HORMONES
and
BODY WATER

ROBERT GAUNT, PH.D.
JAMES H. BIRNIE, PH.D.

HORMONES
and
BODY WATER

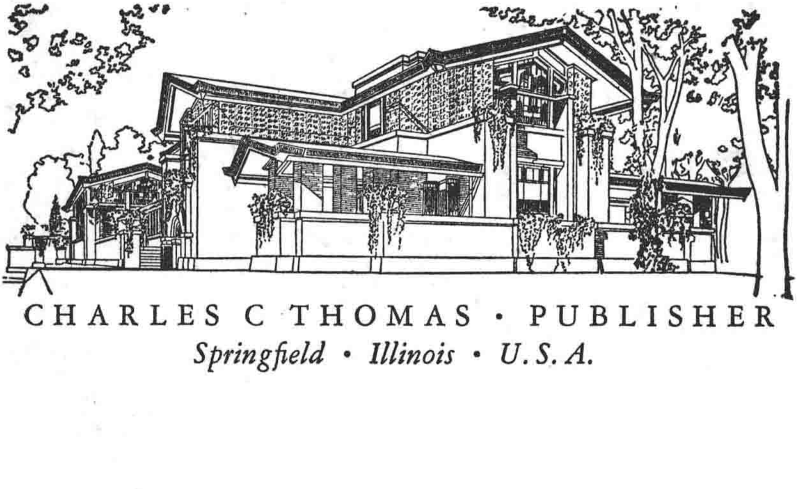
By

ROBERT GAUNT, PH.D.

and

JAMES H. BIRNIE, PH.D.

Department of Zoology
Syracuse University
Syracuse, New York



CHARLES C THOMAS • PUBLISHER
Springfield • Illinois • U.S.A.

CHARLES C THOMAS • PUBLISHER
BANNERSTONE HOUSE
301-327 East Lawrence Avenue, Springfield, Illinois, U.S.A.

Published simultaneously in the British Commonwealth of Nations by
BLACKWELL SCIENTIFIC PUBLICATIONS, LTD., OXFORD, ENGLAND

Published simultaneously in Canada by
THE RYERSON PRESS, TORONTO

Printed in the United States of America

HORMONES
and
BODY WATER

Publication No. 103

AMERICAN LECTURE SERIES

A Monograph in

AMERICAN LECTURES IN PHYSIOLOGY

Edited by

ROBERT F. PITTS, M.D., PH.D.
Professor of Physiology and Biophysics
Cornell University Medical College
New York, New York

Acknowledgments

IN WRITING on this subject, the authors are pleased to acknowledge their indebtedness to a group of collaborators and colleagues at Syracuse University with whom they have studied some of these problems for the last several years. In particular, we refer to Drs. W. R. Boss, W. J. Eversole and C. M. Osborn of the Department of Zoology and Drs. C. W. Lloyd, W. D. Lotspeich, O. W. Sartorius and Robert F. Pitts of the Medical College.

The work discussed here, which originated in this laboratory, was supported by grants from the National Heart Institute, U. S. Public Health Service and Ciba Pharmaceutical Products, Inc.

Contents

HORMONES
and
BODY WATER

1

Introduction

THE ENDOCRINE system in general is involved in the normal and pathological physiology of fluid metabolism. This is clear from modern studies on such clinical entities as diabetes insipidus, Addison's disease, toxemias of pregnancy, menstrual dysfunction and liver disease. It is the purpose of this monograph to attempt a correlation of present knowledge of the role of internal secretions in such phenomena. Much material basic to this discussion on non-endocrine phases of the subject has been presented in earlier monographs of this series.[81, 88b]

The human body is composed of approximately 70 per cent water. As a result of physicochemical forces, this water is distributed in fairly definite amounts into two main compartments: that which is inside body cells (intracellular fluid) and that which is outside the cells (extracellular fluid). The extracellular fluid, in turn, is subdivided into that present in the blood (plasma) and that which is outside both blood vessels and cells (interstitial fluid), including such minor reservoirs as the synovial, cerebrospinal and intraenteric fluids.

The physicochemical factors which determine this internal partitioning of body water will not be considered in detail here. Mention should be made, however, of the conventional concept that the major influence holding water in the extracellular spaces is the osmotic pressure exerted by the sodium salts, sodium being limited largely to the extracellular fluid as a result of cellular membrane phenomena. Various additional influences, some of which are not well understood, determine the partitioning of the subdivisions of the extracellular fluid. For instance, one long-recognized factor by which the plasma fluid level is maintained, despite the fact that the hydrostatic pressure of the blood is tending to force water through the capillaries into the interstitial spaces, is by the supplementary colloidal osmotic pressure exerted by plasma proteins. Intracellular fluid volume is maintained by the osmotic action of substances more or less restrained by cell membranes to intracellular sites, the most important of which are the potassium salts.

