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A Physiology-Based Approach to Hyponatremia

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Homeostasis refers to the ability of living organisms to maintain a stable internal environment despite significant fluctuations in external conditions. This process is essential for health and survival. The extracellular fluid (ECF) constitutes the body's internal environment, and normal cellular function depends on the ECF maintaining physiological parameters within a narrow range. One such critical parameter is plasma tonicity. The regulation of plasma tonicity is crucial for controlling cell volume: under hypertonic conditions, cells shrink, while under hypotonic conditions, cells swell. Plasma sodium concentration is the primary determinant of plasma tonicity. In 1958, Edelman et al. showed that plasma sodium concentration depends on the sum of total body exchangeable sodium and potassium, as well as total body water. Hypotonic hyponatremia occurs when total body water exceeds the combined total of exchangeable sodium and potassium, creating an electrolyte-free water excess. This imbalance typically arises from increased intake of electrolyte-free water, decreased renal excretion of electrolyte-free water, or both. Despite being the most common electrolyte imbalance encountered in clinical practice, with significant morbidity and mortality, hyponatremia is often misdiagnosed and mismanaged. Traditionally, hyponatremia is diagnosed using an algorithm developed in the 1970s. However, this approach has limitations, primarily due to the poor sensitivity and specificity of volume status assessment. We favor a different approach based on physiology. A strong understanding of physiology is crucial for both diagnosing and treating hyponatremia. This lecture will review the basic physiology and pathogenesis of hyponatremia, using a case study to demonstrate a physiology-based approach. This approach will address three key questions: Is this hypotonic hyponatremia? Is it driven by arginine vasopressin (AVP) secretion? And, is the AVP secretion a response to a physiological stimulus?

Keywords: Plasma tonicity, Plasma sodium concentration, Edelman equation, Arginine Vasopressin, Physiology