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EARLY CIRCULATORY DISTURBANCES FOLLOWING EXPERIMENTAL THERMAL TRAUMA

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with the assistance of
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May 11, 1955

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ABSTRACT

Anaesthetized dogs were scalded by immersion in hot water, and determinations were made, before and after the burns, of cardiac output, liver blood flow, blood volume, ECG and pulse contours. Prompt and severe reductions in cardiac output and marked decreases in liver blood flow were observed and severe ECG and pulse disturbances were found. Plasma volume losses appeared to be inadequate to account for the marked changes observed. Early myocardial depression as one possible cause of these changes is discussed.

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INTRODUCTION

Among the various well-known shock-producing traumata, such as hemorrhage, crush, and burns, the largest volume of experimental data has been collected from studies on hemorrhage[1, 2]. Although experimental studies after burns have been made,[1, 2] the information accumulated is much less for this shock-producing agent; particularly lacking are intensive studies of very early changes involving the circulation. Early circulatory derangements, because of their possible prelude to the subsequent development of postburn shock, are emphasized in this study.

METHODS

General

A large group of apparently healthy mongrel dogs weighing from about 10 to 25 kg. were anaesthetized with sodium pentobarbital, 30 mg./kg. Baseline determinations of cardiac output, liver blood flow, and blood volume; electrocardiograms; and femoral pulse contours were obtained. Thermal trauma was produced by imersion of the closely shaved animal, usually to the axillae, in hot water at temperatures of 80° to 85° C. for 30 seconds. Variations in scalding temperature, skin area, and exposure time were occasionally used and are described below. The determinations listed above were repeated as soon as possible after the burn and at frequent intervals during the postburn course.

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† Read in part by title at the Second World Congress of Cardiology, September 15, 1954, Washington, D.C.

Cardiac Output

Cardiac output was measured by integration of the arterial dilution curve (femoral artery) following the rapid intravenous injection (jugular vein) of 150 microcuries of colloidal chromic phosphate labeled with P^{32}. The principles underlying this method are those described by Hamilton and co-workers for the dye-dilution technique[3, 4, 5]. Values for cardiac output are given as a cardiac index and are expressed as liters/10 kg. of body weight.

Liver Blood Flow

This quantity was determined by the rate of disappearance of colloidal chromic phosphate labeled with P^{32} from venous blood. This method has been described in detail previously[6, 7]. Values for liver blood flow obtained by this method are expressed as disappearance rate constants (k) and represent the fraction of the blood volume perfusing the liver per minute.

Blood Volume

Total volume was measured by the dilution technique. Iodinated (I^{131}) human serum albumin* was usually used because of its commercial availability. The dilution curves of I^{131}-labeled human serum albumin were measured for one to two hours and the volumes calculated by extrapolation. The activity of the dilution-curve samples was measured in whole blood and the plasma volume was calculated from the hematocrit. Correction for plasma hold-up in the cell fraction was not made because of the uncertainty of this value when applied to the high hematocrits seen after thermal injury.

Other Measurements

Hematocrits were determined by the standard Wintrobe method. Using a Sanborn Twin-Viso recorder in combination with a Statham pressure transducer and mercury manometer, simultaneous tracings were obtained of lead II of the electrocardiogram and femoral pulse contours as well as mean femoral arterial pressures.

RESULTS

The most striking result in this study was the promptness and the precipitousness of the changes that were observed following thermal injury.

Cardiac Output Changes

Forty-five measurements on 25 dogs were made after immersion to the axillae in water of 80° to 85° C. for 30 seconds. The time of measurement varied from as early as 8 minutes after thermal injury to approximately 6 hours. The average changes in cardiac output with time are summarized in Table I.

*RISA obtained from Abbott Laboratories.

Table I

Reduction in cardiac output at various time intervals after thermal injury (immersion to axillae in water at 80° to 85° C. for 30 seconds).

Time after injury	0-30 min.	30-60 min.	1-3 hr.	3-6 hr.
Fraction of pre-burn cardiac output	1/3	1/3	1/3	1/4
% reduction in cardiac output	66±2.0*	65±3.1*	66±5.1*	75±5.7*
Stand. Dev.	9.2	8.2	16.8	9.8

*Standard error of the mean.

The data show that with the degree of trauma inflicted a marked reduction in cardiac output occurs within the first half hour, and that this reduction remains essentially unchanged throughout the first six hours.