These concepts are summarized herewith in a modification of one of Dr. J. L. Gamble's well-known diagrams (Figure 1). They are useful generalizations but it should be remembered that, as stated, they are oversimplified in that electrolyte and water distribution of tissues vary among themselves and in different physiological states.[25]

The process of maintaining proper levels of the body fluids is inevitably complex because the rate of water and salt intake is erratic and its extra-renal loss, as by sweating, is variable and relatively independent of the amounts of body water available.

Fortunately the body can tolerate considerable variation in its total water content and the processes of adjustment to such variations although definite are sometimes slow. Quick and viligant effort is made, on the other hand, to maintain constancy of other factors in the extracellular fluids such as hydrogen ion concentration and osmotic pressure. Regulation of osmotic pressure is achieved primarily by regulation of the rate of salt and water excretion.

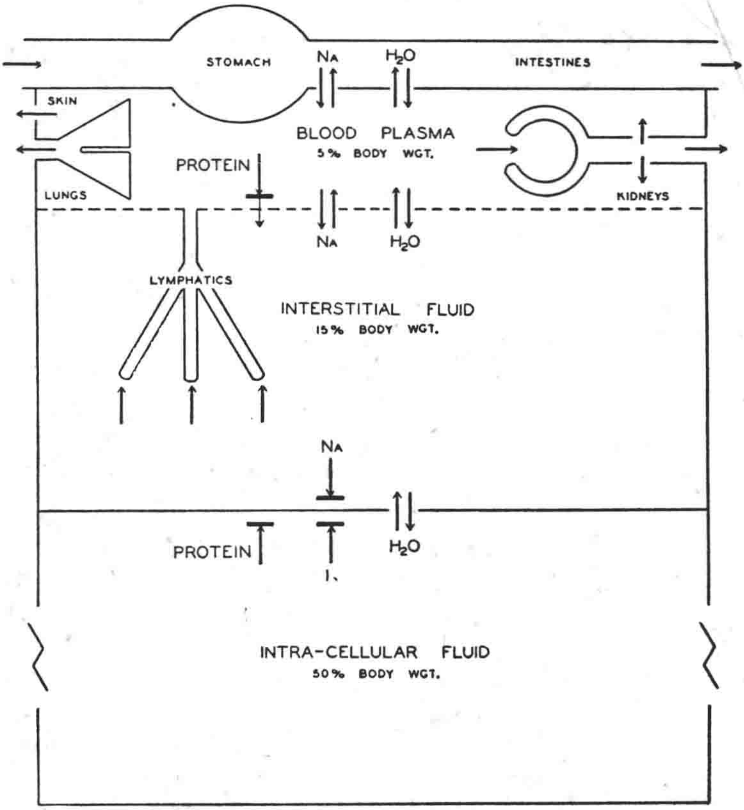


Figure 1. A diagram, modified from Gamble,[38] illustrating some factors which vary and regulate the distribution of body fluids.

Thus, in the maintenance of a constant internal environment the kidney serves as keeper of the gate. In the face of extra-renal influences tending endlessly to vary the body content of salt and water, it adjusts its rate of excretion of these substances to the end of maintaining a constant osmotic pressure. Less sensitively, thirst and salt appetite also help to maintain the *status quo*.

2

Evolutionary Considerations

THE HUMAN BODY and its functional mechanisms are the end-result of over 500 million years of evolutionary processes. These processes could not be brought about by direct wilful change to meet adaptive needs. They depended rather upon the survival of fortuitous mutations in the rugged contest of natural selection. The inevitable consequence of such lack of teleological design is that the result will not be predictable and that it will likely be awkward or even bizarre. While the evolutionary story of our body fluids and the organs which maintain them has been read only dimly, such progress as has been made helps greatly in interpretation of events in the human body.

It was one of the classic concepts of Claude Bernard[7] that the body cells of higher animals actually live and function in an aqueous internal environment, and that the ability to maintain constancy of this internal fluid medium conveys to these organisms an independence in an unstable external environment which lower forms did not possess. "The living organism does not really exist in the *milieu exterieur* . . . but in the liquid *milieu interieur* formed by the circulating organic liquid which surrounds and bathes all tissue elements . . . The stability of the *milieu interieur* is the primary condition for freedom and independence of existence."

The accessory concept that the fluid internal environment of vertebrates — the extracellular fluid — is only modified sea water maintained with the saline concentration which prevailed during the geological epoch in which their ancestors evolved was stated fully by Macallum.[80] The lines of Wordsworth have been pharaphrased[8] as follows:

> "Though inland far we be,
> Our blood has salt from the immortal sea,
> Which brought us hither."

Since its original proposal this theory has received deferentail treatment, if not unequivocal verification. The hypothesis of Macallum is based upon a striking similarity in electrolyte ratio and content between extracellular fluid and the more dilute seas of the early Paleozoic era, periods during which land forms are supposed to have arisen. If this concept be true, then not only do human body cells maintain a constant internal fluid environment, but they maintain an environment to which their ancestors became adapted some 480 million years ago.

