

Novel Haemostatic Dressings

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Introduction

The problem of haemorrhage is well recognised by the deploying military medical community. In 1970 Maughon, after examining the combat deaths of 2600 American servicemen in Vietnam, articulated the simple requirement that more be done - on the battlefield - to prevent death from haemorrhage:

"The striking feature was to see healthy young Americans with a single injury of the distal extremity arrive at the magnificently equipped field hospital, usually within hours, but dead on arrival!"[1]

This was reinforced by Rocko in 1982, who wrote of the need to prevent "public exsanguination" in civilian trauma [2]. Leaving aside unsurvivable CNS trauma, the commonest cause of preventable death in combat remains haemorrhage [3]. In Vietnam 23.9% of casualties that survived to reach a hospital died of haemorrhagic shock [4]. Thirty eight percent of those who succumbed to haemorrhage in the pre-hospital setting bled to death from wounds where control could have been achieved simply by direct pressure [5].

In recent conflicts, extremity trauma has accounted for 54% of wounds by anatomical region [6] and deaths from extremity trauma remain as prevalent in recent conflicts as in Vietnam [7]. Analysis of autopsy data from American casualties sustained in Iraq and Afghanistan has shown that over 80% of casualties with potentially survivable wounds - died from haemorrhage. Of these, approximately 20% died from wounds in the neck, axilla and groin [8]. As death from haemorrhage can occur within minutes of injury, prompt effective treatment of any haemorrhage is paramount [9].

In the Defence Medical Services (DMS) this has seen a re-design of the protocols issued to pre-hospital care providers, with specific indications as to when to employ techniques from an armamentarium of treatments that includes; pressure, elevation, elasticated field dressings, tourniquets and novel haemostatic dressings [10] (Figure 1). The efficacy and rationale behind the use of tourniquets has been discussed in this journal previously [11] and will not be repeated. However, significant numbers of wounds remain that have accessible bleeding points but are not suitable for tourniquet application. These wounds have been described as "nontourniquetable but compressible" [8].

In the tactical situation, application of sustained effective pressure is difficult. There is a poorly defined subgroup of traumatic wounds that due to location [7], complexity [9] or coagulopathy [12] require adjuncts to direct pressure in order to arrest bleeding. It is in dealing with these injuries, particularly in the pre-hospital and transport environment that novel haemostatic dressings have the greatest role to play. It may be where we can have the greatest effect on mortality and morbidity by reducing blood loss and the need for haemostatic resuscitation.

Whilst often controversial, it is always appropriate to regularly examine the scientific basis upon which novel products, techniques and developments are introduced and delivered to the battlefield. The American model has seen a variety of products developed via different research and funding streams and despite frequent joint force operations, there has been a confusing adoption of several different dressings within the individual

American uniformed services. This has not occurred within the DMS. The UK's initial choice of dressing was simply based on pragmatism [13]. It was also, for that reason, to be subject to annual review [11]. DMS clinicians and Medics are happy with the training they receive in utilising all the products currently fielded within the DMS [14], but it is unclear whether the dressings are effective?

Forty four unexpected survivors among British service personnel wounded since 2003 have been reported[15]; it is unknown whether novel haemostatics have played a significant part, or any role at all, in these successes. It may represent a defect in the application injury coding scores unused to severe military blast and ballistic trauma. In written evidence to the Select Committee on Defence, the introduction of several enhanced haemostatic products and devices (HemCon®, QuikClot®, CAT tourniquet and the new FFD (in addition to the team medic)) were credited with saving "over three lives by 2006" [16].

This review examines the scientific evidence that led to the adoption of these novel haemostatic dressings and the clinical evidence as to their effectiveness now available. It will concentrate on those products currently available or recently used within the military environment.

