Dr. Bailey had applied it in solution to bleeding points in several cranial and spinal operations. It did no harm. . . but its effect was entirely transient. Lieutenant Bering then conceived the idea of using fibrinogen, converted into fibrin foam, as a matrix. . . The first applications of fibrin foam were made in cases in which bleeding was difficult to control and the application of muscle was not feasible. The hemostatic effect was evident. . . It was agreed that the material was of extraordinary value as a hemostatic agent in neurosurgery. It had proved of great value in hemophiliacs, in controlling bleeding from traumatic lacerations, and in maintaining hemostasis during minor surgical procedures such as tooth extractions.<sup>10</sup>

Since the 1970s, fibrin glues and sealants produced from either human or bovine donors have been used extensively in fields as varied as abdominal surgery, organ resection, cosmetic surgery, and cardiovascular surgery.<sup>11-16</sup> Initially, there was some fear of disease transmission by fibrin products, but advances in production and purification have virtually eliminated these risks.<sup>16</sup> The chief difficulty now is that liquid fibrin products have a short shelf life and need to be mixed each time they are required for use. This requires added time and extensive laboratory and blood bank support, limiting the usefulness of these products in first-response (field) situations. Because of the limitations of liquid preparations, current investigative efforts have focused on the production of dry fibrin bandages for use in hemorrhage control.

In multiple animal studies, fibrin bandages have proven to significantly decrease blood loss during hemorrhage. Two of these studies were large-animal surgical models (Yorkshire swine), both of which demonstrated that the fibrin bandage treatment achieved faster blood clotting and resulted in less blood loss and a more normal blood pressure profile than a standard gauze pressure bandage treatment, which consists of applying manual pressure to a wound using a gauze pad (Table I).<sup>17,18</sup> A third study was a large-animal ballistic wounding model (Angora goats) which showed that the fibrin dressing was superior to the standard pressure bandage treatment in controlling

Casualty Care Research Center, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814-4799.

This manuscript was received for review in April 2004 and was accepted for publication in May 2004.

TABLE I  
COMPARISON OF TWO SURGICAL FEMORAL INCISION TESTS IN YORKSHIRE SWINE

Reference	Dressing	Incision Size (cm)	Blood Loss in 1 Hour (mL)	$p^a$	Baseline Blood Flow (mL/min)	$p^a$	Initial Mean Arterial Pressure (mm Hg)	$p^a$
Jackson et al. <sup>17</sup>	Control	0.4	82.3 ± 11.1	0.0005	106.7 ± 16.5	0.24	N/A <sup>b</sup>	
	Fibrin	0.4	4.9 ± 4.0	0.0005	114.2 ± 17.4	0.24	N/A	
Larson et al. <sup>18</sup>	Control	1.3	734 ± 134	0.0022	N/A		84.2 ± 6	0.12
	Fibrin	1.3	123 ± 48	0.0022	N/A		81.2 ± 5	0.12

<sup>a</sup>  $p$  values are written as reported in the original journal article.

<sup>b</sup> N/A, Not applicable.

hemorrhage from gunshot wounds inflicted by a 0.308 caliber high-velocity bullet. In equivalent injuries to the experimental subjects, blood loss was significantly lower in the fibrin bandage treatment group than in the control group ( $124 \pm 64$  mL vs.  $377 \pm 64$  mL,  $p = 0.01$ ;  $p$  values are written as reported in the original journal article) and the mean arterial pressure was also maintained higher in the fibrin bandage group ( $95.0 \pm 4.7$  mm Hg vs.  $70.0 \pm 5.0$  mm Hg,  $p = 0.01$ ;  $p$  values are written as reported in the original journal article).<sup>19</sup> A fourth study which compared 10 different hemostatic dressings in an animal surgery model demonstrated that fibrin dressings were as effective in stopping hemorrhage in the surgical repair of a vascular wound as were sutures, with all animals in the fibrin and suture groups surviving the observation period with minimal bleeding in the postocclusion period ( $<37$  mL in each group).<sup>20</sup> Numerous other studies have also demonstrated the efficacy of the dry fibrin bandage in various other surgical uses.<sup>21-25</sup>

