CHEMICAL FINDINGS IN THE BLOOD OF THE DOG AFTER TEMPORARY OBSTRUCTION OF THE PYLORUS.

BY RUSSELL L. HADEN, M.D., AND THOMAS G. ORR, M.D.

(From the University of Kansas, School of Medicine, Kansas City, Kansas.)

(Received for publication, July 2, 1928.)

MacCallum and his coworkers (1), and Hastings, Murray, and Murray (2) in studying pyloric obstruction in the dog noted a marked fall in chlorides and a rise in the CO_2 combining power of the blood. Similar observations in clinical cases were made by Grant (3). The close similarity of such changes with those found in high intestinal obstruction (4) led us to study the non-protein nitrogen of the blood in dogs with the pylorus obstructed (5). The non-protein nitrogen in such animals was found to reach the high levels characteristic of high intestinal obstruction. These observations have since been verified by others in both clinical (6) and experimental work (7, 8).

Our special interest in the subject was the relation of the chloride metabolism to the toxemia as reflected by the non-protein nitrogen level. The observation was made that the toxemia and rise in non-protein nitrogen in high intestinal obstruction do not usually occur until the chloride store of the blood is reduced below a certain level (4). It was also shown that the administration of sodium chloride had a remarkably beneficial effect on the toxemia of intestinal and pyloric obstruction and likewise in preventing the onset of a toxemia if given early (9). No beneficial effects were observed from water alone, other inorganic salts, or glucose. The therapeutic value of NaCl is now well accepted in both pyloric and intestinal obstruction. None of the explanations given for its favorable action is entirely satisfactory.

With the vomiting incident to pyloric obstruction much water and chloride are lost. This dehydration causes a diminution in kidney function with consequent retention of the end-products of protein metabolism. In the toxemias due to upper gastrointestinal tract

obstruction, there is a markedly accelerated nitrogen metabolism with increased tissue breakdown (10, 11). The rise in the non-protein nitrogen in the blood is often too rapid to be accounted for by simple retention. The high level of non-protein nitrogen seems due to both retention and increased tissue destruction.

The exact relation of the chlorides to the toxemia and tissue destruction is as yet undetermined. We suggested originally the possibility that sodium chloride may directly neutralize the bodies responsible for the toxemia. This hypothesis was based on the seeming greater loss of chloride from the blood than could be accounted for in the vomitus and urine and on the striking effect of sodium chloride in relieving and preventing the toxemia. Further studies by Gamble and McIver (8), White and Bridge (12), and Atchley and Benedict (13) indicate that all the chloride lost from the blood and tissues is found in the urine and gastric and intestinal secretions. There is also a fall in the chloride of the tissues (12, 14), and during the toxemia very little chloride is excreted in the urine. These facts render our original theory unlikely.

This still however does not throw any light on the problem of the relation of the chloride level to the tissue metabolism. The proper amount of chloride is necessary to maintain water balance and kidney function. Autolysis may conceivably be more rapid in tissue with a low chloride content. It is also possible that the tissues may be more easily injured by circulating toxins, if such be present, when the salt content is low. These experiments have been made in an attempt to throw some light on the exact relation of the chloride level to the toxemia of upper gastrointestinal tract obstruction.

In studying the relation of the sodium chloride to the blood chemical changes and toxemia, it is most desirable to be able to produce experimentally the characteristic blood changes and toxemia without having to consider mechanical factors, the possibility of infection, and operative risk. We have found that such a condition can be produced by ligating the pylorus and releasing the obstruction in 24 to 72 hours. The thick wall of the pylorus precludes the possibility of rupture of the viscus as frequently happens after ligation of the intestine. The obstruction is easily eliminated by removing the ligature under local anesthesia with little operative risk. In some of the surviving animals

there is produced a characteristic toxemia in which mechanical factors are eliminated making an ideal condition for the study of the blood chemical changes.

Method.

