Chapter I

Introduction and Aims

The pathophysiology of acute renal failure (ARF) has been shown to occur in many clinical situations, for example hemorrhagic shock, myoglobinuria and septicemia. In addition of ARF also occurs in envenomation of Russell's viper (Sitprija and Boonpucknavig, 1974; Harris et al., 1976; Shastrey et al., 1977). The pathophysiology of ARF following Russell's viper envenomation remains uncertain despite a number of experiments and clinical investigations (Aung-Khin, 1978). The effects of venoms on the kidney function are most complex. A broad spectrum of renal lessions, 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. No evidence is available so far to indicate whether the changes in kidney functions are due to direct toxic action of the venom or it occurs indirectly as a consequence of shock, disseminated intravascular clotting, vasculopathies single or in combination.

Previous experimental in dogs given Russell's viper venom showed marked reductions in renal blood flow and glomerular filtration rate which concomittant with an increase in renal vascular resistance. There were obvious decreases in general circulations for example blood pressure, heart rate and cardiac output while a marked increase in

total peripheral resistance was noted (Chaiyabutr, 1985; Tongvanchai, 1984; Tungthanathanich, 1983). After envenomation, the blood pressure increased and approached to the control level within 2 hours. However, renal blood flow, glomerular filtration rate and renal fraction were decreased throughout the period of 2-48 hours after envenomation (Tungthanathanich et al., 1986). These changes were accounted for the local renal vasoconstriction.

According to current concepts, renal circulation regulated by two hormones system. Vasoconstriction, mediated by norepinephrine and/or the renin-angiotensin system; while prostaglandin compounds and the kallikrin-kinin system act as vasodilators. Interestingly, Thamaree (1987) demonstrated the pretreated animals with indomethacin, an inhibitor of prostaglandin synthesis, decreased the renal hemodynamic effects of Russell's viper venom. A possible endogenous mechanism for releasing the hormone induce vasoconstriction after envenomation 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). Direct evidence for the involvement of renin-angiotensin activity in response to renal vasoconstriction after envenomation has been noted by Chaiyabutr et al. (1985) in pretreated envenomize rats with intrarenal angiotensin II blockage (MK 422, enalapril maleate). Resulted in increases in urine flow, glomerular filtration rate and renal blood flow were demonstrated, when compared with the nonpretreated rats.

However, many evidences indicate that experimental animal recieved lethal doses of endotoxins caused rapid and severe haemodynamic changes. The response of animals is charecterized by an

immediate sustained rise in angiotensin levels and a later variable rise in catecholamine levels (Hall and Hodge, 1971; Nykiel and Glaviano, 1961; Schaller et al., 1985; Heiffer et al., 1958). Recently, Koyoma (1984) reported that intravenous (i.v.) injection of E.coli endotoxin (1 mg/kg) in anesthetised cats, the blood pressure falls together with the reduction in sympathetic outflow. During the period of maximal drop in mean arterial pressure (MAP), a compensatory increase in the integrated nerve discharge proceding a transient increase in MAP. However, it has been known that catecholamine or renal nerve stimulation are involved in modulating a number of aspects of renal physiology, including renal blood flow, glomerular filtration and renal vascular resistance (Insel and Snavely, 1981).

From this contribution, catecholamine might be an important mediator of Russell's viper venom induced ARF. To examine this hypothesis prazosin which is α_1-adrenergic blocker was used in experimental dogs, whether changes in renal function are affected by changes in renin-angiotensin system, thromboxane A_2, catecholamine or combination during envenomation.