

**Harvard Medical School Department of
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Cardiology Rounds
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The Road to Wasting is Paved with Lost Minerals

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This issue of *Cardiology Rounds* presents a novel pathophysiological approach to congestive heart failure (CHF) by considering it as more than a failing heart and a state of salt and water retention. Dr. Weber provides evidence that supports the view that CHF is a systemic illness with features that include oxidative stress; a proinflammatory phenotype; and wasting of soft tissues and bone. Indeed, secondary hyperparathyroidism is proposed as a co-variant of CHF produced by urinary and fecal losses of Ca^{2+} and Mg^{2+} promoted by aldosteronism, and augmented by urinary losses of these cations induced by furosemide and hypovitaminosis D.

Questions:

1. CHF is a clinical syndrome with characteristic signs and symptoms. The pathophysiologic origins of CHF are rooted in a salt and water retention process mediated largely by effector hormones of the renin-angiotensin-aldosterone system (RAAS).
True False
2. In patients with chronic cardiac failure and systolic dysfunction, the extent of reduction in depressed left ventricular ejection fraction (LVEF) predicts the degree of activation of the circulating RAAS and, accordingly, the presence or absence of salt and water retention.
True False
3. Beyond the traditional cardio-renal perspective, CHF is accompanied by a systemic illness with the following pathophysiologic feature(s).
 - a. oxidative stress in diverse tissues;
 - b. an immuno-stimulatory state with activated lymphocytes and monocytes;
 - c. increased circulating proinflammatory chemokines and cytokines;
 - d. a catabolic state with wasting of soft tissues and bone that eventuates in cardiac cachexia;
 - e. all of the above
4. Secondary hyperparathyroidism (SHPT) appears in the setting of chronic aldosteronism because aldosteronism is accompanied by increased urinary and fecal excretion of Ca^{2+} and Mg^{2+} , which leads to a fall in plasma-ionized $[\text{Ca}^{2+}]_o$ and $[\text{Mg}^{2+}]_o$, each of which are potent stimuli to the parathyroid glands' elaboration of parathyroid hormone (PTH).
True False

5. In a rat model of aldosterone excess, it is possible to demonstrate that spironolactone is more effective than a K⁺-sparing diuretic. In this model, spironolactone attenuates urinary and fecal excretion of Ca²⁺ and Mg²⁺ and prevents SHPT, which serves to prevent bone resorption. Hence, it rescues bone mineral density and strength.

True False

6. In African-Americans (AAs), SHPT appears to be a covariant of CHF and is related to a tenuous balance between Ca²⁺ and hypovitaminosis D, the presence of aldosteronism with augmented urinary and fecal excretion of Ca²⁺ and Mg²⁺, and is exacerbated by a loop diuretic augmenting urinary Ca²⁺ and Mg²⁺ excretion.

True False

7. Both angiotensin-converting enzyme (ACE) inhibitors and AT₁ receptor antagonists (angiotensin receptor blockers) increase serum zinc.

True False

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