All experiments have been made on dogs. All primary operations were done under ether anesthesia with aseptic technique. Obstruction of the pylorus was

TABLE I.
Typical Changes in Blood of Dog after Simple Obstruction of Pylorus.

Dog No.	Blood					Remarks
	Amount per 100 cc.				CO ₂ combining power	
	Day after operation	Total non-protein nitrogen	Urea nitrogen	Chlorides		
		mg.	mg.	mg.	vol. %	
1	0	35.7	11.2	460	24.0	Pylorus obstructed
	1	46.0	14.5	320	52.0	
	2	111.0	49.0	230	37.7	Died
2	0	37.5	7.9	500	35.4	Pylorus obstructed
	1	38.9	15.4	470	30.5	
	2	57.3	30.8	360	50.2	
	3	129.0	70.0	310	56.0	Died
3	0	28.9	12.6	490	27.5	Pylorus obstructed
	1	27.0	11.2	450	44.7	
	2	61.0	25.2	380	42.8	
	3	76.5	28.7	340	53.9	
	4	181.0	128.2	260	45.3	Died
4	0	33.7	12.6	500	30.5	Pylorus obstructed
	1	46.0	21.0	480	36.2	
	2	155.0	47.6	330	29.4	Died

effected by ligating with a piece of narrow tape. The tape was fixed to the anterior abdominal wall so that it could be easily located at the second operation. The obstruction was released by making a short incision under local anesthesia, cutting and removing the tape. At autopsy after such a procedure no permanent anatomic changes in the pylorus could be observed. The most desirable time for the second operation is usually 48 hours after the obstruction is made. The dogs were kept in metabolism cages. No food was given during the experiment and usually none for 48 hours before operation. Water was allowed *ad libitum*.

TABLE II.
*Course of Toxemia in Dogs Recovering after Temporary Obstruction of Pylorus
without Treatment.*

Dog No.	Blood					Remarks
	Amount per 100 cc.				CO ₂ combining power	
	Day after operation	Total non-protein nitrogen	Urea nitrogen	Chlorides		
		mg.	mg.	mg.	vol. %	
5	0	37.5	10.3	480	30.5	Pylorus obstructed
	1	34.5	8.4	440	40.9	
	2	61.0	26.6	350		Obstruction released
	3	79.0	30.1	310	54.9	
	4	50.0	9.8	330	36.2	
	5	27.3	18.9	330	40.0	
	6	26.3	15.4	370	56.0	
	7	30.0	9.1	360	40.9	
	8	31.2	10.7	380	49.4	
	9	30.3	6.5	430	42.8	
10	27.3	7.5	460	48.5	Well	
6	0	27.7	13.1	460	41.9	Pylorus obstructed
	1	37.5	14.7	370	50.4	
	2	65.5	30.8	330	58.7	
	3	42.8	14.0	330	56.8	
	4	40.0	16.8	340	59.6	
	5	39.5	16.8	340	56.5	
	6	40.0	18.2	340	47.5	
	7	37.5	17.5	350	55.8	
	9	38.0	9.1	370	57.7	
	10	30.9	8.4	400	52.2	
	11	33.0	10.7	420	48.5	
	12	57.3	7.5	450	51.3	Well
7	0	28.5	13.1	500	38.1	Pylorus obstructed
	1	25.9	9.8	440		
	2	30.0	9.1	440	41.9	
	3	33.0	16.1	380	40.0	Obstruction released
	4	50.8	22.9	330	53.2	
	5	34.5	20.7	370	61.7	
	6	42.8	23.7	370	57.9	
	7	125.0	73.6	330	57.7	
	8	32.3	9.1	380	53.9	
	9	31.6	16.1	410	50.2	
	10	42.2	14.0	390	67.1	
	11	32.3	11.7	420	57.7	
	12	41.0	15.4	400	46.6	
	13	50.0	13.1	420	58.7	Well

