Coagulopathy after Major Combat Injury:

Occurrence, Management, and Pathophysiology

J. JUDSON McNAMARA, M.D., EDWIN L. BURRAN, B.S.,
J. F. STREMPLE, M.D., MARK D. MOLOT, M.D.

From the Division of Surgery,
University of Hawaii School of Medicine and
The Queen's Medical Center, Honolulu, Hawaii

COAGULOPATHIES following operation for massive trauma have been widely reported to constitute a frequent and major postoperative complication.[3,6,7] The present report consists of a 6-month clinical experience with bleeding problems following operation for combat casualties in a busy evacuation hospital in Vietnam. It further reports the results of extensive screening coagulation studies performed in both the pre- and postoperative period in a group of 80 randomly selected patients treated at this hospital.

Materials and Methods

The period of clinical study extends from Dec. 1, 1968 to June 1, 1969. During this period some 2965 patients underwent general anesthesia and operation for trauma resulting from combat injuries. The majority of these patients had multiple systems involved in their injury.

During the first 3 months of this period 80 patients underwent clotting studies preoperatively and were subsequently followed with similar studies postoperatively for 5 days or until the time of their evacuation or death. Studies were done preoperatively, immediately postoperatively, and on postoperative days 1 and 3. Studies included platelet counts (phase microscopy), partial thrombo plastin time,[7] prothrombin time (Quick), thromboelastograms, fibrinolysin titers, euglobulin clot lysis,[11] fibrinogen,[1] ethanol gelatin[4] and hematocrit. Careful clinical summaries were recorded on each patient for correlative purposes.

Submitted for publication July 14, 1971.

Results

Clinical Series: A subjective judgment of postoperative coagulopathy was made in 112 patients. All patients had major trauma with involvement of one or more organ systems. Only three patients had not received over five units of blood before and during operation. The significant fact is that in none of these patients was persistent coagulopathy a major postoperative complication. All were controlled with fresh blood and/or fresh frozen plasma. In 18 patients where diffuse oozing was clearly a major potential problem and where over 20 units of blood had been administered, control of the oozing was accomplished by sequential administration of fresh blood requiring between 4–8 units (average 5.5 units).

Investigative Series: One patient with extensive burns was not included in the series. Of the remaining 79 patients, 19 comprised a control group who had only minor soft tissue injuries and received little or no blood transfusions but required general anesthesia for debridement of their injuries. None of the control patients demonstrated clinical oozing problems. Minor depression of platelet count and fibrinogen was noted immediately following operation. A significant fibrinogen re-

bound was noted by POD 3. Platelet counts remained in a normal range throughout. Partial thromboplastin time and prothrombin time were prolonged in the control patients (Table 2).

The remaining 60 patients all had major injuries as defined by penetrating wounds of head, chest or abdomen, major extremity injury involving amputation, major arterial injury or long bone fracture in the legs or a combination of these injuries. Massive transfusion was required in the majority of these patients (Table 1). Fifteen patients were in hypovolemic shock at the time of the initial, preoperative study. These patients did not appear to constitute a unique group and were not considered separately. Other patients with some previous resuscitation had undoubtedly experienced some hypovolemia and thus the distinction would be artificial.

Partial thromboplastin time and prothrombin time were significantly ($p < 0.01$) prolonged from control laboratory values but did not differ significantly from minor injury patient values ($< 0.1 > 0.05$) (Table 2). Mean platelet counts immediately postoperatively were approximately 50% less than admission values. This difference was significant as was the comparison with the corresponding control group. In three instances, immediate post-injury fibrinogen values were significantly depressed. This was not true for the mean value of the group as a whole. Mean values for fibrinogen on POD 1 and 3 were significantly higher than pre- or immediate postoperative values.

Twelve of the patients demonstrated significant clinical oozing (coagulopathy) as determined subjectively by both the surgeon and the investigators studying the patient. The group is not tabulated separately because values do not differ significantly from the seriously injured group as a whole. All 12 patients had required over 10 units of blood for operation and all had multiple major injuries. In all instances all clotting factors were depressed though no single value was depressed to the point usually necessary to produce bleeding difficulties. In all 12 patients, oozing was easily controlled with the administration of 4–6 units of fresh whole blood. Two patients studied had abnormal values for fibrinolysin titer and euglobulin clot lysis (Table 3). One of these developed coagulopathy 4 days after massive head and facial injury. The patient had significant sepsis at the time. He did not respond to heparin but did to fresh whole blood. The other patient had no clinical coagulopathy. Thromboelastography showed abnormal fibrinolysis in both of these patients. The remainder of the thromboelastograms were qualitatively normal though minor prolongations of clotting time (r + k) where observed in 23 patients immediately after operation. This had reverted to normal in all but one patient by the third postoperative day. This prolongation resulted entirely from abnormally long K value in the immediate postoperative period in the seriously injured group of patients (Table 4). Ethanol gelation studies were negative in all but one patient. This was the patient with demonstrated fibrinolysis whose bleeding ceased with administration of fresh blood.

TABLE 2. *Prothrombin Time (sec)*

	Pre-Op	Post-Op	Pod-1	Pod-3
Minor Injury	23.4*	24.9*	20.1*	17.9
Major Injury	19.3*	20.5*	20.0*	19.3*
	Partial Thromboplastin Time (sec)			
Minor Injury	56.9	69.6*	63.5*	46.3
Major Injury	54.0	62.2*	62.2*	53.1
	Hematocrit (%)			
Minor Injury	39	37	35	33
Major Injury	38	35	33	32
	Platelet Count/mm³			
Minor Injury	335	270*	299	286
Major Injury	324	204*	227*	243*
	Fibrinogen mg./100 ml.			
Minor Injury	235	268	365*	472*
Major Injury	221	246	366*	478*

* Values differ significantly (p 0–05) from baseline or control values.

Discussion

The present study demonstrated that coagulopathy with resultant diffuse oozing in the postoperative period is an unusual complication of injury. When it occurred the patients invariably had extensive trauma, frequently associated with shock and usually required multiple blood transfusions (over 20) during the course of resuscitation and initial surgical care. In each instance it was controlled by fresh blood with or without fresh frozen plasma and required 4–6 units of fresh blood administered sequentially to correct the clinical bleeding defect.

Why such coagulopathy should occur is not clear from the present coagulation data. Though some depression of

TABLE 1. *Number of Transfusions Received—Totals and Means*

	Pre-Op	OR	Post-Op	Total
Control (19)*	3(.2)	15(0.8)	2(0.1)	20(1.1)
Test (60)	82(1.4)	346(5.8)	82(1.4)	510(8.5)

* Numbers in parenthesis indicate mean units of blood transfused.

TABLE 3.

Fibrinolysin titers)	
) positive in two patients	
Euglobulin clot lysis)	
Ethanol gelatin—one positive fifth postoperative day in patient bleeding with massive soft tissue sepsis.	

TABLE 4

	Pre-op			Post-op			POD-1			POD-3		
Thromboelastogram	r	k	r + k	r	k	r + k	r	k	r + k	r	k	r + k
Control	11.57	8.12	19.69	13.25	5.89	19.11	12.29	7.20	20.23	11.57	5.10	16.67
Test	11.02	6.43	17.02	14.27	10.67	24.46	12.25	13.81	25.48	13.99	8.79	22.82

r = rate of thromboplastin generation. Mean r for reconstituted plasma is 18 (range 15–25)—values for whole blood somewhat less.
k = a thrombin value responsive to platelet profactors and to a lesser extent plasma—generally unaffected by prothrombin complex. Mean I value for plasma is 6.5 (range 4.5–8.3)—similar values for whole blood.
r + k = analogous to clotting time or heparin tolerance test. Mean normal r + k value for plasma is 24.5 (range 20–29)—values for fresh whole blood somewhat less.

all clotting parameters is observed in the immediate postoperative period in a number of patients, this is rarely profound in any one parameter. Furthermore, it is usually promptly corrected by the body, having returned to normal in almost every instance by the first postoperative day. Whether across-the-board depression of clotting factors, individually of relatively minor proportions, was responsible for the clinical oozing cannot be answered. If this were the case, the quantities of fresh blood required to reverse the defect is surprisingly large. Presumably a single unit of fresh blood should replenish many of the mild abnormalities observed, yet, usually over 4 units were required.[10] The combination of continued bleeding with consequent loss of clotting factors by actual hemorrhage as well as consumption of clotting factor on the injured surface of large soft tissue wounds may explain the necessity for 4 or more fresh units administered sequentially in most patients.

