CHANGES IN BLOOD COAGULABILITY IN DOGS FOLLOWING FLASH BURNS

by

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THE PROBLEM

One severely burned patient places an enormous burden upon the facilities of the average hospital. In the event of nuclear war, mass burn casualties can be expected, making the present individualized treatment techniques largely impractical. Any relatively simple therapy favorably altering the course of the disease or decreasing the severity of the injury would therefore be helpful. The reports that heparin improves both survival and wound healing in experimental burns and the implication of intravascular clotting as possibly being of importance in the etiology of other forms of shock focus interest upon the blood coagulation mechanism in burns. Data concerning the clotting mechanism in burns are incomplete. A controlled study of general clotting parameters after burns in dogs was therefore undertaken to elucidate the rationale for altering blood coagulation as well as to provide a basis for further study if indicated.

FINDINGS

An elevation of the plasma fibrinogen, prolongation of the partial thromboplastin time and Lee-White siliconed clotting times, and decreased fibrinolytic activity occurred between 12 and 96 hours after burn. No significant changes were noted in the thrombocyte count or prothrombin time and no evidence for a period of hypercoagulability was found.

RECOMMENDATION

It was concluded that the changes developed too late to explain previous experimental observations and that the study of the relationship of blood coagulability to specific problems related to burns, rather than as a general phenomenon, would be more profitable for future studies.

ADMINISTRATIVE INFORMATION

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CHANGES IN BLOOD COAGULABILITY IN DOGS FOLLOWING FLASH BURNS

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INTRODUCTION

One severely burned patient places an enormous burden upon the facilities of the average hospital. In the event of nuclear war, mass burn casualties can be expected, making the present individualized treatment techniques largely impractical. Any relatively simple therapy favorably altering the course of the disease or decreasing the severity of the injury would therefore be helpful.

The reports that heparin improves both survival and wound healing in experimental burns

and the implication of intravascular clotting as possibly being of importance in the etiology of other forms of shock focus interest upon the blood coagulation mechanism in burns. The use of anticoagulants has theoretical merit in preventing the studding phenomenon described by Brooks, et al, the systemic clotting described in shock and the local intravascular clotting precipitated by thermal injury to the vascular endothelium.

Data concerning the clotting mechanism in burns are incomplete. A controlled study of general clotting parameters after burns was therefore undertaken to elucidate the rationale for altering blood coagulation as well as to provide a basis for further study if indicated.

MATERIALS AND METHODS

The study was divided into two parts. The first part was designed to rule out any possible effect of sodium pentobarbital anesthesia upon blood clotting. The second section represented the actual study of blood coagulability after burns.

Part I

Twenty mongrel dogs had blood drawn in both the unanesthetized and anesthetized states. Sodium pentobarbital anesthesia (30 mg. kg.) was used for all dogs in this study. The blood samples were obtained on separate days, with half of the animals being anesthetized on the first day and the remainder on the second.

All blood samples were drawn from the jugular vein by a nontraumatic venipuncture through an 18-gauge disposable needle. The hair on the neck had been clipped but no attempt was made to maintain a sterile technique. The first 5 cc.

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of blood were drawn into a glass syringe and discarded. A total of 25 cc. was then drawn into two Tomar disposable syringes and transferred immediately to the appropriate siliconized or acid-washed anticoagulant tubes. When a free flow was not obtained or when the needle did not enter the vein cleanly, the samples were discarded and redrawn from the contralateral jugular vein.

**Part II**

For the actual study of blood coagulability after burns, 40 mongrel dogs, paired by sex and weight, were divided equally to produce two sham-burn and two flash-burn groups. This was done so that no more than four 30 cc. blood samples would be drawn from any dog. The scheduled times for venipuncture in each group are shown in Table I. After the control samples were drawn, the animals were shaved and the flash-burn dogs subjected to a 10 cal. cm.- (third degree) burn over approximately 20 per cent of their body surface. The sham-burn dogs were treated in exactly the same way as the flash-burn animals except that the heat source was not activated. The burn technique was designed to simulate an atomic flash burn and has been previously described. Each matched pair was studied simultaneously. No further sodium pentobarbital was given during the study. For humane reasons, all burned dogs were sacrificed after the last blood sample was taken.

The Quick one-stage prothrombin time, the thromboocyte count by phase
## TABLE III

Mean Blood Coagulation Values Before and After Flash Burn

<table>
<thead>
<tr>
<th>Blood Coagulation Test</th>
<th>Time After Burn</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>Fibrinogen (mg. per cent)</td>
<td>224.0*</td>
</tr>
<tr>
<td></td>
<td>226.1†</td>
</tr>
<tr>
<td></td>
<td>N.S.‡</td>
</tr>
<tr>
<td>Thrombocyte count (thousands)</td>
<td>316.0</td>
</tr>
<tr>
<td></td>
<td>312.8</td>
</tr>
<tr>
<td></td>
<td>N.S.</td>
</tr>
<tr>
<td>Clotting time (minutes)</td>
<td>16.0</td>
</tr>
<tr>
<td></td>
<td>16.2</td>
</tr>
<tr>
<td></td>
<td>N.S.</td>
</tr>
<tr>
<td>Prothrombin time (seconds)</td>
<td>10.5</td>
</tr>
<tr>
<td></td>
<td>10.7</td>
</tr>
<tr>
<td></td>
<td>N.S.</td>
</tr>
<tr>
<td>Partial thromboplastin time (seconds)</td>
<td>17.8</td>
</tr>
<tr>
<td></td>
<td>18.9</td>
</tr>
<tr>
<td></td>
<td>N.S.</td>
</tr>
<tr>
<td>Erythrocyte lysis time (minutes):</td>
<td>58.3</td>
</tr>
<tr>
<td>I</td>
<td>85.7</td>
</tr>
<tr>
<td>H</td>
<td>90.3†</td>
</tr>
<tr>
<td>I</td>
<td>83.1†</td>
</tr>
<tr>
<td>H</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

