JCI The Journal of Clinical Investigation

STUDIES OF SERUM ELECTROLYTES: *VII. The Total Base and Protein Components of the Serum during Lobar Pneumonia with a Note on the Gastric Secretion*

F. William Sunderman

J Clin Invest. 1931;9(4):615-633. https://doi.org/10.1172/JCI100325.

STUDIES OF SERUM ELECTROLYTES

VII. The Total Base and Protein Components of the Serum during Lobar Pneumonia with a Note on the Gastric Secretion

By F. WILLIAM SUNDERMAN[1]

(From the John Herr Musser Department of Research Medicine, University of Pennsylvania and the Medical Wards and Chemistry Department of the Pennsylvania Hospital, Philadelphia)

(Received for publication September 22, 1930)

In previous papers (1) (2) (3), the variations in the composition of blood serum and some features of the metabolism of electrolytes during the course of lobar pneumonia have been described. Among the changes in the serum it was found that during the precritical period there is a decrease in total base concentration and a tendency to a decrease in protein concentration. This investigation has here been extended to include measurement of the separate components of the total base and protein of the serum.

There is comparatively little available data as to the concentration of sodium, potassium, calcium, and magnesium in the serum during pneumonia. This is to be expected because of the lack of appropriate methods, since most of the earlier methods required large amounts of blood. Peabody (4) reviewed the early literature and studied the concentration of calcium and magnesium in the serum during the course of lobar pneumonia. He found that both tended to be slightly lower during the febrile period than in convalescence. The average of 6 magnesium analyses during the febrile period was 19 per cent lower than the average of 4 analyses made after the crisis. The average of 7 measurements of calcium concentration during the febrile period was 10 per cent lower than the average of 4 measurements made after the crisis.

Gerstenberger, Burhans, Smith, and Wetzel (5) studied the con-

[1] Robert M. Girvin Fellow.

centration of calcium and inorganic phosphorus in the blood of children suffering from pneumonia and found a reduction in both. Jansen (6) concluded that the calcium concentration is lowered during the precritical period and increased in the epicritical.

There is a large literature on the excretion of the various components of base in the urine during various fevers. The early literature was extensively reviewed by Garratt (7). The essence of the findings is that there is a decreased urinary excretion of sodium and calcium and an increased excretion of potassium during the height of the fevers, not infrequently continuing after the fall in temperature. Peabody observed these changes in pneumonia and also found magnesium to be excreted normally or in excess. Recently (8) we have reported a lowered excretion of total fixed base in the urine during the precritical period associated with the lowered excretion of chloride.

Attempts to explain the alteration in the concentration of the electrolytes during pneumonia have been made repeatedly but with doubtful success. In a recent contribution Binger, Christie, Davis, and Hiller (9) attacked the problem by measuring the serum chlorides in dogs, first, during experimental pneumococcus infection; second, during anoxemia; third, after tissue destruction; fourth, in anaphylactic shock; fifth, in experimental leucocytosis; and sixth, during fever. A significant decrease in serum chloride was found in all three animals infected by bronchial insufflation with the pneumococcus but in none of the other conditions studied. This study excludes from the entire complex of mutually dependent processes in a pneumococcus infection many of the individual factors which might be considered in seeking an explanation for the electrolyte disturbance.

Geill (10) has recently reviewed the literature on the albumin and globulin concentrations in the serum under normal and pathological conditions. His review brings out the fact that globulin is increased at the expense of albumin in most infections. Limbeck and Pick (11) have shown that in acute infections an increase in globulin may occur even when there is a decrease in total nitrogen.

In a series of five cases of pneumonia studied before and after the crisis Loeper, Ravier, and Lebert (12) have shown in each case a rise in globulin after the crisis. There was a 4 to 37 per cent increase in the ratio of globulin to total nitrogen in the serum after the crisis as compared with the serum before the crisis.

Horvath and Little (13) measured the nitrogen fractions of the serum taken from cows suffering with bronchopneumonia. During the course of the disease they found a rise in the globulin, fibrin, and nonprotein nitrogen.

METHODS

Inasmuch as we were interested in the changes coincident with the ordinary course of the disease, the patients studied were given no unusual treatment. They were on an average caloric intake of 800 calories per day during the febrile period. It is our experience that except when beverages containing glucose have been added to the diet this is the largest daily caloric intake tolerated as a rule by the patient acutely ill with pneumonia without the development of tympanites.

The blood from the patients studied was obtained in the morning before breakfast and was withdrawn by venipuncture into 50 cc. pyrex centrifuge tubes. The blood was collected under paraffin oil, out of contact with air, and was immediately centrifuged at high speed. The clear serum was removed under oil and was used for analysis. The serum was separated within twenty minutes after the blood was withdrawn. Brems (14) believes that high potassium values are found when serum is not separated immediately from the cells, due to the diffusion of potassium from the red blood cells. For this reason we have taken precaution to separate the serum at once.

