Topical Hemostatic Agents

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- In combat:
  - Hemorrhage before evacuation accounts for 49% of all battle field deaths
- In Korea, Vietnam and Somalia:
  - 7 – 14% of those dying from combat wounds died from extremity hemorrhage

Coagulation is a complicated process

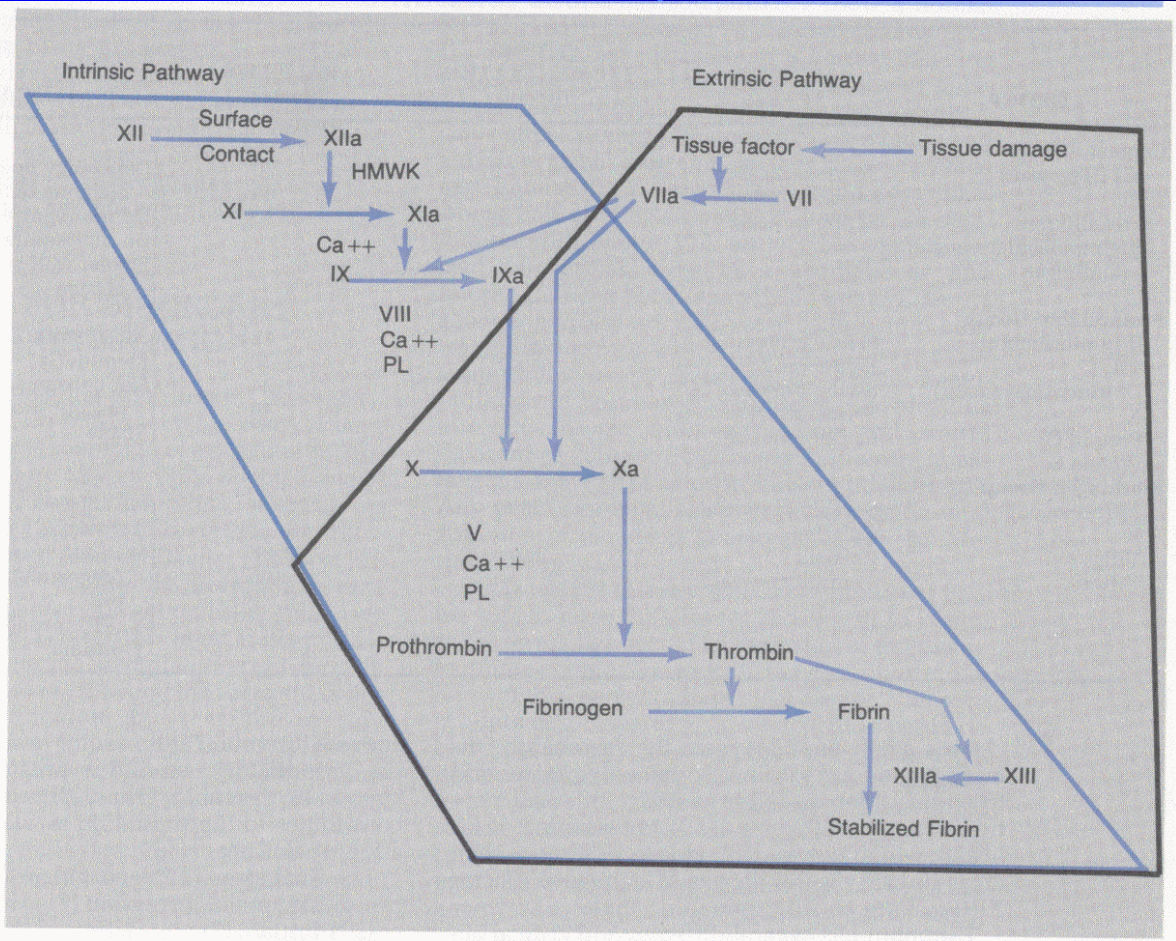


FIGURE 56–1. Simplified pathways of blood coagulation. The area inside the blue line is the intrinsic pathway, measured by APTT. The area inside the black line is the extrinsic pathway, measured by PT. The area encompassed by both lines is the common pathway.

