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A Model For Renal-Electrolyte Regulation

by

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SUMMARY

The present report provides a detailed systems analysis of the kidney and the associated electrolyte regulatory mechanism; which will be referred to, for purposes of brevity, as the renal chemostat. The model explicitly incorporates the effect of water and salt intake, pulmonary CO_2 tension, as well as the main features of renal physiology as it is presently understood. Thus the regulatory function of both aldosterone and antidiuretic hormone are included as well as the effect of such parameters as pH, salt concentration, plasma volume and osmotic factors. The present work thus provides a basis for the development of an electronic analog of the renal-electrolyte system.

A MODEL FOR RENAL-ELECTROLYTE REGULATION

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A theoretical analysis and related analog of the electrolyte composition of the bodily fluids and the associated renal system is of considerable potential value in advancing our understanding of renal physiology as well as in such applied pursuits as the design and control of artificial kidneys. Moreover, because of the central role of the renal chemostat in the regulation of the internal chemical environment an analog would be of value in predicting the adoption limits for the environmental conditions encountered in manned space flights, submarine and other life support systems. The present report presents an analytical model of the renal-electrolyte system which takes into explicit consideration some of the main features of renal physiology as it is presently understood. In addition, the model also incorporates the regulatory function of both aldosterone (A) and antidiuretic hormone (ADH) as well as the relevant systems parameters which influence pH, water, and electrolyte homeostatis. This analysis provides the basis for an electric analog presently under investigation. The present investigation is thus much broader in scope than the interesting studies reported earlier by Landahl[1].

Formulation

It is convenient, at the outset, to state explicitly the physiological mechanisms which will be taken into account in the present study:

(a) Sodium readsorption in the proximal tubules occurs against an electrochemical potential by an active mechanism. Active transport of potassium probably also occurs in the proximal tubules[2,3].

(b) It is also reasonably well established that in the distal tubules, cation exchange occurs between sodium ions and potassium or hydrogen ions.

(c) Chloride and bicarbonate ion absorption in the proximal tubule is probably a passive accompaniment to the cation absorption[4].

(d) It is well established now that water readsorption occurs as the result of osmotic pressure gradients arising from the active cation transport.

(e) The water permiability of the renal tubule wall (particularly at the distal and collecting tubules) is enhanced by ADH.

(f) The rate of ADH secretion is increased by a rise in plasma osmotic pressure or a decrease in blood volume. There are, however, many unresolved problems associated with identification of the volume receptor system.

(g) It is also well established that sodium reabsorption is enhanced by aldosterone.

(h) Aldosterone plasma levels increase (via the renin-angiotensin II mechanisms) when the renal blood flow decreases (renal ischemia) or when the plasma sodium ion concentration decreases.

The general scheme that will be employed in the present analysis is in effect the four compartment model shown in figure 1. The notation is listed in table 1. The renal compartments consist of a distributed urinary tubule section which exchanges, by various mechanisms, electrolyte and water with the compartment representing the flow of blood through the renal capillary system. The appropriate variables will be generally designated by the subscripts u and C respectively. A lumped compartment representing the extra renal plasma circulation is also shown. Into this compartment flows the extra renal plasma and ingested water containing dissolved sodium and potassium chlorides and bicarbonates. A portion of the plasma permiates the capillary membranes to enter the intercellular fluid space as indicated. The plasma compartment also vents into the systemic venous circulation as does also the return flow from the intercellular compartment. Finally, the venous return is pumped via the right heart (RH) through the lungs where equilibration occurs with alveolar CO_2 and O_2 following which the blood is pumped by the left heart (LH) into the aortic artery. Though the pulmonary system appears here as a fifth compartment it plays a comparatively minor role in the present analysis.

It is interesting to note in passing that the above scheme provides a convenient model for the analysis of the edema associated with right and left heart failure. Thus it is immediately evident that diminution of the pumping capacity of RH, in figure 1, must result in systemic fluid accummulation while failure of LH must result in a reduced $\dot{V}_R$ and hence in increased sodium retention (because of items (g) and (h) above) with consequent edema.

However, in order not to unduly complicate the present analysis the hemodynamics of the system will be simplified somewhat by neglecting the intercellular fluid compartment, the pulsatile character of the blood flow and the viscoelelastic character of the vasculature.

