Chapter IV

Results

Effect of Russell's Viper Venom on General Circulation

Group I : Intact dogs

Intrarenal arterial infusion of Russell's viper venom produced a marked changes in general circulation as shown in table 1. Mean arterial blood pressure (MAP) increased significantly from 109.37 $\pm$ 6.20 to 126.46 $\pm$ 9.04 mm.Hg ($p<0.05$) within 1 hour and remained significnt increase ($p<0.001$) over 5 hours period. Pulse pressure (PP) decreased significantly from 47.50 $\pm$ 2.67 to 28.13 $\pm$ 1.31 mm.Hg ($p<0.05$) within 1/2 hour and remained significant decrease ($p<0.05$ over 5 hours period. There was no significant decrease in heart rate (HR) at the first 30 minutes untill 2 hours after venom infusion. However, it gradually increased and returned to the control level within 4 hours. And this rate showed a tendency to increase higher than the control level after the period of 5 hours. No significant increase in packed cell volume (PCV) was apparent throughout the period of the experiment.

Group II : Thyroparathyroidectomized (TPTX) dogs

Effect of intrarenal arterial infusion of Russell's viper venom on general circulation in TPTX dogs are shown in table 2. The venom caused a significant increase in mean arterial blood pressure from 103.33 $\pm$ 5.59 to 113.54 $\pm$ 7.08 mm.Hg ($p<0.01$) within 1 hour

after venom infusion and still significant increased ($p<0.05$) till

Table 1 Effect of intrarenal arterial infusion of Russell's viper venom on general circulation of eight intact dogs. (Mean±SE)

Variables	0	1/2	1	1 1/2	2	3	4	5 (hr.)
			*	***	***	***	**	***
MAP (mm.Hg)	109.37	106.25	126.46	136.25	143.54	140.42	137.08	143.96
	±6.20	±6.81	±9.04	±9.28	±7.38	±7.86	±8.03	±7.75
		***	**	*	*	*	*	*
PP (mm.Hg)	47.50	28.13	32.50	33.75	35.00	34.38	34.38	33.75
	±2.67	±1.31	±1.34	±2.45	±2.31	±3.05	±3.71	±4.60
HR(Beat/min)	123.88	119.75	116.63	109.88	115.13	113.38	122.88	128.0
	±10.24	±9.38	±6.77	±6.51	±7.52	±7.80	±6.77	±10.53
PCV (%)	33.13	35.25	35.44	35.13	35.13	34.38	35.38	37.31
	±1.55	±1.55	±1.61	±1.39	±1.39	±1.67	±1.74	±2.25

P-value with respect to control, * $p\leq .05$, ** $p< .01$, *** $p<.001$.

the end of the experiment. Pulse pressure decreased significantly from 43.75 ± 2.95 to 36.25 ± 2.79 mm.Hg ($p<0.01$) at the first 30 minutes and gradually returned to the control level within 2 hours. And this level was not altered throughout the experimental period. Heart rate decreased slightly at 1 1/2 hours and returned to the control level within 3 hours, this change was not statistically significant. The significant increase in heart rate from the control of 124.75 ± 5.60

to 136.63 ± 5.95 beat/min ($p<0.05$) was noted at the fourth hour after envenomation and maintained at higher level till the end of the experiment. During experiment, no change in packed cell volume was observed.

Table 2 Effect of intrarenal arterial infusion of Russell's viper venom on general circulation of seven TPTX dogs. (Mean ± SE.)

Variables	0	1/2	1	1 1/2	2	3	4	5 (hr.)
				*	*	*	**	**
MAP (mm.Hg)	103.33 ± 5.59	104.79 ± 6.89	110.42 ± 6.79	113.54 ± 7.08	112.28 ± 6.52	115.83 ± 6.04	120.63 ± 5.64	118.33 ± 6.05
		**	**	*				
PP (mm.Hg)	43.75 ±2.95	36.25 ±2.79	35.00 ±2.08	36.88 ±2.49	38.75 ±4.30	38.13 ±2.30	41.25 ±3.24	43.13 ±4.11
							*	*
HR(Beat/min)	124.75 ± 5.60	123.50 ± 7.05	119.75 ± 7.05	118.25 ± 7.79	127.88 ± 4.83	125.63 ± 6.53	136.63 ± 5.95	141.75 ± 5.57
PCV (%)	34.69 ±2.11	35.69 ±2.18	35.06 ±1.92	34.50 ±1.83	34.25 ±1.74	34.0 ±1.84	33.81 ±2.11	33.75 ±2.12

P-value with respect to control, * $p<0.05$, ** $p<0.01$.

The effect of intrarenal arterial infusion of Russell's viper venom on general circulation showed increase in MAP following the slight decrease in both intact and TPTX groups (Fig 1). The response

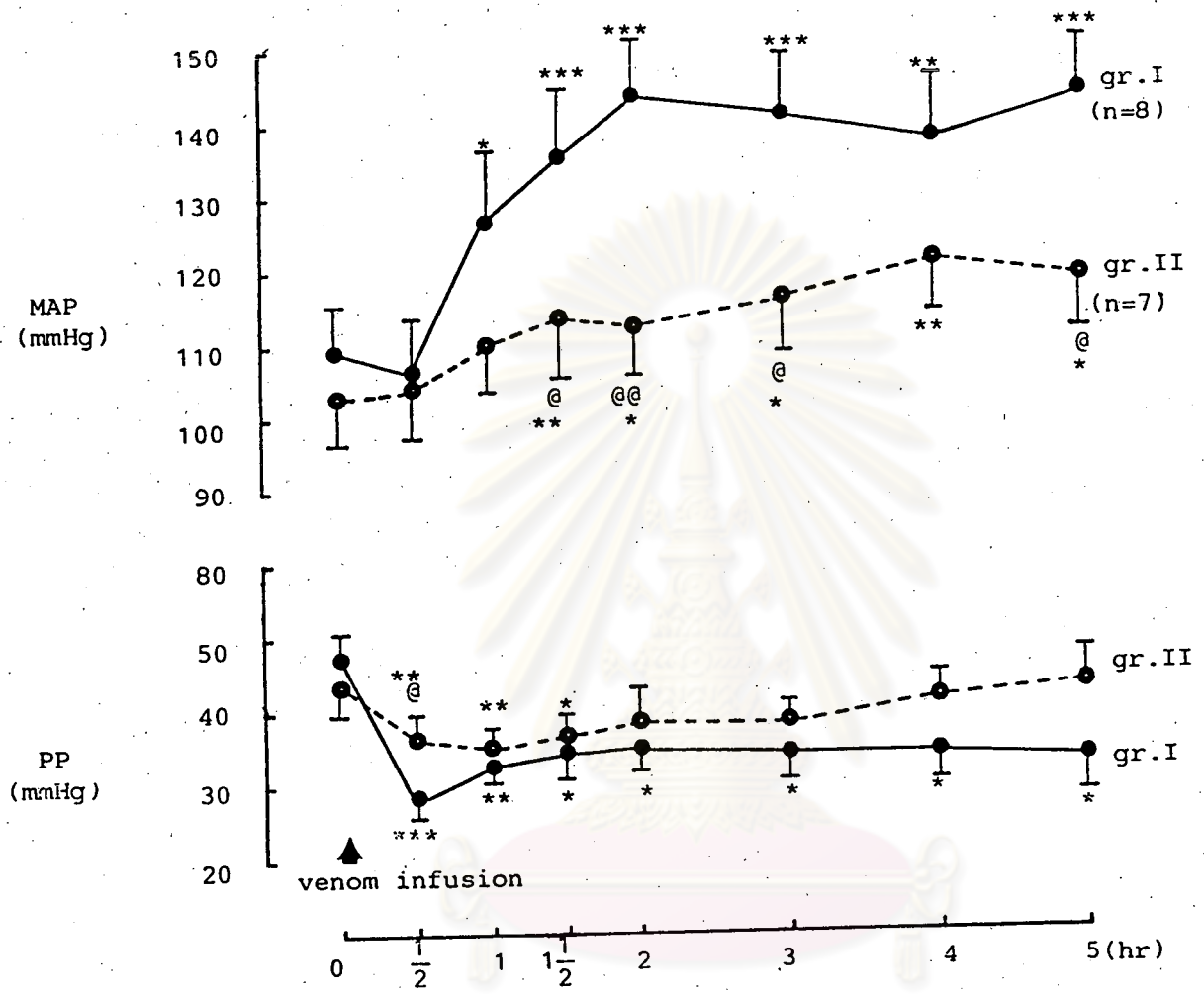

Figure 1 : Effect of intrarenal arterial infusion of Russell's viper venom on mean arterial pressure (MAP) and pulse pressure (PP) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval @ $P < 0.05$,@@ $P < 0.01$.

P-value with respect tocontrol condition of each group,* $P < 0.05$,** $P < 0.01$,*** $P < 0.001$.

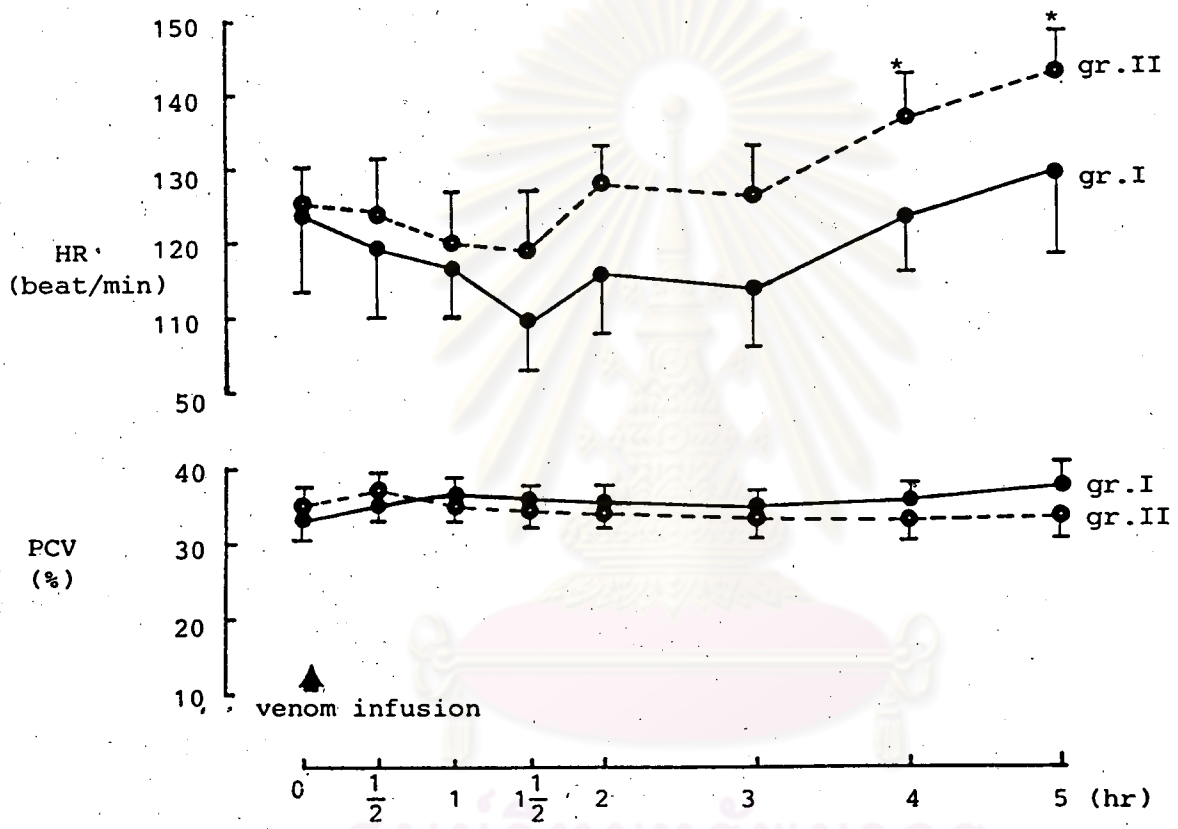

Figure 2 : Effect of intrarenal arterial infusion of Russell's viper venom on heart rate (HR) and packed cell volume (PCV) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE.

P-value with respect to control condition of each group,

* P < 0.05.

of an increase of MAP in intact animals was higher than that of TPTX animals. There was statistically significant difference in MAP response between intact and TPTX animals. However, the MAP of TPTX animals showed a tendency to recovery to control level, which did not occur in intact animals. It should be noted that pulse pressure of intact animals yielded a sharp reduction with slow recovery to the control level as compared to TPTX animals (Fig 1). Heart rate of both groups slightly declined in the same pattern within 2 hours and gradually increased to the control level (Fig 2). The significant increase in heart rate of the TPTX group was observed at the fourth and fifth hours periods and did not differ significantly when compared to the intact group. However, the magnitude of increment was higher in TPTX group after envenomation. There was no significant difference in packed cell volume in both groups (Fig 2).

Effect of Russell's Viper Venom on Renal Hemodynamics.

Group I : Intact dogs

The results are summarized in table 3. Effective renal plasma flow (ERPF) and effective renal blood flow (ERBF) decreased significantly ($p<0.001$) within the first 30 minutes and reached a lower level within 1 hour after venom infusion. It decreased in a low levels over 5 hours, whereas renal vascular resistance (RVR) increased nearly 30 folds after venom infusion and still increased significantly ($p<0.05$) throughout the experimental period (Fig 3). There were significant decreases in glomerular filtration rate (GFR), urine flow (V) and osmolar clearance (C_{Osm}) at the first 30 minutes after venom infusion, (21.17 $\pm$ 1.91 to 4.97 $\pm$ 1.54 ml/min) (0.65 $\pm$ 0.19 to 0.07 $\pm$

Table 3 Effect of intrarenal arterial infusion of Russell's viper venom on renal hemodynamics in the left kidney of eight intact dogs. (Mean ± SE)

Variables	0	1/2	1	1 1/2	2	3	4	5 (hr.)
		***	***	***	***	***	***	**
ERPF (ml/min)	65.16 ±6.57	12.10 ±2.91	5.42 ±1.00	12.29 ±3.70	21.08 ±5.70	23.48 ±5.18	23.79 ±5.06	25.66 ±6.94
		***	***	***	***	***	***	**
ERBF(ml/min)	98.38 ±10.66	15.50 ±4.43	8.27 ±1.45	18.61 ±6.09	33.03 ±9.18	36.58 ±8.12	36.97 ±7.58	40.53 ±10.25
		***	***	***	***	***	***	**
GFR (ml/min)	21.17 ±1.91	4.97 ±1.54	1.90 ±0.41	4.03 ±1.28	7.86 ±2.43	8.47 ±1.97	8.11 ±2.14	8.34 ±2.52
		*	*	*	*	*	*	*
V (ml/min)	0.65 ±0.19	0.07 ±0.01	0.03 ±0.007	0.05 ±0.01	0.08 ±0.02	0.12 ±0.03	0.15 ±0.04	0.19 ±0.06
		**	***	***	***	**	**	*
C_{Osm} (ml/min)	0.81 ±0.13	0.16 ±0.04	0.06 ±0.01	0.10 ±0.03	0.14 ±0.04	0.20 ±0.05	0.26 ±0.08	0.33 ±0.11
C_{H_2O} (ml/min)	-0.17 ±0.11	-0.09 ±0.03	-0.03 ±0.007	-0.04 ±0.01	-0.06 ±0.02	-0.09 ±0.03	-0.10 ±0.05	-0.14 ±0.06
FF (%)	35.31 ±5.23	40.05 ±3.05	36.03 ±4.87	33.13 ±2.86	35.75 ±4.03	36.08 ±2.21	31.45 ±3.04	38.33 ±2.74
		*	**	*	*	*	**	*
RVR(10^3 dyne-sec/cm^5)	97.34 ±43.81	709.53 ±200.15	2265.40 ±533.63	1476.66 ±617.71	816.09 ±342.73	527.69 ±164.57	392.06 ±84.83	583.90 ±208.83
P_{Na} (mEq/L)	142.50 ±1.38	141.00 ±1.68	139.63 ±2.10	141.63 ±1.50	141.50 ±1.89	143.50 ±1.86	143.00 ±1.82	142.00 ±0.98
			**	***	***	***	***	**
P_K (mEq/L)	2.90 ±0.12	2.98 ±0.12	3.18 ±0.12	3.41 ±0.13	3.59 ±0.09	3.93 ±0.11	3.80 ±0.13	3.73 ±0.16
P_{cl} (mEq/L)	117.63 ±2.15	115.63 ±2.44	120.00 ± 3.94	117.50 ±1.77	117.75 ± 3.73	115.00 ± 2.44	121.13 ± 2.38	124.38 ± 2.57
P_{Ca} (mEq/L)	4.84 ±0.27	4.61 ±0.21	4.79 ±0.45	4.52 ±0.24	4.84 ±0.41	4.76 ±0.23	4.86 ±0.33	4.47 ±0.20
P_{Pi} (mEq/L)	5.24 ±0.61	5.34 ±0.50	5.59 ±0.52	5.60 ±0.38	5.26 ±0.53	6.13 ±0.63	5.89 ±0.68	6.73 ±0.87
					*	*	**	**
P_{Osm} (mOsm/kg)	285.63 ±2.12	285.38 ±2.59	287.75 ±1.39	289.88 ±2.05	290.13 ±1.90	291.63 ±1.59	293.63 ±2.18	296.50 ±2.43
		***	***	***	***	***	**	**
FL_{Na} (mEq/min)	3.01 ±0.26	0.70 ±0.22	0.27 ±0.06	0.57 ±0.19	1.11 ±0.03	1.22 ±0.28	1.16 ±0.30	1.18 ±0.36
		***	***	***	**	**	**	**
FL_K (mEq/min)	0.06 ±0.007	0.02 ±0.007	0.007 ±0.001	0.01 ±0.004	0.03 ±0.007	0.03 ±0.007	0.03 ±0.007	0.03 ±0.007
		***	***	***	***	***	***	**
FL_{Cl} (mEq/min)	2.84 ±0.22	0.59 ±0.26	0.23 ±0.05	0.47 ±0.16	0.94 ±0.19	0.99 ±0.24	0.97 ±0.25	1.00 ±0.28
			*	*				
FL_{Ca} (mEq/min)	0.26 ±0.10	0.06 ±0.03	0.03 ±0.02	0.02 ±0.007	0.05 ±0.01	0.05 ±0.01	0.06 ±0.01	0.05 ±0.01
			***	**				
FL_{Pi} (mEq/min)	0.12 ±0.01	0.06 ±0.03	0.02 ±0.007	0.03 ±0.01	0.14 ±0.03	0.11 ±0.06	0.08 ±0.03	0.12 ±0.07
U_{Osm} (mOsm/kg)	519.9 ±362.2	505.9 ±203.6	560.9 ±159.4	506.9 ±155.2	499.6 ±150.3	494.6 ±124.9	533.8 ±195.8	491.6 ±122.5