The average change in cardiac output shown in Table I (66% reduction) represents a fall to one-third of the preburn value. Figure 1 illustrates an extreme example in which the cardiac output fell to one-seventh of the preburn value. The area under each dilution curve is inversely proportional to the cardiac output. At 22 minutes there is a very pronounced increase in the area under this curve, together with a marked delay in appearance time. These marked changes are not transient, but persist essentially unaltered for five hours.

A few measurements were made following lesser degrees of thermal injury, and again the cardiac output was observed to fall in every instance. When immersion to the axillae was in water at 70° C. for 30 seconds, the initial fall was less marked; however, the reduction after two hours was just as great as in the 80° to 85° C. group. When the immersion time at 70° C. was reduced to 12 seconds, the degree of reduction of cardiac output was less throughout the period of measurement (3 hr. postburn).

Liver Blood Flow Changes

A total of 115 colloidal chromic phosphate disappearance curves were measured on 60 dogs. The data are summarized in Table II and represent the liver blood flow measured as the disappearance rate constant, k. Because impaired phagocytic efficiency occurs at about three hours after experimental burn injury,[8] the data after three hours represent a combination of altered

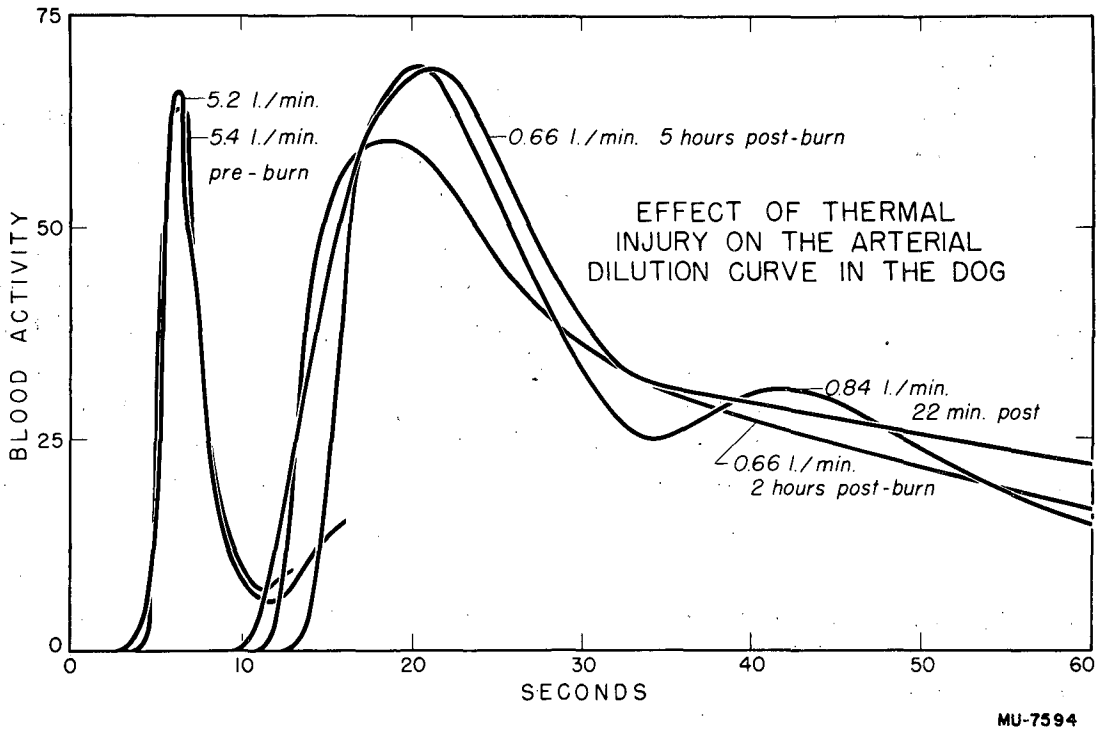

Fig. 1. Serial arterial dilution curves before and after thermal injury. The area under the curves is inversely proportional to the cardiac output.

liver blood flow and depressed phagocytic removal efficiency, whereas prior to three hours the disappearance rate constant k accurately represents the fraction of the blood volume perfusing the liver per minute.

