Chapter I

Introduction and Aims

Acute renal failure (ARF) often occurs in patients bitten by Russell's viper. A broad spectrum of renal lesions, including arteritis (Sitprija et al., 1974), tubular necrosis (Chugh et al., 1975; Shastry et al., 1977; Sitprija et al., 1974; Sitprija and Boonpucknavig, 1977), cortical necrosis (Chugh et al., 1975), interstitial nephritis (Sitprija et al., 1982) and glomerulonephritis (Sitprija and Boonpucknavig, 1980) have been reported, but tubular necrosis is most common. The pathophysiology of ARF following viperine envenomation remains unclear despite a number of studies and clinical investigation. However, very few evidences are available to indicate that the changes in renal functions are due to directly nephrotoxic effect or indirectly as a consequence of shock, disseminated intravascular coagulation, vasculopathies single or in combination.

Previous experimental in dogs, marked changes in systemic and renal hemodynamic occured during the early phase of envenomation intravenously. There were obvious decreases in general circulations for example: blood pressure, heart rate and cardiac output while a mark increase in systemic vascular resistance was apparent (Chaiyabutr et al., 1984). An increase in renal vascular resistance has been suggested to be due to local vasoconstriction which may play a role in the initial pathogenesis of ARF (Schrier and Conger, 1980; Tungthanathanich et al., 1986).

According to current concepts, A number of intrarenal hormones act locally on the nephrons and renal vasculature. Vasodilation, regulated by prostaglandins and kallikrein-kinin system while vasoconstrictors mediated by norepinephrine and renin-angiotensin system (RAS). Prostaglandins are formed within the kidney and appear to exert natriuretic effect. Antinatriuresis is also induced by blocking the synthesis of prostaglandins with indomethacin. The study in the pretreated dogs with indomethacin, results in reducing the renal hemodynamics effects of Russell's viper venom was reported by Thamaree et al., (1987). A possible mechanism may be due to the lack of dilatory prostaglandins (e.g. PGE_2) and/or overproduction of thromboxane A_2 (TXA_2), a powerful renal vasoconstriction (Gerber et al., 1978). The other hormones, Renin-angiotensin system and norepinephrine also involve in renal vasoconstriction. Evidence in pretreated envenomized rats with angiotensin II inhibitor (MK-422, enalapril maleate), showed a tendency to increases in urine flow, glomerular filtration rate and renal blood flow, (Chaiyabutr et al., 1985). Interestingly, pretreated dogs with enalapril maleate and imidazole (thromboxane synthetase inhibitor) associated with left renal artery infusion of prazosin, α_1-adrenergic blocker, throughout the experiment in viperine envenomation has been presented by Kidmungtandee (1989). The results showed the improvement of renal function after envenomation and suggested that catecholamine may be an important mediator of Russell's viper venom induced ARF, But no evidence to report the changing of catecholamine level in general circulation relating to kidney function after envenomation.

From this contribution, the change of catecholamines for

example norepinephrine level might be a modulator in Russell's viper venom induced ARF and/or as a consequence with changing in renin-angiotensin system and prostaglandins. To examine this hypothesis prazosin (α_1-adrenergic blocker), enalapril maleate (converting enzyme inhibitor) and indomethacin (cyclooxygenase inhibitor) were used in experimental dogs, whether changes in renal function and renal circulation are affected by changes of circulating norepinephrine during envenomation.