P. value with respect to control, * $p<0.005$. ** $p<0.01$, *** $p<0.001$.

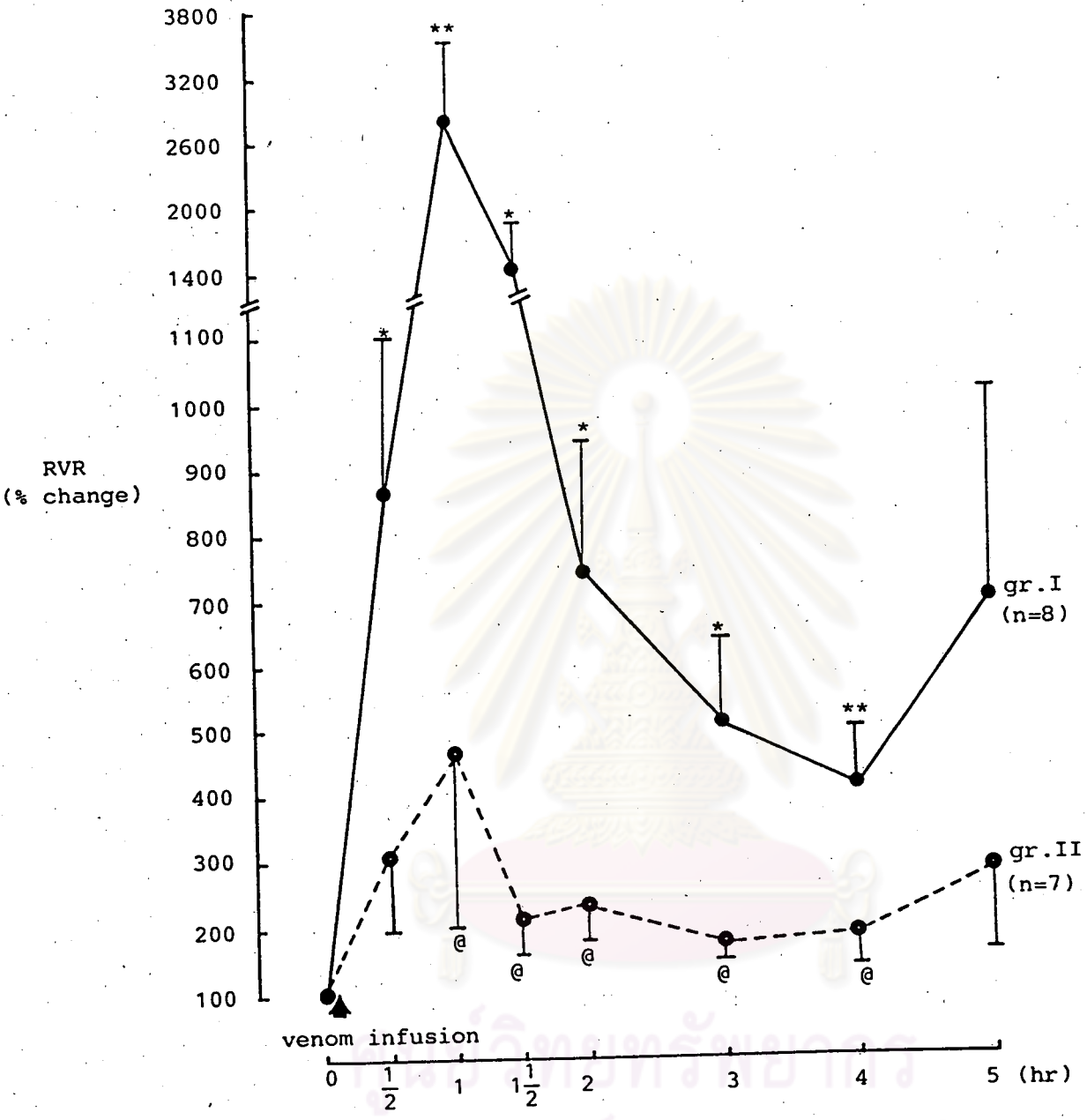

Figure 3 : Changes in percentage of renal vascular resistance (RVR) after intrarenal arterial infusion of Russell's viper venom in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group,* $P < 0.05$,** $p < 0.01$.

0.01 ml/min) (0.81 ± 0.13 to 0.16 ± 0.04 ml/min) and maintained at significant level till the end of the experiment. Whereas free water clearance (C_{H_2O}) and filtration fraction (FF) showed no significant change after envenomation.

The data in table 3 shows that plasma sodium (P_{Na}), chloride (P_{Cl}), calcium (P_{Ca}) and inorganic phosphorus (P_{pi}) were constant throughout the experimental period, while plasma potassium (P_K) increased significantly from 2.90 ± 0.12 to 3.18 ± 0.12 mEq/L ($p<0.01$) within 1 hour after envenomation and maintained at high level ($p<0.001$) till the end of experiment. Plasma osmolarity (P_{Osm}) increased significantly from the control of 285.63 ± 2.12 to 290.13 ± 1.90 mOsm/kg ($p<0.05$) at 2 hours period after venom infusion and remained at significant range ($p<0.01$) over 5 hours. It should be noted that filtered load of sodium (FL_{Na}), potassium (FL_K) and chloride (FL_{Cl}) decreased significantly ($p<0.001$) from 3.01 ± 0.26 to 0.70 ± 0.22 mEq/min, 0.06 ± 0.007 to 0.02 ± 0.007 mEq/min and 2.84 ± 0.22 to 0.59 ± 0.26 mEq/min respectively within 30 minutes after envenomation and remained at significant range over 5 hours. However, a significant decrease in filtered load of calcium (FL_{Ca}) ($p<0.05$) and inorganic phosphorus (FL_{Pi}) ($p<0.001$) at 1 hour period after envenomation were observed. Urine osmolarity (U_{Osm}) was not significant change.

Group II : Thyroparathyroidectomized (TPTX) dogs

Results in table 4 showed that effective renal plasma flow and effective renal blood flow decreased significantly from 110.68 ± 12.49 to 50.85 ± 13.39 ml/min and from 116.80 ± 16.44 to 78.19 ± 21.19

Table 4 Effect of intrarenal arterial infusion of Russell's viper venom on renal hemodynamics in the left kidney of eight TPTX dogs. (Mean ± SE)

Variables	0	1/2	1	1 1/2	2	3	4	5 (hr.)
			*	*	*	*		
ERPF	110.68	59.58	50.85	61.65	60.53	69.79	88.24	74.76
(ml/min)	±12.49	±19.99	±13.39	±13.47	±13.32	±10.67	±17.42	±14.65
			*	*	*			
ERBF	166.80	92.29	78.19	89.55	91.87	105.60	132.66	112.40
(ml/min)	±16.44	±31.32	±21.19	±18.88	±20.85	±16.56	±27.30	±23.27
		*						
GFR	31.94	21.28	19.03	21.55	19.47	22.16	23.59	24.65
(ml/min)	±4.31	±6.81	±5.20	±4.93	±4.98	±4.24	±4.95	±6.34
V (ml/min)	0.59	0.17	0.15	0.18	0.19	0.28	0.35	0.35
	±0.22	±0.06	±0.05	±0.05	±0.05	±0.08	±0.11	±0.12
C_{Osm} (ml/min)	0.58	0.28	0.24	0.30	0.33	0.42	0.40	0.67
	±0.13	±0.09	±0.06	±0.07	±0.08	±0.09	±0.14	±0.08
C_{H_2O} (ml/min)	0.08	0.11	0.09	0.12	0.14	0.16	0.26	0.32
	±0.11	±0.03	±0.03	±0.05	±0.05	±0.05	±0.05	±0.07
FF (%)	31.28	35.33	36.71	33.49	30.39	30.57	25.77	31.10
	±4.44	±3.89	±3.18	±1.38	±1.54	±2.04	±2.01	±3.15
RVR(10^3 dyne-sec/cm^5)	55.10	171.56	318.41	139.73	115.68	88.90	92.60	141.98
	±6.79	±59.48	±187.57	±46.74	±28.73	±14.13	±25.77	±61.65
P_{Na} (mEq/L)	140.75	140.00	141.38	140.88	139.00	143.38	141.75	141.38
	±1.10	±1.15	±0.94	±1.60	±1.51	±1.63	±2.28	±2.46
			**	*	*	**	*	*
P_K (mEq/L)	2.98	3.06	3.23	3.31	3.40	3.50	3.60	3.63
	±0.11	±0.10	±0.13	±0.13	±0.13	±0.13	±0.20	±0.19
P_{Cl} (mEq/L)	123.13	121.88	117.38	117.38	118.00	121.13	121.63	126.13
	±2.00	±2.09	±2.94	±2.91	± 1.63	± 2.17	± 2.98	± 4.72
P_{Ca} (mEq/L)	2.94	2.82	2.74	2.82	2.76	2.65	2.58	2.51
	±0.22	±0.19	±0.22	±0.23	±0.21	±0.20	±0.15	±0.18
				**	*	*		
P_{Pi} (mEq/L)	3.99	4.41	4.69	4.79	4.88	5.09	5.02	4.97
	±0.27	±0.32	±0.26	±0.16	±0.22	±0.30	±0.35	±0.31
					**	**	***	***
P_{Osm} (mEq/L)	283.13	286.13	289.88	287.13	888.75	291.88	294.13	294.13
	±2.10	±1.41	±2.42	±1.25	±1.54	±2.65	±1.90	±2.14
					*			
FL_{Na} (mEq/min)	4.47	3.01	2.69	3.01	2.86	3.20	3.36	3.51
	±0.58	±0.98	±0.73	±0.71	±0.81	±0.62	±0.72	±0.94
FL_K (mEq/min)	0.10	0.07	0.06	0.07	0.07	0.08	0.08	0.09
	+0.01	+0.02	+0.02	+0.02	+0.02	+0.02	+0.02	+0.03
FL_{Cl} (mEq/min)	3.93	2.63	2.31	2.60	2.34	2.73	2.91	2.96
	+0.55	+0.86	+0.66	+0.60	+0.63	+0.56	+0.63	+0.69
FL_{Ca} (mEq/min)	0.09	0.06	0.06	0.06	0.05	0.03	0.06	0.06
	+0.01	+0.02	+0.02	+0.01	+0.01	+0.01	+0.01	+0.02
			*		*			
FL_{Pi} (mEq/min)	0.13	0.10	0.09	0.11	0.10	0.11	0.11	0.12
	+0.02	+0.04	+0.03	+0.03	+0.03	+0.02	+0.02	+0.03
U_{Osm} (mOsm/kg)	535.6	553.4	685.5	548.0	558.1	556.8	590.1	634.8
	±341.1	±359.5	±515.9	±294.6	±260.7	±237.6	±149.5	±227.4

P. value with respect to control, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

min ($p<0.05$) within 1 hour after venom infusion respectively and its returned to control level within 4 hours. There was no significant increased in renal vascular resistance, whereas significant decrease in glomerular filtration rate from 31.94 $\pm$ 4.31 to 21.28 $\pm$ 6.81 ml/min ($p<0.05$) was apparent at the first 30 minutes after envenomation and then it returned toward control level within 1 hour period. No significant changes in urine flow, osmolar clearance, free water clearance and filtration fraction were noted over the study period.

The plasma sodium, chloride and calcium concentration were constant throughout the study period, while plasma potassium concentration increased significantly from 2.98 $\pm$ 0.11 to 3.23 $\pm$ 0.13 mEq/L ($p<0.01$) at the first 1 hour and remained at high level ($p<0.05$) over the study period. Plasma inorganic phosphorus concentration increased significantly from 3.99 $\pm$ 0.27 to 4.79 $\pm$ 0.16 mEq/L ($p<0.01$) at one and half hours after envenomation and returned to control range within four hours. A progressive increase in plasma osmolarity was recorded at the first 30 minutes after venom infusion and reached a significant level at 2 hours ($p<0.01$), then it remained in significant level throughout the remainder periods of experiment ($p<0.001$). Filtered load of sodium decreased to the significant level at 1 hour period after venom infusion ($p<0.05$) and increased to control condition within 1 1/2 hours, whereas filtered load of potassium, chloride and calcium were not significant decrease throughout the trial period. Filtered load of inorganic phosphorus showed significant decrease at 1 and 2 hour periods ($p<0.05$) after envenomation. Urine osmolarity was not change throughout the study.

In comparison of the results, the intact and TPTX groups revealed that a decrease in effective renal plasma flow and effective renal blood flow of TPTX showed a lesser extent ($p<0.001$) as compared to intact group by approximately 40% throughout the experimental period (Fig 4,5). These changes were concomitant with the less renal vascular resistance in TPTX group after venom infusion (Table 3,4). The decrease in percentage of glomerular filtration rate in TPTX group was less than intact group throughout the experiment period (Fig 9). The rate of urine flow in control period of both groups were not different. After venom infusion, a decline in urine flow rate of both groups were noted, but the TPTX group was lesser and not significant decreased (Fig 10). The differences were significant at 1 and 1 1/2 hours ($p<0.05$). The osmolar clearance of TPTX group did not significant decrease after venom infusion, whereas it decreased significantly in the intact group over 5 hours ($p<0.05$) (Fig 11). The significant difference between two groups appeared at the first 1 hour and disappeared within 4 hours period. Four hours after venom infusion, free water clearance of the TPTX one was significant lower than the intact group and remained at significant level over 5 hours period ($p<0.05$) (Fig 12). Filtration fraction was not significantly different throughout the study period (Fig 13). In the control period of both intact and TPTX animals showed no significant difference in plasma concentration of sodium, chloride, potassium (Fig 6) and inorganic phosphorus (Fig 7). While plasma calcium concentration in TPTX animals showed significantly less than those intact group ($p<0.001$) throughout the study period (Fig 7). There was no significant difference in plasma sodium and chloride concentration

between intact and TPTX animals (Fig 6), while plasma potassium increased significantly in both groups after envenomation. It should be noted that plasma inorganic phosphorus concentration in TPTX group was lower than intact group during control period and significant difference was observed at 1 1/2, 3 and 5 hours after venom infusion ($p<0.05$). A significant difference in plasma osmolarity between TPTX group and intact group were not observed during the experiment (Fig 8). Filtered load of sodium, potassium and chloride in control period of TPTX dogs were higher than intact dogs and these differences were statistically significant ($p<0.05$) (Fig 14,15,16). After venom infusion, pararell decreases of these three parameters were obtained and there were significantly different throughout the experimental period. However, the intact group showed more decreases and slow recovery than TPTX group. Before administration of the venom, filtered load of calcium of the TPTX dog was significantly less than the intact dog ($p<0.05$) (Fig 17). After venom infusion, filtered load of calcium in the intact group markedly decreased when compared with the TPTX group and it continue decreased to significance different level at 1 1/2 hours period ($p<0.05$). After that filtered load of calcium increased to the nonsignificance different rank within 2 hours. In figure 18, it demonstrated that the venom produced a less decrease in filtered load of inorganic phosphorus in TPTX group than intact group. This difference was significant at 1 and 1 1/2 hour periods ($p<0.05$) after envenomation. There was no significant difference in urine osmolarity between group.