The dc hydraulic equations for the renal system can now be readily written down by a straightforward application of the hydraulic analog of Ohm's and Kirchoff's laws. It is convenient at this point to introduce the hydraulic conductance, $G = R^{-1}$, and the effective hydraulic pressure defined as the difference between the hydrostatic and colloidal osmotic pressures P_o. Then there follows that

$$\dot{V}_R = G_A(P_A - P_G) = G_E(P_G - P_V) + G_M(P_G - P_B - P_O) \tag{1}$$

From (1) it follows that the hydrostatic pressure in the glomerulus is given by

$$P_G = \frac{G_A P_A + G_E P_V + G_M(P_B + P_O)}{G_A + G_E + G_M} \tag{2}$$

and hence the renal arterial input is

$$\dot{V}_R = \frac{G_A(G_E + G_M)}{G_A + G_E + G_M} \left\{ P_A - \frac{G_E P_V + G_M(P_B + P_O)}{G_E + G_M} \right\} \tag{3}$$

Under steady state conditions continuity requires

$$\dot{V}_{UO} + \dot{V}_{CO} = \dot{V}_R \tag{4}$$

The flow through the extra renal system is simply

$$\dot{V}_S = G_S(P_A - P_V) \tag{5}$$

It is evident that by means of equations (3) and (5) it is possible in principle to calculate the renal and extra renal flows from the systems parameters.

Renal Transport Equations

We next develop a simple model of the kidney which takes into account the above indicated physiological mechanisms. For this purpose we regard the renal tubule as consisting of a tube of uniform radius r but divided into a proximal section (whose function also encompasses the loop of Henle mechanism) of length g, and a distal section of length (h-g), as indicated in figure 2. Close by and parallel to the tubule is a capillary also of uniform radius r containing the plasma. Under steady state conditions in the kidney, which is assumed here, the flux of electrolyte and water out of the tubule is equal to that entering the capillary. The distance along the tubule will be specified by the variable y.

With this three compartment model the ions in the renal tubule are transported to the extra tubular region and the ions in the latter region are transported into the capillary, as indicated in figure 2. However, it can be shown (see appendix III) that when the ions in the extra tubular region are at the steady state concentration then the expressions for the flux are of the standard form and involve only the concentrations in the tubule and the capillary and not that in the extra tubular space.

The transport of sodium and potassium involves an active or so called pumping mechanism. Though the details of this pump are not known, the mechanism probably involves the combination of the sodium ions with the active transport sites at the lumen of the renal tubule. This type of mechanism gives rise to the well known Michealis-Menton type of expression for the active component of the flux associated with sodium reabsorption:

$$J = \frac{K_{1S}(Na)_u}{1 + K_{2S}(Na)_u} \tag{5}$$

where K_{1S} and K_{2S} are parameters which depend on the rate constants. A similar expression applies to the potassium reabsorption.

Other transport mechanisms contribute to the cation flux, namely diffusion arising from concentration gradients, electromotive transport due to the transtubular potential gradient, and possibly ion transport resulting from the flux of water through the membrane. However, in what follows we shall neglect the latter and related ion or solvent drag mechanisms. The relevant expressions for the sodium and potassium fluxes are respectively

$$J_S = \frac{K_{1S}(Na)_u}{1 + K_{2S}(Na)_u} + D_S \left\{ (Na)_u - (Na)_C \right\} - \mu_S (Na)_C \nabla\phi \tag{6}$$

$$J_K = \frac{K_{1k}(K)_u}{1 + K_{2K}(K)_u} + D_K \left\{ (K)_u - (K)_C \right\} - \mu_K (K)_C \nabla\phi \tag{7}$$

The transport of water depends mainly on the osmotic presure differential resulting from the transtubular sodium salt gradient so that

$$J_w = D_w \left\{ (Na)_C - (Na)_u \right\} \tag{8}$$

As is well known, the actual operation of the loop of Henle mechanism is complicated by a counter current multiplier processes. More explicit consideration of the counter current concentration mechanism will be provided in a subsequent paper.

Chloride and bicarbonate fluxes, J_C and J_B respectively, are governed by the transtubular potential gradient and the membrane mobilities μ_C and μ_B and are given by

$$J_C = \mu_C (Cl)_u \nabla\phi \tag{9}$$

$$J_B = \mu_B (HCO_3)_u \nabla\phi \tag{10}$$

since

$$J_C + J_B = J_S + J_K \tag{11}$$

there follows

$$\nabla\phi = \frac{J_S + J_K}{\mu_C (Cl)_u + \mu_B (HCO_3)_u} \tag{12}$$

The main processes at the distal tubule is the well known exchange between sodium and the extra tubular potassium and hydrogen ions. Using the added subscript D to designate the distal tubular processes we have for the sodium pump

$$J_{SD} = \frac{K_{1SD} (Na)_u}{1 + K_{2SD} (Na)_u} + D_S \left\{ (Na)_u - (Na)_C \right\} - \mu_S (Na)_C \nabla\phi \tag{13}$$

