CHAPTER II

Background Information

Russell's viper is found in Thailand and in some areas in the world. Generally it is a quiet and peaceful snake. It prowls in the night to search of prey which consists of mice, rats, frogs etc. It attacks man in self defense only when provoked. The venom is secreted from the salivary gland. The venom is a mixture of physiologically and toxicologically active substances. The compositions of the venom are lipid, carbohydrate, amino acid, nucleosides, nucleotides, organic phosphate compounds and many enzymes including phosphodiesterase, ATPase, hyaluronidase. The venom also consists of toxin protein and necrotizing properties. (Iwanaga and Suzuki, 1979). A bleeding manifestration are frequently following a bite was reported (Chugh et al., 1975). Early signs of systemic poisoning were blood stained spit, non clotting blood and other hemorrhagic signs, bleeding from gums, ecchymosis and positive tourniquet test followed in 1-3 hours. Hematemesis, hematuria and shock developed in severe cases (Trisna-nanda, 1979). These signs were also reported in experimental animals injected with Russell's viper venom (Tungthanathanich, 1983). It has been known for many years that the venom of Russell's viper has powerful coagulant properties so it can be used as substitute for tissue thromboplastin in the determination of the prothrombin time (Kleinman et al., 1945). Lee et al, (1955) demonstrated that the Formosan daboia (Russell's viper) venom had a potent coagulation action in vivo as well as in vitro and its action was resembles that of thromboplastin but not that of thrombin.

Effects of Russell's viper venom on cardiovascular functions.

The action of Russell's viper venom on the circulatory system
was studied by Chopra and Chowhan (1934). A small doses of venom was
injected intravenously in the cat produced a slight initial rise in
blood pressure followed by sudden fall in blood pressure and the
animal sometimes died suddenly from convulsion and heart failure.
Lee (1944) proved that the sudden death produced by Russell's viper
venom was due to intravascular clotting. The systemic blood vessels
were founded to be contracted and those of the splanchnic area were
widely dilated as in histamine shock. The nervous center was not
much affected after envenomation. It has been shown that in
decerebrated animals exactly the same results were produced (Lee,
1948). The symptoms of shock in daboia (Russell's viper) poisoning
were the local dilatation of the splanchnic area not due to the
reflex impulses.If the mesenteric arteries are clamped, large doses
of the venom did not produce any marked effect in the blood pressure.
The paralytic action of the venom seemed to be confined to the
capillaries only (Lee,1948). In the perfusion experiment it showed
that the veins and arteries were not dilated, but showed a tendency
to constrict. The paralytic action of the venom on the capillaries
was observed to be similar to that of histamine, since the venom did
not give only fall of blood pressure after large doses of histamine
and vice versa (Ishvariah and Davis,1932; Chopra and Chowhan,1934).
Drugs like ether and chloroform which depress the capillaries,
potentiated the action of venom. Epinephrine and pituitrin tone up
the capillaries, while glucose, gelatin and gum-saline increased
the total volume and the viscosity of the blood tend to increase the

blood pressure.

Vick et al., (1967) concluded that Russell's viper venom produced an intermediate and irreversible decline in arterial blood pressure. Pulse pressure narrowed and heart rate decreased as arterial pressure fell. Respiration was not affected in the initial post injection period. After approximately 10 minutes, respiratory movement ceased abruptly and profound bradycardia was noted. Evisceration prevented the initial hypotension and bradycardia. Vagotomy did not prevent the sharp fall in arterial blood pressure. However, bradycardia was prevented and a significant increase in heart rate occured.

Effects of Russell's viper venom on renal functions.

Acute renal failure is an important cause of death in patients who survived from the early effects of viper's toxin (Aunkhin, 1978). Many investigators believed that viper's venom had a direct cytotoxic effect on renal tubular cells (Schreiner and Maher, 1965; Hadler and Brazil, 1966; Raab and Kaiser, 1966). Because of the kidney receives the largest volume of blood per unit weight of tissue (Starling and Lavatt, 1962). Hypotension due to the cardiovascular effect of the venom can cause the sudden decrease in renal blood flow which may induce ishemic renal failure. However, renal failure has been noted in some cases of Russell's viper bite without hypotension (Sitprija and Boonpucknavig, 1979). The pathological findings in the kidney following a snake bite were acute tubular necrosis, bilateral diffused cortical necrosis, proliferative glomerulonephritis, hemorrhagic nephritis and hemorrhagic interstitial nephritis

(Oram et al., 1963; Sant and Purandare, 1972; Sitprija and Boonpuck-navig, 1977). The pathogenesis of ARF following a bite has been attributed to hemorrhage leading to circulatory failure, shock, collapse, acute intravascular hemolysis and disseminated intravascular clotting (Oram et al, 1963; Reid, et al, 1963).

Sitprija and Boonpucknavig (1974) reported that necrotizing arteritis in patients following the Russell's viper's bite were due to the deposition of B_1C globulin in the arterial wall. No immuno-globulins were noted in the lesion. None of fibrin deposition was seen. The vein showed wall necrosis and luminal occlusion by platelet thrombus. Arteritis was present at the level of interlobar and arcuate arteries. The arterioles and capillaries showed no changes. Deposition of complement in the arterial lesion without immunoglobulin suggested a nonimmunologic activation of the complement system through an alternate pathways (Bruninga, 1971; Ruddy et al, 1971).

Sarangi et al, (1980) indicated that the most common type of renal function impairment following Russell's viper bite was oliguria with an incidence of hematuria. Tungthanathanich (1983) reported that the effects of Russell's viper venom injection on dog's renal function were the decrease in renal function, such as renal plasma flow, renal blood flow, glomerular filtration rate and urine flow rate.

Acute renal failure in splenectomized animals.

Epinephrine infusion in monkeys and rabbits produced coagulation in the peritubular capillaries with consequent ischemia. (Whitaker et al., 1969). Mandal et al., (1978) studied the changes

in renal morphology induced by epinephrine injection between intact and splenectomized dogs. The splenectomized dogs had significantly less tubular and glomerular damage with renal congestion but no evidence of coagulopathy as in intact dogs. This suggested that the spleen might play a role in pathogenesis of ARF. It was found that intact dogs had more severe ARF than splenectomized dogs and also had a higher packed cell volume. The higher packed cell volume might be the significant factor responsible for the renal lesion. Bell et al., (1981) confirmed that an intravenous infusion of epinephrine caused acute tubular necrosis by approximately 75% of intact, but only 13% of splenectomized dogs.

It is well known that spleen contains large amount of erythrocytes, leukocytes, platelets and other clotting factors. Sympathetic stimulation causes intense splenic contraction and release its contents. This effect caused the increment of packed cell volume, blood viscosity and blood coagulability. Epinephrine infusion in intact dogs was sustained depression of renal blood flow and urine flow. It has been suggested that the protective effects of splenectomy may involve by a reduction of blood coagulability or facilitation renal prostaglandin release (Bell et al., 1981). The experiment of Mandal (1982) supported hypothesis that renal protection might be mediated by an effective vasodilator prostaglandin attested by reversal of the renal protection after pretreatment with indomethacin in splenectomized animal.