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SUBJECT

A Simple Model of Fluid Flow and Electrolyte Balance in the Body

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A SIMPLE MODEL OF FLUID FLOW

AND

ELECTROLYTE BALANCE IN THE BODY

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I. INTRODUCTION

Mathematical modeling of various body functions is a relatively new area of scientific endeavor, dating back only about thirty years. The field of modeling of physiologic processes is interdisciplinary requiring expertise from diverse disciplines for its success. By its very nature, this type of modeling requires considerable pooling of knowledge from applied mathematics, chemistry and physiology. It is all too often true that experts in the area of physical science and experts in the area of life science have little in common that permits them to contribute meaningfully to the same research project. What is superficial or even trivial for one group may be abstruse for the other. It is only through a mutual understanding of the strengths and weaknesses of each group that work in the area of physiological modeling can bear fruit.

This simple model of fluid and electrolyte balance in the human system has been prepared in the hope that it will foster such mutual understanding between those developing models and those ultimately using similar models. The present model, a modification of a basic model[1] of the subsystems regulating fluid and electrolyte balance, allows one to follow the changes in the body accompanying oral ingestion of water. This dynamic model is able to qualitatively predict the changes in twenty-three variables for an average man after varied oral input loads. It is hoped that personnel not familiar with models may learn by actual usage what to expect from simple models and perhaps how to improve them.

II. THE MODEL

The model for fluid and electrolyte balance is a modification of an earlier developed model[1]. This model is basically a three compartment

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[1] Superscript refers to Table of References at end of report.

model, the three compartments being the plasma, interstitial fluid and cellular fluid. Sodium, potassium, chloride and urea are the only major solutes considered explicitly. The control of body water and electrolyte distribution is affected via drinking and hormone levels. Basically, the model follows the effect of various oral input water loads on solute and water distribution throughout the body. Figure 1 gives a flow diagram for the model.

Solute Distribution and Flow

The processes which govern water and solute flow between various compartments are diffusion, osmosis and ultrafiltration[2,3]. The normal osmolarity of the body fluid, O_T^o, is taken to be 300 mosmols/l and the normal total body water, V_T^o, is taken as 40 l. Initial amounts of solutes present are (in mosmols):

$Q_{NA}^o = 5200$, $Q_K^o = 224$, $Q_{CL}^o = 5424$, $Q_U^o = 200$ and $Q_S^o = 952$ where NA = sodium, K = potassium, CL = chloride, U = urea, and S = other solutes. It is assumed that initially the total solute is evenly distributed throughout the body and that the amount of solute in the cells does not change with time.

The solute loss rate through the feces, L_F, is assumed constant at 0.03 mosmols/min and similarly the solute loss rate from the lungs and skin, L_I, is taken as constant at 0.1 mosmols/min. The gain rates of the various solutes (from metabolism) are taken as constant and are (mosmols/min):

$A_{NA} = 0.206$, $A_K = 0.0424$, $A_{CL} = 0.248$, $A_U = 0.376$, and $A_S = 0.0403$. All solutes are assumed to enter the system through the plasma and diffuse into the interstitial space. Losses occur through the urine, feces, lungs and skin.

The material balance equations for the total solute in the plasma and interstitial spaces are (the cells are assumed to have a fixed quantity of solute):

$$\frac{d}{dt} Q_P = A_P^T - L_P^T \quad (1)$$

and

$$\frac{d}{dt} Q_{ISF} = A_{ISF}^T - L_{ISF}^T \quad (2)$$

where A_i^T and L_i^T represent total solute gain and loss rates from the relevant compartments. These gain and loss rates are (mosmols/min):

$$A_P^T = A_P^{ISF} + A_{NA} + A_K + A_{CL} + A_U + A_S, \quad (3)$$

$$L_P^T = L_P^{ISF} + L_U + L_F, \quad (4)$$

$$A_{ISF}^T = A_{ISF}^P, \quad (5)$$

and

$$L_{ISF}^T = L_{ISF}^P + L_I. \quad (6)$$

The diffusive gain rate of solute by the plasma from the interstitial space, A_P^{ISF}, is taken as zero. The diffusive loss of solute from the plasma to the interstitial space, L_P^{ISF}, is given by the Fick's law result

$$L_P^{ISF} = k_{56} (O_P - O_{ISF}) \quad (7)$$

where O_i represents the osmolar concentration of solutes in the plasma or interstitial space. The gain rate of solute by the interstitial space is taken to be the same as the loss rate of solute by the plasma to the interstitial space, since the cells do not lose solute in this model. Thus

$$A_{ISF}^T = L_P^{ISF}. \quad (8)$$

Similarly the loss rate L_{ISF}^P is assumed to be the same as the gain rate A_P^{ISF} which is zero. Note that $A_P^T = 0.913$ and $L_{ISF}^T = 0.1$ mosmols/min.

The total urinary loss rate of solute is given by the sum of the loss rates for the individual species considered. Thus

$$L_U = l_{NA} + l_K + l_{CL} + l_U + l_S \tag{9}$$

where l_i is the urinary loss rate of species i. The assumption is made that l_S is constant

$$l_S = 0.03 \text{ mosmols/l.} \tag{10}$$

Sodium and potassium loss rates are assumed to be controlled by the aldosterone level in the plasma. An additional controlling factor for sodium is the body level of sodium. Note that potassium level does not influence potassium loss directly. It does have an indirect influence by affecting aldosterone production. Hence

$$l_{NA} = M_1 \; O^T_{NA} - M_2 \; O_A \tag{11}$$

where M_1 and M_2 are constants and O^T_{NA} is the osmolarity of sodium in the body, $O^T_{NA} = \frac{Q_{NA}}{V_T}$, and O_A is the aldosterone level (in the plasma). For potassium loss

$$l_K = M_3 \; O_A \tag{12}$$

where M_3 is constant. Loss of chloride is taken as passive loss caused by charge balance

$$l_{CL} = l_{NA} + l_K. \tag{13}$$

Urea loss rate is assumed to depend on the osmolarity of urea in the body and the urinary excretion rate of water. The relationship used is

$$l_U = k_1 \left\{ 1 + k_2 \left(1 - e^{-k_3 \lambda^U_P}\right) \right\} O_U \tag{14}$$

where O_U is the osmolarity of urea in the body, $O_U = \frac{Q_U}{V_T}$, and λ^U_P is the urinary excretion rate of water (discussed in Section III).

