Nephrogenic Diabetes Insipidus: Essential Insights into the Molecular Background and Potential Therapies for Treatment

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The water channel aquaporin-2 (AQP2), expressed in the kidney collecting ducts, plays a pivotal role in maintaining body water balance. The channel is regulated by the peptide hormone arginine vasopressin (AVP), which exerts its effects through the type 2 vasopressin receptor (AVPR2). Disrupted function or regulation of AQP2 or the AVPR2 results in nephrogenic diabetes insipidus (NDI), a common clinical condition of renal origin characterized by polydipsia and polyuria. Over several years, major research efforts have advanced our understanding of NDI at the genetic, cellular, molecular, and biological levels. NDI is commonly characterized as hereditary (congenital) NDI, arising from genetic mutations in the AVPR2 or AQP2; or acquired NDI, due to for example medical treatment or electrolyte disturbances. In this article, we provide a comprehensive overview of the genetic, cell biological, and pathophysiological causes of NDI, with emphasis on the congenital forms and the acquired forms arising from lithium and other drug therapies, acute and chronic renal failure, and disturbed levels of calcium and potassium. Additionally, we provide an overview of the exciting new treatment strategies that have been recently proposed for alleviating the symptoms of some forms of the disease and for bypassing G protein-coupled receptor signaling.

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