THE UNIFORM PRODUCTION OF EXPERIMENTAL SHOCK BY CRUSH INJURY: POSSIBLE RELATIONSHIP TO CLINICAL CRUSH SYNDROME

GEORGE W. DUNCAN,* M.D., AND ALFRED BLALOCK, M.D.

BALTIMORE, MD.

FROM THE DEPARTMENT OF SURGERY OF THE JOHNS HOPKINS SCHOOL OF MEDICINE, BALTIMORE, MD.

IN RECENT MONTHS a number of clinical reports[1, 2, 3, 4, 5] have appeared on the condition which results from the compression of extremities by heavy objects for periods of several hours or longer. Most of these accidents have occurred in association with air raids in which persons have been pinned beneath fallen débris. The essential clinical features are these: The patient is usually in fairly good condition at the time of release of the compression; evidences of shock generally develop within a few hours; the immediate response to therapy is usually favorable; and subsequently, after a period of hours or days, the patient develops signs of progressive renal damage. The urinary output diminishes at this time; there is nitrogenous retention; and the urine contains albumin and large orange or brown granular casts. In approximately half of the reported cases death occurred in three to eight days following the compression.

The present study was undertaken in an attempt to reproduce experimentally the so-called crush syndrome. The first efforts consisted in compressing the extremity of the experimental animal by various means, including the use of tourniquets, encircling layers of rubber dam, and pressure between two smooth boards. The results which followed the use of these methods showed considerable variation. It then appeared to be advisable to use objects for compression which did not have a smooth surface and which would exert an uneven pressure, resulting in greater injury to tissues. This method, which will be described in detail, has resulted, in our hands, in the more uniform production of peripheral circulatory failure than we have been able to accomplish by other procedures.

It cannot be stated with certainty that our method has resulted in the causation of the so-called crush syndrome; in fact, it has not been proved conclusively that the crush syndrome as observed in patients is a distinct clinical entity, with features which may not be found following other types of injury. Regardless of whether or not the crush syndrome has been reproduced, the present studies have yielded what appears to be a rather uniform method of causing shock, in which an increase in the concentration of the blood and a fall in blood pressure occur early following the release of the compression.

The present communication presents a description of the method; a report of the effects of compression of one of the posterior extremities of the

* William Stewart Halsted Fellow in Surgery.

anesthetized animal; and the results of attempts to influence the course of the animals following the release of the compression.

EXPERIMENTAL METHOD

The experiments were performed upon dogs weighing between 7 and 11 Kg. Morphine sulphate in doses of .030 Gm. was given subcutaneously at the beginning of the experiments. Approximately 30 minutes later sodium pentobarbital, .020 Gm. per Kg. of body weight, was given intravenously. One or two subsequent doses of .006 Gm. per Kg. of body weight were usually necessary to maintain anesthesia during the following 18 to 24 hours. The mean arterial blood pressure was determined repeatedly by direct needle puncture of the femoral artery. Hematocrit readings were made with Wintrobe tubes. The bladder was catheterized at the beginning of the experiment and the catheter left in place, so that the character and volume of the urine could be observed at one- to two-hour intervals. Nonprotein nitrogen, plasma creatine, and plasma creatinine levels were determined by the method of Folin and Wu.[6] Blood samples were taken at the beginning of the experiment, immediately before the compression of the limb was released, at one hour, four hours, and six hours subsequently. Creatine and creatinine levels in the urine were determined at corresponding intervals (on individual specimens) by the methods of Folin.[7] All colorimetric determinations were made with an Evelyn photo-electric colorimeter. Urine samples were examined at the beginning of the experiment, and every one to two hours threafter during the experiment, as to volume, gross appearance, presence or absence of albumin, benzidine reaction, hydrogen ion concentration (litmus), and microscopic appearance.

Compression of a limb was produced by an apparatus (Fig. 1) consisting of two three-quarter-inch boards, 15 inches long and seven inches wide, on the inner surface of which were fixed triangular strips of wood measuring 1½x1½x2¼ inches. These strips were placed so that when the boards were approximated their coaptation resulted in a cog or gear-like arrangement. In the center of each strip a groove, one inch in diameter and three-quarters of an inch deep, was made corresponding to the course of the femur. This groove prevented interference with the approximation of the strips and thus ensured the crushing of a larger mass of muscle. Holes, which were three-quarters of an inch in diameter, were drilled in the four corners of the boards. Into these were inserted one-half-inch iron bolts, which were 11 inches long. Threads extended half the length of the shaft and these were fitted with large wing-tipped nuts. Steel compression springs, four inches long, fifteen-sixteenths of an inch in diameter, one-eighth of an inch wire diameter, with 13 effective coils, were placed on the bolts on the upper board. Suitable steel washers were used to protect boards and springs. The springs were calibrated by placing them between the boards and measuring the millimeters of shortening produced by a weight of 500 pounds, which was placed on the upper board.