Material balance is required for the individual solutes just as for the total solute. The relevant equations are

$$\frac{d}{dt} Q_{NA} = A_{NA} - l_{NA} - (L_F + L_I) \frac{Q_{NA}}{Q_T}, \tag{15}$$

$$\frac{d}{dt} Q_K = A_K - l_K - (L_F + L_I) \frac{Q_K}{Q_T}, \tag{16}$$

$$\frac{d}{dt} Q_{CL} = A_{CL} - l_{CL}, \tag{17}$$

$$\frac{d}{dt} Q_U = A_U - l_U - (L_F + L_I) \frac{Q_U}{Q_T}, \tag{18}$$

and

$$\frac{d}{dt} Q_S = A_S - l_S - (L_F + L_I) \frac{Q_S}{Q_T}, \tag{19}$$

where Q_T is the total amount of solute in the body.

Water Distribution and Flow

Oral water ingestion is simulated via a two-compartment system which delays the entrance of water into the plasma. The two compartments, the stomach and intestines, are simply reservoirs from which water flows into the plasma. Thus

$$\frac{dV_S}{dt} = r_I - k_{11} V_S \tag{20}$$

and

$$\frac{dV_G}{dt} = k_{11} V_S - k_{12} V_G \tag{21}$$

where V_i is the water volume in compartment i (S = stomach, G = gut) and r_I is the input flow rate of water. This input flow rate is due to salivation and drinking, with drinking occurring only once at time T_0. Salivation is considered constant at 0.64 ml/min.

From the intestine water flows into the plasma. The assumption is made that the red cell volume is constant. The plasma is in direct contact with the interstitial space and water flow may also occur because of metabolism, urinary loss and fecal loss. The relevant flow equation is

$$\frac{dV_P}{dt} = \alpha_P^G + \alpha_P^{ISF} + \alpha_P^M - \lambda_P^{ISF} - \lambda_P^U - \lambda_P^F \tag{22}$$

where α_P^i represents a gain rate of water by the plasma from i and λ_P^i represents a corresponding loss rate. The superscripts have the meanings: G: gut, ISF: interstitial fluid, M: metabolism, U: urine, F: feces. The metabolic rate of volume gain is considered constant (1.0 ml/min) as is the fecal loss rate (0.1 ml/min). The gain rate from the intestines is

$$\alpha_P^G = k_{12} V_G \tag{23}$$

Water flow between the plasma and interstitial space is assumed to occur by lymph flow and by filtration at the arterial end and reabsorption at the venous end.[3] The lymph flow rate is taken as constant, $\alpha_P^L = 1.7$ ml/min, and the flow into the plasma from the interstitial space is thus

$$\alpha_P^{ISF} = \alpha_P^L + k_{13} (P_{ISF} - P_V + \pi_P - \pi_{ISF}) \tag{24}$$

where k_{13} is constant, P_{ISF} is the hydrostatic pressure of the interstitial space, P_V is the venous capillary hydrostatic pressure, π_P is the plasma colloid osmotic pressure and π_{ISF} is the interstitial space colloid osmotic pressure. Similarly filtration is given by:

$$\lambda_P^{ISF} = k_{14} (P_A - P_{ISF} + \pi_{ISF} - \pi_P) \tag{25}$$

where k_{14} is assumed to equal k_{13} and P_A is the arterial capillary hydrostatic pressure. P_A is considered to vary linearly with the total blood volume (red cell volume plus plasma volume)

$$P_A = k_{15} V_B \tag{26}$$

where $V_B = V_P + V_R$ with V_R, the volume of the red cells, fixed at 2.0 l.

$$P_V = k_{16} V_B. \tag{27}$$

P_{ISF} is taken to be normally negative and is assumed to vary linearly with the volume of the interstitial space

$$P_{ISF} = P^o_{ISF} + k_{17}\,(V_{ISF} - V^o_{ISF}) \tag{28}$$

where $P^o_{ISF} = -7$ mm Hg and $V^o_{ISF} = 12000$ ml. The interstitial oncotic pressure, π_{ISF}, is taken as constant (4.5 mm Hg), but the plasma oncotic pressure, π_P, is assumed to depend linearly on the plasma protein concentration

$$\pi_P = X/V_P \tag{29}$$

where X is related to the amount of plasma protein. X is initially taken to be constant but whenever π_P drops below 26 mm Hg (by V_P increasing) protein is produced at a fixed rate

$$\frac{dX}{dt} = k_{18} \tag{30}$$

until π_P exceeds 26 mm Hg.

The urinary loss rate of water from the plasma, λ^U_P, is assumed to depend on the vasopressin (ADH) level in the plasma, C_{ADH} $(= Q_{ADH}/V_P)$, and on the rate of solute excretion. The kidney is assumed to have different responses to ADH levels depending on past experiences. A sensitivity parameter Z is created with

$$\frac{d}{dt}\,Z = Z_1. \tag{31}$$

If $Z_1 > 0$, the urine flow rate of water due to ADH effect is

$$\lambda^U_{P,1} = \frac{k_{19}}{k_{20} + C_{ADH}} \tag{32}$$

but if $Z_1 \leq 0$ this rate increases to

$$\lambda^U_{P,1} = \frac{k_{19}}{k_{20} + C_{ADH}} - Z_1\,\left(k_{21} + \frac{k_{22}}{k_{20} + C_{ADH}}\right). \tag{33}$$

The parameter Z_1 has a time-delay mechanism

$$Z_1(t) = Q_{ADH}(t) - k_{23} \; Z(t-\tau) \tag{34}$$

with $\tau = 1$ min. The total urinary loss rate of water is, taking solute excretion into account

$$\lambda_P^U = \lambda_{P,1}^U + k_{24} L_U \tag{35}$$

where L_U is given by Eqn. (9).