For the potassium and hydrogen ion fluxes, J_{KD} and J_{HD} respectively, into the tubule we must have

$$J_{KD} + J_{HD} = J_{SD} \tag{14}$$

The current evidence seems to support a passive potassium-hydrogen ion flux so that

$$J_{KD} = \mu_K (K)_C \nabla\phi \tag{15}$$

$$J_{HD} = \mu_H (H)_C \nabla\phi \tag{16}$$

Hormone Regulation

Having written down the main equations governing renal transport the expressions for aldosterone and ADH control must next be considered. As indicated, ADH increases the water permeability of the tubules. Since in general such physiological effects tend to saturate toward a limiting value it is reasonable to write the permeability coefficient in equation (8) as

$$D_W = D_{WO} + \frac{D_{WS}(ADH)}{1 + \alpha_W (ADH)} \tag{17}$$

Here D_{WO} is the permeability at zero concentration of ADH and D_{WS} the increment at saturation. Similarly, aldosterone increases the sodium readsorption at the distal tubules so that

$$K_{1D} = K_{1DO} + \frac{K_{1DS}(A)}{1 + \alpha_S(A)} \tag{18}$$

In order to complete the feedback loops it is necessary to relate the aldosterone and ADH concentrations to the physiological variables. The dependency, given by items (f) and (h) above, may be expressed in terms of deviations about the normal or operating value of the variables. Thus in the case of ADH we may write for the net rate of ADH production

$$\dot{(ADH)} = \dot{(ADH)}_O - \beta_1[V_e - V_{Oe}] + \beta_2[(Na) - (Na)_O] - k_1(ADH) \tag{19}$$

where k_1 is the rate constant for the removal of ADH in the liver or through excretion and $\dot{(ADH)}_O$ is the normal or reference production rate. Similarly the rate equation for aldosterone is

$$(\dot{A}) = (\dot{A})_O - \gamma_1[V_R - V_{RO}] - \gamma_2[(Na) - (Na)_O] - k_2(A) \qquad (20)$$

Concentration Equations

There remains the tasks of relating the fluxes given above to the concentrations in the tubule and capillary as well as that of interrelating the concentrations in the various compartments. The tubular concentration of substance $(X)_u$ at some position y (fig.2) when steady state conditions apply is shown in appendix II to be given by

$$(X(y))_u = \frac{(X)_u(O)\dot{V}_u(O) - 2\pi rN\int_o^y J_x dy}{\dot{V}_u(O) - 2\pi rN\int_o^y J_W dy} \qquad (21)$$

A second relationship, derived in Appendix I, gives the time rate of change of X in the extra renal or systemic compartment of volume V (figure 1)

$$(\dot{X})_S = \frac{\sum_i \{(X)_i - (X)\}\dot{V}_i + (\dot{X})_G V}{V} \qquad (22)$$

where $(X)_i$ and $\dot{V}_i$ are the concentrations and the rate of flow of X into the compartment and $(\dot{X})_G$ is the rate per unit volume at which X is generated within the compartment. These results may now be applied to determining the concentrations of the various chemical species.

Applications and Discussions

The concentration of sodium will be considered now as an example of the previous analysis. It is evident from the above that the

present results assure that the renal concentrations correspond to steady state. The relevant equations for the sodium concentrations in the urinary output $(Na)_{uO}$ and renal vein $(Na)_{CO}$ are obtained by application of expression (21). Hence $(Na)_u$ at the position g in figure 2 is designated by $(Na)_{ug}$ and given by

$$(Na)_{ug} = \frac{\dot{V}_{uI}(Na) - 2\pi rN\int_O^g J_S dy}{\dot{V}_{uI} - 2\Pi rN\int_O^g J_W dy} \tag{23}$$

where J_S is given by (6). To find the sodium in the urine we have

$$(Na)_{uO} = \frac{\dot{V}_{ug}(Na)_{ug} - 2\pi rN\int_g^h J_{SD} dy}{\dot{V}_{uI} - 2\Pi rN\int_o J_W dy} \tag{24}$$

