# CLINICAL METABOLISM OF BODY WATER AND ELECTROLYTES

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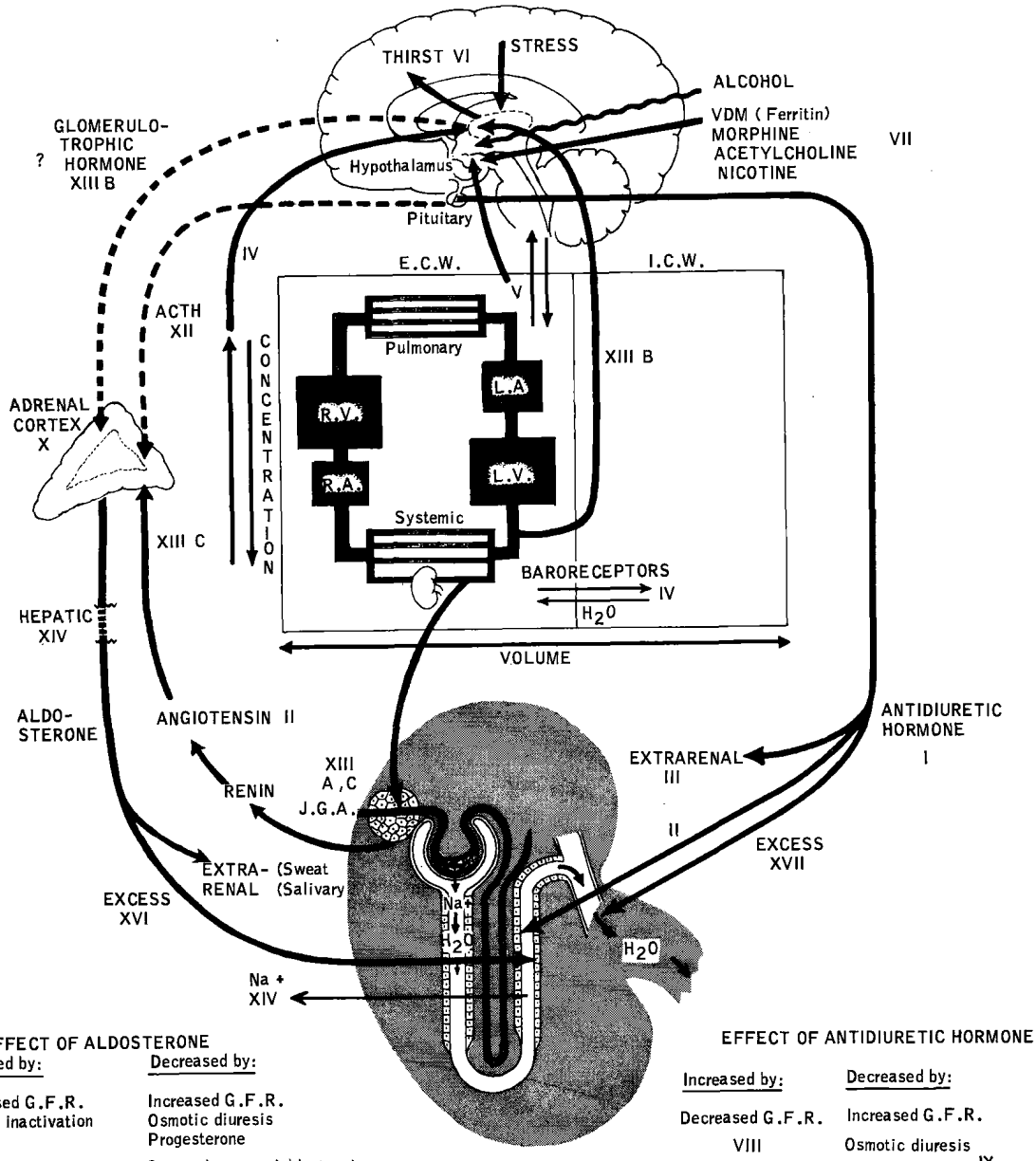


**EFFECT OF ALDOSTERONE**

| Increased by: | Decreased by: |
|---|---|
| Decreased G.F.R. | Increased G.F.R. |
| Hepatic inactivation | Osmotic diuresis |
| | Progesterone |
| XIV | Spironolactones (aldactone) |
| | 11-hydroxy adrenal steroids |
| | Potassium depletion |
| | Renal tubular damage |
| | ? hormonal natriuretic agent |

