Chapter IV

Results

Effects of Russell's viper venom on general circulation

Group I : Control dogs

Intravenous injection of Russell's viper venom produced a marked change in general circulation. Results are show in Table I. Mean arterial blood pressure (MAP) decreased significantly from 128.98 ± 13.60 to 79.99 ± 15.58 mm.Hg. ($P < 0.01$) within 1 hour period and returned to control level within 3 hour period. Heart rate (HR) decreased as mean arterial blood pressure fell and remained significant decrease ($P < 0.05$) over the 3 hour period. Packed cell volume (PCV) increased promptly near 30% within 3 hours after venom injection. Cardiac output (CO) decreased and maintained at a lower level. It was found that plasma volume (PV) and blood volume (BV) remained constant after envenomation. Total peripheral resistance (TPR) increased after venom injection by approximately 176% of the control value in a 3 hour period

Group II : Splenectomized dogs

Effect of Russell's viper venom injection on general circulation in splenectomized dogs are show in Table II. Post venom injection caused a significant decline in mean arterial blood pressure from 113.64 ± 14.90 to 90.65 ± 16.45 mm.Hg ($P < 0.05$) within 1 hour. Mean arterial blood pressure gradually recovered and returned to

Table I Effects of intravenous injections of Russell's viper venom on general circulation of five control dogs.

parameter	control	1 hr	2 hrs	3 hrs
MAP (mm. Hg.)	128.98	79.99**	89.98*	106.46NS
	± 13.60	± 15.58	± 22.96	± 19.06
HR (Beat/min)	162	134NS	137**	139*
	± 32	± 38	± 36	± 45
PCV (%)	34	43NS	43NS	41NS
	± 5	± 11	± 12	± 10
CO (ml/min/kg.bw.)	170.49	-	104.99*	76.84NS
	±136.18	-	95.12	± 36.41
PV (ml/kg.bw.)	42.37	-	40.01NS	39.47NS
	± 3.88	-	± 11.27	± 8.51
BV (ml/Kg/bw.)	64.30	-	70.69NS	81.70NS
	± 4.64	-	± 14.63	± 44.87
TPR (%)	100	-	128.13	176.68
		-	± 16.88	± 85.64

Abbreviation: MAP, mean arteria blood pressure; HR, heart rate; PCV, packed cell volume; CO, cardiac output; PV, plasma volume; BV, blood volume; TPR, total peripheral resistance. Results are given as mean ± S.D. P - Value with respect to control * $P < 0.05$, ** $P < 0.01$, NS = not significant.

Table II Effects of intravenous injection of Russell's viper venom on the general circulation of five splenectomized dogs.

parameter	control	1 hr	2 hrs	3 hrs
MAP (mm. Hg)	113.64	90.65*	103.3NS	100.31NS
	± 14.9	± 16.45	± 7.07	± 19.28
HR (beat/min)	178	172NS	171NS	164NS
	± 42	± 41	± 43	± 42
PCV (%)	26	26NS	25NS	24NS
	± 5	± 6	± 6	± 7
CO (ml/min/kg.bw.)	139.34	-	98.68NS	92.33NS
	± 40.52	-	± 60.16	± 88.13
PV (ml/kg.bw.)	46.49	-	42.52NS	44.86NS
	± 10.32	-	± 11.98	± 21.63
BV (ml/kg.bw.)	63.66	-	55.92NS	58.66NS
	± 12.2	-	± 12.81	± 27.75
TPR (%)	100	-	152.11	179.18
		-	± 55.06	± 86.05

Abbreviation are defined in Table I.

control level in 2 hours. Similar decrease of heart rate was recorded from 178 ± 42 to 164 ± 42 beat/min over the 3 hour period. However, no change in packed cell volume was noted. There was no significant decreased in cardiac output, plasma volume or blood volume, Total peripheral resistance increased to 179% of control level over the 3 hours after venom injection.

Group III : The dogs pretreated with indomethacin

Effects of Russell's viper venom injection in dogs given indomethacin showed a decrease slightly in mean arterial blood pressure in the first hour after venom injection and remained unchanged over a 3 hour period (Table III). Heart rate decreased slightly in the first hours, and then it increased from the control of 165 ± 19 to 178 ± 21 beat/min (9%) at the end of the experiment. Packed cell volume increased from 30% ± 5 to 40% ± 14 in the first hour after envenomation and remained at a high level over 3 hours. Cardiac output showed a marked decrease in the 3 hour period from 200.81 ± 113.88 to 93.26 ± 43.76 ml/min/kg.bw. ($P < 0.05$). Plasma volume decreased from 56.41 ± 8.6 to 43.16 ± 10.29 ml/kg/bw. ($P < 0.05$), whereas blood volume showed no significant decrease after envenomation. Total peripheral resistance increased to 208% of the control value on the 3 hours after venom injection.

Group IV : Splenectomized dogs pretreated with indomethacin

The results are summarized in Table IV. Splenectomized animals given indomethacin showed a slight decline in mean arterial blood pressure and heart rate after venom injection, with a rapid return to control level. No change in packed cell volume was observed.

Table III Effects of intravenous injection of Russell's viper venom on general circulation of five dogs pretreated with indomethacin.

parameter	control	1 hr	2 hrs	3 hrs
MAP (mm. Hg)	130.67	124.67^{NS}	129.66^{NS}	127.33^{NS}
	± 15.39	± 10.57	± 9.82	± 7.13
HR (beat/min)	165	158^{NS}	166^{NS}	178^{NS}
	± 29	± 15	± 28	± 21
PCV (%)	30	40^{NS}	37^{NS}	36^{NS}
	± 5	± 14	± 13	± 12
CO (ml/min/kg.bw.)	200.81	-	95.07^{NS}	93.26*
	±113.88	-	± 51.93	± 43.76
PV (ml/kg.bw.)	56.41	-	39.99**	43.16*
	± 8.6	-	± 9.99	± 10.29
BV (ml/kg.bw.)	80.74	-	64.69^{NS}	69.6^{NS}
	± 8.3	-	± 14.49	± 22.4
TPR (%)	100	-	217.18	208.58
		-	±111.79	± 67.91

Abbreviation: are defined in Table I .

Table IV Effects of intravenous injection of Russell's viper venom on general circulation of four splenectomized dogs pretreated with indomethacin.

parameter	control	1 hr	2 hrs	3 hrs
MAP (mm. Hg.)	118	117^{NS}	112^{NS}	111^{NS}
	± 21.79	± 31.9	± 38.45	± 43.56
HR (beat/min)	183	190^{NS}	183^{NS}	192^{NS}
	± 14	± 12	± 16	± 15
PCV (%)	26	25^{NS}	24^{NS}	22^{NS}
	± 2	± 3	± 3	± 4
CO (ml/min/kg.bw.)	291.77	-	114.75*	128.24*
	± 85.44	-	± 41.66	± 44.92
PV (ml/kg.bw.)	64.51	-	61.68^{NS}	55.4^{NS}
	± 8.57	-	± 18.62	± 11.71
BV (ml/kg.bw.)	87.43	-	81.68^{NS}	72.4*
	± 10.66	-	± 28.32	± 12.81
TPR (%)	100	-	254.74	241.23
		-	±127.28	±142.57

Abbreviation: are defined in Table I.

After envenomation cardiac output decreased significantly from 291.77 ± 85.44 to 114.75± 41.66 and 128.24 ± 44.92 ml/min/kg.bw. ($P < 0.05$) in the 2 hours and 3 hours respectively. Plasma volume decreased 14% from 64.51 ± 8.57 to 55.4 ± 11.71 ml/kg.bw. Blood volume decreased significantly from 87.43 ± 10.66 to 72.40 ± 12.81 ml/kg.bw. ($P < 0.05$) in the 3 hour period. Total peripheral resistance increased to 241% of the control level by the end of the experiment.

In comparison, the effects of Russell's viper venom on general circulation showed a reduction in mean arterial blood pressure in all of four groups (Fig 1). Animal without indomethacin pretreatment produced a sharp reduction in mean arterial blood pressure with slow recovery to the control level as compared to animals pretreated with indomethacin. There was no significant difference in mean arterial blood pressure response between intact and splenectomized animals. It should be noted that heart rate of splenectomized animal under the control condition was higher than of intact animals. (Fig 2) After evenomation there were variable respones in all of the four group. An increase in packed cell volume was observed in intact animals, which did not occur in splenectomized animals after envenomation. (Fig 3) Cardiac output, plasma volume and blood volume in animals pretreated with indomethacin were significantly greater than in non pretreated animals. After envenomation, cardiac output, plasma volume and blood volume of four groups of animals decreased in the same pattern and did not differ significantly when compared between indomethacin pretreated and non pretreated animals (Fig 4-5). However, the percentage of increment in total peripheral resistance was higher in animals pretreated with indomethacin after venom injection (Fig 6)

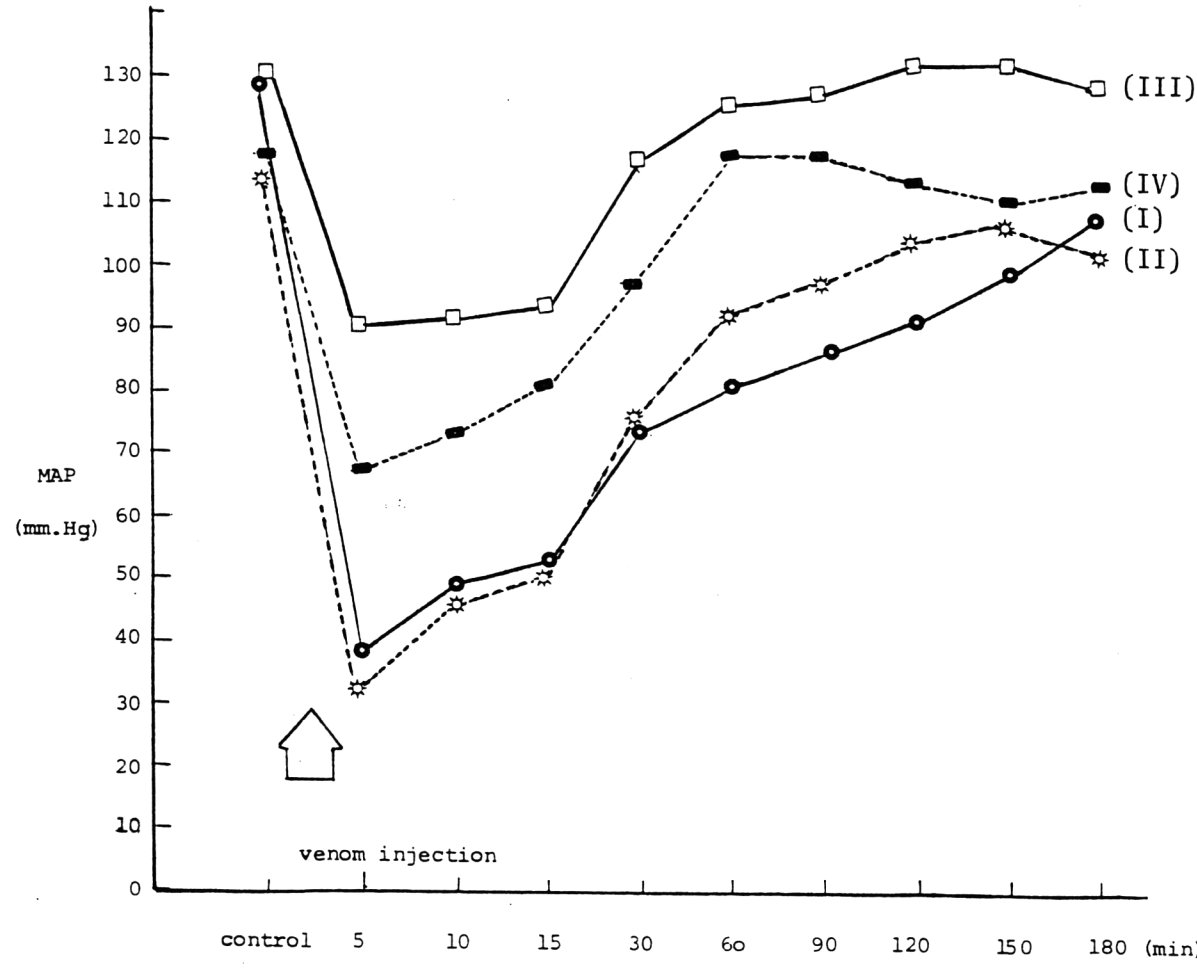


Figure 1 : The effects of intravenous injection of Russell's viper venom on mean arterial blood pressure (MAP) The values are mean ± S.D. group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin).

