Estimation of Body Water and Salt Contents from Plasma Sodium, Protein Concentrations, and Hematocrit

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SUMMARY

New formulae for the estimation of change in water (ΔW) and salt (ΔNaCl) contents of the body from hematocrit, plasma Na, and protein concentrations were proposed based on a compartment model of body fluid regulation: $\Delta W = 0.4(\Delta V_i/V_{i0}) + 0.2(\Delta V_e/V_{e0})$ litres/Kg of body weight; $\Delta \text{NaCl} = 1.64[(\Delta V_e/V_{e0} + 1)/(\Delta V_i/V_{i0} + 1) - 1]$ Gms/Kg of body weight; where $\Delta V_i/V_{i0}$ and $\Delta V_e/V_{e0}$ are relative increment of intra and extracellular fluid volume. $\Delta V_i/V_{i0}$ is considered equal to $([\text{Na}]_0/[\text{Na}] - 1)$ under the condition of normal cell membrane, whereas $\Delta V_e/V_{e0}$ may be a nonlinear function of relative increment of plasma volume and hematocrit or sodium concentration. Thus a nomograph was presented to obtain ΔW and ΔNaCl simultaneously. This nomograph could predict ΔW and ΔNaCl with satisfactory accuracy in the experiments with the dogs to which fluid of various osmolarity was given intravenously. It was also confirmed in a case of mixed water depletion in which the clinical estimation agreed with that of the present method. The conventional formulae of calculation based on either pure dehydration or pure salt loss proved not to be applicable in the usual cases of body fluid disturbances.

Additional Indexing Words:

Body fluid disturbance Compartment model Water depletion
Salt depletion Dehydration

IT is a common practice in clinical medicine to intravenously infuse fluid of various electrolyte contents to patients suspected of water and/or salt deficiencies. However, precise determination of the deficit is not always achievable because of individual variations in clinical signs and symptoms, and in laboratory data with which the patients react to the body fluid dis-

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turbances. One of the methods is to utilize plasma sodium, protein concentrations or hematocrit for the estimation of body water and sodium contents. Familiar formulae for the estimation of change in water (ΔW) or sodium (ΔNa) contents are: $\Delta W = 0.6([Na]_0/[Na] - 1)BW$; $\Delta Na = 0.6([Na] - [Na]_0)BW$.¹⁾⁻⁴⁾ They are based on the assumption that body is lacking in either water or salt only. In the usual clinical cases of body fluid disturbances, where water and salt are lost simultaneously to varying degrees, the formulae are thus not applicable. Relative loss of blood plasma which can be estimated from hematocrit or plasma protein in the absence of abnormal production or destruction of red blood cells and plasma protein is often assumed to be parallel to relative loss of the whole extracellular fluid volume.²⁾⁻⁴⁾ This assumption may not be true in view of the complex dynamic relationship between intravascular and interstitial fluid volumes.

We are proposing in this paper a new nomographic method of estimating body water and sodium deficits (or excesses) simultaneously from plasma Na and protein or hematocrit based on the recent development of physiology of body fluid regulation. The proposed nomograph was tested in the animal experiments as well as in the analysis of a clinical case.

THEORETICAL ANALYSIS

1. The compartment model (Fig. 1):

The compartment model^{5),6)} assumes that the body fluid is divided into 3 compartments; intracellular fluid space (ICF), interstitial fluid space (ISF), and plasma space (PF). ISF and PF are combined and termed extracellular fluid space (ECF). Water contents of the compartments are designated as fluid volume and abbreviated by V_i , V_s , V_p , and V_e for ICF, ISF, PF, and ECF respectively. Ratios of the fluid volumes in litres to body weight in kilograms (BW) are 0.4 for ICF,

Fig. 1. Compartment model of body fluid space. For abbreviations see the text.

0.16 for ISF, and 0.04 for PF in average normal male adults.²⁾ V_i and V_e are balanced by quality of osmolarity in both sides of cell membranes. Main cations of the solutes which exert osmotic forces are sodium in ECF and potassium in ICF, so that sodium ion concentration in ECF ($[Na]$) is considered parallel to potassium ion concentration in ICF ($[Ki]$) in the steady state. Sodium content and potassium content of the body are usually approximated by $[Na] \cdot V_e$ and $[Ki] \cdot V_i$, for these ions are almost exclusively located in the respective spaces.