TABLE II—*Concluded.*

Dog No.	Blood					Remarks
	Amount per 100 cc.				CO ₂ combining power	
	Day after operation	Total non-protein nitrogen	Urea nitrogen	Chlorides		
8		mg.	mg.	mg.	vol. %	
	0	24.6	7.7	450	37.2	Pylorus obstructed
	1	28.0	16.8	400	40.0	
	2	89.0	52.5	330	41.0	Obstruction released
	3	72.3	40.6	320	38.1	
	4	34.5	17.5	380	36.2	
	6	40.0	18.2	420	35.3	
	7	38.0	16.1	400	31.5	
	8	34.5	14.7	420	43.8	
	9	30.0	9.1	440	39.0	
10	29.4	17.5	440	41.9	Well	

Blood was obtained for analysis from the jugular vein just before operation and at 24-hour intervals thereafter.

The non-protein nitrogen of the blood was determined by the method of Folin and Wu (15), urea nitrogen by the Van Slyke and Cullen modification of the Marshall method (16), CO₂ combining power by the method of Van Slyke (17), and the chlorides in the tungstic acid filtrate after the technique suggested by Gettler (18). For the non-protein nitrogen in the urine Folin's micro method (19) was used, and for the chlorides a modified Volhard-Arnold method.

EXPERIMENTAL OBSERVATIONS.

The blood chemical changes in four dogs in which the obstruction was not released are shown in Table I. These all show the characteristic findings, namely, a fall in chloride and a rise in CO₂ combining power, and in non-protein and urea nitrogen. The animals died in 48 to 96 hours after operation.

In eight dogs the obstruction was released but no treatment was given. Four recovered, and four died. In the animals recovering (Table II) there was a gradual rise in the blood chloride until the normal level was reached. No food was given during the experiment so it is quite evident that there was a shift in the store of body chloride so that the diminished supply of blood chloride was restored. The four dogs which died showed a progressive fall in chloride and rise in

TABLE III.

Effect of Sodium Chloride Given by Mouth on Toxemia Induced by Temporary Obstruction of Pylorus.

Dog No.	Blood					Remarks
	Amount per 100 cc.				CO ₂ combining power	
	Day after operation	Total non-protein nitrogen	Urea nitrogen	Chlorides		
		mg.	mg.	mg.	vol. %	
9	0	34.9	15.4	430	32.4	Pylorus obstructed
	2	31.6	14.0	330	46.6	
	3	30.0	16.1	300	60.0	Obstruction released
	4	33.3	17.5	310	50.2	
	5	37.5	20.3	290	55.0	
	6	42.2	12.6	320	53.6	
	7	60.0	18.2	360	59.6	
	9	79.0	35.0	360	40.0	
	10	67.5	37.8	320	52.0	10 gm. NaCl by mouth
	11	38.9	21.0	350	45.7	10 gm. NaCl by mouth
	12	23.3	10.5	470	41.9	10 gm. NaCl by mouth
	13	25.7	15.4	500	41.9	Well
	10	0	30.9	14.0	470	28.7
1		31.6	13.8	450	38.1	
2		39.5	14.0	360	39.0	
3		111.0	52.5	300	53.9	Obstruction released
4		67.0	39.3	350	45.7	
5		60.0	36.4	310	46.6	
6		55.0	30.8	340	47.5	
7		51.8	31.5	350	53.0	
8		70.0	38.5	340	52.2	
9		72.8	48.3	340	52.0	
10		79.0	49.0	370	50.2	10 gm. NaCl by mouth
11		34.1	21.7	390	57.7	10 gm. NaCl by mouth
12		34.9	20.3	470	39.0	
13		34.1	19.6	470	52.0	
14		33.0	19.6	500	48.5	
15		39.5	23.8	470	50.2	
16		28.5	16.1	520	46.6	
17	27.0	17.5	600	40.0	Well	
11	0	61.0	26.6	510	30.5	Pylorus obstructed
	1	68.8	35.0	500	38.1	
	2	117.0	51.1	400	59.6	Obstruction released
	3	137.0	75.7	370	55.8	
	4	123.0	56.7	350	49.4	
	5	120.0	60.2	380	45.7	
	6	120.0	64.4	400	51.3	
	7	100.0	55.3	400	53.9	

