On the Swelling of Erythrocytes in Isotonic Solution of Various Cations in Cases of Several Internal Diseases

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When a pathological mechanism occurs in a human body, many remarkable abnormal phenomena, namely symptoms come into sight and at the same time some delicate changes can be seen directly or indirectly. Taking the phenomenon of swelling of erythrocytes under a certain condition, the problem has been investigated in cases of various diseases.

With regard to the swelling of tissue and substance Loeb¹⁾ and others²⁾⁻⁷⁾ have made fundamental investigations of the human tissue and especially the muscle, gelatine and some glue board. In our laboratory Sato,⁸⁾ Oyama and Sone,⁹⁾ Shimizu and Takahagi¹⁰⁾ have made experiments on the swelling of some tissues. The research on the swelling of erythrocytes which play the greatest role in keeping the vital activity of human body and reacting quickly upon the pathological mechanism, have been done by Koeppe¹¹⁾ and others.¹²⁾⁻¹⁵⁾ However these studies were only basic and theoretical and no investigation has been made directly on patient's blood. To this date, the true mechanism of swelling is still unclassified. Hofmeister²⁾ considered it as a nonchemical phenomenon between the swelling body and the medium: Loeb and others considered that the swelling in a body was due to a gelatinous compound of protein and water; Schwarz,¹⁷⁾ Spiro and Ostwald¹⁸⁾ and others have proved experimentally and theoretically that pH, salts, and the other conditions cause complicated effects to the gelatine compound to induce a complicated reaction; but, whatever be the case, the swelling is merely to be considered that the volume of the swelling body increases as the result of absorbing the surrounding water in itself. Needless to say, the swelling body in an organism is protein. It is a self-evident truth that a medium including protein absorbs water into it and is influenced by quantitative and qualitative change of that protein. Oyama and Sone⁹⁾ in our laboratory proved that there is a parallel relation between the degree of the swelling of tissue

and the colloid-osmotic pressure when the tissue protein is changed into a condition of sol, so therefore, as erythrocytes consists of a great deal of protein, it can be stated that the major cause for the swelling of erythrocyte is protein in the erythrocytes.

Nakazawa¹⁹⁾ has previously reported that protein and colloid-osmotic pressure of blood plasma show various changes in various diseases. Therefore I believe that protein in erythrocytes may disclose some changes in various grades in various diseases and that the swelling of erythrocytes under a certain condition will be able to show minute variations. As there are many complicated factors in a human body, the phenomenon of swelling may become very complicated; however, we can experiment on the swelling in vitro in constant condition very easily. It is my hope that this work will give some convenience to the diagnosis and judgment of prognosis of diseases, by undertaking the study on the swelling of erythrocytes in various diseases under the above mentioned condition.

EXPERIMENTAL

Method

As medium solution I used the isotonic chloride solutions of 4 kinds of cations: Na, K, Ca and Mg (0.9% NaCl, 1.14% KCl, 2.52% CaCl₂ and 2.34% MgCl₂). Most of the examines were the inpatients of Prof. Nakazawa's Medical Clinic. Blood samples were taken from patient's cubital vein free from congestion prior to the patient's breakfast time, and immediately after defibrination, centrifuged in an electric centrifuge (3000 R.P.M.) for 30 minutes, mixed thoroughly after removing the blood serum, a layer of leucocytes and a small amount of erythrocytes. 4 test-tubes each containing 2.5 cc. of above mentioned isotonic cation solutions were prepared and to which 0.5 cc. of erythrocytes was added respectively. A homogenous suspensive fluid of erythrocytes was thereby obtained by gently mixing the solutions. The test-tubes were then allowed to stand 30 minutes in an incubator at 37°C. The measuring of the swelling was undertaken immediately after removing the test-tubes from the incubator. In order to measure the swelling, I used a small graduated tube for precipitation which was especially made for this purpose: a glass-tube 100 mm. long, with a true inside diameter of 5 mm., graduation of 150 and 1.5 cc. volume.

Examination procedure was as follows: 1.5 cc. of the mixture of erythrocytes and cation solution was poured into each of the 4 tubes for precipitation, and centrifuged at 3,000 R.P.M. for 20 minutes. Then, noted the volume of swelling by reading the height of the layer of erythrocytes at the bottom of the tubes. As an aiding factor, the rest of mixture of erythrocytes and cation solutions were placed in Westergren's

tubes for blood sedimentation rate, and read the sedimentation rate every hour for 6 hours while being kept in a box whose temperature was constantly kept at 20°C. However, by Westergren's method, the results cannot be clearly observed because of the hemolysis which occurs in the course of observation, therefore Westergren's method is suitable for reference purposes only. For sake of convenience, the swelling in the Na solution is represented by Na-swelling and likewise: K-swelling represents the swelling in K-solution. Ca-swelling represents the swelling in Ca-solution. etc.

