P. E.—Well developed and nourished. Conscious and rational. Face flushed, breathing somewhat heavily. Stuporous. Head: Cranial bones large compared with size of face. Nasal bones undeveloped and nose of saddle-back type. Upper lip short; drawn upward. Eyes: Pupils small, react sluggishly to light and distance. Motions normal. No strabismus or ptosis. Mouth: Slight pyorrhea. Tongue protruded straight, moist, coated. Ears: Small, not abnormal. Throat: Slight inflammation of pharynx. Neck: No glands. No stiffness. Chest: Pigmentation of left nipple. Heart: Apex in fifth space inside nipple line. Right border 2 cm. to right, left border 10 cm. to left of median line. No thrill. Slight systolic at apex. A2 greater than P2. Lungs: Expansion equal. Resonance, vocal fremitus, and whispered voice normal. Breathing over left lung near scapula intensified and with an occasional rle. Abdomen rounded, tympanitic, no tenderness, spasm or tumors. Extremities; No oedema. Motions normal. Knee jerks present.

Laboratory Reports. Wassermann negative. Widal negative, February 17 and February 18. W. B. C., February 10, 7,200; February 18, 9,400. Blood pressure: Systolic, 145 mm.; diastolic, 90 mm. Urine: February 13 and 15, pale, acid, 1006-1007, no albumen, no sugar. Lumbar Punctures: February 10, 15 cc., clear fluid with 20 cells per cubic mm.; February 18, 18 cc. clear fluid under slight pressure with no organisms present. At entrance, temperature, 102.0; pulse, 80; respiration, 30. February 13, 1917: Temperature, 101.8; pulse, 94; respiration, 25. Patient dull mentally, incontinent of urine and faeces. No complaint or apparent discomfort. Physical examination negative except for a definite Babinski sign on the right for the past three days, and neck slightly rigid. Pupils unequal but react to light and distance. February 17: Condition unchanged. Temperature still elevated, cause not determined. Mentally still very dull. Answers questions fairly well. Physical examination as at last note. February 21: X-ray of brain shows a large sella turcica, 25 mm. in diameter, with thinning of the walls, and obliteration of the clinoid process. Probable enlargement of the pituitary body. Neurological consultant makes a diagnosis of cerebral tumor or brain abscess. February 24: Aural consultant re-

ports "profuse discharge of pus from left sphenoid and ethmoid sells, left maxillary antrum apparently discharging pus." February 27: Temperature normal. Parents refuse operation. Discharged with the diagnosis of cerebral abscess and acromegaly.

REFERENCE.

¹ The Meningeal Syndrome and Other Sources of Error in Pyelitis, BOSTON MEDICAL AND SURGICAL JOURNAL, Nov. 15, 1917.

BLOOD PLASMA CHLORIDES VERSUS RENAL FUNCTION.

By W. C. RAPPLEYE, M.D., SAN FRANCISCO,

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THE significance of the chloride content of the blood is imperfectly understood. Widal, Ambard and their associates and, more recently, McLean at the Rockefeller Hospital, have brought out several interesting features of this problem. The threshold for excretion of sodium chloride, *i.e.*, the concentration of sodium chloride in the blood plasma necessary to start excretion of the salt into the urine, is fairly constant at about 562 mgm. per 100 cc. of plasma. When the concentration of sodium chloride in the plasma falls below this threshold value, excretion of chloride practically ceases. The threshold of sodium chloride secretion is not fixed but varies in health and is much influenced by the administration of drugs and by disease processes. It can be considered to represent a regulatory mechanism for the maintenance of a fairly constant composition of the blood. In this respect, it resembles the mechanism in regard to water and sugar excretion and differs from the excretion of nitrogenous substances, which have no threshold value below which excretion does not take place. From the relationships of plasma and urine chlorides to this threshold, Ambard, Chabanier, and Onell have developed their work on the sodium chloride-secretion-constant.

In dropsical renal disease, the secretion threshold is elevated and points to a lowered ability of the kidneys to excrete sodium chloride. On the other hand, the slight retention frequently seen in the nephropathies may be quite independent of any defect in the sodium chloride elimination. Because of the variation seen in health and in disease, calculation of the threshold value for clinical purposes, in an en-

deavor to secure the sodium chloride permeability of the kidneys, is of little value in the presence of mild degrees of retention. It is early in disease processes that we wish to secure evidence of impaired function—at a stage when something can be done therapeutically—and it is because of the features mentioned above that the threshold studies of sodium chloride give us but little aid in early recognition of decreased renal excretion.