The dog's thigh was placed in this press and a pressure of 500 pounds was applied for a period of five hours, at the end of which time the press was removed. Approximately half the animals were given no treatment after release of the compression, and observations were made at the intervals de-

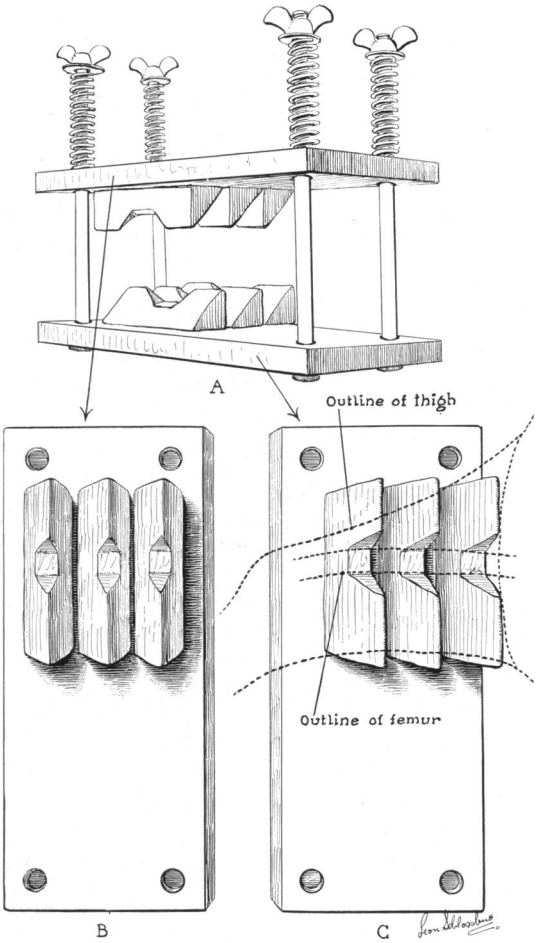

FIG. 1.—Drawings of apparatus used for limb compression. (A) Side view of assembled apparatus with upper board elevated to show relative position of its parts. Pressure is applied to the upper board by tightening the wing-tipped nuts and shortening the springs. (B) Apparatus taken apart to show position of triangular strips of wood and the groove in their centers to fit the approximate course of the femur. These strips are so arranged that their apices fit into the spaces between the strips of the opposite board. In other words, the sharp edges are so placed that they do not touch each other but fit into the corresponding spaces.

scribed above. The other half were treated by the application of a pneumatic rubber cuff (Fig. 2) which was applied to the injured extremity immediately upon release of compression. This cuff consisted of an outer layer of thick rubber which was cylindrical in shape, 17 inches long and five inches in diameter, and an inner layer of thinner rubber which was conical in shape

in order to fit the contour of the extremity snugly. The cuff was fitted with a valve which was connected to the compressed air supply. A mercury column valve was interposed to ensure constant pressure. By means of this cuff a pressure of 40 Mm.Hg. was applied to the extremity for periods of 13 hours in some experiments and 18 hours in others. The loss of fluid into and near the injured area of the animals which died was determined by a bisection method that was described previously.[8]