Hemostatic Dressing Pad

- Alltracel Labs, Czech Republic
- Sandwich of hemostatic contact layer with two superabsorbent layers
- Active substance is “quasi-nonwoven” form of oxidized cellulose
- Pure physical effect- swelling after saturation of blood that aids in formation of a clot

ARC Dressing

- American Red Cross, Rockville, MD
- Dry fibrin dressing
  - Human fibrinogen, human thrombin, factor XIII, CaCl all freeze dried onto a dressing
    - Thrombin converts fibrinogen to fibrin
  - Polygalactin mesh backing

Hemostatin bandage

- Analytical Control Systems, Inc. (Fishers, IN)
- Bandage soaked in Hemostatin
  - Active ingredient = propyl gallate
  - Propyl gallate is a possibly a procoagulant with enhanced placelet activity, or through activation of Factor XII

Hemarrest dressing

- Clarion Pharmaceuticals, Inc. (Westlake, OH)
- Thin pad with epsilon aminocaproic acid and thrombin
  - EACA is an antifibrinolytic
    - Interferes with breakdown of fibrin by plasma

Avitene Dressing

- Davol, Inc (Woburn, MA)
- Microfibrillar collagen
  - Collagen provides matrix for clotting; absorbable
  - Collagen attracts and activates platelets

Surgicel dressing

- Ethicon, Inc. (Somerville, NJ)
- Fibrillar, knitted fabric of regenerated cellulose
  - Cellulose provides a matrix for clotting, absorbable
  - Some degree of physical effect as well from swelling

Sorbstace Microcaps

- Hemostace, LLC (New Orleans, LA)
- Aluminum sulfate microcaps with 6% ethyl cellulose coating, applied to sponges
  - Alum is an astringent- controls capillary and small vessel bleeding

RDH

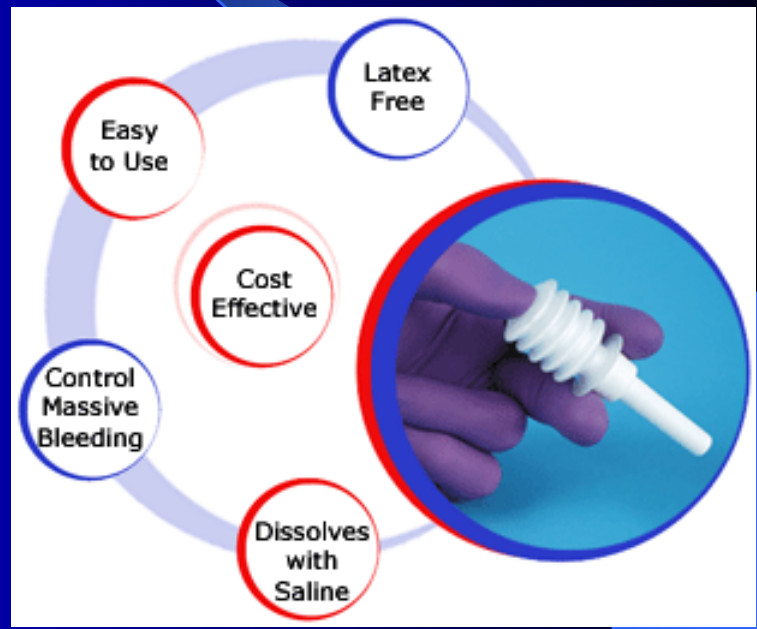
- Marine Polymer Technologies (Danvers, MA)
- Poly-N-acetyl glucosamine dressing
  - An amino sugar normally found in the body
  - Accelerates the concentration of RBCs, clotting factors and platelets at the bleeding site to the critical levels needed for clot formation by a mechanical, not chemical, function

TachoComb-S dressing

- Nycomed (Linz, Austria)
- Human fibrinogen and thrombin on equine collagen
  - Attracts and activates platelets