That there is some degree of selective excretion by the kidneys seems established. In some cases, urea excretion may be normal while that of uric acid may be definitely impaired. The same selective excretion probably pertains to sodium chloride also. Evidence pointing in that direction may be noted in the "concentration" and "dilution experiments" worked out by Hefter and Siebeck, the "fixation of specific gravity" studies reported by Hedinger and Schlayer and the extensive studies on excretory response to varying diets as worked out by Mosenthal and others.

McLean has summarized our information relative to the problem as follows:

1. The normal and usual range of concentration of blood plasma chloride is from 562 to 625 mgm. per 100 cc. of plasma or higher, according to the amount ingested. On the excess over 562 mgm. per 100 cc. of plasma depends the rate of excretion.

2. There is a relative increased concentration in certain cardiac and renal diseases.

3. Under certain conditions, notably fevers and diabetes, or by the action of diuretics or heart tonics, the chloride threshold may be temporarily or permanently lowered.

4. Failure to excrete chlorides in pneumonia is associated with a lowered concentration of chlorides in the plasma.

5. Edema is usually accompanied by a relatively increased concentration of chlorides in the plasma.

6. Chlorides and urea functions are quite independent of each other.

Most of the work in the blood chlorides has been done on young, healthy adults without evidence of renal disease or on patients suffering from active diseases, acute or chronic. During studies on renal functions here, determination of the plasma chloride values were made by a method described recently.¹ These values were compared with the elimination of phenolsulphonaphthalein, the blood urea find-

ings, the blood pressure readings and the urine specific gravity. Other features of the urine analyses were disregarded (there were no cases of glycosuria in the group) for in the type of patient studied, no value can be ascribed to the findings of albuminuria and cylindruria. The cases studied in this connection were active institutional cases, all were workers in the industrial rooms, wards or on the farm, none of them (unless noted) showed any edema, cyanosis, dyspnoea, or other features which are known to compromise excretory rate. The ages of the patients varied from 40 to 85 years, the majority were over 50. None of them were taking drugs of any kind. The blood in every instance was drawn before breakfast, some 12 hours after the preceding meal. The urea determinations were made by the Marshall urease method, the aeration and titration procedure being employed. Determinations of plasma chlorides were made on 5 cc. of plasma, the urea analyses on 5 cc. of citrated blood. The phenolsulphonaphthalein test of Rountree and Geraghty was done in the usual manner. The blood pressure values represent the variations from time to time over a period of months, some are the mean of numerous readings.

Table I gives the figures in a group so studied.

TABLE I.

NUMBER	PLASMA CHLORIDE (Mgm. per 100 cc.)	PHENALEIN	BLOOD UREA NITROGEN	BLOOD PRESSURE	URINE SP. GR.
1	594	60%	8.4	140-95	1030
2	512	15%	23.3	120-60	1024
			29.9	165-55	
3	560	30%	10.1	180-95	1022
			14.0	210-80	
4	570	40%	12.8	185-85	1012-22
				230-90	
5	570	50%	13.4	165-105	1019-22
			13.7	190-110	
6	550	65%	13.4	175-105	1024
	534			130-90	
7	546	60%	19.0	125-75	1020
			21.8	155-90	
			17.4		
8	618	55%	13.4	190-94	1014
			15.1	210-85	
			9.2		
9	662	60%	22.4	165-85	1012-24
		35%	15.4	180-95	
10	570	35%	17.3	165-95	1010
		55%		170-95	
11	570	50%	16.0	160-100	1014
	572		15.4		
12	570	30%	12.2	135-90	1010-30
13	560	40%	9.5	140-90	1010
			16.2	175-90	

TABLE I. (continued)