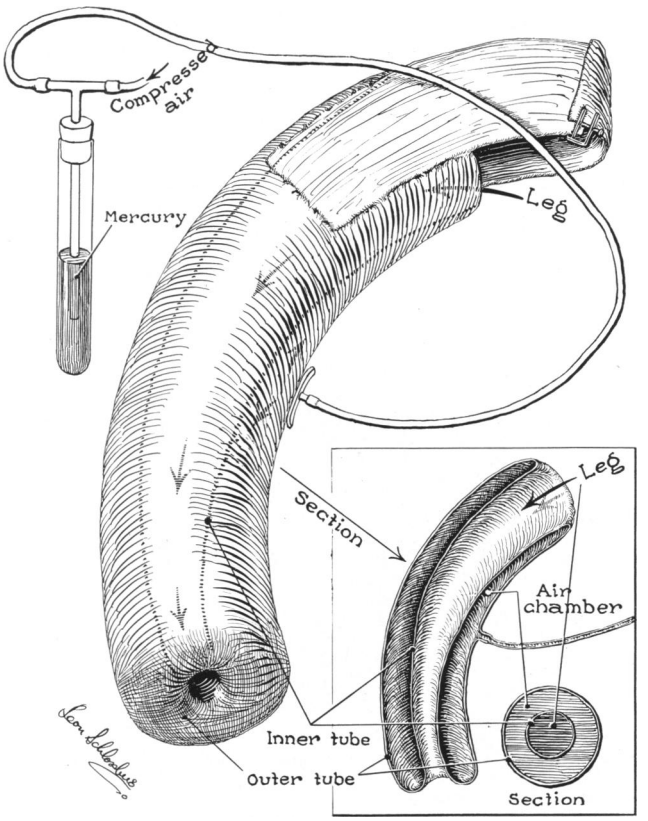

FIG. 2.—Drawing of the pneumatic cuff used in treatment of crushed extremities. The rubber strips at the upper end of the cuff encircle the animal's lower abdomen and are held together by a screw-clamp. Insert—Longitudinal section of the cuff showing air space and conical shape of inner tube which is in contact with the extremity.

RESULTS

The results are summarized in Tables I, II and III. For purposes of description the results of the experiments will be divided into: (1) Crush period, or period of five hours of compression of the extremity; (2) the period following release of compression, no therapy being employed (half of experiments); and (3) the period following release of compression, pressure therapy being used (half of experiments).

TABLE I

THE EFFECTS OF CRUSH INJURIES (UNTREATED GROUP)

Exper. No.	Mean Blood Pressure Mm.Hg.		Pulse Rate per Min.		Hematocrit Reading		Respiratory Rate per Min.		Temperature Degrees F.		Hours Press Applied	Hours Survived After Press Removed	Fluid Loss% Body Weight (Local)
	Control	Reading 2–6 Hrs. After Press Removed	Control	Reading 2–6 Hrs. After Press Removed	Control	Reading 2–6 Hrs. After Press Removed	Control	Reading 2–6 Hrs. After Press Removed	Control	Reading 2–6 Hrs. After Press Removed			
1	130	95	120	172	48.2	71.8	8	12	101.4	102.4	5	6	3.04
2	130	50	68	200	50.2	72.2	10	6	99.6	99.0	5	16 hrs. 15 min.	3.39
3	115	95	56	160	48.3	55.4	6	6	98.9	99.6	5	8	3.02
4	125	75	140	200	44.3	64.7	6	12	98.0	98.0	5	12	3.42
5	125	100	120	200	39.4	43.4	10	16	99.4	102.1	5	Recovered	....
6	125	50	140	200	42.9	67.5	12	6	98.8	98.0	5	7	....
7	115	115	96	108	40.7	58.0	8	8	99.4	99.4	5	12	3.97
8	120	90	84	200	50.4	76.8	10	16	100.0	99.4	5	4 hrs. 35 min.	3.81
9	130	45	120	200	51.3	67.0	8	20	99.0	102.2	5	10	3.40
10	115	75	140	200	56.0	71.1	10	20	99.4	99.0	5	14	3.12
11	125	120	120	160	41.7	72.7	16	16	100.2	98.9	5	6	2.97
12	125	70	120	...	48.4	74.3	6	16	100.1	102.1	5	2 hrs. 20 min.	2.94
13	115	85	120	186	55.0	74.0	10	24	101.2	103.6	5	6	3.46
14	110	75	100	200	56.6	75.8	6	40	100.1	103.1	5	12	3.88
15	130	50	112	200	42.2	72.7	10	40	100.8	103.5	5	2 hrs. 15 min.	3.51
16	120	45	172	200	50.4	76.4	10	40	100.9	103.5	5	5 hrs. 15 min.	3.04
17	130	60	104	180	53.2	78.0	8	40	99.8	102.6	5	5 hrs. 15 min.	3.22
18	125	40	96	172	53.7	72.7	6	10	100.8	102.5	5	11	2.64
19	120	88	140	200	42.7	74.0	6	6	100.6	102.4	5	6	2.67
	Average fall 49.89 Mm.Hg.		Average rise 72.7 per min.		Average rise 44.0% over control values		Average rise 12.00 per min.		Average rise 1.17° F.			Average 7.55 hrs. (excluding survival)	Average 3.26%