Total base, sodium, and potassium analyses were made on ashed sera. The ashing was carried out by digesting the serum in silica beakers on an electric sand bath using 0.5 cc. concentrated H_2SO_4 and 1 cc. concentrated HNO_3 to each cc. of serum. The heat of the sand bath was raised gradually over a period of twenty-four hours and the contents in the beaker were evaporated to dryness. The beakers were then transferred to an electric furnace and the contents were ashed to a dark cherry heat (approximately 600°C.) for twenty minutes. When cool, one drop of 4 N H_2SO_4 was added and the material was heated again in the furnace to dark cherry heat for twenty minutes. With this method of ashing no excess of H_2SO_4 was present and the ash dissolved readily in water.

Sodium. The procedure recommended by Barber and Kolthoff (15) was employed in which sodium is measured gravimetrically as a precipitate of uranyl zinc sodium acetate, $(UO_2)_3ZnNa(CH_3COO)_9 \cdot 6H_2O$. Analyses were made on 1 cc. of serum. Although phosphates in large amounts affect the final result, in amounts of 12 mgm. per 100 cc., theoretical results were obtained. The precipitation and washing were carried out at the same temperature to avoid change in solubility coefficient.

Potassium was measured by the titrimetric method of Shohl and Bennett (16) using 2 cc. amounts of serum. Known solutions of potassium were analyzed with each series as a check. The values obtained on known solutions were always high by 0.2 to 0.6 mM. and the corresponding correction was subtracted from the results obtained on the unknown.

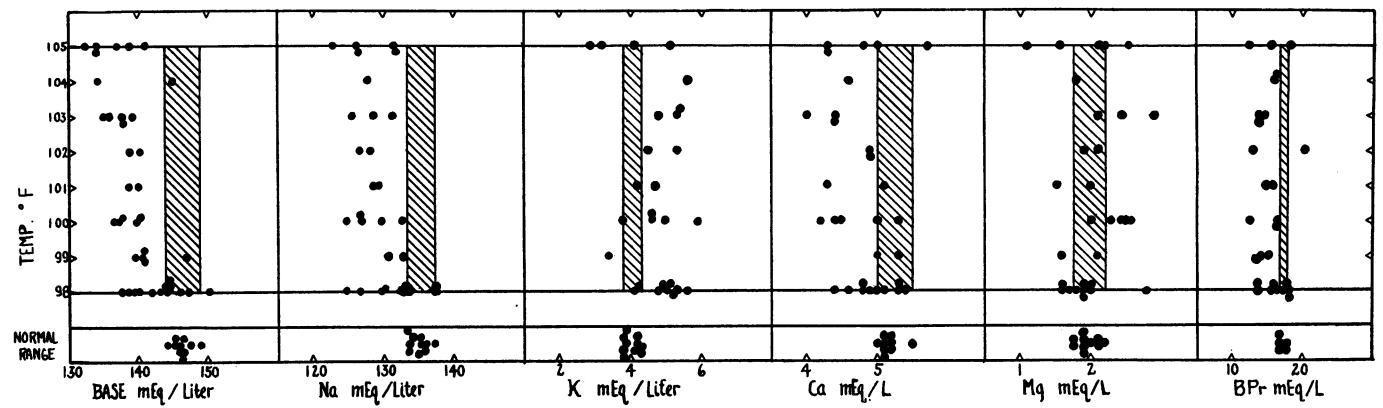

FIG. 1. BASE COMPONENTS PLOTTED AGAINST AVERAGE TEMPERATURE

Calcium was measured by the method recommended by Clark and Collip (17).

Magnesium was measured in serum from which the calcium had been precipitated. The procedure was carried out by Briggs' method (18) in which magnesium is precipitated as $MgNH_4PO_4 \cdot 6H_2O$. The phosphorus content was then determined according to the colorimetric method of Fiske and Subbarow (19).

Total base was analyzed according to the method of Stadie and Ross (20).

Albumin and globulin measurements were made by the method of Howe (21) with a macro-Kjeldahl technique.

Base bound by protein. This value was calculated by the equation of Van Slyke, Hastings, Hiller, and Sendroy (22).

$$BPr = 0.78 \text{ (Albumin N) (pH} - 5.16) + 0.48 \text{ (globulin N) (pH} - 4.89)$$

A constant pH of 7.35 was assumed.

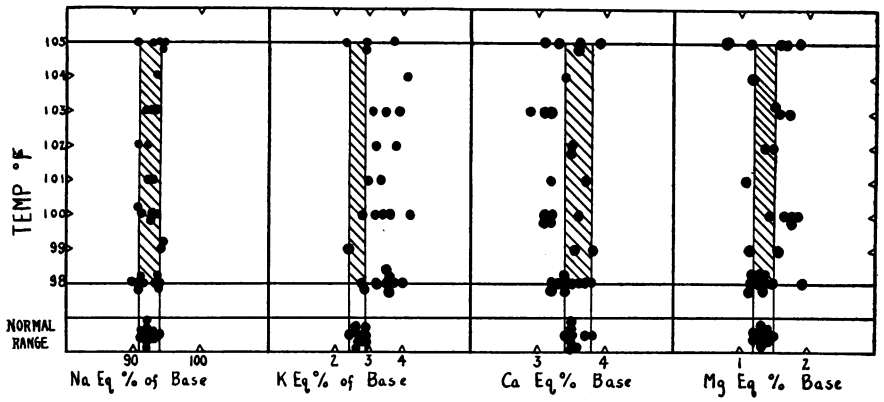

FIG. 2. EQUIVALENT PERCENTAGE OF BASE COMPONENTS PLOTTED AGAINST AVERAGE TEMPERATURE

Chlorides were analyzed by means of the Wilson and Ball modification (23) of the Van Slyke method. CO_2 analyses were made by the Van Slyke and Neill method (24). The Fiske and Subbarow (19) method of measuring *inorganic phosphates* was employed.

