Adrenomedullin (ADM) Overview

Overview:
Adrenomedullin (ADM) is a vasoactive peptide originally discovered in human pheochromocytoma tissue. It plays a crucial role in cardiovascular homeostasis, fluid balance, and vascular integrity. It is a 52-amino acid peptide with broad physiological effects.

Mechanism of Action:
ADM exerts its biological effects by binding to calcitonin receptor-like receptor (CLR) and its accessory protein, receptor activity-modifying protein 2 (RAMP2 or RAMP3). This receptor complex is a G-protein coupled receptor (GPCR) that, when activated by ADM, stimulates:

- Adenylate cyclase activity → increased cyclic AMP (cAMP)
- Nitric oxide (NO) synthesis → vasodilation
- Endothelial barrier function → reduced vascular permeability

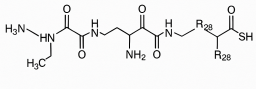
These pathways lower blood pressure, improve endothelial stability, and regulate vascular tone.

Physiological Functions in the Body:
Vasodilation: ADM causes relaxation of vascular smooth muscle, leading to lower blood pressure.
Cardioprotection: It reduces cardiac afterload and protects against ischemic injury.
Fluid Homeostasis: ADM helps regulate sodium and water balance in the kidneys by enhancing diuresis and natriuresis.
Anti-Inflammatory Effects: ADM has anti-inflammatory properties, including reducing vascular permeability in inflammatory states.
Endothelial Protection: Maintains vascular integrity, especially during sepsis or cardiovascular stress.

Clinical & Research Use:

- ADM is not currently used as a direct therapeutic peptide, but ADM analogs and receptor agonists are being researched for heart failure, septic shock, and other cardiovascular conditions.
- Elevated ADM levels are often a biomarker for heart failure, sepsis, and endothelial dysfunction.

Dosing (Experimental & Clinical Context):
Endogenous ADM: Circulating plasma levels vary by health status, generally 10-20 pg/mL in healthy individuals.
Recombinant/Analog Dosing (in trials): Dosing regimens are typically continuous intravenous infusions in a range of 10-50 ng/kg/min for acute cardiovascular or septic shock studies.
No approved ADM-based drug – research-based dosing only.

Conclusion:
Adrenomedullin is a promising endogenous peptide with significant roles in vascular regulation, fluid balance, and cardiovascular protection. While it is not yet an approved therapeutic agent, ongoing research highlights its potential in treating heart failure, septic shock, and other vascular disorders. Its unique mechanism of action and broad physiological functions make ADM a key focus in cardiovascular and critical care research, with future studies likely to determine its full clinical impact.

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