NUMBER	PLASMA CHLORIDE (Mgm. per 100 c.c.)	PTHALEIN	BLOOD UREA NITROGEN	BLOOD PRESSURE	URINE SP. GR.
14	554	40%	16.8	120-60	1002-10
15	603	40%	15.4	130-85	1020
16	566	30%	19.6	130-80	1012
		15%			
17	590	35%	18.5	130-90	1030
			19.9		
18	590	35%	10.1	150-85	1026
19	554	40%	18.5	155-85	1025
		30%	8.4	135-90	
20	558	50%	9.5	180-100	1012
			12.3	210-110	
21	542	5%	24.4	150-90	1021
		10%		160-95	
22	562	70%*	17.9	160-80	1013-22
		55%†	15.7	210-90	
		40%‡			
23	572	35%	10.6	185-120	1022
	578		13.4	190-110	
24	580	35%*	9.5	150-95	1020
		50%†	13.7	180-100	
		70%‡	14.6		
25	572	5%	15.7	190-130	1015-30
		5%		150-100	
26	572	30%	16.5	170-115	1006-12
27	540	40%	15.4	170-95	1028
			19.0	180-100	
28	572	40%	12.0	150-100	1018
29	510	45%	12.9	200-120	1020
	522		13.4		
30	498	25%	19.6	160-105	1016
			18.5	170-110	
31	570	25%	11.2	160-90	1015
		35%		175-95	
32	560	30%	11.8	125-75	1020
				170-100	
33	522	10%	17.4	145-90	1025
		5%			
34	520	40%	17.6	170-80	1012-35
			17.6		
35	730?	45%	15.1	150-85	1020
			11.7	180-90	
36	596	25%	10.1	120-85	1025
	522		11.2	170-110	
			15.2		
37	542	60%	11.2	135-80	1024
			15.9	120-80	
38	536	50%	14.5	145-95	1020
			14.0	165-110	
39	590	45%	12.9	160-110	1028
40	570	10%	21.3	165-110	1012-20
41	596	15%	11.2	150-120	1012-22
				190-130	
42	580	30%	22.9	150-95	1012-20
			23.5		
43	658	55%	14.0	175-95	1020-28
44	590	40%	10.6	150-100	1025-30
		55%	11.8	180-100	
45	514	50%	7.2	185-85	1030
46	558	50%*	10.1	200-110	1028
		20%†	12.3	190-105	
47	566	40%	6.7	170-90	1008-18
48	630	40%†	14.0	145-85	1010-20
		30%‡			
49	558	45%	11.2	185-80	1010-14
50	558	65%	9.2	170-100	1016-18
			10.1	240-90	
51	610	40%	7.3	180-60	1008
52	560	50%	12.3	160-65	1008-20
				220-90	

TABLE I. (concluded)

NUMBER	PLASMA CHLORIDE (Mgm. per 100 c.c.)	PTHALEIN	BLOOD UREA NITROGEN	BLOOD PRESSURE	URINE SP. GR.
53	530	60%	12.4	165-85	1016
54	566	25%	7.3	170-100	1004-40
55	546	45%*	18.4	210-130	1002-15
		15%†			
56	610	40%	11.7	220-140	1010
	612	10%			
57	606	45%	12.4	135-85	1012-22
58	620	55%	12.3	210-140	1032
				250-70	
59	672	60%	15.4	160-85	1004-10
	540	40%	13.2	200-110	
60	620	65%	12.3	180-90	1022-24
			10.1	220-105	
			12.8	210-130	
61	558	40%	7.6	125-95	1012
62	575	50%	11.4	135-90	1016
63	602	35%	14.4	230-120	1010-14
64	638	15%	8.4	190-110	1020-23
65	670	40%	14.6	260-120	1024
	576				
66	594	60%	14.2	145-95	1030-31
67	560	55%	9.4	155-80	1014
68	602	30%	18.3	175-90	1010-14
69	578	15%	17.5	150-75	1020-24
70	590				
	594	35%	8.6	125-70	1030
			13.4		
71	566	40%	17.6	170-110	1015-35
72	586	50%	10.3	115-75	1022-30
73	586	30%	16.8	180-115	1008-22
74	578	70%	14.3	200-140	1016-30
			16.5	210-120	
75	562	25%	15.4	130-70	1022
			15.9		
76	590	30%	13.4	150-90	1002-24
77	550	45%	—	155-90	1020
78	646	40%	18.2	120-70	1024-30
79	586	45%	16.4	130-75	1032
80	566	28%	18.5	140-75	1020
		25%			
81	708	15%	23.6	230-100	1018-0
	708		22.2		
82	520	40%	17.6	170-80	1012-35
			17.6		
83	540	—	14.3	180-100	1020
84	658	55%	9.2	145-85	1017-26
85	570	25%	25.2	200-85	1020
86	558	40%	—	120-78	1010-18
87	578	60%	—	220-110	1030
88	558	40%	—	155-75	1020
89	586	25%	—	138-85	1012-22
90	590	35%	—	195-110	1010-18
91	540	40%	—	185-70	1030-32
92	594	25%	—	170-100	1008-14
93	590	50%	—	145-85	1020
94	558	35%	—	140-100	1020
95	560	65%	—	140-85	1024
96	588	50%	—	105-65	1010
97	606	40%	—	140-85	1012-26
98	550	45%	—	210-110	1020-22
99	526	25%	—	172-85	1012-20
100	594	50%	—	135-55	1024
101	582	25%	—	120-85	1021-24
102	566	70%	—	155-100	1026
103	554	30%	—	160-95	1020
104	558	60%	—	160-90	1070

* 1917.