RESULTS

We are presenting our data of our base fractionations by plotting each type of base against the average temperature of the day on which the blood was withdrawn. It is often difficult to estimate correctly the day of crisis or even the day of the disease. For this reason we preferred to consider our findings in relation to the temperature (figure 1). Such an arrangement at least dissociates the febrile from the afebrile periods.

TABLE 1

Individual case analyses

Case number	Date	Temperature	Serum Na	Serum K	Serum Ca	Serum Mg	Serum total base			Serum protein N	Albumin N	Globulin N	Nonprotein N	Calculated BPr	Serum Cl	Serum CO_2	Serum P (inorganic)
							Sum of cations	Stadie and Ross method	Average								
	1930	*°F.*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*grams per liter*	*grams per liter*	*grams per liter*	*grams per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*mM. per liter*	*mgm. per 100 cc.*
C1	February 14	101	128.7	4.2	5.3	2.0	139.4	140.0	139.7								
	February 24	99	132.8		5.0	1.6		140.6		10.00	5.30	4.70	0.30	14.8	99.6		
C2	February 15	105	131.5	3.2	5.7	1.1	141.2	137.0	139.1				0.24				
	February 24	98	124.8	5.6	4.8	1.6	137.1	139.5	138.8				0.28				
C3	March 17	104	127.9	5.6	4.6	1.8	139.7	134.3	137.0				0.33				
	March 20	99	130.7	3.4	5.3	2.1	141.5	137.6	139.6				0.40		89.7		
	March 24	98	132.9	5.0	5.3	1.8	145.0	138.6	141.8				0.33				
	March 31	98	133.8	4.8	5.1	1.9	145.6	150.4	148.0	11.47	5.50	5.96	0.33	15.6			
	April 10	98			5.3	2.0		147.2		11.94	7.77	4.17	0.38	18.2	97.8		4.2
C4	March 3	105	123.0	2.9	4.3	2.2	132.4	132.4	132.4								
	March 6	98	126.6	4.9	4.4	2.0	137.9	137.6	137.8								
C5	March 10	100	124.9	4.6	4.4	2.4	136.4	137.3	136.9								
C6	March 10	103	125.6	4.8	4.0	2.9	138.6	135.1	136.9						90.2		
	March 17	100	129.7	5.9	4.3	2.0	141.9	137.8	139.9				0.26		88.9		
C7	March 25	103	131.4	4.3	4.4	2.2	142.3	139.3	140.8	10.07	5.62	4.45	0.28	14.8	98.0		2.3
	March 31	98	129.7	5.3	4.8	1.9	141.7	143.3	142.5								
	April 14	98	137.6	4.1	5.0	2.8	149.5	144.1	146.8	11.88	6.50	5.38	0.28	17.5			

C8	March 27	105	131.8	4.1	5.0	1.6	142.5	138.8	140.7	12.96	6.55	6.41	0.27	18.4			
	March 31	102	128.3	4.5	4.9	1.9	139.6	138.9	139.3								
	April 3	102	126.8	5.3	4.9	2.1	139.0	140.4	139.7	13.13	7.38	6.75	0.32	20.4			
	April 7	100	127.0	5.0	5.0	2.6	140.5	139.9	140.2	11.38	5.72	5.66	0.31	16.5			
	April 10	101	129.4	4.7	5.1	1.5	140.7	138.8	139.3	10.86	5.70	5.16	0.29	15.8			
	April 23	98	130.2	4.2	5.4	1.6	141.4	144.9	143.2	12.68	6.17	6.51	0.26	18.2	97.4		
C9	April 3	103	128.7	5.4	4.4	2.1	140.6	137.8	139.2	9.76	5.49	4.26	0.35	14.1	91.8		2.1
	April 7	100	132.6	4.6	4.5	2.5	144.2	140.4	142.3	11.35	5.60	5.75	0.32	16.4	93.1		
	April 14	98	137.5	5.1	4.9	1.7	149.2	144.6	146.9	11.48	5.33	6.15	0.25	16.4			4.4
	April 23	98	133.2	5.2	4.6	1.9	144.9	140.2	142.6	12.55	6.12	6.43	0.28	18.0	98.0		
C10	April 7	100	126.8	3.8	4.2	2.3	137.1	136.6	136.9	8.87	4.22	4.65	0.41	12.7	89.6		4.2
C11	April 8	105	126.3		4.8	2.1		134.1		10.03	6.92	3.11	0.31	15.5			
C12	April 22	105	126.6	5.1	4.3	2.6	138.6	141.0	139.8								
	1929																
C13	February 11	104								10.63	6.47	4.16	0.42	16.0	98.0	26	
	February 14	104						145.0		11.12	6.23	4.89	0.50	16.4	101.0	28	
	February 18	99						141.0		10.48	5.63	4.85	0.42	15.4	99.0	27	
	March 4	98						146.0		10.85	5.77	5.08	0.20	16.0	99.0	31	
C14	February 13	105						134.0		8.09	5.62	2.47	0.32	12.5	97.0	22	
	February 16	102								8.27	6.09	2.18	0.49	13.0	95.0	24	
	February 20	99						147.0		9.75	5.02	4.69	0.42	14.1	96.0		
	February 28	98						144.0		9.36	5.18	4.18	0.27	13.8	97.0	32	
C15	March 10	103						136.0		9.28	5.51	3.77	0.49	13.9	86.0	27	
	March 13	99						141.0		9.04	5.58	3.46	0.52	13.6	91.0	31	
	March 19	98						142.0		9.33	5.24	4.09	0.30	13.8	96.0	28	