* Upper figure in all cases = flash burn group; † Lower figure in all cases = sham burn group; ‡ N.S. = Non-significant; § Sig. = Significant; Flush burn group.

Homogeneity of the four groups was tested by the Kruskal-Wallis one-way analysis of variance by ranks.27 The median test28 was used to determine whether the two experimental groups had been drawn from the same population. The 0.05 level was chosen to evaluate significance.
RESULTS

None of the blood coagulation tests used in this study was affected significantly by the sodium pentobarbital anesthesia.

The four experimental groups were homogeneous for all parameters except the euglobulin lysis time. Therefore, the sham-burn and flash-burn groups were each treated as one group in presenting the data for the other five blood coagulation tests.

No significant changes suggesting a hypercoagulable state were noted. The partial thromboplastin time and the Lee-White siliconed clotting time became prolonged at 24 and 96 hours, respectively, after the burn. A significant elevation of the plasma fibrinogen and a concomitant prolongation of the euglobulin lysis time were also noted. No changes were found in either the thrombocyte count or the prothrombin time.

DISCUSSION

Changes in blood coagulability after various types of trauma are well documented. Innes and Sevitt, in a study of 42 patients, noted an increased fibrinolytic activity, decreased platelet count, prolongation of the prothrombin time and a transient shortening of the heparin-retarded clotting time during the first six hours after injury. After the early acceleration, the clotting time often became slightly or moderately prolonged. Concomitantly the fibrinogen rose and the fibrinolytic activity decreased. These data generally confirm the previous work of Scott and Crosby and Warren, et al., although some minor discrepancies are present. In experimental trauma, Penick, et al., have emphasized the paradoxical situation of intravascular hypercoagulability resulting in a hemorrhagic state secondary to the depletion of clotting factors.

The situation after burns is much less clear. Sevitt, in a review of the literature in 1957, stated that "a variable decrease in the number of blood platelets and a variable fall in the plasma prothrombin commonly follow extensive burning, and not infrequently the plasma fibrinogen rises. However, the whole blood clotting and bleeding times rarely show any significant abnormality." Sevitt's conclusions are based partly on the work of Campbell, et al., which, although comprehensive, was uncontrolled. Holder, et al., in another uncontrolled study, noted hypercoagulability in flash burned female mice. They attributed this to a thromboplastic substance from burned skin. Hypercoagulability has also been described in rats immediately following burns, with the subsequent development of a hypocoagulable state 12 hours later.
The results of this study (and others) must be interpreted with the reservations that plague all burn experimentation. The variety of burn techniques, experimental animals, and environmental conditions make interpretation, comparison, and especially extrapolation to human thermal injury difficult.

In future studies, it might be more profitable to determine the relationship of blood coagulability to the pathophysiology of burns with regard to specific problems rather than as a generalized phenomenon. Examples of such problems include the possible beneficial effect of heparin, the causes of sludging and the effect of local blood clotting upon the extent of tissue damage.

CONCLUSIONS

A controlled study of blood coagulability after burns in dogs revealed an elevation of the plasma fibrinogen, prolongation of the partial thromboplastin time and Lee-White siliconed clotting times, and decreased fibrinolytic activity occurring between 12 and 96 hours after burn. No significant changes were noted in the thrombocyte count or prothrombin time and no evidence for a period of hypercoagulability was found. It was concluded that the changes developed too late to explain previous experimental observations and that the study of the relationship of blood coagulability to specific problems, rather than as a general phenomenon, might be more profitable.
REFERENCES


25. Wilson, I. D. and Jackson, R. Data to be published.
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An interim report was conducted by Wilson, I. Dodd, LT, MC, USNR, Taylor, Dean R., LT, MC, USNR, and Nicholson, Thomas C., ENS, MC, USNR, from the U.S. Naval Medical Field Research Laboratory, Camp Lejeune, North Carolina 28542.

### Abstract

A controlled study of blood coagulability after burns in dogs revealed an elevation of the plasma fibrinogen, prolongation of the partial thromboplastin time and Lee-White siliconed clotting times, and decreased fibrinolytic activity occurring between 12 and 96 hours after burn. No significant changes were noted in the thrombocyte count or prothrombin time and no evidence for a period of hypercoagulability was found. It was concluded that the changes developed too late to explain previous experimental observations and that the study of the relationship of blood coagulability to specific problems, rather than as a general phenomenon, might be more profitable. (U)