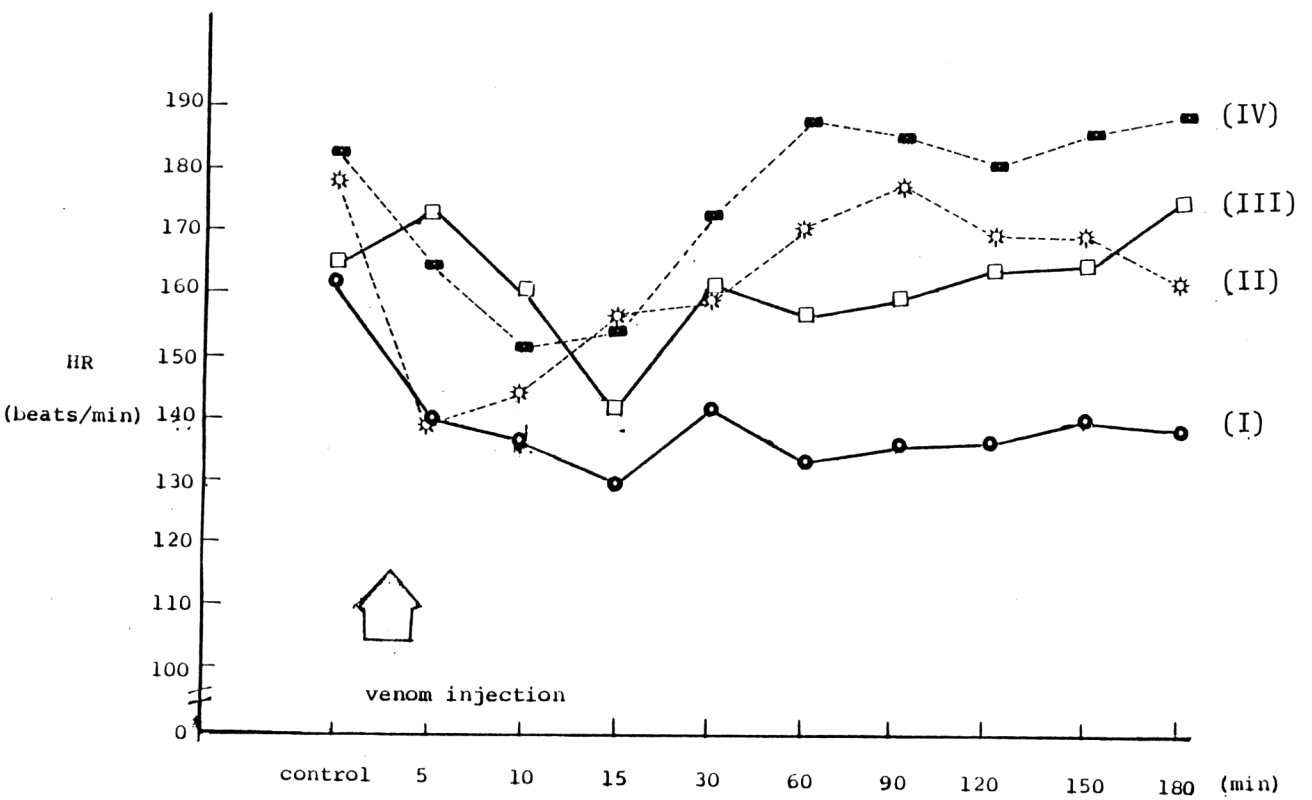


Figure 2 : The effects of intravenous injection of Russell's viper venom on heart rate (HR). The values are mean ± S.D. group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin)

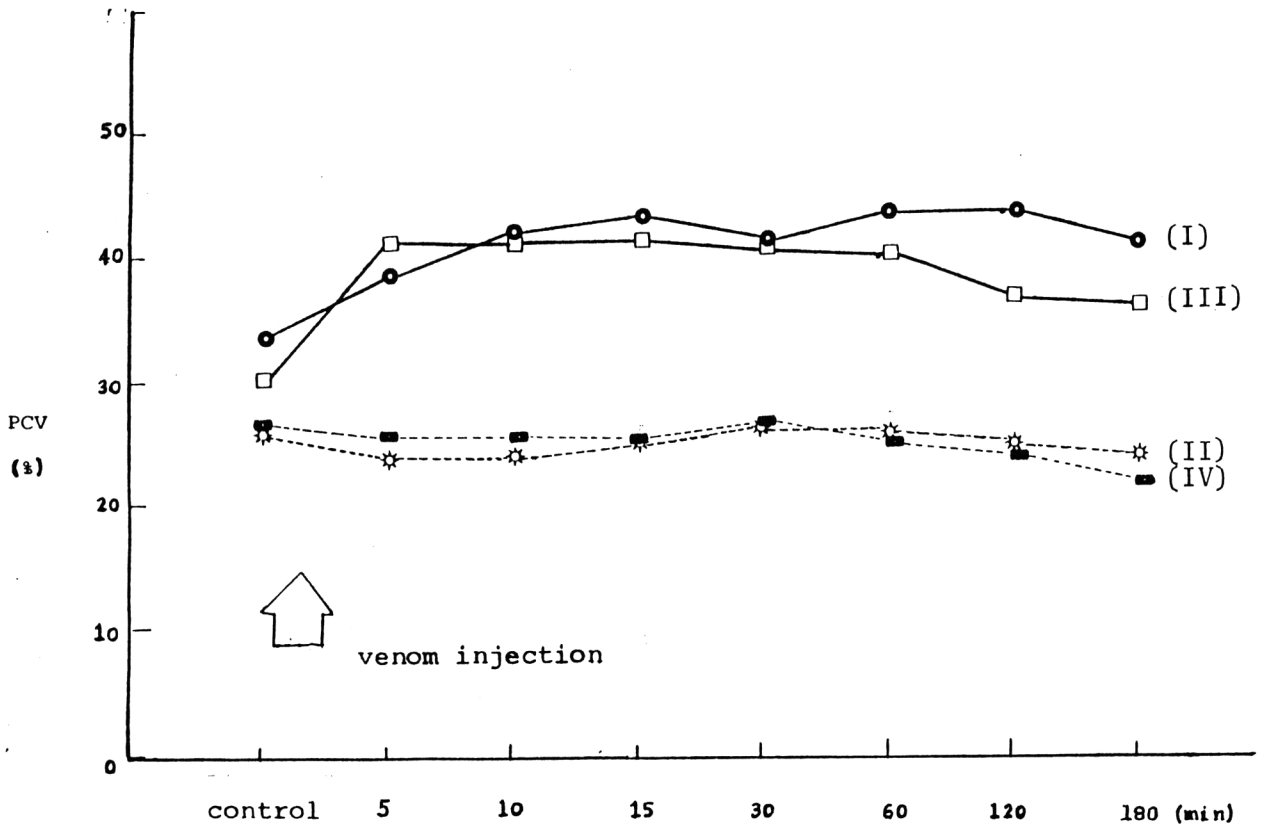


Figure 3 : The effects of intravenous injection of Russell's viper venom on packed cell volume (P.C.V.) in group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin). The values are mean ± S.D.

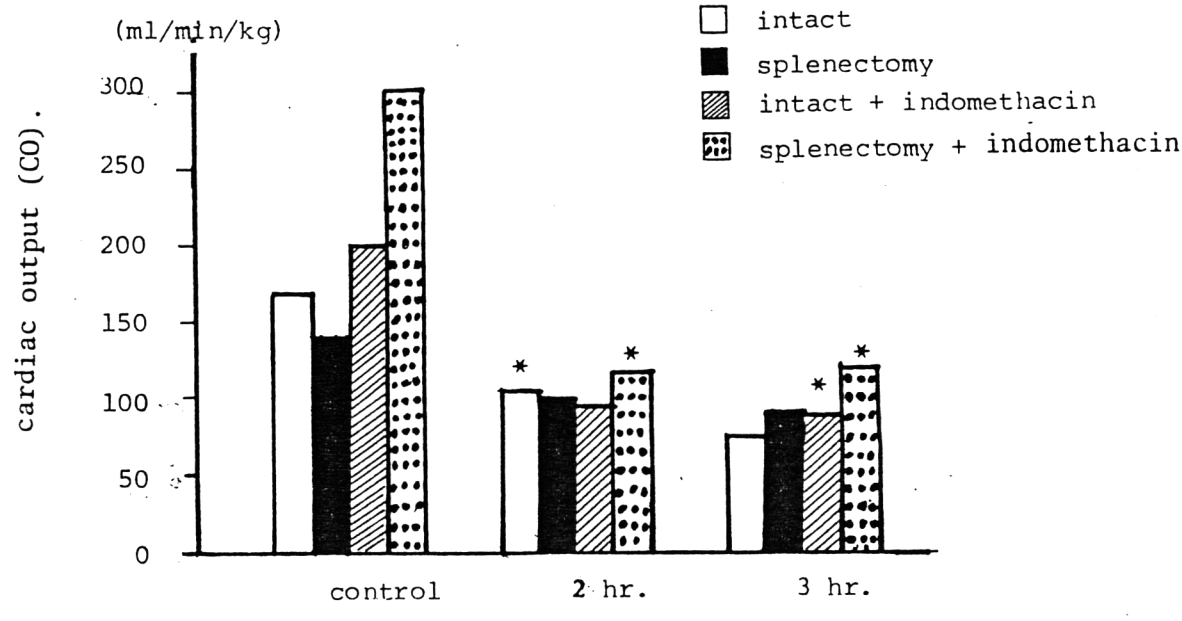


Figure 4 : The effects of intravenous injection of Russell's viper venom on cardiac output (CO). The values are mean ± S.D. P-value with respect to control,* $P < 0.05$,

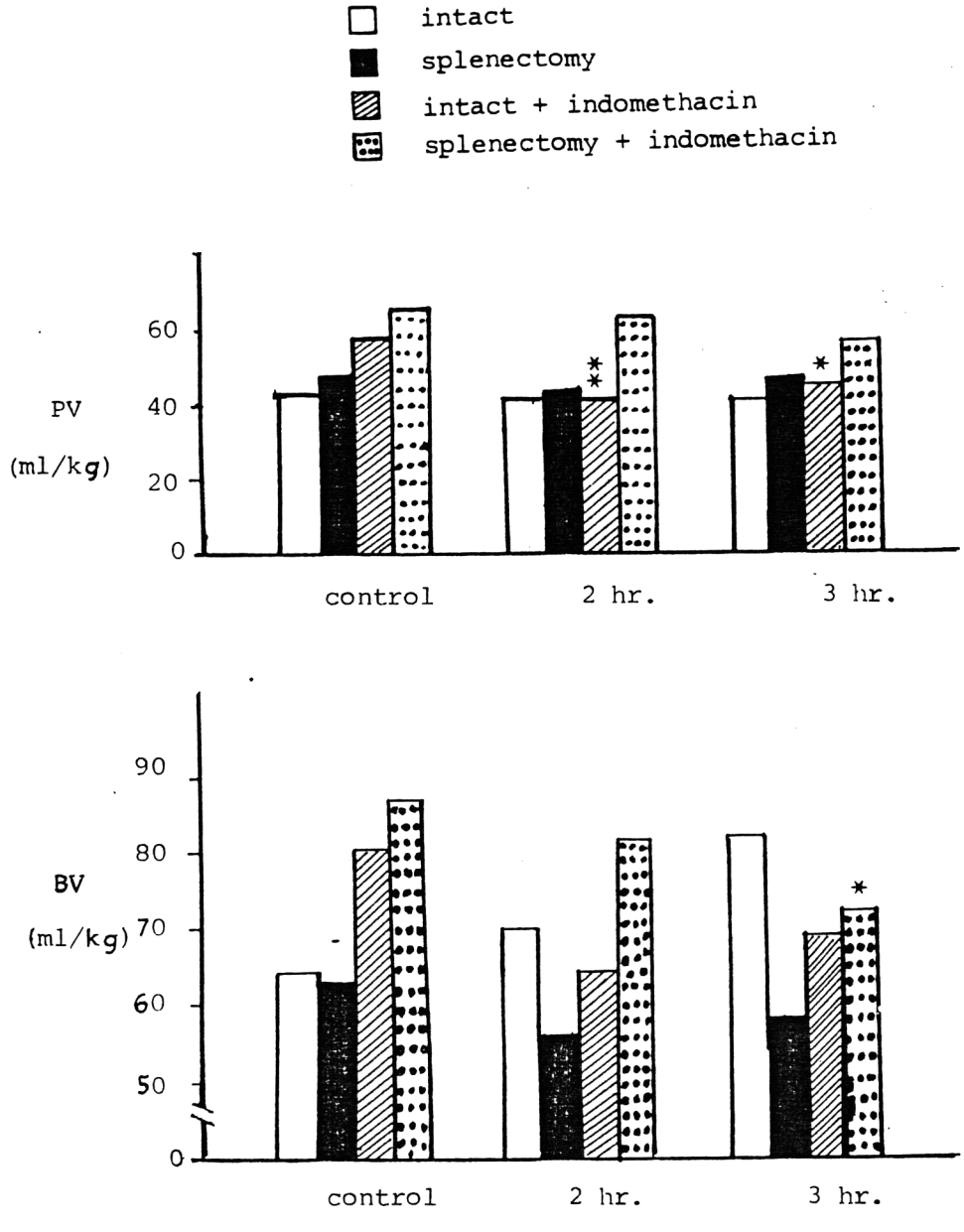


Figure 5 : The effects of intravenous injection of Russell's viper venom on plasma volume (PV) (upper panel) and blood volume (BV) (Lower panel). The values are mean ± S.D, P- values with respect to control, * $P < 0.05$, ** $P < 0.01$.

