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A Study of Anuria in Experimental Shock.*

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In experiments on the effect of thermal trauma on the G.I. tract it was frequently observed that the urine output after burns was low even after large infusions of saline. While this has been known some time,[1] no comparative study has been made on anuria in different types of shock, using approximately the same experimental approach in each.

Experimental Procedure. Large dogs were used for this study and all animals were deeply anesthetized throughout the experimental period with nembutal or sodium barbital. An excess of anesthetic was administered at the termination of each experiment. Each ureter was cannulated and connected to a sensitive drop recorder which registered on a kymograph the drops of urine from each kidney.[2] Each drop of urine represents 0.052 cc. Blood pressure was recorded on the same kymograph so that an immediate correlation between the effects of shock on blood pressure and urine secretion was possible. Repeated determinations of plasma CO_2, hemoglobin, hematocrit, and, in some experiments of serum N.P.N. were made. Hemorrhagic, burn, and traumatic shock were studied. Duncan-Blalock clamps[3] were used for the production of traumatic shock because this method produces little if any hemorrhage.

Results. The total of 43 experiments may be divided into 4 groups. (1) Two control experiments of 18 and 32 hours duration. (2) Five hemorrhage experiments. (3) Twenty-three thermal trauma experiments. (4) Thirteen traumatic shock experiments. Analysis of the experiments is done most effectively by examining and comparing individual experiments of each group. Therefore, from the 43 experiments 8 will be discussed in detail because they illustrate the most consistent findings. However, the remaining 35 experiments deviated slightly from them by the severity of the anuria and oliguria. The extent of kidney damage was frequently dependent on the degree of injury (thermal, traumatic, or hemorrhagic) suffered by the animal, and the duration of time before treatment of the shock. But it was apparent that in most experiments the type of anuria or oliguria could be divided into definite characteristic groups.

Several interesting observations were made in the 2 control experiments. In the first control, without infusion, the kidneys secreted well for 17 hours. At that time the following changes occurred: blood pressure had dropped only 10 mm Hg. (to 115), hematocrit increased 11% (to 64%), CO_2 had fallen 8 vol. % (to 39 vol. %), and a decrease of urine secretion to 22 drops per 15 minutes from the control average of 30 drops. In the second control experiment, without infusion, the following changes occurred in the animal after a 21-hour period: Blood pressure dropped to 95 mm Hg., hematocrit had risen to 64%, the CO_2 had fallen to 18 vol. % from the control value of 50 vol. %, and the urine decreased to 16 drops per 15 minutes from the control value of 28 drops per 15 minutes. Five hundred cc of plasma i.v. increased urine secretion to 95 drops. These experiments demonstrated that the operative procedure, anesthesia, and lack of asepsis did not produce anuria in 17 or in 21 hours. The kidneys responded immediately to an infusion of plasma after this time. The second experiment was continued for an additional 11

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1 Harkins, Henry N., *The Treatment of Burns*, Charles C. Thomas, 1942, 33.