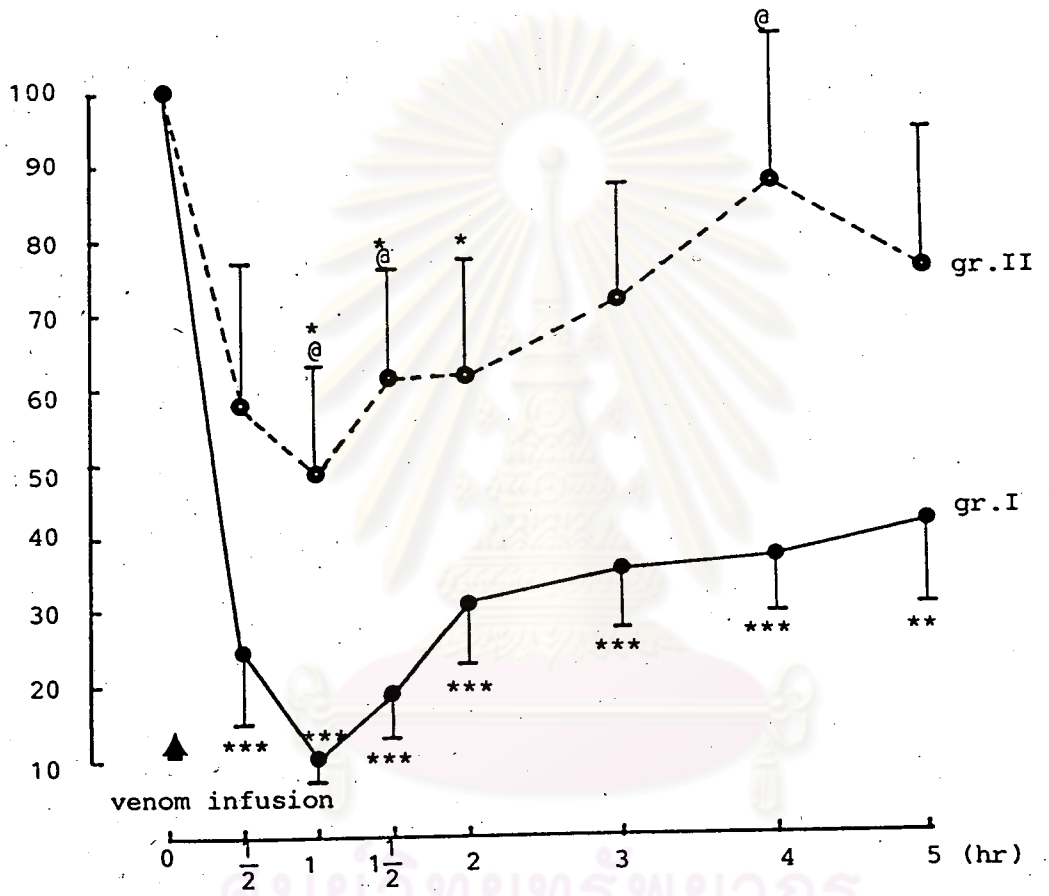

Figure 4 : Percentage changes in effective renal plasma flow as compaired to control period of each group after intrarenal arterial infusion of Russell's viper venom in group I (intact) and group II (thyroparathyroidectomized). The value are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

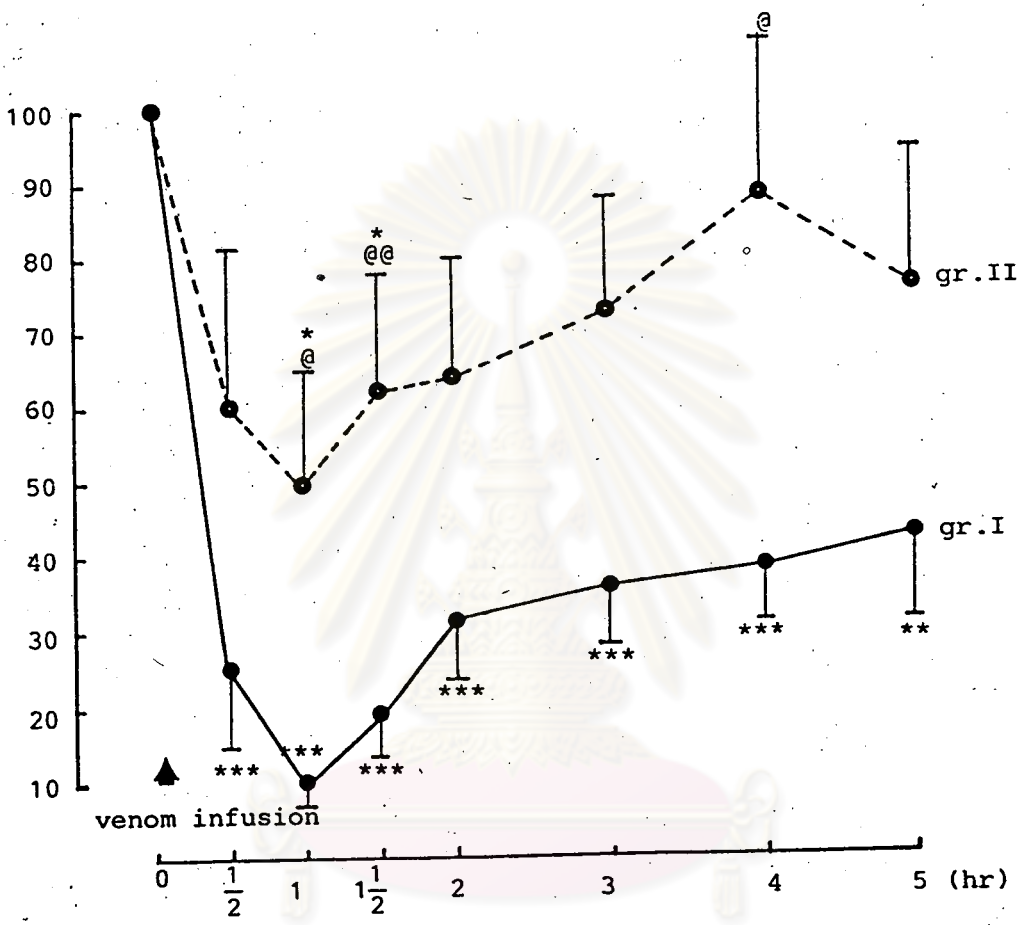

Figure 5 : percentage changes in effective renal blood flow as compaired to control period of each group after intrarenal arterial infusion of Russell's viper venom in group I (intact) and group II (thyroparathyroidectomized).The value are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$,@@ $P < 0.01$.

P-value with respect to control condition of each group,* $P < 0.05$, ** $P < 0.01$,*** $P < 0.001$.

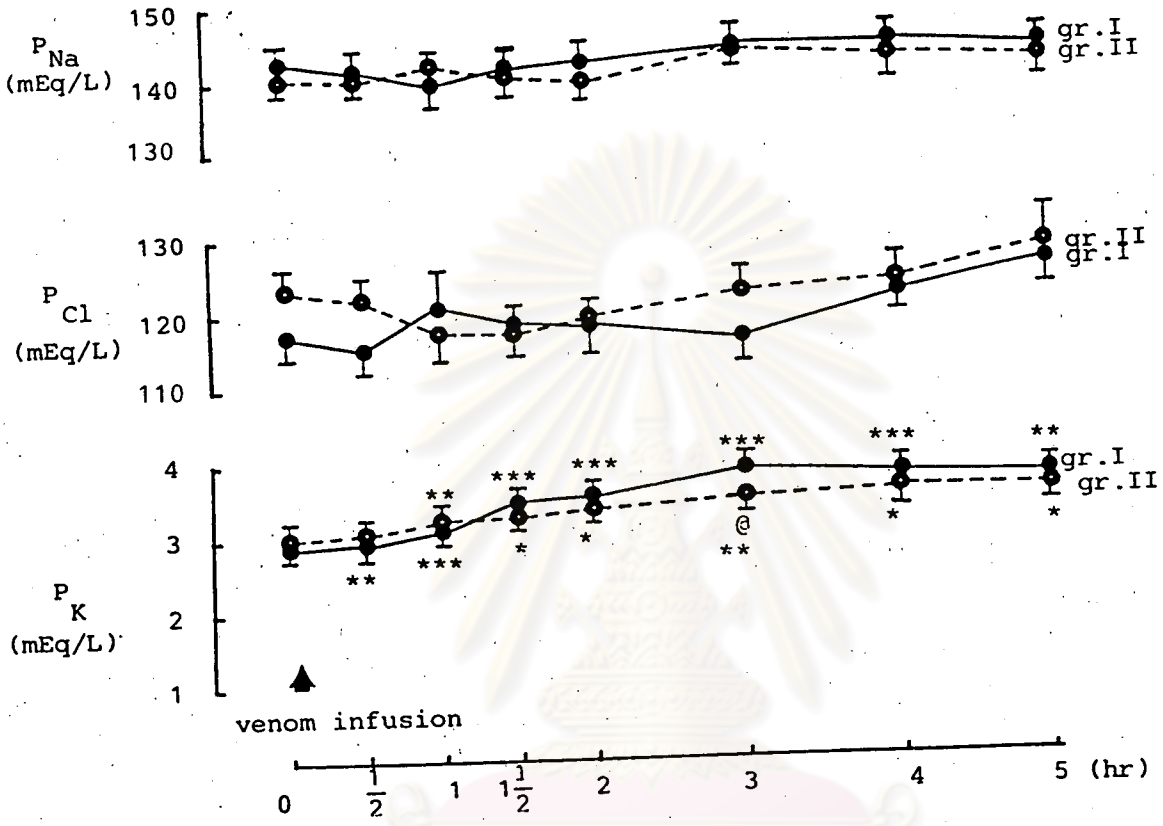

Figure 6 : Effect of intrarenal arterial infusion of Russell's viper venom on plasma sodium (P_{Na}) chloride (P_{Cl}) and potassium (P_K) concentration in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group,* $P < 0.05$, ** $P < 0.01$,*** $P < 0.001$.

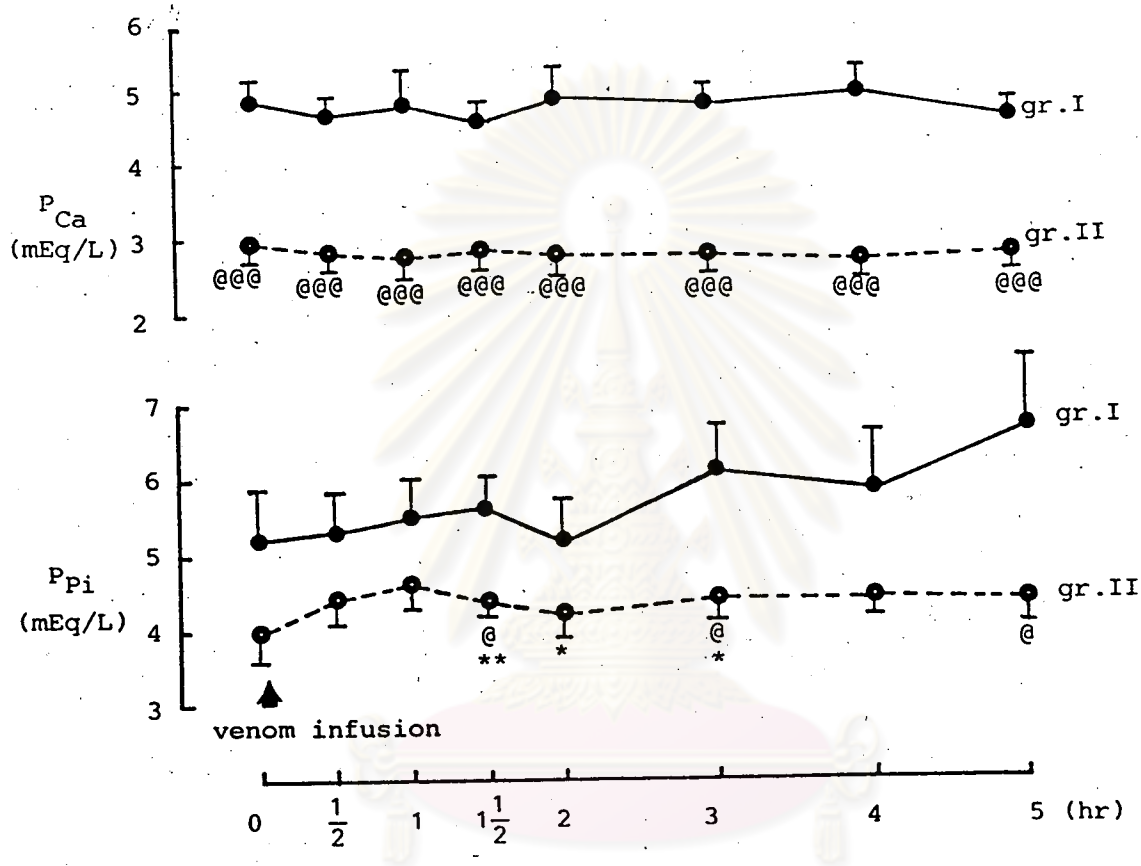

Figure 7 : Effect of intrarenal arterial infusion of Russell's viper venom on plasma calcium (P_{Ca}) and inorganic phosphorus (P_{Pi}) concentration in group I (intact) and group II (thyroparathyroidectomized). The values are mean $\pm$ SE..

P-value with respect to intact group at the same time interval, @@@ $P < 0.001$.

P-value with respect to control condition of each group,* $P < 0.05$,** $P < 0.01$,*** $P < 0.001$.

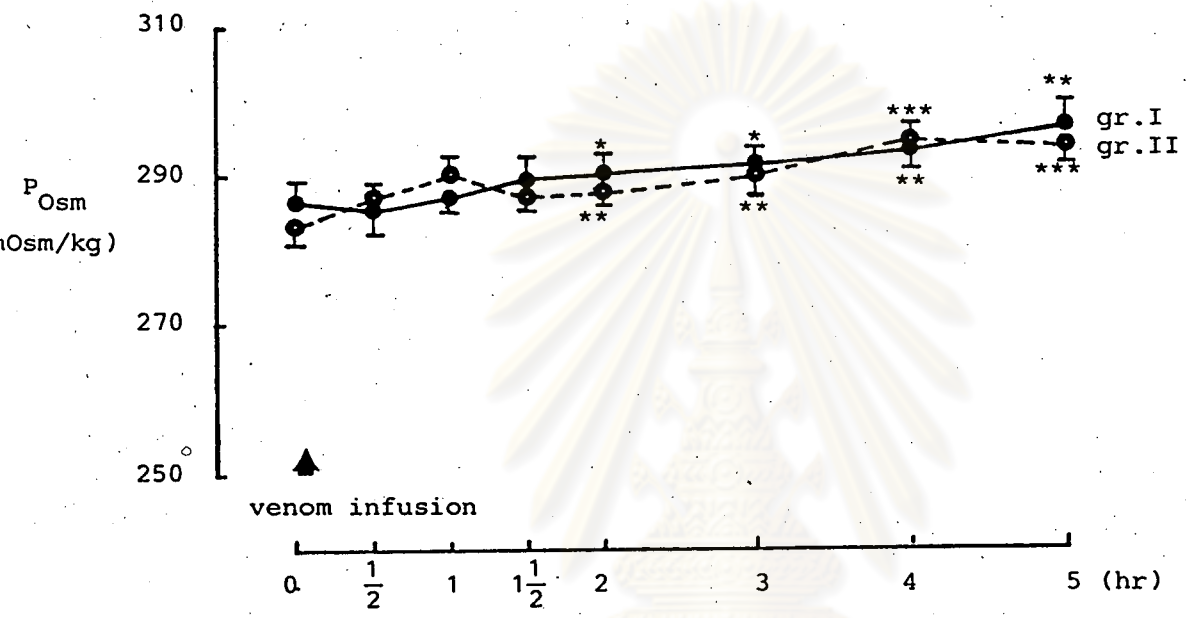

Figure 8 : Effect of intrarenal arterial infusion of Russell's viper venom on plasma osmolarity (P_{Osm}) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE.
P-value with respect to control condition of each group,* $P < 0.05$,** $P < 0.01$,*** $P < 0.001$.