TraumaDex

- Manufactured by Medafor, Inc., sold by Emergency Medical Products
- Bioinert, microporous particles synthesized to a controlled porosity and spherical diameter from raw materials derived form plants- potato starch?
- Absorbs fluid, concentrating platelets. Thrombin and fibrinogen on particle surface



QuikClot

- Proprietary formulation of zeolyte- a mineral; derivative of volcanic rock; no botanical or biological substances
- Rapid absorption of fluid concentrates clotting factors around the wound
- Non-allergenic

HemCon dressing

- Made of chitosan, a naturally occuring protein found in shrimp shells
- Potentially allergenic

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 and Hepatic Injury in Swine

- Pusateri AE, et al. , J Trauma 2003; 55:518-25.
- Swine prepared with vascular catheters, and splenectomized
- Standardized liver injuries induced; portal vein and parenchymal damage
- Dressing applied and resuscitation initiated
- Blood loss, hemostasis and 60 min survival quantified

Nine Hemostatic Dressings in a Model of Severe Large Venous and Hepatic Injury in Swine

- After 6 animals completed in each treatment group, 4 dressings eliminated:
  - Hemarrest, Surgicel, Sorbstace Microcaps, and RDH
- ARC similar to Tachocomb-S dressing, but much more effective

Pusateri AE, et al. , J Trauma 2003; 55:518-25.