**EFFECT OF ANTIDIURETIC HORMONE**

| Increased by: | Decreased by: |
|---|---|
| Decreased G.F.R. | Increased G.F.R. |
| VIII | Osmotic diuresis IX |
| | Hypercalcemia |
| | Renal tubular damage |
| | Increased hepatic inactivation |

Proposed mechanisms for the release of antidiuretic hormone and of aldosterone, their site of action, and the factors which modify their action. (Solid lines indicate stimulation, and wavy lines inhibition. Red lines relate to aldosterone, and the blue to the antidiuretic hormone.) The Roman numerals refer to sections in the text in which the various factors are discussed. Abbreviations: ECW, extracellular water; ICW, intracellular water; RA, RV, LA, LV, right and left atria and ventricles; GFR, glomerular filtration rate; JGA, juxtaglomerular apparatus. (See Chapter 4, pages 66–68.)

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# "Water is Best"
# A Substrate for Life

It was assuredly not chance that led Thales to found philosophy and science with the assertion that water is the origin of all things. Whether his belief was most influenced by the wetness of animal tissues and fluids, or by early poetic cosmogonies, or by the ever-present importance of the sea to the Ionians, however vague his conception of water may, indeed must, have been, he at least expressed a conclusion which proceeded from experience and serious reflection.

Water, of its very nature, as it occurs automatically in the process of cosmic evolution, is fit, with a fitness no less marvelous and varied than that fitness of the organism which has been won by the process of adaptation in the course of organic evolution.

If doubts remain, let a search be made for any other substance which, however slightly, can claim to rival water as the milieu of simple organisms, as the milieu intérieur of all living things, or in any other of the countless physiological functions which it performs either automatically or as a result of adaptation. —L. J. Henderson: *The Fitness of the Environment.* Boston, Beacon Press, 1958.

# PREFACE

This book needs no apology, but does require explanation. The author-editor has read 12 books on this subject since 1956; because so many are available, an author and editor must provide a clear statement of aims before embarking on the exorbitant procedure of writing a further one.

A main aim of the book is to emphasize clinical medicine as it relates to laboratory research, to bridge the gap between basic and clinical investigation and bedside medicine. Contributors were asked to bring their field up to date in regard to progress in research in areas relevant to and usable in clinical medicine. Wherever such data have equivocal or doubtful clinical implications he has tried to convey this. The author's responsibility is to convey his own experience and views, relate biochemical and biophysical research to clinical events. The highest level of patient care occurs in the environment of research and education. Clinical science and skills require re-emphasis; active participation in clinical medicine is necessary to the medical student, intern, resident, practicing clinician and clinical investigator.

There have been major advances in the past five years, especially in the areas of anatomy of body water and electrolytes, total body composition, intracellular hydrogen ion concentration (even intramitochondrial hydrogen ion regulation), aldosterone and antidiuretic hormone regulation of water and electrolyte metabolism, transport systems and the relations among water, electrolyte, hydrogen ion and the connective tissue system. This new information is incorporated in the text.

There is need for a better expression of water and electrolyte metabolism; the author and editor believes that he has learned to present and edit the material with greater precision and clarity.

It is believed that one person can no longer encompass the field; thus the decision for a multi-author clinical book on water and electrolyte metabolism.

The book is done in the traditional way, relating the biochemical and physiologic data to disease states. The mechanisms responsible for the maintenance of normal volume, tonicity, composition and pH of body liquids become disturbed in disease states; i.e. disease is change from normal equilibrium or disruption of basic physiologic processes. Abnormalities are considered in terms of physiologic mechanisms; it is believed that description in terms of general areas of disease has greater clinical usefulness than general descriptions of the basic physiology. The first part of the book and several reference chapters are devoted to basic biochemical and physiologic description; later chapters deal with general areas of disease.