If there is any osmolarity shift as expressed by that of plasma sodium concentration from $[Na]_0$ to $[Na]$, the balance of intracellular and extracellular osmolarity will be accomplished by trans-cell membrane water shift under the condition of normal cell membranes (Osmosis). The following equation will hold:

$$\frac{V_i}{V_{i0}} = \frac{[Na]_0}{[Na]} \quad (1)$$

Partition of V_e between ISF and PF is determined by the opposing forces across the capillary membranes; hydrostatic capillary pressure (P_c)+interstitial oncotic pressure (π_s) vs. plasma oncotic pressure (π_p)+interstitial hydrostatic pressure (P_s). The difference between the forces may be called filtration pressure (P_f):

$$P_f = P_c + \pi_s - P_s - \pi_p \quad (2)$$

The net filtration through the capillary membranes (U_f) is driven by P_f at the rate of the whole body capillary filtration coefficient (CFC): $U_f = \text{CFC} \cdot P_f$. The capillary filtration (U_f) will be equal in turn to lymphatic flow (U_l) in the steady state.

The steady state relationship between V_s and V_p appears to be highly complex,⁷⁾ but we derived the following quadratic equation in terms of V_p from eq. (2) on the assumption that $P_c = 23.0(V_b/V_{b0}) - 6.0$ ⁸⁾ (V_b : blood volume), $\pi_p = 28(V_{p0}/V_p)$, $\pi_s = 5(V_{s0}/V_s)$,⁹⁾ $P_s = \max[-15, 4.90 - 7.42/(V_s/V_{s0} - 0.338)]$, and $P_f = U_l/\text{CFC} = \max[0, 20.9(1 - 5.31/(P_s + 11.7))]$,¹²⁾

$$23.0(V_p/V_{p0})^2(100 - H_{t0})/(100 - H_t) + [5/(V_s/V_{s0}) - P_s - P_f - 6.0](V_p/V_{p0}) - 28 = 0 \quad (3)$$

where suffix 0 means standard values and H_t is hematocrit. Pressures (mmHg) for the standard conditions are: $P_c = 17$, $\pi_s = 5$, $\pi_p = 28$, $P_s = -6.31$, $P_f = 0.31$.^{7), 11)} The detailed derivation of eq. (3) and methods of the numerical solution are given in Appendix.

Hematocrit (H_t) and plasma volume (V_p) are related by way of plasma sodium concentration ($[Na]$) as follows.

Definition of H_t will give for the 2 states

$$\frac{H_{t0}}{100} = \frac{V_{r0}}{V_{b0}} \quad (4)$$

$$\frac{H_t}{100} = \frac{V_r}{V_b} \quad (5)$$

where V_r 's are red blood cell volumes.

V_p/V_{p0} will be from eqs. (4) and (5)

$$\frac{V_p}{V_{p0}} = \frac{100/H_t - 1}{100/H_{t0} - 1} \cdot \frac{V_r}{V_{r0}} \quad (6)$$

If osmolarity changes from one state to another, the red blood cell volume will be changed by osmosis (ΔV_r),

$$\Delta V_r = V_r - V_{r0} \quad (7)$$

Suppose that the free water fractions of the red blood cell volume for both states are C_0 and C respectively, V_r will also be given by

$$\Delta V_r = C \cdot V_r - C_0 \cdot V_{r0} \quad (8)$$

If the total solute contents within the cells are unchanged, and ratio of ECF osmolarity of one state (0) to another is approximately represented by $[Na]_0/[Na]$, as in eq. (1),

$$\frac{[Na]_0}{[Na]} = \frac{C \cdot V_r}{C_0 \cdot V_{r0}} \quad (9)$$

Eliminating ΔV_r and C from eqs. (7)–(9),

$$\frac{V_r}{V_{r0}} = 1 + C_0 \left(\frac{[Na]_0}{[Na]} - 1 \right) \quad (10)$$

C_0 can be obtained from changes in Na and Ht of blood samples immersed in the saline solutions of various osmolarity. Mean $\pm$ SE of C_0 for 10 young healthy subjects were 0.52 ± 0.15 .¹⁰⁾