Results

1. Healthy persons

26 persons were selected for experiment—12 males and 14 females—from a group of healthy laboratory workers, laboratory assistants and nurses. These persons were examined and their swelling of erythrocytes was measured as shown in Tab. I.

The values of swelling by this method, under average conditions, were: 2.0–2.7 on Na-swelling, 2.0–2.6 on K-swelling, 2.0–2.5 on Mg-swelling and 1.4–2.0 on Ca-swelling. Ca-swelling showed the least visual change. It was difficult to read the values of the swelling of other solution by Table observations only. Statistical examination was made as 26-persons by use of various cations as indicated in Fig. 1: On comparing Na-swelling with K-swelling, no significant difference was found: the level of significance is 5%, because the mean of the difference of individual values (M) is $+0.042$ and the unbased estimate of population variance (U^2) is 0.052.

When comparing K-swelling with Mg-swelling, $M=+0.173$, and $U^2=0.045$, were obtained. In such a case the significant difference, though very small, existed and the fact was recognized that Mg-swelling is less than K-swelling. In the next instance, comparing Mg-swelling with C-swelling, $M=+0.519$ and $U^2=0.093$, were obtained and thereby showing a remarkable and a significant difference. The value of Ca-swelling was very small compared with that of Mg-swelling, i.e., the fact was established that Ca-swelling was the least of the 4 kinds of cations, and accordingly, the order of the value of swelling of erythrocytes in each of the cation solution was: $\text{Na}=\text{K}>\text{Mg}>\text{Ca}$.

According to the former study on the swelling of a piece of liver by Sato,⁸⁾ Oyama and Sone,⁹⁾ and Shimizu and Takahagi¹⁰⁾ in our laboratory, the order of the values of swelling in Na, K, Mg and Ca, for swelling of liver tissue was found to be as follows: $\text{K}>\text{Na}>\text{Ca}>\text{Mg}$. This order has a quite different appearance as compared with that of erythrocytes, and especially it showed a remarkable difference i.e., Ca-swelling was less than

TABLE I

Nr.	Age and gender	NaCl	KCl	MgCl ₂	CaCl ₂
1	26, ♂	2.5	2.5	2.1	2.0
2	30, ♂	2.5	2.35	2.0	2.0
3	31, ♂	2.3	2.3	2.3	1.8
4	41, ♂	2.35	2.8	2.75	2.0
5	18, ♂	2.3	2.25	2.15	1.7
6	20, ♂	2.4	2.35	2.1	1.05
7	14, ♂	2.4	2.3	2.5	1.2
8	20, ♂	2.0	2.05	2.15	1.7
9	19, ♂	2.4	2.4	2.3	1.4
10	42, ♂	2.6	2.1	2.4	1.9
11	32, ♂	2.4	2.5	2.3	1.7
12	60, ♂	1.8	2.0	2.1	1.6
13	22, ♀	2.7	2.4	2.5	1.9
14	21, ♀	2.4	2.35	2.0	2.0
15	21, ♀	2.5	2.4	2.25	1.4
16	20, ♀	2.5	2.4	2.5	2.0
17	53, ♀	2.8	2.5	2.8	2.3
18	30, ♀	2.7	2.0	2.35	1.7
19	22, ♀	2.8	2.6	2.4	2.1
20	20, ♀	2.5	2.4	2.15	1.7
21	18, ♀	2.15	2.4	2.0	1.6
22	19, ♀	2.3	2.5	1.75	1.7
23	19, ♀	2.5	2.45	2.1	1.9
24	27, ♀	2.6	2.6	2.6	2.0
25	23, ♀	2.4	2.5	2.1	1.6
26	25, ♀	2.4	2.5	2.3	1.8

Mg-swelling. It is recognized the fact that there is a peculiarity pertaining to the swelling of erythrocytes.

2. Tuberculous diseases

The advancement of tuberculous diseases and the erythrocyte sedimentation rate are closely related to each other as proved by numerous scholars, such as: Westergren²⁰⁾ and after him Benninghof²¹⁾ and others.²²⁾⁻²³⁾ These writers have reported that the cause of above fact is due to the increase of globulin and fibrinogen in blood. Ito, Seki and Nakazawa²⁴⁾ have proved that the colloid-osmotic pressure of the blood of phthisical patients is generally within the range of normal values among the light cases and decreases in serious cases. Referring to the reports on this problem and from our own observations it is concluded that some change must have occurred in its colloid-chemical state, that is, the quality