Similarly for the concentration of sodium in the renal capillary flow we have

$$(Na)_{cg} = \frac{\dot{V}_{cI}(Na) + 2\pi rN\int_o^g J_S dy}{\dot{V}_{cI} + 2\pi rN\int_o^g J_W dy} \tag{25}$$

$$(Na)_{cO} = \frac{\dot{V}_{cg}(Na)_{cg} + 2\Pi rN\int_g^h J_{SD} dy}{\dot{V}_{cI} + 2\pi rN\int_o^g J_W dy} \tag{26}$$

The renal venous output $(Na)_{cO}$ then mixes with the systemic venous flow according to the expression

$$(Na) = \frac{(Na)_{cO}\dot{V}_{cO} + (Na)_e\dot{V}_e}{\dot{V}_{cO} + \dot{V}_e} \tag{27}$$

where the systemic venous output is given by equation 22:

$$(\dot{Na})_e \dot{V}_e = \{(Na) - (Na)_e\} \dot{V}_S + \{(Na)_D - (Na)_e\} \dot{V}_D \qquad (28)$$

Similar arguments lead to the expressions for the other cations and anions. The carbonic acid system, however, requires special consideration because of the multiple equilibria that are involved.

The mass balance equations for the $H_2CO_3/HCO_3/H+$ system will now be derived taking into account the relevant equilibrium conditions. The expressions relating to the flow through the proximal section of the capillaries will be derived first. The plasma entering the capillary is assumed to have been brought to equilibrium with the alveolar CO_2 so that if $(pCO_2)_{a\ell}$ is the partial pressure of CO_2 in the alveolar space then

$$(H_2CO_3) = K_S(pCO_2)_{a\ell} \qquad (29)$$

The sum of the carbonic acid plus bicarbonate flowing out of this section must be equal to that flowing in plus the amount that has diffused into the capillary. Similarly the hydrogen ions flowing out must equal that entering minus the amount that has combined with the bicarbonate. Assuming equilibration and recalling that water is also transported the following equations are readily obtained:

$$\{(HCO_3^-)_{Cg} + (H_2CO_3)_{Cg}\} \dot{V}_{Cg} = K(pCO_2)_{a\ell} + (HCO_3^-) \dot{V}_{CI} + 2\pi rN \int J_B dy \qquad (30)$$

$$(H^+)_{Cg} \dot{V}_{Cg} = (H+)\dot{V}_{CI} - \{(HCO_3^-)\dot{V}_{CI} + 2\pi rN \int J_B dy - (HCO_3^-)_{Cg}\dot{V}_{Cg}\} \qquad (31)$$

since

$$K_A = \frac{(H^+)_{Cg}(HCO_3^-)_{Cg}}{(H_2CO_3)_{Cg}} \qquad (32)$$

we have from (30) and (32)

$$(HCO_3)_{Cg} = \frac{\left\{ K(pCO_2)_{a\ell} + (HCO_3) \right\} \dot{V}_{CI} + 2\pi rN \int J_B dy}{\left[1 + \frac{(H^+)_{Cg}}{K_A} \right] \dot{V}_{Cg}} \tag{33}$$

The last three expressions clearly permit the calculation of the desired concentrations provided (HCO_3^-), the aortic concentration of bicarbonate, is known. Expressions for the latter will be obtained below. At the distal end of the capillary sodium is exchanged in part for hydrogen ions which flow out of the capillary and leave behind bicarbonate ions. In addition H^+ ions are generated by the dissociation of carbonic acid. Considering then the renal venous output mass balance and equilibrium conditions the following expressions are obtained

$$(HCO_3)_{CO} + (H_2CO_3)_{CO} \dot{V}_{Cg} = (HCO_3)_{Cg} + (H_2CO_3)_{Cg} \dot{V}_{Cg} \tag{34}$$

$$(H^+)_{CO} \dot{V}_{CO} = \left\{ (H^+)_{Cg} + (HCO_3)_{CO} - (HCO_3)_{Cg} \right\} \dot{V}_{Cg} - 2\pi rN \int_g^h J_{HD} dy \tag{35}$$

From (32) and (34) we have

$$(HCO_3)_{CO} = \frac{(HCO_3)_{Cg} \left[1 + \frac{(H^+)_{Cg}}{K_A} \right]}{\left[1 + \frac{(H^+)_{CO}}{K_A} \right]} \tag{36}$$

