CHAPTER V

DISCUSSION

The present investigation was designed to determine whether any alterations of renal functions during intrarenal infusion of hypertonic and hypotonic saline in either hypothyroidism or hyperthyroidism were due to change of extrarenal or intrarenal factors.

Effect of hypertonic saline infusion :

During hypertonic saline infusion in the control group (Group I), an increase in renal blood flow (RBF), effective renal plasma flow (ERPF) and urinary electrolyte excretion cannot be attributed to an increase in renal fraction since cardiac output, mean arterial blood pressure and glomerular filtration rate (GFR) did not change. The decrease in renal vascular resistance (RVR) was observed in the infused kidney. Thus, an increase in RBF may be due primarily to local vasodilatation. In the present study, hypertonic saline infusion (537 mOsm/kg) caused an elevation of plasma sodium concentration in the renal artery to 2.67 ± 1.81 mEq/ml/min. The rate of infusion was adjusted to equal the rate of urine flow plus the amount of blood withdrawn to prevent a change in plasma fluid volume. Many studies indicated that the fall in sodium reabsorption associated with volume expansion was found to take place in the proximal tubule (Landwehr and Giebisch, 1947, Rector *et al*, 1964, Dirk, Cirksum; and Berliner, 1965, Cortiney *et al*, 1965, Hayslett *et al*, 1967). However, volume expansion in the present study might not expect since plasma

volume and packed cell volume remained unchanged during all recorded periods.

An increase in C_{Osm} in the infused kidney indicates hypertonic saline infusion generated local osmotic diuresis. If hypertonic saline infusion affected an increase in hyperosmolarity of the plasma, the contralateral control kidney should show parallel changes to those in the ipsilateral infused kidney. These were not shown in this study. Changes in the rate of urine flow, urinary excretion of sodium, chloride and C_{Osm} during the infusion of hypertonic saline can be assumed to be a direct response to a change in sodium chloride concentration in the renal artery. These results were consistent with the result of early study (Chaiyabutr and Malila, 1977). With a hypertonic saline infusion, the increase in filtered load and the retention of solutes within the tubular lumen has been suggested to depress proximal tubular reabsorption (Giebisch *et al*, 1964).

This study is shown that serum T_4 level in the hypothyroid is lower than that of the control dogs. In hypothyroid animals, there was a reduction in renal hemodynamic. These results were similar to the results also noted by previous investigators (Chaiyabutr, 1981, Williams, 1981). During hypertonic saline infusion in hypothyroid animals, the rate of urine flow increased by 63% while GFR and RBF decreased markedly in the infused kidney. The depression in GFR and RBF of the infused kidney were related to an increase in RVR by approximately 24%. Therefore, the reduction of renal hemodynamics cannot be attributed solely to a decrease in cardiac output

since there was clear evidence of additional local vasoconstriction. However, in the infused kidney, the filtration fraction increased in accompany with the reduction of GFR which was disproportion to that of RBF. The study showed that there are relatively rapid effects on the diuresis as hypertonic saline infusion in the hypothyroid dog. But the question arises of whether the changes in renal functions during the infusion of hypertonic saline in the hypothyroid group simply reflect a change back to normality, as part of a process of deadaptation from the normal state. There were a reduction of the activity of the renin-angiotensin system in the hypothyroid state, but the mechanism is not clear (Bradley, 1978, Williams, 1981, Dzau and Herrmann, 1982, Ganong, 1982, Resnick and Laragh, 1982). However, the increases in the rate of urine flow and urinary electrolyte excretion in the infused kidney of the hypothyroid dogs might occur to be due to solutes entering the tubules. It cannot pass through the membrane and it will be retained within the tubular lumen. Creation of the osmotic gradient will interfere the reabsorption of a normal fraction of isosmotic sodium resulting in osmotic diuresis.

The present data showed that general circulation and renal hemodynamics of the hyperthyroid were higher than the control dogs. These results were similar to previous studies (Pronina, 1971, Chaiyabutr, 1981, Williams, 1981). During hypertonic saline infusion in hyperthyroid dog, the marked rise in RVR of the infused and the contralateral kidneys indicate renal vasoconstriction. However, these results show no relationship between RVR and other renal variables. An increase in fractional and urinary electrolyte

excretion of the infused kidney showed a greater degree than the contralateral kidney. This difference could be due to an increase in filtered solutes induced the effect towards natriuresis in the infused kidney. Since, urinary sodium and chloride excretion of the infused kidney increased by approximately 14% and 11% respectively.

An increase in urinary electrolyte excretion despite a slight decrease in RBF and GFR of the infused kidney in the hyperthyroid group indicates no relationship between renal hemodynamics and the regulation of electrolyte balance. Early investigators reported that there was an increase in the activity of the renin-angiotensin system during hyperthyroid state (Bounik, 1981, Dzau and Herrman, 1982, Resnick and Laragh, 1982). The present results seem to support the finding that the intrarenal renin-angiotensin system plays an important role in regulating renal hemodynamic, but does not contribute to the regulating of water and electrolyte balance (Levens *et al*, 1981).

Effects of hypotonic saline infusion

Infusion of hypotonic saline (27 mOsm/kg) caused a decrease in renal plasma sodium concentration to 2.87 ± 1.94 (Mean ± S.D.) μEq/ml/min. In control dogs, there were a marked decrease in RBF which related to marked increase in RVR of both kidneys during hypotonic saline infusion. In hyperthyroid dogs, there was a significant decrease in GFR but RVR increased slightly of both kidneys. The urine flow rate and urinary excretions of eletrolytes in the infused and the contralateral kidneys were decreased slightly. These

results point that there is a vasoconstriction of both kidneys during the infusion of hypotonic saline in the control and hyperthyroid dogs. The vasoconstriction would expect to be prominant in afferent arterioles.

Hypotonic saline infusion in the hypothyroid dogs caused a significant decrease in the rate of urine flow, urinary excretion of sodium whereas a slight decrease in GFR, RBF, U_KV and $U_{Cl}V$. There was a slight increase in RVR in the infused kidney. But the contralateral kidney changed slightly. These results indicate that local vasoconstriction still occurs in the infused kidney during hypotonic saline infusion in hypothyroid dogs. The infusion of hypotonic saline solution in the hyperthyroidism showed more potent effect than the hypothyroidism. There was an evidence that hyperthyroidism would be expected to be associated with increased renin secretion and hypothyroidism would be associated with decreased plasma renin activity (Ganong, 1982). If this hypothesis is accepted, the alterations of renal functions during hypotonic saline infusion in hypothyroid and hyperthyroid groups may be the result of changes in the renin-angiotensin system. The early report has been presented to support the hypothesis that macula densa acts as a sensor to detect a signal provided by the renal tubular fluid and alters in some way of the rate of renin release (Davis and Freeman, 1976). The previous study suggested that an increase in sodium load to the macula densa might be the signal that block the rise in renin release (Vander and Miller, 1964), and therefore the rate of renin release, but the specific mechanism has not been established (Mayer and Stein, 1981).

The present experiment has demonstrated that major changes occur in the kidney of hyperthyroid dog during hypertonic saline infusion. Varied of physiological changes which occur in the contralateral kidney of hyperthyroid dog have been shown to be the result of systemic effect. Although, we know a great deal of the change of renin-angiotensin system during hypotonic saline infusion, we do not know the physiological signal which increase local vasoconstriction during hypertonic saline infusion in both hypothyroid and hyperthyroid dogs. There is still a need for more information, for example; intrarenal hormonal changes and/or local regulatory mechanism which is mediated to be responsible for the renal vascular tone during hypertonic saline infusion.