Fig. 1

TABLE II

Nr.	Age and gender		NaCl	KCl	MgCl ₂	CaCl ₂
1	20,	♂	2.1	2.4	2.25	1.9
2	16,	♂	2.5	2.5	2.4	2.15
3	26,	♂	2.3	2.4	2.1	1.8
4	28,	♂	2.4	2.4	2.35	1.8
5	22,	♂	2.3	2.5	2.35	2.1
6	24,	♂	2.35	2.5	2.3	1.7
7	21,	♂	2.3	2.5	2.25	2.0
8	59,	♀	2.2	2.3	2.3	1.7
9	26,	♀	2.3	2.35	2.15	1.7
10	20,	♀	2.3	2.4	2.35	2.1
11	19,	♀	2.35	2.6	2.4	1.8
12	24,	♀	2.55	2.6	2.4	1.8
13	18,	♀	2.4	2.5	2.55	1.8
14	19,	♀	2.5	2.6	2.3	1.7
15	32,	♀	2.4	2.45	2.25	1.8
16	28,	♀	2.4	2.5	2.3	1.75
17	31,	♀	2.6	2.75	2.25	1.7

of bloodprotein must have changed in cases of tuberculous diseases. With regard to the quantitative change of mineral matters in blood in cases of tuberculous diseases, Otto⁸⁶⁾ and others^{86), 40)} have made numerous re-

Fig. 2.

ports during their days. Some variations have been found in their reports, though scarcely no scholar has denoted any special important variations. Close observation of qualitative change of bloodprotein which is closely connected with swelling, discloses that there are some qualitative changes in the erythrocyte colloid, and therefore, I undertook the problem of tuberculous diseases and its relation to the swelling of tubercular patients erythrocytes.

Tubercular patient were divided into 3 groups; i.e. 1) slight cases, 2) serious cases of pulmonary tuberculosis, 3) tuberculous pleurisy, peritonitis and meningitis.

i) *Slight cases of pulmonary tuberculosis.* Observation on 17 slight cases of pulmonary tuberculosis resulted in data as stated in Tab. II. These patients appeared to have slight symptoms as clearly indicated by clinical diagnosis and X-ray examinations. The patient's swelling results were: Na-swelling 2.3–2.5; K-swelling 2.4–2.6; Mg-swelling 2.2–2.4 and Ca-swelling 1.7–2.0. At a glance, we can not recognize the great difference comparing with healthy persons on the volume and the order of the each swelling. Statistic figures as in Fig. 2, show that a slight difference can be detected. No significant difference exists between Na-swelling and K-swelling as in healthy persons, and there is no significant difference between K-swelling and Mg-swelling, because $M=+0.150$, $U^2=0.044$, as found when observing healthy persons. When the value of Mg-swelling

of slight pulmonary patients was compared with healthy persons statistically, minute significant differences were observed and also the fact that Mg-swelling at the beginning of pulmonary tuberculosis is greater than that of healthy person was demonstrated, and a significant difference between Mg-swelling and Ca-swelling was also noted. In other words, there is little change of Na-swelling, K-swelling and Ca-swelling: only the value of Mg-swelling becomes greater and it can be described that there 3 swellings (Mg, Na and K) generally stand on the same level.

$$\text{Na} = \text{K} = \text{Mg} > \text{Ca}.$$

ii) *Serious cases of pulmonary tuberculosis.* Observations were made on 23 patients possessing marked lung cavities and with No. 4 or more of Gaffky's scale, due to pulmonary tuberculosis on both side, whose body temperatures showed little or no variation due to their being in the hospital. (Tab. III and Fig. 3).

Observation showed that: Na-swelling was 2.1–2.5, K-swelling 2.2–2.6, Mg-swelling 1.9–2.5 and Ca-swelling 1.7–2.0, as shown in the Table.

TABLE III

Nr.	Age and gender		NaCl	KCl	MgCl ₂	CaCl ₂
1	21,	♂	2.4	2.6	1.9	1.8
2	28,	♂	2.4	2.3	2.1	1.9
3	33,	♂	2.1	2.2	1.95	2.0
4	70,	♂	2.35	2.5	2.3	2.1
5	27,	♂	2.3	2.35	2.1	2.0
6	27,	♂	2.2	2.4	2.1	1.9
7	38,	♂	2.3	2.25	2.2	1.8
8	19,	♂	2.1	2.4	2.2	1.9
9	29,	♂	2.25	2.4	2.45	2.0
10	32,	♂	2.1	2.3	2.2	1.9
11	27,	♀	2.1	2.8	2.1	1.8
12	22,	♀	2.1	2.25	2.1	2.1
13	22,	♀	2.3	2.4	2.4	1.9
14	27,	♀	2.2	2.3	2.2	2.0
15	24,	♀	2.5	2.4	2.3	1.7
16	23,	♀	2.4	2.3	2.15	1.65
17	32,	♀	2.1	2.2	2.2	1.9
18	50,	♀	2.2	2.3	2.4	1.9
19	32,	♀	2.1	2.2	2.3	1.8
20	25,	♀	2.55	2.6	2.4	1.8
21	18,	♀	2.4	2.5	2.55	1.8
22	18,	♀	2.5	2.6	2.3	1.7
23	21,	♀	2.35	2.5	2.25	1.7

Fig. 3.