Plasma total protein concentration (T_p) can be used to estimate plasma volume, if intravascular protein content is held constant:

$$\frac{V_p}{V_{p0}} = \frac{T_{p0}}{T_p} \quad (11)$$

On the other hand, hematocrit alone can not predict change in plasma volume unless osmolarity is constant. Eqs. (6) and (10) will give

$$\frac{V_p}{V_{p0}} = \left[1 + C_0 \left(\frac{[Na]_0}{[Na]} - 1 \right) \right] \cdot \frac{100/H_t - 1}{100/H_{t0} - 1} \quad (12)$$

$(100 - H_{t0})/(100 - H_t)$ in eq. (3) is thus related to V_p/V_{p0} by

$$\frac{100 - H_{t0}}{100 - H_t} = 1 - \frac{H_{t0}}{100} \left\{ 1 - \frac{V_{p0}}{V_p} \left[1 + C_0 \left(\frac{[Na]_0}{[Na]} - 1 \right) \right] \right\} \quad (13)$$

This relationship is given by Nomograph 1 (Fig. 2).

Relative increment of ECF ($\Delta V_e/V_{e0}$) as a function of that of plasma ($\Delta V_p/V_{p0}$) was computed utilizing eqs. (3), (13) and the relationship

$$\frac{\Delta V_e}{V_{e0}} = 0.2 \frac{\Delta V_p}{V_{p0}} + 0.8 \frac{\Delta V_s}{V_{s0}} \quad (14)$$

and their equiosmolar relationships are depicted in Fig. 3. (For computation details, see Appendix.) This sigmoid curve will have the following physiological

Fig. 2. Nomograph 1 relating hematocrit, Na, and Vp (eq. (13)).

Fig. 3. The relationship between relative changes in plasma volume (V_p/V_{p0}) and extracellular volume (V_e/V_{e0}) under various iso-osmolar conditions; isotonic ($[Na]_o/[Na] = 1.0$), hypotonic ($[Na]_o/[Na] = 1.4$), and hyper-tonic ($[Na]_o/[Na] = 0.6$).

significance: When plasma volume is increased to a limited degree, interstitial fluid volume is relatively kept constant due to increase in lymphatic flow and non-linear characteristics of tissue compliance, which Guyton summarized as an 'edema protecting factor'.⁷⁾ If extracellular fluid volume is decreased, partition of fluid between the extracellular 2 compartments will be in favor of keeping plasma volume

relatively constant due to the same mechanism. We might call the latter a 'hypovolemic shock preventing factor'.

2. Body fluid disturbances:

Most basic concepts pertaining to the body fluid disturbances are excesses or deficits of water (ΔW) and/or salt (ΔNaCl) contents in the body. These states can be expressed by changes in V_e and V_i as follows (Fig. 4).

Changes in water content (l) per Kg of body weight will be given

$$\begin{aligned} \frac{\Delta W}{BW} &= \frac{\Delta V_i}{V_{i0}} \frac{V_{i0}}{BW} + \frac{\Delta V_e}{V_{e0}} \cdot \frac{V_{e0}}{BW} \\ &= 0.4 \frac{\Delta V_i}{V_{i0}} + 0.2 \frac{\Delta V_e}{V_{e0}} \end{aligned} \quad (15)$$

Fig. 4. Content of body water and salt defined by axes of extra and intracellular volume. a. Plane of relative changes in V_e and V_i . b. Excess and/or loss of water and salt content expressed on V_e - V_i plane. c. Clinically possible range of salt and water deficit. d. Pure water and salt loss or excess vs. pure ICF and ECF loss or excess.

and changes in salt content in Gms per Kg of body weight, assuming $[Na]_0=140$ mEq/L,

$$\begin{aligned}\frac{\Delta NaCl}{BW} &= 0.0585 \frac{([Na] \cdot V_e - [Na]_0 \cdot V_{e0})}{BW} \\ &= \frac{0.0585 [Na]_0 V_{e0}}{BW} \left(\frac{V_e}{V_{e0}} \cdot \frac{[Na]}{[Na]_0} - 1 \right) \\ &= 1.64 \left(\frac{V_e}{V_{e0}} \cdot \frac{[Na]}{[Na]_0} - 1 \right)\end{aligned}\quad (16)$$

or using eq. (1),

$$\begin{aligned}\frac{\Delta NaCl}{BW} &= 1.64 \left(\frac{V_e}{V_{e0}} \cdot \frac{V_{i0}}{V_i} - 1 \right) \\ &= 1.64 \left[\left(\frac{\Delta V_e}{V_{e0}} + 1 \right) / \left(\frac{\Delta V_i}{V_{i0}} + 1 \right) - 1 \right].\end{aligned}\quad (17)$$

The lines given by $\Delta W/BW=0$ in eq. (15) and $\Delta NaCl/BW=0$ in eq. (17) divide the $\Delta V_i/V_{i0} - \Delta V_e/V_{e0}$ plane into 4 quadrants of combinations of water excess or

Fig. 5. Nomograph 2 to obtain $\Delta W/BW$, V_e/V_{e0} , and $\Delta NaCl/BW$ from V_p/V_{p0} , $(100-Ht_0)/(100-Ht)$ and $[Na]_0/[Na]$. The dotted lines show an example: $V_p/V_{p0}=0.761$ enters at A and goes along surrounding curves to the crossing point C with the vertical line from B at which $(100-Ht_0)/(100-Ht)$ is given. C is then brought horizontally to V_e/V_{e0} bar and D ($=0.67$) is obtained. The line which goes through D and E (at which $[Na]_0/[Na]=1.014$ is given) crosses with the bars of $\Delta W/BW$ and $\Delta NaCl/BW$ at F (6%) and G (0.56 Gm/Kg) respectively.

loss and salt excess or loss (Fig. 4-b). Water and salt deficiencies of varying extent are independently defined on the same plane (Fig. 4-c). Ranges of the clinically encountered deficits per Kg of body weight are according to Marriott:⁵⁾ $\Delta W = -4\%$ (early), $= -6\%$ (moderately severe), $= -7 \sim -14\%$ (very severe); and $\Delta \text{NaCl} = -0.5 \text{ Gm}$ (slight to moderate), $= -0.5 \sim -0.75 \text{ Gm}$ (moderate to severe), $= -0.75 \sim -1.25 \text{ Gm}$ (severe to very severe). Pure dehydration or pure salt depletion may be only a theoretical concept.^{1),5)} The real situation will be somewhere between the 2 extreme conditions (Fig. 4-d): Hypertonic, isotonic, and hypotonic saline losses.

According to eqs. (15) and (16), estimation of water or salt loss relative to body weight can be ascribed to estimation of V_e/V_{e0} and V_i/V_{i0} . The latter is equal to $[\text{Na}]_0/[\text{Na}]$ if cell membranes are normal, whereas V_e/V_{e0} is a complicated function of V_p/V_{p0} and H_t . We made Nomograph 2 to obtain V_e/V_{e0} , V_i/V_{i0} , $\Delta W/\text{BW}$, and $\Delta \text{NaCl}/\text{BW}$ simultaneously from T_p , T_{p0} , H_t , H_{t0} , Na , Na_0 , based on eq. (3) (Fig. 5). If either one of H_t or T_p is lacking, we could obtain the latter using Nomograph 1 (Fig. 3).

3. Special cases (Fig. 4):

(1) Pure water depletion or excess may be defined $\Delta \text{NaCl} = 0$, in eq. (17), which gives to $\Delta V_e/V_{e0} = \Delta V_i/V_{i0}$. In this state, eq. (15) will become

$$\frac{\Delta W}{\text{BW}} = 0.6 \frac{\Delta V_i}{V_{i0}} = 0.6 \left(\frac{[\text{Na}]_0}{[\text{Na}]} - 1 \right) \quad (18)$$

(2) If only salt is lost from or added to the body, $\Delta W = 0$ in eq. (15). This leads to $\Delta V_e/V_{e0} = -2 \cdot \Delta V_i/V_{i0}$. Then the eq. (17) will be

$$\begin{aligned} \frac{\Delta \text{NaCl}}{\text{BW}} &= 1.64 \left[\left(1 - 2 \frac{\Delta V_i}{V_{i0}} \right) / \left(\frac{\Delta V_i}{V_{i0}} + 1 \right) - 1 \right] \\ &= 0.035([\text{Na}] - [\text{Na}]_0) \end{aligned} \quad (19)$$

(3) If isotonic disturbance of body fluid occurs, $[\text{Na}]_0 = [\text{Na}]$, which means that $\Delta V_i/V_{i0} = 0$ in eqs. (15) and (17). Then,

$$\frac{\Delta W}{\text{BW}} = 0.2 \frac{\Delta V_e}{V_{e0}} \quad (20)$$

$$\frac{\Delta \text{NaCl}}{\text{BW}} = 1.64 \frac{\Delta V_e}{V_{e0}} \quad (21)$$