TABLE III—*Concluded.*

Dog No.	Blood					Remarks
	Amount per 100 cc.				CO ₂ combining power	
	Day after operation	Total non- protein nitrogen	Urea nitrogen	Chlorides		
		mg.	mg.	mg.	vol. %	
12	8	103.0	59.5	380	51.3	
	9	115.0	57.4	390	47.4	
	10	98.8	45.5	400	55.8	
	11	143.0	82.9	380	28.7	
	12	100.0	50.4	420	45.7	
	13	126.0	60.2	400	36.2	10 gm. NaCl by mouth
	14	88.4	44.1	480	4.0	10 gm. NaCl by mouth
	15	60.0	23.1	440	30.5	
	16	71.3	43.9	530	32.4	
	17	57.3	35.0	570	31.5	
	18	42.2	15.4	580	24.0	
	19	35.7	14.0	520	28.7	
	20	38.9	19.6	480	30.5	Well
13	0	51.8	26.2	430	42.1	Pylorus obstructed
	1	30.3	12.6	340	67.1	
	2	68.2	43.3	210	72.7	Obstruction released
	3	132.2	72.9	260	74.5	
	4	83.3	57.1	230	80.1	
	5	77.3	38.2	270	74.5	
	6	107.0	63.9	260	74.5	
	7	158.0	98.8	350	56.9	
	8	208.0	123.3	290	58.8	
	9	173.0	100.8	250	67.5	
	10	230.0	141.5	270	65.3	
	11	250.0	159.7	270	71.8	10 gm. NaCl by mouth
	12	136.0	78.5	410	61.6	Died immediately after intra- venous injection of 25 per cent NaCl

non-protein nitrogen after the obstruction was released. The course of the toxemia was not influenced by the release of the obstruction.

Five animals were treated with sodium chloride by mouth after a toxemia had been established for a sufficiently long period to indicate that it would not adjust itself spontaneously (Tables III and IV). The sodium chloride was given by mouth in 1 gm. tablets with a small

TABLE IV.

Blood and Urine Findings after Temporary Obstruction of the Pylorus.