The editor regards medicine as an empiric science; its descriptive phase is only now beginning to terminate. Perhaps it is better described as a polyscience, a combination of sciences in which one, if he is to do scientific investigation, must be trained in depth in at least one of the medical sciences. Medicine is becoming a proper science. We now use the tools of physicists and chemists in everyday work. Medical investigators work on a more sophisticated level than they did a short time

ago. Physicists are now becoming biophysicists, apparently thinking that particle physics has not the challenge it once had and that the physics of biological molecules is the domain where the future lies. Medicine is a biological science; medicine is human biology. Water and electrolyte metabolic investigation is one of the most active areas in medical investigation and practice. There is now need for a book written by experts in several areas of the field.

In a sense one might say that water and salt metabolism from a clinical point of view began with Charles Darwin, who developed the thesis that the external environment, in the final analysis, determines the nature and behavior of the organism. Specifically, he proposed that external forms of organisms were best explained by adaptations which had survival value, permitting survival in a fluctuating environment of organisms having the most valuable genetic endowment. Darwin proposed that the animal not only arises from the external environment, but also functions so that it adapts to resist environmental change; failure to adapt means death. Homeostatic mechanisms were established for survival in and for adaptation to an unkind world.

Claude Bernard in France introduced into biology the idea of an internal environment consisting of extracellular water, blood plasma and interstitial liquids; environment was constant, and survival depended upon its constancy of chemical structure or resistance to change. By this means the organism avoided pressures of the external environment. A heated, warm, watery envelope full of electrolytes and nutrients kept life secure. Actually, Bernard based his concept on shaky experimental data; it was a brilliant intuition not settled on firmly established experimental fact. How much has grown out of the idea! Bernard defined the internal environment and strongly intimated that the purpose of most physiologic processes was to keep this environment constant.

Walter B. Cannon of Harvard made the next major contribution in which he evolved the term "homeostasis" and the idea of a "wisdom of the body." He implied that physiologically controlled processes were guarding the body. The body behaved in ways that were "good for it." The good could be defined in terms of a series of dynamic equilibriums, a stable internal environment, the extracellular system. He described constancy in terms of closed system thermodynamics. Closed systems are defined by their complete reversibility. A given force produces a displacement from the constant state, and the displacement starts operation of forces returning the system to its original state. In a thoughtful critique of Cannon's approach Drabkin has emphasized the fact that biological systems are really open, not closed, thermodynamic systems.*

Open systems differ from closed systems in being critically dependent on a flow of energy from the external environment; they are therefore in a constant state of change, and their over-all direction is downhill. Their ultimate nature is irreversible. In open systems the idea of "wisdom of the body and homeostasis" cannot effectively operate. *The only constant thing in such systems is change, and when change ceases, life ceases.* Perhaps we are on the edge of a resynthesis and development of new concepts in water and salt metabolism.

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* D. L. Drabkin: Imperfection: Biochemical Phobias and Metabolic Ambivalence. *Perspectives in Biol. & Med.*, 2:473, 1959.

# ACKNOWLEDGMENTS

This book presents a focus of the interests and efforts of contributors representing eleven schools of medicine. The book maintains a clinical orientation, and all its contributors are first, last and always physicians who believe in working at the bedside and being perpetually aware of changing and developing concepts and advances in human biology. They have pride in intellectual achievement, in the medical sciences and in craftmanship in writing. The book is in keeping with the traditions of teaching with a full, orderly, systematic stepwise presentation of concepts.

I am first indebted to all twenty-one contributors whose manuscripts and galley proofs arrived with all dispatch. We often agreed to disagree on certain points of English usage in scientific writing.

I am grateful for criticism of all kinds, that which is gentle and nontraumatic and that which withers and is iconoclastic. Since publication of the Second Edition of this book I have received an abundance of all sorts from teachers, students, house staff and practicing physicians. All have been nourishing, indeed. The crow was so artfully prepared and pleasantly served that I have grown on its ingestion.

I am grateful to Professor E. L. Amidon, Chairman of the Department and Professor of Medicine at the University of Vermont, in whose department each member has freedom and latitude to work at his own depth and taste as he sees it. He gave me every facility, encouragement and time to complete the book.