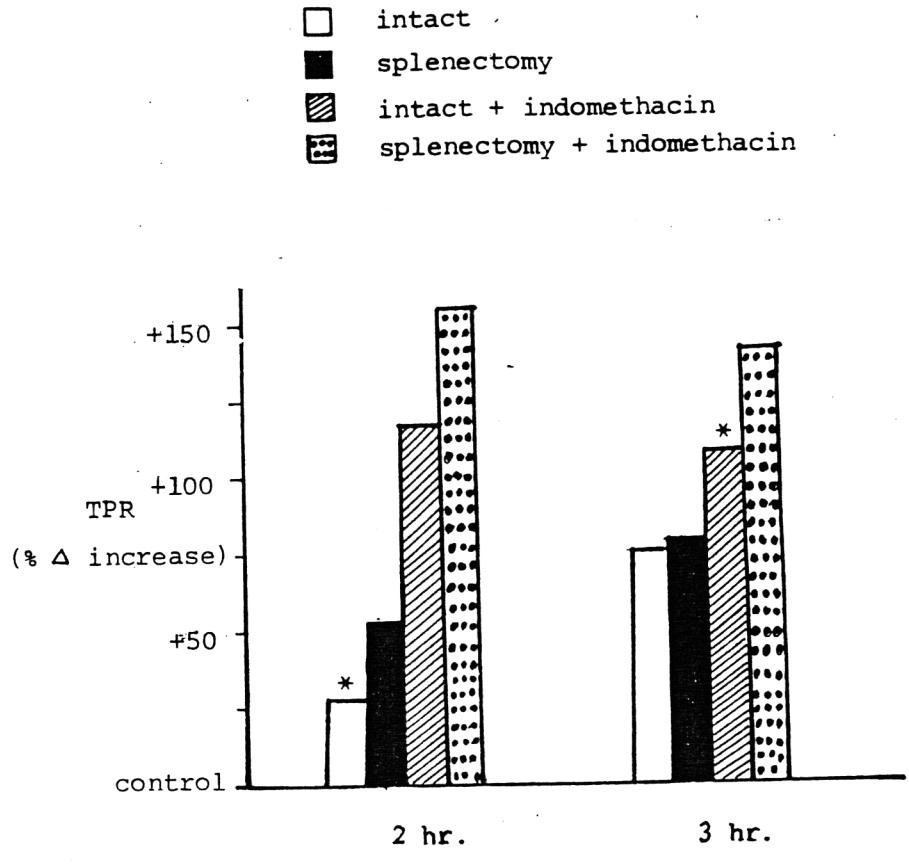


Figure 6 : Percentage changes in total peripheral resistance (TPR) as compared to control period of each group after intravenous injection of Russell's viper venom. The values are mean ± S.D.

Effects of Russell's viper venom on renal functions.

Group I : Control dogs

The results in Table V shows that after envenomation the rate of urine flow (V) did not significantly alter from 37.77 ± 25.77 to 36.40± 61.90 µl/min/kg.bw. in the 3 hour period of the experiment. Glomerular filtration rate (GFR) significantly decreased from 3.55 ± 1.30 to 1.33 ± 0.95 ml/min/kg.bw. ($P < 0.05$) in the first hour and maintained at low levels over 3 hours. Renal plasma flow (RPF) and renal blood flow (RBF) decreased significantly ($P < 0.05$) after envenomation. Filtration fraction (FF) increased significantly from 28.96% ± 11.61 to 51.91 ± 5.05 ($P < 0.01$) over 3 hour after venom injection. Renal fraction (RF) decreased by approximately 60%, whereas renal vascular resistance (RVR) increased nearly 12 fold after venom injection.

The data in Table VI and Table VII indicated that plasma concentrations of sodium and chloride were constant throughout the experiment, while urinary concentrations of sodium, chloride and urinary osmolality decreased makedly by approximately 62%, 83% and 33% respectively in the 3 hours period. Plasma concentration of potassium decreased slightly and return to control level in the 3 hour period, while urinary concentration of potassium increased 33%. Plasma osmolality increased slightly and returned to control levels in the 3 hour period after envenomation. Urinary excretion of sodium decreased by approximately 64% from mean value of 7.95 ± 4.54 to 2.86 ± 4.99 µl/min/kg.bw., potassium decreased by 46% from mean value of 1.57 ± 0.74 to 0.84 ± 0.52 µl/min/kg.bw. and chloride decreased by approximately

Table V Effects of intravenous injection of Russell's viper venom on renal functions of five control dogs.

parameter	control	1 hr	2 hrs	3 hrs
V (µl/min/kg.bw.)	37.77	24.96^{NS}	40.84^{NS}	36.40^{NS}
	± 25.77	± 28.56	± 63.72	± 61.90
GFR (ml/min/kg.bw.)	3.55	1.33*	1.61^{NS}	1.73^{NS}
	± 1.30	± 0.95	± 1.11	± 1.61
RPF (ml/min/kg.bw.)	12.58	4.46*	3.78*	3.37*
	± 2.01	± 3.38	± 2.83	± 3.09
RBF (ml/min/kg.bw.)	19.23	7.64*	6.40*	5.27*
	± 3.80	± 5.64	± 4.10	± 4.40
F.F. (%)	28.96	34.91^{NS}	45.79*	51.91**
	± 11.61	± 10.78	± 7.95	± 5.05
R.F. (%)	16.52	-	6.80^{NS}	6.60^{NS}
	± 9.53	± -	± 4.20	± 6.16
RVR. (%)	100	336.76	410.93	1206.78
	-	±351.23	±396.41	±1810.35

Abbreviation: V, urine flow rate; GFR, glomerular filtration rate; RPF, renal plasma flow; RBF, renal blood flow; FF, filtration fraction; RF, renal fraction; RVR, renal vascular resistance. Results are given as mean ± S.D. P -values with respect to control, * $P < 0.05$, ** $P < 0.01$, NS = not significant

Table VI Effects of intravenous injection of Russell's viper venom on renal hemodynamics of five control dogs.

parameter	control	1 hr	2 hrs	3 hrs
P_{Na} (mEq/L.)	145.8	143.0^{NS}	142.8*	145.0^{NS}
	± 3.7	± 5.83	± 5.50	± 2.92
P_{K} (mEq/L.)	3.22	2.78^{NS}	2.76*	3.14^{NS}
	± 0.34	± 0.27	± 0.33	± 0.24
P_{Cl} (mEq/L.)	116	115.8^{NS}	113.6^{NS}	115.8^{NS}
	± 4.69	± 4.6	± 9.34	± 3.27
P_{Osm} (mOsm/Kg.)	287.28	292.8*	286.08^{NS}	287^{NS}
	± 5.71	± 7.40	± 8.04	± 15.90
U_{Na} (mEq/L.)	204.0	80.2^{NS}	81.4^{NS}	75.8^{NS}
	±112.1	± 66.97	± 87.26	± 91.09
U_{K} (mEq/L.)	65.2	67.2^{NS}	72.0^{NS}	86.4^{NS}
	± 52.71	± 40.22	± 61.14	± 73.18
U_{Cl} (mEq/L.)	170	42*	31.4*	28.2*
	± 84.46	± 46.40	± 45.13	± 40.85
U_{Osm} (mOsm/Kg.)	813.48	497.24*	498.71^{NS}	549.92^{NS}
	±250.8	±175.08	±263.16	±345.19

Abbreviation: P_{Na}, Plasma concentration of sodium; P_{K}, Plasma concentration of potassium; P_{Cl}, Plasma concentration of chloride; P_{Osm}, Plasma osmolality; U_{Na}, urinary concentration of sodium; U_{K}, urinary concentration of potassium; U_{Cl}, urinary concentration of chloride; U_{Osm} urinary osmolality. P - values with respect to control, * $P < 0.05$, ** $P < 0.01$, NS = not significant.

Table VII Effects of intravenous injection of Russell's viper venom on renal hemodynamics of five control dogs.

parameter	control	1 hr	2 hrs	3 hrs
$U_{Na}V$ (μEq/min/kg.bw.)	7.95	2.86^{NS}	2.54*	1.91*
	± 4.54	± 4.99	± 3.04	± 2.44
$U_{K}V$ (μEq/min/kg.bw.)	1.57	0.84^{NS}	0.87^{NS}	0.82^{NS}
	± 0.74	± 0.52	± 0.54	± 0.79
$U_{Cl}V$ (μEq/min/kg.bw.)	6.93	1.74*	1.31*	0.77*
	± 4.36	± 3.14	± 1.71	± 1.06
FE of Na (%)	1.52	0.92^{NS}	0.77^{NS}	0.47*
	± 0.99	± 1.25	± 0.76	± 0.41
FE of K (%)	14.98	24.03*	23.38^{NS}	21.08^{NS}
	± 7.84	± 4.67	± 7.8	± 11.33
FE of Cl (%)	1.72	0.67*	0.5*	0.23*
	± 1.22	± 1.03	± 0.61	± 0.25
$U_{Osm}V$(μOsm/min/kg.bw.)	26.06	10.31*	9.77*	9.11*
	± 10.72	± 11.69	± 11.18	± 8.71
C_{Osm} (μl/min/kg.bw.)	91.15	35.62*	39.29*	32.28*
	± 38.08	± 41.08	± 35.24	± 31.38
C_{H_2O} (μl/min/kg.bw.)	- 53.38	- 10.66*	+ 1.53*	+ 4.12^{NS}
	± 23.60	± 16.41	± 40.77	± 49.70

Abbreviation: $U_{Na}V$, urinary excretion of sodium; $U_{K}V$, urinary excretion of potassium; $U_{Cl}V$, urinary excretion of chloride; FF of Na, fractional excretion of sodium; F.E of K, fractional excretion of potassium; F.E of Cl, fractional excretion of chloride; $U_{Osm}V$. urinary osmolar excretion; C_{Osm}, osmolar clearance; C_{H_2O}, Free water clearance. P-value with respect to control, * $P < 0.05$, NS = not significant.

75% from mean value of 6.93 ± 4.36 to 1.74 ± 3.14 µl/min/kg.bw. within the first hour after venom injection. Electrolyte excretion remained at the lower level throughout the period of the experiment. Fractional excretion of sodium and chloride decreased by approximately 39% and 61% respectively at the first hour after envenomation. The lower level was maintained until the end of the experiment. Fractional excretion of potassium was increased by approximately 60% at the first hour and remained at the higher level until the end of the experiment. Urinary osmolar excretion and osmolar clearance decreased significantly ($p < 0.05$) and remained at the lower level until the end of experiment. While, the free water clearance increased after envenomation approximately by 93% after 3 hours

Group II : Splenectomized dogs.

Effects of Russell's viper venom on renal function in splenectomized dogs are shown in Table VIII. Decreases in urine flow rate (26%), glomerular filtration rate (33%), renal plasma flow (48%) and renal fraction (34%) were recorded in splenectomized animals injected with Russell's viper venom. Renal blood flow decreased 51% from the control level of 18.09 ± 7.83 to 7.68 ± 3.68 ml/min/kg.bw. within the 3 hour period after venom injection. An increase in filtration fraction and renal vascular resistance (40% and 282% of control level, respectively) were observed at the end of the experiment. While renal fraction decreased 34%

Table IX and Table X show the effects of Russell's viper venom on renal hemodynamics. Plasma concentration of sodium and chloride were constant throughout the experiment, while urinary concentrations of sodium, chloride and urinary osmolality decreased 37%, 75% and 21% respectively in the 3 hour period. plasma concentra-

Table VIII Effects of intravenous injection of Russell's viper venom on renal function of five splenectomized dogs.

parameter	control	1 hr	2 hrs	3 hrs
V (µl/min/kg.bw.)	53.57	39.06^{NS}	38.34^{NS}	26.45^{NS}
	± 49.43	± 53.58	± 38.83	± 23.59
GFR (ml/min/kg.bw.)	3.33	2.47^{NS}	2.31^{NS}	2.03^{NS}
	± 0.91	± 1.05	± 0.78	± 0.40
RPF (ml/min/kg.bw.)	12.93	8.88^{NS}	7.03^{NS}	5.87^{NS}
	± 5.60	± 3.96	± 2.98	± 2.98
RBF (ml/min/kg.bw.)	18.09	12.02^{NS}	9.35^{NS}	7.68^{NS}
	± 7.83	± 5.22	± 3.77	± 3.68
FF (%)	27.57	28.60^{NS}	34.60^{NS}	38.76^{NS}
	± 6.80	± 9.00	± 11.59	± 12.60
RF (%)	15.01	-	11.36^{NS}	9.94^{NS}
	± 11.49	± -	± 5.91	± 4.66
RVR (%)	100	143.89	222.77	282.67
		± 88.06	±181.35	±261.55

Abbreviation: are defined in Table V.