Dog No.	Day after operation	Blood					Urine					Remarks	
		Non-protein nitrogen	Urea nitrogen	Chlorides	CO ₂ combining power	Hematocrit (% plasma)	Amt.	Chlorides		Nitrogen			
		mg.	mg.	mg.	vol. %	%		cc.	%	gm.	%	gm.	
14	0	44.0	10.3	470	38.1	51							Operation
	1	28.0	9.3	430	45.7	41							
	2	125.0	36.0	470	49.4	42	250	0.50	1.50	0.96	2.40	Obstruction released	
	3	175.0	92.2	450	50.2	43	900	0.01	0.09	0.33	2.97		
	4	276.0	126.6	380	40.0		320	0.01	0.032	1.38	4.4		
	5	220.0	132.6	370	40.9	53	680	0.01	0.068	0.44	2.99		
	6 a.m.	236.0	154.1	370	41.9	58	560	0.22	1.23	0.68	3.80	100 cc. 10 per cent NaCl by stomach tube	
	6 p.m.	169.0	98.5	430	38.1	59							
	7	78.0	57.0	490	38.1	61	1330	0.63	8.38	0.68	9.0		
	8	75.0	47.2	450	32.4	67	270	0.11	0.30	2.00	5.4		
	9	27.7	17.3	490	38.1	65	240	0.06	0.14	2.50	6.0		
	10	24.4	14.9	480	38.1	72	140	0.07	0.09	3.30	4.6		
	11						190	0.15	0.29	2.85	5.4		
12	28.1	8.9	580	34.4		150	0.35	0.53	2.00	3.0	Recovered		
13													
15	0	33.0	8.4	470	34.3	55							Operation
	2	68.3	33.6	420	48.3	42							
	3	132.0	98.1	430	50.2	52	730	0.35	2.56	0.64	4.67	Obstruction released	
	4	173.0	112.8	320	47.5	48	340	0.07	0.24	1.77	6.02		
	5	159.0	91.1	440	41.6		275	0.05	0.14	3.00	8.25		
	6						355			3.00	10.65		
	7		44.8	410	45.7		195	0.03	0.06	3.00	5.05		
	8	37.5	23.8	410	52.0		220	0.03	0.06	1.02	4.22		
	9	40.6	16.8	410	55.8		220						
	10	29.1	14.0	450	59.6		210	0.05	0.11	1.00	2.1	Recovered	
16	0	30.0	13.3	490	38.1								Operation
	1	30.3	12.4	420	41.9								
	2	59.5	38.5	330	57.7		1000	0.05	0.50	0.92	9.2	Obstruction released	
	3	41.6	15.4	390	52.0		625	0.05	0.31	1.23	7.7		
	4	41.0	22.4	380	48.8		610	0.05	0.30	1.04	6.3		
	5	32.6	16.1	380	52.0		500	0.02	0.10	1.92	9.6		
	6	38.9	14.0	390	50.2		235	0.03	0.70	3.00	7.05		
	7	31.9	15.4	400	55.8		365	0.06	0.22	1.44	5.3	Recovered	
8	27.0	16.8	400	54.6		265	0.03	0.08	1.10	2.9			

amount of water in four animals and in 10 per cent solution in another. A very large amount of salt was required for each animal. The four recovering showed a rapid return of blood findings to normal, and a disappearance of the signs of toxemia. The animal which did not recover showed a marked fall in non-protein nitrogen after the administration of 10 gm. of salt by mouth. The following morning an intravenous injection of 25 per cent sodium chloride was attempted with immediate death of the animal.

In three animals chemical studies were also made on the urine after the pyloric obstruction was released (Table IV). After the release there was no vomiting, so accurate urine collections could be made. Distilled water was allowed *ad libitum*. No food was given. In one animal (No. 13) the non-protein nitrogen continued to rise and the chlorides to fall after the removal of the obstruction. There was a marked diuresis, with a high nitrogen and low chloride excretion. Even with this marked diuresis and high nitrogen output the non-protein nitrogen in the blood continued to rise indicating the continuation of the increased protein destruction. The hematocrit reading before operation was 51, and 4 days after the release operation it was 58. When the non-protein nitrogen was 236 mg. per 100 cc. the animal was given 100 cc. 10 per cent sodium chloride by stomach tube in broken doses over several hours time. In the afternoon the non-protein nitrogen had fallen to 169 mg. with practically no change in the hematocrit reading. The following day there was a marked diuresis with a high nitrogen excretion. Almost all the chloride given was excreted within 48 hours. The non-protein nitrogen rapidly returned to normal and remained so. In two other animals there was also a marked diuresis after release of the obstruction. The nitrogen excretion was very high. The non-protein nitrogen returned to normal without treatment. The blood chloride returned to normal in one animal and almost to normal in the other.

DISCUSSION.

Temporary obstruction of the pylorus is a procedure by which the characteristic toxemia of upper gastrointestinal tract obstruction may be produced without having to consider mechanical factors, infection, or operative risk. It gives an opportunity for studying the toxemia factor alone.

The animals which recovered after the release of the obstruction showed the findings now known as characteristic of pyloric obstruction. The animals which recovered spontaneously all showed a quite low blood chloride at the height of the toxemia. The lowest level of chloride always occurred with the highest non-protein nitrogen. As the non-protein nitrogen returned to normal the chloride rose and gradually returned to normal with the animal receiving nothing by mouth except distilled water. These results can be explained only on the basis of a redistribution of the body chlorides. Some of the chloride lost from the blood must have been stored somewhere within the body only to return to the blood after the toxemia is relieved. The level of chloride in the blood is evidently not a true index of the chloride in the body.