For the interstitial space the analogue to Eqn. (22) is

$$\frac{dV_{ISF}}{dt} = \alpha_{ISP}^P - \lambda_{ISF}^P - \lambda_{ISF}^{ICF} - \lambda_{ISF}^I \tag{36}$$

where α_{ISF}^P is the gain rate in interstitial fluid from the plasma, λ_{ISF}^P is the corresponding loss rate to the plasma, λ_{ISF}^{ICF} is the osmotic flow rate to the cells, and λ_{ISF}^I is the insensible loss rate through the skin and lungs. λ_{ISF}^I is taken as constant (0.5 ml/min), $\alpha_{ISF}^P = \lambda_P^{ISF}$, and $\lambda_{ISF}^P = \alpha_P^{ISF}$. The rate of volume flow due to osmotic flow to the cells is given by Fick's law

$$\lambda_{ISF}^{ICF} = k_{25} \left(O_{ICF} - O_{ISF}\right) \tag{37}$$

where O_i represents the total osmolarity of i in mosmols/l.

Aldosterone Production

Aldosterone is assumed to be produced via a renin, angiotensin, aldosterone mechanism sensitive to blood volume and potassium level. All three of these substances are considered to be produced by similar means. For aldosterone the relevant expression is

$$\frac{d}{dt} Q_A = k_4 \frac{Q_G}{V_P} + k_5 \frac{Q_K}{V_T} - k_6 Q_A. \tag{38}$$

Q_i represents the quantity of i (A = aldosterone, G = angiotensin, K = potassium, R = renin). For angiotensin the rate equation is

$$\frac{d}{dt} Q_G = k_7 \frac{Q_R}{V_P} - k_8 Q_G. \tag{39}$$

For renin the production rate is taken as zero if the blood volume, V_B, exceeds 7000 ml. Otherwise

$$\frac{d}{dt} Q_R = k_9 \, (B_1 - V_B) - k_{10} \, Q_R \tag{40}$$

where $B_1 = 7000$ ml.

Vasopressin (ADH) Production

The production of ADH is assumed to depend on the blood volume and the plasma osmolarity. The time delay involved in ADH production is simulated by requiring flow through five hypothetical states between initiation of production and flow into the plasma. The rate equations for these five states are

$$\frac{dQ_1}{dt} = K(P_{ADH} - Q_1),$$

$$\frac{dQ_2}{dt} = K \, (Q_1 - Q_2) \; ,$$

$$\frac{dQ_3}{dt} = K \, (Q_2 - Q_3) \; ,$$

$$\frac{dQ_4}{dt} = K \, (Q_3 - Q_4) \; , \tag{41}$$

and

$$\frac{dQ_{ADH}}{dt} = Q_4 - k_{26} \, Q_{ADH}$$

where

$$K = \frac{8}{40 + C_{ADH}}$$

with $C_{ADH} = Q_{ADH}/V_P$

The initial production rate, P_{ADH}, has two components

$$P_{ADH} = p_1 + p_2 \tag{42}$$

where p_1 is the production rate due to blood volume and p_2 is the production rate due to plasma osmolarity. In both cases p_i is taken as non-negative. The form of p_1 is

$$p_1 = k_{27} - k_{28}\Delta_1 - k_{29} \exp(k_{30}\Delta_1) \tag{43}$$

where

$$\Delta_1 = \frac{V_P - V_P^o}{V_B} .$$

The rate p_2 has the form

$$p_2 = k_{31} + k_{32}\Delta_2 - k_{33} \exp(-k_{34}\Delta_2) \tag{44}$$

where

$\Delta_2 = O_P - O_T^o$ (O_T^o is the normal total body osmolarity).

III. NUMERICAL METHODS

Most of the equations of the preceding section are differential and require approximation if a numerical solution is to be obtained. With the exception of Eqns (20) and (21) which are solved exactly, all of the differential equations are solved by using Euler's method. This method has severe limitations as to both accuracy and stability, but it is a very simple method to use and probably does not lead to serious error during the meaningful time durations being examined by the model. The results, however, should be interpreted qualitatively, not quantitatively.

The general form of the differential equations encountered in section II is

$$\frac{d}{dt}y = f(t,y) \tag{45}$$

with some initial condition $y(t_o)$ specified. Euler's method generates $y(t_1)$ where $t_1 = t_o + h$, with h being a fixed parameter called the step size. The function y is assumed analytic in the vicinity of t_o (y has a Maclaurin expansion) so that

$$y\,(t_o + h) = y\,(t_o) + h\,y'\,(t_o) + \frac{h^2}{2}\,y''\,(t_o) + \ldots \quad (46)$$

and h is assumed small enough so that the terms beyond first order in h may be neglected. This gives

$$y\,(t_o + h) = y\,(t_o) + h\,y'\,(t_o). \quad (47)$$

The Eqn (45) is used to calculate $y'\,(t_o)$

$$y'\,(t_o) = f\left(t_o,\ y(t_o)\right) \quad (48)$$

and this is used in Eqn (47) resulting in

$$y\,(t_o + h) = y\,(t_o) + h\,f\left(t_o,\ y\,(t_o)\right). \quad (49)$$

This process is repeated until $y(t)$ is generated for the t desired.

In this work h = 1 min. and the reported values of the y are at 10 minute intervals.

IV. THE USE OF THE PROGRAM

A Fortran IV version of this model is listed in Appendix A. This program simulates the changes in levels of the twenty-three quantities listed in Table 1 when a person of average size consumes a quantity of water after having no oral water intake for six hours.

The user of the program may select as many as nine of the twenty-three quantities and have their levels printed out in column form at ten minute increments after consumption of the water (sixty minute increments before consumption).