The extra renal plasma is next considered. If the carbon dioxide partial pressure in the extra renal venous blood is $(pCO_2)_e$ then

$$(H_2CO_3)_e = K_S(pCO_2)_e \tag{37}$$

The bicarbonate ion concentration in this compartment is equal to that in the arterial input plus that arising from the ionization of carbonic acid

$$(HCO_3^-)_e = (HCO_3^-) + (H^+)_e - (H^+) = (HCO_3^-) + K_S K_A \left\{ \frac{(pCO_2)_e}{(HCO_3^-)_e} - \frac{(pCO_2)_{a\ell}}{(HCO_3^-)} \right\} \tag{38}$$

The final concentration in the caval return is determined by the mixing of renal and extra-renal plasma given by

$$(H_2CO_3)_V = \frac{(H_2CO_3)_e \dot{V}_e + (H_2CO_3)_{CO} \dot{V}_{CO}}{\dot{V}_e + \dot{V}_{CO}} \tag{39}$$

$$(HCO_3^-)_V = \frac{(HCO_3)_e \dot{V}_e + (HCO_3)_{CO} \dot{V}_{CO}}{\dot{V}_e + \dot{V}_{CO}} \tag{40}$$

Finally the venous blood equilibrates with alveolar CO_2 in the pulmonary system. The output concentration of bicarbonate ion is equal to the input concentration minus the bicarbonate which associates with hydrogen ions to form carbonic acid.

$$(HCO_3) = (HCO_3)_v - \left\{ (H^+)_v - (H^+) \right\} \tag{41}$$

$$(HCO_3) = (HCO_3)_v - K_S K_A \left\{ \frac{(pCO_2)_v}{(HCO_3)_v} - \frac{(pCO_2)_{a\ell}}{(HCO_3)} \right\} \tag{42}$$

This last result relates, as mentioned earlier, the aortic bicarbonate concentration to that of the venous return.

All of the above expressions for the various ionic species are interrelated through the expressions for the flux so that the solution of the equations becomes very difficult and it is desirable to program the system of equations on a computer.

An analog computer has been selected for this purpose and the result will be presented in a subsequent publication.

Appendix I

The concentration and volume change may be derived in general for a reservoir initially having plasma volume V and in which is dissolved a substance X of concentration (X). If the ith input of (X) occurs at a rate $\dot{V}_i$, then the concentration of X in this input is designated by $(X)_i$. In the general case we must also consider the possibility that the X substance is generated by a chemical reaction. We consider the case of n inputs and j outputs V_{oj} and we assume concentration uniformity within the reservoir at the same rate $(\dot{X})_G$ per unit volume. In a small interval of time Δt at the instant t, conservation of X requires that

$$(X(t+\Delta t)) = \frac{X(t)V(t) + \Delta t \sum_{i=1}^{n} (X)_i \dot{V}_i - \Delta t \sum_{i=1}^{j} (X(t)) V_{oi} + (\dot{X})_G V(t) \Delta t}{V(t+\Delta t)} \quad (1)$$

We now multiply both sides by $V(t+\Delta t)$ and expand $X(t+\Delta t)$ and $V(t+\Delta t)$ in a Taylors series about the values at t

$$(X(t+\Delta t)) = (X(t)) + (\dot{X})\Delta t \quad (2)$$

$$V(t+\Delta t) = V(t) + \dot{V}\Delta t \quad (3)$$

We now take the limit as $\Delta t \to 0$ and find that

$$(\dot{X})(V) + (X)\dot{V} = \sum_i (X)_i \dot{V}_i - (X) \sum_j V_{oj} + (\dot{X})_G V \quad (4)$$

A second relationship follows from the incompressibility of the liquid and neglecting the volume change due to the concentration effect:

$$\dot{V} = \sum_i \dot{V}_i - \sum_j \dot{V}_{oj}$$

so that

$$\dot{X} = \frac{\sum_i (X)_i \dot{V}_i - (X) \sum_j \dot{V}_i + (\dot{X})_G V}{V} \tag{5}$$

$$\dot{X} = \frac{\sum_i \left\{(X)_i - (X)\right\} \dot{V}_i + (\dot{X})_G V}{V} \tag{6}$$