Table IX Effects of intravenous injection of Russell's viper venom on renal hemodynamics of five splenectomized dogs.

parameter	control	1 hr	2 hrs	3 hrs
P_{Na} (mEq/L.)	135.6	140.0^{NS}	136.4^{NS}	132.4^{NS}
	± 5.73	± 9.92	± 19.35	± 5.08
P_{K} (mEq/L.)	3.52	2.74*	2.8*	2.96^{NS}
	± 0.46	± 0.45	± 0.41	± 0.42
P_{Cl} (mEq/L.)	120.4	117.6^{NS}	121.8^{NS}	121.2^{NS}
	± 3.97	± 3.78	± 2.17	± 5.26
P_{Osm} (mOsm/Kg.)	268.04	277.72^{NS}	277.36^{NS}	279.84^{NS}
	± 13.53	± 12.7	± 6.42	± 7.78
U_{Na} (mEq/L.)	101.0	60.0^{NS}	51.8^{NS}	64.4^{NS}
	± 76.87	± 52.69	± 48.08	± 49.81
U_{K} (mEq/L.)	103.4	106.8^{NS}	100.6^{NS}	122.2^{NS}
	± 77.20	± 73.21	± 89.24	± 97.71
U_{Cl} (mEq/L.)	90.2	21.4*	25.6*	22.0*
	± 50.45	± 13.94	± 22.49	± 20.19
U_{Osm} (mOsm/Kg.)	895.08	741.84^{NS}	680.32^{NS}	703.66^{NS}
	±627.0	±603.9	±464.36	±575.44

Abbreviation: are defined in Table VI.

Table X Effects of intravenous injection of Russell's viper venom on renal hemodynamics of five splenectomized dogs.

parameter	control	1 hr	2 hrs	3 hrs
$U_{Na}V$ (μEq/min/kg.bw.)	3.02	1.20^{NS}	1.09^{NS}	1.19^{NS}
	± 2.27	± 0.80	± 0.78	± 0.80
$U_{K}V$ (μEq/min/kg.bw.)	2.47	1.87^{NS}	1.33*	1.60*
	± 0.65	± 0.57	± 0.48	± 0.26
$U_{Cl}V$ (μEq/min/kg.bw.)	2.62	0.42^{NS}	0.58^{NS}	0.82^{NS}
	± 2.04	± 0.20	± 0.40	± 1.02
FE of Na (%)	0.70	0.36^{NS}	0.31^{NS}	0.42^{NS}
	± 0.48	± 0.22	± 0.16	± 0.24
FE of K (%)	21.38	29.70*	22.72^{NS}	27.77^{NS}
	± 1.66	± 5.83	± 10.39	± 6.40
FE of Cl (%)	0.64	0.15*	0.19^{NS}	0.14*
	± 0.36	± 0.05	± 0.10	± 0.06
$U_{Osm}V$ (μOsm/min/kg.bw.)	21.02	12.39^{NS}	9.67*	9.76*
	± 4.51	± 4.70	± 3.19	± 2.08
C_{Osm}(μl/min/kg.bw.)	79.07	44.21^{NS}	34.77*	34.89*
	± 19.73	± 15.22	± 10.98	± 7.46
C_{H_2O} (μl/min/kg.bw.)	- 39.50	- 5.15^{NS}	+ 3.58*	- 8.45*
	± 44.64	± 46.70	± 41.99	± 24.44

Abbreviation: are defined in Table VII.

tion of potassium decreased 16%, Whereas urinary concentration of potassium increased by approximately 18% in the 3 hour period after envenomation. Urinary excretion of sodium, potassium and chloride decreased by approximately 61%, 35% and 68% respectively in the 3 hours after venom injection. Fractional excretion of sodium and chloride decreased by approximately 40% and 78% respectively, whereas fractional excretion of potassium increased by approximately 30%. Both urinary osmolar excretion and osmolar clearance decreased significantly ($P < 0.05$) with increase free water clearance (78%) throughout the experiment.

Group III : The animals pretreated with indomethacin.

After venom injection, urine flow rate did not change over 3 hours. However, there were reductions in glomerular filtration rate (19%), renal plasma flow (25%) and renal blood flow (20%) within 3 hours. Filtration fraction and renal fraction increased slightly by approximately 9% and 34% respectively in 3 hours after venom injection, while renal vascular resistance increased to 147% of the control level. (Table XI)

The data in the Table XII and Table XIII indicate that after envenomation, plasma concentration of sodium and chloride were not altered from control values, while plasma osmolality increased slightly. Urinary concentration of sodium, chloride and urine osmolality decreased approximately 29%, 47% and 22% respectively in the first hour and remained low level throughout the experiment. Plasma concentration of potassium increased 11% in the 3 hour period, while urinary concentration did not alter from control level. Urinary excretion of sodium

Table XI Effects of intravenous injection of Russell's viper venom on renal function of five dogs pretreated with indomethacin.

parameter	control	1 hr	2 hrs	3 hrs
V (μl/min/kg.bw.)	9.19	8.92^{NS}	10.11^{NS}	10.08^{NS}
	± 1.00	± 3.16	± 3.18	± 3.05
GFR (ml/min/kg.bw.)	3.12	2.70^{NS}	2.64^{NS}	2.49^{NS}
	± 0.27	± 0.70	± 0.75	± 1.11
RPF (ml/min/kg.bw.)	7.11	3.67^{NS}	5.46^{NS}	5.21^{NS}
	± 1.12	± 2.23	± 1.71	± 2.29
RBF (ml/min/kg.bw.)	10.32	9.03^{NS}	8.56^{NS}	7.83^{NS}
	± 2.34	± 2.25	± 1.48	± 2.32
F.F. (%)	44.36	51.17^{NS}	48.72^{NS}	48.25^{NS}
	± 4.28	± 7.99	± 2.81	± 7.34
R.F. (%)	6.85	-	10.35^{NS}	9.20^{NS}
	± 3.94	-	± 3.89	± 2.64
RVR (%)	100	112.69	124.46	147.31
		± 28.71	± 43.85	± 83.12

Abbreviation: are difened in Table V.

Table XII Effects of intravenous injection of Russell's viper venom on renal hemodynamics of five dogs pretreated with indomethacin.

parameter	control	1 hr	2 hrs	3 hrs
P_{Na} (mEq/L.)	134.6	136.0^{NS}	136.0^{NS}	137.0^{NS}
	± 4.51	± 10.27	± 8.37	± 12.25
P_{K} (mEq/L.)	3.06	3.0^{NS}	3.14^{NS}	3.4^{NS}
	± 0.34	± 0.37	± 0.27	± 0.35
P_{Cl} (mEq/L.)	114.8	115.6^{NS}	113.4^{NS}	116.4^{NS}
	± 8.44	± 6.66	± 6.15	± 7.44
P_{Osm} (mOsm/Kg.)	283.4	281.4^{NS}	285.08^{NS}	285.68^{NS}
	± 20.38	± 7.46	± 11.49	± 11.44
U_{Na} (mEq/L.)	165.0	116.8^{NS}	109.2^{NS}	131.2^{NS}
	±113.38	± 92.45	± 78.85	±103.98
U_{K} (mEq/L.)	190.8	206.4^{NS}	193.2^{NS}	187.6^{NS}
	± 66.68	± 60.11	± 89.94	± 60.69
U_{Cl} (mEq/L.)	52.4	27.8^{NS}	21.8^{NS}	19.1^{NS}
	± 45.60	± 16.08	± 12.93	± 12.3
U_{Osm} (mOsm/Kg.)	2002.3	1564.12**	1454.72*	1344.08*
	± 72.07	±160.11	±325.82	±403.57

Abbreviation: are defined in Table VI.

Table XIII Effects of intravenous injection of Russell's viper venom on renal hemodynamics of five dogs pretreated with indomethacin.

parameter	control	1 hr	2 hrs	3 hrs
$U_{Na}V$ (μEq/min/kg.bw.)	1.64	1.19^{NS}	1.12^{NS}	1.55^{NS}
	± 1.01	± 0.97	± 0.72	± 1.37
$U_{K}V$ (μEq/min/kg.bw.)	1.71	1.75^{NS}	1.87^{NS}	1.96^{NS}
	± 0.48	± 0.58	± 0.79	± 0.99
$U_{Cl}V$ (μEq/min/kg.bw.)	0.50	0.26^{NS}	0.23^{NS}	0.22^{NS}
	± 0.48	± 0.18	± 0.15	± 0.18
FE of Na (%)	0.37	0.31^{NS}	0.29^{NS}	0.37^{NS}
	± 0.28	± 0.26	± 0.18	± 0.27
FE of K (%)	17.88	21.72^{NS}	22.81^{NS}	23.08^{*}
	± 4.79	± 4.16	± 7.74	± 4.69
FE of Cl (%)	0.15	0.08^{NS}	0.07^{NS}	0.07^{NS}
	± 0.16	± 0.05	± 0.04	± 0.05
$U_{Osm}V$ (μOsm/min/kg.bw.)	18.39	14.09^{NS}	14.81^{NS}	14.43^{NS}
	± 1.98	± 5.80	± 5.16	± 7.60
C_{Osm}(μl/min/kg.bw.)	65.27	50.25^{NS}	51.88^{NS}	50.67^{NS}
	± 9.37	± 21.15	± 17.87	± 27.85
C_{H_2O} (μl/min/kg.bw.)	- 55.48	$- 41.32^{NS}$	$- 41.77^{NS}$	$- 40.61^{NS}$
	± 8.60	± 18.60	± 15.53	± 25.09

Abbreviation: are defined in Table VII.

decreased (27%) in the first hour and returned to control level in 3 hour period. Whereas urinary excretion of potassium increased slightly (15%) throughout the experimental period. Urinary excretion of chloride decreased (48%) in the first hour and remained at a lower level over the course of experiment. Fractional excretion of sodium showed a tendency to fall in the first two hours. while fractional excretion of potassium increased 29% from the control level. After venom injection, fractional excretion of chloride decreased by approximately 52% from the control level. Urinary osmolar excretion and osmolar clearance decreased by approximately 23% in the first hour and remained low throughout the remainder of the experiment. Free water clearance increased approximately 27% from the control level at the end of the experiment.

Group IV : Splenectomized dogs pretreated with indomethacin.

The effect of Russell's viper venom on the renal function was studied in splenectomized dogs pretreated with indomethacin. In the first hour after venom injection the rate of urine flow decreased by approximately 13% and remained in a low level throughout the experimental period. There were reductions in glomerular filtration rate (22%), renal plasma flow (16%) and renal blood flow (16%) whithin the first hour period and remained at a low level over the 3 hour period. No change in filtration fraction was recorded. After venom injection, renal fraction increased 64% in the 3 hour period. Renal vascular resistance increased to 140% of the control level by the end of the experiment. (Table XIV)

The data in table XV and Table XVI indicated that after envenomation, plasma concentration of sodium and chloride were not changed

Table XIV Effects of intravenous injection of Russell's viper venom on renal functions of four splenectomized dogs pretreated with indomethacin

parameter	control	1 hr	2 hrs	3 hrs
V (µl/min/kg.bw)	16.60 ± 6.24	14.46^{NS} ± 1.68	14.86^{NS} ± 3.18	11.85^{NS} ± 4.67
GFR (ml/min/kg,bw.)	3.69 ± 1.10	2.85^{NS} ± 0.95	3.25^{NS} ± 1.05	2.82^{NS} ± 1.12
RPF (ml/min/kg.bw.)	9.20 ± 1.25	7.86^{NS} ± 2.19	7.87^{NS} ± 1.81	7.55^{NS} ± 3.43
RBF (ml/min/kg.bw.)	12.33 ± 1.40	10.58^{NS} ± 2.79	10.28* ± 2.15	9.57^{NS} ± 4.10
F.F. (%)	39.70 ± 9.21	35.88^{NS} ± 2.40	41.43^{NS} ± 10.49	39.58^{NS} ± 11.52
R.F. (%)	4.58 ± 1.45	- -	9.67^{NS} ± 2.51	7.50^{NS} ± 1.41
RVR (%)	100	119.62 ± 20.21	116.0 ± 28.97	140.09 ± 84.05

Abbreviation: are defined in Table V.

Table XV Effects of intravenous injection of Russell's viper venom on renal hemodynamics of four splenectomized dogs pretreated with indomethacin.

parameter	control	1 hr	2 hrs	3 hrs
P_{Na} (mEq/L.)	139	136.25^{NS}	139.5^{NS}	138.75^{NS}
	± 3.56	± 8.02	± 12.15	± 12.23
P_{K} (mEq/L.)	2.98	2.93^{NS}	3.1^{NS}	3.33^{NS}
	± 0.33	± 0.29	± 0.36	± 0.22
P_{Cl} (mEq/L.)	108.25	110.25^{NS}	110.75^{NS}	106.75^{NS}
	± 8.18	± 12.53	± 8.73	± 9.46
P_{Osm} (mOsm/ Kg.)	287.5	293.85^{NS}	297.45^{NS}	296.6^{NS}
	± 15.38	± 11.45	± 6.72	± 6.22
U_{Na} (mEq/L.)	161.5	145.0^{NS}	126.5^{NS}	103.25^{NS}
	±167.39	± 94.43	± 65.50	± 57.70
U_{K} (mEq/L.)	99.25	110.25^{NS}	102.75^{NS}	150.5^{NS}
	± 44.48	± 55.94	± 32.99	± 22.59
U_{Cl} (mEq/L.)	126.5	68.5^{NS}	48.25^{NS}	40.0^{NS}
	±166.46	± 63.54	± 46.81	± 39.61
U_{Osm} (mOsm/ Kg.)	1397.15	1124.68^{NS}	1222.15^{NS}	1189.33^{NS}
	±281.53	±181.42	± 45.43	±174.37

Abbreviation: are defined in Table VI.