Table II

Pre- and postburn colloid disappearance rate constants k and the percent reduction in liver blood flow at various time intervals after thermal injury (immersion to axillae in water at 80° to 85° C. for 30 seconds).[a]

Time after injury	Preburn	0-30 min	30-60 min	1-3 hr	3-6 hr
Disap. rate constant k (min^{-1})	0.52±0.01	0.29±0.01	0.27±0.03	0.22±0.01	0.18±0.01
Standard Deviation	0.09	0.06	0.08	0.02	0.04
% reduction in liver blood flow		44	48	58	b____

[a] The percent reduction in liver blood flow is given without correction for reduction in blood volume. If blood volume decreases are included the reductions in liver blood flow are greater than shown.

[b] Cannot be accurately calculated due to impaired phagocytic efficiency after three hours.[8]

The data in Table II show an immediate and sustained fall in liver blood flow. The gradual additional fall after three hours reflects the change in efficiency of the liver phagocytes mentioned above.

Figure 2 shows a series of pre- and postburn disappearance curves of colloidal chromic phosphate. The disappearance rates are expressed as half times and can be converted to disappearance rate constants (k) by division into 0.693. Eight minutes after thermal trauma of 85° C. for 30 seconds, the disappearance half time has been prolonged to 2.5 minutes, representing a reduction in liver blood flow of 56%. With increasing time after injury there is a progressive decrease in colloid disappearance rate.

As was noted in the cardiac output data, lesser degrees of thermal trauma always produced a fall in liver blood flow, but the magnitudes were less than in the 80° to 85° C. group.

Blood Volume and Hematocrit Changes

Since blood volume was measured with a plasma diluent, the data are expressed as plasma volume in percent of body weight. Forty-six measurements were made on 22 dogs. Table III summarizes the changes in plasma volume