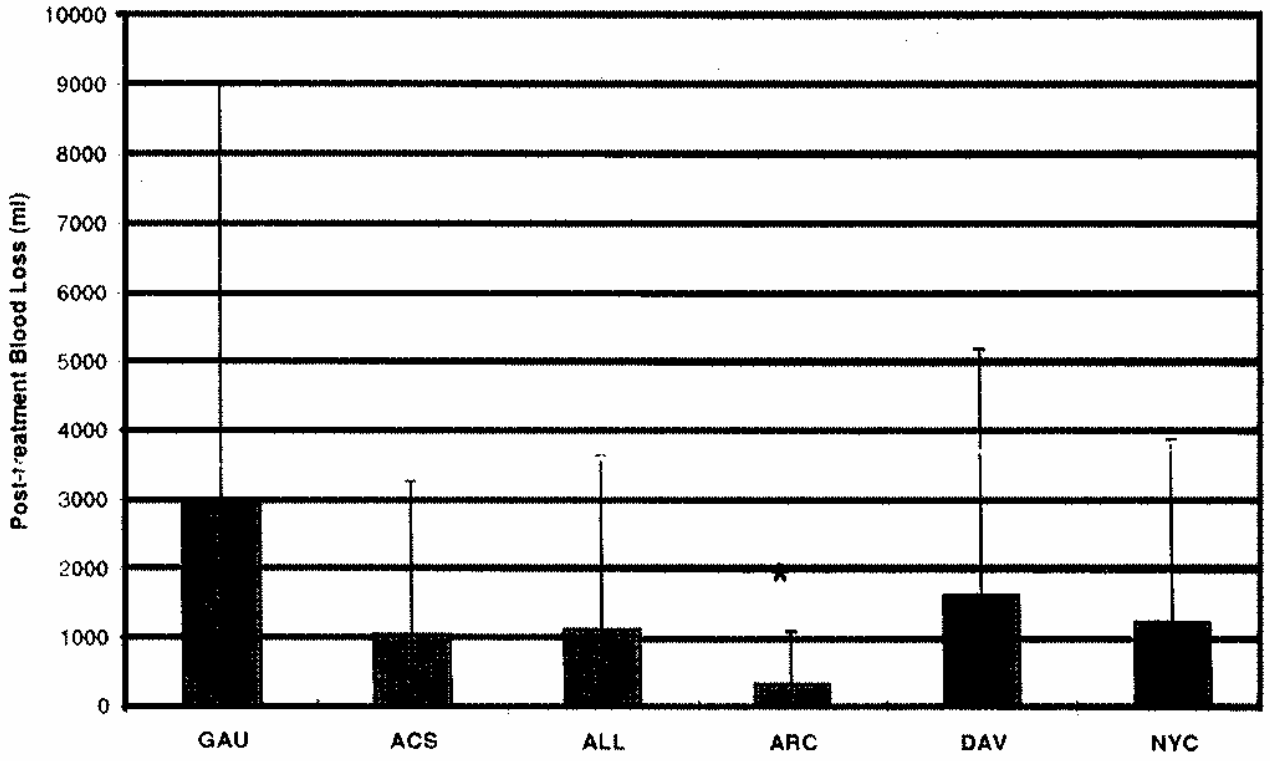


Fig. 1. *Effect of hemostatic dressing type on posttreatment blood loss. *Different from gauze control* ($p < 0.01$). *Means and 95% confidence intervals are shown.*

Table 3 Survival and Hemostasis in Animals Included in the Full Study

Group	Survival (%)	Hemostasis (%)			
		1 Min	2 Min	3 Min	4 Min
ACS	82	0	9	9	18
ALL	50	9	9	18	18
ARC	91	9	27	64[a]	73[b]
DAV	64	0	9	18	18
NYC	73	0	0	18	36
GAU	55	0	0	0	0

[a] Different from GAU ($p < 0.05$).
[b] Different from GAU ($p < 0.01$).

Nine Hemostatic Dressings in a Model of Severe Large Venous and Hepatic Injury in Swine

- Post treatment blood loss reduced in the ARC group compared to the Gauze control ($p < 0.01$)
- No other differences noted

Pusateri AE, et al. , J Trauma 2003; 55:518-25.

Comparison of 10 Different Hemostatic Dressings in an Aortic Injury

- Sondeen JL, et al. J Trauma 2003;54:280-85.
- 11 groups of pigs
  - 9 dressing groups
  - 2 controls (gauze and suture)
- Instrumented with catheters and splenectomized
- 4.4 mm aortotomy, dressing applied to spraying jet of blood, pressure held 4 minutes
- Survival, blood loss,other variable measured over 1 hour period

Table 3 Survival Number and Time, and Hemorrhage and Resuscitation Volumes

Dressing Group*	No. of Survivors/ Total	Survival Time (min)**	Initial Hemorrhage (mL)	Hemorrhage Postocclusion (mL)	LR Solution Volume (mL)
Gauze	2/9	20 ± 8 [8]	120 ± 14	785 ± 179	391 ± 285
Suture	5/5	60 ± 0^{+++} [60]	50 ± 11^{+}	8 ± 8^{+++}	766 ± 311
FD	5/5***	60 ± 0^{+++} [60]	147 ± 12	12 ± 7^{+++}	1,659 ± 739^{++}
Avitene	0/5	8 ± 1 [8]	127 ± 20	1,098 ± 95	0
Surgicel	0/5	7 ± 1 [7]	151 ± 28	1,049 ± 63	0
D1	0/5	11 ± 2 [8]	131 ± 20	1,104 ± 65	0
D2	0/5	8 ± 1 [8]	148 ± 18	994 ± 79	0
D3	0/5	8 ± 1 [7]	152 ± 14	1,003 ± 138	0
D4	0/5	12 ± 4 [9]	129 ± 20	1,126 ± 59	0
D5	0/5	11 ± 3 [8]	141 ± 16	1,059 ± 121	0
D6	0/5	7 ± 1 [8]	133 ± 19	1,231 ± 77	0

* Groups are described in the text and Table 1. Comparisons of proportional survival rate involved only the dressing groups because the suture group survival rate is expected to be 100% and is not directly relevant to the hypothesis under test.

** Median survival time in brackets.

*** For proportional survival with FD vs. gauze: $p = 0.036$ after Bonferroni correction for nine comparisons with gauze. For other variables: $^{+}p < 0.05$; $^{++}p < 0.01$, $^{+++}p < 0.001$ (vs. gauze control group, Dunnett's test). Data are given as mean ± SEM.

