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Effect of Adrenal Insufficiency on Distribution of Chlorides Between  
Plasma and Erythrocytes.

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Lucas<sup>1</sup> was probably the first to observe a decrease of the plasma chloride concentration in the suprarenalectomized dog. Since then, numerous other authors confirmed his findings in various species of experimental animals.<sup>2-12</sup> Although several investigators obtained negative or contradictory results,<sup>13-16</sup> it is now a generally accepted fact that adrenal insufficiency results in a decrease in blood chlorides.

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<sup>14</sup> Urechia, C. L., *Gr. Benetato et Retezeanu: Bull. Acad. Méd. Roum.*, 1936, **1**, 141.

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<sup>16</sup> Simpson, S. Levy, Dennison, M., and Korenchevsky, V., *J. Path.*, 1934, **39**, 569.

In the course of our previous studies on the effect of various stimuli on blood chlorides,<sup>17</sup> we found that the red cell chloride concentration is usually a more sensitive test of beginning hypochloremia than the whole blood or plasma chloride concentration. Since most of the above mentioned investigators used whole blood, plasma or serum for their determinations, it appeared of interest, therefore, to establish whether this would also be true in the case of hypochloremia induced by adrenalectomy. For this purpose, we removed the adrenals from 10 male „hooded“ rats weighing 160—190 g. They received food and water *ad libitum* during the first 24 hours after the operation. Then food was withdrawn for 24 hours so as to eliminate the possible effect of varying food intake. At the end of this fasting period, these and 24 control animals of the same strain; weight and sex and fasted for the same length of time were killed. Their blood was collected, clotting being prevented by sodium oxalate. The

TABLE I.

Chloride Concentrations Are Expressed in mg of Chloride per 100 cc of Material.

No.	Hematocrit	Whole Blood Chlorides	Plasma Chlorides	Red Cell Chlorides	Cl <sub>c</sub> :Cl <sub>p</sub>
Normal Animals.					
1	40	298	369	189	.51
2	41	291	362	188	.52
3	43	277	355	175	.50
4	40.5	284	355	180	.50
5	42	284	362	174	.50
6	42	291	362	184	.50
7	41.5	284	362	174	.49
8	42.5	277	355	172	.49
9	42	284	362	174	.50
10	41	291	369	192	.52
11	42.5	277	348	181	.52
12	42	291	376	183	.49
13	42	284	369	172	.48
14	41.5	291	362	190	.52
15	42	298	376	190	.50
16	43	284	362	182	.50

<sup>17</sup> Karady, S., Selye, H., and Browne, J. S. L., *Proc. Am. Physiol. Soc.*, Toronto, April, 1939.

No.	Hematocrit	Whole Blood Chlorides	Plasma Chlorides	Red Cell Chlorides	Cl <sub>C</sub> :Cl <sub>P</sub>
17	42	291	369	183	.50
18	43	284	369	190	.52
19	41	298	376	185	.49
20	43	284	362	182	.50
21	43	277	355	175	.49
22	42.5	291	369	186	.50
23	41.5	291	376	179	.48
24	42	284	362	176	.49
Avg	42	287	364	182	.5
Adrenalectomized Animals.					
1	43	263	348	151	.44
2	42	263	355	136	.38
3	44	242	340	139	.41
4	44	248	355	114	.32
5	42	254	340	136	.40
6	44	254	362	118	.33
7	45	248	362	111	.31
8	44	254	355	125	.35
9	45	270	369	149	.42
10	43	263	355	142	.40
Avg	43.6	256	354	134	.38

chlorides were then directly determined in the plasma and the whole blood while red cell chlorides were calculated from these values and from the hematocrit reading. This indirect method was used because it proved difficult to measure pure red cells accurately and because direct determinations showed that there is no significant difference between the calculated and the directly determined values. The determinations were performed with the Rusznyak<sup>18</sup> micro-method which in our experience gives results which check well with those obtained by the Van Slyke method. Table I. summarizes our results.

As the table indicates, there is a relatively slight decrease in plasma chlorides, a somewhat more marked decrease in whole blood chlorides and a very pronounced decrease

<sup>18</sup> Rusznyak, S., *Biochem. Z.*, 1920, **114**, 23.

in the red cell chloride concentration. As a result of this, the index  $Cl_C:Cl_{PI}$  (that is, the chloride concentration of the cells divided by the chloride concentration of the plasma) falls considerably. In 7 of 10 animals in the adrenalectomized group the plasma chloride concentration was within the limits of normal variation while in No. 11 among the normals, for instance, the plasma chloride concentration was below the average of the adrenalectomized group. This may explain why many of the authors who based their conclusions merely on plasma chloride determinations obtained inconclusive results. It will be seen that the red cell chloride concentration in all adrenalectomized animals is considerably lower than it is even in the lowest of the normal figures. Similarly the  $Cl_C:Cl_{PI}$  index in all the adrenalectomized animals is lower than the lowest value in the normal group.

*Conclusions.* Experiments on adrenalectomized rats indicate that the red cell chloride concentration decreases much more markedly during adrenal insufficiency than does the plasma or whole blood chloride content. In cases of slight hypochloremia caused by moderate adrenal insufficiency, the direct or indirect determination of the red cell chloride concentration or of the index  $Cl_C:Cl_{PI}$  is a more sensitive index of a change in chloride metabolism than the more commonly determined plasma or whole blood chloride concentration.