We found the total base measurements agreed with the summation of the individual cations to within approximately ±2 per cent and with maximum deviations of −4.5 and +3.2 per cent. In figure 2 where the ratios of individual cations to base are plotted, the base represents the average of the total base measurements and the sum of all of the cations. The complete chemical data on the pneumonia patients are given in table 1. Protocols of these patients are in the appendix. In table 2 appear the serum values obtained on ten healthy adults, for the most part members of the medical staff or medical students. Our normal values for total base are considerably lower than those reported by Sunderman, Austin, and Camac in 1926. The 1926 analyses were made on the trichloracetic acid filtrate from serum obtained from defibrinated blood. The filtrate, after digestion with H_2SO_4 and HNO_3, was ashed in the final step over a Meeker burner. The analyses of total base reported in this paper were made without removal of the protein, directly on the serum obtained from blood which had been permitted to clot spontaneously before centrifuging. The final step in the ashing was carried out in an electric furnace at dark cherry heat.

In our series of protein fractionations, the conspicuous feature found was the decrease in the albumin concentration not only during the active infection but also in the period of convalescence. The globulin content was increased enough to compensate for the albumin loss in most of the sera excepting before the crisis in cases C14 and C15; in these two patients there was a significant decrease in total protein content of the serum. Values for nonprotein nitrogen were usually high at the time of crisis.

Taking the normal values for base bound by protein as between 16 and 19 m.Eq. per liter, it will be seen in figure 1 that this quantity is usually decreased during the febrile period.

We have shown previously (1) that the total base of serum during the active infection may fall as low as 83 per cent of the mean normal value and that this loss is almost equalled by the decrease in chloride. Sodium normally constitutes between 91 and 94 equivalents per cent of the total base. The sodium level was decreased in all of our cases before and for a considerable period after the crisis and this loss was approximately equal to the decrease in total base.

TABLE 2

Normal subjects

Subject	Serum Na	Serum K	Serum Ca	Serum Mg	Serum total base			Serum protein N	Albumin N	Globulin N	Nonprotein N	Serum chloride	Calculated BPr
					Sum of cations	Stadie and Ross method	Average						
	m.Eq. per liter	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*grams per liter*	*grams per liter*	*grams per liter*	*grams per liter*	*m.Eq. per liter*	*m.Eq. per liter*
FWS	137.3	4.2	5.2	2.1	148.8	149.1	149.0	11.3	7.9	3.4	0.29		16.9
R	133.7	3.9	5.1	2.2	144.9	147.1	146.0	11.3	8.3	3.0	0.26	98.5	17.8
P	133.6	3.8	5.2	2.0	144.6	149.3	146.5	11.4	7.9	3.5	0.26	101.3	17.6
CLS	136.0	4.1	5.1	1.9	147.1	147.8	147.5	11.0	7.4	3.6	0.24	103.4	16.8
RO	135.4	3.8	5.1	1.8	146.2	142.0	144.1	11.1	6.9	4.2	0.26		16.8
B	134.1	3.8	5.0	1.9	144.8	145.5	145.2				0.27	104.5	
SHER	135.1	4.2	5.3	1.9	146.6	144.0	145.3				0.25		
SHEF	135.9	4.3	5.2	2.1	147.5	145.6	146.6				0.22	102.5	
SCOT	133.9	3.9	5.1	1.9	144.8	147.1	146.0				0.24		
BE	135.1	4.3	5.5	1.8	146.8	145.7	146.3				0.22		
Maximum	137.3	4.3	5.5	2.2		149.3		11.4	8.3	4.2	0.29	104.5	17.8
Minimum	133.6	3.8	5.0	1.8		142.0		11.0	6.9	3.0	0.22	98.5	16.8
Average	135.0	4.0	5.2	1.96		146.32		11.22	7.68	3.54	0.25	102.1	17.2
Number of determinations	10	10	10	10		10		5	5	5	10	5	5

Our normal values for potassium in serum are slightly lower than those generally given in the literature. They vary from 3.8 to 4.3 mM. per liter with an average of approximately 4.0 mM. per liter. The serum potassium was increased during the febrile period above our normal range in twelve out of eighteen measurements. This increase tended to persist after the crisis. Normally our potassium values represent from 2.4 to 2.9 equivalents per cent of the total base; in pneumonic sera, however, the percentage of potassium rose as high as 4.2 per cent.