TABLE II

THE EFFECTS OF CRUSH INJURIES AND OF COMPRESSION THERAPY

Exper. No.	Mean Blood Pressure Mm.Hg.		Pulse Rate per Min.		Hematocrit Reading		Respiratory Rate per Min.		Temperature Degrees F.		Hours Press Applied	Hours Pneumatic Cuff Applied	Hours Survived After Press Removed*	Fluid Loss% Body Weight (Local)
	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed				
20	120	115	152	180	40.8	58.8	6	10	100.8	98.2	5	13	Recovered	
21	120	105	132	180	50.2	80.4	12	8	101.2	103.6	5	12	12	3.12
22	130	115	136	192	49.5	69.8	12	16	99.6	104.6	5	13	30	3.14
23	135	110	140	160	52.8	68.4	10	16	98.9	101.4	5	13	30	3.25
24	120	105	96	150	33.4	50.0	6	6	100.6	101.0	5	13	Recovered	
25	125	130	120	116	49.4	51.2	10	8	100.1	98.9	5	13	Recovered	
26	125	105	66	172	42.2	43.3	8	10	103.2	102.4	5	13	Recovered	
27	130	120	160	192	43.7	60.3	10	16	102.4	102.4	5	18	Recovered	
28	130	120	132	180	50.0	66.4	10	12	100.6	99.3	5	18	Recovered	
29	120	120	112	160	46.3	53.6	6	12	101.2	102.4	5	18	30	....
30	125	114	84	160	44.0	54.2	10	10	98.8	98.8	5	18	Recovered	
31	115	140	120	192	47.7	63.0	8	12	99.0	98.2	5	18	Recovered	
32	125	115	120	200	55.8	76.3	16	12	98.4	103.6	5	18	{ 25 hrs. 25 min. }	3.29
33	130	115	104	160	43.5	60.3	6	8	99.7	104.4	5	18	Recovered	
34	125	115	120	120	52.3	60.7	6	8	101.2	99.0	5	18	Recovered	
35	126	120	72	72	53.0	67.5	10	8	100.8	99.8	5	18	Recovered	
36	110	110	140	180	52.0	60.0	16	14	101.6	99.8	5	18	Recovered	
37	130	110	110	150	....	....	12	10	101.4	102.3	5	18	Recovered	
38	135	100	112	188	55.2	66.7	10	16	102.2	104.3	5	18	Recovered	
39	132	80	72	160	37.0	44.2	8	8	100.2	102.6	5	18	Recovered	
40											5	7	7	3.50
	Average fall 16.88 Mm.Hg.		Average rise 53.00 per min.		Average rise 28.5% over control values		Average rise 1.88 per min.		Average rise .85° F.				Average survival time 26.33 hrs. (excluding survivals)	Average 3.26%

* The animals listed as recovered were in most instances sacrificed three to four days following removal of the pneumatic cuff. Longer survival periods are being studied at the present time.

TABLE III

BLOOD AND URINARY FINDINGS FOLLOWING EXPERIMENTAL CRUSH INJURIES

Exper. No.	Plasma Creatine* Mg.%		Plasma Creatinine* Mg.%		N. P. N. Mg.%		Urinary Creatine* Mg./Cc.		Urinary Creatinine* Mg./Cc.		Urine Output Cc.		Urine Benzidine Reaction		Urine Albumin	
	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Total While Press on Thigh	Total for 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed
1	1.9	2.0	1.5	1.4	25.0	90.0	0.5	5.7	1.4	1.5	46	48	Neg.	Pos.	Neg.	Pos.
2	2.2	3.9	.6	.9	32.5	43.7	1.0	4.5	3.2	1.2	20	45	Neg.	Pos.	Neg.	Pos.
3	1.9	17.4	.9	1.5	32.0	70.5	2.8	1.1	2.2	1.7	67	4	Neg.	Pos.	Trace	Pos.
4	.8	3.6	.9	1.9	30.0	84.0	.5	3.2	2.4	1.7	30	26	Neg.	Pos.	Neg.	Pos.
5	.4	12.8	1.0	3.2	35.2	84.0	.8	6.2	.9	1.6	36	3	Neg.	Pos.	Trace	Pos.
6	1.1	20.1	1.0	1.8	31.0	71.6	.9	.4	2.5	1.5	31	3	Neg.	Pos.	Neg.	Pos.
7	2.3	11.6	.9	2.3	30.0	63.7	1.1	6.7	2.1	.7	39	20	Neg.	Pos.	Neg.	Pos.
8	.4	5.5	1.1	1.5	27.5	81.0	1.0	3.4	2.5	1.1	27	42	Neg.	Pos.	Neg.	Pos.
	Average rise 8.2 mg.%		Average rise .8 mg.%		Average rise 43.2 mg.%		Average rise 2.8 mg.%		Average fall .7		Av. 37 cc.	Av. 23.9 cc.				