Comparing these results, $M = -0.110$, $U^2 = 0.026$ were obtained between Na-swelling and K-swelling; this fact is quite opposed to cases in healthy persons who show $M = +0.042$. Next, comparing K-swelling with Mg-swelling, $M = +0.120$, $U^2 = 0.040$ were obtained. In comparison with that of healthy persons Mg-swelling value approximates that of K-swelling. That is, Mg-swelling shows a greater comparative value, Ca-swelling is always the least and shows scarcely any change. In other words, Na-swelling tends to be lesser, whereas Mg-swelling a little larger in the serious cases of pulmonary tuberculosis.

$$\text{Na} < \text{K} = \text{Mg} > \text{Ca}$$

iii) *Tuberculous pleurisy, peritonitis and meningitis.* Observations were made on 23 cases suffering from tubercular pleurisy, peritonitis and tuberculous meningitis. The results are shown in Tab. IV and Fig. 4. As shown in the table, Na-swelling was 2.1–2.5, K-swelling 2.3–2.6, Mg-swelling 1.8–2.4 and Ca-swelling 1.7–2.5. It was observed by comparing these results that $M = 0.100$, $U^2 = 0.010$ between Na-swelling and K-swelling. This fact is opposite to the cases of healthy persons from whom $M = +0.042$ was obtained, and the contraction of Na-swelling as well as in the serious cases of pulmonary tuberculosis was recognized. Comparing K-swelling with Mg-swelling, $M = +0.170$ and $U^2 = 0.044$ were obtained; Mg-swelling approximates K-swelling when compared with the cases of healthy persons—this fact shows that Mg-swelling is augmenting. Ca-

TABLE IV

Nr.	Age and gender	NaCl	KCl	MgCl ₂	CaCl ₂
1	17, ♂	2.3	3.3	1.75	2.5
2	19, ♂	2.1	2.2	2.3	1.55
3	35, ♂	2.15	2.3	2.1	1.6
4	22, ♂	2.1	2.3	2.2	1.4
5	22, ♀	2.5	2.4	2.5	2.0
6	21, ♀	2.1	2.3	2.4	2.5
7	23, ♀	2.5	2.6	1.9	2.6
8	26, ♀	2.55	2.6	2.4	1.8
9	22, ♀	2.6	2.8	2.55	1.8
10	21, ♀	2.35	2.5	2.1	2.4
11	21, ♀	2.2	2.25	2.5	1.9
12	23, ♀	2.1	2.3	2.2	1.8
13	29, ♀	2.1	2.3	2.0	1.4
14	59, ♀	2.2	2.3	2.3	1.7
15	18, ♀	2.2	2.15	1.8	1.4
16	32, ♀	2.4	2.6	2.4	1.7
17	41, ♀	2.2	2.3	1.7	1.55
18	23, ♀	2.4	2.3	1.8	1.65
19	23, ♀	2.25	2.45	2.3	2.1
20	19, ♀	2.35	2.6	2.35	1.95
21	27, ♀	2.1	2.3	2.05	1.8
22	25, ♀	2.55	2.6	2.4	1.8
23	19, ♀	2.6	2.6	2.6	1.9

swelling is always the least and shows scarcely any changes compared with that of healthy persons. As stated above, the order of the swelling is the same as during the serious cases of pulmonary tuberculosis. It is obvious that the lesser value of Na-swelling, the greater is the increasing of the value of Mg-swelling.

$$\text{Na} < \text{K} = \text{Mg} > \text{Ca}$$

The above mentioned measurements were made on such patients who had entered the critical stages of their illness, and therefore, in order to examine the recovery stage, 13 patients were selected for observation, those who are in the convalescent stage as based on the findings of clinical examination. The results are shown in Tab. V and Fig. 5, which show: Na-swelling 2.1-2.4; K-swelling 2.2-2.4; Mg-swelling 2.0-2.3; and Ca-swelling 1.7-1.9. Comparing these results, $M = -0.031$, $U^2 = 0.007$ were obtained between Na-swelling and K-swelling; the significant difference which have existed among the same group of patients at their critical stages disappears, and the value of Na-swelling approximates that of K-

Fig. 4.

TABLE V

Nr.	Age and gender		NaCl	KCl	MgCl ₂	CaCl ₂
1	17,	♂	2.35	2.3	2.2	2.1
2	41,	♂	2.2	2.25	1.9	1.9
3	19,	♂	2.1	2.1	2.0	1.7
4	30,	♂	2.1	2.2	2.25	1.9
5	28,	♂	2.2	2.25	2.2	1.85
6	37,	♀	2.4	2.3	2.3	2.0
7	21,	♀	2.3	2.2	1.95	1.9
8	29,	♀	2.2	2.25	2.2	1.8
9	19,	♀	2.25	2.3	2.0	1.9
10	18,	♀	2.2	2.3	2.1	1.7
11	27,	♀	2.3	2.35	2.25	1.9
12	32,	♀	2.3	2.35	2.3	1.7
13	27,	♀	2.5	2.45	2.3	1.7

swelling and the fact that the order of swelling approximates that of healthy persons was established. This fact will also be found when comparative examinations on the Na-swelling of healthy persons is made statistically. Comparing K-swelling with Mg-swelling, $M=+0.107$, $U^2=0.019$ which show less significant difference than in healthy persons. Between Mg-swelling and Ca-swelling there is a relationship that $M=+0.300$, $U^2=$

Fig. 5.

0.036, and significant difference is recognized in this case. Observations confirmed the fact that the order of erythrocytes swelling comes near to that of healthy person. That is: $\text{Na}=\text{K} > \text{Mg} > \text{Ca}$.

3. Cardiovascular diseases

The swelling measurements were made on 13 patients (11 patients with valvular diseases and 2 patients with aortic aneurysm) and the results are shown in Tab. IV and Fig. 6. Na-swelling is 2.2–2.4, K-swelling

TABLE VI

Nr.	Age and gender		NaCl	KCl	MgCl ₂	CaCl ₂
1	35,	♂	2.25	2.3	2.35	1.85
2	52,	♂	2.4	2.5	2.3	2.0
3	50,	♂	2.4	2.4	2.3	1.9
4	51,	♂	2.3	2.4	2.2	1.6
5	39,	♂	2.25	2.1	2.0	1.6
6	22,	♂	2.4	2.5	2.2	2.0
7	19,	♂	2.2	2.05	2.1	1.8
8	46,	♂	2.2	2.4	2.2	1.9
9	47,	♀	2.4	2.5	2.4	1.9
10	40,	♀	2.3	2.5	2.2	1.9
11	57,	♀	2.4	2.45	2.2	2.0
12	25,	♀	2.3	2.05	2.0	1.75
13	24,	♀	2.3	2.0	2.05	1.8

2.1-2.5, Mg-swelling 2.0-2.3 and Ca-swelling 1.6-2.0. By statistical investigation, it was found that $M=+0.030$, $U^2=0.037$ between Na-swelling and K-swelling and no significant difference existed. Next, $M=+0.090$, $U^2=0.033$ were obtained between K-swelling and Mg-swelling. Mg-swelling is rather small than K-swelling, and $M=+0.34$, $U^2=0.016$ were obtained between Mg-swelling and Ca-swelling. These values show that Ca-swelling too is very small. This relationship is similar to the case of healthy persons and the order is:

$$N=K>Mg>Ca.$$

There is no remarkable change in this cases. In addition, as shown in Table VII and Fig. 7, 6 cases of essential hypertension were examined, but they can not be objects of the accuracy of the statistical examination.

4. Nephritis

It is well known fact that in cases of nephritis there is always some

TABLE VII

Nr.	Age and gender	NaCl	KCl	MgCl ₂	CaCl ₂
1	57, ♂	2.4	2.5	2.65	1.9
2	53, ♂	2.3	2.4	2.2	1.8
3	56, ♂	2.4	2.6	2.5	1.9
4	62, ♂	2.2	2.4	2.4	2.0
5	56, ♀	2.45	2.6	2.5	1.9
6	46, ♀	2.5	2.6	2.4	2.0

Fig. 7.

variations of the colloid contained in the human tissue. Therefore, as it can be expected that there is some variation in the protein of erythrocyte, the swelling measurements were made on 9 nephritis patients, and as shown in Tab. VIII and Fig. 8, which show Na-swelling 2.2–2.4, K-swelling 2.3–2.4, Mg-swelling 2.2–2.4 and Ca-swelling 1.9–2.0. As sufficient patients for observation in this particular case were not available and also difficult to express statistically and theoretically, however, as shown in Fig. 8, no remarkable difference existed between Na-swelling and K-swelling, and it is also difficult to recognize the significant difference between

TABLE VIII

Nr.	Age and gender	NaCl	KCl	MgCl ₂	CaCl ₂
1	44, ♂	2.4	2.4	2.5	2.0
2	29, ♂	2.2	2.3	2.4	1.8
3	30, ♂	2.4	2.4	2.6	1.6
4	40, ♂	2.4	2.4	2.3	1.9
5	51, ♂	2.2	2.25	2.2	1.9
6	50, ♂	2.4	2.35	2.4	2.0
7	55, ♀	2.4	2.5	2.2	1.9
8	19, ♀	2.4	2.3	2.15	1.85
9	32, ♀	2.3	2.4	2.4	1.9

Fig. 8.