In thirteen out of twenty calcium measurements made during the febrile period the calcium level was below the normal range. This invites consideration of the associated changes in serum protein. Csapó and Faubl (25) concluded that 1.89 and 3.89 m.Eq. of Ca were bound respectively to every 100 grams of globulin and albumin. Inasmuch as approximately one half the serum Ca is bound by protein in the non-diffusible form, the tendency to lower calcium concentrations may have been explained in part by the decreased amount of albumin which is uncompensated in Ca binding power by the increased amount of globulin during the course of the disease, however, our measurements do not reveal consistent correlation of serum calcium with the fractions of serum protein.

The magnesium values showed throughout the period of the pneumonic infection, a tendency to scatter about the normal range. Seven analyses were below the lower normal limits, seventeen were within the normal limits, and six were above the upper limit. No particular rise was observed at the time of crisis. Stary and Winternitz (26) showed that there is a non-dialyzable fraction of Mg in serum averaging 28 per cent. Only a very small part of the fluctuation observed in magnesium can be attributed presumably to fluctuations in the serum protein.

Note on gastric secretion during lobar pneumonia

In the course of studies on the chloride metabolism in pneumonia, the absence of free HCl in the gastric contents of two of the patients was noted during the precritical period. We have studied this phenomenon in a series of fourteen gastric analyses on four patients during the course of the disease. Two of the patients (C13 and C14)

received no unusual treatment while the other two (C15 and C16) received a salt mixture containing: KCl, 6 grams; $NaHCO_3$, 5.9 grams; and $MgCl_2$, 1.2 gram; and approximately two liters of beverages containing 10 per cent glucose supplementing the diet each day until after the crisis. One half of the salt mixture when added to the ordinary food intake of the patient provides a mean normal salt ration. The dilute alcohol test meal as described by Bloomfield and

TABLE 3

Gastric analyses

Case number	Day of disease	Temperature	Maximal free acidity		Maximal total acidity		Maximal gastric chloride	Serum total base	Serum Cl
			Without histamine	With histamine	Without histamine	With histamine			
		°F.	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*
C13	−7	104	3		14		104		99
	−4	104	0		7		101	145	101
	0	99	0	0	19	47	112	141	100
	+14	98	30	33	36	42	92	146	99
C14	−4	105	0		11		99	134	97
	−1	102	0	42	11	68			95
	+3	99	9	39	40	67	123	147	96
	+11	98	26	30	57	50	109	144	98
C15	−3	103	19		26		104	136	86
	0	99	37	31	51	51	121	141	91
	+6	98	36	76	55	76	130	142	96
C16	−3	103	0	19	3	35	79	131	92
	0	100	18	34	26	42	94	134	99
	+7	98	49	46	58	53	95		98

Keefer (27) was used for the study of the gastric secretion. Specimens of gastric contents were taken at ten minute intervals for sixty minutes after which time the stomach was emptied and a solution of histamine (0.1 mgm. per 10 kgm. of body weight) was injected subcutaneously. Thereafter, the gastric contents were removed at ten minute intervals for thirty or forty minutes. The specimens were analyzed for free HCl and total acidity by fractional titration using

Topfer's and phenolphthalein indicators and for total chloride by the method used for serum. Total base and chloride of the serum were measured on specimens obtained just before the introduction of the stomach tube.

Convenient values for comparison are the maximal values of free HCl, total acidity, and chloride concentration observed in any one specimen of a given day. These values are given in table 3 together with the average temperature, the day of the disease in relation to the crisis, and the total base and chloride concentration of the serum.

The acidity tended to be lowered until after the crisis. In three of the four subjects there was no significant free HCl without histamine stimulation until after the crises. Histamine induced the appearance of free HCl in two of the three instances in which it was given during the precritical period in a patient who had shown no free HCl after the alcohol meal. Absence of free HCl during the febrile period is to be expected frequently in view of Meyers, Cohen, and Carlson's (28) experimental studies and the clinical observations of others upon gastric contents during fever.

We found no apparent correlation between the changes of either total base or chloride of the serum and the gastric acidity. The highest precritical total gastric acidity was observed in C3 who had at the same time the lowest precritical total base and chloride concentration in the serum. The maximal gastric concentration of chloride showed no variation beyond what may be expected normally in three out of the four subjects.

DISCUSSION

It is difficult to evaluate clearly the significance of changes in the concentration of serum electrolytes until more precise information is obtained concerning their complete metabolism under normal and pathological conditions. This will require a knowledge of the rate of utilization of the electrolytes by the tissues; the rate at which they are excreted by the body; the quantity in each tissue of the body; and a knowledge of the physiological conditions which bring about changes in their distribution. While awaiting such data, however, one may note such occurrences as seem to be correlated with the changes in concentration of electrolytes in the serum and suggest plausible relationships.

