appears preferable to plasma for potassium determinations since hemolysis seems to be much more readily prevented.

35 (1617)

On the elimination of phenolsulphonephthalein in acute mercuric chloride intoxication.

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In two recent publications [1,2] on the toxic effect of mercuric chloride in normal and in naturally nephropathic animals, observations have been made concerning the relationship between the development of an acid intoxication and the acute kidney injury. In these animals the poison was given in large doses, 15 mgs. per kilogram, which eliminated the study of the development of the intoxication in the early stages.

The following preliminary note has as its object a study of the early stages of the development of an acid intoxication from mercuric chloride and the relationship of such a disturbance to renal function as is shown by the elimination of phenolsulphonephthalein.

Fourteen normal dogs have been used in the study. The animals were kept in metabolism cages, fed on bread with a small amount of cooked meat and given 500 c.c. of water by stomach tube daily. The animals were catheterized once a day and the urine examined for albumin and glucose. Centrifugalized samples were examined for casts. The phenolsulphonephthalein test was conducted according to the technique of Rowntree and Geraghty. Blood urea determinations were made by the method of Marshall as modified by Van Slyke and Cullen. The reserve alkali of the blood (R.p.H.) was determined by the method of Marriott. After the commencement of the intoxication the urine was ex-

[1] MacNider, Wm. deB., "A Study of Acute Mercuric Chloride Intoxication In The Dog with Special Reference To The Kidney Injury," *Jour. Exp. Med.*, Vol. XXVII, 519, 1918.

[2] MacNider, Wm. deB., "The Susceptibility of Naturally Nephropathic Animals to Acute Mercuric Chloride Intoxications," *Jour. Med. Research*, Vol. XXXIX, 461, 1919.

amined for the presence of mercury by the method of Elliott. Following two days of normal observations, the animals were given 4 mgs. per kilogram of mercuric chloride by stomach tube. Prior to administering the mercury the dogs were partially narcotized by a subcutaneous injection of 0.25 c.c. of a 4 per cent. solution of morphine sulphate per kilogram. Such a procedure prevents the vomiting of the mercury. After the introduction of the poison the animals were studied by the methods just outlined. At definite periods during the course of the intoxication, 6, 12 and 24 hours, the animals were killed without the use of an anesthetic and autopsied. The liver and kidney were studied histologically.

The course of two experiments that are representative of the condition of the fourteen animals in the very early stages of poisoning by mercuric chloride are outlined in Table I. At the com-

TABLE I.

ELIMINATION OF PHENOLSULPHONEPHTHALEIN IN ACUTE MERCURIC CHLORIDE INTOXICATIONS

Number of Experiment.	Duration of Experiment.	Mercuric Chloride Mgs. per Kg.	Urine in 24 Hours.	Albumin and Casts.	Phthalein per Cent.	R. p. H.	Blood Urea Mgs. per 100 Cc.	Mercury in Urine.
10	Normal Observation	0	368 c.c.	0	56	8.4	18	0
	Normal Observation 6 hours	0	478 c.c.	0	53	8.4	20	0
	Animal killed	4 mgs. per kg.	571 c.c.	Trace no Casts	68	8.1	12	0
13	Normal Observation	0	281 c.c.	0	72	8.3	22	0
	Normal Observation 12 hours	0	310 c.c.	0	70	8.3	24	0
		4 mgs. per kg.	365 c.c.	0	78	8.3	17	Trace
	24 hours; animal killed		491 c.c.	Trace	74	8.1	17	Trace

mencement of each experiment normal observations are recorded for two days prior to the commencement of the intoxication. A study of this normal record shows the urine to be free from both albumin and casts. The total output of urine in a twenty-four hour period has varied with the fourteen animals from 281 c.c. to 576 c.c. The elimination of phenolsulphonephthalein in a two

hour period has ranged from 53 to 84 per cent. Blood urea determinations have varied from 18 to 27 mgs. per 100 c.c. of blood. The alkali reserve determinations in all of the animals have only shown a variation between 8.3 to 8.4.

The animal of Experiment 10, six hours after receiving the mercury showed a distinct increase in the output of urine. The urine in this six hour interval amounted to 571 c.c., as opposed to the normal maximum output for a twenty-four hour period of 478 c.c. At this early period a trace of albumin appeared in the urine. Casts were not present. Associated with the development of the albuminuria the reserve alkali of the blood was reduced from the normal of 8.4 to 8.1. The elimination of phenolsulphonephthalein was increased from the normal maximum output of 56 per cent. to 68 per cent. The blood urea showed a decrease from the normal maximum of 20 mgs. per 100 c.c. of blood to 12 mgs. The urine did not show the presence of mercury.