* No selection was made as to sex, age or regulation of carbohydrate and protein intake of the animals prior to the experiments. This probably accounts for the high plasma creatine and creatinuria of the control specimens. Control values on 12 animals under the same conditions showed similar results and human specimens showed normal values.

TABLE III—*Continued*

Exper. No.	Urine Reaction (Litmus)		Gross Appearance of Urine		Microscopic Examination of Urine—Catheterized		Blood Pressure		Pulse		Hematocrit		Therapy and Result
	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	Control	Reading 4–6 Hrs. After Press Removed	
1	Acid	Alk.	Clear yellow	Grossly bloody	Occasional leukocyte and epithelial cell. No erythrocytes or casts.	Loaded with erythrocytes. Numerous leukocytes and epithelial cells. Numerous red cell casts and granular casts.	130	120	132	180	50.0	66.4	Pneumatic cuff applied. Recovered.
2	Acid	Acid	Clear amber	Grossly bloody	Occasional leukocyte and epithelial cell. No erythrocytes or casts.	Loaded with erythrocytes. Few leukocytes and epithelial cells. No casts.	130	115	160	192	43.7	60.3	Pneumatic cuff applied. Recovered.
3	Acid	Alk.	Clear yellow	Dark brown	Occasional leukocyte. No casts. No erythrocytes. Occasional epithelial cell.	30–40 erythrocytes. Numerous epithelial cells. Few leukocytes.	130	85	112	200+	42.2	67.7	No therapy. Died.
4	Alk.	Acid	Slightly cloudy, yellow	Cloudy, grossly bloody	2–3 epithelial cells. Occasional leukocyte and erythrocyte.	Loaded with erythrocytes. Numerous epithelial cells. 6–8 leukocytes/H.P.F. No casts.	135	100	112	188	55.2	66.7	Pneumatic cuff applied. Recovered.
5	Acid	Alk.	Clear yellow	Grossly bloody	Occasional leukocyte and epithelial cell. No casts or erythrocytes.	Loaded with erythrocytes. 3–4 granular and red cell casts/H.P.F. Numerous epithelial cells and crystals.	120	45	172	200+	50.4	76.4	No therapy. Died.
6	Acid	Alk.	Clear amber	Grossly bloody, brown tinge	Occasional erythrocyte, epithelial cell and leukocyte. No casts.	No casts. Loaded with erythrocytes. Numerous epithelial cells and crystals.	130	60	104	180	53.2	78.0	No therapy. Died.
7	Acid	Acid	Clear yellow	Grossly bloody, brown tinge	Occasional granular cast. Occasional epithelial cell and leukocyte. Occasional erythrocyte.	Loaded with erythrocytes. Numerous red cell casts and large brown granular casts.	125	120	132	180	50.2	73.6	Pneumatic cuff applied. Died.
8	Acid	Alk.	Clear yellow	Grossly bloody, brown tinge	Occasional leukocyte and epithelial cell. No casts or erythrocytes.	Loaded with erythrocytes. Numerous epithelial cells. Occasional granular cast.	120	115	152	180	40.8	55.3	Pneumatic cuff applied. Recovered.
							Average fall 32.5		Average fall 53/min.		Average rise 41.1% over control values		

CRUSH PERIOD

During the crush period there was no significant change in blood pressure in any of the animals. A slight increase in the concentration of the red blood corpuscles was noted in 22 experiments and a slight decrease in 18, the average being an increase of .61 per cent. The pulse rate increased in 30 experiments, decreased in eight and remained unchanged in two, the average being a rise of 20.8 beats per minute. The respiratory rate increased in 23 experiments, decreased in 12 and remained unchanged in five. The average was an increase of 2.3 per minute. The temperature rose in 21 animals and fell in 16, the average being a rise of .36° F. There was an average fall in plasma creatinine of .69 mg.%, and an average increase in plasma creatine of .48 mg.% was observed. Nonprotein nitrogen values increased an average of 4.05 mg.%. Urinary creatine decreased .07 mg. per cc. Urinary creatinine decreased .30 mg. per cc. Microscopic examination showed red blood cells in the urine in every case within two to three hours after the press was applied. The benzidine reaction became positive in two to three hours. Albumin was present in the urine in two to four hours. Except for the urinary findings, it is to be observed that the alterations in most of the functions were minimal.