(4) If extracellular fluid volume is not changed, $\Delta V_e/V_{e0} = 0$, which leads from eqs. (15) and (17) to

$$\frac{\Delta W}{\text{BW}} = 0.4 \left(\frac{[\text{Na}]_0}{[\text{Na}]} - 1 \right) \quad (22)$$

$$\frac{\Delta \text{NaCl}}{\text{BW}} = 0.0117([\text{Na}] - [\text{Na}]_0) \quad (23)$$

Eqs. (18) and (19) are familiar formulae in the text book of fluid therapy.¹⁾⁻⁴⁾

EXPERIMENTAL STUDIES

Methods:

In order to confirm the result of the theoretical analysis, experiments were carried out on 8 mongrel dogs of either sex varying in weight between 13 and 32 Kg. The dogs were anesthetized with sodium pentobarbital (25 mg/Kg iv) and cannulated in left femoral artery for arterial pressure determination, left femoral vein for venous pressure determination, right femoral artery for blood sampling, and right femoral vein for infusion of fluid. Infused fluids were 6% dextran C (mwt: 6000-9000) in Ringer sol., Ringer sol., and Ringer sol. diluted to half by distilled water. Blood samples were taken before, during, and after the infusion every 10-30 min. for determinations of hematocrit, [Na] (flame photometry), and total protein (refractometry). Urine was collected through the catheters inserted into both ureters and analyzed for Na concentration. In some of the experiments both renal arteries were ligated prior to the infusion. Blood pressures were monitored with pressure transducer and recorded on a polygraph (Nihon Koden). Net intake of water (ΔW) and salt (ΔNaCl) were calculated as (infused amount—urine output). $[\text{Na}]_0$, Ht_0 , Tp_0 before the infusion and the corresponding values after the infusion—Na, Ht, Tp—when these values reached a steady state, were

Table I. Summary of the Experimental Results

Fluid	Dextran C		Ringer		Ringer : Water = 1 : 1			
Exp. No.	1*	2*	3	4	5*	6*	7	8
Inpul (ml)	400	250	500	500	500	300	600	600
BW (Kg)	21.0	20.8	17.7	17.6	13.2	13.0	32.0	28.0
ΔW (ml)	400	250	450	452	500	300	580	528
NaCl (gm)			4.1	4.2	2.0	1.2	2.4	2.4
$[\text{Na}]_0$ (meq/l)			153.0	150.0	152.7	149.6	143.7	150.9
[Na]			153.0	149.4	147.5	145.2	142.6	148.6
Ht ₀ (%)	46	52	65.4	48.5	62.6	47.0	59.4	43.4
Ht	37	44	61.6	45.4	57.6	44.5	58.6	40.8
Tp ₀ (g/dl)				7.0		5.3	7.8	5.8
Tp				5.8		4.6	6.8	5.3
$\Delta \hat{V}_p^{**}$ (eqs. 11, 12)	408	259	87	126	100	76	97	133
$\Delta \hat{V}_e$ (Nomo. 2)			389	415	422	215	432	392
$\Delta \hat{V}_i$ (Nomo. 2)			0	42	186	158	93	173
$\Delta \hat{W}^\dagger$ (Nomo. 2)	408	259	389	457	608	373	525	565
$\Delta \hat{\text{NaCl}}$ (Nomo. 2)			3.2	3.3	2.4	1.1	3.1	2.5
$\Delta \hat{V}_e^{***}$			630	612	671	359	941	605
$\Delta \hat{W}'$ (eq. 18)			0	63	186	237	148	260
$\Delta \hat{\text{NaCl}}'$ (eq. 19)			0	-0.4	2.4	2.0	1.2	2.3

* Renal arteries ligated; ** $V_{p0}=0.04 \text{ BW}$; *** $\Delta V_e'=0.2 (V_p/V_{p0})\text{BW}$; $\dagger \Delta W=V_p$ for Exp. No. 1 and 2; ^ means an estimated value.