First aid (professional)

Treatment guidelines 2b

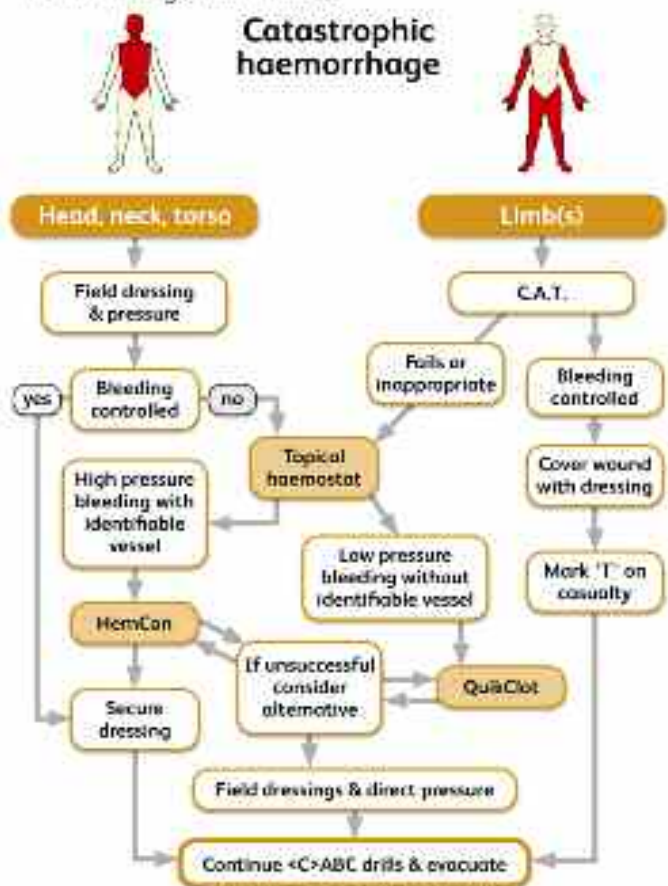


Figure 1. Treatment algorithm for Catastrophic haemorrhage taken from Clinical Guidelines for Operations, 2008 [10]

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The Ideal Haemostatic Dressing

The ideal haemostatic dressing should clearly be cheap, effective, simple to apply by either the patient or provider, easy to remove, stable at extremes of temperature, safe to both patient and provider, and logistically acceptable. One American working group also defined a requirement to “stop large vessel arterial and venous bleeding within two minutes of application to a wound, in an actively bleeding environment through a pool of blood” [17]. It is difficult to attribute all of those qualities to any currently issued dressing. Current novel haemostatic dressings can be grouped as follows (Table 1).

Class	Product	Active Agent	Cost	FDA approval	Deployed
Factor Concentrators	QuikClot®	Zeolite	£10	Yes	Yes
	QuikClot ACSTM™+		£16	Yes	Yes
	TraumaDex™	Polysaccharide Hemospheres	£20	Yes	
	WoundStat™	Smectite mineral clay	£30	Yes	Withdrawn
Mucoadhesive Agents	Hemcon®	Chitosan	£66	Yes	Yes
	Celox™		£20	Yes	
	TraumaStat™		£66	Yes	
	RDH	Poly-N-Acetyl Glucosamine	N/A	Yes	
	mRDH		£250	Yes	
	Super QR	K Fe Oxyacid Salt Hydrophilic polymer	£10	No	
Procoagulant Supplements	Dry Fibrin Sealant	Fibrinogen Thrombin C++ FXIII	>£550	No	Yes (1 pt)
	TachoComb H®	Collagen Thrombin Fibrinogen	N/A	No	
	CombatGauze	Kaolin	£30	Yes	Yes

Table 1 Currently available novel haemostatics and their characteristics

Factor Concentrators

These include products such as QuikClot®, QuikClot ACS™+, WoundStat™, TraumaDex™, and Self-Expanding Hemostatic Polymer (SEHP).

