CXXIV. THE CHLORIDES AND INORGANIC CONSTITUENTS OF THE SERUM AND CEREBROSPINAL FLUID IN NEPHRITIS AND ACIDOSIS.

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IN view of the constant relationship of the chlorides of the cerebrospinal fluid to the chlorides of the blood-serum in normal conditions [Hamilton, 1925] and in meningitis [Linder and Carmichael, 1928], it appeared to us of interest to investigate the conditions which obtain in nephritis and in ammonium chloride acidosis. The few observations which we have found in the papers of Hamilton and of Pincus and Kramer [1923] have not revealed any striking changes.

It has been reported [Greenfield and Carmichael, 1925] that in uraemia the cerebrospinal fluid chloride may rise from the normal level of 720–745 mg./100 cc. to 900 or even 1000 mg./100 cc. We have found no record of serum analyses in these cases, but, if we assume the normal relationship to hold, the serum-chloride corresponding to these figures would be 745 and 830 mg. per 100 cc. of serum (127 and 142 *mM*). That this is the case with any but the lesser increases seems highly improbable, for Bulger, Peters, Eisenman and Lee [1926] in 77 cases of nephritis found 5 with a serum-chloride exceeding 100 *mM* and none exceeding 128 *mM*, and Atchley and Benedict [1930] found that a decrease in serum-chlorides and total serum-electrolytes was the rule in uraemic acidosis. No patient presenting such gross increase in cerebrospinal fluid chloride has been available for us to study, but the suggestion that the usual relationship of cerebrospinal to serum-chlorides is abrogated was supported by one of our observations.

EXPERIMENTAL.

Cerebrospinal fluid and arterial blood-serum were obtained and investigated by the methods described in our earlier paper [1928] with the exceptions that the inorganic phosphorus was determined by the method of Fiske and Subbarow [1925], and that the water content of the serum was calculated from a serum-protein determination by the formula, water = $(990 - 0.8 \times \text{protein})$ g. per litre [Van Slyke, Wu and McLean, 1923]. As before the concentration of the inorganic constituents was recorded in *mM* concentration in serum-water and in cerebrospinal fluid.

Table I.

Case no.	Diagnosis	Blood urea (mg./100 cc.)	Blood pressure (mm. Hg)	Chloride		Bicarbonate		Total base		Inorganic phosphorus		Protein		Other acids		Remarks							
				Serum-water		Serum-water		Serum-water		Serum-water		Serum		Serum- water									
				mM	CSF	mM	CSF	mM	CSF	mM	CSF	mM	CSF	mM	CSF		mM	CSF					
I	Hydraemic nephritis	116	125/60	119	129	Cl _{ser} /Cl _{csf}	mM	BHCO _{3ser} /BHCO _{3csf}	mM	B _{ser} /B _{csf}	mM	mM	g./100 cc.	mM	mM	Serum CSF							
II	Azotaemic nephritis	95	265/160	98	116	0.85	0.85	33.5	28.65	1.17	170	161	0.95	1.8	0.7	8.1	0.02	17	15	7.52	7.37	Alkali therapy	
III	Azotaemic nephritis, uraemia	200	180/120	118	130	0.91	0.91	12.5	17.8	0.70	164	152	0.93	2.1	0.3	7.9	0.03	13	4	7.23			
IV	Azotaemic nephritis, uraemia	380	240/120	98	127	0.77	0.77	13.0	13.2	0.98	164	133		4.7	5	7.0	0.09	26		7.26			
Mean normal				111	124	0.89	0.89	25	21	1.19	164	156	0.95	1.2	0.6	—	—	—	—	—	—	—	Hamilton's series

Table II.

Exp.	Chloride		Bicarbonate		Total base		Inorganic phosphorus		Protein		Other acids		pH		Remarks		
	Serum-water	CSF	Serum-water	CSF	Serum-water	CSF	Serum-water	CSF	Serum	CSF	Serum-water	CSF	Serum	CSF			
mM	mM	mM	mM	mM	mM	mM	mM	mM	mM	mM	mM	mM	mM				
I a	105	122	32	27.6	1.16	157	154	1.5	0.55	6	0.09	3	3	7.45	7.44	Before NH ₄ Cl	
b	117	127	0.92	20.1	0.86	154	158	1.03	1.55	0.6		- 1	7	7.35	7.38	After 2 days on 12 g./day	
c	111	127	0.88	20.15	0.91	155	154	0.99	1.18	0.47	6.5	1	4.5	7.41	7.40	After 4 days on 12 g./day	
II a	107	120	0.89	30.5	26.7	1.14	160	150	0.92	1.18	0.48	7	0.05	2	2	7.52	Before NH ₄ Cl
b	114	123.5	0.92	22.7	22.8	1.00	161	151	0.94	0.95	0.47	9	0.04	3	5	7.43	After 2 days on 12 g./day

Nephritis.