The effect of sodium chloride given by mouth in the toxic animals was immediate and most striking. In no instance was the salt given until it was quite apparent that the toxemia would not be relieved by water alone. In every animal so treated there was a rapid return of the blood to normal except the one in which a fatal result followed a later intravenous injection.

The study of the urine after temporary obstruction of the pylorus emphasizes again the high nitrogen excretion which can be explained only on the basis of increased protein destruction. There is a marked diuresis after the obstruction is released probably due to the increased urea content of the blood. The administration of sodium chloride caused a transient increase in the diuresis and output of nitrogen and salt with a rapid return to normal. The assumption seems justified that the restoration of the chlorides has stopped the increased protein destruction.

CONCLUSIONS.

The toxemia characteristic of upper gastrointestinal tract obstruction may be produced by temporary obstruction of the pylorus. This procedure affords an opportunity for studying the toxemia in the absence of mechanical factors, operative risk, and infection.

Animals which spontaneously recover from the toxemia may show a return of the blood chloride to normal when only distilled water is given. In such instances there must be a redistribution of the body store of chlorides.

The administration of sodium chloride by mouth to animals which show a toxemia without evidence of spontaneous recovery causes a rapid return of the blood to normal.

There is a marked diuresis with high nitrogen excretion during the toxemia. This is evidently due to the increased protein destruction.

The return of the blood chlorides to normal causes a cessation of the increased protein destruction.

REFERENCES.

1. MacCallum, W. G., Lintz, J., Vermilye, H. H., Leggett, T. H., and Boas, E., *Bull. Johns Hopkins Hosp.*, 1920, xxxi, 1.
2. Hastings, A. B., Murray, C. D., and Murray, H. A., Jr., *J. Biol. Chem.*, 1921, xlii, 223.
3. Grant, S. B., *Arch. Int. Med.*, 1922, xxx, 355.
4. Haden, R. L., and Orr, T. G., *J. Exp. Med.*, 1923, xxxvii, 365.
5. Haden, R. L., and Orr, T. G., *J. Exp. Med.*, 1923, xxxvii, 377.
6. McVicar, C. S., *Am. J. Med. Sc.*, 1925, clxix, 224.
7. Murray, H. A., Jr., *Arch. Surg.*, 1923, vii, 166.
8. Gamble, J. L., and McIver, M. A., *J. Clin. Inv.*, 1925, i, 531.
9. Haden, R. L., and Orr, T. G., *J. Exp. Med.*, 1923, xxxviii, 55.
10. Whipple, G. G., Cooke, J. V., and Steams, T., *J. Exp. Med.*, 1917, xxv, 479.
11. Haden, R. L., and Orr, T. G., *J. Exp. Med.*, 1927, xlv, 433.
12. White, J. C., and Bridge, E. M., *Boston Med. and Surg. J.*, 1927, cxcvi, 893.
13. Atchley, D., and Benedict, E. M., *J. Biol. Chem.*, 1927, lxxv, 697.
14. Haden, R. L., and Orr, T. G., *J. Exp. Med.*, 1926, xlii, 419.
15. Folin, O., and Wu, H., *J. Biol. Chem.*, 1919, xxxviii, 81.
16. Van Slyke, D. D., and Cullen, G. E., *J. Am. Med. Assn.*, 1914, lxii, 1558.
17. Van Slyke, D. D., and Cullen, G. E., *J. Biol. Chem.*, 1919, xxx, 289.
18. Gettler, A. O., *J. Am. Med. Assn.*, 1921, lxxvii, 1652.
19. Folin, O., and Dennis, W., *J. Biol. Chem.*, 1916, xxvi, 473.