

Vander A J. Control of renin release. *Physiol. Rev.* 47:359-82, 1967.

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The paper critically reviews the various theories proposed for the control of renin release. It then analyzes data from the many physiological and pathological situations associated with altered renin release, in the context of their consistency with these theories. [The SCI® indicates that this paper has been cited in over 605 publications since 1967.]

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"Until 1963, I had been a traditional renal physiologist at the University of Michigan, studying the handling of sodium and water by the kidneys. That year, I heard James O. Davis present Louis Tobian's intrarenal-baroreceptor hypothesis for the control of renin secretion, i.e., that the renin-secreting cells respond directly to the pressure within the renal arterioles.<sup>1</sup> It struck me, while listening to him, that changes in renal vascular pressure also caused important changes in the flow of fluid through the renal tubules and in sodium reabsorption, and I wondered whether one of these variables, acting via the macula densa, might be the actual controller of renin release. An experiment to distinguish between the baroreceptor and macula densa theories was easy to formulate, but I knew nothing about the methodology (then very crude) for measuring renin. At this time, a brilliant medical student, Richard Miller, came to work with me for the summer and began a totally unrelated project. However, we talked about the hypothesis and experiment I had been toying

with, and without hesitation, Rick abandoned his original project, set up the necessary methods, and we were off.<sup>2</sup>

"My lab produced a large number of experiments dealing with the control of renin secretion and, in 1966, I was asked by James W. McCubbin and Irvine H. Page to contribute a chapter<sup>3</sup> on this subject to a book that they were editing. After reading my manuscript, Page stated that he thought it deserved a wider audience and he suggested I submit it to *Physiological Reviews*, explaining to the editors of this journal that a very similar version would be appearing in the forthcoming book. Happily, this was not deemed a problem and the review was accepted.

"I believe there are several reasons for the paper being cited so often. It was the first comprehensive review of a subject that is not only of basic physiological significance but has very important implications for a variety of common diseases, including hypertension. Also, during the previous five years, there had been remarkable advances in our understanding of the role of the renin-angiotensin-aldosterone system, and many of the system's functions and properties had been reviewed. The methodology for quantitative studies of the controls over renin secretion itself had also been rapidly improving, and the growing number of studies in this critical area had generated considerable controversy. Perhaps the major value of my review was its attempt to analyze the various theories that had been proposed and the body of literature underlying them. I hope that the theoretical analysis provided by the review helped to stimulate the deluge of experiments on this subject that began about that time and still continues. Of course, whether or not my review really played a stimulatory role, the authors of all these papers were obliged to cite it for the next nine years, until the next comprehensive review was published."<sup>4</sup>

1. Tobian L. Relationship of juxtaglomerular apparatus to renin and angiotensin. *Circulation* 25:189-92, 1962. (Cited 160 times.)
2. Vander A J & Miller R. Control of renin secretion in the anesthetized dog. *Amer. J. Physiol.* 207:537-46, 1964. (Cited 400 times.)
3. Bunag R D, Vander A J & Kaneko Y. Control of renin release. (Page I H & McCubbin J W, eds.) *Renal hypertension*. Chicago: Year Book Medical Publishers, 1968, p. 100-17. (Cited 40 times.)
4. Davis J O & Freeman R H. Mechanisms regulating renin release. *Physiol. Rev.* 56:1-56, 1976. (Cited 595 times.)