Current literature supports effectiveness of the dry fibrin bandage; unfortunately, the bandage is very expensive (approximately \$1,000 per 4-inch square) and it has not yet been approved for routine use by the Food and Drug Administration (FDA).<sup>22</sup> Research is being directed at augmenting the fibrin to enhance its effectiveness and reduce the amount needed for each bandage, thus lowering the cost. However, this is still experimental and has so far only showed limited promise.<sup>26,27</sup> The bandage itself is also brittle and is subject to damage in rough use, limiting both its ability to be applied by a less experienced provider and its effectiveness in the military field setting. It is also difficult to insert into deep wounds because of its brittleness, further limiting its utility for military applications.<sup>28</sup>

### Microporous Polysaccharide Hemisphere

Another approach to improving hemostasis has been to apply substances that decrease the local tissue fluid and therefore increase the relative concentration of clotting factors in the wound without actually adding exogenous clotting factors such as fibrin. A small number of these types of hemostatic agents have been marketed over the past few years and have received FDA approval. The microporous polysaccharide hemisphere compound is an example of one of these recently developed agents. The microporous polysaccharide hemisphere made for first responders is sold as TraumaDEX (Medafor, Inc., Minneapolis, Minnesota) and comes in a powder that is poured into open wounds (Fig. 1). It assists in clotting by absorbing water and low molecular weight products from the blood, allowing clotting factors and platelets to become more concentrated.<sup>29</sup>

TraumaDEX is relatively safe and simple because it is bio-inert, contains no human proteins, has an extended shelf life, and can be applied in a one-step process.<sup>30</sup> Studies suggest that TraumaDEX is effective in accelerating hemostasis time in animal and human wounds.<sup>31</sup> However, a recent study has shown that TraumaDEX may be ineffective in clotting severe external hemorrhages. Alam et al.<sup>32</sup> studied TraumaDEX and other hemostatic substances in a lethal Yorkshire swine animal model created by transecting the femoral artery and vein. In that study, swine were separated into five groups with each group receiving one of five treatments: (1) no dressing, (2) standard dressing (consisting of an  $8 \times 10$ -inch absorbent pad and elastic bandage [Cinch Tight, H&H Associates, Bena, VA]), (3) standard dressing and Rapid Deployment Hemostat bandage (Marine Polymer Technologies, Danvers, MA), (4) standard dressing and QuikClot (Z-Medica, Newington, CT), and (5) standard dressing and TraumaDEX. As compared with standard treatment, the TraumaDEX dressing did not cause a statistically significant decrease in mortality.<sup>32</sup> Thus, the powder appears to be effective in accelerating hemostasis time in minor to moderate wounds,<sup>31</sup> but not in severe hemorrhaging wounds.<sup>32</sup> Because of these results, neither the USA nor the USMC chose to use TraumaDEX to treat their wounded during Operation Iraqi Freedom.

### Mineral Zeolite

Another recently developed hemostatic agent that increases the clotting factor concentration in the wound by adsorbing liquid is the mineral zeolite powder QuikClot (Fig. 2). The pow-

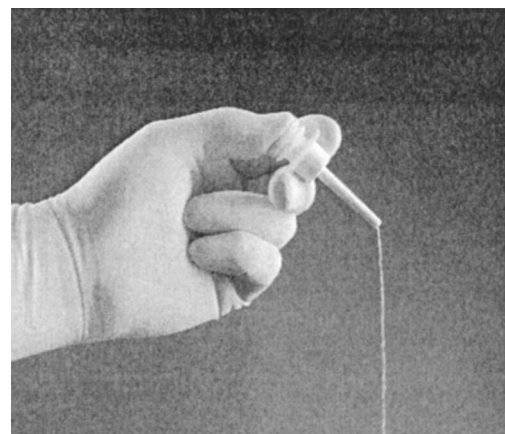


Fig. 1. TraumaDEX.