RELEASE OF CRUSH WITHOUT THERAPY

There were 19 experiments in this group, the results of which are given in Table I. The press was applied to the thigh for a period of five hours. At the end of this time it was removed and the animal was observed, no form of therapy being employed. All animals died except one. Upon removal of the press there was usually a sudden sharp decline in blood pressure to 50 to 60 Mm.Hg. The pressure returned within a few minutes to, or almost to, its former level and subsequently a progressive decline occurred. An increase in the concentration of the red blood cells occurred as soon as the press was removed. This increase was progressive and an average rise of 44 per cent over the control values was observed at the end of periods varying from two to six hours. The pulse rate rose an average of 72.7 per minute. The respirations increased an average of 12 per minute. The rectal temperature increased an average of 1.17° F. The average duration of life in this group was 7.55 hours.

The urine usually became grossly bloody within an hour after the press was removed. The output of urine in this group during the two- to six-hour period following removal of the press averaged 3.3 cc. Although granular and red blood cell casts were frequently found, the dark granular casts, which have been described in clinical cases of crush injury, were not observed.

In three dogs of this group, in which blood chemical and urinary chemical changes were observed, the plasma creatine increased an average of 15.6 mg.% above the control levels. Plasma creatinine levels showed an average increase of 3.45 mg.%, and nonprotein nitrogen an average rise of 44.8 mg.%. Uri-

nary creatine increased an average of 1.03 mg. per cc. Urinary creatinine decreased an average of .25 mg. per cc.

RELEASE OF CRUSH WITH THERAPY

There were 21 experiments in which, following the removal of the press, a pneumatic rubber cuff was applied to the injured thigh at a pressure of 40 Mm.Hg. When the cuff was applied for a period of 13 hours, three of six animals died. When the time of application was increased to 18 hours, three of 15 died. The average survival time of these six animals was 26.3 hours. The average fall in blood pressure of the entire group in the first four- to six-hour period was 16.9 Mm.Hg. Hematocrit volumes increased in this same period an average of 28.5 per cent over the control values. The respiratory rate showed an average increase of 1.88 per minute, and the average elevation of body temperature was .85° F. The pulse rate increased an average of 53 per minute.

Just as in the untreated group, the urine became discolored and showed gross blood within one hour after the press was removed. The average urinary output for the same period of time was 36.2 cc. On microscopic examination of the urine, several animals showed granular and red blood cell casts and an occasional hyaline cast. Two animals of this group showed in the urine large dark brown granular casts which were similar in appearance to those described in clinical cases of crush injury. The urinary creatine output averaged 3.67 mg. per cc. The creatinine output showed an average decrease of 1.27 mg. per cc. Plasma creatine increased an average of 3.60 mg.% and plasma creatinine an average of .57 mg.%.

PATHOLOGIC CHANGES

The pathologic changes in the treated group of animals which ultimately succumbed were, as a rule, more marked than those of the untreated group, probably because the duration of life was longer, and there was a longer period of time in which anoxia could exert its ill effects. There was patchy, bluish discoloration of the lungs, which was most noticeable in the more dependent portions. Microscopically, there was engorgement of the alveolar vessels and extravasation of fluid and cells into the alveolar spaces. The liver showed dark discoloration and the cut surface was moist. On microscopic examination, engorgement of capillaries and degenerative changes in the hepatic cells were noted. The adrenals showed red discoloration on the cut surface, which was most pronounced in the medullary portion, and the vessels were engorged in both cortex and medulla. Degenerative changes were present in the cortical cells, and there was moderate infiltration of polymorphonuclear leukocytes in the zona fasciculata. The gastro-intestinal tract of several animals showed gross hemorrhage; this was greatest in the duodenum and the jejunum. The mucosa of the duodenum and the jejunum was hyperemic, and, on microscopic examination, there was evidence of vascular engorgement. The peritoneal cavity of two animals, and the pleural cavities

of one, contained free fluid. The kidneys were of normal size and on external examination showed no change. The cut surface was darkly discolored in both medulla and cortex. Red radial streaks, indicative of vascular engorgement, were present. Microscopic examination showed engorgement of the glomerular capillaries with extravasation of blood into Bowman's capsules. In some animals homogeneous, amorphous eosinophilic material was present in Bowman's capsules. Vascular engorgement was evident in both cortex and medulla. The collecting tubules in many areas were dilated but empty, and the lining epithelium was flattened. No large brown casts were found.

Examination of the injured extremity revealed massive swelling of the thigh, and to a lesser extent of the leg and foot. There was some swelling of the flank and of the adjacent anterior abdominal wall. Upon section, the swelling was seen to be due to the presence of clear yellow fluid in the subcutaneous tissues, the fascial planes, and the bellies of the muscles. In only two animals which succumbed was there extravasation of whole blood into the tissues of the limb, and in these the amount was very small. The swelling persisted for at least several days. Necrosis and sloughing of the skin were frequently noted at the site at which the maximum pressure had been applied. The pressure resulted in temporary paralysis of the extremity.