2 Olson, Wm. H., and Necheles, H., *J. Lab. and Clin. Med.*, 1942, **27**, 802.

3 Duncan, G. W., and Blalock, Alfred, *Surg.*, 1942, **115**, 684.

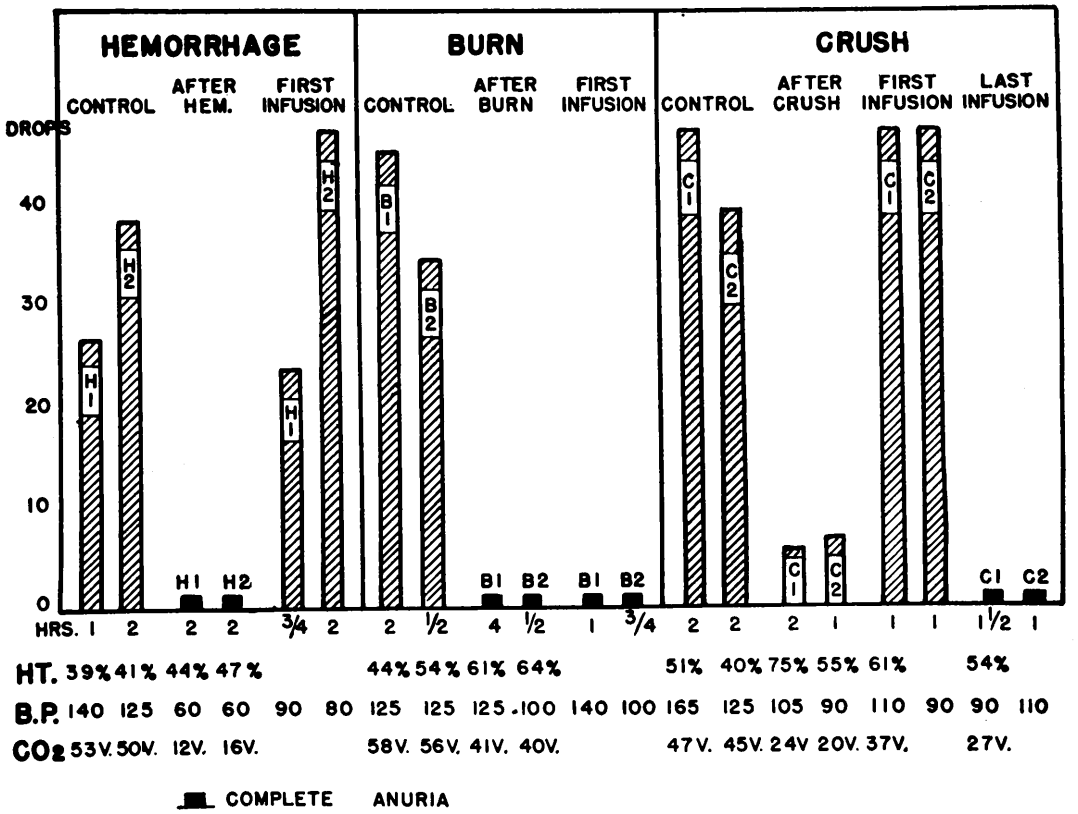

CHART 1.

Data of 6 experiments representing 3 types of anuria. The columns represent average urine secretion of both kidneys in drops per 15 minutes during the interval of time (Hrs) marked below each column. The values below each column are hematocrit, blood pressure in mm Hg and arterial plasma CO_2 in volumes percent. Control values were determined before and values during shock after the time interval. C1 and C2 secreted a total of 210 and 130 drops of urine respectively after infusion (not drawn fully on chart).

hours, when the animal died. The kidneys secreted following all subsequent infusions of plasma. No complete anuria was observed until shortly before death.

Chart 1 gives the significant data for 6 experiments, two experiments from each of the 3 types of shock studied. The first hemorrhage experiment (HI) was performed under nembutal on a dog weighing 20 kg. Control BP 140, hematocrit 39, and CO_2 53. During one hour, the average urine secretion was 27 drops per 15 minutes. The animal was bled 700 cc and the blood pressure dropped to 90. During the next 1½ hours, the average secretion was 26 drops per 15 minutes and the BP rose to 100. This period is not shown on the chart. The animal was then bled 375 cc and urinary secretion was completely suppressed for 2 hours. At that time blood pressure was 60, hematocrit was 44, and CO_2 12. A saline infusion of 300 cc raised BP to 90 and for ¾ hours stimulated a urinary secretion of 23 drops per 15 minutes; then the animal died. The second hemorrhage experiment (H2) was performed on an 18-kg dog under nembutal. Control BP was 125, hematocrit 41, and CO_2 50. For 2 hours the control urine secretion was 38 drops per 15 minutes. Then, the animal was bled 450 cc; BP dropped to 50, and for ¾ hours the average urine secretion was 10 drops per 15 minutes. During this time the BP rose to 85. The animal was then bled an additional 270 cc. BP dropped to 30, and urine secretion was completely suppressed for 2 hours. A 270 cc saline infusion, however, stimulated an average urine secretion of 50

drops per 15 minutes for 2 hours. BP rose to 80 mm Hg. The animal was then sacrificed.

Burn experiment B1 was performed on a 19.5 kg dog under nembutal. Control BP was 125, Ht. 44, CO_2 58, and urine secretion was 47 drops per 15 minutes. Thermal trauma by a torch was applied for 10 minutes. The BP rose to 155 during this time, and urine secretion stopped completely. Four hours later the Ht. was 61, BP 125, and CO_2 41. The plasma contained 1385 mg % of Hb. No urine was secreted during this time. A 300 cc saline infusion had no effect on the anuria, although the BP rose to 140. However, a second infusion, not shown in Chart 1, produced a urine secretion of 10 drops per 15 minutes for 1 hour. At this time the animal was sacrificed.

Burn experiment B2 was performed on a 15.5 kg dog under morphine-sodium barbiturate anesthesia. Control Ht. was 54, BP 125, and CO_2 56. During ½ hour control period, the average urine secretion was 35 drops per 15 minutes. Then a severe thermal trauma was administered. Urine secretion was completely inhibited. At ¾ hours after the burn the Ht. was 64, BP 100, CO_2 40, and urine secretion 0. The plasma contained 3680 mg % Hb. The animal was given an infusion of saline, 6 cc per minute. After 270 cc had been given, the rate of infusion was increased to 12 cc per minute. Blood pressure was 100. An additional 2160 cc of saline was given over a 3-hour period. No urine was secreted during this period, which terminated with the animal's death.