QuikClot®

QuikClot® (Z-Medica, Wallingford, CT) is a granular preparation composed of sodium, silicon, aluminium and magnesium oxides with small amounts of quartz [18] that works by adsorbing the water component of blood in an exothermic reaction, thereby concentrating clotting factors, it also supplies Ca²⁺ ions and activates platelets as further adjuncts to coagulation [19]. The exact mode of action of QuikClot® has never been proven experimentally [20]. In 2002 it was approved by the Federal Drugs Administration (FDA) “as an external temporary traumatic wound treatment to achieve hemostasis for moderate to severe bleeding” [21].

In 2003 both the United States Navy and Marine Corps adopted QuikClot®. In the planning for Operation Iraqi Freedom the intent was to issue it to every Marine engaged in combat operations. This was in part due to its performance in an Office of Navy Research grant funded comparative study, utilising a swine complex groin wound model of haemorrhage to examine the effectiveness of QuikClot® against other commercially available dressings [22]. This model involved transecting the femoral vasculature and soft-tissues of a pig at the level of the inguinal ligament. After a five-minute delay the dressing in question and direct pressure were applied. After a further 30 minutes 1000mls of normal saline 0.9% was administered over a thirty-minute period. Mortality was 83% without treatment, 33.4% with standard gauze and 0% with QuikClot® [22].

When QuikClot® was compared against HemCon®, using the same injury model but a different resuscitation protocol (6% Hetastarch in 500mls 0.9% normal saline given over 30 minutes, begun 15 minutes following injury) it outperformed its rival reducing quoted mortality to 0% compared with 28.6% for HemCon® [23]. The performance of HemCon® was noted as providing either complete arrest of haemorrhage (5/7 animals) or being completely ineffective (2/7 animals). This was postulated to be related to ‘manufacturing issues’ and variability in the quality of the HemCon® end product.

The main criticisms of QuikClot® have involved the exothermic nature of the reaction of the zeolite. When added to water alone temperatures of 100°C are produced [24]. Information regarding its use is rather mischievously included on the US Army Medical Material Agency website under “Hot Topics.” [25]. In his 2003 study Alam recorded maximum temperatures of 42–44°C, and the following year zeolite preparations achieved wound temperatures of 51–57°C [22, 23]. Other investigators have reported wound temperatures of 58°C using either the original granules or the ACS preparation [30]. Applied to a 6mm swine femoral arteriotomy wound through a pool of blood, wound temperatures of 70.8°C have been recorded [27].

When United States Air Force (USAF) investigators examined the exothermic nature of the reaction in a swine model of tissue injury they demonstrated full thickness burns at the edges of the groin wounds. Even greater increases in temperature (over 100°C at the wound edge) were reported. It is unclear what exact deep wound temperatures were recorded when QuikClot® was used as per the manufacturers instructions [28].

Criticisms of the granular nature of the agent and the difficulty in applying it to an actively bleeding wound [29] has seen the product converted into a “teabag” with granules placed into a meshed bag (QuikClot® Advanced Clotting Sponge (ACS)) and now QuikClot® beads within a bag with interior baffles creating four compartments (QuikClot ACS+™). The beads are zeolite with a larger diameter (1.7–2.4 mm) than the granules (0.4–0.8 mm) and are equally as effective in a swine groin injury model with the same maximum wound temperatures achieved [30]. The bagged preparations are said to be easier to remove at the definitive care facility and ACS+ has a silicon rod within the bag for ease of location on wound radiographs [31].

Clinical reports are now being published regarding the use of QuikClot® in military and civilian trauma settings. The only case series published, examined the use of QuikClot® in 103 cases ranging from the US military in Iraq to first responders and trauma surgeons in a civilian EMS [32]. It is a retrospective, non-consecutive observational study. The data was collected by completion of “self reporting survey sheets” with three-quarters of those completing the sheets being interviewed by the lead investigator. A representative example of a completed sheet is at figure 2.