Table XVI Effects of intravenous injection of Russell's viper venom on renal hemodynamics of four splenectomized dogs pretreated with indomethacin .

parameter	control	1 hr	2 hrs	3 hrs
$U_{Na}V$ (μEq/min/kg.bw.)	2.12	2.10^{NS}	1.78^{NS}	1.09^{NS}
	± 1.83	± 1.42	± 0.74	± 0.60
$U_{K}V$ (μEq/min/kg.bw.)	1.60	1.60^{NS}	1.62^{NS}	1.73^{NS}
	± 0.67	± 0.87	± 0.74	± 0.63
$U_{Cl}V$ (μEq/min/kg.bw.)	1.79	1.00^{NS}	0.72^{NS}	0.53^{NS}
	± 1.77	± 0.96	± 0.79	± 0.68
FE of Na (%)	0.39	0.52^{NS}	0.39^{NS}	0.27^{NS}
	± 0.27	± 0.31	± 0.07	± 0.04
FE of K (%)	15.67	20.36^{NS}	18.44^{NS}	20.10^{NS}
	± 7.58	± 11.15	± 11.11	± 9.84
FE of Cl (%)	0.32	0.28^{NS}	0.17^{NS}	0.14^{NS}
	± 0.39	± 0.22	± 0.12	± 0.13
$U_{Osm}V$ (μOsm/min/kg.bw.)	22.32	16.36^{NS}	18.21^{NS}	13.56^{NS}
	± 5.96	± 3.84	± 4.15	± 4.47
C_{Osm} (μl/min/kg.bw.)	78.51	55.98^{NS}	61.14^{NS}	45.66^{NS}
	± 25.38	± 14.43	± 14.05	± 15.02
C_{H_2O} (μl/min/kg.bw.)	- 61.91	- 41.53^{NS}	- 46.26^{NS}	- 33.63^{NS}
	± 19.92	± 13.06	± 11.01	± 10.94

Abbreviation: are defined in Table VII.

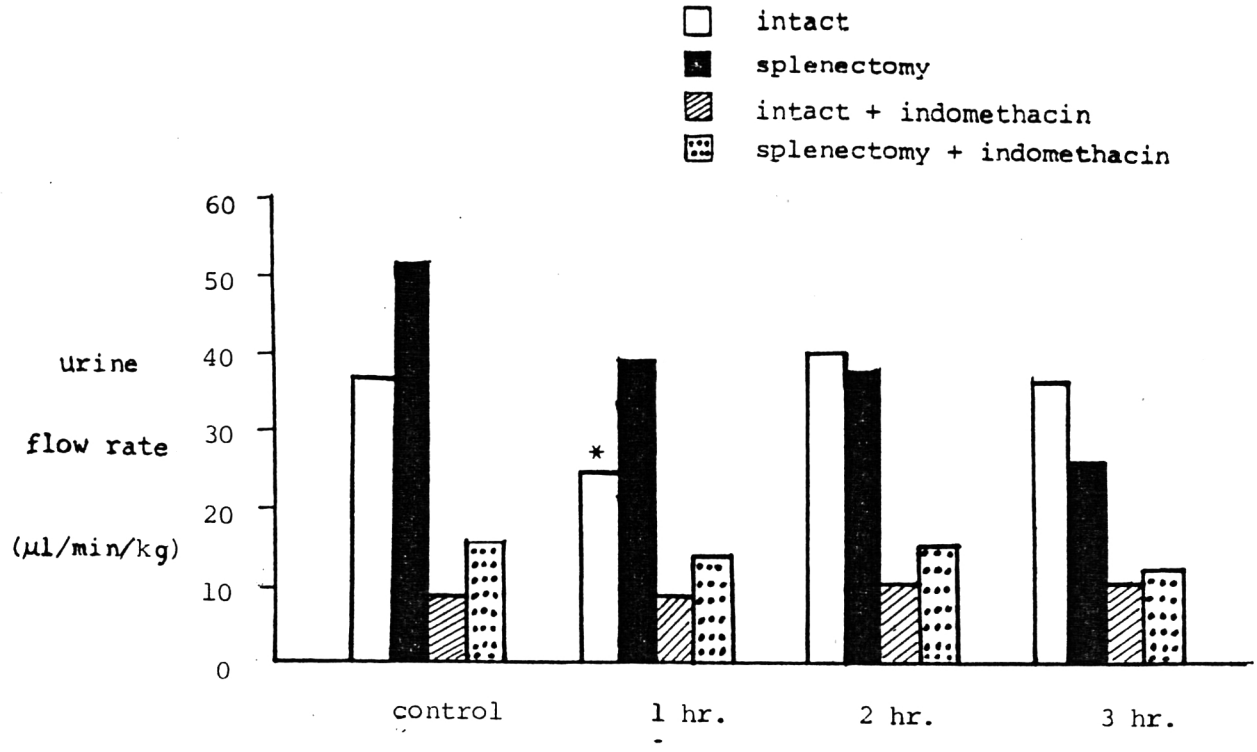
from control values, while plasma osmolity increased slightly. Urinary concentrations of sodium, chloride and urine osmolality decreased by approximately 36%, 68% and 15% respectively by the end of experiment. Plasma and urinary concentrations of potassium showed an increase of approximately 11% and 52% respectively after 3 hour period. Urinary excretion of sodium was unchanged in the first hours and then decreased 16% and 48% of control within the second and third hours after venom injection. Urinary excretion of chloride decreased progressively by 44%, 60% and 70% within 1, 2 and 3 hours respectively. Fractional excretion of sodium decreased 30% in the 3 hours. A similar progressive decline in fractional excretion of chloride was recorded within the first hour and maintained a low level over the 3 hour period. Fractional excretion of potassium increased by approximately 30% in the first hour, then remained high throughout the remainder of the experiment. Urinary osmolar excretion and osmolar clearance decreased by approximately 39% and 42% respectively in the 3 hour period, while free water clearance increased 45% by the end of the experiment.

Comparing the effect of Russell's viper venom on renal function in each of four groups of animals.

In the control period both intact and splenectomized animals pretreated with indomethacin showed less urine output than non pretreated animals. After venom injection, animals in all four groups showed similar declines in the rate of urine flow (Fig 7). It is also noted that animals pretreated with indomethacin showed a significant decreased in renal plasma flow than those of non pretreated

animals (Fig 8).There was no significant difference in glomerular filtration rate in the control period among the four group (Fig 9). After venom injection, renal plasma flow, renal blood flow and glomerular filtration rate decreased markedly in control animals (group 1) as compared with the other groups. Renal vascular resistance also increased markedly near 12 fold. While renal vascular resistance of animals in the other groups showed a 1-3 fold increase after venom injection (Fig 10).In the control period, the filtration fraction of animals pretreated with indomethacin was significantly higher than non-pretreated animals. After venom injection filtration fraction of the four groups changed simultaneously. In animals pretreated with indomethacin the renal fraction in the control period was less than that in non pretreated animals. After venom injection, renal fraction increased in the pretreated animals, while decreased in non pretreated animals (Fig 11). However, these changes were not significant between groups. Plasma concentration of sodium and chloride were constant throughout the experiment in all groups. Indomethacin pretreated groups showed an increase in plasma potassium concentration, while non pretreated groups showed a decrease. Similar slight increases in plasma osmolality were found in all groups. There were similar decreased in urine concentrations of sodium and chloride throughout the experiment. Whereas, urinary concentration of potassium increased. It should be noted that indomethacin pretreated animal produced a higher urinary osmolality (Fig 12-15) than non pretreated animals before and after venom injection. Urinary excretion and fractional excretion of sodium and chloride in animals pretreated with indomethacin were less than in non pretreated animals during the control period. There were similar declines in these

variables in all groups after venom injection. Urinary excretion of potassium decreased in non pretreated animals, while increased in pretreated animals. Similar increases in fractional excretion of potassium were recorded in all groups. (Fig 16-18)



Pigure 7 : The effects of intravenous injection of Russell's viper venom on urine flow rate (V). The values are mean ± S.D. P - values with respect to control, * $P < 0.05$.

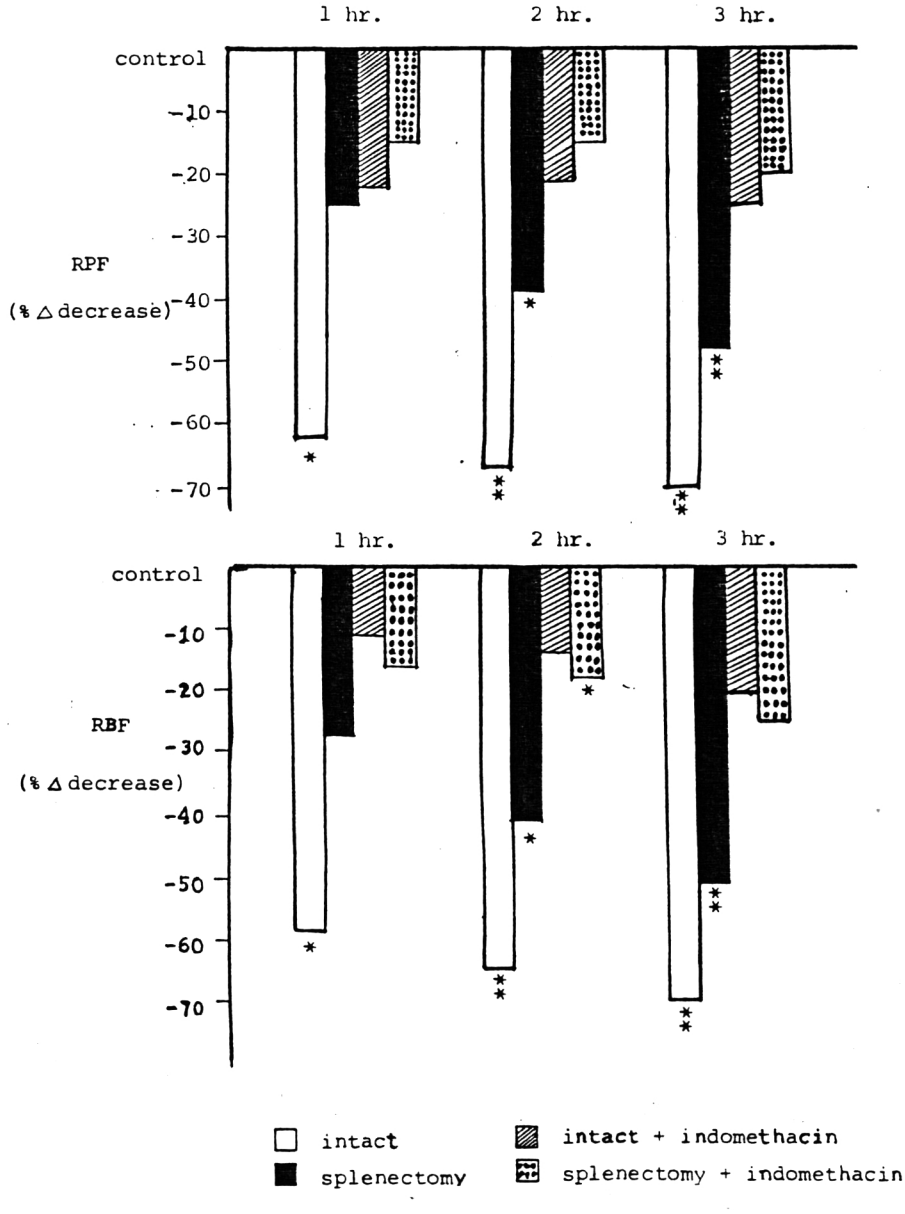


Figure 8: Percentage changes in renal plasma flow (upper panel) and renal blood flow (Lower panel) as compared to control period of each group after intravenous injection of Russell's viper venom. The values are mean ± S.D. P - values with respect to control, * $P < 0.05$, ** $P < 0.01$.