Crush experiment C1 was done on an 18 kg dog under nembutal. Control Ht. was 51, BP 165, CO_2 47, and average urine secretion over a 2-hour period was 48 drops per 15 minutes. Two Blalock clamps were applied for 5 hours, during which time the average urine secretion was 31 drops per 15 minutes (not shown on this chart); for a 2-hour period after removal of the clamps it fell to 6 drops per 15 minutes. After that period, the Ht. was 75, BP 105, and CO_2 24. The first infusion of 500 cc of plasma produced an average urine secretion of 210 drops per 15 minutes for a period of one hour, and of 30 drops per 15 minutes during the next 3 hours (the latter not shown on the chart). The response of the kidney to plasma infusion decreased slowly. At 19 hours after the first infusion, Ht. was 54, BP 90, and CO_2 27. However, even after a 500 cc plasma infusion, no urine was secreted. Complete anuria was present. This animal was sacrificed 1½ hours later, when its BP was 100.

Crush experiment C2 was done on a 15 kg dog under nembutal anesthesia. Control values were: Ht. 40, BP 125, CO_2 45, and average urine secretion for 2 hours was 40 drops per 15 minutes. Two clamps were applied for 5 hours. For one hour after the clamps were removed the average urine secretion was 7 drops. After that period the Ht. was 55, BP 90, and CO_2 20. The first infusion of 500 cc of plasma stimulated an average urine secretion of 130 drops per 15 minutes for one hour. At each subsequent plasma infusion, the kidneys secreted less, so that at 17 hours after the first infusion no urine was secreted after a 500 cc plasma infusion. The blood pressure rose to 100 during the infusion, but the animal died one hour later.

Discussion. In the present series of experiments we have attempted to find the conditions under which complete anuria would occur, and therefore kidney function was determined only by the volume of urine secreted.

The immediate effects of the 3 different types of shock on urine secretion was a marked depression. In the crush experiments the injury did not immediately produce complete anuria. Undoubtedly, if the BP had dropped lower, as in the hemorrhage experiments, an early anuria would have been present.

By the reactions to intravenous infusions, 3 different types of anuria became evident. The first type is produced mainly by low blood pressure and a reduced blood volume, such as occurred after hemorrhage and immediately after crushing. Infusion stimulated urine secretion in all these cases, regardless of the severity of the shock. In the hemorrhage experiments the BP was 60 and the CO_2 at a very low level: in one experiment the animal was infused shortly before death; yet, in all cases the infusion stimulated urinary secretion. In the early stages of the crush experi-

ments, urinary secretion was similar to that following hemorrhage. During this stage, considerable hemoconcentration (75% in one of the experiments) was present, yet the infusion stimulated considerable kidney secretion. It seems evident from these 2 groups of experiments that acidosis and hemoconcentration are not the important factors in complete anuria of shock. We may therefore assume, that reduced blood volume, hemoconcentration, low blood pressure, and acidosis do not lead to a permanent anuria, *i.e.*, one which is not abolished by infusions.

The second type of anuria may be called burn anuria. This type did not always respond to an infusion fluid. In experiment B1 the kidneys secreted urine only after the second infusion. In experiment B2 a total amount of 2,430 cc of saline had no effect on kidney secretion. The difference in response might be attributed to different amounts of hemoglobin in the plasma. In B1 the plasma hemoglobin was 1385 mg %, whereas in experiment B2 it was 3680 mg %. The severity of the anuria in all burn experiments frequently could be associated with the degree of hemoglobinemia.

The third type of anuria may be called crush anuria. It should not be mistaken for the first type, *i.e.*, the anuria of low blood pressure and diminished blood volume. In crush anuria, the kidneys always secreted well after the first infusion as in the first type, but the urine was deeply pigmented, presumably with myohemoglobin.[4] This was a sign of impending damage to the kidneys. Unlike following burns, the anuria developed very slowly and only after 18 hours or longer the kidneys might stop secreting, even after infusion. It was important to give infusions in order to determine the extent of damage to the kidneys. It seemed possible to prevent the crush anuria by giving certain infusion fluids early. Saline and plasma did not prevent it in all cases. In many cases complete anuria did not occur either in burns or in crush injuries, but all experiments exhibited some degree of oliguria.

Summary and Conclusions. I. Three different types of anuria were observed in these experiments.

1. Anuria following a severe hemorrhage or a reduced blood volume.
2. Anuria following a severe burn.
3. Anuria following a crush injury: this type developed much later, 18 to 36 hours, after injury.

II. The possible factors for the appearance of anuria are: low blood pressure, a reduced blood volume, the hemoglobinemia present in burns, and an unknown substance. This substance may be myohemoglobin or a toxic agent released from the damaged limb.

III. Permanent damage to the kidneys and anuria may develop following crushing or burning, because renal function seems to be most impaired following these two traumatic agents.

[4] Morison, J. Edgar, *Brit. Med. J.*, 1942, **2**, 736.

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Absorption of Galactose by Renal Tubules of the Dog.

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In previous papers from this laboratory evidence was presented to show that in the rat and in man, thyroid hormone increases the rate of the intestinal absorption of substances that are transferred actively by a mechanism generally considered to involve phosphorylation; the hormone was without influence on the rate of absorption of those substances that