Fig. 2. QuikClot package and powder.

der is poured into the wound and increases hemostasis by adsorbing water and concentrating clotting factors in the blood. QuikClot has properties similar to those of TraumaDEX in that it is bio-inert, nonallergenic, sterile, a one-step application, and inexpensive (\$20 per packet, average wholesale price).<sup>33</sup>

Results from the study performed by Alam et al.<sup>32</sup> demonstrated that QuikClot effectively increased survival and decreased hemorrhage in a lethal groin injury model as compared to standard methods of hemorrhage control. In that animal study, the control group, which was treated with no dressing, had an 83% mortality, the group treated with only the standard dressing (which consisted of an 8 × 10-inch absorbent pad and elastic bandage) had a 33.4% mortality, and the group treated with the standard dressing and QuikClot had a 0% mortality. In addition, the group treated with both the standard dressing and QuikClot had the lowest volume of blood lost; however, this was not statistically significant compared with the control group.<sup>32</sup>

A unique side effect of QuikClot is that the adsorption of water causes an exothermic reaction. The temperature quickly rises after application to between 42°C and 44°C.<sup>32</sup> This temperature rise is transient, lasting only a few minutes. Local tissue burn injury has been shown to occur in a number of animal models; however, the investigators concluded that the risk of tissue damage was far outweighed by the benefit of increased survival when QuikClot is used to treat an otherwise uncontrollable exsanguinating hemorrhage.<sup>34</sup>

At the request of the USMC, a multiservice panel was convened at the Uniformed Services University in February 2003 to review the results of the study by Alam et al.<sup>32</sup> and to make recommendations regarding the safe use of QuikClot.<sup>34</sup> Some of these recommendations were that the product should be: used only where there is a life-threatening hemorrhage; used only on external wounds; used only after standard methods have failed to control hemorrhage; issued only to personnel who are adequately trained to apply the product; and reported each time a packet is used to ensure that the product is not used for less severe injuries.<sup>34</sup>

After the recommendations by the panel were reviewed, QuikClot was issued to U.S. Navy corpsmen to be used in treating casualties during combat operations in Iraq. Comments from a USMC after-action report showed that QuikClot might have not been as effective as the USMC had hoped. Some of the comments were:

- Wounded Iraqi civilian. Shot near brachial artery. QuikClot was applied per the instructions. The substance dried

but was flaking off. Standard direct pressure applied by corpsman proved more effective on the patient.

- Iraqi civilian shot in back with punctured spine. QuikClot applied to severe bleeding. Pressure from bleeding sprayed QuikClot away. According to LT Webb, “QuikClot was everywhere but the wound.”
- Iraqi civilian, female, shot in femoral artery. She suffered severe arterial bleeding. Patient bled out. QuikClot unable to be applied effectively due to pressure of blood flow from wound. Patient died.
- An LAR Marine was shot in the femoral artery. QuikClot was applied to the heavily bleeding wound. The pressure from the blood soon caused the QuikClot to be pushed out of the wound and rendered ineffective. A tourniquet was applied instead. The patient died.<sup>35</sup>

Although comments from the USMC report suggest that QuikClot was ineffective in the treatment of these specific wounds, the USMC comments do not reflect every individual application of QuikClot in Operation Iraq Freedom. Furthermore, in some of the above instances, QuikClot was not used according to the manufacturer's directions or USMC guidelines. On the other hand, perhaps QuikClot was ineffective in the above instances because combat setting wounds are different than laboratory-simulated wounds. The lethal groin injury model that Alam et al.<sup>32</sup> used on swine could have had blood pooling in the inguinal cavity, causing the blood to flow slower and to be more apt to clot. However, a brachial artery transection in a human might be different because of the high flow and absence of pooling at the site of application. Consequently, researchers cannot draw a definite conclusion as to its effectiveness in the overall combat setting based solely on these anecdotal reports.