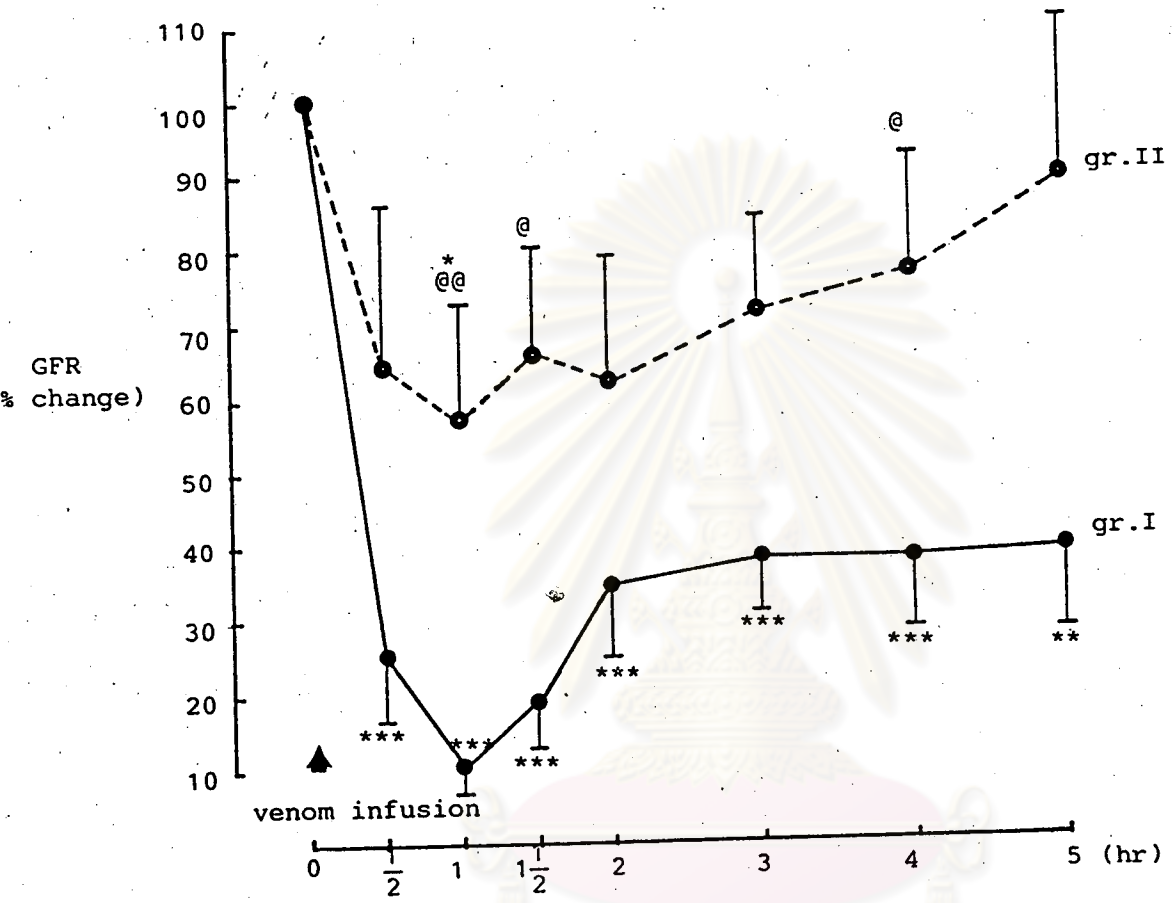

Figure 9 : Percentage changes in glomerular filtration rate as compaired to control period of each group after intrarenal arterial infusion of Russell's viper venom in group I (intact) and group II (thyroparathyroidectomized).The value are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$,@@ $P < 0.01$.

P-value with respect to control condition 0f each group,* $P < 0.05$, ** $P < 0.01$,*** $P < 0.001$.

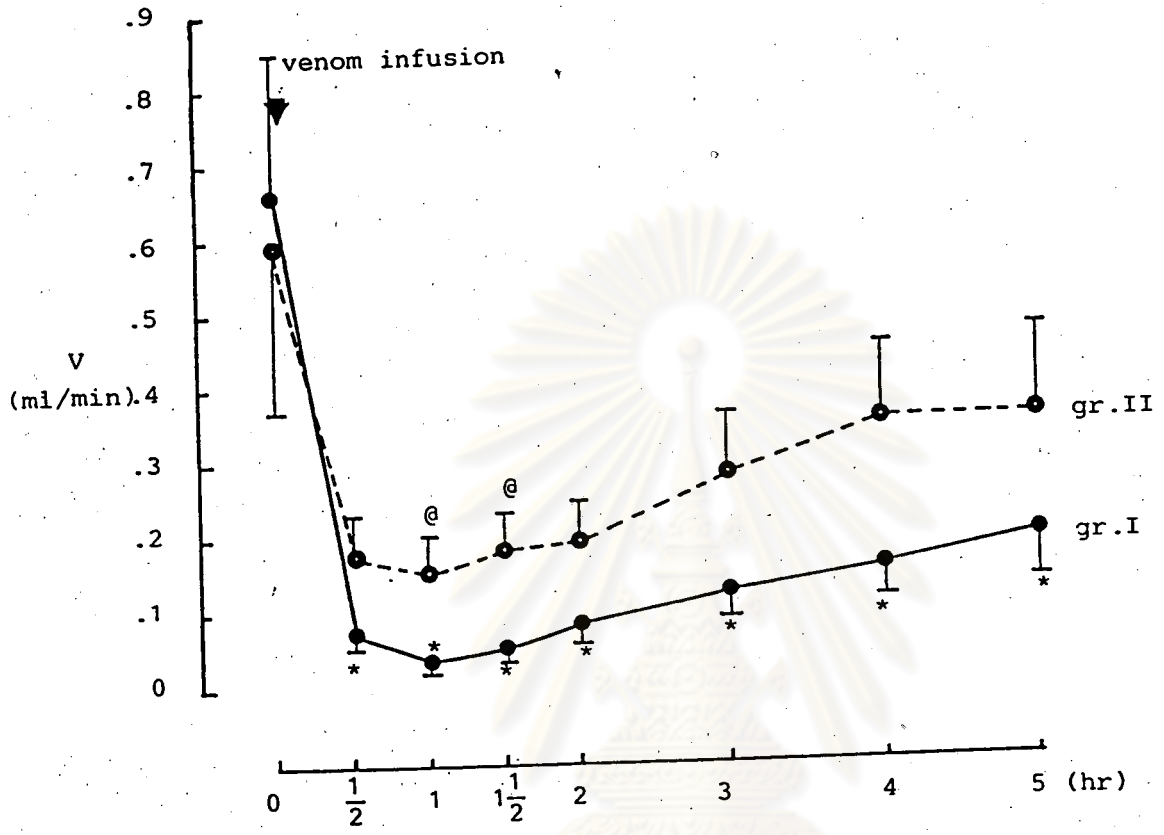

Figure 10 : Effect of intrarenal arterial infusion of Russell's viper venom on urine flow (V) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group,* $P < 0.05$.

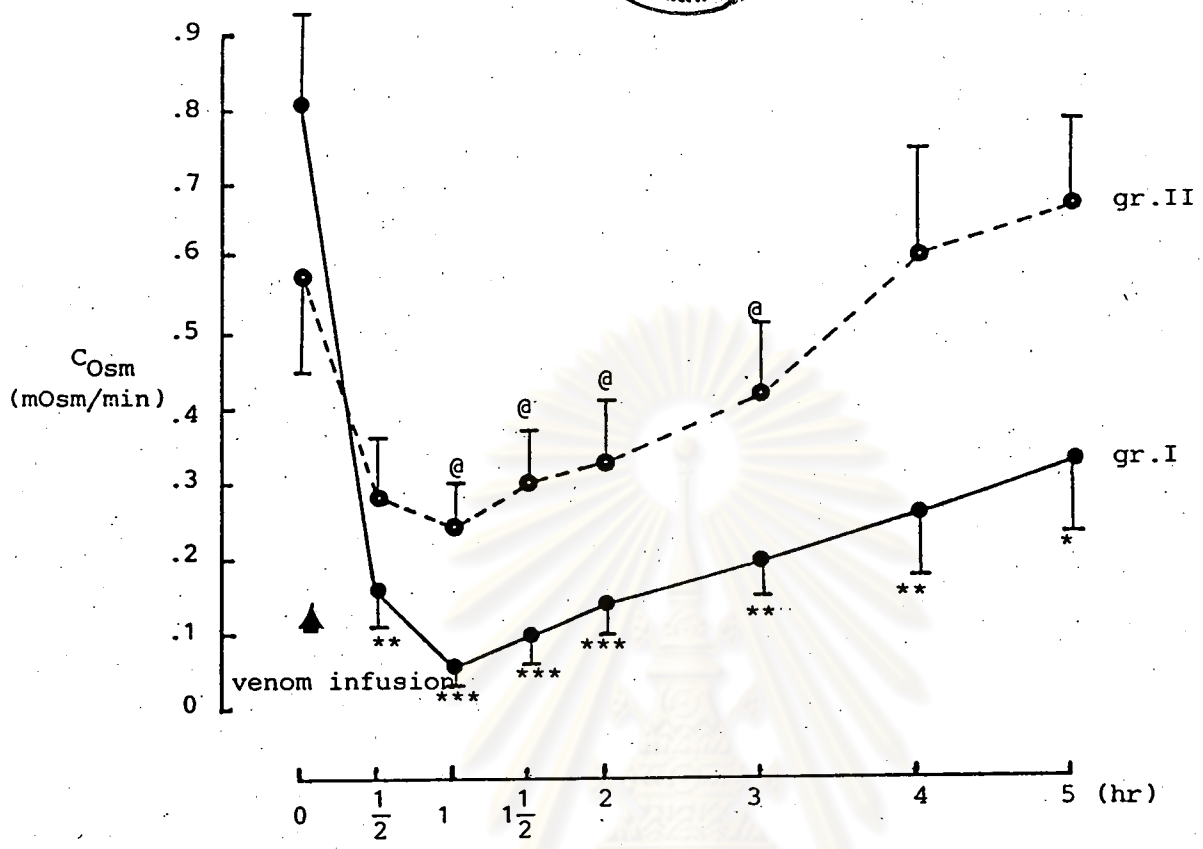

Figure 11 : Effect of intrarenal arterial infusion of Russell's viper venom on osmolar clearance (C_{Osm}) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group,* $P < 0.05$,** $P < 0.01$,*** $P < 0.001$.

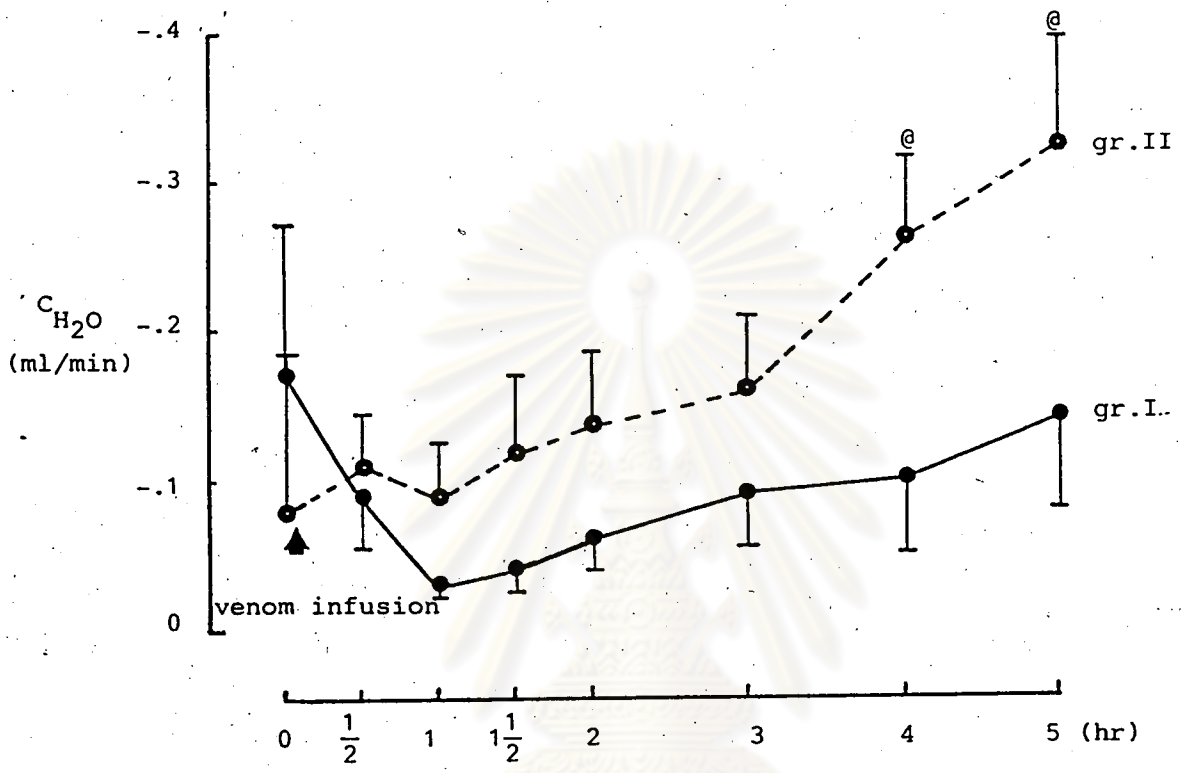

Figure 12 : Effect of intrarenal arterial infusion of Russell's viper venom on free water clearlance (C_{H_2O})in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE. P-value with respect to intact group at the same time interval, @ $P < 0.05$.

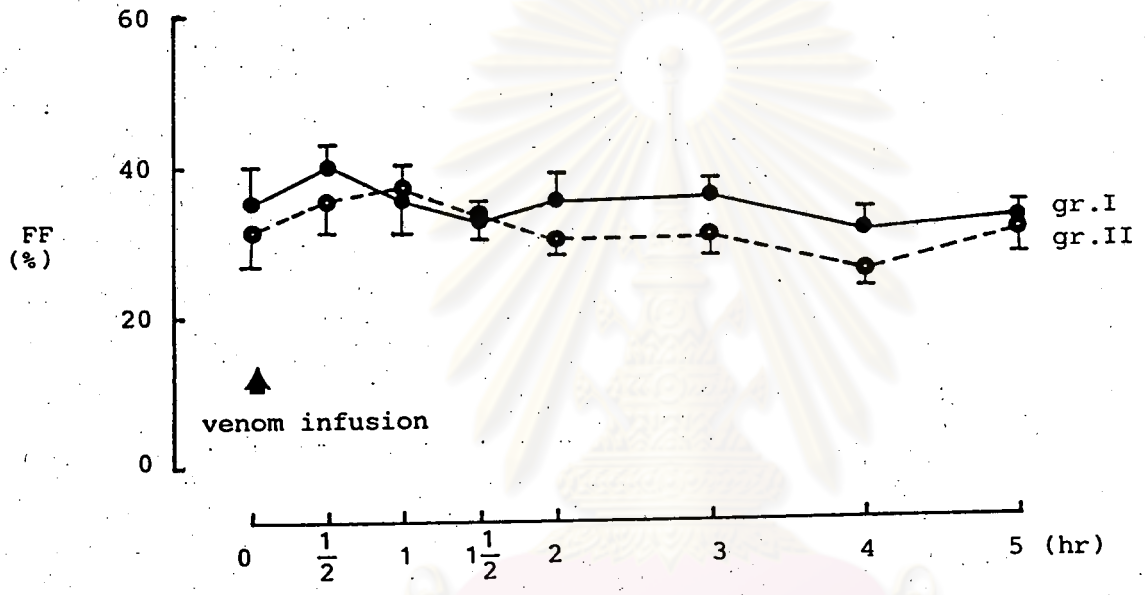

Figure 13 : Effect of intrarenal arterial infusion of Russell's viper venom on filtration fraction (FF) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE.

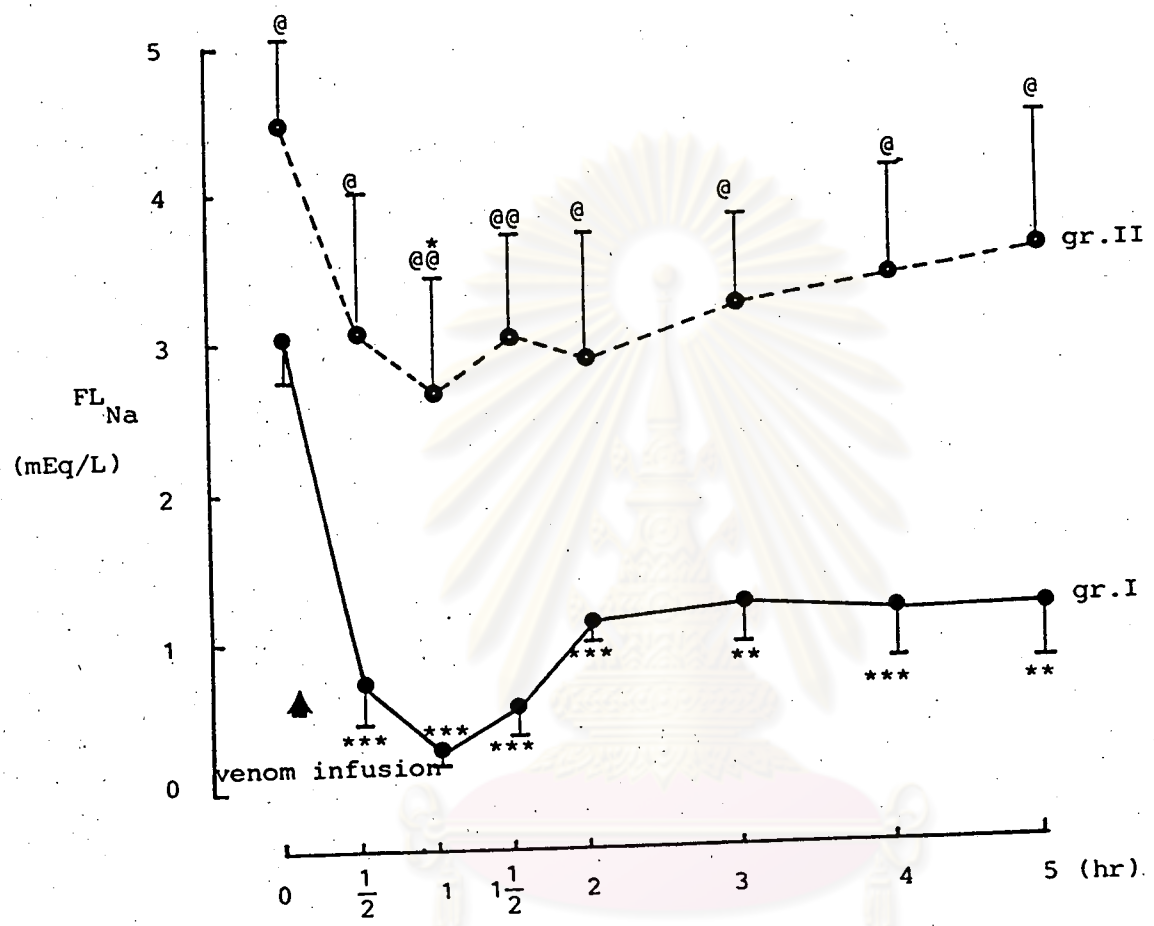

Figure 14 : Effect of intrarenal arterial infusion of Russell's viper venom on filter load of sodium (FL_{Na}) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$, @@ $P < 0.01$.