Analysis of all 103 cases demonstrated an overall efficacy rate of 92%. Of the eight failures, five occurred in non-body cavity wounds making QuikClot® 94% effective in achieving haemostasis on extremity and superficial thoraco-abdominal wounds, in those cases included in this study. Only medical officers and trauma surgeons reported failures of the product to achieve haemostasis. This was thought to be due to the moribund condition of the patient or the inability to place QuikClot® adjacent to the site of haemorrhage. There were three cases of burn injury attributed to the use of QuikClot® and one of these required formal skin grafting.

Surprisingly for a product never intended for intra-corporeal use the study documented 20 such episodes, one of which had been previously reported in the literature [33]. In each instance application of QuikClot® was deemed a “last resort” measure but was effective in 18/20 cases with only one serious complication. The complication manifested itself two months following application of QuikClot® to a ballistic injury involving the sacro-iliac joint. Ureteric obstruction occurred secondary to scarring

from an “intense foreign body reaction”. Complex ureteric reconstruction surgery was then required [32]. Although last-ditch use in an *in extremis* patient in the field setting was deemed too severe a test of QuikClot® by the authors, it is interesting to note that this last-ditch off-licence intra-corporeal use was surprisingly effective. Surgical exposures clearly allow accurate direct placement of the product onto the site of bleeding by surgeons.

Whilst QuikClot® is biologically inert, it is not broken down or metabolised by the body and needs physical removal. As military and trauma wounds will require surgical debridement this can be performed in the operating theatre either by sharp debridement or copious irrigation. The consequences of leaving QuikClot® within a swine wound model are granuloma and abscess formation [28]. Whereas the original FDA reports stated that QuikClot® is “*designed and packaged to be easily packed, carried and applied using only one hand*”; [21] in the DMS the effective application of QuikClot® is deemed a two-person technique. It involves wiping away excess blood, pouring the zeolite granules into the wound and then applying compression through a standard dressing [10]. There are currently no reports relating to the use of QuikClot® by DMS personnel within open source material, but successful intra-corporeal use has been observed in patients evacuated to the Royal Centre for Defence Medicine (RCDM) [34].

[22]. Based on the results of this study neither the United States Army nor Marine Corps adopted TraumaDex™ [29].

S.E.H.P

Self-Expanding Hemostatic Polymer SEHP (Payload Systems Inc, Cambridge, MA) comprises a powder polymer within a small permeable bag that can be utilised in a “set and forget” manner in that once placed into the defect, there is no stated requirement for the provider to apply external compression. On packing into a wound it controls bleeding by expanding to exert a pressure on the wound surface and by absorbing the “aqueous phase” of blood, concentrating clotting factors locally [36]. SEHP appears to absorb water in a non-exothermic reaction. Early animal experimental work is again ‘promising’ but it is not currently licensed for use in humans.

WoundStat™

WoundStat™ (Trauma Inc, Bethesda, MD) is a granular preparation of compounds including a smectite clay mineral and a cross-linked poly-acrylic acid. The non-biodegradable powder is poured into wounds where it absorbs water concentrating clotting factors in a non-exothermic manner [24]. It also exhibits a degree of adherence to the wound to aid haemostasis.

In two early comparative swine studies utilising a 6mm femoral arteriotomy wound all WoundStat™ animals survived compared with none treated with [37,38]. The resuscitation component of this study was criticised as being too aggressive, thereby creating a vicious circle of bleeding, fluid administration, dilutional coagulopathy and further bleeding. These results are also clearly at odds with the original QuikClot® studies [22,23,30].

The United States Army was in the process of replacing HemCon® and QuikClot® with WoundStat™ in some theatres of operation [39] and 17000 sachets were purchased in October 2008. [40] However, as of July 2009 a permanent suspension of its use was implemented by the US military due to local tissue damage [38], and observed significant remote embolic phenomena in test animals [41].

Mucoadhesive Agents

HemCon®

HemCon® (HemCon® Medical Technologies Inc, Portland, OR) is a chitosan-based dressing. Chitosan is the predominately (70%) de-acetylated form of chitin (poly-β[1→4]=N-acetyl-D-glucosamine) a complex polysaccharide naturally occurring in shrimp exoskeletons. The original dressing came in a variety of sizes and has a wafer like consistency.