The program is presently designed to use cards as the input mechanism and printed page (132 columns) as the output mechanism. Each data card should have an integer right justified in card column 5. The integer in the first data card tells the quantity of water consumed (in milliliters). The integer in column 5 of the second data card tells how many (from 1 to 9) columns of information are requested. Then that number of data cards follows, one for each column of information requested, arranged in the order in which the user wants the columns to be printed. Each of these remaining data cards should have an integer from one to twenty-three right justified to card column 5 together with any appropriate column heading (preferably centered) in columns 10 thru 17 for the quantity which that integer represents, according to the list in Table 1.

The output will consist of a statement of the quantity of water consumed followed by the column headings which the user selected (in the order in which the data cards are arranged) and the levels of these quantities at ten minute increments after the water is consumed. The output may be considered accurate to at most three significant figures in spite of the figures given.

REFERENCES

1. The basic model was constructed by Thomas G. Cleaver of the University of Louisville.

2. P. H. Abbrecht, Compartments and Body Fluids, Biomed. Engrg. XX:161, 1971.

3. C. A. Widerhielm, Dynamics of Transcapillary Fluid Exchange, Journal Gen. Physiol. 52:29s, 1968.

APPENDIX A

A Fortran IV Version of a Model which Simulates Fluid and Electrolyte Balance in the Body.

```
C      AFTER FASTING FOR 6 HOURS, THE SUBJECT CONSUMES A GIVEN
C      QUANTITY OF WATER.  SPECIFY THIS QUANTITY IN ML AS AN
C      INTEGER RIGHT JUSTIFIED IN COLUMN 5 OF THE FIRST DATA
C      CARD.
C
C      FROM THE FOLLOWING LIST YOU MAY SELECT AS MANY AS NINE OF
C      THE TWENTY-THREE QUANTITIES THAT YOU ARE INTERESTED IN.
C      THE PRINT OUT WILL CONSIST OF A COLUMN OF THE INDEPENDENT
C      TIME VARIABLE IN TEN MINUTE INCREMENTS AFTER CONSUMPTION
C      (60 MIN INCREMENTS BEFORE CONSUMPTION) FOLLOWED BY
C      COLUMNS OF THE INFORMATION THAT YOU REQUEST, IN THE ORDER
C      IN WHICH THEY ARE REQUESTED, AT EACH TEN MINUTE
C      INCREMENT.  THE INPUT SHOULD CONSIST OF A SECOND DATA
C      CARD HAVING AN INTEGER FROM 1 TO 9 IN COLUMN 5 TELLING
C      HOW MANY QUANTITIES YOU SELECT, FOLLOWED BY THAT
C      NUMBER OF DATA CARDS, EACH HAVING AN INTEGER FROM 1
C      TO 23 RIGHT JUSTIFIED IN COLUMN 5 TOGETHER WITH ANY
C      APPROPRIATE COLUMN HEADING (PREFERABLY CENTERED) IN
C      COLUMNS 10 THRU 17 FOR THE QUANTITY WHICH THAT INTEGER
C      REPRESENTS, ACCORDING TO THE FOLLOWING LIST:
C       1 - VOL OF WATER IN STOMACH
C       2 - VOL OF WATER IN INTESTINES
C       3 - VOL OF WATER IN PLASMA
C       4 - VOL OF WATER IN INTERSTITIAL FLUID
C       5 - VOL OF WATER IN CELL FLUID
C       6 - TOTAL WATER VOLUME IN PLASMA, INTERSTITIAL SPACE,
C           AND CELLS
C       7 - RATE OF PRODUCTION OF URINE
C       8 - TOTAL SOLUTE IN PLASMA
C       9 - TOTAL SOLUTE IN INTERSTITIAL FLUID
C      10 - TOTAL SOLUTES IN PLASMA, INTERSTITIAL SPACE,
C           AND CELLS
C      11 - RATE OF PRODUCTION OF SOLUTES IN URINE
C      12 - ADH
C      13 - RENIN
C      14 - ANGIOTENSIN
C      15 - ALDOSTERONE
C      16 - SODIUM LOSS
C      17 - POTASSIUM LOSS
C      18 - CHLORIDE LOSS
C      19 - UREA LOSS
C      20 - PLASMA OSMOLARITY
C      21 - INTERSTITIAL FLUID OSMOLARITY
C      22 - CELL FLUID OSMOLARITY
C      23 - URINE OSMOLARITY
C
C      VOLUME IS GIVEN IN ML, TIME IN MINUTES, AMOUNTS OF SOLUTE
C      IN MILLIOSMOLS, AND OSMOLARITY IN MILLIOSMOLS/LITER
C
C**** THIS IS THE PROGRAM FOR BODY WATER AND ELECTROLYTE
C**** BALANCE.  VARIABLES AND CONSTANTS USED IN THIS PROGRAM
C**** WILL BE USED ACCORDING TO THE FOLLOWING FORMAT.
```

```
C**** ALPHABETIC VARIABLES AND CONSTANTS
C**** A - ALDOSTERONE