The RDH Bandage: Hemostasis and Survival in a Lethal Aortotomy Hemorrhage Model

- Vournakis JN, et al. J Surg Research, 2003
- Swine model; 4 mm aortic punch wounds created
- Dressing applied (RDH or Army First Aid Field Bandage)
- Bandages removed at 2 hrs, and monitored for 30 more mins
- 80% of RDH treated animals survived the entire protocol vs 40% surviving to removal of AFAFB, none survived until the end
- RDH also studied in liver injury model
  - Jewelewicz DD, et al, J Trauma, 2003;55:275-81

But wait. . .

EMS personnel aren't often called upon to control hemorrhage from the liver and aorta. . .

TraumaDEX

Animal studies conducted at the Minneapolis Medical Research Foundation

- Porcine topical wound model- lesions created in the skin and muscle
  - "proved efficacy of TraumaDEX to conventional dressings
- "More severe test"- rabbit femoral artery severed
  - In 11/12 trials (92%), TraumaDEX was successful in controlling hemorrhage
  - While in only 3 of 12 trials (25%) was bleeding controlled by manual pressure

TraumaDEX

- Human Trial conducted at Mayo Clinic
- Two matched, controlled incisions created on the forearms of volunteers (n = 30)
  - Treated with TraumaDEX and pressure, or pressure alone
  - In 29/30 (97%), TraumaDEX stopped bleeding faster than controls

Old surgeon's adage:

All bleeding stops. . .

Comparative Analysis of Hemostatic Agents in a Swine Model of Lethal Groin Injury

- Alam HB, et al, J Trauma 2003; 54:1077-1082
- Complex groin injury created in swine
  - Semitransection of the thigh with complete division of the femoral artery and vein
- After 5 minutes, animals randomized to:
  - No dressing (ND)
  - Standard dressing (SD)
  - SD and RDH
  - SD and QuikClot
  - SD and TraumaDEX

Comparative Analysis of Hemostatic Agents in a Swine Model of Lethal Groin Injury

- Measurements:
  - Blood loss
  - Early mortality (180 minutes)
  - Physiologic markers of hemorrhagic shock
    - Cardiac Output
    - BP
    - Hgb
    - Acidosis

Alam HB, et al, J Trauma 2003; 54:1077-1082

Comparative Analysis of Hemostatic Agents in a Swine Model of Lethal Groin Injury