One may question first whether the changes observed in the cation concentrations in the serum are secondary to partial inanition and a lowered intake of salts. We have shown in previous studies that negative nitrogen balances are even higher in patients with pneumonia than in fasting subjects and that of the total cations ingested during the active infection in our patients, calcium alone is taken in a quantity similar to that found in an adequate daily ration of salt. From Morgulis' (29) studies of the cation concentration in the serum during the early stages of fasting in dogs, and from Gamble, Ross, and Tisdall's (30) studies of the cation concentrations in the serum of fasting epileptic children, there would appear to be a constancy in the electrolyte concentrations in the serum during inanition in contrast to the changes which we observed in pneumonia. It is possible that the more rapid catabolism of body tissue during the course of pneumonia than during inanition may be related to the change in electrolyte concentration of the serum in pneumonia.

Morgulis observed that when his fasting dogs progressed beyond a twenty per cent loss in weight, there was a decrease in the calcium concentration in the serum. He argues that the calcium bound by protein must be decreased since Csapó and Faubl estimate that approximately twice as much calcium is bound by albumin as by globulin and from the literature there is an apparent increase in the globulin-albumin ratio during starvation. Furthermore, he contends if it be accepted that tetany is due to a decrease in the dialyzable calcium content in the serum, then this quantity must have remained above the tetany limit, since Morgulis' animals showed no evidence of tetany. We believe that the fraction of calcium bound by protein in the serum of our patients may be diminished but, as already noted, our measurements do not reveal consistent correlation of the decrease in the concentration of serum calcium with the decrease in the concentration of serum protein or of the albumin fraction of the serum protein.

The disproportionate changes in the individual cation concentrations constitute evidence against the view that the changes we report can be accounted for by simple dilution of the serum with water. That the phenomena observed, however, may be due partially to the administration of large quantities of water deserves consideration. During the precritical period of pneumonia copious quantities of water

are generally consumed. Greene and Rowntree (31) studied the changes in the blood of dogs after the forced administration of water and found that the serum electrolytes were decreased and that both chloride and sodium concentrations were decreased to a greater extent than could be accounted for by the degree of dilution measured by the increase in plasma volume and by the lowered hemoglobin and serum protein concentrations.

By comparing our studies on the serum with those in the literature on the urinary excretion of bases during pneumonia there is a suggestion that the excretion of each of the electrolyte components may in general be correlated with its concentration in the serum. Thus during the precritical period of pneumonia there appears to be a decreased concentration in the serum of sodium and calcium and there is reported a decreased excretion of these ions in the urine; there is an increased concentration of potassium in the serum and there is reported an increase of potassium in the urinary excretion; the magnesium concentration in the serum appears to fluctuate in either direction from the normal, and the same is reported of its excretion (4, 7).

I am indebted to Miss Priscilla Williams for assistance in the analytical work.

CONCLUSIONS

The total base and protein components of the serum have been studied before and after the crisis in patients suffering with lobar pneumonia.

The sodium concentration in the serum was decreased in all of the cases studied before and for a considerable period after the crisis. The decreased concentration of sodium was approximately equal to the decreased concentration of total base.

The potassium concentration in the serum was increased in over one half of the determinations made before the crisis. This increase tended to persist after the crisis.

The calcium values were generally decreased during the febrile period.

Magnesium values were scattered about the normal range throughout the period of infection.

The albumin concentration in the serum was diminished not only during the period of active infection but also during convalescence. The globulin fraction was usually increased, so that the total protein tended to remain within the normal or lower normal limits.

Base bound by protein was usually decreased during the febrile period.

From studies of fourteen gastric analyses on four patients suffering with lobar pneumonia it was noted that:

1. The gastric acidity tended to be lowered until after the crisis.
2. When lowered it was generally increased by histamine stimulation.
3. There was no apparent correlation of either total base or chloride of the serum with the gastric acidity.

PROTOCOLS

Case C1 (Number 14743). Colored, male, age 20, janitor. The patient was admitted with consolidation of the right lower lobe. He was dyspneic, cyanotic, and jaundiced. Sputum yielded a Type I pneumococcus. The highest leukocyte count occurred just before the crisis, and was 40,000. Blood Wassermann was positive. The patient gave a history of having had lobar pneumonia confined to the right lower lobe two years previously which was followed by an empyema. Convalescence was uneventful.

Case C2 (Number 14860). Colored, male, age 23, laborer. The patient was admitted to the hospital with a lobar pneumonia confined to the left lower lobe. Respirations were quite labored and restricted over the left lower chest. A pericardial friction was audible over the precordium. The patient's temperature fell by crisis on the eighth day of the disease. However, there were daily rises in temperature to 100° until after the eighteenth day of the disease. Leukocyte count varied from 9000 to 20,000. Sputum yielded a Type I pneumococcus. Blood Wassermann was positive.

Case C3 (Number 15328). Irish, male, age 57, sailor. The patient entered the hospital with a history of exposure on shipboard followed by severe pain in the right chest of 5 days' duration. Physical examination revealed a consolidation of the right lower lobe. Temperature fell by crisis on the eighth day of the disease. Highest leukocyte count was 24,000 with 80 per cent polymorphonuclears. Convalescence was uneventful.

Case C4 (Number 15085). Colored, male, age 30, cook. The patient had an upper right lobar pneumonia with a crisis on the fifth day of the disease. Group

IV pneumococci were isolated in the sputum. Leukocyte count on admission was 23,000 with 86 per cent polymorphonuclears. Convalescence was uneventful.

