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ENDOCRINOLOGY BOARD REVIEW MANUAL

STATEMENT OF EDITORIAL PURPOSE

The *Hospital Physician Endocrinology Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in endocrinology. Each manual reviews a topic essential to the current practice of endocrinology.

Disorders of Water Metabolism

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Table of Contents

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INTRODUCTION

Disorders of water metabolism are associated with disturbances of normal plasma osmolality. In clinical practice, these disorders present primarily as problems associated with hyponatremia or, less commonly, hypernatremia. The near-synonymity of disorders of water metabolism with derangement of the normal serum sodium concentration reflects the primacy of sodium as the dominant cation of extracellular fluid (ECF).

To correctly solve problems involving hyponatremia or hypernatremia, one must remember that hormones affecting osmolality respond to changes in plasma osmolality as well as changes, real or perceived, in circulating plasma volume. Many apparent clinical problems arise under conditions in which osmoregulatory hormones are secreted inappropriately with regard to plasma osmolality but entirely appropriately with regard to perceived plasma volume signaling. When addressing problems of hypo- and hypernatremia, it is crucial to recall that when osmolar signaling is at odds with volume signaling, volume signaling is quantitatively (and qualitatively) more dominant.

PHYSIOLOGY OF WATER METABOLISM

Total Body Water and Plasma Osmolality

Total body water (TBW) constitutes approximately 60% of the total body weight in young adult men (50% in young adult women). Older age and higher percentage of body fat correlate with lower TBW as a percentage of body weight. A simple calculation for TBW (in L) is to multiply patient body weight (in kg) by 0.6 (for an adult male), 0.5 (adult female), 0.5 (elderly male), or 0.45 (elderly female).

Roughly two thirds of TBW is contained in the intracellular fluid (ICF) compartment, with one third in the ECF compartment. Movement of water between the ECF and ICF is governed primarily by the osmolality of each compartment. Under normal conditions, ECF osmolality and ICF osmolality are approximately the same. Thus, plasma osmolality is a useful indicator of the osmolality within cells. For practical purposes, plasma osmolality (in mOsm/kg) can be estimated from the concentrations of the major osmotically active ECF solutes using the following formula:

$$(2 \times Na^+) + (glucose/18) + (BUN/2.8)$$

where sodium (Na^+) is expressed in mEq/L and glucose and blood urea nitrogen (BUN) are expressed in mg/dL. If BUN and glucose concentrations are normal, plasma osmolality can be estimated using the following simplified formula:

$$(2 \times Na^+) + 8$$

A comparison of estimated versus directly measured plasma osmolality is an important checkpoint prior to initiating therapy for hyponatremia, since instances of pseudohyponatremia may be associated with normal or even elevated plasma osmolality. Directly measured plasma osmolality should agree with estimated plasma osmolality within 20 mOsm/kg; a larger discrepancy suggests the presence of an unmeasured osmole, such as an alcohol, a lipid, or a paraprotein. Although clinical situations featuring osmolal gaps are unusual, the recognition that one is present may lead to a diagnosis of otherwise-unsuspected poisoning, for example with ethylene glycol or methanol. Severe hypertriglyceridemia or paraproteinemia should be obvious from measurement of plasma lipids (the serum should appear grossly lipemic) and total protein.

Normal Governance of Plasma Osmolality

Normal plasma osmolality is maintained primarily by a balance of renal excretion and oral intake of water, since daily solute excretion is largely of an obligate nature.

Vasopressin-mediated renal water handling. The dominant osmoregulatory hormone is vasopressin (antidiuretic hormone [ADH]). Vasopressin is synthesized by neurosecretory neurons in the paraventricular and supraoptic nuclei of the hypothalamus and migrates along axons within the pituitary stalk to the posterior pituitary, where it is ready for release in response to osmotic or nonosmotic stimuli.

Vasopressin release is triggered by plasma osmolality as it rises above 288 mOsm/kg. Rising plasma osmolality is perceived by osmoreceptors located in