K-swelling and Mg-swelling. But by calculation, the difference between K-swelling and Mg-swelling, $M=+0.020$, $U^2=0.022$ were obtained and both were regarded as being nearly equal. A remarkable difference existed between Mg-swelling and Ca-swelling. Here, Ca-swelling is always the least, and the order of swelling is as follows:

$$Na=K=Mg>Ca.$$

In nephritis, Mg-swelling increases as compared with that of a healthy person.

5. Anemia

Observations were undertaken mainly on 9 patients with simple anemia, and as shown in Tab. IX and Fig. 9 which show: Na-swelling 2.0–2.4, K-swelling 2.0–2.5; Mg-swelling 2.0–2.6 and Ca-swelling 1.7–2.0. The value of Ca-swelling showed a slight decrease whereas Mg-swelling an increase. In this case, a statistical examination in the strict sense of the term can not be conducted, but, when experimented on patients, calculation was tried on the assumption that it is possible to do so. It was found that $M=-0.120$, $U^2=0.124$ between Na-swelling and K-swelling mean a minute contraction of Na-swelling. There is a relation that $M=-0.06$, $U^2=0.080$ between K-swelling and Mg-swelling, and any difference is not to be recognized. It is obvious that there is a comparative augment of Mg-swelling in such a case. Here, it is needless to say that Ca-swelling is the least, and therefore the order of swelling is

TABLE IX

Nr.	Age and gender		NaCl	KCl	MgCl ₂	CaCl ₂
1	48,	♂	2.2	2.5	2.4	1.8
2	58,	♂	2.4	2.35	2.5	1.7
3	20,	♂	2.1	2.0	2.1	1.7
4	19,	♂	1.9	2.65	1.5	2.0
5	51,	♀	2.8	2.6	2.6	2.1
6	31,	♀	2.4	2.05	2.6	1.7
7	16,	♀	2.2	2.35	2.4	2.0
8	16,	♀	2.4	2.3	1.9	2.0
9	28,	♀	2.4	2.9	2.6	2.0

Fig. 9.

supposed to be as follows:

$$\text{Na} < \text{K} = \text{Mg} > \text{Ca}.$$

The comparative augment of Mg-swelling and contraction of Na-swelling will be recognized in a case of noticeable anemia.

6. Gastric cancer

Observations were made on 19 patients with gastric cancer as shown in Tab. X and Fig. 10, and Na-swelling was 2.3–2.5, K-swelling 2.3–2.5, Mg-swelling 2.2–2.5 and Ca-swelling was 1.6–2.0; it seems that Mg-swelling augments comparatively. There is the relation which is: $M =$

TABLE X

Nr.	Age and gender		NaCl	KCl	MgCl ₂	CaCl ₂
1	52,	♂	2.5	2.4	2.5	1.6
2	49,	♂	2.7	2.5	2.1	1.8
3	56,	♂	2.65	2.3	2.2	1.9
4	36,	♂	2.3	2.4	2.15	1.95
5	56,	♂	2.3	2.5	2.3	2.0
6	53,	♂	2.4	2.45	2.25	1.7
7	62,	♂	2.5	2.55	1.95	2.3
8	25,	♂	2.3	2.25	2.2	1.8
9	62,	♂	2.4	2.6	2.5	2.0
10	29,	♂	2.3	2.35	2.4	1.9
11	55,	♂	2.3	2.3	2.5	2.1
12	66,	♂	2.6	2.5	2.4	1.9
13	63,	♂	2.5	2.3	2.4	2.0
14	38,	♂	2.45	2.4	2.35	1.9
15	62,	♂	2.3	2.5	2.4	2.0
16	49,	♂	2.5	2.5	2.4	1.6
17	46,	♀	2.7	2.6	2.2	1.8
18	66,	♀	2.1	2.4	2.2	2.0
19	49,	♀	2.4	2.2	2.3	2.0

Fig. 10.

+0.005, $U^2=0.028$ between Na-swelling and K-swelling. Here, of course, no significant difference exists, but U^2 and M are small, compared with a healthy person. This fact proves that the value of Na-swelling is nearly equal to that of K-swelling, i.e. a slight decrease of Na-swelling. Next, K-swelling was compared with Mg-swelling, and so the results were $M=+0.100$, $U^2=0.002$. And there was no significant difference between K-swelling and Mg-swelling; and therefore comparative augment of Mg-swelling was proved. There was a very remarkable difference between Mg-swelling and Ca-swelling, the latter was the least. Therefore the order of swelling can be stated as:

$$\text{Na} \approx \text{K} = \text{Mg} > \text{Ca}.$$

It was considered that there is a comparative augment of Mg-swelling and that comparative contraction of Na-swelling was probable in the cases of gastric cancer.