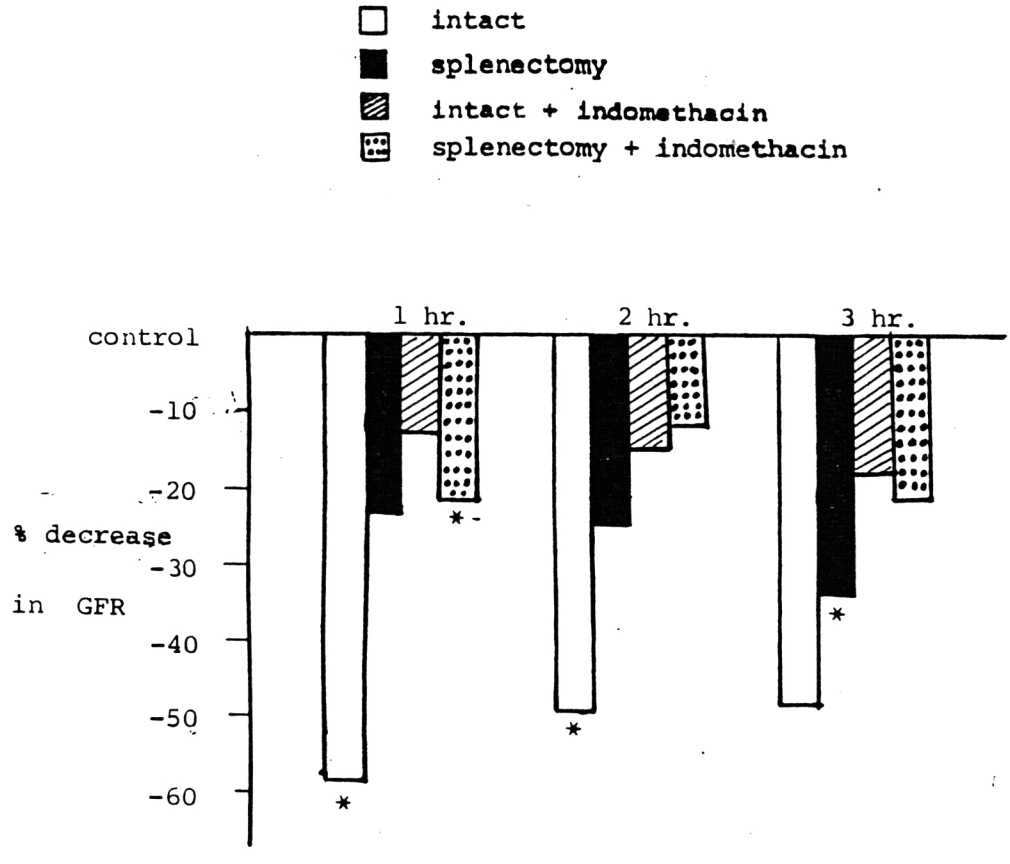


Figure 9 : Percentage changes in glomerular filtration rate (GFR) as compared to control period of each group after intravenous injection of Russell's viper venom. The values are mean ± S.D. P - value with respect to control, * $P < 0.05$.

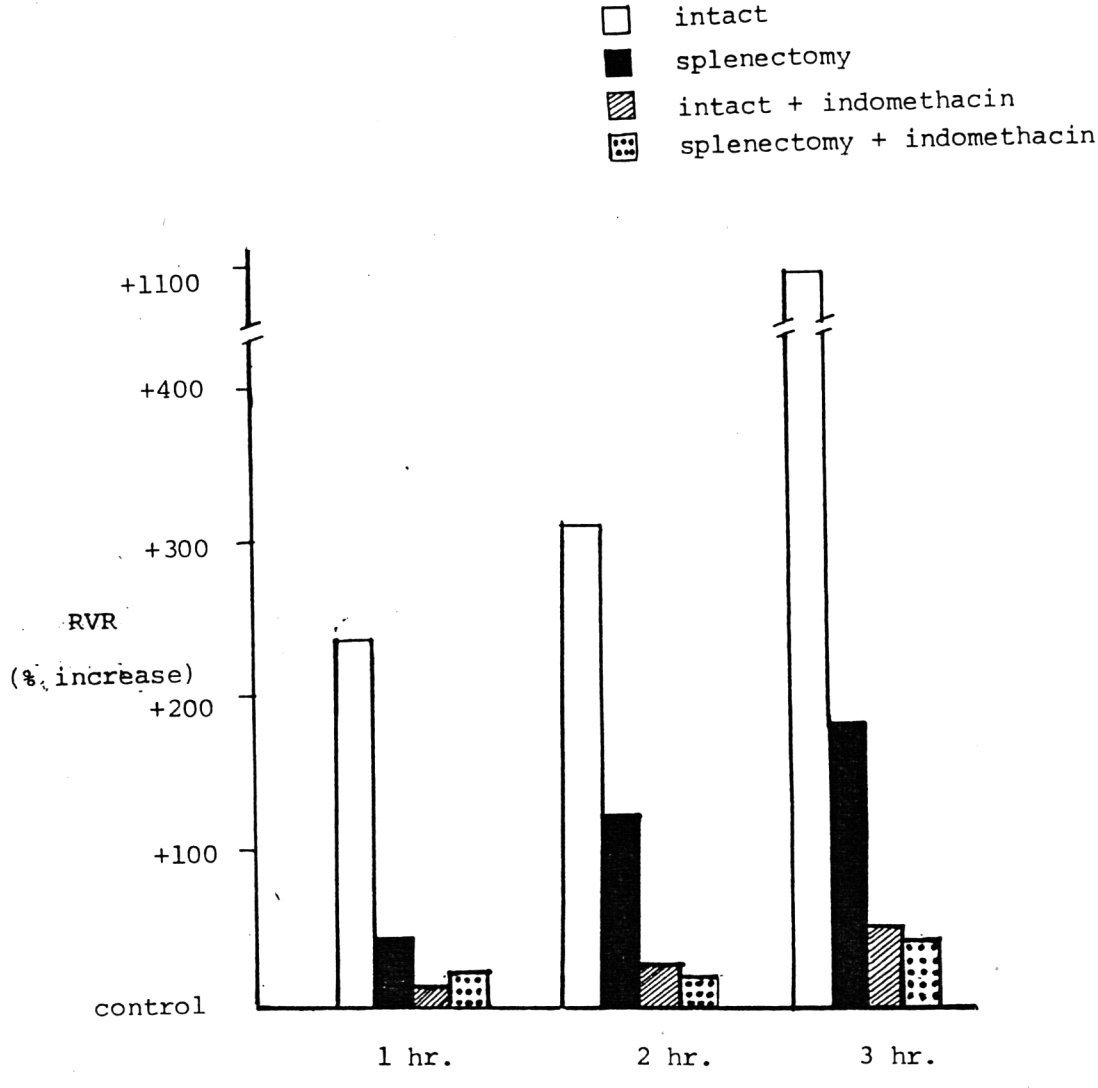


Figure 10 : Percentage changes in renal vascular resistance (RVR) as compared to control period of each group after intravenous injection of Russell's viper venom. The values are mean ± S.D.

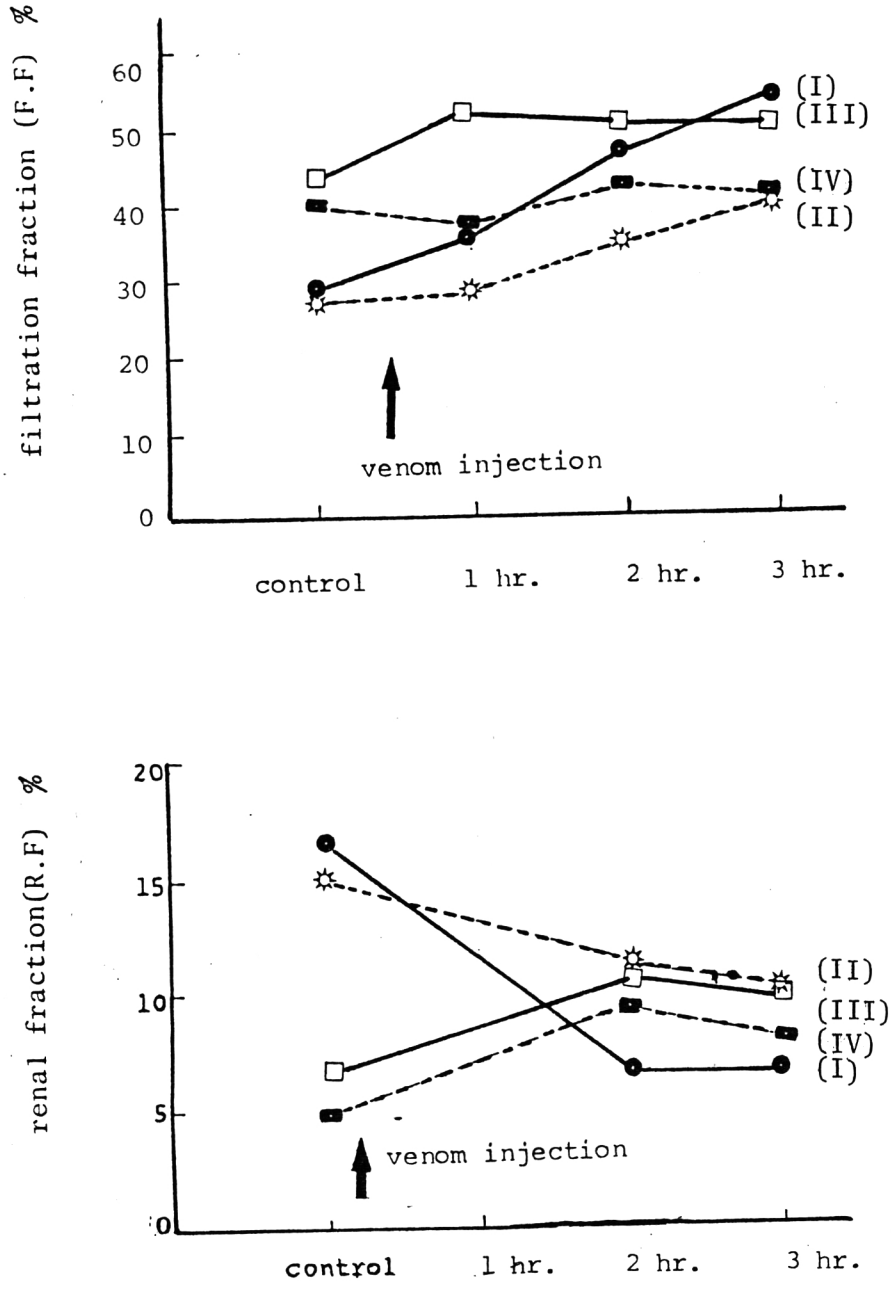


Figure 11 : The effects of intravenous injection of Russell's viper venom on filtration fraction (F.F) (upper panel) and renal fraction(R.F) (lower panel) : group 1 (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin and group IV (Splenectomized dogs pretreated with indomethacin). The values are mean ± S.D.

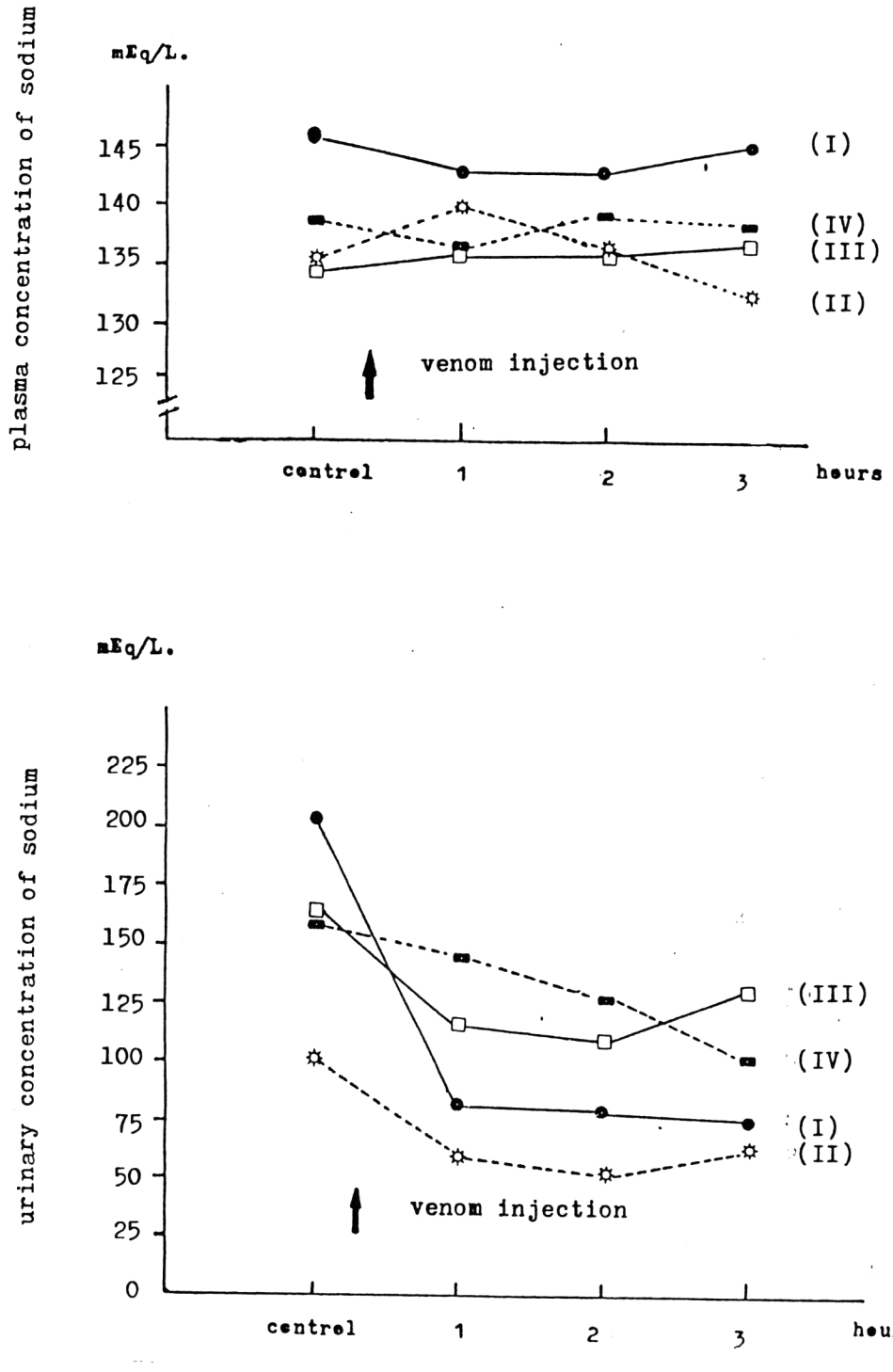


Figure 12 : Shows the effects of intravenous injection of Russell's viper venom on plasma concentration of sodium (upper panel) and urinary concentration of sodium (lower panel): group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV(splenectomized dogs pretreated with indomethacin) The values are mean ± S.D.

