Chapter I

Introduction and Aims

The pathophysiology of acute renal failure following viperine envenomation remains uncertain despite a number of experiments and clinical investigations (Aung - Khin, 1978). The early reports have been shown that the changes in renal functions are due to indirectly as a consequence of shock, disseminated intravascular coagulation, vasculopathies singly or in combination (Chugh et al., 1975; Jeyarajah, 1984). However, acute renal failure has been noted in some case of Russell's viper bite without hypotension (Sitprija and Boonpucknavig, 1977) or correlation between the severity of renal failure and coagulopathies (Shastry et al., 1977). The observation in isolated perfused kidney showed a direct nephrotoxicity of Russell's viper venom as that seen in acute tubular necrosis from the other causes (Retcliffe and Pukrittayakamee, 1985). However, the mechanisms responsible for the development of acute renal failure following envenomation have not been clear, although many of the profound histopathological, immunological,electrophysiological, biochemical and physiological alterlations that occur in the kidney and other organs have been described (Richard et al., 1965; Kocholaty et al., 1971; Chugh et al., 1975; Sitprija et al., 1982 Stolc, 1985).

Many renal functions are altered during envenomation. For example: glomerular filtration rate and renal blood flow decreased, renal vascular resistance and filtration fraction

increased, while fractional electrolytes excretion varied (Tungthanathanich et al., 1986). It is interesting that fractional excretion of inorganic phosphorus increased many folds after envenomation. The phosphaturic effect of Russell's viper venom remains unclear. Many factors have been shown to be related with phosphaturic effect, such as volume expansion, glycosuria, parathyroid hormone (Denis et al., 1979; Jastack et al., 1968), c - AMP (Agus et al., 1971; Butten and Jard, 1972; Hammerman and Hruska, 1982), acidosis (Gyory et al., 1968; Hulter, 1984) and inhibition of sodium - phosphate cotransport system (Denis et al., 1979). As part of present study aimed to elucidate the factors responsible for the hyperphosphaturia and mechanism of acute renal failure following Russell's viper envenomation. Since previous investigations indicated that the Russell's viper venom induced depolarization of proximal renal tubular cell (Chaiyabutr et al., 1985) and enhanced c - AMP formation in human mononuclear and polymorphonuclear leukocytes (Stolc, 1985). These effects have been considered to be a direct physical interaction to the specific sites or the composition in the cell membrane which interposed the membrane permeability that govern the transport of ions across tubular cell. Therefore, the present study has been made in order to determine, first, whether an alteration of inorganic phosphorus excretion occur as a direct effect of Russell's viper venom on the renal tubular cell and, secondly, whether, hyperphosphaturia occurs as a consequence of acidosis or the secondary hyperparathyroidism during envenomation. Acutely thyroparathyroidectomized animal (TPTX) was performed to exclude the effect of parathyroid hormone. This investigation will gain deeper

insight into the mechanism(s) responsible for the development of acute renal failure following Russell's viper envenomation.