Case C5 (Number 15210). Hebrew, male, age 18, clerk. The patient was admitted on the sixth day of the disease with signs of consolidation of the right lower lobe. Temperature became normal by lysis four days after admission. X-ray evidence was suggestive of active pulmonary tuberculosis but the clinical course proved it to be otherwise. Sputum examination did not reveal the presence of any tubercle bacilli. Leukocyte counts varied from 17,500 to 10,000.

Case C6 (Number 14965). Colored, male, age 24, laborer. The onset of the disease began with a peritonsillar abscess. Physical examination pointed to consolidation of the right lower lobe. Lung abscess was considered but later excluded. Postural drainage proved unsuccessful. Sputum yielded Group IV pneumococci and Friedlander's bacilli. Convalescence was uneventful.

Case C7 (Number 15447). Colored, male, age 34, laborer. The patient entered the hospital with a typical lobar pneumonia confined to the right lower lobe. Crisis occurred on the fifth day of the disease. Leukocyte count on admission was 16,700. The sputum yielded Group IV pneumococci. Blood Wassermann was positive. Convalescence was uneventful.

Case C8 (Number 15499). Colored, male, age 30. The patient was first studied on the seventh day of a left lower lobar pneumonia. Pleural frictions were audible in the left axilla. The patient did not become afebrile until after the twenty-fourth day of the disease. Sputum yielded a Type III pneumococcus. Leukocyte count on admission was 30,000 with 80 per cent polymorphonuclears. Convalescence was protracted but uncomplicated.

Case C9 (Number 15564). Italian, male, age 34, laborer. The patient entered the hospital with a major complaint of right abdominal pain. Physical examination revealed a right lower lobar pneumonia and evidences of a frontal sinus infection. Leukocytes ranged from 29,000 to 12,000. Wassermann was positive. Sputum contained Group IV pneumococci. Patient did not become afebrile until 12 days after admission.

Case C10 (Number 15645). White, male, age 63, machinist. On admission patient was apneic, jaundiced, and cyanotic. Physical signs gave evidence of a consolidation of the right lower lobe. Sputum yielded Group IV pneumococci and Friedlander's bacilli. The patient died two days after admission.

Case C11, (Number 15663). Hebrew, female, age 15, student. The patient on admission was prostated, cyanotic, and had consolidation of the right lung. She developed pulmonary edema in twenty-four hours after admission and died. Leukocyte count on admission was 5,000.

Case C12, (Number 15862). Colored, male, age 28, laborer. Patient was admitted to the hospital in a critical condition, apneic, perspiring profusely, and comatose. Percussion note over right chest was impaired, over which area rhonchi were audible. Leukocytes ranged from 18,000 to 19,000. Sputum contained Group IV pneumococci. Wassermann was strongly positive. The patient died on what was regarded as the ninth day of his disease.

Case C13, (Number 9352). Colored, male, age 23, laborer. The patient entered on the fourth day of the disease and showed evidence of consolidation of the right lower lobe. The crisis occurred on the twelfth day of the disease. Highest leukocyte count occurred at the time of crisis and was 27,000. Sputum yielded Group IV pneumococci. Convalescence was uneventful.

Case C14 (Number 9393). White, male, age 30, laborer. The study was begun on the sixth day of the disease. The patient had a right upper and lower lobar pneumonia. The urine contained a cloud of albumin and granular casts during the febrile period. Crisis occurred on the ninth day of the disease. A Type II pneumococcus was recovered from sputum. Convalescence was protracted for four weeks.

Case C15, (Number 9750). White, male, age 31, chauffeur. The patient was brought into the hospital in a delirious state. He had been sick at home complaining of severe pain in left chest, coughing, hemoptysis and high fever for six days previous to admission. Physical examination revealed consolidation of left lower lobe and congestion of right lower lobe. On the seventh day after admission, temperature and pulse fell by crisis and the patient made an uneventful recovery. Sputum yielded both Group IV pneumococci and influenza bacilli. Leukocytes ranged from 9,600 to 18,000.

Case C16, (Number 10025). Colored, male, age 25, laborer. The patient entered the hospital with evidences of incomplete consolidation in both lower lobes and complete consolidation in the right upper lobe. Crisis occurred on the seventh day of the disease. No pneumococci were isolated from the sputum. Convalescence was uneventful. Wassermann and Kahn reactions were strongly positive.

BIBLIOGRAPHY

1. Sunderman, F. William, Austin, J. Harold, and Camac, J. G., J. Clin. Invest., 1926, iii, 37. Studies in Serum Electrolytes. I. Concentration of Electrolytes and Non-electrolytes in the Serum During Lobar Pneumonia.