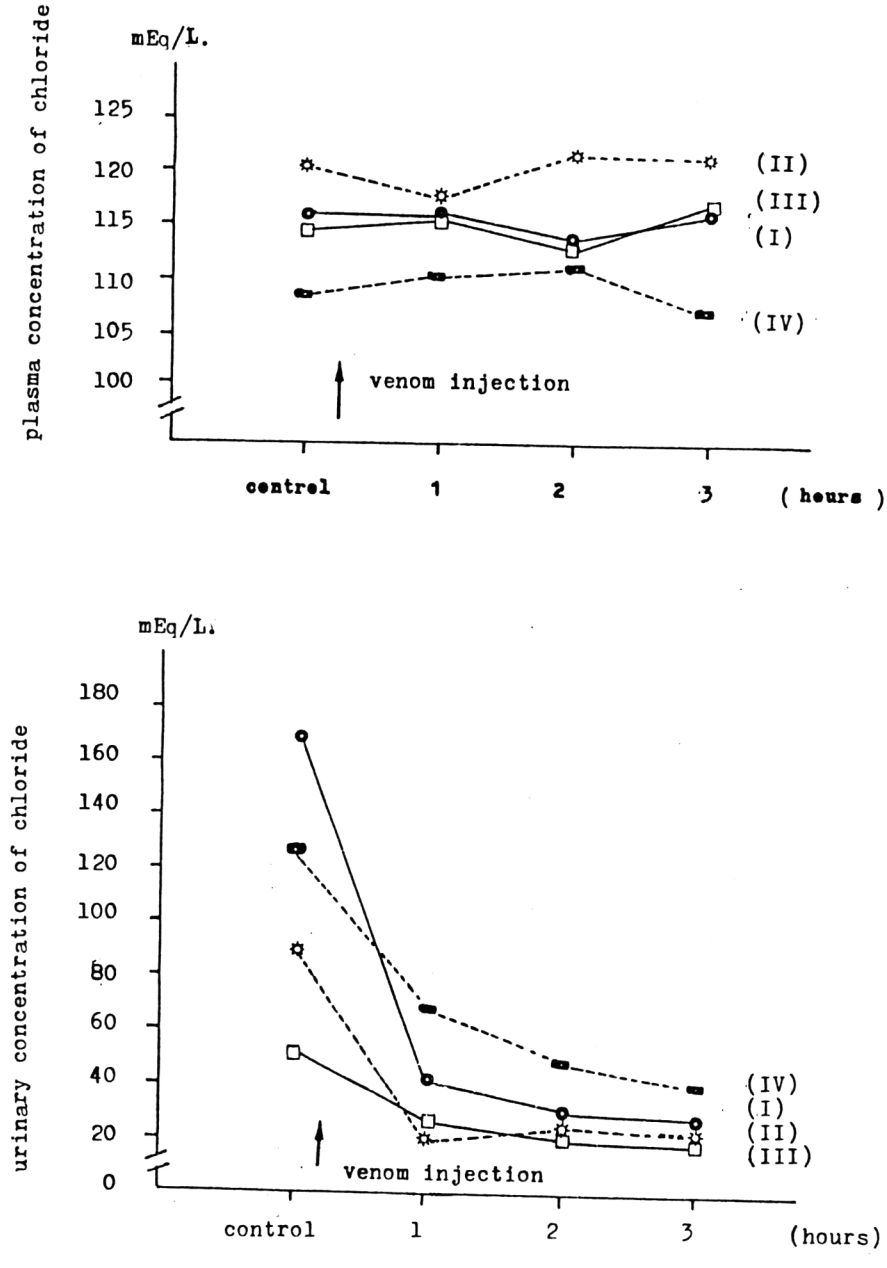


Figure 13: Shows the effects of intravenous injection of Russell's viper venom on plasma concentration of chloride (upper panel) and urinary concentration of chloride (lower panel) group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin). The values are mean ± S.D.

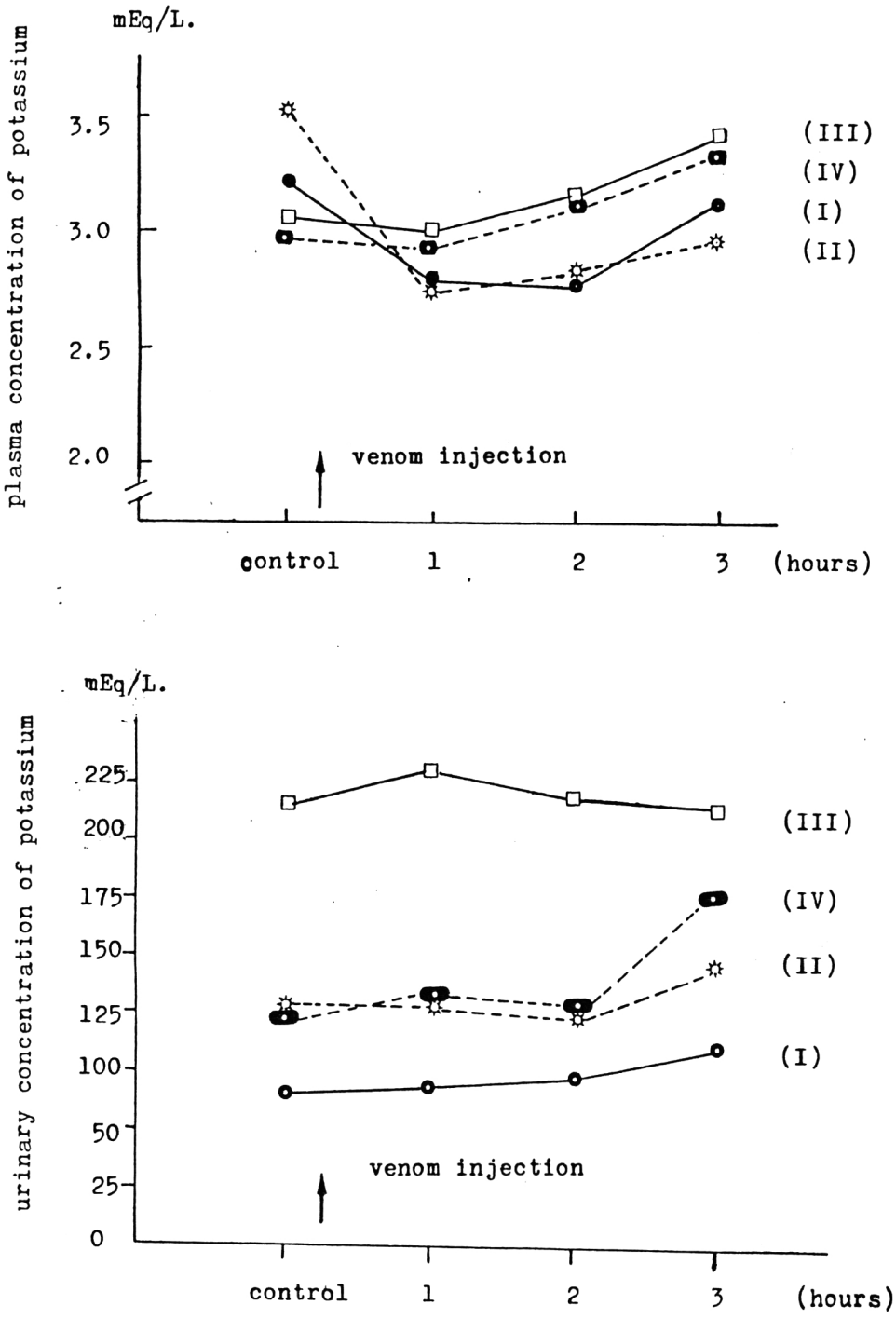


Figure 14 : Shows the effects of intravenous injection of Russell's viper venom on plasma concentration of potassium (upper panel) and urinary concentration of potassium (lower panel) group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin). The values are mean ± S.D.

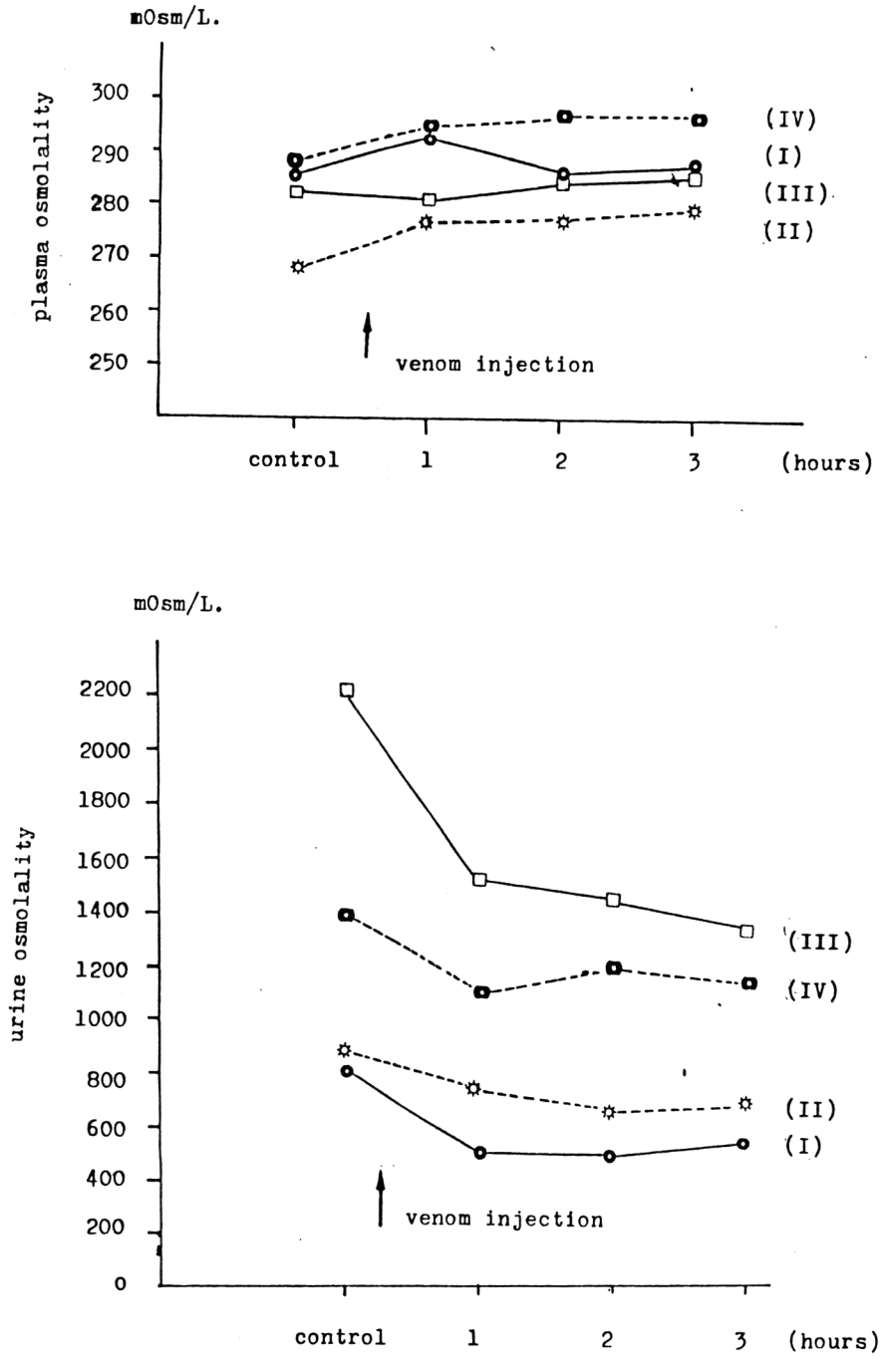
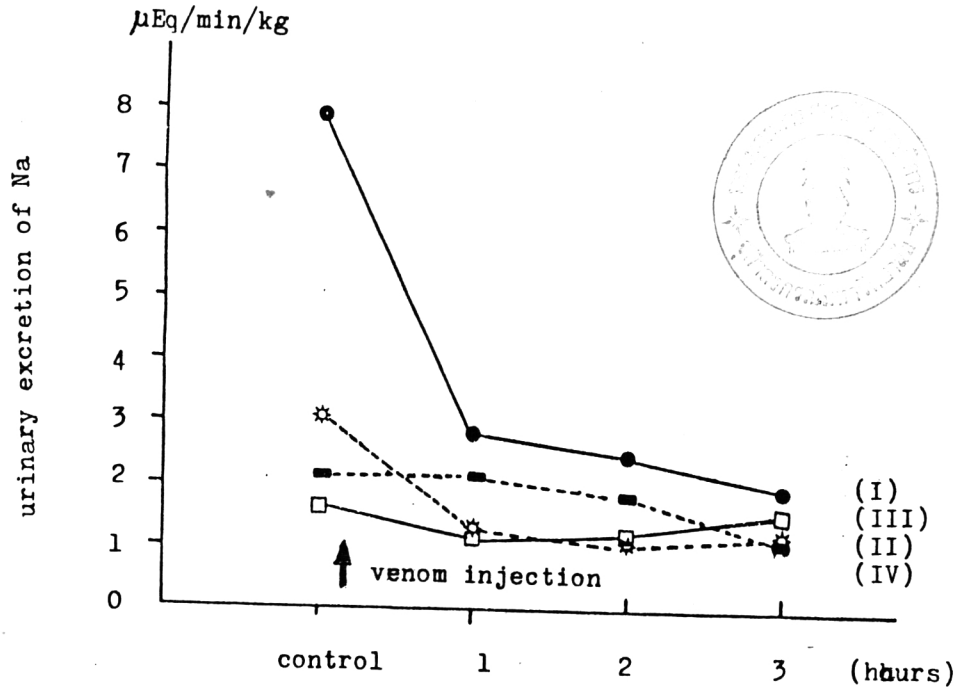