The dressing received FDA approval in 2002 for the emergency treatment of external haemorrhage and was adopted by the United States Army, who had funded its development [17]. It was decided to make them widely available with “*an issue of one for every deployed soldier, three for every Combat Life Saver, and five to every Medic in the combat theatre.*” [42] This was funded as part of a \$30 million requirements contract for haemostatic control bandages [43].

Chitosan had been noted to effect haemostasis in a variety of live animal models including feline brain bleeding [44] and human intestinal incisions [45]. This is due to direct adherence to the wound [46], although it may also aid recruitment of red blood cells and platelets [47]. There is limited evidence to suggest that it may have some bactericidal action in a murine contaminated wound model [48]. It may also aid wound healing [49].

A United States Army funded study found HemCon® to be superior to standard gauze in improving survival when applied to a swine model of severe liver injury [50]. This is considered a model of severe venous bleeding, low pressure high-flow, and may not be representative of the wounds encountered in the pre-hospital environment.

As previously documented, in early studies, when HemCon® was applied to mixed arterial and venous groin wounds in swine it was

QuikClot® Sealed Hemostatic Agent Evaluation Sheet

Evaluator Information
 Name & Rank: On File
 Company/Organization: -
 City, State, Zip, Country: 10th Mountain Div
 Phone: DSO 318-251-2411 Email: 1 Date of Use: 15Oct09

Description of Injury
 Location on Body: R lower leg and R lower thigh
 Size and Shape: R Lower Leg = severed limb, and inner thigh = incision 6 inches
 Arterial, Venous, Capillary, Unknown: R Lower leg: Arterial and venous and lower thigh was Arterial
 Source/ Cause of Wound: Mine Blast

Treatment Prior to the Use of QuikClot® Hemostat
 Length of time between injury and initial treatment: 1 min.
 Treatment attempted before QuikClot® hemostat: Tourniquet and pressure dressing
 Result of treatment: Used quik clot sup on lower thigh wound due to amount of bleeding. And used QC on stump for further action in awaiting bleeding stopped.

Additional Information / Comments:
 I have used the video of the rig and see how easy at the quick positive results of the inner lack of bleeding. Not aware.

Application of QuikClot® Hemostat
 Estimate blood pressure at time of application: 90/66
 Describe application of QuikClot® Hemostat: Wiped wound clear to T.D. blood source and used approx. 1/2 - 1/3 of the bag to stop the bleeding
 Wipe away blood first? Yes
 Amount used: 1/2 - 1/3
 Action immediately after application: dropped my jaw in complete amazement and then applied an ace 4x8's and then an Ilevu pressure dressing
 Degree to which QuikClot® hemostat controlled bleeding: 100%
 Time to control: 1-3 seconds. And viewed no blood through the top layer of QC applied to the wound

Estimated blood pressure after application: Keep on hand 1 into vein. 134. 4 mg of Morphine. And you I know that I should have done a slow push through the IV.

Fluid Resuscitation
 Previous to or Following QuikClot® Hemostat Application: 500 ml of Hemotack 6% followed by 1,000 ml of Ringer's
 Effect, if any: yes elevated BP to approx 100/40

Follow Up
 Follow up time: None
 Complications: Unknown
 Remarks: Hopefully a man gets home to his kids soon because of QC

Overall Evaluation
 Did QuikClot® Hemostat improve outcome? Most definitely
 Would you use QuikClot® Hemostat again? Yes very much so
 Additional Information: It would be a shame to EVER see this item fail in the theatre do so negative press or some
 Comments: our most respected opinion is that it cause to much additional work on these behalf to repair the injury in a whole. Sorry for the negativity I just really believe in the positive effects of this product and will continue to be more than passionate about my feelings for this product. It has given me more confidence in what body I have available to me and that I can honestly look a wounded soldier in his eyes and say don't worry brother I won't let you down. You will make it home alive. Please do everything in your power to keep this in our military inventory. Again thank you for making me to provide a human the basic right to live and to someday be able to function in life once again. US Army Combat Medic and Ranger