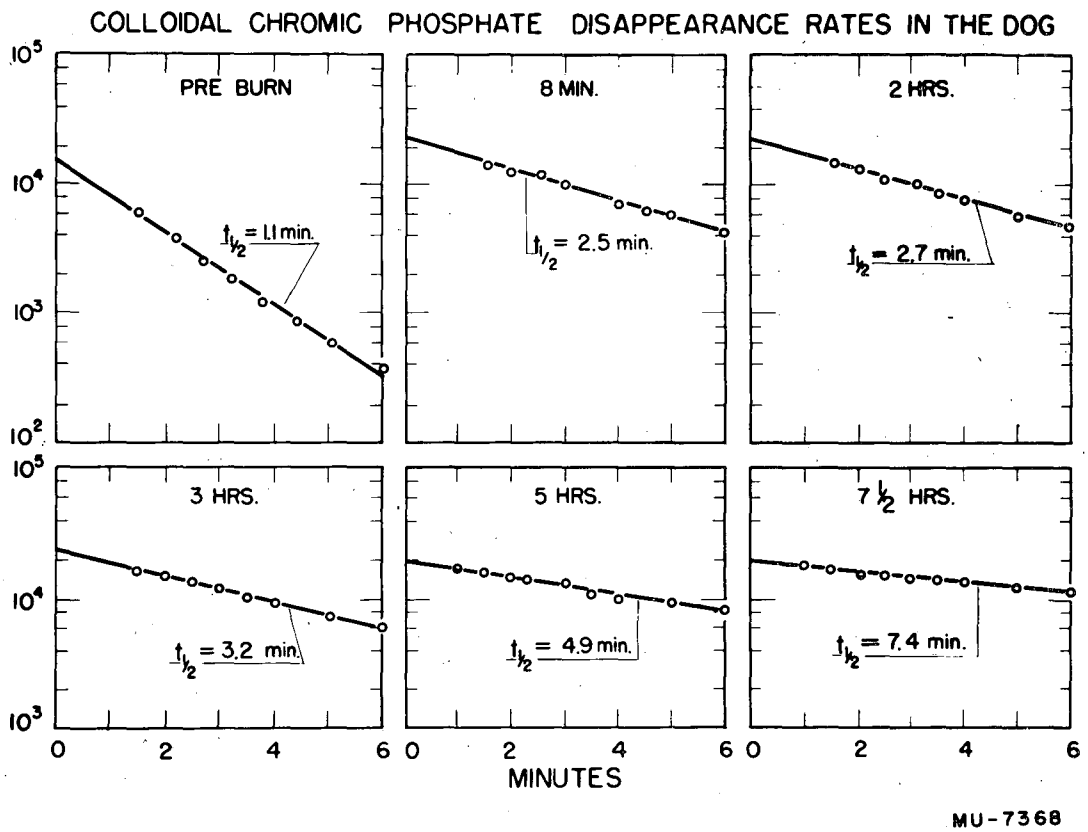

Fig. 2. Serial disappearance curves of colloidal chromic phosphate before and after thermal injury. The t 1/2's of the curves are inversely proportional to the volume of blood perfusing the liver per minute (liver blood flow). After 3 hours, however, the disappearance slopes represent a combination of altered liver blood flow and depressed phagocytic removal efficiency.

and hematocrit seen after thermal trauma.

Table III

Pre- and postburn hematocrit and plasma volume determinations, and the percent reduction in plasma volume, at various times after thermal injury (immersion to axillae in water at 80° to 85° C. for 30 seconds).

Time after injury	Preburn	0-30 min	30-60 min	1-3 hr	3-6 hr
Hematocrit, % cells	43±1	54±3	55±3	56±4	61±1
Standard Deviation	6	8	7	9	2
Plasma volume % body weight	5.3±0.3	4.1±0.6	3.4±0.6	3.7±0.7	2.8±0.8
Standard Deviation	1.6	1.4	1.3	1.5	1.3
% reduction in plasma volume		23	36	30	47

In contrast to the cardiac output, the plasma volume and hematocrit show progressive changes with time. An extensive reduction in plasma volume occurs promptly, but the percent reduction in the 3 to 6 hour interval is twice the reduction seen in the first half hour.

The plasma volume and cardiac output data do not substantiate the general impression that cardiac output reductions are completely explained by plasma losses. In Figure 3 the percent reduction in cardiac output is plotted against the percent reduction in plasma volume for dogs subjected to the same degree of injury (80° C. to axillae for 30 seconds). A complete lack of correlation is shown by the scatter.

Blood Pressure and Electrocardiographic Changes

In the first three hours after thermal injury, mean femoral arterial pressures showed marked changes, ranging from a 36% reduction to a 34% increase. The average postburn value, however, was only 7% below the preburn value, and hypotensive levels were seldom reached before 6 or more hours.

Although mean arterial pressures did not parallel the reduction in cardiac output, pulse pressures showed a high degree of correlation with cardiac output.

Simultaneous lead II electrocardiograms and femoral arterial pulse contours were obtained in 11 dogs before and at frequent intervals after thermal injury. Pulsus alternans appeared in 5 of the animals, usually within the first half hour. ECG changes also occurred within the first half hour after