C**** B - BLOOD VOLUME
C**** C - CHLORIDE
C**** D - DELTA T (THE INTEGRATING TIME INTERVAL)
C**** E - ERYTHROCYTE VOLUME
C**** F
C**** G - ANGIOTENSIN
C**** H - ADH
C**** I - CONSTANTS RELATED TO CAPILLARIES
C**** J - CONSTANTS RELATED TO CELL-INTERSTITIAL INTERFACE
C**** K - POTASSIUM (MILLIOSMOLS)
C**** L - CONSTANTS RELATED TO ADH PRODUCTION
C**** M - CONSTANTS RELATED TO ALDOSTERONE PRODUCTION
C**** N - SODIUM (MILLIOSMOLS)
C**** O - OSMOLARITY (MILLIOSMOLS/LITER)
C**** P - PRESSURE (MILLIMETERS OF MERCURY)
C**** Q - TOTAL SOLUTE (MILLIOSMOLS)
C**** R - RENIN
C**** S - SOLUTE OTHER THAN NA, K, CL, U (MILLIOSMOLS)
C**** T - TIME CONSTANT OR TIME (MINS)
C**** U - UREA (MILLIOSMOLS)
C**** V - VOLUME (MILLILITERS)
C**** W - CONSTANTS RELATED TO THE KIDNEY
C**** X - PLASMA PROTEIN
C**** Y - CONSTANTS RELATING URINE OUTPUT TO UREA OUTPUT
C**** Z - A MEASURE OF KIDNEY SENSITIVITY TO ADH
C**** SUBSCRIPTS
C**** 0 - AVERAGE, DESIRED OR REFERENCE VALUE
C**** 1 - D/DT (TIME DERIVATIVE)
C**** 2 - EXTERNAL INPUT OR OUTPUT
C**** 3 - STOMACH
C**** 4 - INTESTINE
C**** 5 - PLASMA
C**** 6 - INTERSTITIAL FLUID
C**** 7 - CELL FLUID
C**** 8 - URINE
C**** 9 - OTHER
C
C     NOMLWC IS THE NUMBER OF ML. OF WATER CONSUMED.
      READ (5,2000) NUMLWC
 2000 FORMAT(I5)
      WRITE (6,2010) NUMLWC
 2010 FORMAT(34X,'AFTER FASTING FOR 6 HOURS, THE SUBJECT'
     *' COMSUMES'I5,1X,'ML OF WATER.'/)
C     VWC = VOLUME OF WATER CONSUMED = NOMLWC
      VWC=NUMLWC
      REAL  L0,L1,L2,L3,L4,L5,M1,M2,M3,M4,M5,M6,M7,M8,N3,K3,N2
      REAL  V(167),Q(167),O(9),N,K,I1,I2,I3,I4,I5,I6,J,K2,N1
      REAL  K34,K45
C
      DIMENSION COL(23), ALPHA(9), BETA(9)
```

```
C      NOREQ = NUMBER OF COLUMNS OF INFORMATION REQUESTED
       READ (5,2200) NOREQ
 2200  FORMAT(I5)
C***************** INITIALIZE VARIABLES AND DEFINE CONSTANTS **
C****
C**** THE SUBJECT TAKES A DRINK OF WATER AT TIME T5
       T5 = 361.
C**** V(50), V(60) AND V(70) ARE THE NORMAL VALUES OF THE
C**** PLASMA, INTERSTITIAL FLUID AND CELLS, RESPECTIVELY IN ML
C      ACCORDING TO GUYTON'S TEXTBOOK OF MEDICAL PHYSIOLOGY,
C      V(50)=3000, V(60)=12000, V(70)=25000, AND E=2000 ML.
C      V(50) = 3200.
       V(50) = 3000.
C      V(60) = 13800.
       V(60) = 12000.
C      V(70) = 28000.
       V(70) = 25000.
C**** OO IS THE NORMAL OSMOLARITY OF BODY FLUID IN MOSMOL/LITER
       OO = 300.
C**** V(90) IS NORMAL TOTAL BODY WATER
       V(90)=V(50)+V(60)+V(70)
C**** D IS THE INTEGRATING INTERVAL IN MINUTES
       D=1.
C**** V(23) IS THE INPUT WATER LOAD
C      V(23)=.64
C      .64 ML/MIN OF WATER ARE SWALLOWED IN SALIVA.
       RATE=.64
C**** N, K, C, AND U ARE THE TOTAL AMOUNTS OF THE SOLUTES NA,
C**** K, CL AND UREA DISSOLVED IN THE BODY FLUIDS, RESPECTIVELY
C***************** GENERAL ***************************************
       N=V(90)*130./1000.
       K=V(90)*5.1/1000.
       C=N+K
       U=V(90)*5.0/1000.
C**** S IS ALL OTHER SOLUTES IN THE BODY FLUID
       S=(OO/1000.)*V(90)-N-K-C-U
C**** Q(9) IS THE TOTAL INITIAL SOLUTE IN THE BODY
       Q(9)=N+K+C+U+S
C**** V(34) IS THE VOLUME THAT HAS FLOWED FROM STOMACH TO
C**** INTESTINE IN ML
C***************** STOMACH ***************************************
C      V(34)=0.
       T3=20.
       K34=1./T3
C***************** GUT *******************************************
C      V(45)=0.
       T4=18.
       K45=1./T4
C***************** BLOOD *****************************************
       V(156)=0.
       V(165)=0.
       V(18)=0.
```

```
      V(159)=.1
      V(125)=1.
      V(5)=V(50)
      Q(156)=0.
      Q(165)=0.
      Q(18)=0.
      Q(159)=U0*V(159)/1000.
      Q(5)=Q(9)*V(50)/V(90)
C***************** INTERSTITIAL FLUID *************************
      V(167)=0.
      V(162)=.5
      Q(162)=.2*V(162)
      V(6)=V(60)
      Q(6)=Q(9)*V(60)/V(90)
C***************** CELLS ***************************************
      V(7)=V(70)
      Q(7)=Q(9)*V(70)/V(90)
C***************** CAPILLARIES *********************************
