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Maack T, Marion D N, Camargo M J F, Kleinert H D, Laragh J H, Vaughan E D & Atlas S A. Effects of auriculin (atrial natriuretic factor) on blood pressure, renal function, and the reninaldosterone system in dogs. *Amer. J. Med.* 77:1069-75 1984 [Depts. Physiol., Surg., and Med., and Hypertension Center, Cornell Univ. Med Coll., New York, NY]

Infusion of synthetic atrial natriuretic factor (ANF) in dogs was shown to increase fluid and electrolyte excretion and glomerular filtration rate and filtration fraction, while blood pressure fell, hematocrit increased, and total renal blood flow was unchanged. ANF also decreased renin secretion and plasma levels of renin and aldosterone. These properties indicated that ANF has an important role in the regulation of renal function and in volume-pressure homeostasis. [The *SCI*® indicates that this paper has been cited in more than 600 publications.]

The Ways of a New Hormone

Thomas Maack and Steven A. Atlas Departments of Physiology and Medicine and Cardiovascular Center Cornell University Medical College New York, NY 10021

The discovery of a new hormone and the initial studies describing its functional properties are a rare and exciting event in biology. This study stemmed from the discovery of atrial natriuretic factor (ANF)[1] and followed quickly upon the elucidation of the biochemical structure and synthesis of ANF.[2,3] Our particular focus was based on our previous work showing that atrial extract has remarkable renal hemodynamic and vascular effects and antagonizes angiotensin II-induced vasoconstriction in the isolated rat kidney[4] and inhibits aldosterone biosynthesis in isolated adrenal glomerulosa.[5]

Our study, together with that of J.C. Burnett, Jr., et al.,[6] showed that ANF has a unique combination of functional properties. The data summarized above, as well as the questions and hypotheses raised in the article's discussion section, stimulated further studies by many investigators, who then cited our paper in their work. As reviewed recently,[3] this included work that unveiled mechanisms by which ANF inhibits renin and aldosterone secretion, decreases blood pressure and plasma volume, affects electrolyte excretion, and regulates renal and glomerular hemodynamics. Importantly, the study also encouraged the infusion of ANF in humans, resulting in effects that are similar to those described in dogs.[3]

To unveil the functional properties of ANF in vivo, we dedicated nearly our entire stock of precious synthetic peptide, once the final purification was completed. The studies employed classical renal clearance techniques. With D.N. Marion, we performed the actual experiments, a rare treat for senior scientists. Each experiment lasted approximately eight hours, and the entire series of dogs was completed in less than one month. The lull periods within each experiment were a time for intense scientific discussions by all the authors. Sometimes we became so loud as to attract investigators of neighboring labs. On these occasions it was not uncommon to have one anesthetized dog surrounded by 10 loquacious people, who were promptly expelled from the room when we had to concentrate on the experimental procedure. It was an exciting atmosphere. Over the next few years, much of the subsequent work by members of the team originated from these discussions.

As with other pioneering observations on ANF, including its discovery,[1] our manuscript was initially rejected by another journal. Perhaps a factor contributing to these rejections was that the initial ANF discoveries originated from experiments using simple methodologies and a nonreductionist approach, at a time when high technology and minimalism were (and still are) the main propellers of forefront biological research. The impact of these articles attests to the fact that whole animal physiologic studies continue to have an irreplaceable role in unveiling novel biological phenomena.

We are pleased that our article contributed to the ANF research explosion. Our recent review on the subject[3] contains almost 1,000 references, and this represents less than 20 percent of the publications in the field since 1984.

1. **de Bold A J, Borenstein H B, Veress A T & Sonnenberg H.** A rapid and potent natriuretic response to intravenous injection of atrial myocardial extract in rats. *Life Sci.* 28:89-94, 1981. (Cited 1,845 times.) [See also: de Bold A J. The discovery of atrial natriuretic factor. Citation Classic®. *Current Contents®/Life Sciences* 34(26):8, 1 July 1991.]
2. **Atlas S A, Kleinert H D, Camargo M J, Januszewicz A, Sealey J E, Laragh J H, Schilling J W, Lewicki J A, Johnson L K & Maack T.** Purification, sequencing and synthesis of natriuretic and vasoactive rat atrial peptide. *Nature* 309:717-9, 1984. (Cited 455 times.)
3. **Atlas S A & Maack T.** Atrial natriuretic factor. (Windhager E E. ed.) *Handbook of physiology Section 8: renal physiology* New York: Oxford University Press, 1992. Vol. 2. p. 1577-673.
4. **Camargo M J F, Kleinert H D, Atlas S A, Sealey J E, Laragh J H & Maack T.** Ca-dependent hemodynamic and natriuretic effects of atrial extract in isolated rat kidney. *Amer. J. Physiol.* 246:F447-F456, 1984. (Cited 305 times.)
5. **Goodfriend T L, Elliott M E & Atlas S A.** Actions of synthetic alrial natriurctic factor on bovine adrenal glomerulosa *Life Sci.* 35:1675-82. 1984.
6. **Burnett J C, Jr., Granger J P & Opgenorth T J.** Effects of synthetic atrial nalriuretic faclor on renal function and renin release *Amer. J. Physiol.* 247:F863-F866. 1984. (Cited 560 times.)

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