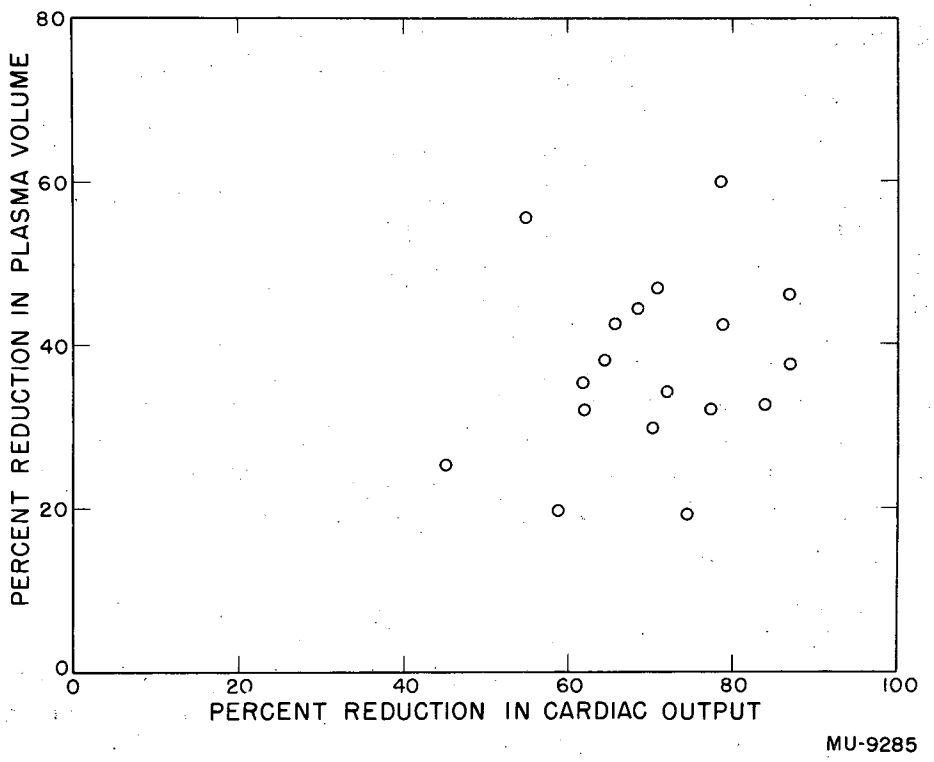

Fig. 3. Demonstration of the lack of correlation between the reduction in cardiac output and the reduction in plasma volume in dogs subjected to the same degree of thermal injury.

thermal trauma and consisted of a marked decrease in QRS voltage in 8 dogs, the appearance of either a biphasic or a tall peaked T-wave in 5, and an increase in P-wave voltage in 2. When pulsus alternans did occur, it was usually preceded by electrocardiographic changes. Representative ECG and pulse-contour changes are shown in Figures 4, 5 and 6.

DISCUSSION

As denoted by the data presented, the most striking change produced by experimental thermal injury is a prompt and severe fall in cardiac output with consequent reduction of blood flow to vital tissues. This reduction in cardiac output following experimental burns has been described or alluded to by others.[9, 10] The depression in cardiac output has hitherto usually been assumed to result solely from plasma losses at the area of injury. These plasma losses presumably lead to a decrease in circulating blood volume with a consequent reduction in venous return to the heart.

The early reduction in plasma volume recorded in Table III amounts to 23%. This represents a reduction of only about 12% in total circulating blood volume. This small reduction would not be expected to produce as great a change in cardiac output as is observed. To further delineate this, a small series of hemorrhage experiments were performed. Dogs were acutely bled by 1.5% of their body weight (removal of 15% of total blood volume). Cardiac output reductions in these animals averaged 30%, a much smaller reduction than was obtained in the burn experiments (Table I). Furthermore, even acute removal of 30% of the total blood volume produced a smaller reduction in cardiac output than the burn. It appears, therefore, that in experimental burn injury simple reduction in blood volume alone cannot completely account for the marked reductions in cardiac output.

Since plasma is presumably progressively lost into the burn area, one would also expect a progressive reduction in cardiac output with time. The fall in cardiac output which appears initially remains essentially unchanged, however, while plasma volume continues to fall, thus producing the lack of correlation between these two factors noted in Figure 3.

That some partial connection between cardiac output and plasma volume exists, however, is indicated when therapeutic efforts are made to increase the circulating blood volume. In a limited number of experiments, replacement of calculated blood losses by the use of whole blood with high hematocrits (55% to 70%) produced only a slight return toward normal of the depressed cardiac output. On the other hand, replacement of blood losses by the infusion of 6% Dextran resulted in a fall in hematocrit and a prompt return of cardiac output to values approximating the normal preburn level. Furthermore, reduction of hematocrit without a net increase in total blood volume, as accomplished by volume-for-volume replacement of blood with Dextran,