† 1918.

‡ 1919.

Of the 104 cases enumerated in Table I, 40 showed plasma chloride values ranging from 554 to 575 mgm. per 100 cc., there were 20 that showed values below 554 mgm. and the other 44 gave figures over 575 mgm. An attempt to relate the values found with the other findings, *i.e.*, the blood urea nitrogen, rate of elimination of phenolsulphonephthalein and blood-pressure readings, showed that of the cases showing a plasma chloride of 560 mgm. or less, 68% of such cases had a red test of 40% or higher, 60% had a blood urea nitrogen of 16.0 mgm. or less and 34% had a systolic blood-pressure of 150 mm. or less, while 26% had a systolic reading of 180 mm. or over. A review of similar findings in the whole group shows that 60% of them showed a red test of 40% or higher, 66% had a blood urea nitrogen of 16.0 mgm. or less, 38% had a systolic blood pressure of 150 mm. or less, and 27% had a pressure reading of 180 mm. or higher. The close relative approximation of these two groups of figures does not permit one to draw a conclusion that the plasma chloride figures bear any relationship to the other features taken as evidence of renal function.

It must be borne in mind that the plasma chloride values depend in part on the alkaline reserve of the plasma and, since the latter is quickly altered by exposure to air, the blood must be centrifuged promptly to minimize the alteration so produced, or drawn under oil to prevent the escape of carbon dioxide, consequent depression of bicarbonate in the plasma and resulting high chloride reading. In the group of cases studied here, the bicarbonate content of the plasma was not determined.

A second group of 40 cases was studied and the plasma chlorides of blood drawn 12 hours after the preceding meal were determined and compared with figures determined three to four hours after a regular meal. The values so found are given in Table II, together with the blood-urea-nitrogen, phenolsulphonephthalein output, blood pressure and urine specific gravity. 85% of the cases showed a definite rise in plasma chlorides after the meal, but an attempt to correlate the rise with any feature of the renal function as evidenced by the other findings enumerated, failed. In both series there was little tendency toward a low fixation of the specific gravity of the urine.

TABLE II.

NUMBER	PLASMA CHLORIDE (before breakfast)	PLASMA CHLORIDE (3-4 hours after meal)	PHTHALEIN	BLOOD UREA NITROGEN	BLOOD PRESSURE	URINE SP. GR.
1	590	676	15%	32.8	180-100	
2	564	642	50%	10.4	215-100	1020-30
					160-70	
3	560	668	50%	9.5	140-90	1012-18
	522			14.0	175-120	
4	594	730	55%	13.2	160-120	1008-20
5	610	746	50%	12.2	130-70	1012-30
6	620	660	45%	16.0	130-60	1010-30
7	560	648	20%	20.2	165-95	1018-22
				21.3	180-85	
8	608	716	45%	17.0	135-90	1010-28
9	554	610	55%	7.3	140-70	1020-22
10	538	652	55%	10.4	120-70	1004-14
11	554	530	10%	7.6	155-90	1012-22
12	586	704	45%	8.8	125-75	1010-12
13	560	644	30%	16.3		
14	570	584	40%	10.6	160-90	1025-30
15	546	606	35%	11.7	150-75	1004-20
			15%	12.3	170-80	
16	608	600	15%	18.6	170-100	1022-30
					140-95	
17	618	652	60%	15.4	170-80	1008-30
				15.6	210-120	
				12.0	195-100	
18	600	642	40%	13.4	170-95	1013-14
		686			190-120	
19	590	634	65%	6.2	125-70	1014
20	602	716	45%	15.6	165-85	1078
				11.5		
21	570	572	35%	8.4	130-65	1005-25
22	582	648	45%	16.4	120-100	1032
23	582	660	15%	26.4	170-120	1015-21
			5%			
24	618	742	40%	14.6	170-120	1030
25	590	684	45%	12.9	155-110	1018-28
26	562	674	30%	19.0	115-70	1020-30
27	616	584	15%	18.4	160-90	1012-16
28	574	610	35%	10.6	150-80	1010-20
29	578	660	55%	6.7	205-85	1034
30	558	672	40%	13.2	140-90	1020-22
31	604	636	50%	10.6	160-75	1010-26
32	558	602	10%	17.4	145-80	1028
33	560	584	45%	12.4	130-85	1010-16
34	574	712	—	—	100-55	1010-20
35	562	570	70%	8.4	135-75	1010-20
36	598	596	40%	14.2	140-80	1014-16
37	578	714	40%	8.4	120-80	1025-30
38	610	602	30%	—	145-70	1020-28
39	580	608	—	16.8	160-100	1025
	576				210-120	
40	616	584	15%	22.4	180-100	1012-14