C     F=3000.
      E=2000.
      P0=E+V(50)
      I1=25.3/80
      I2=9.0/80
      P6=-7.
      I3=1./280.
      X2=63.
      P7=26.
      X=28.0*V(50)
      I4=1.7
      P5=4.5
      I5=1.7
      I6=1400.
C***************** ADH *****************************************
      J=400.
      L0=.9
      L1=20.
      L2=90./L0
      L3=U0
      L4=.2
      L5=1440./L0
      H6=600.
      H7=H6
      H8=H6
      H9=H6
      H5=5.0*V(50)
      T9=24.4
C***************** ALDOSTERONE *********************************
      R1=7000.
      T0=100.
      T1=T0
      T2=T0
      R1=V(50)
```

```
      M2=V(50)
      M3=V(50)
      M4=(.755-.148)/(T0*T1*T2*(B1-B0))
      R2=M1*(B1-B0)*T0
      G2=R2*M2*T1/V(50)
      A2=G2*M3*T2/V(50)
      M6=.04/((B1-B0)*T0*T1*T2)
      M7=(1.0/.0051)*A2/T2
      M8=.5
      M5=.755*V(90)/N
C****************** KIDNEY ****************************************
      H=5.
      T8=180.
      Z=H*T8
      W1=3.
      W2=.4
      W3=.8
      Y1=50.
      Y2=1.5
      Y3=.3
      N3=.15+0.13*N/Q(9)
      K3=.04+0.13*K/Q(9)
      C3=N3+K3
      U3=.32+0.13*N/Q(9)
      S3=.03+0.13*S/Q(9)
      Q(125)=N3+K3+C3+U3+S3
      N2=0.
      K2=N2
      U2=N2
      C2=N2
      S2=.03
C****************** STOMACH ***************************************
C     DO 3900 NT=1,1701
      DO 3900 NT=1,1061
      T=NT
C     IF (T-T5) 2230,2220,2220
C2220 V(23)=1500
C2230 V(3)=V(23)-V(34)
      V(3)=(RATE/K34)*(1.-EXP(-K34*T))
      IF (T-T5) 2230,2220,2220
 2220 V(3)=V(3)+VWC*EXP(-K34*(T-T5))
C     V(134)=V(3)/T3
C     V(34)=V(34)+V(134)*D
C****************** GUT*******************************************
C     V(4)=V(34)-V(45)
 2230 V(4)=(K34*RATE/(K45-K34))*((1./K34)*(1.-EXP(-K34*T))-
     *                 (1./K45)*(1.-EXP(-K45*T)))
      IF(T-T5) 2250,2240,2240
 2240 V(4)=V(4)+(K34*VWC/(K45-K34))*(EXP(-K34*(T-T5))-
     *                 EXP(-K45*(T-T5)))
C     V(145)=V(4)/T4
 2250 V(145)=V(4)/T4
```

```
C      V(45)=V(45)+V(145)*D
C***************** BLOOD ******************************************
      V(15)=V(145)+V(165)-V(156)-V(18)+V(125)-V(159)
      V(5)=V(5)+V(15)*D
      Q(15)=Q(165)-Q(156)-Q(18)+Q(125)-Q(159)
      Q(5)=Q(5)+Q(15)*D
      U(5)=Q(5)*1000./V(5)
C***************** INTERSTITIAL SPACE *************************
      V(16)=V(156)-V(165)-V(167)-V(162)
      V(6)=V(6)+V(16)*D
      Q(16)=Q(156)-Q(165)-Q(162)
      Q(6)=Q(6)+Q(16)*D
      U(6)=Q(6)*1000./V(6)
C***************** CELLS ******************************************
      V(17)=V(167)
      V(7)=V(7)+V(17)*D
      U(7)=Q(7)*1000./V(7)
C***************** CAPILLARIES ************************************
      V(9)=V(5)+V(6)+V(7)
      B=E+V(5)
      P1=I1*B
      P2=I2*B
      P3=P6+I3*(V(6)-V(60))
      P4=X/V(5)
      IF (P4-P7) 2790,2800,2800
 2790 X=X+X2*D
 2800 V(156)=I4*(P1-P3-P4+P5)**2/(P1-P2)
      V(165)=I4*(P2-P3-P4+P5)**2/(P1-P2)+I5
      Q(156)=I6*(U(5)-U(6))/1000.
C***************** CELL-INTERSTITIAL INTERFACE ***************
      V(167)=J*(U(7)-U(6))/1000.
C***************** ADH ********************************************
      H1=(1.-L0)*(L2*(B0*U0/B+L1-U0)-L5*EXP(L4*(L3-B0*U0/B)))
      H2=L0*(L2*(U(5)+L1-U0)-L5*EXP(L4*(L3-U(5))))
      IF (H2) 3040,3050,3050
 3040 H2=0.
 3050 IF (H1) 3060,3070,3070
 3060 H1=0.
 3070 H3=H1+H2
      T6=20.0+H/2.
      H6=H6+(H3-H6)*D*4.0/T6
      H7=H7+(H6-H7)*D*4.0/T6
      H8=H8+(H7-H8)*D*4.0/T6
      H9=H8+(H8-H9)*D*4.0/T6
      H5=H5+(H9-H5/T9)*D
      H=H5/V(5)
C***************** ANGIOTENSIN *********************************
      R1=M1*(B1-B)
      IF (R1) 3316,3320,3320
 3316 R1=0.
 3320 R2=R2+(R1-R2/T0)*D
      R=R2/V(5)
```

```
      G1=M2*G
      G2=G2+(G1-G2/T1)*D
      G=G2/V(5)
      A1=M8*M3*G+(1.0-M8)*M7*K/V(9)
      A2=A2+(A1-A2/T2)*D
      A=A2/V(5)
      N1=M4*A
      N2=M5*N/V(9)-N1
      IF (N2) 3430,3440,3440
 3430 N2=0.
 3440 K2=M6*A
C****************** KIDNEY *************************************