Figure 2 An example of the self reporting sheets. Reproduced from J Trauma with permission [32]

TraumaDex™

TraumaDex™ (Medafor, Minneapolis MN) is a powder of microporous polysaccharide hemospheres that acts as a “molecular sieve” [35] absorbing the water component of blood and therefore concentrating clotting factors. It was not as effective as QuikClot® in a swine groin wound model of haemostasis, with overall mortality using TraumaDex™ no different from standard dressings

either completely effective (5/7 animals) or ineffective, this was thought to be due to quality assurance issues [23]. These were addressed and the new dressings were tested at the USAISR “expeditiously (in one day)” [51] before being declared suitable for utilization in current theatres of operations.

In 2008 HemCon[®] was again examined in a swine femoral vasculature complete transection model. It performed no better than standard gauze with respect to mortality [52]. In this study HemCon[®] was applied after 30 seconds of uncontrolled haemorrhage. Direct manual pressure was maintained for five minutes through an abdominal pack and the wound examined. Failure to achieve haemostasis was defined as “blood pooling outside the wound.” Aggressive fluid resuscitation commenced on application of the dressing, with lactated Ringer’s solution delivered at 165ml/min in an attempt to maintain mean arterial blood pressure (MABP) at pre-injury levels. During the 120-minute study period there were 8/10 dressing failures in the HemCon[®] group with three deaths. Standard gauze dressings resulted in 5/10 dressing failures with one death.

The significant differences between the Alam 2004 [23] and Englehart 2008 [52] studies were the duration of uncontrolled haemorrhage and the resuscitation protocols. The uncontrolled haemorrhage lasted three minutes in 2004 and 30 seconds in 2008, leading to lower MABPs on application of the HemCon[®] in 2004.

The differing resuscitation strategies saw no animal improve MABP in the initial study whereas the high volume crystalloid strategy in 2008 saw MABP rally then fall steadily with failure of haemostasis and further bleeding. Therefore we see how HemCon[®] performed better in the model with lower MABP on application and “hypotensive” style resuscitation. Although in both studies it did not statistically outperform the standard dressing control.

In high pressure uncontrolled models of arterial haemorrhage such as swine 4.4 mm punch biopsy of the aorta, HemCon[®] has been unable to sustain haemostasis despite initial control of bleeding in 5/7 test animals [53]. With a 6mm femoral artery punch biopsy injury HemCon[®] has been unable to influence mortality and although able, once again, to gain control of the initial haemorrhage in 6/10 animals was able to maintain haemostasis in only 1/10 pigs for the 180 minute study period. Notably, failed to control the initial haemorrhage in 0/6 and was therefore excluded from the remainder of the study [38].

Chitoflex

Early user feedback criticised the wafer texture of the original HemCon[®] dressing and its inability to be placed into small wounds or cavities, requiring it to be cut into pieces [42]. This resulted in the development of ChitoFlex. ChitoFlex is a chitosan dressing in a more flexible format with two active sides specifically to be delivered into wound tracts perhaps reflecting the practise of combat medics folding HemCon[®] on itself to create an ad hoc two-sided product [54]. When compared with standard gauze and TraumaStat[™] in a swine groin wound model there was no difference between ChitoFlex and standard gauze, although advocates of ChitoFlex would criticise that it was not used as the manufacturers advised.

Celox[™]

Celox[™] (SAM Medical Products, Newport OR) is a chitosan based dressing in a granular format. When compared against HemCon[®], QuikClot[®] and standard gauze in a swine groin model of fatal haemorrhage as described by Alam et al, Celox[™] performed well with 12/12 animals surviving. There was no statistically demonstrable difference between the remaining dressings in terms of survival. However, QuikClot[®] saved 11/12 and therefore the failure to achieve statistical significance is due to failure in a single animal. Post-mortem inspection of this specimen revealed that the QuikClot[®] had not reached the vessels and had “migrated to an adjacent soft tissue void” [55].