Figure 15: Shows the effects of intravenous injection of Russell's viper venom on plasma osmolality (upper panel) and urinary osmolality (lower panel) : group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin). The values are mean ± S.D.



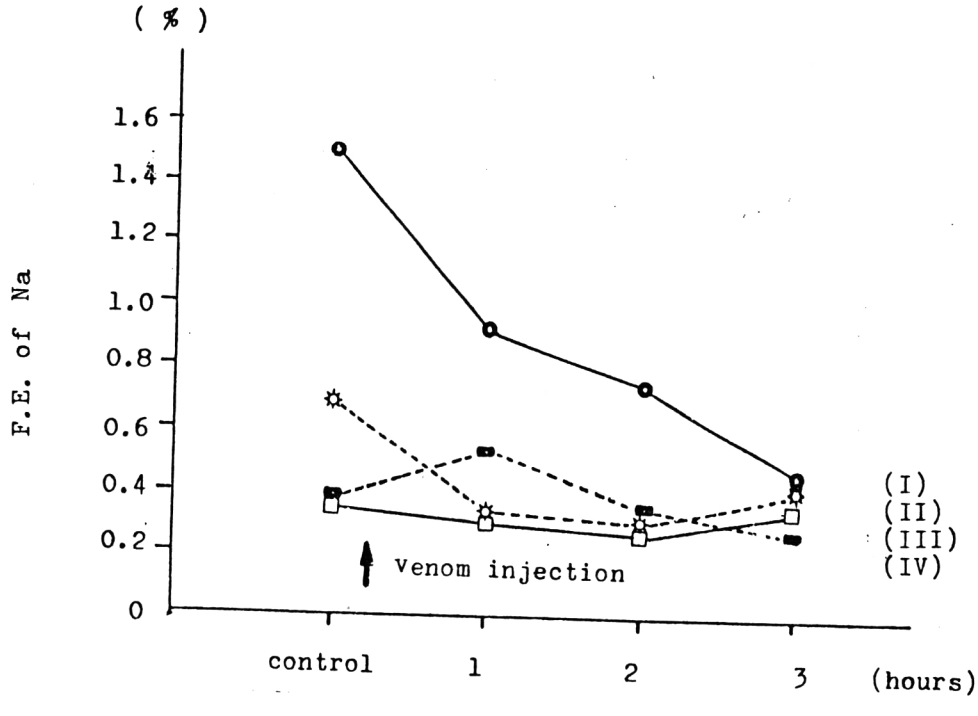


Figure 16 : Shows the effects of intravenous injection of Russell's viper venom on urinary excretion of sodium (upper panel) and Fractional excretion of sodium (lower panel) : group I (control), group II (Splenectomized dogs) group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin). The values are mean ± S.D.

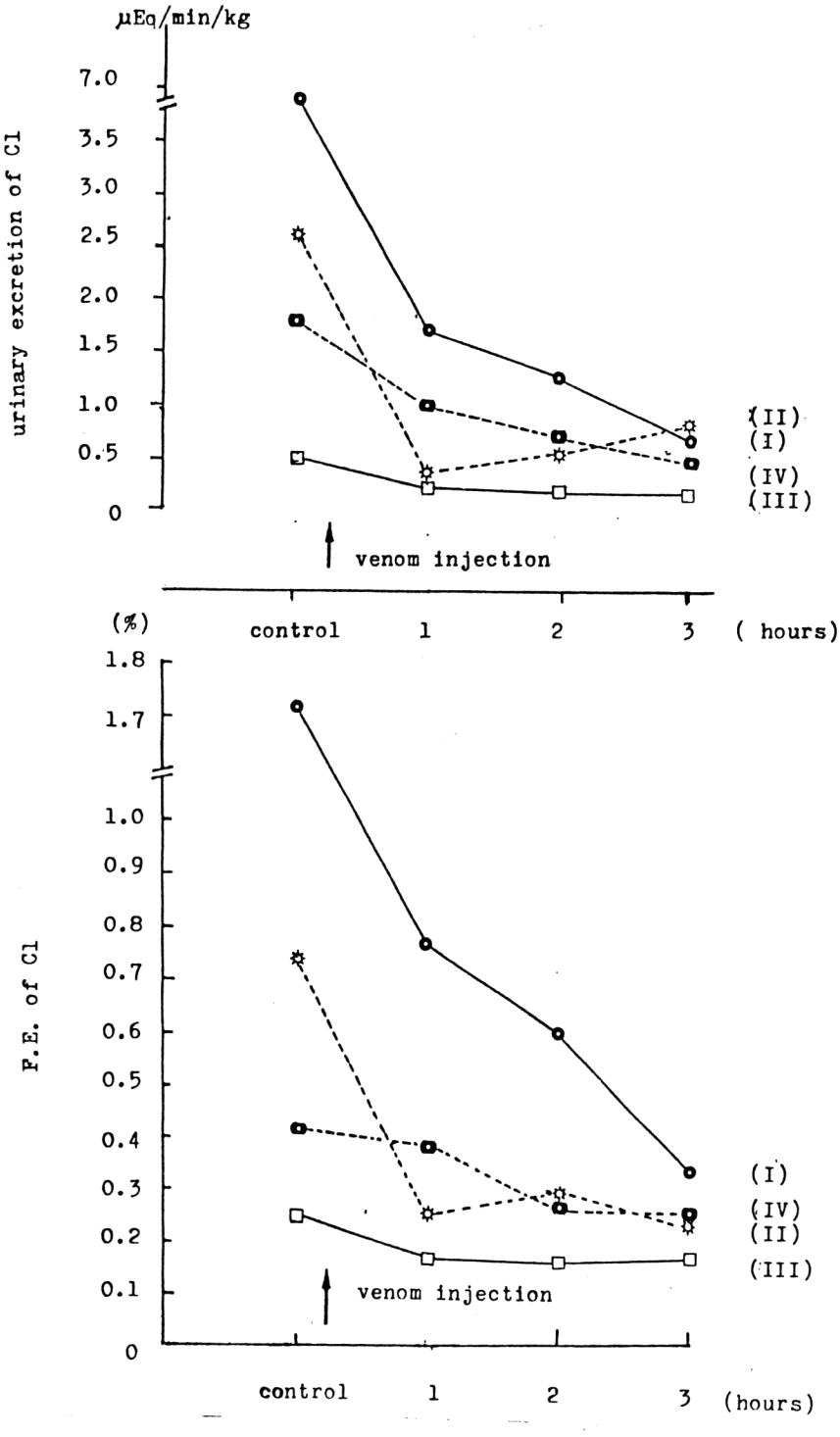


Figure 17 : Shows the effects of intravenous injection of Russell's viper venom on urinary excretion of chloride (upper panel) and Fractional excretion of chloride (lower panel) : group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin). The values are mean ± S.D.

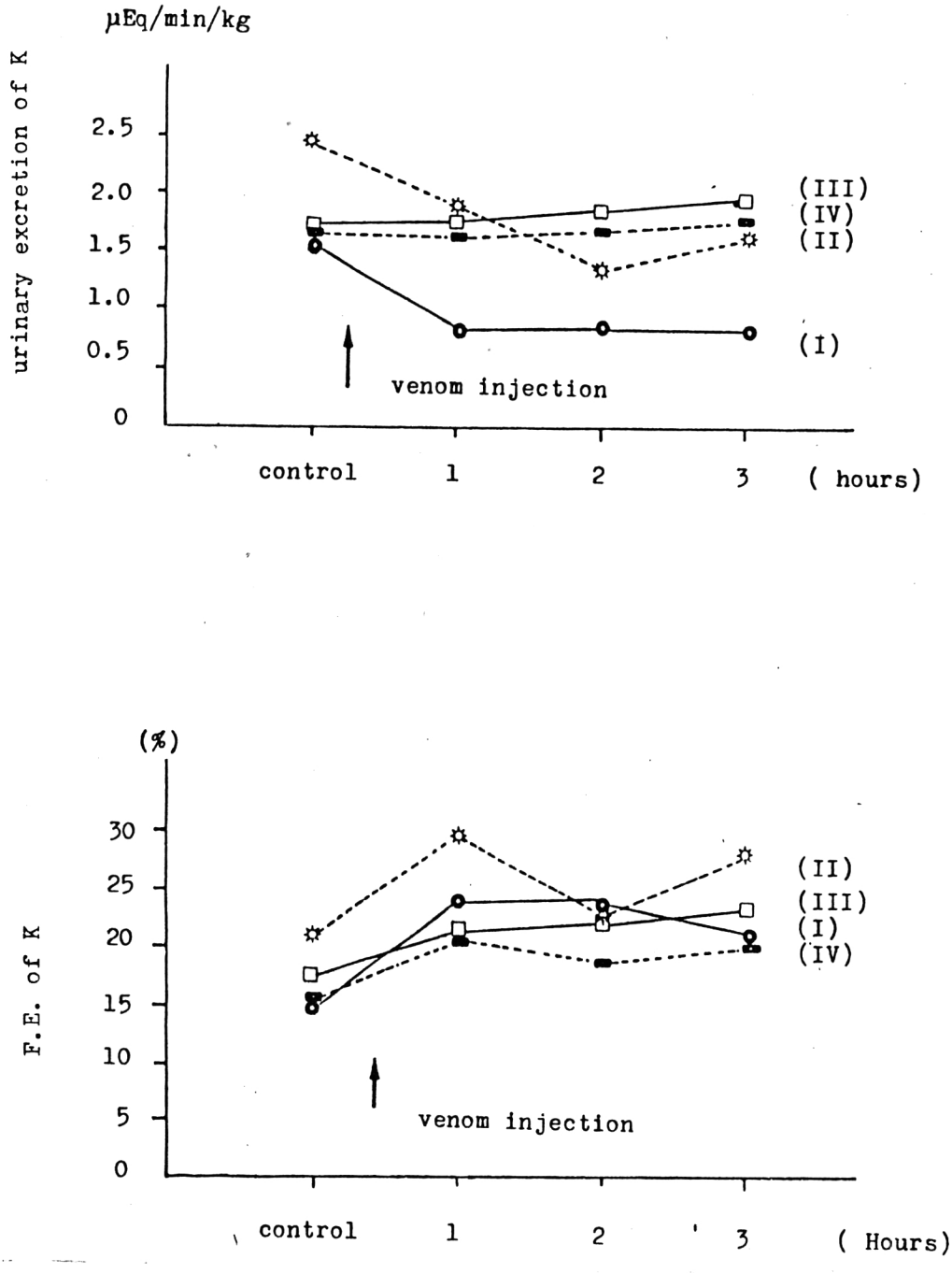


Figure 18 : Shows the effects of intravenous injection of Russell's viper venom on urinary excretion of potassium (upper panel) and Fractional excretion of potassium (lower panel) : group I (control), group II (Splenectomized dogs), group III (The dogs pretreated with indomethacin) and group IV (Splenectomized dogs pretreated with indomethacin). The values are mean ± S.D.