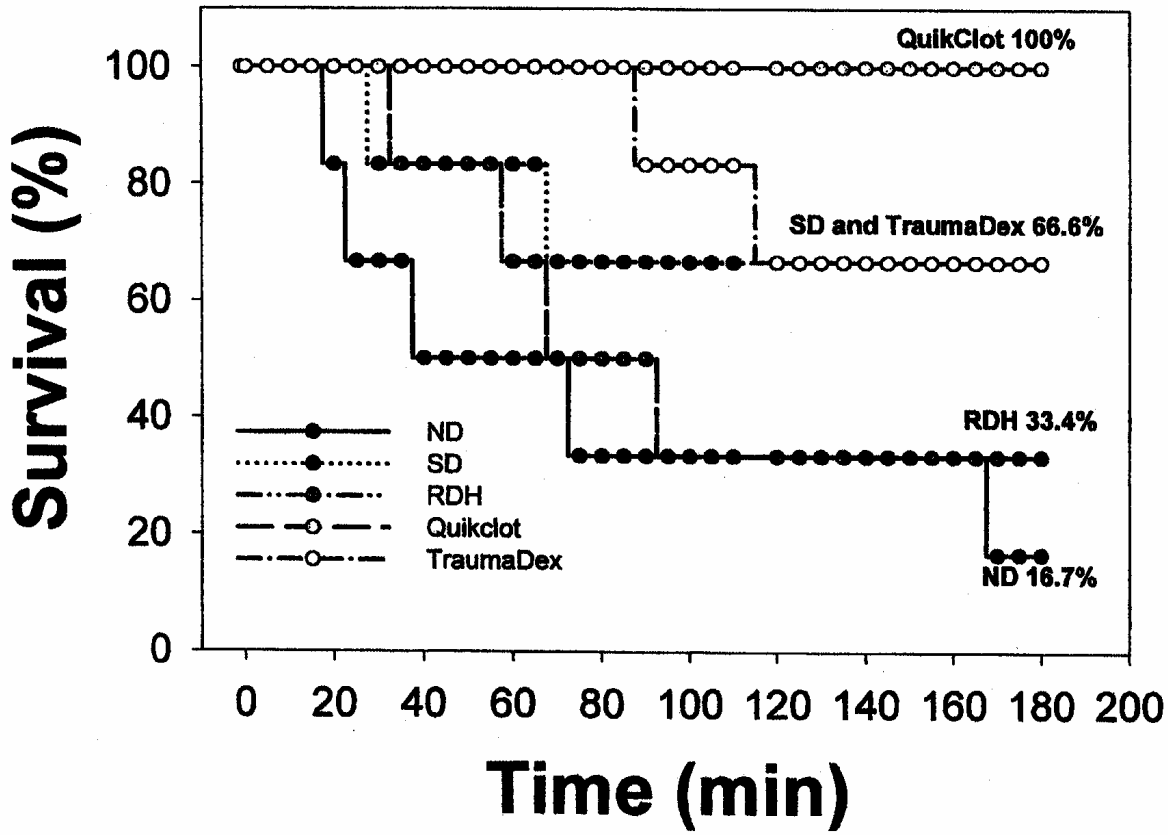
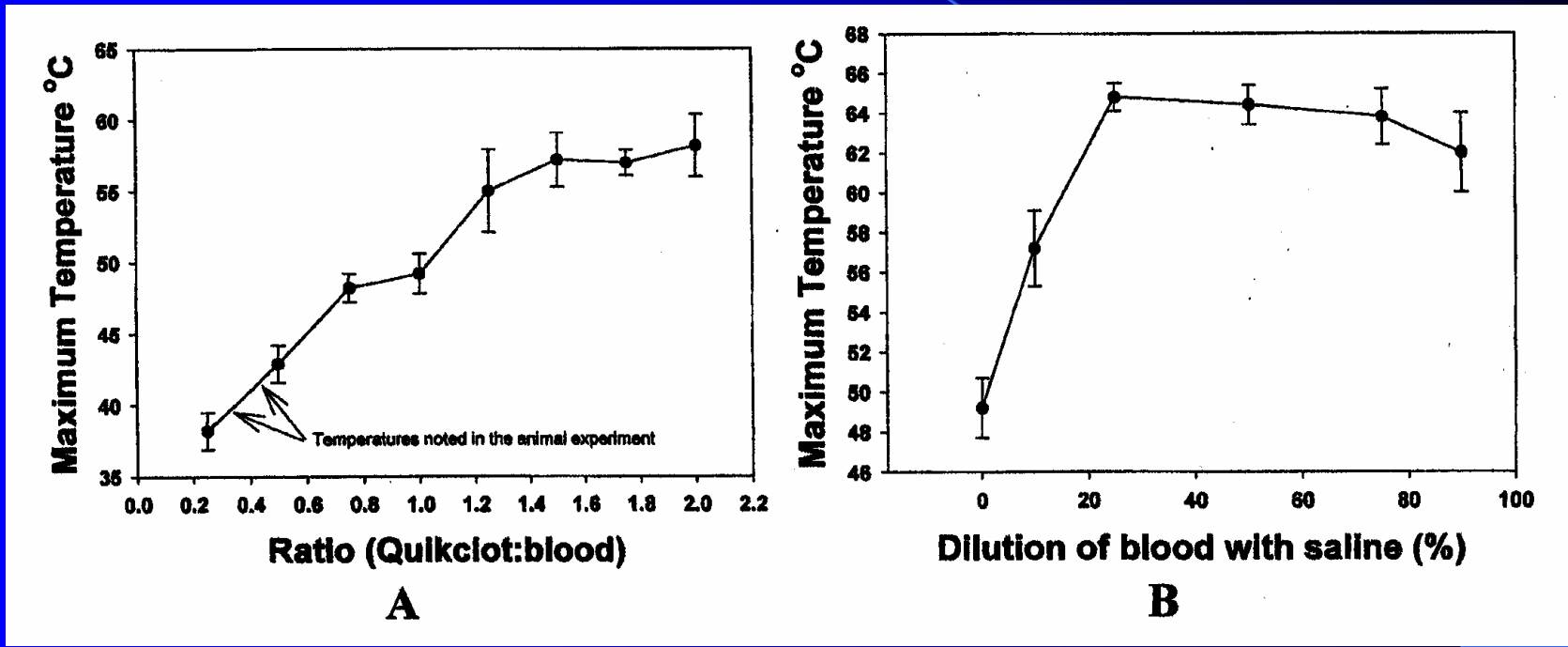