### Poly-N-Acetylglucosamine

Chitin (poly-N-acetylglucosamine) is a polysaccharide biopolymer produced naturally by algae through fermentation. Both chitin and its deacetylated form, chitosan, have been shown to be effective hemostatic agents.<sup>36-39</sup> The exact mechanism of action is still under study but is postulated to be via vasoconstriction and the rapid mobilization of red blood cells, clotting factors, and platelets to the site of the injury.<sup>40</sup> The military is specifically interested in poly-N-acetylglucosamine devices as hemostatic agents because they have stable shelf lives, are easy to use, and are relatively inexpensive.

Although chitin has been shown to be effective in the treatment of minor wounds,<sup>36,37</sup> it is controversial if the product is effective in the treatment of more severe wounds. In a surface splenic laceration animal model, the chitin dressing (made by Marine Polymer Technologies, Danvers, Massachusetts) was proven to provide significantly faster coagulation than fibrin glues (22.9 seconds vs. 172.9 seconds,  $p < 0.01$ ;  $p$  values are written as reported in the original article).<sup>41</sup> However, in a recent study by Pusateri et al.,<sup>42</sup> a chitin dressing (Marine Polymer Technologies) showed no significant advantage over the standard 10.2 × 10.2-cm gauze sponge (Nu Gauze general-use sponges, Johnson & Johnson Medical, Inc., Arlington, Texas) in stopping bleeding from a severe large venous hemorrhage and hepatic injury in swine.

Chitosan has been shown to be more efficacious than chitin in

controlling severe hemorrhage from simulated combat wounds. In another study by Pusateri et al.,<sup>43</sup> chitosan was demonstrated to reduce blood loss (264 mL vs. 2,879 mL,  $p < 0.01$ ;  $p$  values are written as reported in the original article) and increase survival (87.5% vs. 28.6%,  $p = 0.04$ ;  $p$  values are written as reported in the original article) as compared with gauze control groups in a severe hepatic injury in swine. The USA has issued its Special Forces Units specific chitosan dressings manufactured by HemCon Hemorrhage Control Technologies (Lake Oswego, Oregon) (Fig. 3). Anecdotal case reports from Operation Iraqi Freedom about the efficacy of HemCon dressings have been positive, including an isolated report of a gunshot wound to the right foot that suggested superiority of a HemCon dressing with direct pressure over the standard medical dressing. American medical personnel had primarily treated the wound with a standard bandage, but soon after the bandage was soaked with blood. The bandage was removed and a HemCon dressing was applied with 4 minutes of direct pressure. After the pressure on the dressing was removed, the medic noted that hemorrhage control had been achieved (Robert Miller, personal communication).

### Microporous Hydrogel-Forming Polyacrylamide

The BioHemostat (Hemodyne, Richmond, Virginia) is part pressure dressing and part hemostatic dressing. When inserted into a wound, the BioHemostat functions by absorbing fluid and expanding to occlude the wound and create backpressure to stop bleeding. The device consists of two components, a liquid absorbing core attached to a traditional bandage.<sup>44</sup> The core is composed of a microporous hydrogel-forming polyacrylamide that has the potential for rapid expansion.<sup>45</sup> According to Carr et al.,<sup>45</sup> the material has the capacity to absorb 1,400 times its weight. The core's outer shell is composed of an elastomeric polymer, ethylene-vinyl acetate copolymer that can be treated with hemostatic agents, antibiotics, and analgesics.<sup>45</sup> Once applied, the dressing will remain until patient arrives at a facility for definitive care. The manufacturer asserts that the BioHemostat has the potential to stop arterial hemorrhaging while also saving the limb from ischemic damage and amputation. This dressing concept is ideal for far-forward operators because of its small size, simplicity, and low monitoring requirements once inserted. No data are available to assess BioHemostat's efficacy in a combat setting and further research should be performed.



Fig. 3. HemCon dressing.

