CHAPTER V

DISCUSSION AND SUMMARY

The renal pathology in wistar rats following Russell's viper envenomation revealed varying degrees of focal tubular degeneration, intratubular casts, vascular congestion and intraglomerular fibrin thrombi. Significant pathological changes occurred within the first 3 days, but at 10^{th} and 30^{th} day, renal histology was nearly normal. All of these changes in pathology were demonstrated as early as 2 hours after envenomation, though the characteristic of tubular necrosis was more apparent after 24 hours. In an experimental study reported by Chugh et.al. (1984), absence of renal lesions in most animals receiving lethal dosages of the venom might be due to inadequate time for any pathology to be shown.

From our data, both renal tubular lesion and vascular congestion scores are significantly higher than those of the control group. However, only tubular lesions which have been frequently reported in human are generally accepted as a major pathological change in cases of Russell's viper bite. In those cases, biopsy or autopsy was usually performed late in the course of disease, so renal vascular congestion was not demonstrated.

Infact, the feature of renal vascular congestion has been described in many cases of ischemic renal injury in both humans and experimental animals (Mason et.al., 1984). In 1986, Mason proposed the role of medullary hyperemia in the pathogenesis of ischemic renal failure.

Analyzing the correlation between renal functions and degrees of vascular hyperemia, she and her colleagues found that when medullary hyperemia was more severe, renal blood flow, glomerular filtration rate and tubular functions were more compromised. Their subsequent study showed that correction of vascular congestion could restore renal functions.

The possible pathogenetic mechanism of vascular congestion came from a work by the same group of investigators (1987). In post-shocked kidney, congested vasculature almostly contained densely packed erythrocytes, while intravascular plasma water was nearly absent. They concluded that, in ischemic condition, vascular congestion occurred after plasma water had been taken by adjacent swollen tubular cells.

The role of vascular congestion in the pathogenesis of renal failure in cases of Russell's viper bite is still not known. Since this study did not find strongly positive correlation between vascular congestion and tubular lesion, the significance of vascular congestion as a pathogenetic mechanism cannot be proved.

On the other hand, the feature of vascular congestion in our study would support the role of renal ischemia in pathogenesis of tubular lesions. Our findings of patchy distribution of tubular degeneration, tubulorhexis lesion, and vascular congestion resemble many renal pathological changes in various ischemic conditions which have been reported in humans and experimental animals. In addition, our data do not show the correlation between dosages of the venom and severity of tubular lesions. The mean tubular lesion and vascular congestion scores of group A in some intervals were significantly higher than those of group B, even though the animals in group A received lower dosages of the venom. These lines of evidence indicate the significant role of renal ischemia in the pathogenesis of tubular necrosis from Russell's viper venom. The role of

direct nephrotoxicity, albeit not completely excluded, seems less significant.

Mechanisms of ischemic renal damage from the venom may be either through hemodynamic alteration or intravascular congestion. We believe that both mechanisms play roles in the pathogenesis. With aforementioned data, the role of intravascular coagulation has been proposed by many investigators (Chugh et.al. 1984, Date and Shastry 1982). Their evidence came from the studies which demonstrated intraglomerular fibrin thrombi. Our study also demonstrates fibrin thrombi;however, the percentage of cases with positive fibrin is only 25%, while tubular lesion is found in 100%. Thus, we feel that intravascular coagulation would not be the primary pathogenetic mechanism.

Since fibrin and its products can be dissolved readily by fibrinolytic system in a body, its pathogenetic role cannot be excluded only by the reason of negative fibrin stains in specimens. However, though the renal morphological studies were performed as early as 2 and 6 hour by using both light and electron microscope, few of them showed a significant amount of fibrin.

In the experimental work carried out in India by Chugh et.al. (1984), high percentage of glomeruli contained fibrin. In this study,the percentage of demonstrable intraglomerular fibrin is much lower. These conflicting results may be explained by difference in types of animals used or in dosages of the venom. On the other hand, we would like to postulate that the venom of snakes from different regions may contain different components. Since bilateral cortical necrosis from snake bite in India and Srilanka is quite common but has never been reported in our country, it is possible that venom of Russell's viper in those countries may contain stronger pro-coagulant substance causing more fibrin formation

and more ischemic renal damage.

It doesn't mean that intravascular coagulation has no role at all. In this study, there is the correlation between positive fibrin stain and severity of renal tubular lesions. Thus, it is concluded that in cases of Russell's viper bite, hemodynamic alteration plays the primary role in the pathogenesis of tubular damage, while intravascular coagulation plays an additive role in severe cases.