Table II. Relative Errors in the Estimation of Water and Salt Balance

Exp. No.	1	2	3	4	5	6	7	8	Mean	SE
$(\Delta\hat{W}-\Delta W)/\Delta W$ (%)	2.0	3.6	-13.6	1.1	21.6	24.3	-9.5	7.0	4.56	4.62
$(\Delta\hat{NaCl}-\Delta NaCl)/\Delta NaCl$ (%)			-21.9	21.4	10.0	-8.3	32.6	4.2	6.33	8.05
$(\Delta\hat{W}'-\Delta W)/\Delta W$ (%)			-100.0	-86.6	-62.8	-21.0	-74.5	-50.8	-65.95*	11.43
$(\Delta\hat{NaCl}'-\Delta NaCl)/\Delta NaCl$ (%)			100.0	-110.0	21.6	66.7	-50.0	4.2	-21.18	28.69
$(\Delta\hat{V_e}-\Delta V_e)/\Delta V_e$ (%)			62.0	47.5	59.0	6.0	48.4	54.3	56.20*	2.55

* Mean of % difference is statistically significant at 1% level.

used for the estimation of change in water and salt contents of the body. [Na] and Tp were not measured in the experiment of dextran infusion, for we were concerned only with expansion of intravascular space in that case. Data for protein concentration were lacking in some of other experiments. $\Delta V_p = 0.04(\Delta V_p/V_{p0}) \cdot BW$ was calculated both from protein and hematocrit using eqs. (11) and (12). If the values did not agree, we took the arithmetic mean of the two. ΔV_e , ΔV_i , ΔW , and $\Delta NaCl$ were estimated using Nomograph 2 of Fig. 5. $\Delta\hat{V_e}' (=0.2(\Delta V_p/V_{p0}) \cdot BW)$, $\Delta\hat{W}'$ (eq. (16)), $\Delta\hat{NaCl}'$ (eq. (17)) were also calculated for comparison. Percentage deviation from true net intake was statistically analyzed.

Results:

Results of the experiments were summarized in Table I. Estimation of water and salt content by Nomograph 2 seems to be satisfactory. Mean $\pm$ SE of the relative deviation of the estimated from the real ΔW and $\Delta NaCl$ were $4.56 \pm 4.62\%$, and $6.33 \pm 8.05\%$ (Table II). If we assumed $\Delta V_e/V_{e0} = \Delta V_p/V_{p0}$ instead of the relationship given by eq. (3), we might tend to overestimate ΔV_e by $56.2 \pm 2.55\%$. $\Delta\hat{W}'$ on the assumption of pure salt loss (eq. (18)) and $\Delta\hat{NaCl}'$ on the assumption of pure water loss (eq. (19)) were both far from the real inputs: Relative errors were $-65.95 \pm 11.43\%$ and $-28.18 \pm 28.69\%$ respectively.

ANALYSIS OF A CLINICAL CASE

Case Presentation:¹⁴⁾

K.S. 46., male; BW 54 Kg, BH 155 cm.

The patient had been well until 3 days before he visited our out-patient clinic with diarrhea and fever. He had watery stool 3-10 times a day, body temperature of 37° - 38° C. Urine output appeared to have been gradually lowered to probably less than 400 ml in 24 hours prior to his first visit. He complained of headache, vertigo, and postural syncope, and had nausea, vomiting, and sensation of thirst. On physical examination, he showed dry buccal mucosa, prominent furrowed tongue. The presternal skin turgor appeared low, the subaxillar region dry. He had no edema, normal ocular pressure. Pulse rate 120/min, Bp 98/80. The clinical diagnosis was acute enterocolitis. Judging from the anamnesis and the physical findings, we might conclude that he had mixed water depletion of moderate degree: $\Delta W = \text{ca. } -6\%$ BW and $\Delta NaCl = -0.5 \sim -0.75$ Gm/Kg BW.

Among the laboratory data on the day of his first visit, the following data were noted: $H_t=52\%$, $T_p=8$ Gm/100 ml, and $[Na]=138$ mEq/L. Assuming that $H_{t_0}=45$, $T_{p_0}=7.0$, $[Na]_0=140$, $V_p/V_{p_0}=T_{p_0}/T_p=7/8=0.875$ (eq. (11)) and $V_p/V_{p_0}=(1+0.52(140/138-1))(100/52-1)/(100/45-1)=0.761$ (eq. (12)). Taking the mean of them and using $V_p/V_{p_0}=0.818$, $(100-H_{t_0})/(100-H_t)=1.146$, and $[Na]_0/[Na]=1.014$ on Nomograph 2, we obtained $\Delta W=-2.23$ L or -4.1% BW, and $\Delta NaCl=-21.8$ Gms or -0.4 Gm/Kg·BW. These values would indicate mixed water depletion of slight to moderate degree. In view of the fact that the patient could have been losing some protein in the stool, we might as well trust H_t as an indicator of V_p rather than T_p . Then, $\Delta W=-3.25$ L or -6% of BW, and $\Delta NaCl=-30$ Gms or -0.56 Gm/Kg; values corresponding to water and Na depletions of moderate degree.