### Conclusion

Although the literature on new techniques for bleeding control and clotting is extremely limited, we have reviewed current publications as well as anecdotal data from unpublished military reports coming from Operation Iraqi Freedom. Although there is not yet a single hemorrhage control mechanism that will be universally effective, there are a number of products that show promise. One approach is to increase the supply of clotting factors, such as fibrin, to the wound to induce rapid hemostasis. Multiple studies demonstrated that the dry fibrin bandage is effective at enhancing clot formation in hemorrhage situations. Unfortunately, the bandage itself is brittle, making it difficult to insert into deep wounds and subject to being fractured when transported by combat medical personnel. The fibrin bandage is also not yet approved by the FDA because of concern about its production from either human or bovine plasma.

Another approach to hemorrhage control is to add a substance to the wound that increases the concentration of local clotting factors. The recently developed hemostatic agents that fall into this category are microporous polysaccharide hemosphere (TraumaDEX), mineral zeolite (QuikClot), and poly-*N*-acetylglucosamine (HemCon). All three types of products are relatively inexpensive, easy to use, and easy to apply. TraumaDEX appears to be effective in treating minor to moderate wounds<sup>31</sup> but is less effective in treating severe external hemorrhage.<sup>32</sup> QuikClot, on the other hand, demonstrated efficacy in treating severe external hemorrhages in the laboratory, but has been initially reported as less efficient when used to treat the wounded in Iraq.<sup>35</sup> There is anecdotal evidence from Operation Iraqi Freedom that HemCon is effective (Robert Miller, personal communication), but more data about the agent's performance in a combat setting are needed. None of the hemostatic products discussed herein have anything other than anecdotal data supporting their effectiveness in combat settings when applied by combat medical personnel; thus, more research needs to be performed to draw definite conclusions.

Finally, the combination pressure/hemostatic dressing BioHemostat may provide the hemorrhage control of traditional pressure bandages without inducing necrosis of the distal limb and therefore worsening the tissue injury. However, no research yet published has tested the efficacy of this product on combat wounds.

Uncontrolled hemorrhage is the leading cause of death during the prehospital period in combat.<sup>1-3</sup> Immediate hemorrhage control by an on-scene first responder is the most effective method of limiting patient mortality. A hemorrhage control device that is effective, inexpensive, easy to transport, and easy to apply may drastically reduce patient mortality on the battlefield.

### References

1. Bellamy RF: Causes of death in conventional warfare. *Milit Med* 1984; 149: 55-62.
2. Sauaia A, Moore FA, Moore EE, et al: Epidemiology of trauma deaths: a reassessment. *J Trauma* 1995; 38: 185-93.
3. Acosta JA, Yang JC, Winchell RJ, et al: Lethal injuries and time to death in a level one trauma center. *J Am Coll Surg* 1998; 186: 528-33.
4. Regel G, Stalp M, Lehmann U, et al: Prehospital care, importance of early intervention on outcome. *Acta Anaesthesiol Scand* 1997; 110: 71-6.
5. Zimmerman L, Veith I: *Great Ideas in the History of Surgery*, Chap 3, p 31. San Francisco, CA, Norman Publishing, 1993.