7. Bronchial asthma

Bronchial asthma is closely connected with autonomic nerves and blood colloid is influenced by the same nerve too. Now, observations were undertaken on 11 patients of bronchial asthma (Tab. XI and Fig. 11). It was found that Na-swelling was 2.2–2.6, K-swelling 2.3–2.7, Mg-swelling 2.3–2.6 and Ca-swelling 1.6–2.0. It is probable that no marked difference exists among Na-, K- and Mg-swellings, but statistically $M=-0.081$, $U^2=0.020$ were obtained between Na-swelling and K-swelling, therefore a slight difference can be recognized by mathematical calculations. Between K-swelling and Mg-swelling no significant difference can be observed because of $M=+0.150$ and $U^2=0.018$. Taking consideration of decrease of Mg-swelling with the significant difference in the case of healthy persons, comparative augment of Mg-swelling was demonstrated in this case.

TABLE XI

Nr.	Age and gender	NaCl	KCl	MgCl ₂	CaCl ₂
1	21, ♂	2.4	2.5	2.3	1.9
2	24, ♂	2.5	2.55	2.45	2.0
3	31, ♂	2.6	2.7	2.6	1.8
4	20, ♂	2.2	2.5	2.3	1.8
5	25, ♂	2.2	2.3	2.15	1.6
6	31, ♀	2.45	2.7	2.4	2.0
7	26, ♀	2.4	2.25	2.1	1.4
8	23, ♀	2.35	2.2	2.15	1.6
9	20, ♀	2.7	2.6	2.6	2.0
10	59, ♀	2.3	2.5	2.3	1.55
11	19, ♀	2.4	2.6	2.3	2.0

Fig. 11.

Ca-swelling is the least, therefore the order of swelling can be stated as:

$$\text{Na} \approx \text{K} = \text{Mg} > \text{Ca}.$$

It is supposed that there is an augment of Mg-swelling and a little comparative decrease of Na-swelling in bronchial asthma.

8. Beriberi

Observations were made on 13 patients with beriberi as shown in

TABLE XII

Nr.	Age and gender		NaCl	KCl	MgCl ₂	CaCl ₂
1	22,	♂	2.3	2.4	2.0	1.8
2	14,	♂	2.6	2.55	2.3	1.8
3	22,	♀	2.6	2.4	2.5	1.9
4	28,	♀	2.05	2.1	2.1	1.9
5	18,	♀	2.2	2.25	2.1	2.0
6	24,	♀	2.5	2.55	2.3	1.9
7	22,	♀	2.45	2.4	2.35	2.0
8	29,	♀	2.1	2.15	2.2	1.9
9	26,	♀	2.6	2.5	2.0	1.9
10	41,	♀	2.3	2.25	2.3	2.0
11	23,	♀	2.2	2.25	2.1	1.9
12	22,	♀	2.5	2.3	2.3	2.0
13	21,	♀	2.35	2.4	2.2	1.8

Fig. 12.

Tab. XII and Fig. 12. As generally accepted, the present-day beriberi-patients showed only slight cardiovascular and sensory disturbance with or without traces of edema. The results of this experiments is as follows: Na-swelling is 2.2–2.6, K-swelling 2.2–2.5, Mg-swelling 2.1–2.3 and Ca-swelling 1.8–2.0, and the order is the same as of healthy persons. Examination by calculation disclosed that $M = +0.023$, $U^2 = 0.015$ between Na-swelling and K-swelling. There is not so much significant difference as in the case of healthy persons, and where $M = +0.130$, $U^2 = 0.034$ were obtained between K-swelling and Mg-swelling. The value approximates that of healthy persons. Between Mg-swelling and Ca-swelling $M = +0.300$, $U^2 = 0.023$ were obtained which showed a remarkable difference. Therefore, at least, in the cases of beriberi as observed the variation on the order of swelling can not be recognized and therefore:

$$Na = K > Mg > Ca.$$

9. Croupous pneumonia and typhoid fever

Observations were made on 12 patients with acute croupous pneumonia and 9 patients with typhoid fever (Tab. XIII and Fig. 13, Tab. XIV and Fig. 14).

