

**Goldberg L I.** Cardiovascular and renal actions of dopamine: potential clinical applications. *Pharmacol. Rev.* 24:1-29, 1972.

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This paper reviews the studies of the endogenous catecholamine, dopamine, which resulted in discovery of its unique cardiovascular and renal actions and its clinical uses in the treatment of congestive heart failure and shock. [The *SCI*® indicates that this paper has been cited in over 760 publications.]

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Research leading to this review began when I was a graduate student in the Department of Pharmacology of the Medical University of South Carolina under Robert P. Walton. We were searching for a sympathomimetic amine with a positive inotropic action that did not increase blood pressure or heart rate, so that it could be used in the treatment of heart failure. None were found. Several years later I participated in an ongoing study of endogenous amines in the Experimental Therapeutics Section of the National Heart Institute and found that within a specific dose range, dopamine increased cardiac contractile force in the anesthetized dog without changing heart rate or blood pressure—an accidental discovery.<sup>1</sup>

Hemodynamic investigations in collaboration with David Horwitz and Samuel Fox revealed that dopamine produced similar effects in normal subjects.<sup>2</sup> On the basis of these studies, my colleagues and I at Emory University administered dopamine to pa-

tients with refractory congestive heart failure and found that a sodium diuresis occurred.<sup>3</sup> We assumed that the response was secondary to improvement in cardiac function. Accordingly, we were surprised to find that dopamine also increased sodium excretion in normal subjects and in addition increased renal blood flow and decreased renal resistance.<sup>4</sup> These unexpected findings led to the utilization of dopamine in the treatment of congestive heart failure and shock and to investigations in experimental animals to determine the mechanism for the unusual renal vasodilation. After confirmation of these findings by other investigators, I wrote this review. Previous reviews of dopamine were largely limited to the central nervous system, especially the involvement of dopamine in the etiology and treatment of Parkinson's disease.

The unusual pharmacological actions of dopamine and its clinical applications explain the frequent citation of this review. The field has continued to grow rapidly, and recently we identified two peripheral dopamine receptor subtypes: DA<sub>1</sub> and DA<sub>2</sub>. Activation of DA<sub>1</sub> receptors results in vasodilation of the renal and other vascular beds, and activation of DA<sub>2</sub> receptors results in inhibition of norepinephrine released from sympathetic nerves.<sup>5</sup> Medicinal chemists have been very active in this field and selective DA<sub>1</sub> and DA<sub>2</sub> agonists and antagonists are now available.<sup>6</sup> Current research goals are to determine the physiological role of peripheral DA receptors and to develop orally active DA derivatives for treatment of congestive heart failure, hypertension, and renal insufficiency.

I have been involved in this research for more than 30 years and am grateful to the many collaborators with whom I studied dopamine and its derivatives in different animal models, in normal subjects, and in patients. I received the Experimental Therapeutic Award for 1974 of the American Society for Pharmacology and Experimental Therapeutics for this work.

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3. Goldberg L I, McDonald R H, Jr, & Zimmerman A M. Sodium diuresis produced by dopamine in patients with congestive heart failure. *N. Engl. J. Med.* 269:1060-4, 1963. (Cited 100 times.)
4. McDonald R H, Jr., Goldberg L I, McNay J L & Tuttle E P, Jr. Effects of dopamine in man: augmentation of sodium excretion, glomerular filtration rate, and renal plasma flow. *J. Clin. Invest.* 43:1116-24, 1964. (Cited 280 times.)
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