6. Mabry RL, Holcomb JB, Baker AM, et al: United States Army Rangers in Somalia: an analysis of combat casualties on an urban battlefield. *J Trauma* 2000; 49: 515-29.
7. Sierra D: Fibrin sealant adhesive systems: a review of their chemistry, material properties and clinical applications. *J Biomat Appl* 1993; 7: 309-52.
8. Grey E: Fibrin as a hemostatic in cerebral surgery. *Surg Gynecol Obstet* 1915; 21: 452-5.
9. Holcomb JB, Pusateri AE, Hess JR, et al: Implications of new dry fibrin sealant technology for trauma surgery. *Surg Clin North Am* 1997; 77: 943-52.
10. Kendrick B, Coates JB (editor in chief): Medical Department United States Army in World War II, Blood Program in World War II, p 364. Washington DC, Office of the Surgeon General, Department of the Army, 1964.
11. Ochsner G, Maniscalco-Theberge M, Champion H: Fibrin glues as a hemostatic agent in hepatic and splenic trauma. *J Trauma* 1990; 30: 884-7.
12. Brands W, Haselberger J, et al: Treatment of ruptured kidney by gluing with highly concentrated human fibrinogen. *J Pediatr Surg* 1983; 18: 611-13.
13. Saltz R, Dimick A, Harris C, et al: Application of autologous fibrin glue in burn wounds. *J Burn Care Rehab* 1989; 10: 504-7.
14. Marchac D, Pugash E, Gault D: The use of sprayed fibrin glue for facelifts. *Eur J Plast Surg* 1987; 10: 139-42.
15. Steuin J, Frapier J, Colson P: Fibrin sealant for early repair of acquired ventricular septal defect. *J Thorac Cardiovasc Surg* 1992; 104: 748-51.
16. Reiss RF, Oz MC: Autologous fibrin glue: production and clinical use. *Trans Med Rev* 1996; 10: 85-92.
17. Jackson MR, Friedman SA, Carter AJ, et al: Hemostatic efficacy of a fibrin sealant-based topical agent in a femoral injury model: a randomized, blinded, placebo controlled study. *J Vasc Surg* 1997; 26: 274-80.
18. Larson MJ, Bowersox JC, Lim RC: Efficacy of a fibrin hemostatic bandage in controlling hemorrhage from experimental injuries. *Arch Surg* 1995; 130: 420-2.
19. Holcomb JB, MacPhee MJ, Hetz SP, et al: Efficacy of a dry fibrin sealant dressing for hemorrhage control following ballistic injury. *Arch Surg*, 1998; 113: 32-5.
20. Sondeen JL, Pusateri AE, Coppes VG, et al: Comparison of 10 different hemostatic dressings in an aortic injury. *J Trauma* 2003; 54: 280-5.
21. Holcomb JB, Pusateri AE, Harris RA, et al: Effect of dry fibrin sealant dressings versus gauze packing on blood loss in grade V liver injuries in resuscitated swine. *J Trauma* 1999; 46: 49-57.
22. Holcomb JB, Pusateri AE, Harris RA, et al: Dry fibrin sealant dressings reduce blood loss, resuscitation volume, and improve survival in hypothermic coagulopathic swine with grade V liver injuries. *J Trauma* 1999; 47: 233-42.
23. Morey AF, Anema JG, Harris RA, et al: Treatment of grade 4 renal stab wounds with absorbable fibrin adhesive bandage in a porcine model. *J Urol* 2001; 165: 955-8.
24. Cornum RL, Morey AF, Harris R, et al: Does the absorbable fibrin adhesive bandage facilitate partial nephrectomy? *J Urol* 2000; 164: 864-7.
25. Halfpenny W, Fraser JS, Adlam DM: Comparison of 2 hemostatic agents for the prevention of postextraction hemorrhage in patients on anticoagulants. *Oral Surg Oral Med Oral Pathol* 2001; 92: 257-9.
26. Rothwell SW, Fudge JM, Reid TJ, et al:  $\epsilon$ -Amino caproic acid additive decreases fibrin bandage performance in a swine arterial bleeding model. *Thromb Res* 2003; 108: 341-5.
27. Rothwell SW, Fudge JM, Chen W, et al: Addition of a propyl gallate-based procoagulant to a fibrin bandage improves hemostatic performance in a swine arterial bleeding model. *Thromb Res* 2003; 108: 335-40.