P-value with respect to control condition of each group, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

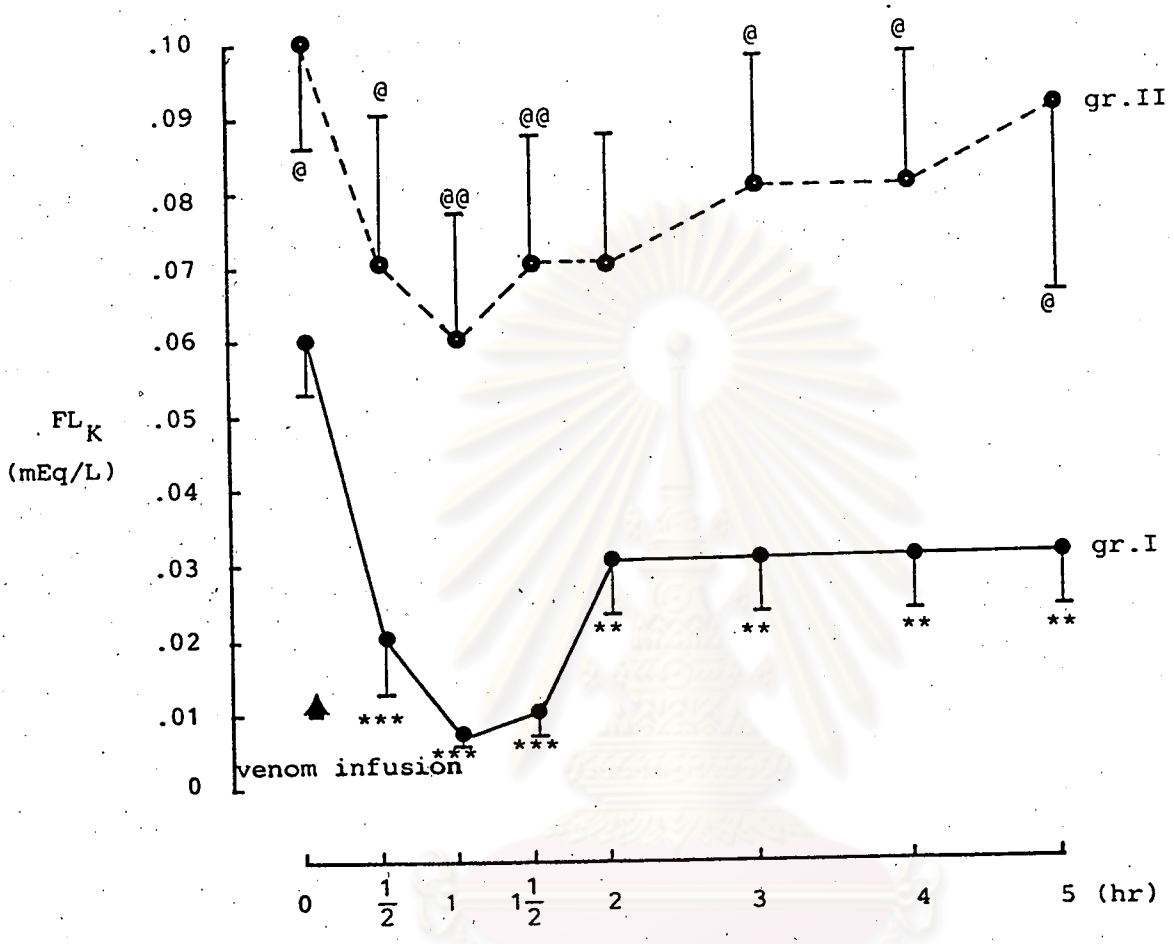

Figure 15 : Effect of intrarenal arterial infusion of Russell's viper venom on filter load of potassium (FL_K) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$, @@ $P < 0.01$.

P-value with respect to control condition of each group, ** $P < 0.01$, *** $P < 0.001$.

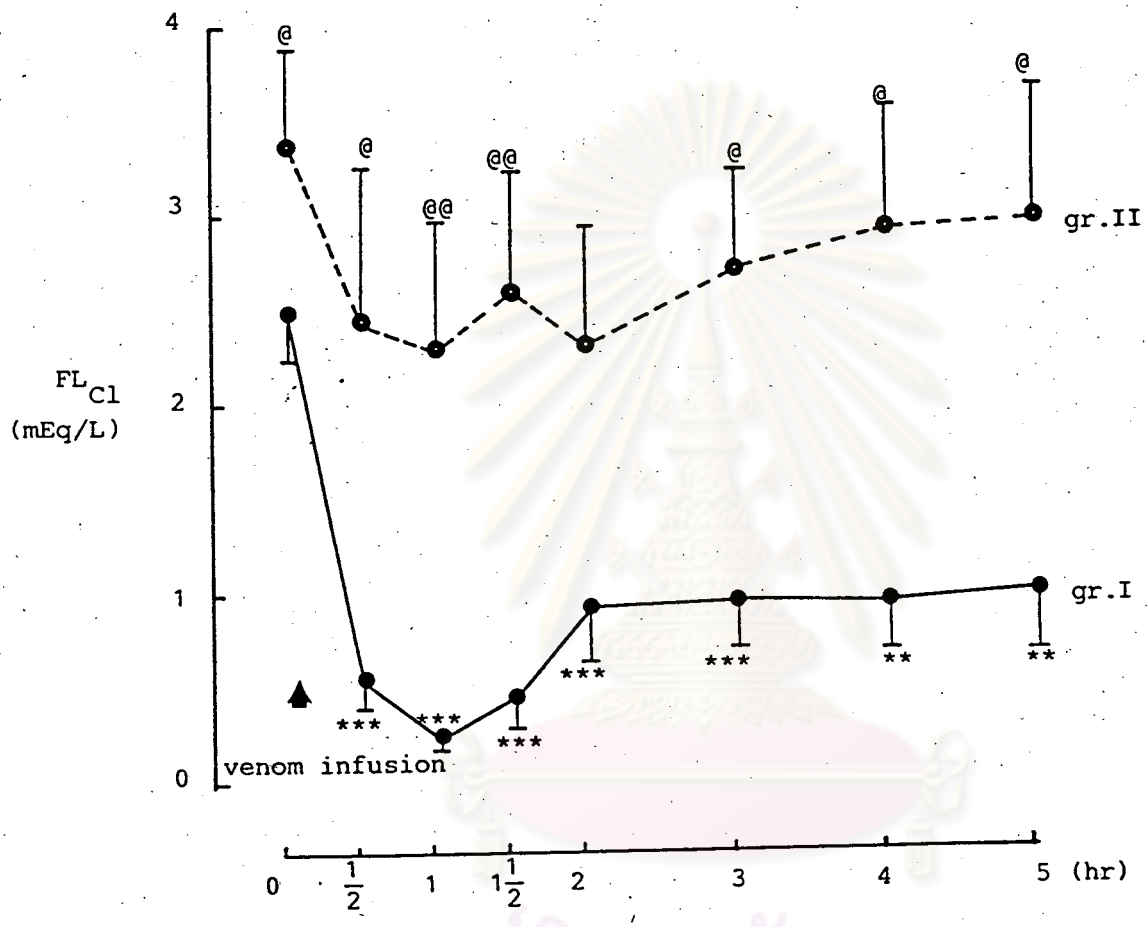

Figure 16 : Effect of intrarenal arterial infusion of Russell's viper venom on filter load of cloride (FL_{Cl}) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$, @@ $P < 0.01$.

P-value with respect to control condition of each group, ** $P < 0.01$. *** $P < 0.001$.

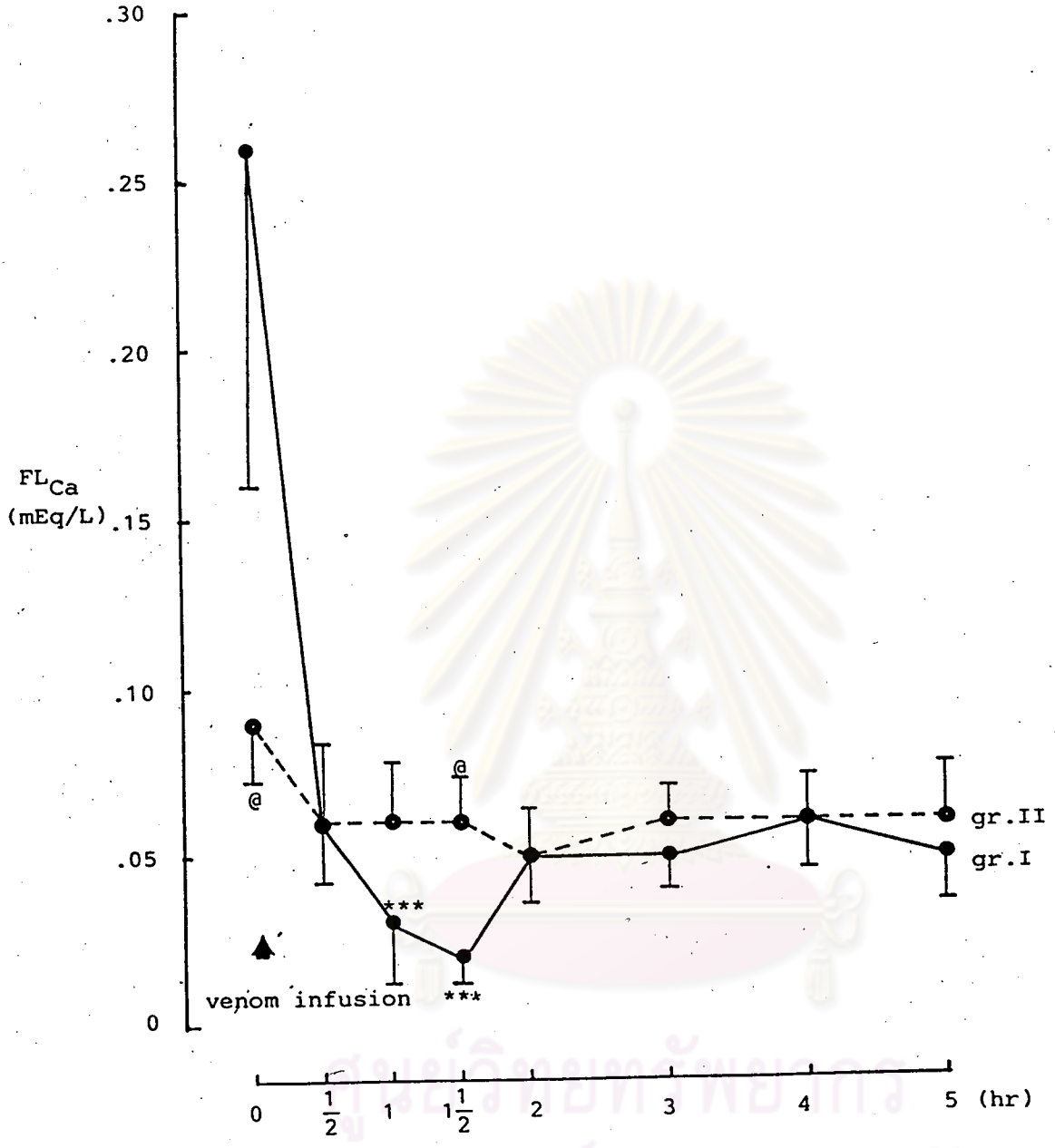

Figure 17 : Effect of intrarenal arterial infusion of Russell's viper venom on filter load of calcium (FL_{Ca}) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group, *** $P < 0.001$.

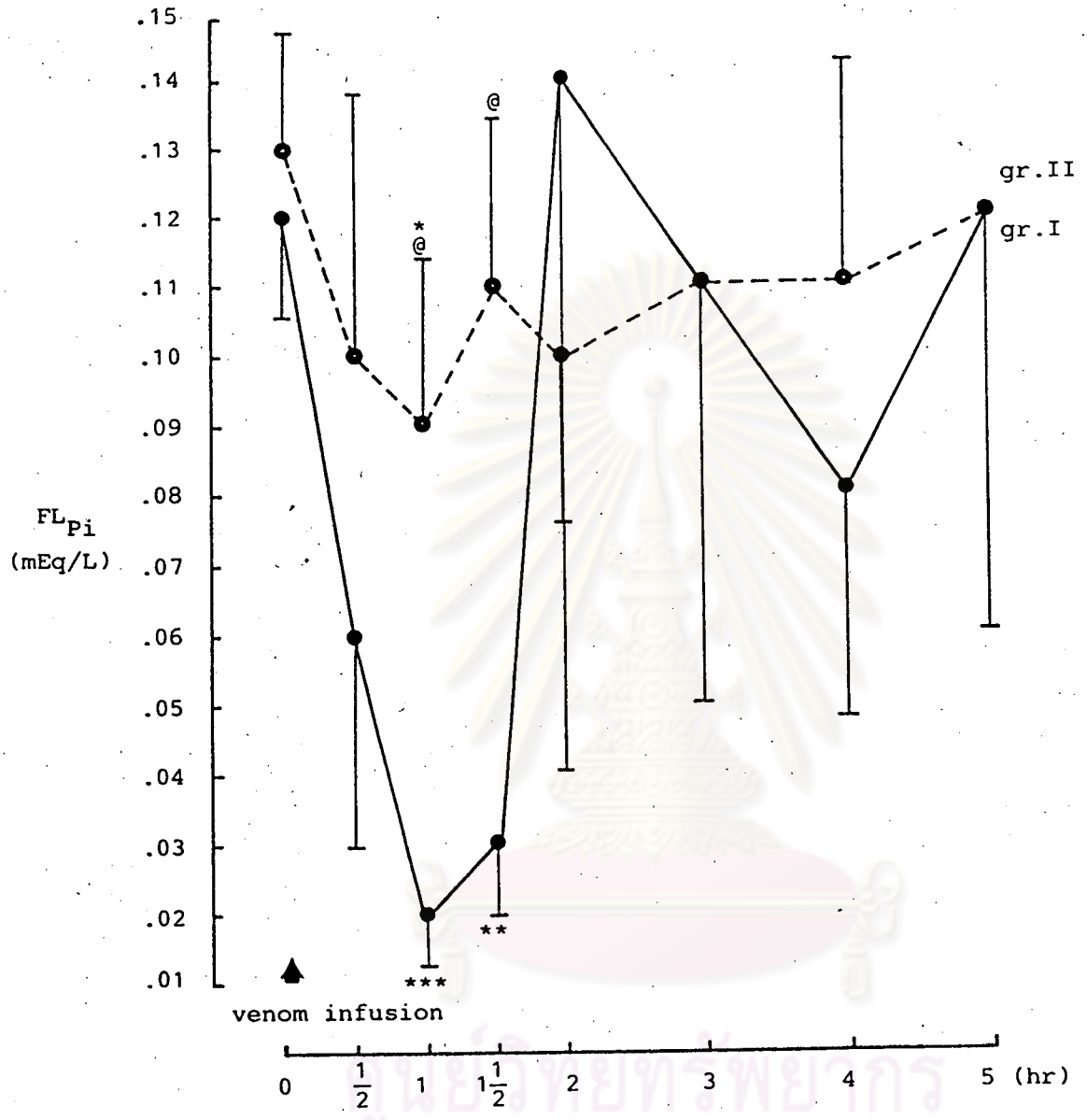

Figure 18 : Effect of intrarenal arterial infusion of Russell's viper venom on filter load of inorganic phosphorus (FL_{Pi}) in group I (intact) and group II (thyroparathyroidectomized).The values are mean $\pm$ SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group,* $P < 0.05$,** $P < 0.01$,*** $P < 0.001$.