If we were to assume that the patient had pure dehydration and use eq. (18), then $\Delta W=+470$ ml, and if we should assume on the contrary that pure salt loss had occurred, then $\Delta NaCl=-1.3$ Gm according to eq. (21). Evidently, these estimations are far from the real.

We might say that the result of the present scheme of calculation generally agreed with the estimation on the basis of clinical signs and symptoms. But, unfortunately, cases of this kind are rather rare in the University Hospital in which majority of the patients have problems in production or destruction of red blood cells and protein in addition to body fluid disturbances. In these cases, water and salt deficits can not be estimated from the blood analysis. Sick cell syndromes will also defy our present analysis, because eq. (1) may not be applicable in the leaky cell membranes.

DISCUSSION

Various states of water loss and/or salt loss of the body have been defined with a different terminology by different investigators.^{1)-3),5)} For instance, Marriott⁵⁾ defined pure dehydration as $\Delta W<0$, $\Delta NaCl=0$, pure salt loss as $\Delta NaCl<0$, $\Delta Vi<0$, and mixed water and salt loss as $\Delta NaCl<0$, $\Delta Vi<0$. Scribner¹⁾ simply defined water depletion $\Delta Vi<0$, and saline depletion $\Delta Ve<0$. However, on the basis of the compartment model of the body fluid, amount of salt loss (or excess) and water loss (or excess) should be expressed by a coordinate which is different from the originally assumed $\Delta V_c/V_{c_0}-\Delta V_i/V_{i_0}$ plane (Fig. 4-d). Thus we define in this paper water and salt losses (or excesses) independently and 'pure' signifies no change in the amount of the counterpart: Pure dehydration is $\Delta W<0$, $\Delta NaCl=0$ and pure salt loss is $\Delta NaCl<0$, $\Delta W=0$.

This point may be rather important, because the formulae given by eqs. (18) and (19) for the estimation of the deficits assume the 'pure' conditions in this sense.²⁾⁻⁴⁾ Use of these formulae is discouraged by these authors because of the limited applicability. Our main contention in this paper is that we might be able to estimate 'mixed' salt and water loss by

combining the informations on ECF, e.g., plasma protein and Ht, and on ICF, e.g., plasma sodium or osmolarity. The equality of $V_i/V_{i0} = [Na]_0/[Na]$ under the condition of normal cell membranes has long been established whereas the relationship between V_e and V_p is more difficult to be determined. Recent developments in overall quantitative analysis of cardiovascular and body fluid regulation^{7)-9),15)} seem to have given us a sufficient basis for obtaining a relative increment of interstitial volume to given relative increments of plasma volume and hematocrit.

In the derivation of eq. (3) which was used to calculate the relationship, we used hyperbolic functions of interstitial hydrostatic pressure and lymphatic flow rate in terms of volume of interstitial space and interstitial pressure respectively according to Cameron.¹²⁾ These functions were found to fit the observations of Guyton et al,¹³⁾ and also the results of their more complex model.^{11),3)} We assumed the mean capillary hydrostatic pressure as a linear function of blood volume. This is based on the fact that Starling's curve of cardiac performance against atrial pressure will be in the range of linearity when blood volume is $\pm 50\%$ of the normal value, and influence of after-load will be negligible.⁸⁾ The proportionality of π 's and protein concentrations is a linear approximation of the 3rd order equations given by Landis and Pappenheimer.¹⁶⁾ This again may be permissible in the narrow range of volume change.

The validity of this model was confirmed in the experimental and clinical studies. It seems also compatible with a number of data in the literatures. For instance, Marriott stated in his classical lecture⁵⁾ that a reasonable rough assumption was that loss of 1 L of plasma volume (normal plasma volume being approximately 3 L) meant a total loss of extracellular fluid of the order of 6-7 L. Giving the values of $\Delta V_p/V_{p0} = -1/3$ or $V_p/V_{p0} = 0.67$, $[Na]_0/[Na] = 1$, and $Ht_0 = 45\%$ (which gives $100 - Ht_0/100 - Ht = 1.21$ (eq. (12)) on Nomograph 2, we obtain $V_e/V_{e0} = -0.58$ or 7-8 L for average adults. The difference between Marriott's result and ours may not be striking for the 'rough' estimations.