DISCUSSION

The type of injury which has resulted in the so-called crush or compression syndrome has, in all reported cases, involved the extremities, and has been of sufficient violence to crush large masses of tissue, especially skeletal muscle. The victims have remained pinned beneath the fallen object for several hours, resulting in great interference with the circulation of the entire extremity and in some instances in the production of necrosis at the site of injury. Following removal of the constricting object, with reestablishment of the blood supply, swelling of the extremity appears. Shortly afterward the patient may present signs of shock and later may develop renal failure. As stated previously, one of the objects of the present experiments was to attempt to reproduce the crush syndrome. When the press described above is applied to an extremity for a period of five hours at a pressure of 500 pounds, the tissues of the thigh are crushed and at least a major portion, if not all, of the blood supply to the part is interrupted for the duration of this period. The popliteal and posterior tibial pulses cannot be felt with the press in place, but are always palpable immediately after its removal. Following the removal of the press there is progressive swelling which seems to reach its maximum in six to eight hours. As can be seen from Table I, shock was produced in all experiments, and was fatal in all animals except one in the untreated group.

The swelling of the extremity is due almost entirely to extravasation of plasma rather than of whole blood. The fluid observed in the tissues of the extremity and the adjacent body wall was a clear yellow; very rarely was there even slight evidence of whole blood loss. At autopsy, the posterior part of the animal's body was bisected and the weights of the injured and uninjured

sides were compared. This comparison revealed a fluid loss in the injured side of 3.26 per cent of the body weight. The results of previous experiments[9] of approximately the same duration in which plasma was removed from the blood stream indicate that the local loss in the present experiments was the major factor in causing the decline in blood pressure and death. Probable explanation for the plasma loss lies in the local mechanical injury to tissues plus the anoxia produced by the constricting or tourniquet effect of the press.

Further evidence of plasma loss is demonstrated by the marked increase in the concentration of the red blood corpuscles which invariably occurred. This rise began immediately after the press was removed and progressed in the untreated group until the animal died. The average rise in the untreated group was 44 per cent above the control values as compared with 28.5 per cent above the control values in the treated group.

In the animals which were successfully treated by application of the pneumatic cuff there was comparatively little swelling of the injured extremity at the time of removal of the cuff after 13 or 18 hours. Swelling became more evident within a few hours and appeared to become greater in those treated for 13 hours than in those to which the cuff was applied for 18 hours. In animals which died in spite of treatment, comparison of the weight of the injured and uninjured sides showed a fluid loss as great as that of the untreated group (3.26 per cent of body weight). The beneficial effect of the pneumatic cuff would appear to be due chiefly to its rôle in lessening local fluid loss into the extremity. It is likely that a partial repair of the increased capillary permeability in the injured extremity takes place following the return of its blood supply during the 18 hours that the pneumatic cuff is in position.

The urinary changes in these experiments are of interest. Blood was present, on microscopic examination of the urine, within two to three hours after the press was applied. The development of hematuria probably precedes an appreciable diminution in blood volume and blood pressure, and also probably precedes the absorption into the general circulation of the major part of the products of injury. There may be some absorption of these metabolic products at the upper end of the press and through collateral channels where the circulation is still intact. Gross blood was present in the urine within an hour after the press was removed. A peculiar brownish discoloration of the urine was often noted during the period following removal of the press. Oliguria was observed in all experiments, most severe in the untreated animals and in those which died in spite of treatment, that is to say, those animals in which shock was most profound. This oliguria was due at least in part to the physiologic imbalances accompanying shock—diminished blood volume and flow, depression of blood pressure, and hemoconcentration. Granular and red blood cell casts were frequently found and occasionally hyaline casts were noted, but in no animals of the untreated group, and in only two of the treated group, were large, brown granular casts observed. In these two animals, histologic examination did not show the selective tubular changes and the casts which have been described in clinical cases of crush injury. Had the

length of life been greater, it is possible that this observation would have been made more often.

Elevated blood creatine levels and creatinuria have been observed in several types of muscular disease.[10] Aub and Wu[11] have reported an increase in blood creatine following injuries to muscle. The values we have obtained are high, and are suggestive of severe muscle damage. Marked disturbance of creatine-creatinine ratios in blood and urine were observed. The levels are higher in the plasma of the untreated group than in that of the treated group, and higher in the urine of the treated group than in that of the untreated group. These observations may indicate failure of excretion of the excessive creatine because of diminished renal function. Destruction of renal function in itself will produce an elevation in blood creatine.[12, 13] Further evidence of diminished renal function and tissue injury is presented by the progressive rise in nonprotein nitrogen seen in all the experiments.