Effect of Russell's Viper Venom on electrolytes excretion

Group I Intact dogs

The data in table 5 reveal a significant decrease in fractional excretion of sodium (FE_{Na}) at 2 and 3 hours after venom infusion ($p<0.05$), while fractional excretion of potassium (FE_K) markedly increased ($p<0.05$). However, changes in fractional excretion of chloride (FE_{Cl}), calcium (FE_{Ca}) and inorganic phosphorus (FE_{Pi}) were not significantly apparent. A simultaneous decreases were observed for urinary sodium ($U_{Na}V$), chloride (U_KV) and calcium ($U_{Ca}V$) excretion at the first 30 minutes after venom infusion and it maintained at low level throughout the experimental period. There were significant decreases in urinary potassium (U_KV) ($p<0.001$) and inorganic phosphorus ($U_{Pi}V$) ($p<0.01$) excretion after 1 1/2 and 2 hours of envenomation. The urinary titratable acid excretion (U_HV) decreased significantly within 1 hour ($p<0.01$) and returned to control condition within 3 hours.

Group II : Thyroparathyroidectomized (TPTX) dogs

The effect of intrarenal arterial infusion of Russell's viper venom on electrolytes excretion are presented in table 6. The remarkable findings was a pregressive increased in fractional excretion of sodium and calcium over 5 hours period, whereas fractional excretion of potassium reached significant level at 4 and 5 hours period after venom infusion. No significant increase in fractional excretin of chloride was recorded. Three hours after venom infusion, fractional excretion of inorganic phosphorus increased significantly till the end of the experiment ($p<0.05$). Urinary

Table 5 Effect of intrarenal arterial infusion of Russell's viper venom on tubuloglomerular activity in the left kidney of eight intact dogs. (Mean ± SE)

Variables	0	1/2	1	1 1/2	2	3	4	5 (hr.)
					*	*		
FE_{Na} (%)	2.64	1.96	3.24	1.36	0.95	0.98	1.66	2.12
	±0.53	±0.53	±1.45	±3.00	±0.21	±0.29	±0.92	±0.84
					*	*	*	**
FE_K (%)	18.17	21.62	23.43	30.74	30.51	38.27	48.03	52.85
	±1.46	±3.67	±3.67	±7.80	±5.86	±6.76	±10.13	±9.41
FE_{Cl} (%)	2.18	2.57	2.23	1.91	1.30	1.35	2.32	2.34
	±0.48	±0.58	±0.43	±0.63	±0.37	±0.50	±1.44	±1.13
FE_{Ca}++	2.16	1.55	1.65	1.85	1.38	1.41	1.76	2.14
	±0.49	±0.42	±0.25	±0.38	±0.34	±0.56	±0.97	±0.85
FE_{Pi} (%)	16.01	16.98	19.57	18.14	17.24	26.17	59.86	61.14
	±3.26	±4.67	±10.56	±4.01	±3.25	±9.04	±33.65	±25.29
		**	**	**	**	**	**	*
U_{Na} V	78.62	10.88	3.77	4.91	6.71	10.74	16.09	23.80
(µEq/min)	±17.05	±2.73	±0.77	±1.27	±1.73	±3.87	±7.10	±10.81
		***	***	**	**			
U_K V	10.79	2.94	1.57	4.35	7.19	10.49	11.77	13.69
(µEq/min)	±0.99	±0.91	±0.45	±1.86	±2.32	±1.98	±1.87	±3.59
		**	**	**	**	**	*	*
U_{Cl} V	76.57	11.39	4.06	5.04	6.45	9.81	15.33	18.71
(µEq/min)	±17.88	±2.69	±0.81	±1.16	±1.78	±2.58	±6.41	±7.59
U_{Ca} V	2.19	0.31	0.13	0.23	0.33	0.35	0.48	0.52
(µEq/min)	±0.57	±0.08	±0.0	±0.15	±0.08	±0.07	±0.17	±0.19
		**	**	**	*			
U_{Pi} V	16.58	4.03	1.09	3.23	6.43	11.64	20.12	24.28
(µEq/min)	±3.06	±1.05	±0.27	±1.46	±2.61	±4.37	±7.68	±8.44
			**	*	*			
U_H V	13.31	7.09	2.30	4.55	5.68	7.21	11.44	15.00
(µEq/min)	±3.15	±4.19	±0.49	±1.21	±1.58	±2.55	±2.82	±5.07

P. value with respect to control, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Table 6 Effect of intrarenal arterial infusion of Russell's viper venom on tubuloglomerular activity in the left kidney of eight TPTX dogs. (Mean ± SE)

Variables	0	1/2	1	1 1/2	2	3	4	5 (hr.)
FE_{Na} (%)	0.51 ±0.11	0.44 ±0.07	0.74 ±0.36	0.39 ±0.09	0.53 ±0.09	0.76 ±0.21	1.39 ±0.54 *	1.57 ±0.71 *
FE_K (%)	14.54 ±1.61	14.56 ±1.36	21.65 ±6.89	22.37 ±7.52	20.41 ±3.45	21.98 ±3.78	23.18 ±2.73	24.31 ±3.34
FE_{Cl} (%)	0.58 ±0.15	0.56 ±0.13	0.55 ±0.11	0.35 ±0.09	0.49 ±0.10	0.74 ±0.21	1.39 ±0.52	1.66 ±0.57 *
FE_{Ca} (%)	0.49 ±0.17	0.45 ±0.12	0.68 ±0.35	0.71 ±0.23	0.55 ±0.17	0.58 ±0.17 *	0.83 ±0.27 *	1.05 ±0.26 **
FE_{Pi} (%)	0.99 ±0.32	1.16 ±0.44	1.18 ±0.35	2.92 ±1.30	5.07 ±1.83	10.12 ±2.97	14.47 ±3.65	16.43 ±3.02
U_{Na} V (μEq/min)	20.11 ±3.11	11.64 ±4.48	10.70 ±4.69 **	14.88 ±5.33 *	18.06 ±6.82	27.55 ±8.44	47.55 ±15.69	55.47 ±19.50
U_K V (μEq/min)	11.16 ±1.79	8.28 ±2.53	7.51 ±1.69	9.82 ±1.88	11.33 ±2.73	14.97 ±3.03	16.87 ±2.62	17.57 ±3.28
U_{Cl} V (μEq/min)	19.33 ±4.29	11.26 ±4.47	9.38 ±4.66	11.10 ±4.53	13.26 ±5.23	21.92 ±6.28	40.63 ±18.85	49.94 ±17.41
U_{Ca} V (μEq/min)	0.49 ±0.13	0.18 ±0.09	0.17 ±0.09	0.19 ±0.09	0.12 ±0.07	0.27 ±0.08 *	0.44 ±0.15 *	0.45 ±0.12 *
U_{Pi} V (μEq/min)	1.16 ±0.33	1.28 ±0.78	1.40 ±0.72	3.92 ±2.28	2.52 ±1.32	12.44 ±4.62	17.57 ±5.24	20.81 ±6.14 *
U_H V (μEq/min)	2.44 ±0.32	2.97 ±0.71	3.74 ±1.65	3.13 ±0.54	3.33 ±0.68	5.13 ±1.33	7.02 ±2.59	10.92 ±3.25

P. value with respect to control, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

sodium, chloride and calcium excretion did not significant change following envenomation. Significant fall in urinary potassium excretion was observed during 1 and 1 1/2 hours after venom infusion. Significant increases in urinary inorganic phosphorus and titratable acid excretion were recorded at 3,4,5 and 5 hours respectively ($p<0.05$).

Comparison the effect of Russell's viper venom on electrolytes excretion intact and TPTX group. Fractional excretion of sodium, potassium, chloride, calcium and inorganic phosphorus in TPTX animals were lower than intact animals throughout the study period (Fig 19,20, 21,22). In comparison the value in the control period between TPTX and intact group. The significant differences were recorded for fractional excretion of sodium ($p<0.01$), chloride ($p<0.05$), calcium ($p<0.01$) and inorganic phosphorus ($p<0.001$), whereas fractional excretion of potassium was not significant difference (Fig 20). It was found that urinary excretion of sodium and chloride in TPTX group were similarly depressed with significant difference from intact group during control period (Fig 24,26), however, it decreased simultaneously after venom infusion. The decrease was marked in intact group, while TPTX group showed a slightly decline in urinary excretion of sodium with tendency to increase higher than control value. There were no significant difference between groups following venom infusion. Urinary excretion of potassium was not different during control condition (Fig 25). After venom infusion, animals with TPTX exhibited less decrease than intact animals and reached a significant difference at 1 hour ($p<0.01$), then it simultaneously increased to the control level with no significant difference between groups. During control condition, urinary excretion of calcium in

TPTX group was significantly less than intact group ($p<0.05$) (Fig 27). The difference between the two groups were not observed throughout the post venom infusion period. Significant decrease in urinary excretion of inorganic phosphorus was noted in TPTX group ($p<0.001$) (Fig 28). The intact animals showed a sharp decrease in urinary excretion of inorganic phosphorus after venom infusion and then it progressively increased to the control level within 3 hours, whereas, it gradually increased throughout the post venom infusion periods in the TPTX group. The significant difference between groups were not observed following venom infusion. The urinary excretion of titratable acid in TPTX and intact groups were also significant different during control period ($p<0.01$) and did not alter after venom infusion (Fig 29).

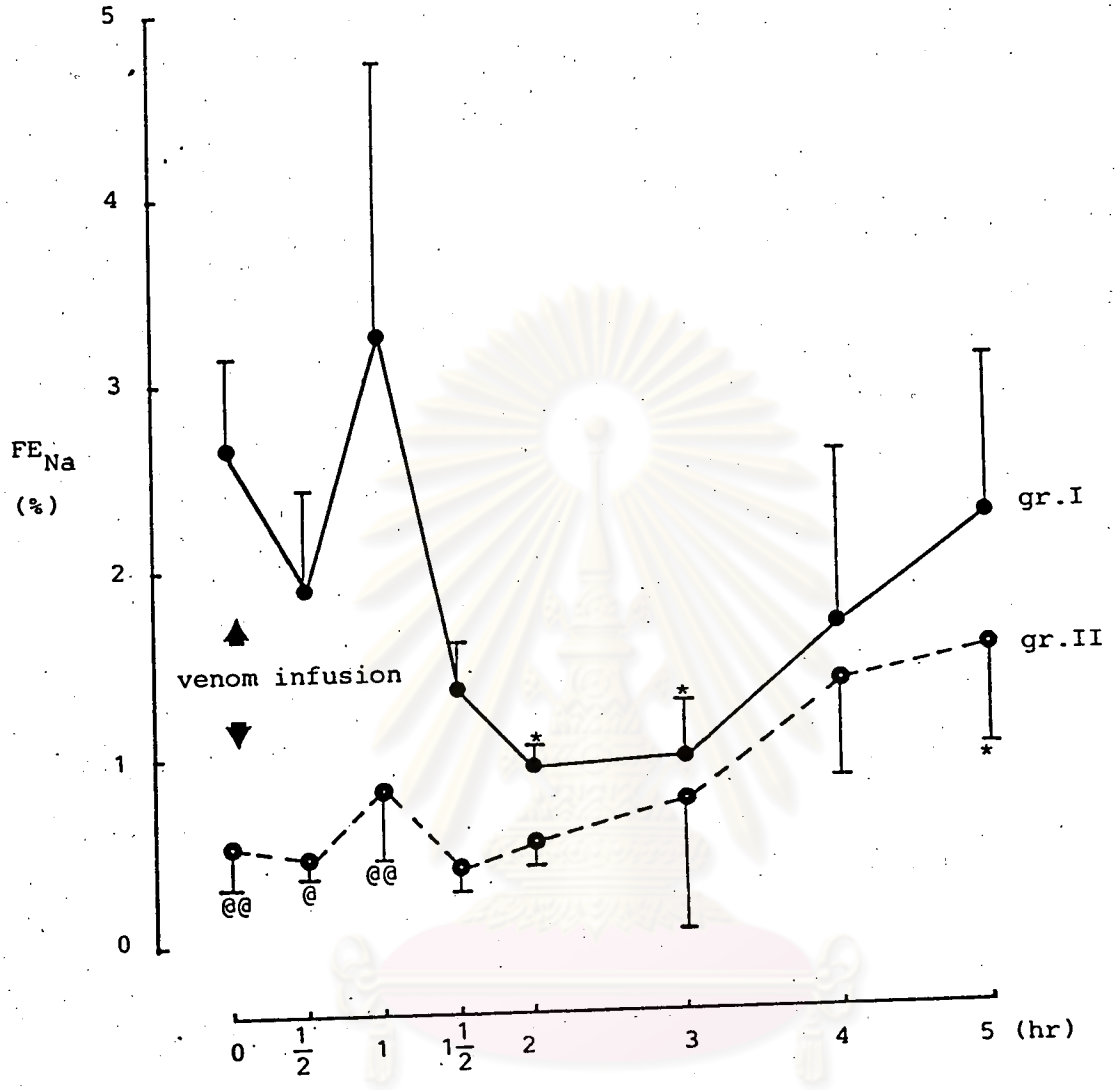

Figure 19 : Effect of intrarenal arterial infusion of Russell's viper venom on fractional excretion of sodium (FE_{Na}) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$, @@ $P < 0.01$.

P-value with respect to control condition of each group, * $P < 0.05$.

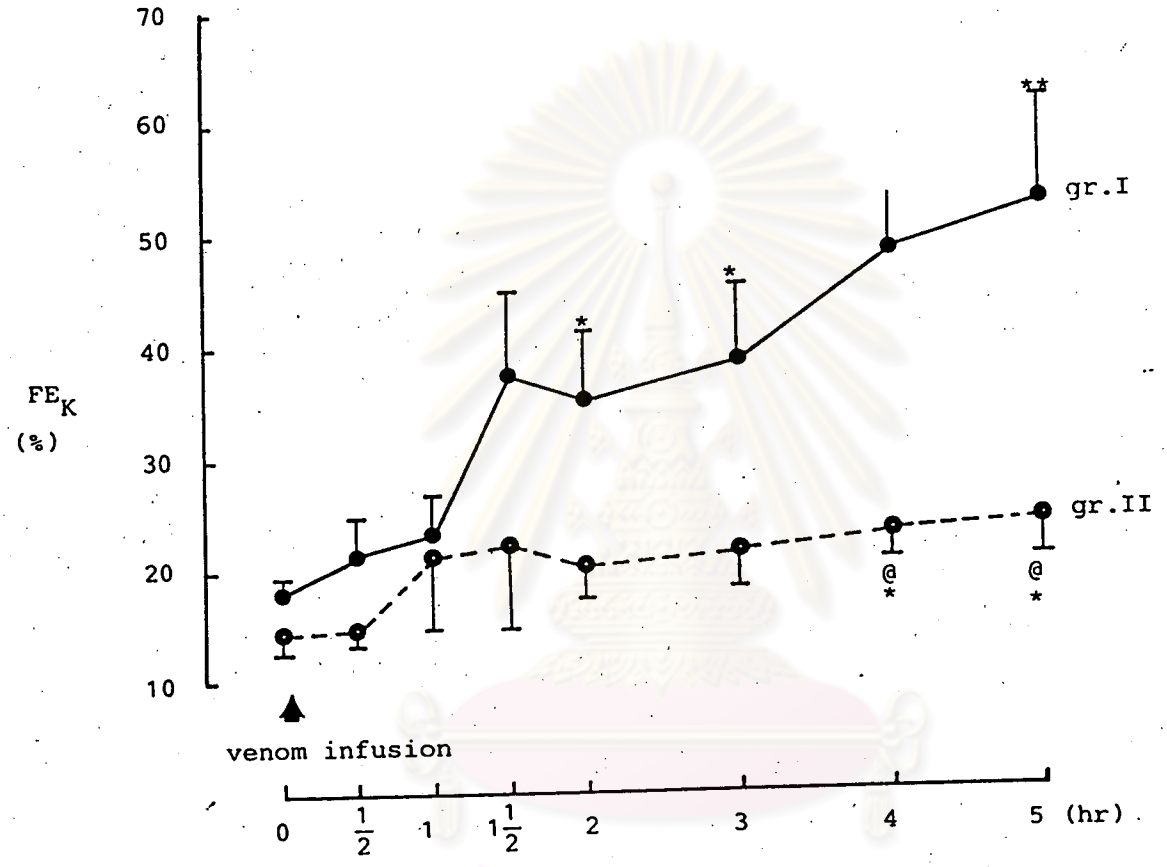

Figure 20 : Effect of intrarenal arterial infusion of Russell's viper venom on fractional excretion of potassium (FE_K) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ±SE. P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group,* $P < 0.05$,** $P < 0.01$.