There are two clinical case series examining the use of HemCon[®] in military [42] and civilian [56] trauma systems. Wedmore

reported the early military experience based upon the verbal reports from Special Forces medical providers in far forward positions. 64 case reports were deemed suitable and the dressing was successful in 97% of these cases. In two-thirds of episodes standard gauze dressings had been unsuccessful prior to the application of HemCon[®]. There were no reported adverse effects attributable to the dressings. [42]

Civilian emergency medical providers have had a less successful but still positive experience with HemCon[®]. A retrospective questionnaire based survey of the experience of Portland firefighters, 60% of whom were also trained as paramedics is presented. Over a 15-month period 37 episodes were recorded of which 34 had sufficient data recorded to be included in the study. HemCon[®] controlled haemorrhage in 79% of cases. In 25/34 direct pressure with gauze and adjuncts such as elevation had failed to stop the bleeding. The bleeding was ascertained by the acute responder as being venous (13/34), arterial (12/34) or unknown (9/34). Review of the cases where HemCon[®] had proven ineffective concluded that user error had contributed to the failure of haemostasis (6/7 cases). Again there were no reported adverse effects [56].

TraumaStat[™]

TraumaStat[™] (Ore-Medix, Lebanon, OR) is a sponge like dressing composed of silica fibres coated in chitosan. Polyethylene maintains the porous nature of the sponge that together with the number of silica fibres gives each sponge a vast surface area (110m²/g) [52]. One Oregon based group has utilised a swine groin wound model to examine its effectiveness against HemCon[®] and ChitoFlex in two separate studies concluding that TraumaStat[™] was more effective [54].

Procoagulant Supplementors

Combat Gauze[™]

Combat Gauze[™] (Z-Medica, Wallingford, CT) sees Kaolin bonded to a polyester/ rayon gauze that can be stuffed into cavity wounds or applied onto open wounds like a standard dressing. Kaolin is a layered clay that has as its active ingredient aluminium silicate. It has historically been utilised to monitor the effects of heparin therapy, as it is a potent activator of the intrinsic clotting system [57]. It has been shown to be as effective as QuikClot[®] in causing in vitro porcine blood to coagulate without any excess heat being generated [24]. Z-Medica is currently the recipient from the United States Department of Defense of a US\$ 3.2 million grant for ongoing trials.

Live animal modeling has seen a kaolin coated gauze stop haemorrhage in a swine model of femoral artery and vein transection as well as injuries to the liver, spleen and mesentery. This work was presented as an abstract at the Special Operations Medical Association Meeting (SOMA) 2007 [58] but has yet to surface as part of the mainstream medical literature.

Combat gauze is currently issued to US service personnel deployed on operations, and since the withdrawal of WoundStat[™] from frontline use it is the preferred haemostatic dressing [41].

Dry Fibrin Sealant Dressing

Dry Fibrin Sealant Dressing (DFSD, American Red Cross Holland Laboratory, Rockville, MD) consists of supra-physiological concentrations of human fibrinogen (15mg/cm²), human thrombin (37.5 U/cm²) and calcium chloride (117 µg/cm²) affixed to a Vicryl mesh (Ethicon, Somerville, New Jersey) [17]. These agents were in increasingly common utilisation towards the end of World War II but fell out of favour and were subsequently abandoned due to the transmission of hepatitis [59]. DFSD mimics and potentiates the final stages of the coagulation process forming a robust clot that adheres to tissues [60]. DFSD for trauma was re-visited by the US Army in the early 1990s, and together with the American Red Cross, they were able to solve the

problem of infective transmission of viral pathogens due to post war technological developments [61].