2. Sunderman, F. William, J. Clin. Invest., 1929, vii, 313. Studies of Serum Electrolytes. IV. The Chloride and Nitrogen Balances, and Weight Changes in Pneumonia.
3. Sunderman, F. William, and Austin, J. Harold, Am. J. Med. Sci., 1930, clxxix, 167. Studies of Serum Electrolytes. VI. Water Metabolism in Pneumonia.
4. Peabody, Francis W., J. Exp. Med., 1913, xvii, 71. Studies of the Inorganic Metabolism in Pneumonia with Especial Reference to Calcium and Magnesium.
5. Gerstenberger, H. J., Burhans, C. W., Smith, D. N., and Wetzel, N. C., Am. J. Dis. Child., 1923, xxvi, 329. The Blood Serum Content of Inorganic Phosphorus and Calcium in Pneumonia.
6. Jansen, W. H., Deutsch. Arch. f. klin. Med., 1924, cxliv, 14. Kalkstudien am Menschen. III. Der Kalkgehalt des menschlichen Blutes unter pathologischen Verhältnissen.
7. Garratt, G. C., Medico-Chirurgical Trans., 1904, lxxxvii, 163. Observations on Metabolism in the Febrile State in Man.
8. Austin, J. Harold, and Sunderman, F. William, J. Clin. Invest., 1929, vii, 333. Studies of Serum Electrolytes. V. Urinary Electrolyte Excretion in Pneumonia.
9. Binger, C. A. L., Christie, R. V., Davis, J. S., Jr., and Hiller, A., J. Exp. Med., 1929, xlix, 603. Blood Chlorides in Conditions Associated with Pneumonia.
10. Geill, Torben, Klin. Wchnschr., 1927, vi, 221. Über den Gehalt an albumin und globulin im Blutserum unter normalen und pathologischen Verhältnissen.
11. Limbeck, R. v., and Pick, F., Prag. Med. Wchnschr., 1893, xviii, 165. Ueber die quantitativen Verhältnisse der Eiweisskörper im Blutserum von Kranken.
12. Loeper, M., Ravier, J. de Sèze and Lebert, Mlle., Compt. rend. Soc. de Biol., 1929, ci, 423. La Globulinémie a la Période Critique de la Pneumonie.
13. Horvath, A. A., and Little, R. B., J. Clin. Invest., 1928, v, 541. Studies in Blood Composition of Animals under Pathological Conditions. I. Bronchopneumonia in Cows.
14. Brems, A., Acta Med. Skandinav., 1927, lxvi, 207. Untersuchungen über das Verhältnis zwischen dem Kalium- und Calcium-Gehalt des Blutserums und der probatorischen Adrenalinreaktion.
15. Barber, H. H., and Kolthoff, I. M., J. Am. Chem. Soc., 1928, l, 1625. A Specific Reagent for the Rapid Gravimetric Determination of Sodium.
16. Shohl, A. T., and Bennett, H. B., J. Biol. Chem., 1928, lxxviii, 643. A Micro Method for the Determination of Potassium as Iodoplatinate.
17. Clark, E. P., and Collip, J. B., J. Biol. Chem., 1925, lxiii, 461. A Study of the Tisdall Method for the Determination of Blood Serum Calcium with a Suggested Modification.
18. Briggs, A. P., J. Biol. Chem., 1924, lix, 255. Some Applications of the Colorimetric Phosphate Method.

19. Fiske, C. H., and Subbarow, Y., J. Biol. Chem., 1925, lxvi, 375. The Colorimetric Determination of Phosphorus.
20. Stadie, W. C., and Ross, E. C., J. Biol. Chem., 1925, lxv, 735. A Micro Method for the Determination of Base in Blood and Serum and Other Biological Materials.
21. Howe, P. E., J. Biol. Chem., 1921, xlix, 109. The Determination of Proteins in Blood—A Micro Method.
22. Van Slyke, D. D., Hastings, A. B., Hiller, A., and Sendroy, J., J. Biol. Chem., 1928, lxxix, 769. Studies of Gas and Electrolyte Equilibria in Blood. XIV. The Amounts of Alkali Bound by Serum Albumin and Globulin.
23. Wilson, D. W., and Ball, E. G., J. Biol. Chem., 1928, lxxix, 221. A Study of the Estimation of Chloride in Blood and Serum.
24. Van Slyke, D. D., and Neill, J. M., J. Biol. Chem., 1924, lxi, 523. The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement. I.
25. Csapó, J., and Faubl, J., Biochem. Ztschr., 1924, cl, 509. Calciumgehalt der Serumeiweissfraktionen.
26. Stary, Z., and Winternitz, R., Ztschr. f. Physiol. Chem., 1929, clxxxii, 107. Über das physikalisch-chemische Verhalten des Magnesiums im Serum.
27. Bloomfield, A. L., and Keefer, C. S., Arch. Int. Med., 1926, xxxvii, 819. A Method for the Continuous Quantitatve Estimation of Gastric Secretion and Discharge in Man.
28. Meyer, Jacob, Cohen, S. J., and Carlson, A. J., Arch. Int. Med., 1918, xxi, 354. Contribution to the Physiology of the Stomach. Gastric Secretion during Fever.
29. Morgulis, S., Am. J. Physiol., 1928, lxxxiv, 350. Chemical Changes in the Blood During Fasting and Subsequent Refeeding. II. Inorganic Components.
30. Gamble, J. L., Ross, G. S., and Tisdall, F. F., J. Biol. Chem., 1923, lvii, 633. The Metabolism of Fixed Base During Fasting.
31. Greene, Carl H., and Rowntree, Leonard G., Am. J. Physiol., 1927, lxxx, 209. The Effect of the Experimental Administration of Excessive Amounts of Water. I. On the Volume and Concentration of the Blood.