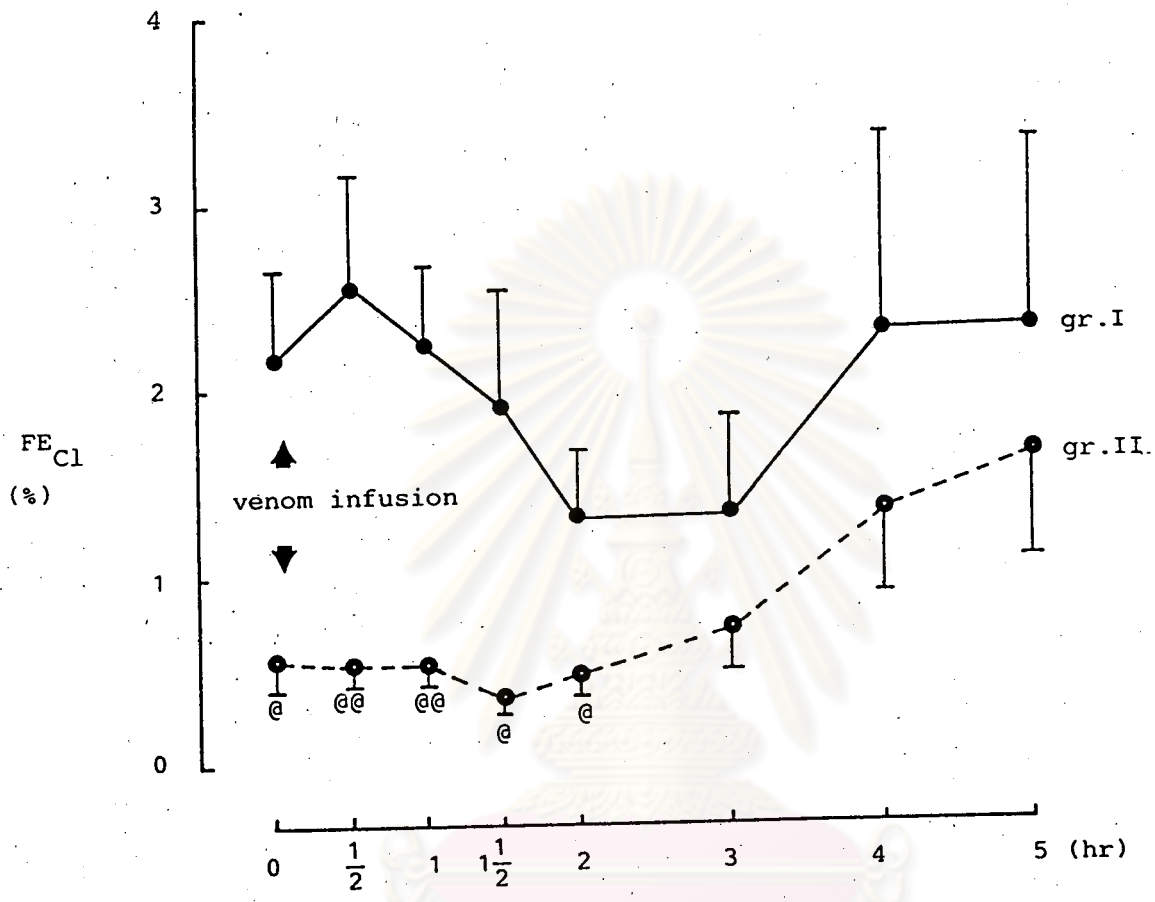

Figure 21 : Effect of intrarenal arterial infusion of Russell's viper venom on fractional excretion of chloride (FE_{Cl}) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE. P-value with respect to intact group at the same time interval, @ $P < 0.05$, @@ $P < 0.01$.

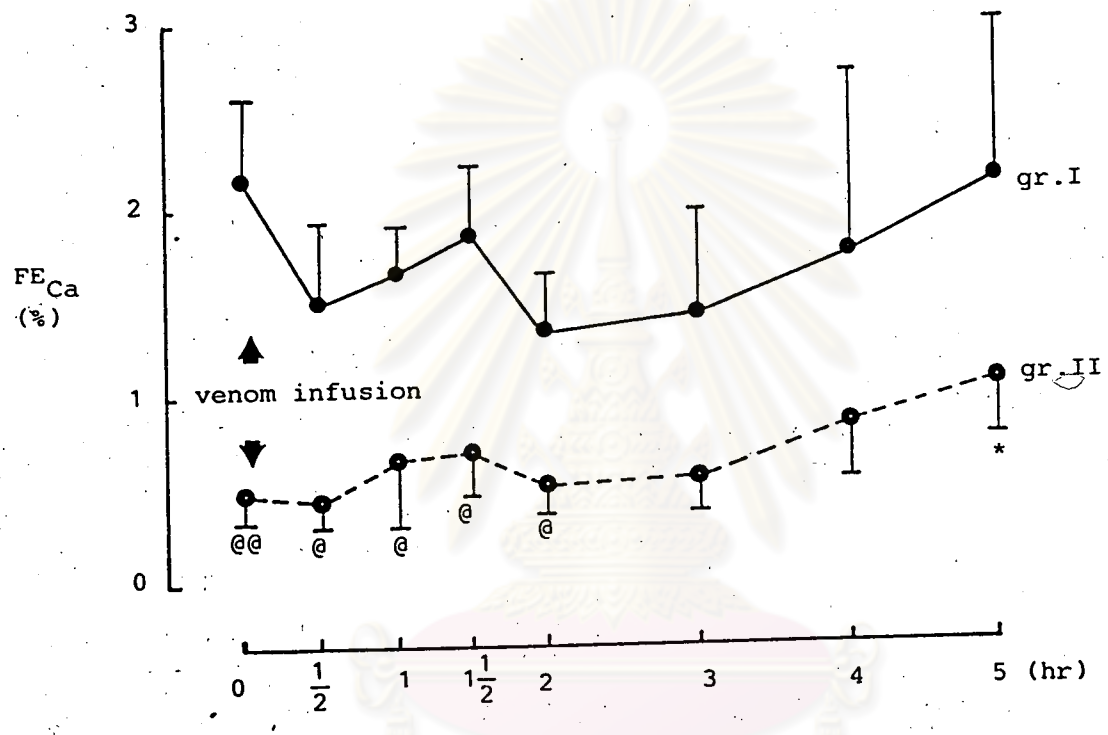

Figure 22 : Effect of intrarenal arterial infusion of Russell's viper venom on fractionnal excretion of calcium (FE_{Ca}) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$, @@ $P < 0.01$.

P-value with respect to control condition of each group, * $P < 0.05$.

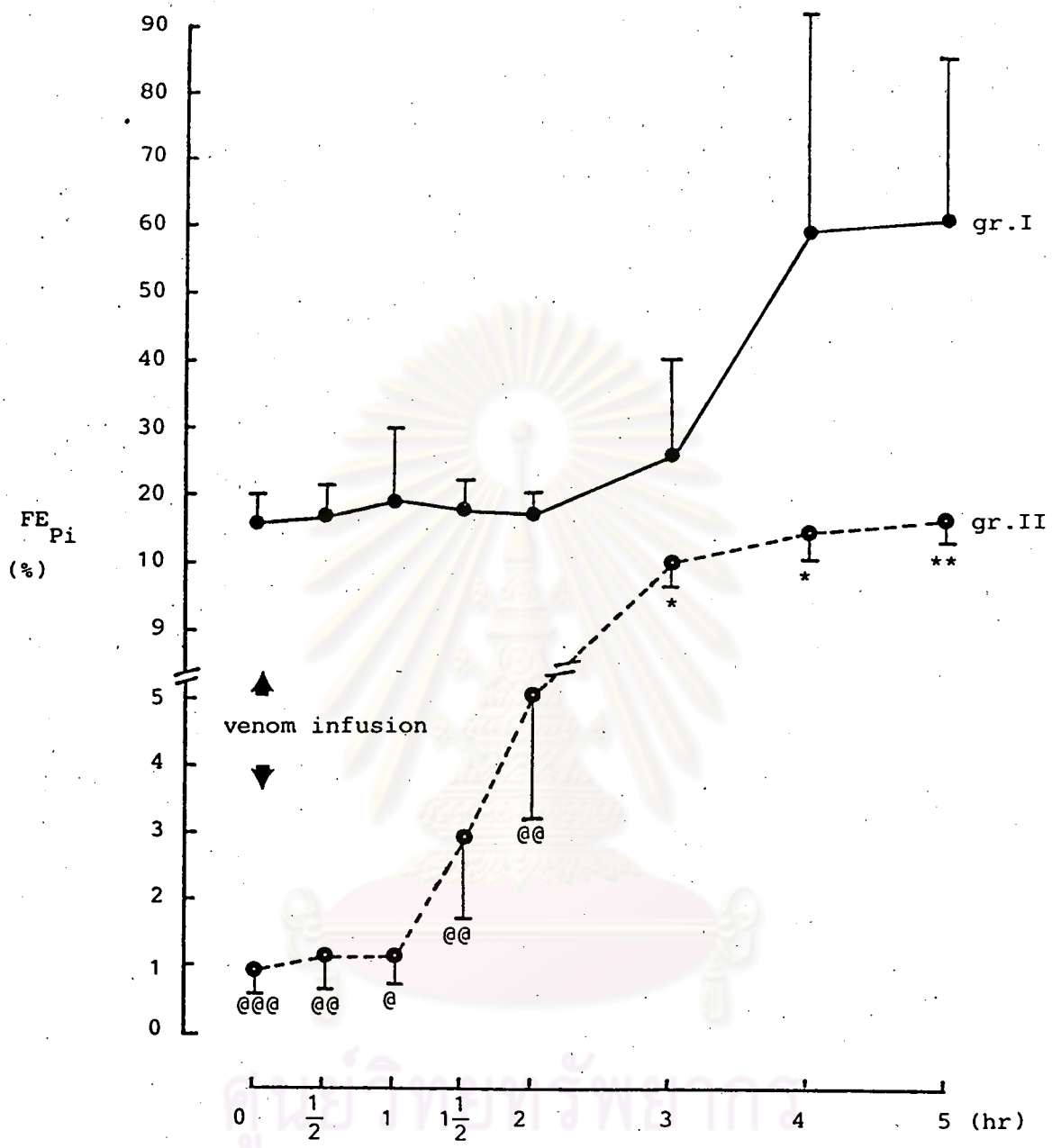

Figure 23 : Effect of intrarenal arterial infusion of Russell's viper venom on fractional excretion of inorganic phosphorus (FE_{Pi}) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE. P-value with respect to intact group at the same time interval,@@ $P < 0.01$,@@@ $P < 0.001$. P-value with respect to control condition of each group,* $P < 0.05$,** $P < 0.01$.

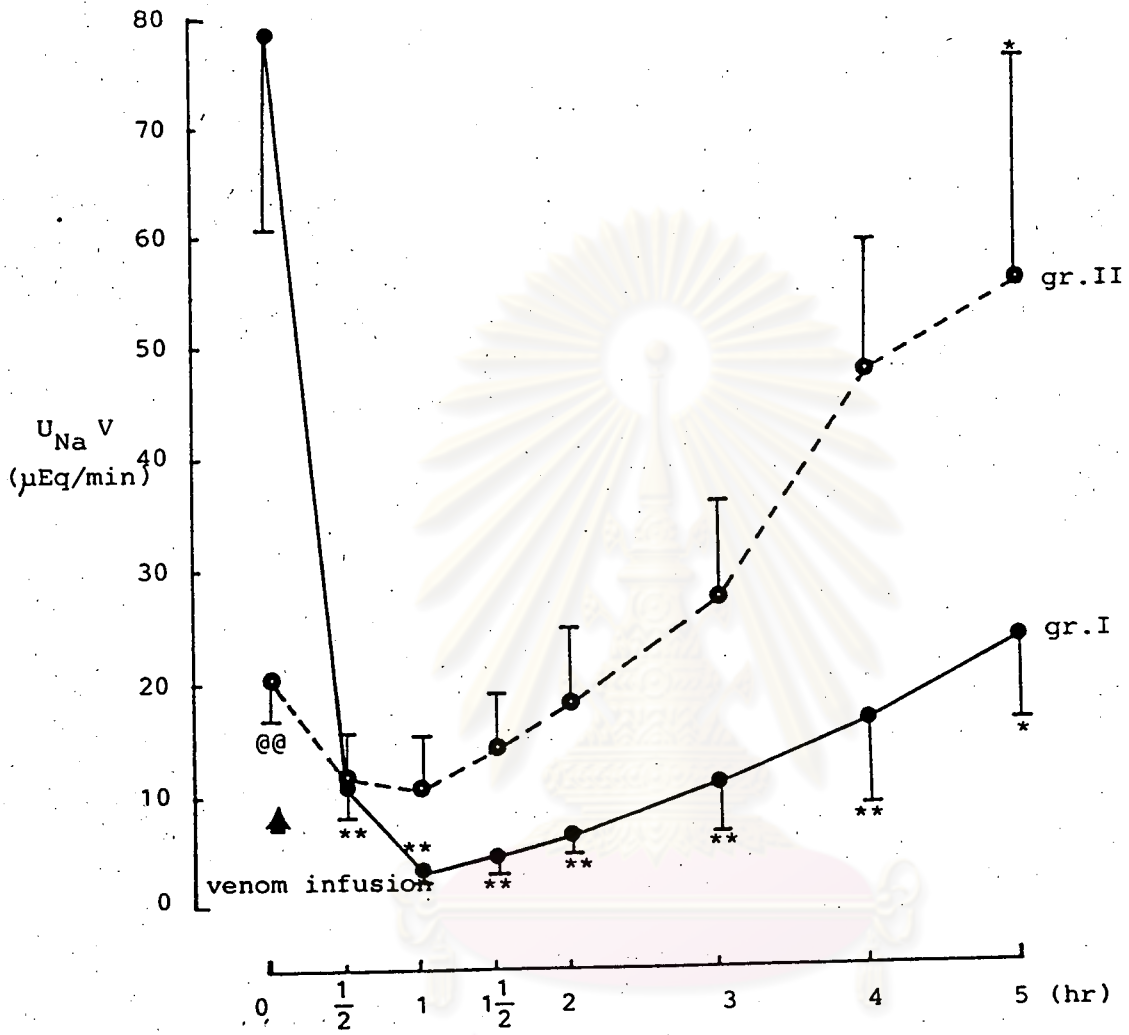

Figure 24 : Effect of intrarenal arterial infusion of Russell's viper venom on urinary excretion of sodium ($U_{Na}V$) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @@ $P < 0.05$.

P-value with respect to control condition of each group, * $P < 0.05$, ** $P < 0.01$.

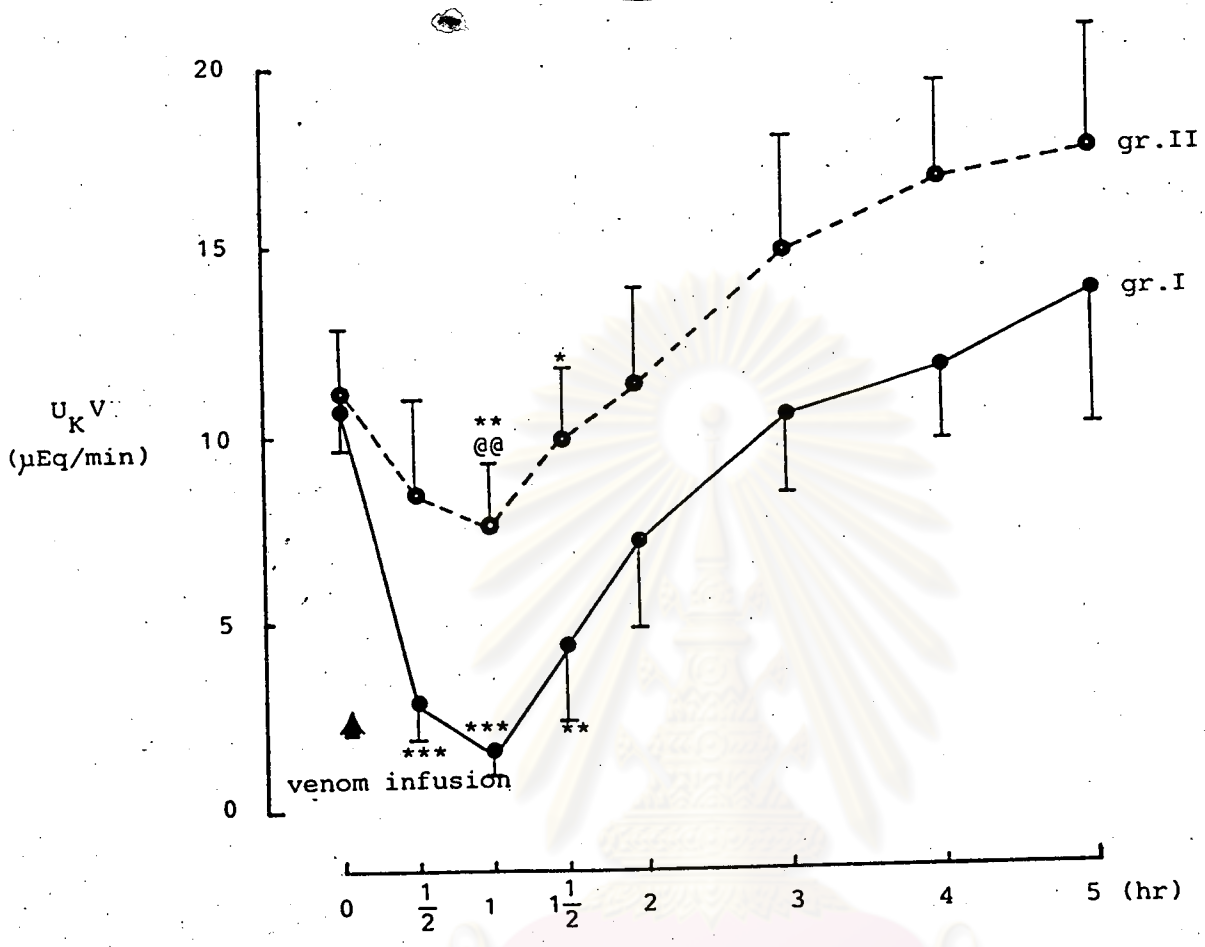

Figure 25 : Effect of intrarenal arterial infusion of Russell's viper venom on urinary excretion of potassium ($U_K V$) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @@ $P < 0.01$.