APPENDIX II

The Tubule Equation

The transport equation for the tubule will now be derived. We consider a small section of tubule of height Δy and radius r. Let the concentration of a substance at y at time t be represented by $(X(y,t))_u$. The substance enters the top section at a rate $(X)\dot{V}(y,t)$ where $\dot{V}(y,t)$ is the volume of fluid entering per unit time. We assume that the substance in question is transported through the wall of the tubule at a rate given by $2\pi r\Delta YJ$ where J is the outward flux given in such units as moles/cm^2 sec. In addition a volume ΔV of fluid leaving given by $J_V 2\pi r\Delta Y$where J_V is the volume flux given in such units as volume/cm^2 sec. The change of (X) is then

$$\pi r^2 \Delta y \frac{\partial (X)}{\partial t} = (X)\dot{V} - \left\{(X) + \frac{\partial (X)}{\partial y}\Delta y\right\}\left\{\dot{V} + \frac{\partial \dot{V}}{\partial y}\Delta y\right\} - 2\pi r\Delta y J + (\dot{X})_G \pi r^2 \Delta y$$

where $(\dot{X})_G$ is the rate at which X is generated per unit volume and unit time. On going to the limit $\Delta y \to 0$ we have

$$\frac{\partial (X)}{\partial t} = \frac{1}{\pi r^2}\frac{\partial (X\dot{V})}{\partial y} - \frac{2J}{r} + (\dot{X})_G \qquad (1A)$$

From the continuity condition on the fluid volume we have that

$$(\dot{V} + \frac{\partial \dot{V}}{\partial y}\Delta y) - \dot{V} = -2\pi r J_V \Delta y \qquad (2A)$$

$$\frac{\partial \dot{V}}{\partial y} = -2\pi r J_V$$

hence,

$$\dot{V}(y) = -2\pi r \int_0^y J_V \, dy + \dot{V}(0) \qquad (3A)$$

On integrating (1A) under the steady state assumption we have

$$(X(y))_u \dot{V}(y) - (X(0))_u \dot{V}(0) = -2\pi r \int_0^y J \, dy + \pi r^2 \Delta y \int_0^y (\dot{X})_G dy \qquad (4A)$$

From (3A and 4A) we have

$$(X(y)) = \frac{-2\pi r \int_0^y J \, dy + \pi r^2 \int_0^y (\dot{X})_G \, dy + (X(0))\dot{V}(0)}{\dot{V}(0) - 2\pi r \int_0^y J_V \, dy} \qquad (5A)$$

When $\dot{V}(0)$ represents the total flow into the kidney then the integrals must be multiplied by N the number of active nephrons.

Appendix III

Steady State Flux

We consider the flux in a three compartment system shown in figure 3, where the concentration of the transported species is indicated by (X_1), (X_2), and (X_3). Let

$$J_1 = D_1\left\{ (X_1) - (X_2)\right\} + \frac{K_1(X_1)}{1 + K_2(X_1)} - (X_2)\mu\nabla\phi$$

where $\nabla\phi$ is a potential gradient which tends to drive the transported species from right to left in figure 3. Let

$$J_2 = D_2((X_2) - (X_3)).$$

When the concentration in the middle compartment has reached the steady state then $J_1 = J_2$ and hence

$$(X_2) = \frac{D_1(X_1) + D_2(X_3) + \dfrac{K_1(X_1)}{1 + K_2(X_1)}}{D_1 + D_2 + \mu\nabla\phi}$$

The steady state flux can now be found upon substituting the steady state value for (X_2) given above into the expression for J_1. It is found that the steady state flux J_{1S} is

$$J_{1S} = \frac{D_2}{D_1+D_2+\mu\nabla\phi}\left\{D_1\left\{ (X_1) - (X_3)\right\} + \frac{K_1(X_1)}{1+K_2(X_1)} - \mu\nabla\phi(X_3)\right\}$$

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TABLE No. I

(A)	=	aldosterone concentration
(ADH)	=	antidiuretic hormone concentration
D_K	=	permeability constant of potassium
D_S	=	permeability constant of sodium
D_W	=	permeability constant of water
g	=	length of proximal section of tubule
G	=	hydraulic conductance
h	=	length of distal plus proximal sections of tubule
J_{XD}	=	flux of X in distal tubule
J_{XP}	=	flux of X in proximal tubule
k_1	=	rate constant for ADH removal
k_2	=	rate constant for aldosterone removal
K_{1X}, K_{2X}	=	constants characterizing the active transport of X
N	=	number of active nephrons
P_A	=	effective arterial pressure
P_B	=	filtrate pressure in Bowman's capsule
P_G	=	blood pressure in capillaries of glomerulus
P_I	=	pressure of interstitial fluid
P_{OI}	=	osmotic pressure of interstitial fluid
P_O	=	colloidal osmotic pressure of plasma
P_V	=	systemic venous pressure
$(pCO_2)_{al}$	=	alveolar CO_2 partial pressure