Table I presents the results obtained in four cases of nephritis. The mean of Hamilton's series is given as a guide to the normal.

Chloride. In one patient, Case II, the cerebrospinal fluid chloride was less than normal. The serum-chloride was also low and so the ratio of Cl_{sw} to Cl_{csf} was the same as in the normal series. The bicarbonate was rather high, and both of these abnormalities were attributed to the fact that until the preceding day the patient had been taking large doses of alkali.

In the remaining patients the cerebrospinal fluid chloride was just above the normal range. In two, Cases I and III, there was a proportionate increase in the serum-water chloride, but in the third, Case IV, the cerebrospinal fluid chloride was high whereas the serum-water chloride was low, and the ratio $\text{Cl}_{\text{sw}}/\text{Cl}_{\text{csf}}$ fell to the very unusual figure of 0.77. Such a low ratio appears to be exceptional. Among Hamilton's observations there were two as low as 0.83, one from a case of cerebral tumour and the other from a case of uraemia. In the latter the cerebrospinal fluid chloride was high, 142 *mM* (830 mg./100 cc.); the serum-bicarbonate was 15 *mM*, so there was a moderately severe acidosis. In our own case there was advanced acidosis, the serum-bicarbonate being 12.1 *mM*, the p_{H} 7.26 and the inorganic phosphorus 4.4 *mM* (13.6 mg./100 cc.).

Bicarbonate. The serum-bicarbonate was very low in Cases III and IV, and was below normal in Case I; in the remaining patient it was high, probably as a result of alkali therapy.

Chart showing relation of serum-water bicarbonate to cerebrospinal fluid bicarbonate. The numbers correspond to the case numbers. The points joined by thin lines are from the same case and the arrows indicate the order in which the points are to be read. Two meningitis cases with very high bicarbonate are omitted.

Hamilton found that the serum-water bicarbonate (X) showed a relationship to the cerebrospinal fluid bicarbonate (Y), which was expressed best for his series by the equation $Y = 9.7 + 0.46 X$, X and Y being measured in *mM*. We have plotted the points for our observations in meningitis [1928], nephritis and ammonium chloride acidosis, and found that they tended to lie along a line parallel to but a little higher than Hamilton's; our line corresponded

to the equation $Y = 11.8 + 0.49 X$. Three points out of 14 lay far away from this line; two were from meningitic patients, one having a very high and the other a very low serum-bicarbonate, and the third was Case IV of this paper, who had severe acidosis and the abnormal chloride ratio commented upon above.

It is noteworthy that in Case III a still greater degree of acidosis was present, but both the cerebrospinal fluid chloride and bicarbonate were at the levels expected from the normal chloride ratio and the bicarbonate equation.

Total Base. There was no abnormality of total base in these cases, but in Case IV the determination in the cerebrospinal fluid was obviously erroneous and unfortunately could not be repeated.

Ammonium chloride acidosis.

Table II gives the results of producing an acidosis with ammonium chloride in two patients with quiescent tabes. Twelve grams of ammonium chloride were given daily. Cerebrospinal fluid and arterial blood were taken before and after two and four days' treatment. The results were a reduction of serum-bicarbonate by a third, a moderate fall in p_H , and a rise in serum-chloride and serum-protein. The cerebrospinal fluid chloride followed the serum-chloride with possibly a slight delay; the ratio Cl_{sw}/Cl_{csf} became slightly greater, but the normal balance was maintained. The bicarbonate figures followed the line discussed above very closely. The total base ratio was not disturbed.

SUMMARY AND CONCLUSIONS.

It is apparent from these figures that in moderate disturbances of acid-base balance due to nephritis or to ammonium chloride therapy the normal relationships of the cerebrospinal fluid and arterial blood-serum remain intact.

In severe nephritis with great reduction in serum-bicarbonate and p_H and gross nitrogen retention a breakdown of these relationships may sometimes occur as in Case IV and in Hamilton's case McG-n, in which the cerebrospinal fluid chloride was considerably higher than was compatible with the serum-chloride. In Case IV, too, the cerebrospinal fluid bicarbonate was considerably less than was to be expected from the serum-bicarbonate, and the inorganic phosphorus in the cerebrospinal fluid was vastly increased and practically equal to that in the serum. We are of the opinion that these observations give the key to the situation in those cases of uraemia in which very high cerebrospinal fluid chlorides have been reported and explain why such high cerebrospinal fluid chlorides are of evil prognosis.

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