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# GLOSSARY OF SYMBOLS AND ABBREVIATIONS

A anion component of a salt
ACH hormones (as a group) from the adrenal cortex
ACT activity (physical)
ACTH adrenocorticotropic hormone
ADH antidiuretic hormone of the posterior pituitary
At. wt. atomic weight
ATP adenosine triphosphate
A-V $O_2$ arteriovenous oxygen difference
B cation component of a salt
$B^+HCO_3^-$ bicarbonate salt of any cation
BME basic metabolic expenditure
Bp. blood pressure
$B^+Pr.^-$ cationic salt of serum protein
BUN blood urea nitrogen
B. wt. total body weight
$Ca^{++}$ the cation calcium
C.A. the enzyme carbonic anhydrase
CHO carbohydrate
$Cl^-$ the anion chloride
[ ] chemical symbol for concentration, e.g. the number of particles in unit volume
CNS central nervous system
$CO_2$ carbon dioxide
C.W.D. compulsory water drinking
D.I. diabetes Insipidus
DNA deoxyribonucleic acid
$D_2O$ deuterium oxide (heavy water)
DOCA synthetic desoxycorticosterone acetate
Subscript e denotes extracellular water; e.g. $K_e^+$ means extracellular potassium; $[Na^+]_e$ means concentration of extracellular sodium
ECW extracellular water
Eq. equivalent
Eq. vol. equivalent volume
Eq. wt. equivalent weight
F fat
F.F.S. fat-free solids
FLS fibrous long spacing
$\varphi$ flux of neutral particles against a chemical gradient or charged particles against an electrochemical gradient
G.F.R. glomerular filtration rate
gm. gram or grams
$H^+$ the hydrogen ion
HA fixed acid of any sort
Hb. Hemoglobin
$HCO_3^-$ the anion bicarbonate
$H_2CO_3$ carbonic acid
HHb. reduced hemoglobin, weakly acid
$HHbCO_2$ carbhemoglobin; carbamino compound of hemoglobin
$HHbO_2$ oxyhemoglobin, relatively strong acid
$H^+HCO_3^-$ carbonic acid
Hct. hematocrit or volume of packed red blood cells
$HPO_4^=$ the anion phosphate
HPr. serum protein represented as its buffering function; functioning as one of the buffer anions.
$HPrCO_2$ carbamate; the carbamino compound of an amino group of serum protein with carbon dioxide
Subscript i denotes intracellular water, e.g. $[Na]_i$ means sodium concentration of intracellular water

ICW intracellular water
ILA insulin-like activity
ISW interstitial water
IWL insensible water loss
JGA juxtaglomerular apparatus
$K^+$ the cation potassium
KCl the salt potassium chloride
KHb the potassium salt of reduced hemoglobin, HHb
$KHbO_2$ the potassium salt of oxyhemoglobin, $HHbO_2$
L. liter
M. mol, or gram-molecular weight. A one-molar (M) solution contains 1 gram-molecular weight per liter, or one mol
mEq. milliequivalent
$Mg^{++}$ the cation magnesium
ml. milliliter (essentially used in the same sense as cc. or cubic centimeter; ml. has advantage of more accuracy)
mM. millimol
mm. millimeter
mol gram-molecule. The molecular weight in grams of an element or compound
Molal molal solution is 1 gm. molecular weight of a substance in 1 kg. of solvent
mOsm. milliosmol
N normal. A normal (N) solution contains one equivalent per liter
$Na^+$ the cation sodium
NaCl sodium chloride
NaPr. sodium salt of serum protein
NPN nonprotein nitrogen of blood
Org. ac. organic acids, lactic, pyruvic, betahydroxybutyric, acetoacetic acids
Osm. osmol
$\pi$ osmotic pressure
P the element phosphorus
PAH para-aminohippurate
$pCO_2$ partial pressure of carbon dioxide
pH concentration of hydrogen ion
$PO_4$= the anion phosphate
Pr. protein
Rbc. red blood cells, erythrocytes
R.B.F. renal blood flow
RNA ribonucleic acid
SDA specific dynamic action
S.G. specific gravity
SLS segment long spacing (collagen)
$T.E._K$ total extracellular potassium
$T.E._{Na}$ total extracellular sodium
TSH thyroid-stimulating hormone
$\Phi$ transmembrane coulomb potential
UDPAG uridine diphosphate acetyl glucoseamine
UDPGA uridine diphosphate glucuronic acid
$\beta$ or $\eta$ viscosity
Vol. % volumes per cent

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