Attention was later turned to the so-called cases of essential vascular hypertension as seen in the out-patient clinics and wards of a general hospital. In these patients, no evidence of nitrogen retention or depressed phenolsulphonephthalein output is obtained to suggest that the origin of the hypertension is failing excretory function. The group which has been studied is still too small to allow comment, but it seems quite probable that many of these people have a high kidney threshold for salt in relation to their elevated blood-pressure. Attempts to lower the threshold of excretion have

been tried but they introduce new features, such as the effect of ingested alkali on the distribution of salt between plasma, red cells and tissues. In some cases, however, it is possible to secure a markedly increased salt output in the urine with a fall in plasma chlorides, but the mechanism is not entirely clear.

SUMMARY.

The blood plasma chlorides were determined in 104 patients showing no obvious evidence of compromising physical disease, the blood being drawn 12 hours after the preceding meal. The ages ranged from 40 to 85 years. No relationship could be established between the chloride values and the blood urea nitrogen, rate of elimination of phenolsulphonephthalein, blood pressure readings or urine specific gravity.

In a second group of 40 cases, the plasma chlorides on fasting blood and blood drawn four hours after the preceding meal were determined. Although 85% of the cases showed a definite and considerable rise after the meal, the rise would not be associated with any consistency with the parallel determinations enumerated above.

The small group of cases of so-called essential vascular hypertension studied seem to show an elevated renal threshold for sodium chloride. Attempts to lower the threshold have given no conclusive results.

REFERENCE.

- ¹ Rappleye, W. C.: A Simple Application of the Volhard Principle for Blood Plasma Chlorides, *Jour. Bio. Chem.*, Vol. xxxv, No. 3, September, 1918.

INSTITUTIONAL CONTROL OF DIPHTHERIA.

BY FRANCIS A. FINNEGAN, M.D., BOSTON,

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DIPHTHERIA, a communicable disease with an established etiology,—the Klebs-Loeffler bacillus; with a specific curative agent,—antitoxin,—is still responsible for more deaths in the United States than whooping cough, measles, or scarlet fever. It is accountable for 4.4% of the total mortality at ages under 15 years in the registration area, and the average yearly toll is approximately 23,000 lives.

Many reasons are put forth for this still too great mortality, such as failure to call the physician early enough, a delayed use of anti-

toxin and in very severe and late cases the non-use of the intravenous administration of antitoxin. All these facts have been strikingly brought to light by investigators of diphtheria mortality. Failure on the part of the parent or guardian to consult the physician early enough means a late administration of antitoxin and lessens the chances of recovery. Evidence is positive and overwhelming that the earlier the use of antitoxin in any given case the better the result and the greater the chance of recovery.

Dr. J. M. Clements of Hull, England, in discussing diphtheria in elementary schools, and its prevention, said that the mortality among cases coming under his care from 1903 to 1906, classified to the day of the disease on which antitoxin treatment started, that of those coming under treatment on the first day was nil; on the second day 1.5%; on the third day 8%, etc., the mortality percentage rising with each successive delayed day.

The intravenous injection of antitoxin in very late and severe cases lets loose immediately into the blood stream the curative agent and results in a quicker attack upon the diphtheria toxin or poison circulating in the blood.

It would seem, therefore, they must utilize another practical method of immunizing against diphtheria. The Schick test has made it possible readily to detect persons susceptible to the Klebs-Loeffler bacillus or diphtheria bacillus and if susceptible to be actively immunized with three injections of toxin antitoxin at weekly intervals. Schick re-tests should subsequently be made to determine the success of the protection obtained. Already in two institutions in Massachusetts there has been successfully carried out the Schick test and after immunizing with diphtheria toxin antitoxin these two institutions, where formerly diphtheria had been endemic and epidemic at times, have been able to keep their diphtheria rate to almost nil since the advent of this practical method of control. Each inmate on entrance is given the Schick test and if positive (meaning susceptibility to the disease), is given three successive doses of diphtheria toxin antitoxin at weekly intervals. The re-Schick test is tried at intervals of six months, one year, two years, etc. In one institution where the work has been carried out for the past two years under the immediate supervision of the State Department of Health these re-Schick cases on persons once susceptible, that