The improvisations which animals used to maintain a constancy of the internal fluid environment, in the face of radically different external environments, makes one of the most fascinating stories to which the combined sciences of phylogeny and physiology have turned. The story is far from complete in any particular, but as regards the kidney available fact and intelligent speculation has been brilliantly recorded in the writings of Dr. Homer W. Smith.[102] Vertebrate animals, most evolutionists believe, arose in fresh water as fish-like forms from ancestors whose body fluids had been adapted previously to a marine existence. To maintain a saline extracellular fluid in the face of the osmotic inrush of water from a fresh water external environment imposed a serious problem. They met this problem, Smith believes, in two ways. First, they acquired impermeable coats and thus provided a mechanical barrier to osmotic dilution. This could only be a device of limited effectiveness because the problem of survival precluded covering the gills and mucous membranes, through which water could pass freely. The armor typical of the fossilized vertebrates of the Silurian and Devonian periods is thought to bear witness to the attempted defense against the osmotic invasion of fresh water. As a second attempted defense, the circulatory system was connected to the kidney tubules by means of the glomeruli; thus the organism was able to use the energy of the beating heart to pump water out as fast as it came in. Smith feels that the fundamental architecture of the human kidney is based on its original adaptation to serve as a water pump.

After having developed a functional water pump which served to offset the osmotic imbibition of water in a fresh water habitat the descendents of these early vertebrates migrated into many different environments. In these new habitats they were confronted with new problems. Some returned to the ocean, but by this time the seas were saltier than before and hence were hypertonic to the body fluids. Many adaptations appeared in an attempt to prevent dessication and to counteract the heritage of mechanisms designed to offset a constant osmotic inflow rather than outflow of water. In sharks the renal threshold to urea was elevated to the end that enormous amounts of urea were retained in the plasma, thus equalizing the osmotic pressure of their body fluids with that of the hypertonic sea. Other fish consumed salt water and "distilled" it by excreting the salt through the gills and were thus able to resist dessication in a hypertonic environment. As the glomerular filtering apparatus which evolved in fresh water was no longer an asset, some forms became adapted to their hypertonic environment by reducing or obliterating the glomeruli of their kidneys and relying upon the tubular secretion of metabolites.

Other forms migrated to terrestrial environments where they encountered habitats that varied from swampy regions to desert aridity. The land vertebrates, needing to conserve water so that they could leave their water sources and make the best use of their terrestrial domain, employed various stratagems to maintain a constant extracellular medium. The reptiles and birds modified their metabolic processes so as to excrete a supersaturated uric acid solution which precipitates in the cloaca. From this site water could be reabsorbed and a relatively dry urine eliminated. The adaptations which gave mammals their supremacy has made their problem of water conservation more difficult. They developed, along with the birds, the trait of warm-bloodedness, which tends to increase evaporative fluid loss. Further, the higher metabolic rate associated with warm-bloodedness results in the need for the excretion of more metabolites which carry out water as their solvent. Those mammalian forms which help regulate their body temperature by panting or sweating place an additional strain on the water conserving mechanisms. Blood pressure is high in mammals and that tends to filter more fluid through the glomeruli than would otherwise be the case. And lastly, the number of glomeruli is greatly increased thus making available a larger surface area for filtration. The result of these factors is that in man some 125 ml. of fluid is filtered into the renal tubules per minute, most of which is and must be reabsorbed to avoid speedy oblivion. Thus it seems that the heart and kidney tubules are working against each other to provide the human body with an excretory mechanism which while it has the substantial merit of working remarkably well is from the standpoint of energetics grossly inefficient. Smith [102] evaluates it thusly: "There is enough waste motion here to bankrupt any economic system — other than a natural one, for Nature is the only artificer who does not need to count the cost by which she achieves her ends."

A portion of the fluid filtered into the renal tubules is reabsorbed passively along with its solutes. In addition, a new use of an old hormone, that of the posterior pituitary gland, appears in its full-blown form in the mammals. This hormone stimulates a further reabsorption of water from the tubular fluid and permits for the first time the excretion of a true hypertonic urine; by this means a relatively effective conservation of water is achieved. Nevertheless, uncontrollable water loss is of such magnitude as to make water the most immediately essential dietary constituent.

It is now clear that at some stage in these processes other hormones, particularly those of the adrenal cortex, entered the picture, affecting the excretion of both salt and water. The cortical hormones tend to inhibit sodium excretion and enhance the excretion of potassium. Could this action be an adaptation to the relatively low sodium and high potassium diet of the animal that departed from the salty sea first to fresh water and then to the equally salt-poor land? No evidence is at hand on which to base an answer but the peril risked by the wild animal in search of salt and the avidity with which man adopts the salt shaker point to the adaptive significance of such mechanisms.

The comparative physiologist has an inviting task before