Fig. 2. *Time to death. Data presented as the percent of surviving animals over time. ND, no dressing; SD, standard dressing; RDH, Rapid Deployment Hemostat dressing.*

Alam HB, et al, J Trauma 2003; 54:1077-1082

Comparative Analysis of Hemostatic Agents in a Swine Model of Lethal Groin Injury

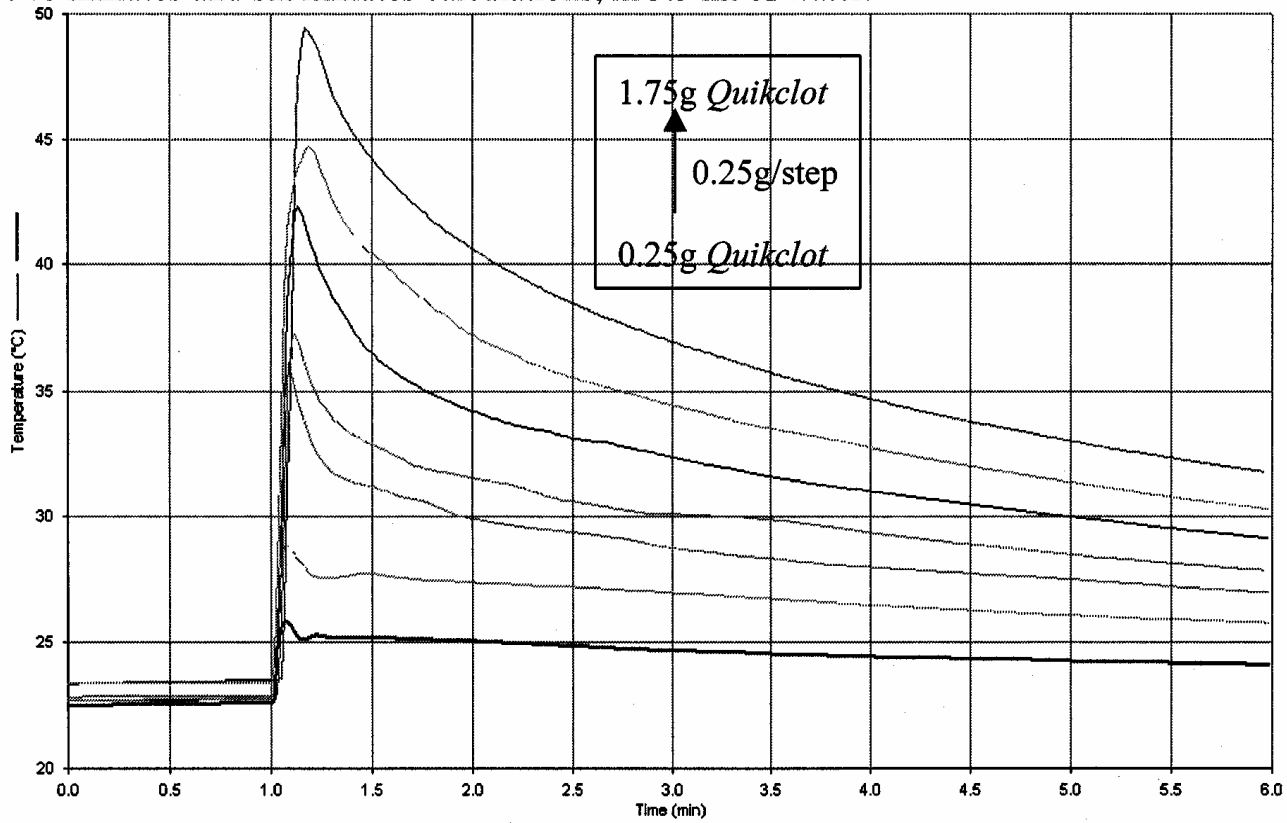


Degree of exothermic reaction influenced by both the ratio of QC to blood and the degree of hemodilution