      Z1=H-Z/T8
      Z=Z+Z1*D
      IF (Z1) 3530,3530,3527
 3527 Z1=0.
 3530 V(18)=W1/(W2+H)+(.05+1.0/(W2+H))*(-Z1)*W3
      IF (V(18)) 3550,3560,3560
 3550 V(18)=0.
 3560 U2=Y1*(1.0+Y2*(1.0-EXP(-Y3*V(18))))*U/V(9)
      C2=N2+K2
      Q(18)=N2+K2+C2+U2+S2
      V(18)=V(18)+Q(18)*1000./1600.
      U2=Y1*(1.0+Y2*(1.0-EXP(-Y3*V(18))))*U/V(9)
      Q(18)=N2+K2+S2+U2+C2
      Q([illegible])=Q(18)*1000./V(18)
      Q8=(Q(159)+Q(162))/Q(9)
      N=N+(N3-N2-N*Q8)*D
      K=K+(K3-K2-K*Q8)*D
      C=C+(C3-C2)*D
      U=U+(U3-U2-U*Q8)*D
      S=S+(S3-S2-S*Q8)*D
      V(9)=N+K+C+U+S
C****************** PRINT OUT ***********************************
      COL(1)=V(3)
      COL(2)=V(4)
      COL(3)=V(5)
      COL(4)=V(6)
      COL(5)=V(7)
      COL(6)=V(9)
      COL(7)=V(18)
      COL(8)=Q(5)
      COL(9)=Q(6)
      COL(10)=Q(9)
      COL(11)=Q(18)
      COL(12)=H
      COL(13)=R
      COL(14)=G
      COL(15)=A
      COL(16)=N2
      COL(17)=K2
      COL(18)=C2
```

```
      COL(19)=U2
      COL(20)=D(5)
      COL(21)=D(6)
      COL(22)=D(7)
      COL(23)=D(9)
      IF(T-1.) 3700,3605,3700
 3605 DO 3619 IT=1,NOREQ
      READ (5,3610) NUMBER, ALPHA(IT),BETA(IT)
 3610 FORMAT(I5,4X,2A4)
      GO TO (3611,3612,3613,3614,3615,3616,3617,3618,3619),IT
 3611 NC1=NUMBER
 3612 NC2=NUMBER
 3613 NC3=NUMBER
 3614 NC4=NUMBER
 3615 NC5=NUMBER
 3616 NC6=NUMBER
 3617 NC7=NUMBER
 3618 NC8=NUMBER
 3619 NC9=NUMBER
      GO TO(3621,3622,3623,3624,3625,3626,3627,3628,3629),NOREQ
 3621 WRITE (6,3631) ALPHA(1),BETA(1)
      GO TO 3700
 3622 WRITE(6,3632) (ALPHA(IS),BETA(IS), IS=1,2)
      GO TO 3700
 3623 WRITE(6,3633) (ALPHA(IS),BETA(IS), IS=1,3)
      GO TO 3700
 3624 WRITE(6,3634) (ALPHA(IS),BETA(IS), IS=1,4)
      GO TO 3700
 3625 WRITE(6,3635) (ALPHA(IS),BETA(IS), IS=1,5)
      GO TO 3700
 3626 WRITE(6,3636) (ALPHA(IS),BETA(IS), IS=1,6)
      GO TO 3700
 3627 WRITE(6,3637) (ALPHA(IS),BETA(IS), IS=1,7)
      GO TO 3700
 3628 WRITE(6,3638) (ALPHA(IS),BETA(IS), IS=1,8)
      GO TO 3700
 3629 WRITE(6,3639) (ALPHA(IS),BETA(IS), IS=1,9)
 3631 FORMAT(57X,'TIME'7X,2A4/)
 3632 FORMAT(50X,'TIME'7X,2A4,6X,2A4/)
 3633 FORMAT(43X,'TIME'7X,2A4,2(6X,2A4)/)
 3634 FORMAT(36X,'TIME'7X,2A4,3(6X,2A4)/)
 3635 FORMAT(29X,'TIME'7X,2A4,4(6X,2A4)/)
 3636 FORMAT(22X,'TIME'7X,2A4,5(6X,2A4)/)
 3637 FORMAT(15X,'TIME'7X,2A4,6(6X,2A4)/)
 3638 FORMAT( 8X,'TIME'7X,2A4,7(6X,2A4)/)
 3639 FORMAT( 1X,'TIME'7X,2A4,8(6X,2A4)/)
C     F1=T-1.
 3700 F1=T-1.
      IF (T-(T5-10.)) 3720,3740,3740
 3720 F2=F1/60.
C     F6=F1
      GO TO 3750
```

```
 3740 F2=F1/10.
C     F6=T-T5
C3750 IF3=F2
 3750 IF6=T-T5
      IF3=F2
      F3=IF3
      F4=F3-F2
      IF (F4) 3900,3800,3900
 3800 GO TO(3801,3802,3803,3804,3805,3806,3807,3808,3809),NOREQ
C3800 WRITE (6,3810) F6,V(5),D(5),V(18),D(8),H
C3800 WRITE (108,3810) F6,V(5),D(5),V(18),D(8),H
C3810 FORMAT (6F15.5)
 3801 WRITE (6,3811) IF6,COL(NC1)
      GO TO 3900
 3802 WRITE (6,3812) IF6,COL(NC1),COL(NC2)
      GO TO 3900
 3803 WRITE (6,3813) IF6,COL(NC1),COL(NC2),COL(NC3)
      GO TO 3900
 3804 WRITE (6,3814) IF6,COL(NC1),COL(NC2),COL(NC3),COL(NC4)
      GO TO 3900
 3805 WRITE (6,3815) IF6,COL(NC1),COL(NC2),COL(NC3),COL(NC4),
     *COL(NC5)
      GO TO 3900
 3806 WRITE (6,3816) IF6,COL(NC1),COL(NC2),COL(NC3),COL(NC4),
     *COL(NC5),COL(NC6)
      GO TO 3900
 3807 WRITE (6,3817) IF6,COL(NC1),COL(NC2),COL(NC3),COL(NC4),
     *COL(NC5),COL(NC6),COL(NC7)
      GO TO 3900
 3808 WRITE (6,3818) IF6,COL(NC1),COL(NC2),COL(NC3),COL(NC4),
     *COL(NC5),COL(NC6),COL(NC7),COL(NC8)
      GO TO 3900
 3809 WRITE (6,3819) IF6,COL(NC1),COL(NC2),COL(NC3),COL(NC4),
     *COL(NC5),COL(NC6),COL(NC7),COL(NC8),COL(NC9)
 3811 FORMAT(57X,I4, F14.2)
 3812 FORMAT(50X,I4,2F14.2)
 3813 FORMAT(43X,I4,3F14.2)
 3814 FORMAT(36X,I4,4F14.2)
 3815 FORMAT(29X,I4,5F14.2)
 3816 FORMAT(22X,I4,6F14.2)
 3817 FORMAT(15X,I4,7F14.2)
 3818 FORMAT( 8X,I4,8F14.2)
 3819 FORMAT( 1X,I4,9F14.2)
 3900 CONTINUE
      STOP
      END
```