Firstly, pneumonia patients were observed and Na-swelling was 2.2–2.5, K-swelling 2.1–2.5, Mg-swelling 2.2–2.5 and Ca-swelling as 1.5–1.9. By comparing these results between Na-swelling and K-swelling, $M = -0.016$, $U^2 = 0.023$ were obtained and there was no significant difference,

TABLE XIII

Nr.	Age and gender	NaCl	KCl	MgCl ₂	CaCl ₂
1	20, ♂	2.2	2.1	2.2	1.5
2	41, ♂	2.15	2.05	2.15	1.3
3	21, ♂	2.3	2.25	2.5	1.8
4	23, ♂	2.3	2.4	2.2	1.6
5	10, ♂	2.8	2.6	3.2	2.1
6	49, ♂	2.3	2.35	2.2	1.9
7	37, ♂	2.3	2.4	2.2	1.7
8	56, ♀	2.4	2.8	2.3	2.0
9	37, ♀	2.5	2.4	2.6	1.9
10	38, ♀	2.1	2.0	2.0	1.4
11	41, ♀	2.4	2.3	2.2	1.5
12	37, ♀	2.5	2.5	2.9	1.9

Fig. 13.

but, in effect it is a probable case that there is a comparative decrease of Na-swelling compared with healthy person. Between K-swelling and Mg-swelling, $M = -0.03$, $U^2 = 0.088$, which showed no significant statistical difference. Comparative augment of Mg-swelling was found the same as healthy persons. There is a remarkable difference between Mg-swelling and Ca-swelling statistically, which is rather greater than in the case of

healthy person, and expressed as:

$$\text{Na} \approx \text{K} = \text{Mg} > \text{Ca}.$$

By this order, the comparative augment of Mg-swelling and that of Na-swelling also was clearly recognized as decreasing comparatively.

TABLE XIV

Nr.	Age and gender	NaCl	KCl	CaCl ₂	MgCl ₂
1	32, ♂	2.1	2.1	1.9	1.55
2	30, ♂	2.1	2.2	1.9	1.6
3	43, ♂	2.1	2.4	2.3	1.5
4	44, ♂	2.1	2.3	2.0	1.95
5	22, ♂	2.0	2.3	1.9	1.9
6	37, ♀	1.9	2.1	1.9	1.4
7	23, ♀	2.0	2.25	1.9	1.5
8	17, ♀	2.15	2.4	2.05	1.9
9	41, ♀	2.1	2.3	2.0	1.9

Fig. 14.

Typhoid fever patients showed the order of swelling as per Tab. XIV as also as follows: $\text{Na} < \text{K} > \text{Mg} > \text{Ca}$. Which shows that the decrease of Na-swelling is a considered fact.

SUMMARY

By summarizing the facts and data obtained from the fore-mentioned experiments:

1. The order of erythrocytes swelling in healthy person is

$$\text{Na}=\text{K}>\text{Mg}>\text{Ca}$$

and being different from Hofmeister's order, and is proper only to erythrocyte.

2. On tuberculous disease, it has been demonstrated that there is a comparative augment of Mg-swelling in the beginning of pulmonary tuberculosis, and a comparative contraction of Na-swelling and comparative augment of Mg-swelling in the serious cases of pulmonary tuberculosis. By these facts, if Na-swelling turns to normal, it may be considered that it indicates an improvement of the malady.

3. In tuberculous pleurisy, peritonitis and meningitis, the comparative contraction of Na-swelling and the comparative augment of Mg-swelling was recognized in the critical stage of the illness, but in the patients of tuberculous pleurisy and peritonitis who are on their way to recovery, this relationship turns to normal.

4. The order of swelling in cardiovascular disease is recognized as $\text{Na}=\text{K}>\text{Mg}>\text{Ca}$, which is the same as with healthy persons.

5. The order of swelling in nephritis is $\text{Na}=\text{K}=\text{Mg}>\text{Ca}$, or a comparative augment of Mg-swelling.

6. The order of swelling in anemia is $\text{Na}<\text{K}=\text{Mg}>\text{Ca}$, or a comparative augment of Mg-swelling and a possible minute contraction of Na-swelling.

7. The order of swelling in gastric cancer is $\text{Na}\approx\text{K}=\text{Mg}>\text{Ca}$, or a comparative augment of Mg-swelling, or it appears that there is a comparative contraction of Na-swelling.

8. The order of swelling in bronchial asthma is $\text{Na}\approx\text{K}=\text{Mg}>\text{Ca}$. There is also a comparative augment of Mg-swelling and, as a matter of fact, there is a minute decrease of Na-swelling.

9. The swelling in beriberi is the same in healthy persons.

10. The order of swelling in croupous pneumonia is $\text{Na}\approx\text{K}=\text{Mg}>\text{Ca}$. Besides there is a comparative augment of Mg-swelling, and possibly there is a comparative contraction of Na-swelling.

11. The order of swelling in typhoid fever is $\text{Na}<\text{K}>\text{Mg}>\text{Ca}$, and possibly there is a comparative contraction of Na-swelling.

To sum up the facts on the above mentioned data in a few words as possible, the swelling of erythrocytes in the case of Na, K, Mg and Ca—4 kinds of cation, have a peculiarity, i.e., having a different appearance against the swelling of tissue of liver or others. In the case of disease, the

order of swelling is varied, but the variations in the cases of K-swelling and Ca-swelling are very small: it is Mg-swelling that causes the main variation, and is Na-swelling is a secondary swelling to a Mg-swelling.

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