P-value with respect to control condition of each group, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

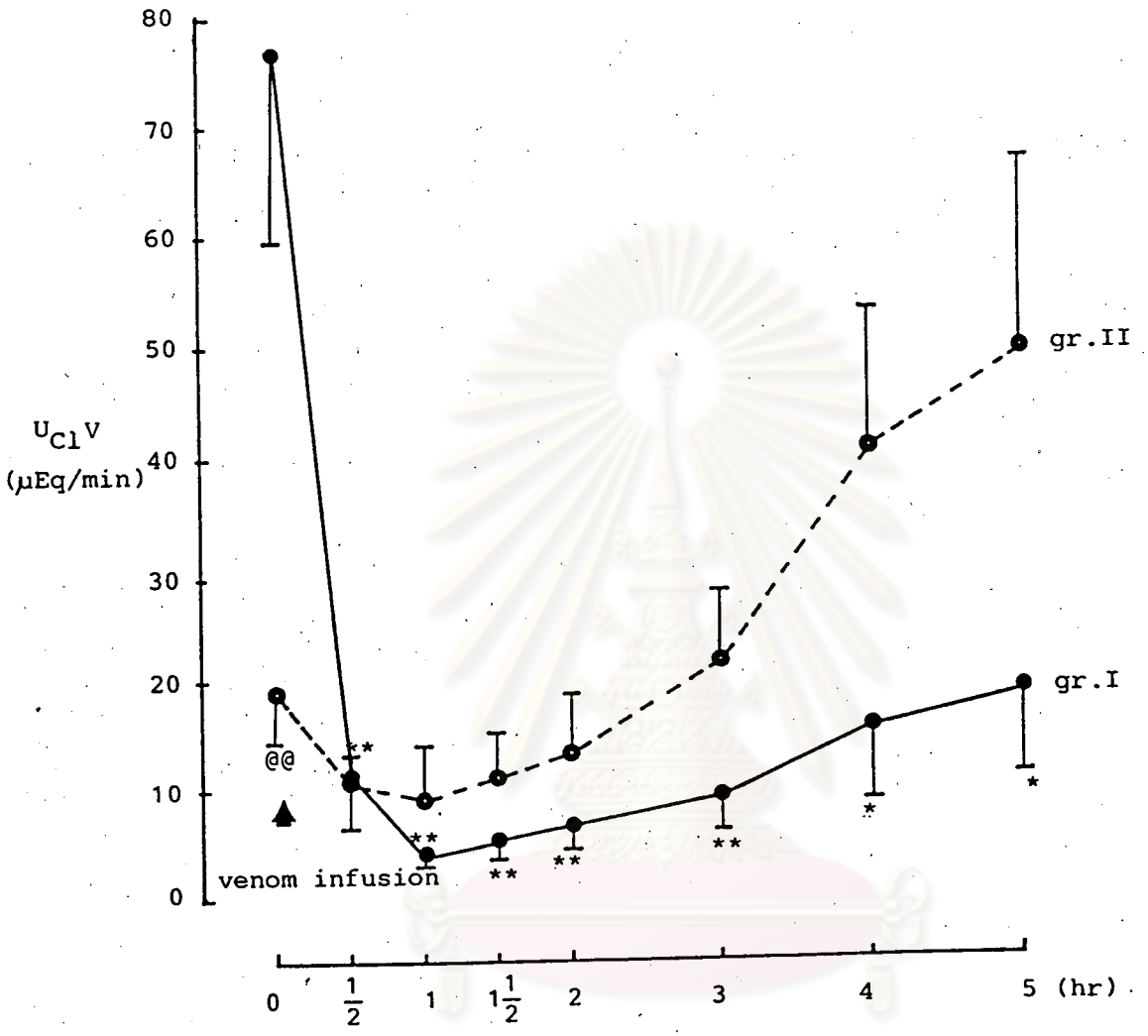

Figure 26 : Effect of intrarenal arterial infusion of Russell's viper venom on urinary excretion of chloride ($U_{Cl}V$) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE.

P-value with respect to intact group at the same time interval, @@ $P < 0.01$.

P-value with respect to control condition of each group,* $P < 0.05$,** $P < 0.01$.

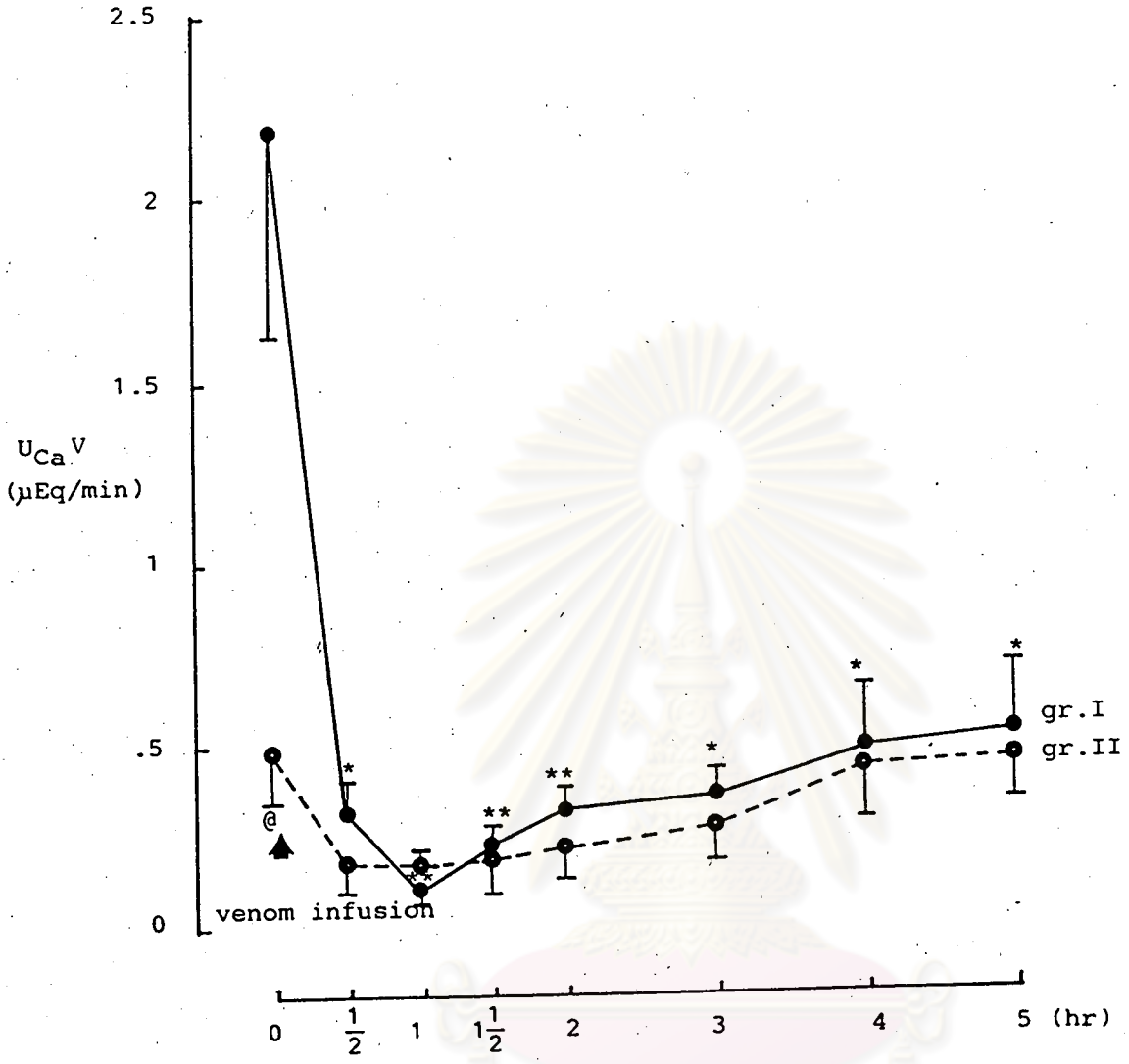

Figure 27 : Effect of intrarenal arterial infusion of Russell's viper venom on urinary excretion of calcium ($U_{Ca}{}^{V}$) in group I (intact) and group II (thyroparathyroidectomized). The values are mean ± SE.

P-value with respect to intact group at the same time interval, @ $P < 0.05$.

P-value with respect to control condition of each group, * $P < 0.05$, ** $P < 0.01$.

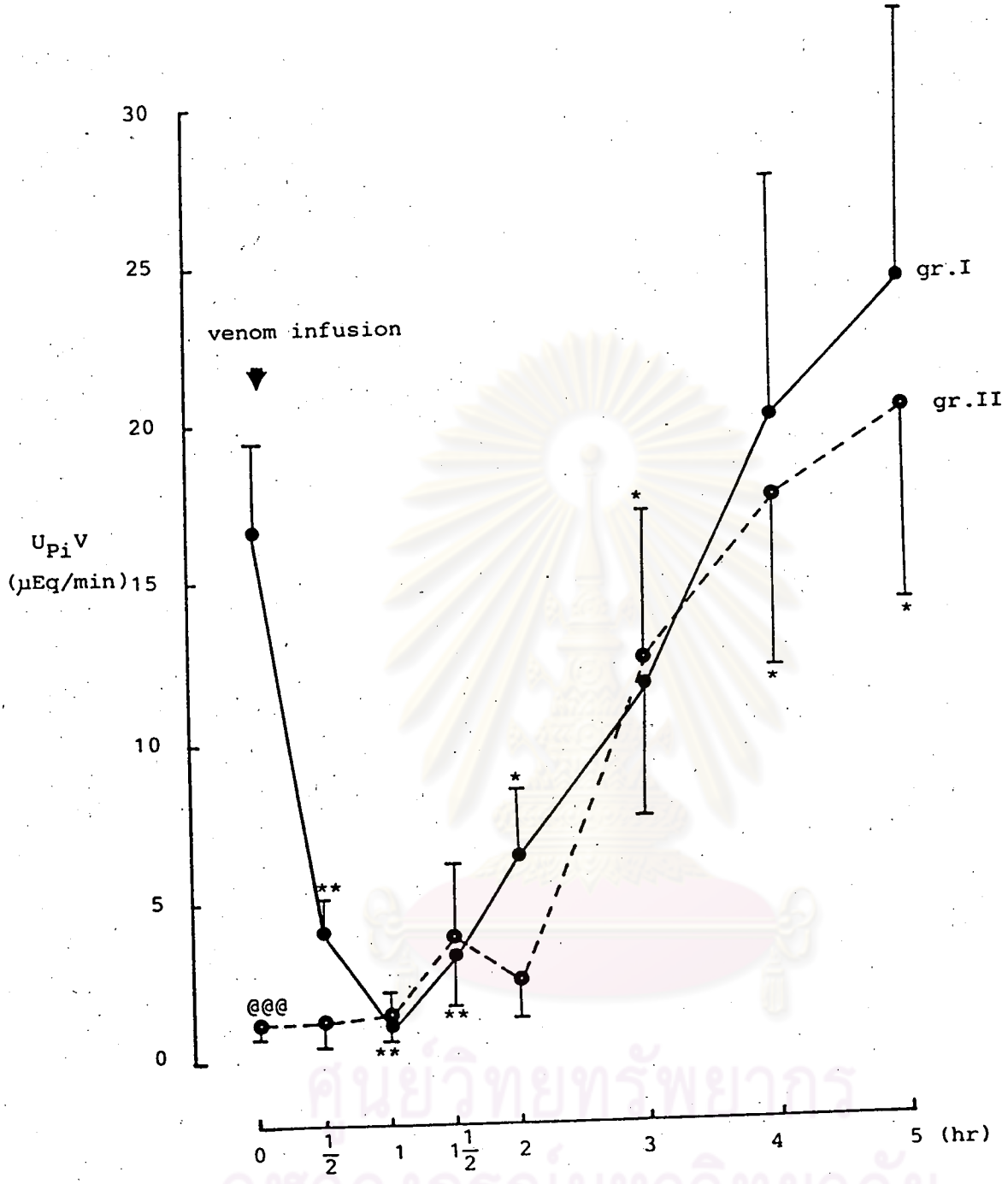

Figure 28 : Effect of intrarenal arterial infusion of Russell's viper venom on urinary excretion of inorganic phosphorus ($U_{Pi}V$) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE.

P-value with respect to intact group at the same time interval, @@@ $P < 0.001$.

P-value with respect to control condition of each group,* $P < 0.05$,** $P < 0.01$.

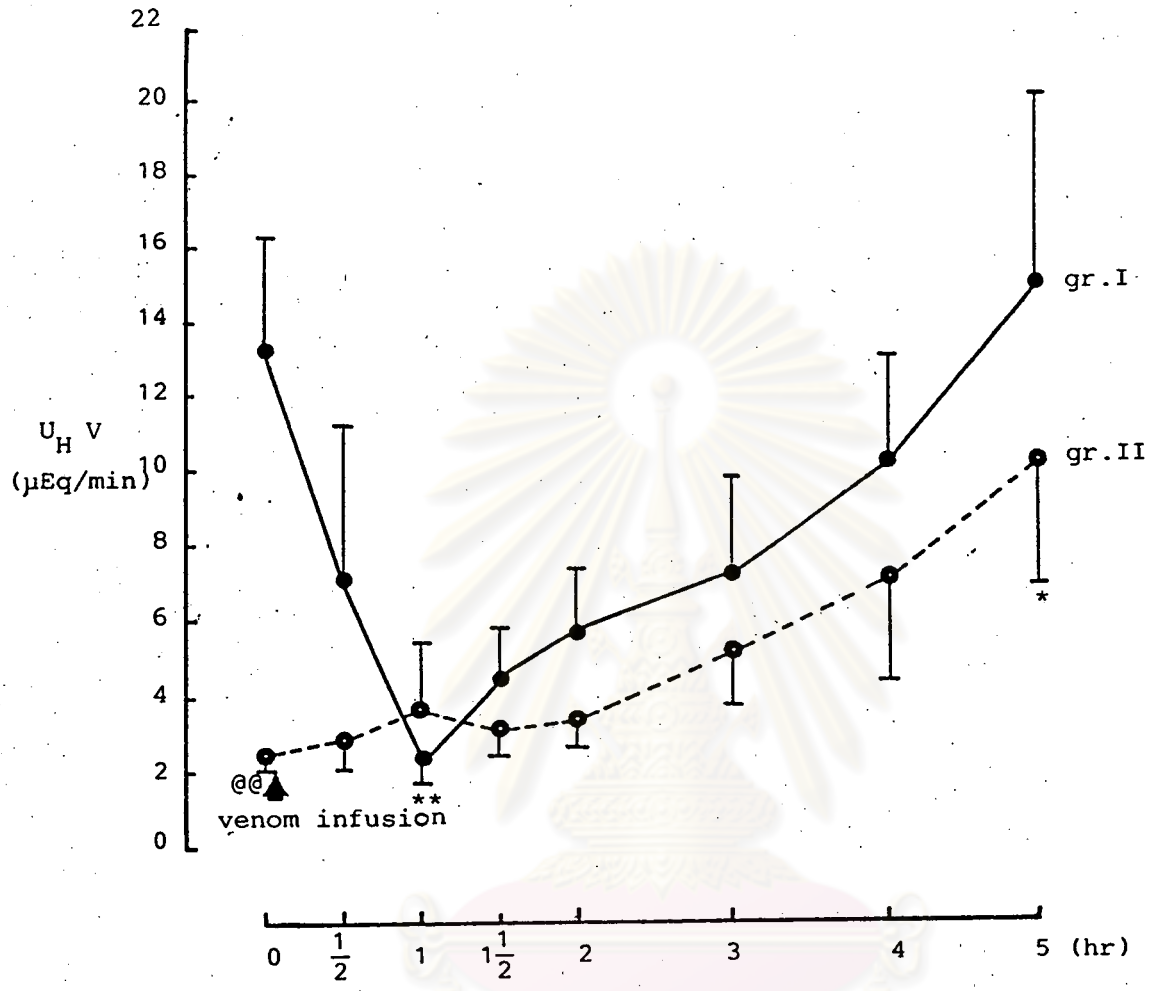

Figure 29 : Effect of intrarenal arterial infusion of Russell's viper venom on urinary excretion of titratable acid (U_H V) in group I (intact) and group II (thyroparathyroidectomized).The values are mean ± SE.

P-value with respect to intact group at the same time interval, @@ $P < 0.01$.

P-value with respect to control condition of each group,* $P < 0.05$, ** $P < 0.01$.