Alam HB, et al, J Trauma 2003; 54:1077-1082

Calorimetric analysis of a granular mineral hemostatic agent

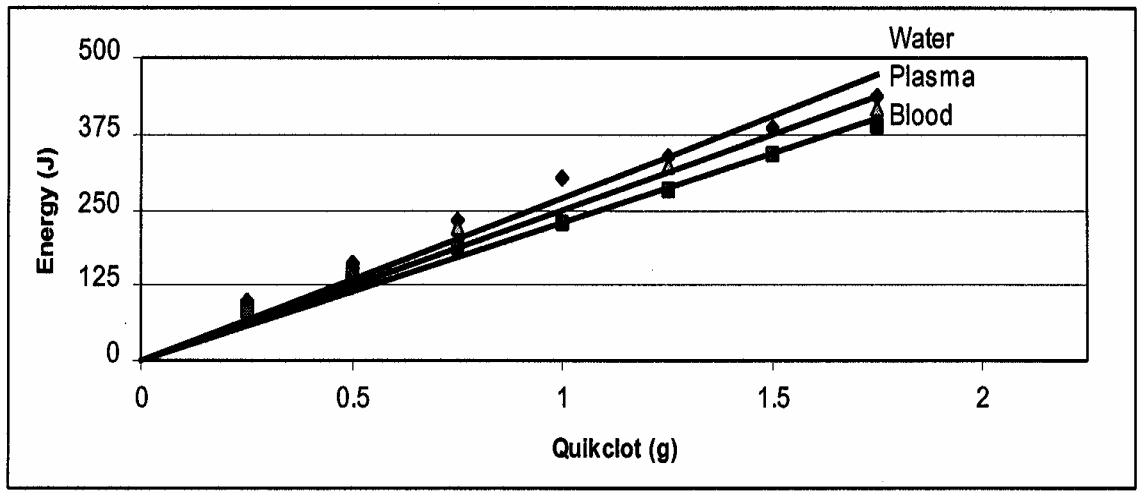
Figure 4. Representative temperature versus time curves for *Quikclot* over six minutes, ΔT at two minutes and six minutes calculations, in 3.5 ml of water.



Hmel PJ, et al, Dept of Blood Research, Walter Reed Army Institute of Research

Calorimetric analysis of a granular mineral hemostatic agent

Figure 9. Predicted plot of energy versus *Quikclot* amount for water, plasma, and whole blood based on the immersion heater energy data.



"The amount of energy released by Quikclot is staggering . . .the substitution of fresh whole blood in place of water yielded comparable results (blood is > 90% water)"

Hmel PJ, et al, Dept of Blood Research, Walter Reed Army Institute of Research

Thermal Injury Resulting from Application of Granular Mineral Hemostatic Agent

- Anesthetized swine were maintained with a MAP > 60 mm Hg
- Skin, muscle, liver, spleen, venous and arterial wounds were created in a standardized fashion
- Topical hemostatic agents were applied
- Application of the agent (QC) resulted in elevated tissue surface temperatures in excess of 95'C and tissue temperatures exceeding 50'C
- Necrosis of fat, muscle, artery and vein were noted as well as nerve injury and full and partial thickness burns

Wright JK, et al

Conclusions

- Experimental models don't correlate well with injuries encountered in civilian prehospital trauma care
- No published civilian prehospital experience with any agent
- Quikclot is associated with an exothermic reaction and may produce collateral tissue damage
- ***No evidence these agents are superior to direct pressure!!***