r = radius of renal tubule and capillary

R_A = hydraulic impedance of venal pre-plomerulus vessels

R_E = hydraulic impedance of renal post glomerulus vessels

R_M = hydraulic impedance of renal glomerulus vessels

R_S = lumped hydraulic impedance of extra renal systemic circulation

$\dot{V}$ = total plasma volume pumped by heart per unit time

CI = rate of arterial flow leaving glomerulus

CO = capillary flow rate at output

$\dot{V}_D$ = injected water flow rate

$\dot{V}_e$ = extra renal venous flow rate

V_{Oe} = reference (normal) plasma volume

$\dot{V}_R$ = renal arterial flow rate

$\dot{V}_S$ = systemic (extra renal) arterial flow rate

$\dot{V}_{uh}$ = flow rate of filtrate entering distal tubules

$\dot{V}_{uI}$ = glomerular filtrate flow rate

$\dot{V}_{uO}$ = flow rate of excreted urine

$\dot{V}_v$ = total venous flow rate

$X)$ = concentration of X in aortic circulation

$C = (X(y))_C$ = concentration of X in plasma at position y in the renal capillary

Cg = concentration of X in plasma at end of the proximal section of the renal capillary

CO = concentration of X in renal vein

$(X)_D$ = concentration of injected substance X

$(X)_e$ = concentration of X in extra renal venous circulation

$(X)_O$ = normal or reference concentration of X in aortic circulation

$u=(X(y))_u$ = concentration of X in filtrate at position y in the renal tubule

$_{ug}$ = concentration of X at end of the proximal section of the renal tubule

$_{uO}$ = concentration of X in urine

$(y,t))_u$ = concentration of X in filtrate at position y and time t in the renal tubule

= emperical constant appearing in equation 18

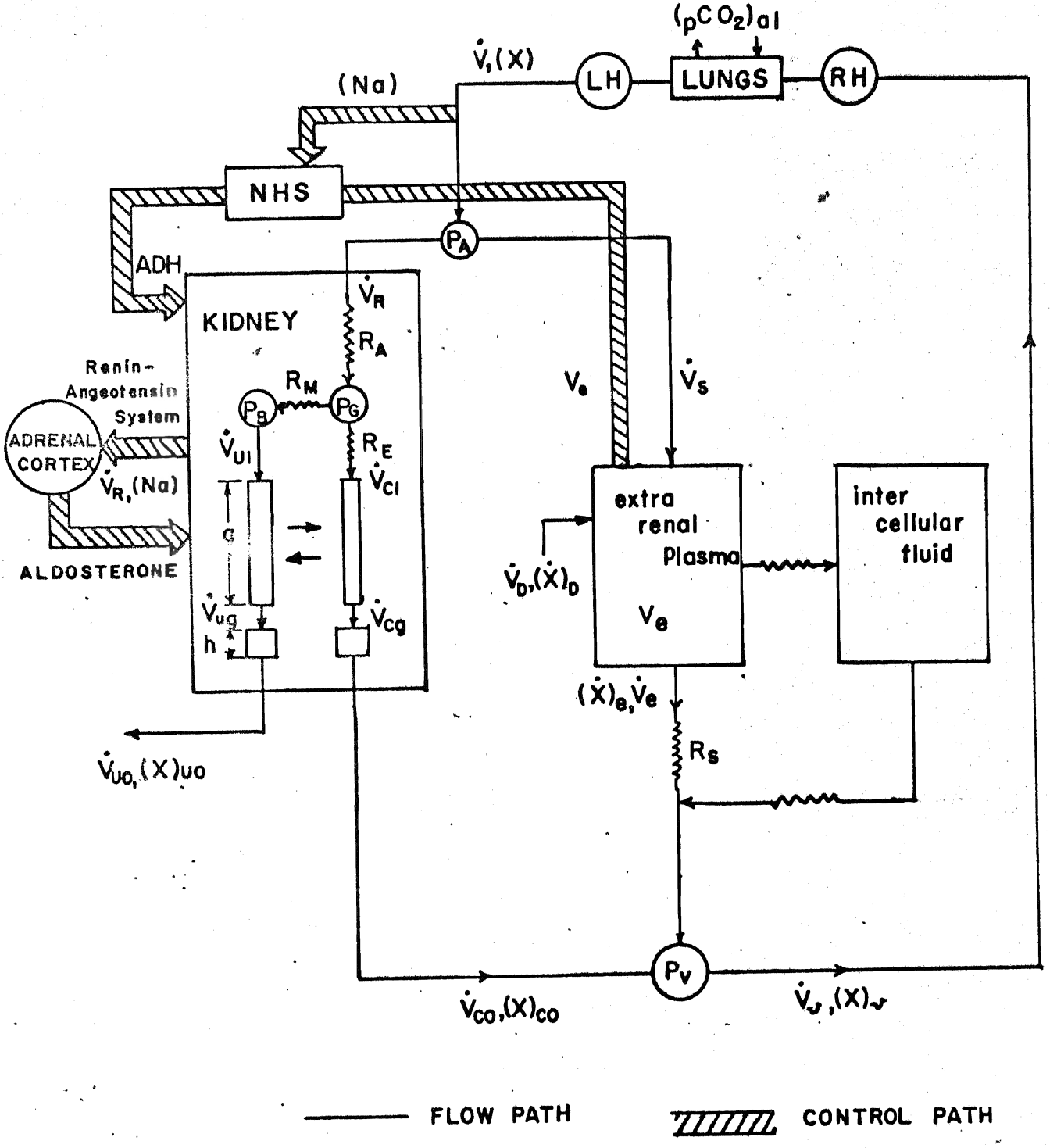
= emperical constant appearing in equation 17