The animal of Experiment 13, Table I, received the same amount of mercury per kilogram as the animal of Experiment 10. The duration of the experiment was twenty-four hours. The course of the intoxication is in general similar to that shown by the previously outlined experiment. Twelve hours after the use of the poison the output of urine gave an increase of 55 c.c. over the normal elimination for the preceding twenty-four hours. By the end of the first twenty-four hours of the poisoning the animal had formed 856 c.c. of urine as opposed to the maximum output for a twenty-four hour normal period of 310 c.c. At the end of the first twelve hours of the experiment the urine was free from albumin but contained a trace of mercury. The elimination of phenolsulphonephthalein had increased from 70 to 78 per cent. The reserve alkali of the blood remained unchanged. The blood urea was reduced from 22 mgs. per 100 c.c. to 17 mgs. At the end of twenty-four hours of the intoxication the urine contained a trace of albumin. The elimination of phenolsulphonephthalein was reduced from 78 per cent. to 74 per cent. The normal elimination of the dye was 72 per cent. The reserve alkali of the blood was reduced from the normal of 8.3 to 8.1. The blood urea remained unchanged, 17 mgs. per kilogram.

The pathology of the liver and the kindey in these animals

early in the intoxication from 4 mgs. of mercuric chloride per kilogram presents the following points of interest. The liver is pale and the lobulations well marked. Histologically the periphery of the loblues show cells which are edematous and necrotic. As the center of the lobule is reached these changes become less marked. The destruction of liver tissue is extensive when the duration of the intoxication and the amount of the poison administered is taken into consideration. The kidneys have appeared normal. On section they drip blood freely. The glomeruli are prominent. Histologically both the vascular and epithelial elements of the kidney have failed to show evidence of degeneration. The capillaries of the glomeruli have been well filled with blood and have generally obliterated the subcapsular space. No exudate or hemorrhage into the subcapsular space has been observed. The tubular epithelium, especially that of the convoluted tubules, has appeared decreased in volume, giving undue prominence to the tubular lumen. The nuclei have appeared large in proportion to the cytoplasm of the cells and have stained intensely.

CONCLUSIONS.

1. When normal dogs are given mercuric chloride in the dose of 4 mgs. per kilogram there develops a well marked and constant diuresis. This mercury diuresis is not solely dependent upon the action of the mercury on the kidney during its elimination, for such a diuretic effect may be obtained when the urine is free from mercury.

2. In the early stages of an intoxication from such small quantities of mercury there is further evidence of its diuretic effect which is shown by an increase in the elimination of phenolsulphonephthalein.

3. Prior to, or associated with, the appearance of albumin alone, or albumin and casts in the urine, there occurs a reduction in the reserve alkali of the blood. This change in the acid-base equilibrium of the blood is not primarily a retention phenomenon dependent upon an injury to the kidney, for at the time of the reduction in the alkali reserve of the blood there is evidence of an increase in the functional capacity of the kidney, as is shown by an increase in the amount of urine formed and by an increase in

the ability of the kidney to eliminate phenolsulphonephthalein. Furthermore, at this stage of the mercury intoxication the kidney shows no evidence of injury but shows on the contrary a convoluted tubule epithelium with nuclear and cytoplasmic changes, indicative of a functionally active state.

4. At this early stage of the intoxication by mercuric chloride there occurs a reduction in blood urea. This decrease in blood urea has been associated with the development of degenerative changes in the liver which first make their appearance in the periphery of the liver lobule.

5. Associated with such changes in the liver and prior to the development of the kidney injury there occurs a reduction in the alkali reserve of the blood.

36 (1618)

Mercury saligenin, a new antiseptic.

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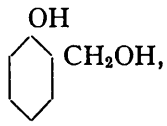
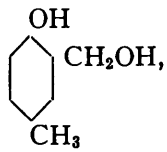
The early studies of G. Cohn on saligenin and homosaligenin and the recent investigations of D. I. Macht on benzyl alcohol have demonstrated that these substances are mild antiseptics. We have studied the action of saligenin,



homosaligenin,



[1] The researches reported in this investigation were made possible by the aid of funds granted by the United States Interdepartmental Social Hygiene Board for the discovery of more efficient medical measures in the treatment and prevention of venereal diseases.