INTRODUCTION

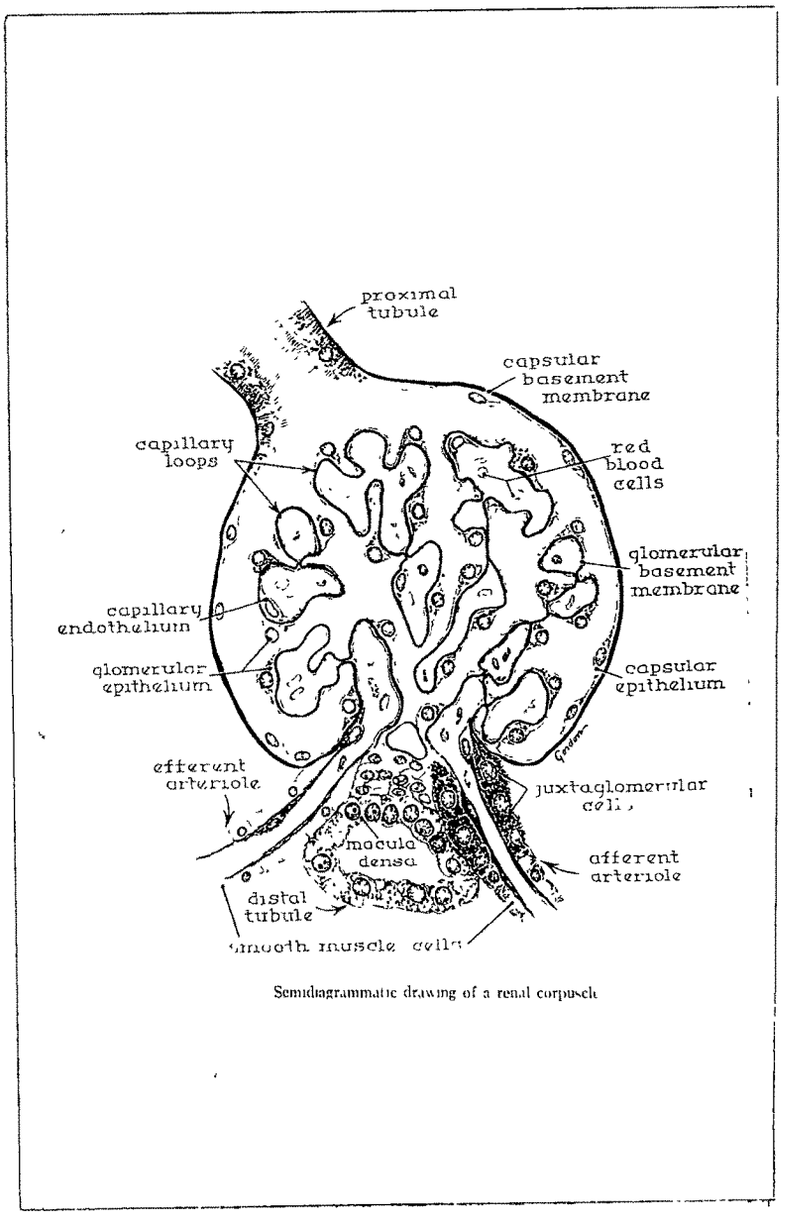
When renal blood flow is reduced renin is released from the juxtaglomerular cells of the nephron of kidney (Gen. fig.1) into the blood where it acts upon a protein to release angiotensin decapeptide (also called angiotensin I). Then another blood enzyme, the converting enzyme, acts on angiotensin I to form angiotensin II, an octapeptide, by removing two amino acids at the end of the chain. The decapeptide is only slightly active, while angiotensin II has a pressor activity about 200 times that of norepinephrine under certain assay conditions (76). The sequence of amino acids in angiotensin I and II is shown below (76).

Amino acids L - aspartyl (1) - L - arginyl (2) - L - valyl (3) -
L - tyrosyl (4) - L - isoleucyl (5) -
L - histidyl (6) - L - prolyl (7) -
L - phenylalanyl (8) - L - histidyl (9) -
L - leucine. (10)

Angiotensin I has amino acids from 1 - 10.

Angiotensin II has amino acids from 1 - 8.

The pressor action of angiotensin has been studied extensively, but there have been relatively few studies of effects of the compound on heart rate and the results

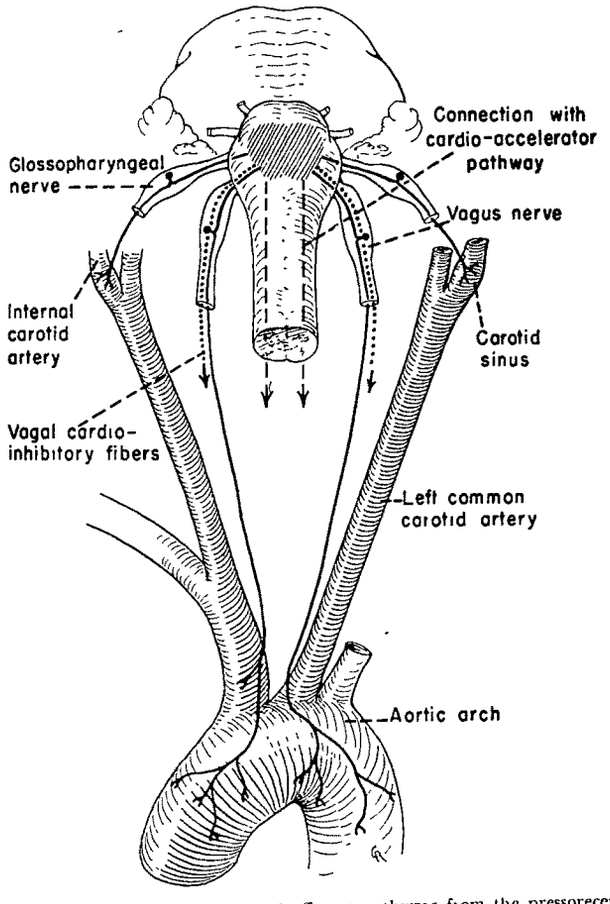


Gen. Fig. I: Juxtaglomerular cells in a renal nephron.

have been variable under different experimental conditions (20,21,63,90).

Marey, in his monograph on circulation of blood published in 1881, referred to the fact that an increase in blood pressure commonly is accompanied by a decrease in heart rate, while a fall in blood pressure commonly is associated with cardiac acceleration. Such patterns of change in heart rate and blood pressure occur when the primary change is in the peripheral resistance, and the mechanism, in large part at least, is that reflex effects on the cardioaccelerator and cardioinhibitory centers are elicited from the sinoaortic pressoreceptors (Gen. Fig. 2). When these receptors are stimulated there is cardiac inhibition, inhibition of vasomotor tonus and inhibition of respiration. Hence any agent which causes a rise in peripheral resistance by direct action on arteriolar tonus may be expected to elicit bradycardia and a brief period of respiratory inhibition.

The idea of studying the effect of angiotensin on heart rate came when it was found that there was no marked cardiac slowing despite the fact that angiotensin has marked vasopressor effect; moreover it showed different effects on heart rate with different doses.



—Diagram of principal afferent pathways from the pressoreceptors of the carotid sinuses and aortic arch. Connections are made in the medulla with the cardioinhibitory and cardioaccelerator centers. Efferent fibers from the cardioinhibitory center are found in the vagus nerve, fibers from the cardioaccelerator center descend in the cord to make connections in the upper thoracic part of the spinal cord with neurons of the sympathetic system.

Gen. Fig. 2 : Pathways for sinoaortic reflexes.

The present studies were performed to determine the effect of angiotensin on heart rate of dogs under morphine and chloralose as influenced by 1) mechanical buffering of blood pressure, 2) rate of injection of angiotensin at various sites, 3) sinoaortic denervation, 4) denervation of the heart, 5) transverse section of spinal cord, 6) blocking of autonomic ganglia, 7) blocking of the adrenal veins, 8) use of the β cell blocking compounds, and 9) use of the sympatholytic compounds.