and β_2 = emperical constants appearing in equation 19

and γ_2 = emperical constants appearing in equation 20

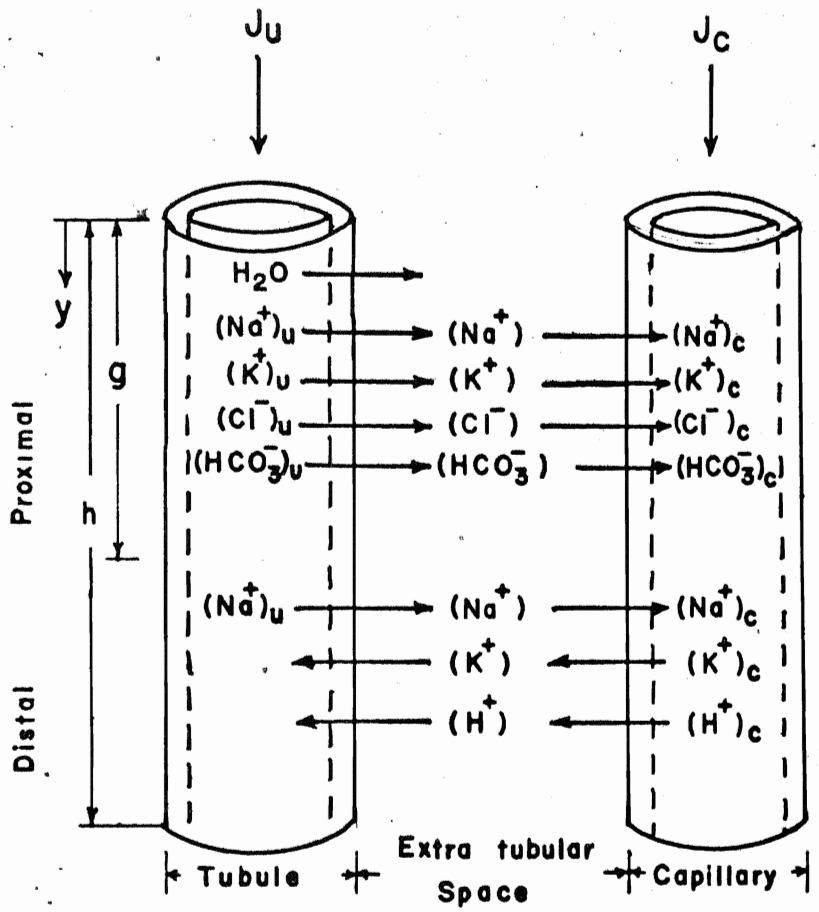
= transtubular potential gradient

= mobility constant



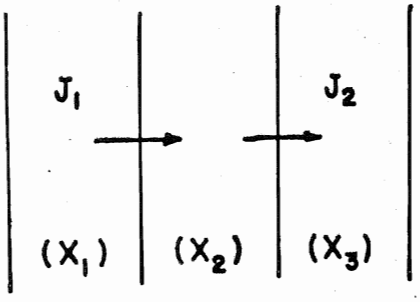
The renal-electrolyte control system showing the regulation due to ADH secreted by the neurohypophysis (NHS) and aldosterone.

Fig. 1



The ionic transport and exchanges occurring in the proximal and distal tubules.

Fig. 2



Three compartment model with fluxes J_1 and J_2 and steady state concentrations (X_i).

Fig.3