TABLE 1. POSSIBLE OUTPUTS OBTAINABLE WITH THIS MODEL

(ƀ means blank space.)

Number (Columns 4 & 5)	Suggested Headings (Columns 10 thru 17)	Quantity (Units)
1	BELLYƀVƀ	Vol. of water in stomach (ML)
2	ƀGUTƀVƀƀ	Vol. of water in intestines (ML)
3	PLASMAƀV	Vol. of water in plasma (ML)
4	INTERSƀV	Vol. of water in interstitial space (ML)
5	CELLƀFƀV	Vol. of water in cell fluid (ML)
6	TOTALƀVƀ	Total water vol. in above 3 (ML)
7	UƀML/MIN	Rate or production of urine (ML/MIN)
8	PLASMAƀS	Total solute in plasma (m Osmols)
9	INTERSƀS	Total solute in interstitial space (m Osmols)
10	ALLƀSOLƀ	Total solute in plasma, interstitial space and cells (m Osmols)
11	UƀSƀRATE	Rate of production of solutes in urine (m Osmols/Min)
12	ƀƀƀADHƀƀ	ADH
13	ƀRENINƀƀ	Renin
14	ANGIOTEN	Angiotensin
15	ALDOSTER	Aldosterone
16	ƀNAƀLOSS	Sodium Loss Rate (m Osmols/Min)
17	ƀƀKƀLOSS	Potassium Loss Rate (m Osmols/Min)
18	ƀƀCLƀLOSS	Chloride Loss Rate (m Osmols/Min)
19	UREAƀLOSS	Urea Loss Rate (m Osmols/Min)
20	PLASMAƀO	Plasma Osmolarity (m Osmols/Liter
21	INTERSƀO	Interstitial Osmolarity (m Osmols/Liter)
22	CELLƀFƀO	Cell Fluid Osmolarity (m Osmols/Liter)
23	URINEƀOƀ	Urine Osmolarity (m Osmols/Liter)

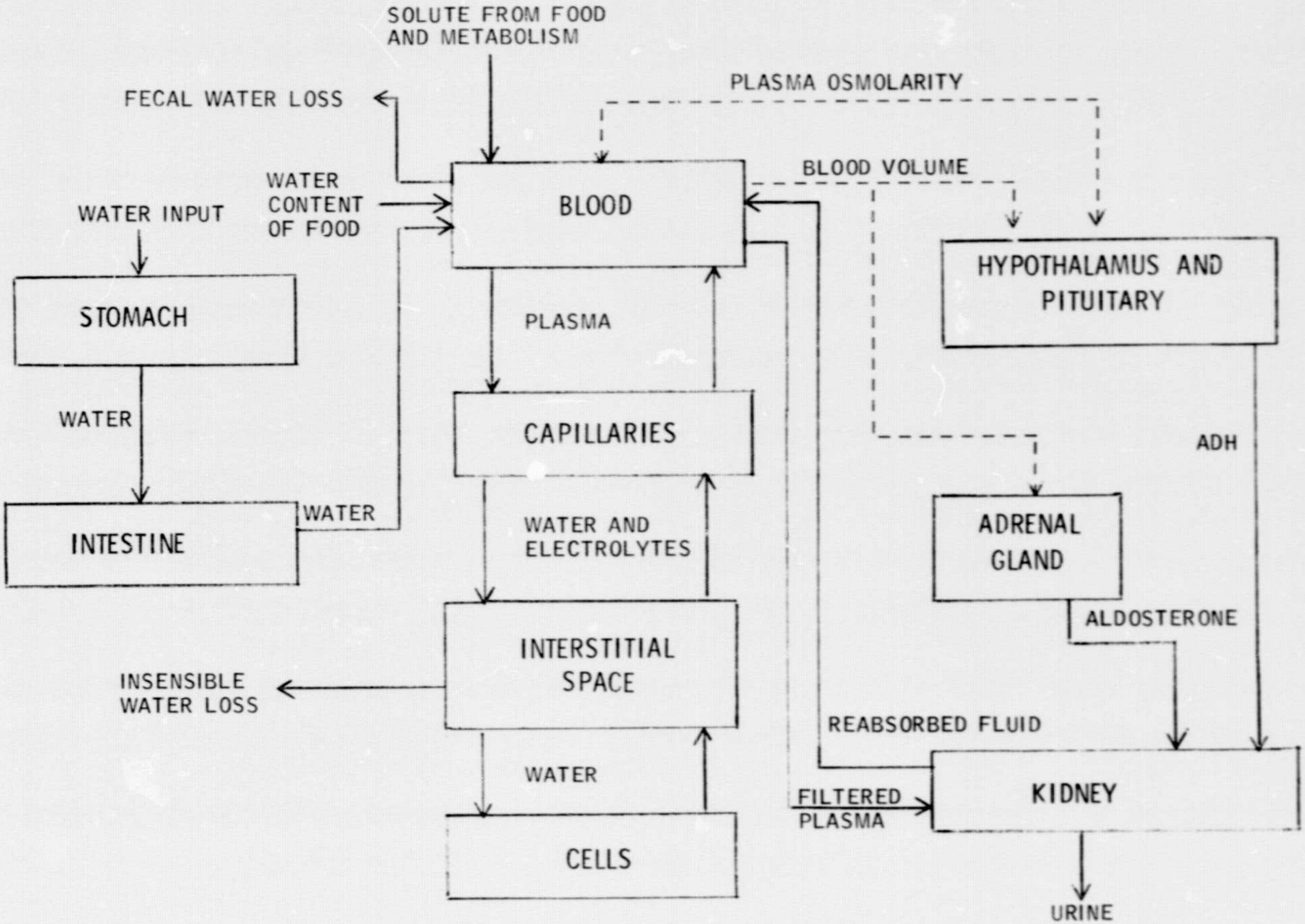

FIGURE 1. GENERAL FLOW CHART OF WATER AND ELECTROLYTE BALANCE.