The method which has been described presents both advantages and disadvantages in the study of shock. Included among the advantages is the observation that there appears to be less individual variation in the responses of animals to this form of injury than to any other that we have studied. This method allows one to study, with greater exactness, the pathogenesis of shock, and to determine, with greater certainty, the effects of various therapeutic procedures. Another advantage which is common to all methods in which one extremity is injured is that the opposite extremity can be used as a control. A disadvantage of the method is that the type of injury which is produced is not encountered as frequently in patients as are burns and some other types of trauma.

It remains to be proved whether or not the crush syndrome as observed in patients can be reproduced by this method. The alterations in the urinary tract in the experimental animals and in the patients are not identical. Most of the animals which survived following treatment with the pneumatic cuff were sacrificed after several days, hence a study of the late effects of injury is incomplete. Such studies are being carried on at the present time. It will probably be necessary to modify the method in such manner that the survival period of untreated animals will be lengthened. It is apparent that a careful study of renal function in this experimental condition is indicated.

SUMMARY

A new method for producing shock, in which an attempt is made to simulate the crush syndrome as observed in patients, is described. The method consists in placing a posterior extremity of the anesthetized animal in an apparatus with uneven surfaces, which exert great pressure on the soft tissues.* Removal of the extremity from the press is followed by swelling of the leg, an increase

* It is to be emphasized that medium sized animals which had a good deal of muscular tissue in the thigh were chosen and that the grooves in the insets of wood on the press allowed the pressure to be made mainly on the soft tissues rather than on the femur.

in the concentration of the blood, a decline in blood pressure, oliguria, abnormal urinary findings, elevated blood creatine and creatinuria, and usually death. The local loss of plasma is great. Recovery usually results if, at the time the press is removed, the injured part is placed immediately in a pneumatic tube with an internal pressure of 40 Mm.Hg.

Whether the experimental conditions have any relationship to the crush syndrome as observed in patients remains to be proved, but it can be stated that the use of this method results in a more uniform production of traumatic shock than any with which we have hitherto worked.

REFERENCES

[1] Bywaters, E. G. L., and Beall, D.: Crush Injuries with Impairment of Renal Function. Brit. Med. Jour., **1**, 427–432, March 22, 1941.

[2] Beall, D., Bywaters, E. G. L., Belsey, R. H. R., and Miles, J. A. R.: Crush Injury with Renal Failure. Brit. Med. Jour., **1**, 432–434, March 22, 1941.

[3] Mayon-White, R., and Solandt, O. M.: A Case of Limb Compression Ending Fatally in Uremia. Brit. Med. Jour., **1**, 434–435, March 22, 1941.

[4] Dunn, J. Shaw, Gillespie, Marjorie, and Niven, J. S. F.: Renal Lesions in Two Cases of Crush Syndrome. Lancet, **241**, 549–552, November 8, 1941.

[5] Report of Royal Society of Medicine: Effects on Kidney of Limb Compression. Brit. Med. Jour., **2**, 884–885, December 20, 1941.

[6] Folin, O., and Wu, H.: A System of Blood Analysis. Jour. Biol. Chem., **38**, 81, 1919.

[7] Folin, O.: On the Determination of Creatine and Creatinine in Urine. Jour. Biol. Chem., **17**, 469, 1914.

[8] Blalock, A.: Experimental Shock: A Cause of Low Blood Pressure Produced by Muscle Injury. Arch. Surg., **20**, 959–996, 1930.

[9] Johnson, G. S., and Blalock, A.: Experimental Shock: Study of the Effects of Loss of Whole Blood, of Blood Plasma and Red Blood Cells. Arch. Surg., **22**, 626–637, 1931.

[10] Hunter, A.: Creatine and Creatinine. London and New York, Longmans, Green and Co., 1928.

[11] Aub, J. C., and Wu, H.: Studies in Experimental Traumatic Shock. Am. Jour. Physiol., **54**, 416, 1920.

[12] Looney, J. M.: Blood Changes in Acute Mercuric Chloride Poisoning. Jour. Biol. Chem., **70**, 513, 1926.

[13] Campbell, W. R.: Observations on Acute Mercuric Chloride Nephrosis. Arch. Int. Med., **20**, 919, 1917.