The new formulae: eqs. (15) and (16) with the aid of Nomograph would provide a useful clue for the quantitative estimation of mixed water and salt losses. However, they are still limited in their applicability as the above mentioned assumptions are necessary and normal values of $[Na]$, Ht, and Tp for the given patient should be known. The clinical signs and symptoms and urine output should make up for the defect and vice versa. For more accurate analysis, we might need a computer assisted numerical calculation instead of the analytical presentations. But crude classification of the body fluid disturbance into 3 categories (moderate, severe, and very severe) may

be all we needed—and all we can wish in most of the clinical cases—to initiate a regimen of fluid therapy.

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APPENDIX

Derivation and numerical solution of eq. (3)

Rewriting eq. (2),

$$P_f = P_c + \pi_s - P_s - \pi_p \quad (2)$$

If we substitute P_c , π_s , and π_p in the eq. (2) by their respective assumed functions and rearrange it, we obtain

$$23.0(V_b/V_{b_0})(V_p/V_{p_0}) + [(5/(V_s/V_{s_0})) - P_s - P_f - 6.0](V_p/V_{p_0}) - 28 = 0.$$

From eqs. (4), (5), and (6), $(V_b/V_{b_0}) = (V_p/V_{p_0})(100 - H_{t_0})/(100 - H_t)$, which changes the above equation into eq. (3).

Inspection of the hyperbolic functions of P_s and P_f would result:

- (1) $0.995 \leq V_s/V_{s_0}$
 $P_s = 4.9(V_s/V_{s_0} - 1.852)/(V_s/V_{s_0} - 0.338)$
 $P_f = 14.215(V_s/V_{s_0} - 0.995)/(V_s/V_{s_0} - 0.785)$
- (2) $0.711 \leq V_s/V_{s_0} < 0.995$
 $P_s = 4.9(V_s/V_{s_0} - 1.852)/(V_s/V_{s_0} - 0.338)$
 $P_f = 0$
- (3) $V_s/V_{s_0} < 0.711$
 $P_s = -15$
 $P_f = 0$

Then, V_s/V_{s_0} for a given combination of V_p/V_{p_0} and $(100 - H_{t_0})/(100 - H_t)$ (which will be abbreviated as R_{ht}) will be obtained by solving the following equations:

- (1) $0.995 \leq V_s/V_{s_0}$
 $A(V_s/V_{s_0})^3 + B(V_s/V_{s_0})^2 + C(V_s/V_{s_0}) + D = 0,$
 where
 $A = 23.0[(V_p/V_{p_0})^2 R_{ht} - 1.092(V_p/V_{p_0}) - 1.217]$
 $B = -25.83[(V_p/V_{p_0})^2 R_{ht} - 1.688(V_p/V_{p_0}) - 1.217]$
 $C = 6.103[(V_p/V_{p_0})^2 R_{ht} - 3.132(V_p/V_{p_0}) - 1.217]$
 $D = 1.327(V_p/V_{p_0});$
- (2) $0.711 \leq V_s/V_{s_0} < 0.995$
 $A'(V_s/V_{s_0})^2 + B'(V_s/V_{s_0}) + C' = 0$
 where
 $A' = 23.0[(V_p/V_{p_0})^2 R_{ht} - 0.474(V_p/V_{p_0}) - 1.217]$
 $B' = -7.774[(V_p/V_{p_0})^2 R_{ht} - 2.072(V_p/V_{p_0}) - 1.217]$

$$C' = -1.690(V_p/V_{p_0});$$

$$(3) \quad V_s/V_{s_0} < 0.711$$

$$V_s/V_{s_0} = 0.217[(V_p/V_{p_0})/(- (V_p/V_{p_0})^2 R_{ht} + 0.391(V_p/V_{p_0}) + 1.217)].$$

V_s/V_{s_0} 's for any given combination of V_p/V_{p_0} and R_{ht} were computed according to all of the 3 equations. A correct value of V_s/V_{s_0} was then picked up from them as one which satisfies the range constraints. The third order equation was solved by Newton's method.

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