HORMONE RESPONSE TO HYPOVOLEMIA

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Control of Extracellular Volume

Volume receptors respond to changes in “effective circulating volume” (defined as the rate of capillary perfusion) which is generally proportional to BCF volume. Renal volume receptors (in the juxtaglomerular apparatus of renal afferent arterioles) govern sodium balance via the renin-angiotensin-aldosterone system; extrarenal volume receptors through the sympathetic nervous system and atrial natriuretic factor (ANF).

These receptors then activate various effector mechanisms that restore volume by varying vascular resistance, cardiac output, and urinary sodium excretion. The hemodynamic changes are primarily compensatory and restoration of normal volume depends on changes in Na⁺ excretion.

The renin-angiotensin-aldosterone system:

1. Aldosterone is the major adrenal steroid in man. It increases the reabsorption of Na⁺ and promotes the secretion of K⁺ and H⁺ in distal segments of the nephron. Lack of aldosterone leads to increased Na⁺ excretion and consequent shrinkage of extracellular volume. Aldosterone deficiency also causes a decrease in K⁺ and H⁺ secretion in the distal nephron resulting in hyperkalemia and metabolic acidosis.

2. Aldosterone secretion is stimulated by an increase in plasma angiotensin II. This peptide hormone is formed by the following reaction:

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\text{angiotensinogen} \rightarrow \text{angiotensin I} \rightarrow \text{angiotensin II}
\]

- (a globulin) (a decapeptide) (an octapeptide)

- The first step in the reaction is catalyzed by renin, a proteolytic enzyme, released into the circulation by granule cells (or juxtaglomerular cells) located primarily on the wall of the afferent arteriole; the second step by an enzyme in the lung (converting enzyme) (see figure on next page).

- Renin is secreted into the lumen of the afferent arteriole in response to at least three factors: 1) renal hypoperfusion, sensed by volume receptors in the afferent arteriole; 2) stimulation of renal sympathetic nerves, which innervate the juxtaglomerular cells, in response to a fall in extrarenal vascular volume; and 3) changes in the volume or composition of the tubular urine reaching the macula densa cells in the nearby distal tubule.

- In addition to its ability to stimulate aldosterone secretion, angiotensin II is also a potent vasoconstrictor. The response of the renin-angiotensin-aldosterone system to hypovolemia involves both the renal and cardiovascular effects of angiotensin II.

- Recent studies suggest that ANF also plays in important role in control of aldosterone. Decreased plasma ANF stimulates and increased ANF inhibits aldosterone secretion, consistent with the reciprocal roles of these two hormones in volume regulation. Aldosterone secretion is also stimulated by other factors including an increase in plasma potassium concentration, an effect important for potassium balance, but not for volume regulation.
3. ANP (or atriopeptin)

- Atrial natriuretic peptide (ANP) is a cardiac peptide hormone. It is released from myocardial cells in the atria in response to expansion of the extracellular volume, sensed by stretch-receptors in the wall of the atria. It has two major effects: it is a potent vasodilator, which lowers blood pressure; and it increases the renal excretion of $\text{Na}^+$ and water. Factors important in the ANP-mediated natriuresis and diuresis include a decrease in distal tubule sodium absorption and inhibition of aldosterone secretion.

- The presence of ANP was first demonstrated in 1981, and its role in normal fluid homeostasis is still not well understood. It was originally called ANP, because of its renal effects, but is now becoming known as atriopeptin since it has effects throughout the body.

- Hormonal control of distal tubular sodium reabsorption, by aldosterone and ANP, may be the primary renal volume regulatory mechanisms in humans. Other factors also influence volume regulation (see, for example, the direct tubular effects of angiotensin II and of sympathetic activity), but it appears that these may only be important in the response to marked changes in volume.

4. Sympathetic nervous system

- Volume expansion decreases sympathetic neural tone and the secretion of epinephrine and norepinephrine from the renal medulla; whereas volume depletion increases their activity.

- The importance of the sympathetic response to hypovolemia can be seen in the acute, compensatory response to hemorrhage by patients with autonomic insufficiency. In these patients, removal of only one pint of blood, a loss well tolerated by normal subjects, may lead to severe hypotension

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\begin{align*}
\text{Decreased effective circulating volume} & \downarrow \\
\text{Decreased cardiac output} & \downarrow \\
\text{Decreased cardiac output} & \downarrow \\
\text{Decreased blood pressure} & \downarrow \\
\text{Baroreceptor stimulation} & \downarrow \\
\text{Increased sympathetic tone} & \\
\text{Increased renin secretion} & \quad \text{Increased tubular } \text{Na}^+ \text{ reabsorption} \\
\text{Increased angiotensin II formation} & \\
\text{Increased aldosterone secretion} & \quad \text{Increased effective circulating volume}
\end{align*}
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References:

