ANESTHESIA AND THE RENIN-ANGIOTENSIN SYSTEM

EDWARD D. MILLER, JR., M.D.

It has been known since the middle of the 1800's that the kidney was an important determinant of blood pressure. Bright was the first to show that kidney disease could result in the elevation of blood pressure. It wasn't until the classic work of Goldblatt in the 1930's that a true relationship between constriction of the renal artery and elevation in blood pressure was made. Once that discovery had been made, though, many investigators thought that the renin-angiotensin system might be extremely important in control of blood pressure for a variety of circumstances. Unfortunately, once the ability to measure plasma renin activity became available in 1967,(1) the correlation between blood pressure and plasma renin activity was not as clear-cut as individuals had originally thought.(2) Some hypertensive patients, and in some other disease states, plasma renin levels were actually lower than had been anticipated, and therefore some believed that the renin-angiotensin system was not important in blood pressure control at all. However, in the early 1970's inhibitors of the renin-angiotensin system became available which specifically inhibited angiotensin II so that investigators could decide what the real role of this peptide was in blood pressure control.(3,4) The following discussion will look at some of those aspects and see how they are related to our management of patients in the operating room and in the intensive care units.

First, let us examine the renin-angiotensin system. Renin is an enzyme that is released from the kidney under a variety of stimuli. Once released into the circulation renin acts on a substrate, angiotensinogen, formed in the liver and cleaves off ten amino acids which form the peptide angiotensin I. Angiotensin I has no known physiologic properties and is converted to angiotensin II in a single pass through the lung. The conversion of the ten amino acids, angiotensin I, to eight amino acids, angiotensin II, occurs by cleavage of two amino acids from the angiotensin I by an enzyme called converting enzyme that is located in the endothelium of the pulmonary vasculature. Angiotensin II has a variety of properties that make it important in blood pressure control. These include constriction of arterioles, stimulation of aldosterone secretion, potentiation of thirst, potentiation of catecholamine release, and a variety of other stimulatory properties. The interaction of the renin-angiotensin system with atrial natriuretic peptide is complex at best, and since there are no specific inhibitors of atrial natriuretic peptide at this time, the relative role of each of these series of peptides remains to be investigated.

The mechanisms that are known to release renin from the afferent arteriole of the kidney include: a decrease in efferent arteriolar pressure (called the baroreceptor theory), changes in sodium which is delivered to the distal nephron, (called the macula densa theory) and neurogenic control, that is stimulation of the nerves that cause the kidney to release renin. As can be seen, these mechanisms all are involved in the regulation of volume and pressure status of the animal or the human.

Over the past twenty years, a variety of inhibitors of the renin-angiotensin system have now been produced. Saralasin, a competitive inhibitor of angiotensin II was the first of such peptides, but had to be used