28. Gillert DJ: New Bandage Stops Hemorrhaging. *Journal American Forces Press Service*, NNMC The Journal January 22, 1999. Available at [http://www.dcmilitary.com/navy/journal/archives/jan22/j\\_c12299.html](http://www.dcmilitary.com/navy/journal/archives/jan22/j_c12299.html); accessed August 2003.
29. Ereth MH, Dong Y, Gordon EA, Nuttall GA, Oliver WC: Microporous Polysaccharide Hemospheres Provides Effective Topical Hemostasis in a Human Modified Bleeding Time Incision Model, Annual Meeting of the American Society of Anesthesiology, September 2002. Available at <http://www.nataonline.com>; accessed July 2003.
30. Medafor Hemostatic Polymer Technologies homepage: MPH technology, MPH Features and Benefits. Available at <http://www.medafor.com/technology.html>; accessed July 2003.
31. Medafor Hemostatic Polymer Technologies homepage: MPH Research. Available at [www.medafor.com/research.html](http://www.medafor.com/research.html); accessed July 2003.
32. Alam HB, Uy GB, Miller D, Koustova E, et al: Comparative analysis of hemostatic agents in a swine model of lethal groin injury. *J Trauma*, 2003; 54: 1077-82.
33. QuikClot homepage: Available at <http://www.quikclot.com>; accessed July 15, 2003.
34. Burris D: Memo to LCDR J.A. DaCorta, Expeditionary Medicine, Marine Corps Warfighting Lab, Quantico, VA, February 26, 2003.
35. Field Report Marine Corps Systems Command Liaison Team, Central Iraq, April 20 to April 25, 2003.
36. Kulling D, Vournakis JN, Woo S, et al: Endoscopic injection of bleeding esophageal varices with a poly-N-acetyl glucosamine gel formulation in the canine portal hypertension model. *Gastrointest Endosc* 1999; 49: 764-71.
37. Cole DJ, Connolly RJ, Chan MW, et al: A pilot study evaluation the efficacy of a fully acetylated poly-N-acetylglucosamine membrane formulation as a topical hemostatic agent. *J Surg* 1999; 126: 510-17.
38. Brandenburg G, Leibrock LG, Shuman R, Mallette WG, Quigley H: Chitosan: a new topical hemostatic agent for diffuse capillary bleeding in brain tissue. *Neurosurgery* 1984; 15: 9-13.
39. Klokkevold PR, Subar P, Fukayama H, Bertolami CN: Effect of chitosan on lingual hemostasis in rabbits with platelet dysfunction induced by epoprostenol. *Oral Maxillofac Surg* 1992; 50: 41-5.
40. Ikeda Y, Young LH, Vournakis JN, Lefer AM: Vascular effects of poly-N-acetylglucosamine in isolated rat aortic rings. *J Surg Res* 2002; 102: 215-20.
41. Chan MW, Schwaizberg SD, Demcheva M, Vournakis J, et al: Comparison of poly-N-acetylglucosamine with absorbable collagen and fibrin sealant for achieving hemostasis in a swine model of splenic hemorrhage. *J Trauma* 2000; 48: 454-8.
42. Pusateri AE, Modrow HE, Harris RA, Holcomb JB, et al: Advanced hemostatic dressing development program: animal model selection criteria and results of a study of nine hemostatic dressings in a model of severe large venous hemorrhage and hepatic injury in swine. *J Trauma* 2003; 55: 518-26.
43. Pusateri AE, McCarthy SJ, Gregory KW, et al: Effect of a chitosan-based hemostatic dressing on blood loss and survival in a model of severe venous hemorrhage and hepatic injury in swine. *J Trauma* 2003; 54: 177-82.
44. Dodes RL: Blood Money. *Washington Business Forward*, December 2001. Available at <http://www.bizforward.com/wdc/issues/2001-12/bioscience/>; accessed October 2003.
45. Carr ME, Wnek G, Cohen K, Ward K, Ivatory R, et al: The BioHemostat-Acute Treatment Modality for High Pressure Bleeding-Changing the Treatment Paradigm to "Saving the Patient and Sparring the Limb." Available <http://www.vcu.edu/vcures/docs/ATACCC200120BioHemostat20Abstract.pdf>; accessed February 2004.