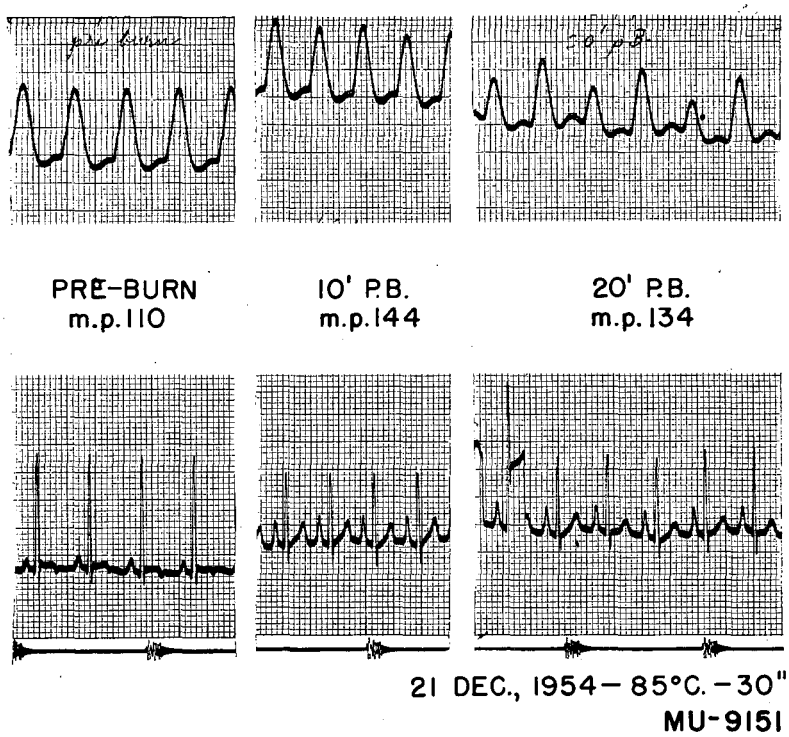

Fig. 4. Femoral arterial pulse contours, mean arterial pressures, and lead II electrocardiograms before and after thermal injury. At 10 minutes postburn: there is an increase in mean arterial pressure, P-wave voltage has increased, QRS voltage is reduced, and the preburn biphasic T-wave has become upright. At 20 minutes postburn: the mean arterial pressure is still above the preburn level, but pulsus alternans is now evident. The ECG changes seen at 10 minutes persist. The cardiac rate is essentially unchanged. Cardiac indices were: preburn, 1.6; 15 minutes postburn, 0.56.

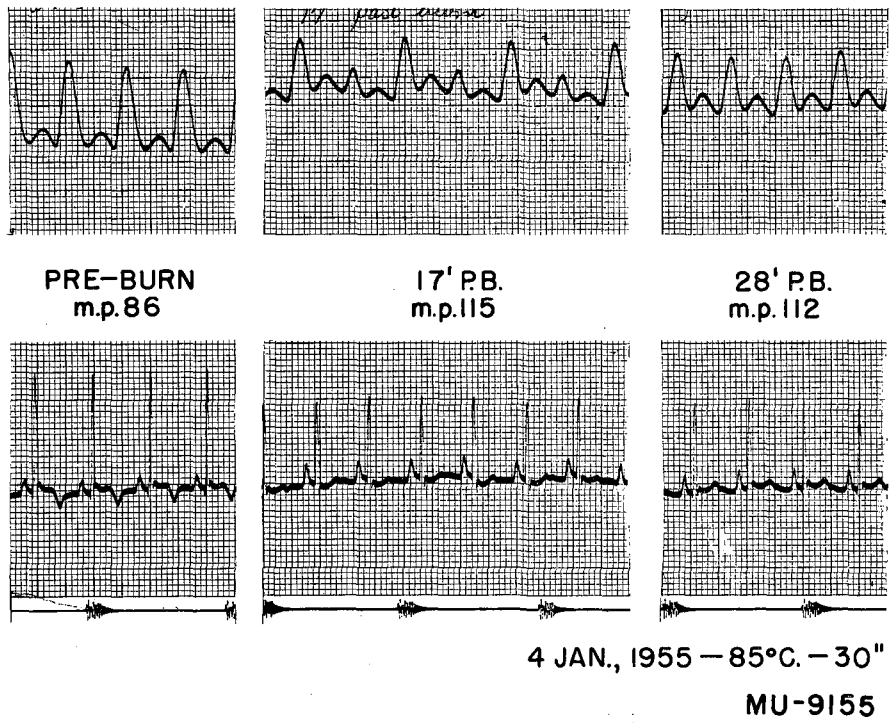

Fig. 5. Femoral arterial pulse contours, mean arterial pressures, and lead II electrocardiograms before and after thermal injury. At 17 minutes postburn: in spite of the appearance of pulsus alternans, the mean arterial pressure has risen, P-wave voltage has increased, QRS voltage has decreased, and the preburn inverted T-wave has become biphasic. At 28 minutes postburn: mean arterial pressure has remained constant, pulsus alternans has disappeared, and pulse pressure is moderately decreased. The ECG changes persist. The cardiac rate remains essentially unchanged. Cardiac indices were: preburn, 2.2; 17 minutes postburn, 1.1; 28 minutes postburn, 0.80.