The mechanism of depletion of clotting factors with major injury remains a source of considerable controversy. The subject has recently been thoroughly reviewed by Salzman.[9] The alternative mechanisms proposed to explain this coagulopathy include dilution of clotting factors, consumption of clotting factors, fibrinolysis or a qualitative defect in platelet function superimposed on any or all of the above.[9,10] In only one of our cases of coagulopathy did fibrinolysis seem to contribute to clinical bleeding and here sepsis may have played a role in his fibrinolytic episode. Disseminated Intravascular Coagulation (DIC) currently is a popularly stated source of such bleeding difficulties.[9] However, the absence of positive ethanol gelatin in any of the patients with immediate post-injury bleeding studied to date, and the prompt control of oozing by fresh blood administration mitigates against this as an important mechanism. DIC occurring with the acute insult but *not* as a continuing process could account for the observed clotting factor depletion. This cannot be excluded but since it does not appear to be an ongoing process it should be of no clinical significance. The present data and our conclusions are in general agreement with similar studies and conclusions by Attar *et al.*[2] Dilution of clotting factors may play a contributing role, particularly with the administration of large volumes of old banked blood. Finally, a qualitative abnormality in platelet function superimposed on mild quantitative depression of other factors has been suggested as the major problem in post-traumatic coagulopathy. The prolonged K values observed with thromboelastography in the present study, in the postoperative period, lend support to this concept since this value is said to reflect the platelet phase of coagulation. Specific alterations in metabolism and function of blood elements following injury and in banked blood following storage may contribute to such a qualitative abnormality in platelet function.[5] Any relationship between these specific abnormalities and the general subjective observation of post operative coagulopathy remain conjectural and beyond the scope of this discussion.

Conclusions

1. Diffuse oozing coagulopathy occurs frequently following massive injury and massive blood transfusion.
2. Such coagulopathy is virtually always reversible with fresh blood given sequentially—usually requires 4 to 5 units.
3. Mechanism of the coagulopathy remains obscure.
   A. Present data favors a qualitative abnormality in platelet function:
      1) Lack of evidence of fibrinolysis
      2) Reversal by fresh blood
      3) Some element of thrombocytopenia
      4) Thromboelastography showing prolonged K value
      5) Bleeding usually develops with administration of multiple units of banked blood.
   B. However, intravascular coagulation, occurring acutely after injury could also be the mechanism because:
      1) Consumption of coagulation factors is suggested by decreases in fibrinogen and platelets.

2) Question reliability of ethanol gelation in excluding DIC.

3) Absence of fibrinolysis not absolutely against DIC.

4) Consumption could occur acutely, leaving resulting alteration in clotting factors in absence of persistent DIC.

References

1. Astrup, T., Brakman, P., and Miseer, V.: The Estimation of Fibrinogen. Scand. I. Clin. Lab. Invest., **17**:57, 1965.
2. Attar, S., Boyd, D., Layne, E., McLaughlin, J., Mansberger, A. R. and Romley, R. A.: Alterations in Coagulation and Fibrinolytic Mechanisms in Acute Trauma. J. Trauma, **9**:939, 1969.
3. Attar, S., Kirby, S. W., Jr., Masaitis, C., Monsberger, A. R., Jr., and Cowley, R. A.: Coagulation Changes in Clinical Shock. Ann. Surg., **164**:34, 1966.
4. Breen, F. A., Jr. and Tullis, J. L.: Ethanol Gelation: A Rapid Screening Test for Intravascular Coagulation. Ann. Intern. Med., **69**:1197, 1968.
5. Hellem, A. J.: Platelet Adhesiveness. Scand. J. Haemat. (Series Haemat.) **1**:99, 1968.
6. Innes, D. and Sevitt, S.: Coagulation and Fibrinolysis in Injured Patients. J. Clin. Path. **17**:1, 1964.
7. Karlson, K. E. and Lerner, B.: The Coagulation Status of Surgical Patients. Ann. N. Y. Acad. Sci., **115**:315, 1964.
8. Nye, S. W., Graham, S. W., and Brinkhous: The Partial Thromboplastin Time As A Screening Test for the Detection of Latent Bleeders. Am. J. Med. Sci., **243**:279, 1962.
9. Salzman, E. W.: Does Intravascular Coagulation Occur in Hemorrhagic Shock in Man? J. Trauma, **8**:867, 1968.
10. Simmons, R. L., Collins, J. A., Heisterkamp, C. A., Mills, D. E., Andren, R. and Phillips, L. L.: Coagulation Disorders in Combat Casualties. Ann. Surg., **169**:455, 1969.
11. Von Kaulla, K. N. and Schultz, R. L.: Methods for Evaluation of Human Fibrinolysis. Am. J. Clin. Path., **29**:104, 1958.