CHAPTER V

Discussion

In the first series of the experiment, the Russell's viper venom was injected intravenously in order to offset variation in the degree of absorption, and to be sure that the dog had recieved exactly the amount of venom required. It was found that the minimal lethal dose for the dog was in the range of 0.2-0.35 mg./kg.bw. But when using these doses in anaesthetized dogs, the dogs were deeply depressed and died easily. The was therefore adjusted at 0.1 mg./kg.bw. The Russell's viper venom in general has a pronounced haematotoxic effect (Lee and Lee, 1979). Some evidence suggested the possibility that the venom affected the central nervous system indirectly as a consequence of anoxia resulting from arterial hypotension (Meldrum, 1965; Sket et al., 1973). The anaesthatic drug is known to depress the respiratory center in the medulla (Meldrum, 1978). Therefore, the present study both venom and anaesthetic drug would symergistically act to decrease oxygen supply of the central nervous system.

In the second series of the experiment, the venom produced an immediate fall in arterial blood pressure, narrow pulse pressure and a decrease of heart rate, which were similar to the results of Vick et al., (1967) and Lee (1948). These workers concluded that hypotension was due to vasodilation of capillaries in the hepato-splanchnic area, and could be

prevented by evisceration. Lee and Lee (1979) reported that the fall in blood pressure was not central in origin, since in decerebrated or despinated animals (Chopra and Chowhan, 1934; Chopra et al., 1935), or after elimination of the brain circulation, exactly the same results were produced.

The present study showed that an increase in total peripheral resistance without alteration of cardiac output 2 hours after envenomation indicating a compensatory mechanism for maintainance of blood pressure. It was observed that the cardiac output markedly decreased in the animal which could not compensate and died within 24 hours after envenomation. (Chaiyabutr et al., unpublished data). Blood pressure, especially diastolic blood pressure decreased 24 hours after envenomation. The decrease in blood pressure was attributed to the decreased total peripheral resistance and decreased blood volume due to bleeding resulted from clotting effect. The total peripheral resistance markedly decreased at 24th hour of venom injection. It is possible that accumulation of waste products following hypoxia during the initial hypotension could account for the decrease in peripheral vascular tone and thus total peripheral resistance (Sullivan et al., 1981). It might be suggested that the Russell's viper venom could possibly cause vasodilation similar to the venom of Bothrop jararaca. Thus postulation remains to be worked out. A slight increase of blood volume during hypotension seemed to be due to splenic contraction (Ganong, 1977). During 24-48 hours, packed cell volume markedly decreased because of

massive bleeding due to clotting defect after envenomation. The changes in haemoglobin concentration in the present experiment was found to correlate to the changes in packed cell volume. Plasma volume was almost constant and mean corpuscular haemoglobin concentration was in normal range throughout the experiment. These results indicate that the increase in the packed cell volume is exactly due to splenic cotraction, not to the extravasation of plasma and swelling of red blood cell.

The increase in total peripheral resistance after envenomation was probably due to vasoconstriction during hypotension, which might be caused by renin-angiotensin activation or sympathetic activity or other compensatory mechanisms of the body (Ganong, 1977). A marked increase in renal vascular resistance after envenomation seemed to be due to the vasoconstriction of the renal arteriole during hypotension. The increase in renal vascular resistance appeared to be more than the increase in total peripheral resistance, by approximate 1.3 folds throughout the experimental period, as shown in figure 7. There was evidence to support that both glomerular filtration rate and effective renal plasma flow decreased after envenomation. The decrease in effective renal plasma flow is more than the decrease in glomerular filtration rate, giving the significant increase in filtration fraction after envenomation.

The determination of tubular activity by transport of PAH, showed decreased tubular function 2 hours after envenomation and returned to normal condition at 48th hour;

when the transport of PAH showed no difference from the control. The osmolar clearance had a markedly significant decrease at 24th hour after envenomation due to the decrease of glomerular filtration rate, and returned to normal level 24 hours after envenomation. Free water clearance had a markedly decrease at 24th and 48th hour. These indicated that tubular cell activity had a normal function to reabsorb water during hypovolemic condition due to bleeding by clotting defect. Apart from these, there was no statistically significant difference in plasma creatinine concentration between the control and the experimental period, as shown in figure 7. These results indicate that the secretory function of tubular cell is still normal. The present study reviewed no evidence of tubular necrosis from histopathological examination and renal tubular function remained intact. These results were different from previous reports inwhich haemorrhage and intravascular coagulation with subsequent tubular necrosis and acute renal failure occuring in man (Sitprija et al., 1976) and experimental animals (Aung-Khin, 1978).

However, at the end of the experiment the renal vascular resistance was still higher and the renal fraction was still decreased when compared with the control (figure 4 and 7). An acute renal failure might have been noted if the animals were observed for a longer period of time. Moreover, the antigen-antibody complex from snake venom may trigger the immunologic reactions leading to the development of glomerular

lesion which may further compromise renal function. Sitprija and Boonpucknavig (1979) suggested that vasculotoxic effect of the venom, intravascular coagulation and immunologic reaction due to the antigenicity of the venom were responsible for renal lesion in Russell's viper bite. The absence of renal lesion in the study could be explained by the use of too small dose of venom and the short period of observation.

The filtered load of electrolytes decreased significantly 24 hours after envenomation. This was attributed to the decrease in glomerular filtration rate. Plasma concentration of electrolytes showed no important change statistically throughout the period of experiment. The decrease in urinary sodium concentration, sodium excretion and fractional excretion of sodium was significant during the 2th hour and started to increase at 24th hour. The decrement during the 2th hour was due to the decrease in filtered load; and the increment at 24th hour could be due to the decreased renal vascular resistance and filtration fraction. The changes of excretion and fractional excretion of potassium, chloride and calcium were also similar to sodium; and urinary concentration of only chloride and calcium had the same pattern as sodium. Urinary potassium concentration increased throughout the experiment as compared with the control, especially at 2th hour after envenomation. This may be due to potassium secretion of distal tubule and collecting duct (Pitts, 1968) and haemolysis of red blood cell in urine samples. Urinary phosphorus concentration, phosphorus excretion and fractional

excretion of phosphorus highly increased 24 hours after venom injection (table 5), this could be due to the compensation of the body during metabolic acidosis following hypoxia from hypotension. In acidosis condition, the kidney had a tendency to reserve bicarbonate and excrete hydrogen by excretion of phosphate (Pitts, 1968). Therefore, the urinary phosphorus concentration increased significantly. Increase phosphorus excretion due to tubular injury is also a possibility.

From this study, it is concluded that the Russell's viper venom affected cardiovascular system and renal haemodynamics, which dictated renal function change of minimal magnitude. General circulation returned to normal within 48 hours, while renal haemodynamics incompletely returned to normal. The renal vascular resistance remained higher and renal fraction remained lower when compared with the control.