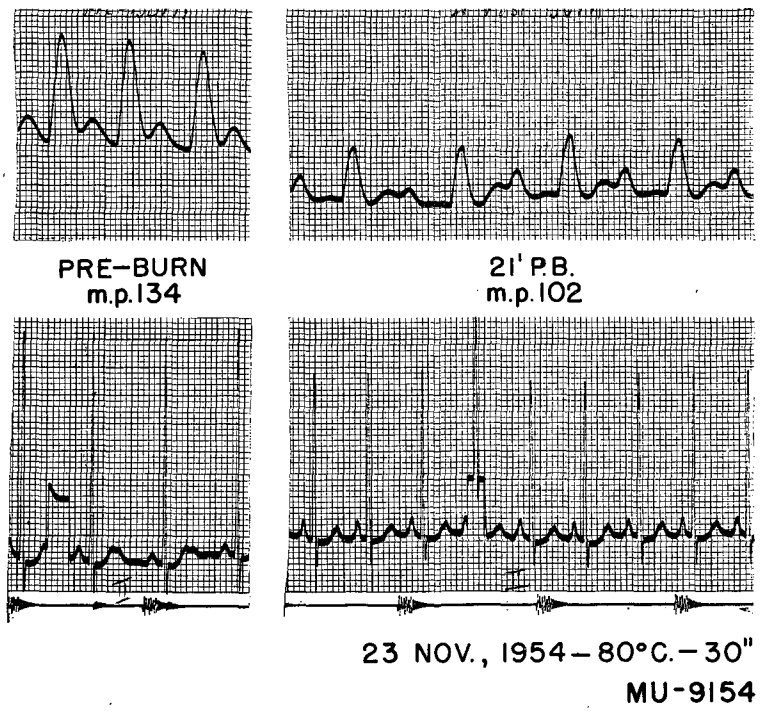

Fig. 6. Femoral arterial pulse contours, mean arterial pressures, and lead II electrocardiograms before and after thermal injury. At 21 minutes postburn; there is a fall in mean arterial pressure, a marked reduction in pulse pressure, and the appearance of pulsus alternans. P-wave voltage has increased, QRS voltage has decreased, and the T-wave has become more peaked. The cardiac rate has increased moderately. Cardiac indices were: preburn, 1.9, 21 minutes postburn: 0.66.

also yielded a definite albeit small, improvement in cardiac output.

Although some relationship between plasma volume and cardiac output exists, the data presented suggest that other important factors are also operating to produce a deleterious effect upon cardiac output. The early appearance of electrocardiographic changes, and on occasion of pulsus alternans, suggests that an intrinsic myocardial depression may exist which participates in the reduction of cardiac output. This initial depression of the myocardium may be caused by several mechanisms acting independently or in combination.

One factor that may be of significance in this connection is the state of the peripheral vascular tree. Failure to obtain an early consistent fall in blood pressure accompanying the marked fall in cardiac output is indicative of a severe generalized vasoconstriction, which, indeed, is readily noted in the major peripheral arteries by simple palpation. If generalized vasoconstriction includes the coronary circulation, the consequent reduction in coronary blood flow may in part account for the depressed myocardial function and the accompanying electrocardiographic and pulse-contour changes observed.

Another factor that may serve to explain the disproportion between cardiac-output reduction and plasma-volume loss is a change in the quality (rather than in the quantity) of the blood accompanying hemoconcentration. An increase in hematocrit is known to produce a marked increase in blood viscosity, and this may impede blood flow to the myocardium as well as to other regions. In this connection it is of interest that Dextran infusions which resulted in cardiac output improvements also produced marked reductions in hemoconcentration, whereas whole-blood infusions which increased the circulating blood volume without changing the hematocrit were relatively ineffective.

SUMMARY AND CONCLUSIONS

1. The most striking change noted after experimental thermal injury is a prompt, severe, and sustained fall in cardiac output, amounting on the average to a 66% reduction.

2. This severe fall in cardiac output is accompanied by a marked decrease in liver blood flow, amounting on the average to a 44% reduction.

3. Although plasma volume shows an initial fall, the severe changes in cardiac output do not appear to be adequately explained by volume losses alone.

4. Electrocardiographic abnormalities and the appearance of pulsus alternans suggest the occurrence of early myocardial depression which may participate in the reduction of cardiac output.

5. Factors that may serve to explain the disproportion between cardiac output reduction and plasma volume loss are discussed.

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