After three revisions [62] the investigators settled upon a dressing that sandwiched thrombin in a polka dot configuration between two layers of fibrinogen, with the critical concentration of fibrinogen proven in large animal modeling [63]. DFSD has proven to be effective in controlling haemorrhage in a goat limb model of ballistic injury [64] and in swine models of femoral arteriotomy [65], grade V liver injury [66] and infra-renal aortotomy [67, 68]. It has successfully been utilised in one patient to arrest traumatic haemorrhage [17] but is currently not available for field use.

Discussion

In the immediate build-up to operations in Iraq and Afghanistan the services within the United States Armed Forces chose novel haemostatic dressings based upon differing mechanisms of action to offer their troops further protection from death by haemorrhage. The Army chose HemCon®, a chitosan based product that although effective in high volume low pressure animal models of haemorrhage [50] was less so in high flow, high volume swine models of groin injury [23,52]. It was thought to be safe with minimum side effect profiles and after early manufacturing issues were resolved it was adopted and issued to every soldier involved in combat operations.

The Navy and Marine Corps chose QuikClot® a volcanic rock with a slightly uncertain mechanism of action and the potential for more dramatic side effects but with much more convincing performance in arresting haemorrhage in a model that could, by some, be considered more realistic of the wounds that it was to be targeted against [23]. This was initially issued to individual Marines and sailors.

The US Army decided also to adopt QuikClot® but limited it to selected medical care providers. Each individual service provided training on their respective haemostatic agents and instructed that they be used as part of a graded response to the control of haemorrhage [18], accepting that neither was perfect and prepared to underwrite the risks in the knowledge that they may reduce the mortality from battlefield haemorrhage. Data collection and re-assessment of these products was to be conducted in order to insure that complications were minimal and documented. The DMS experience essentially mirrors the United States Army, with only our adoption of HemCon® delayed.

Operations in Afghanistan have now lasted longer than those of the Second World War. The necessity to provide improved haemostatic options to our frontline troops remains as urgent as on the eve of battle, however, medical care is now delivered as part of an inclusive trauma system [69] that whilst constantly evolving with changes in the operational tempo is mature, with formalised quality assurance and performance improvement processes [70]. Utilisation of novel haemostatic products cannot happen within this structure without assessment and recording of their effectiveness and potential problems. It is surprising therefore that there are only three studies looking at the effectiveness of these products.

Two of the studies relate to chitosan based dressings [42,56] and one to zeolite preparations [18]. They are all supportive of their effectiveness, but were retrospective questionnaire-based studies with obvious flaws. The questionnaires returned to Alam et al [18] appear to have preconceived ideas about the efficacy of the product which potentially introduces bias to the study. It also raises the possibility that those care-providers less enamoured with the products may not be as keen to participate.

There is no data from the trauma registries as to the usage and effects of novel haemostatics? The escalation philosophy behind novel haemostatic utilisation in the field means that QuikClot® use is confined to those patients where other modalities had failed. It is not unreasonable to expect that all patients that have had

QuikClot® applied will have been seen in a role 2/3 facility, at least for removal of the product and dressing of the wound. There are no reports in the public literature from these facilities regarding novel haemostatics. This is a criticism of all of us who have seen these products utilised, been involved in the care of soldiers where these have been used but have not ensured that these episodes have been documented.

In the DMS the use of QuikClot® was to have been audited by the completion of an A4 form but this "*proved too burdensome for some members of the DMS*" [11]. "*Trauma care should be efficacious, safe, and cost effective,*" according to the American College of Surgeons [71] and it is up to all of us to collect the data to prove that it is.

Worryingly, it is possible to have a product developed, tested, introduced into an operational theatre, used on soldiers then withdrawn due to potential problems [41] and still in the open medical literature have only three articles that pertain to its role as a novel haemostatic. Perhaps the lesson to draw from this review does not relate to perceived flaws with individual dressings but with the way in which after introduction to frontline service our mechanisms for collecting unbiased accurate data on their performance are so lacking.

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