SUMMARY AND CONCLUSIONS

Studies were performed to determine the effect of angiotensin on heart rate in dogs under morphine and chloralose as influenced by mechanical buffering of blood pressure, variations in rate of infusion of the drug, and sinoaortic denervation. The effects were compared with those of Pitressin produced when equipressor doses of the two compounds were given in the same dog and when blood pressure was buffered by means of a compensator.

It was demonstrated that the action of angiotensin when compared with equipressor doses of Pitressin was less effective in producing slowing of the heart rate just after injection. Heart rate returned to normal in the case of angiotensin within about 2 minutes after injection, then it went above the basal level. In the case of Pitressin heart rate had not reached the basal level 15 to 20 minutes after injection of the drug.

Mechanical buffering of blood pressure partially or completely prevented the pressor response to angiotensin and Pitressin. When the pressure was buffered and angiotensin was injected the initial slowing of

heart rate was not observed. In this case only acceleration was observed, while with Pitressin slowing was present although of less magnitude.

With slower infusions of angiotensin when blood pressure was not buffered the cardioinhibitory response proportionately was less and at a rate of 1.25 µg angiotensin/min. no slowing was produced. When rate of injection of angiotensin was increased stepwise from slow rates the cardioinhibitory response was less or absent, although the final level of blood pressure attained remained the same. If 5 µg/min. infusion was given the heart rate decreased 30 beats/min., while the same dose when reached gradually produced a slowing of only 3 beats/min. The later rise of heart rate, however, was proportional to the amount of angiotensin given.

After sinoaortic denervation a marked increase in heart rate was produced by angiotensin. No initial reduction in heart rate occurred. The heart rate rose simultaneously with the increase in blood pressure. This shows that angiotensin has an accelerator action on heart rate which starts just after the beginning of the injection, but in the intact animal reflex effects from baroceptors counteract the accelerator action at first. When the blood pressure reaches the maximum

level and is maintained the accelerator action becomes manifest. When angiotensin is produced in response to physiologic stimuli the blood levels probably rise gradually and hence it would not be expected to cause a decrease in heart rate.

It is postulated that angiotensin has a cardio-accelerator influence which is exerted through the medullary centers and the nerves to the heart. This acceleration effect is present after vagotomy, but it is reduced after transverse section of spinal cord and after bilateral sympathectomy through T_1 to T_6 of sympathetic chain on either side of vertebral column. This showed that a component of cardiac accelerator action of angiotensin is via cardiac accelerator center and via sympathetic fibers to the heart.

However, other component of the cardiac accelerator action which is present after transverse section of spinal cord and after sympathectomy points towards the peripheral action of angiotensin on heart rate.

The presence of cardiac accelerator effect of angiotensin after ganglion blocking and after chemical sympathectomy also point towards the peripheral mode of action of angiotensin.

This peripheral action could be due either to stimulation of post-ganglionic sympathetic nerve endings to the heart or because of the stimulation of sinoatrial node of heart. The possibility of stimulation of adrenal medulla by angiotensin and thereby increasing the heart rate is also there.

It has been observed that a single dose of 10 µg of angiotensin does not release sufficient catecholamines from adrenal medulla so as to cause cardiac acceleration.

After sympatholysis by reserpine and after blocking of Beta cells of pace maker by inderal angiotensin does not show cardiac accelerator effect.

From above findings it may be concluded that angiotensin releases adrenalin from sympathetic supply to the heart which accelerates the heart rate. The other mechanism of acceleration of heart rate is because of its stimulatory effect on cardio-accelerator center of medulla.