

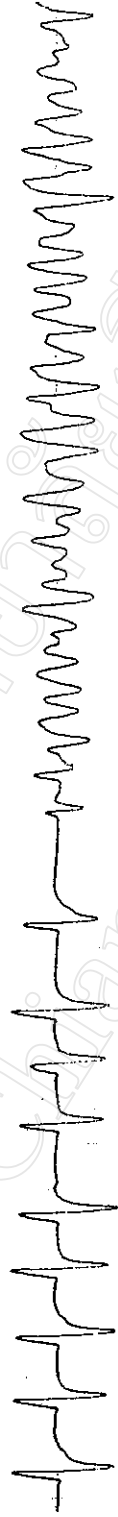
## RESULTS

### Incidence of Hypothermia-Induced Ventricular Fibrillation (VF)

An example of EKG recording showing VF that spontaneously occurred during a hypothermia procedure, is shown in Figure 1. Prior to VF occurrence, there was usually seen a ventricular bradycardia before the irregular waves of VF. These observations were seen commonly in all groups of the animals regardless of their treatments. The incidence of VF in the Control group (n=12/30) of 40 % was reduced to 10 % in Lidocaine-treated group (n = 3/30) and to 6.6 % in Bretylium-treated group (n = 3/45) as shown in Table 1 and Figure 2. The incidence of VF in both Lidocaine-treated and Bretylium-treated groups was significantly less than that of the Control group ( $p < 0.05$ ). However, between Lidocaine-treated and Bretylium-treated groups, there was no significant difference ( $p > 0.05$ ).

### Duration of Hypothermia-Induced Ventricular Fibrillation

The mean durations of VF in each group of the animals are presented in Table 2 and Figure 3. In the Control group, the VF duration was  $58.75 \pm 2.23$  sec (n = 12). In the Lidocaine-treated and Bretylium-treated groups, the VF durations were  $54.67 \pm 4.63$  (n = 3) and  $54.00 \pm 4.75$  (n = 3) sec, respectively. Regarding the VF durations, there were no significant differences between both of the chemical-treated groups and the Control group ( $p > 0.05$ ).



(0.1 mV / 10 mm , 25 mm / sec)

Figure 1. An example of EKG standard limb lead II of hypothermia-induced ventricular fibrillation (VF) in normal rat.

Table 1. Percentage of incidence of hypothermia-induced ventricular fibrillation (VF) in Control, Lidocaine-treated and Bretylium-treated groups.

Group	n	Incidence of VF	
		n	%
Control	30	12	40
Lidocaine	30	3	10*
Bretylium	45	3	6.6*

\*  $p < 0.05$  between Control and Lidocaine-treated groups and between Control and Bretylium-treated groups

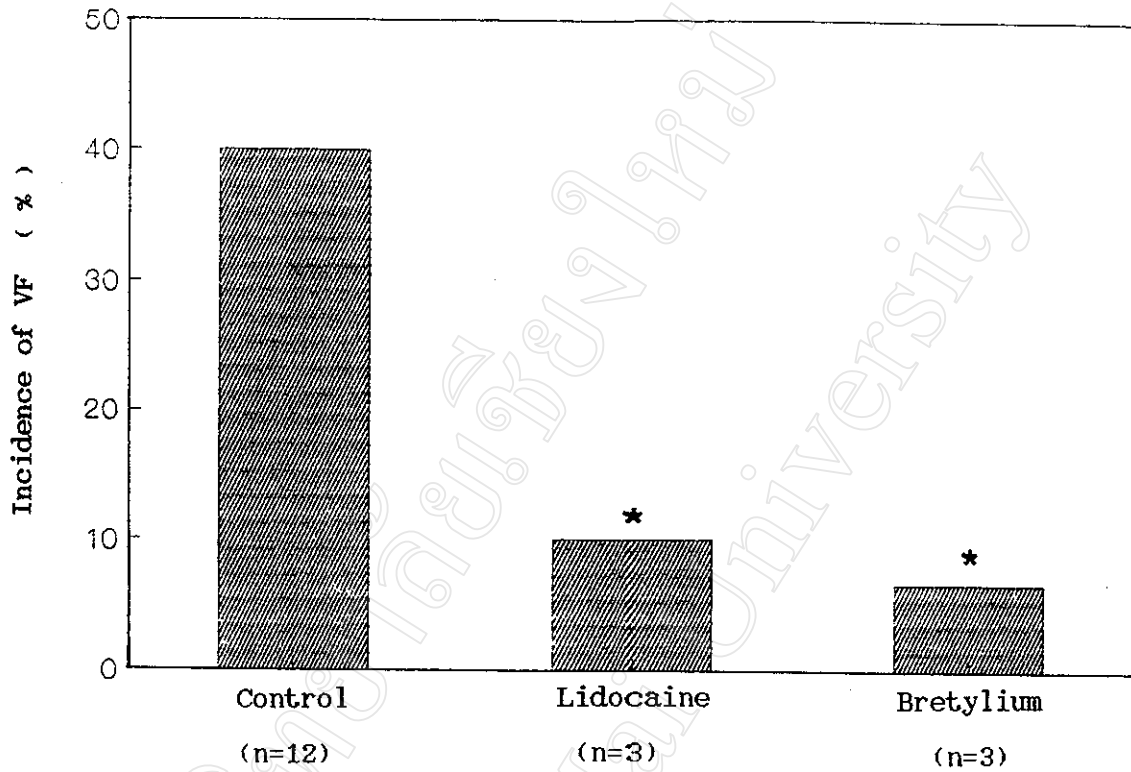


Figure 2. Comparison of the percentage of the incidence of hypothermia-induced ventricular fibrillation among control and both of the chemical-treated rats.

\*  $p < 0.05$  between Control and Lidocaine-treated groups and between Control and Bretylium-treated groups

Table 2. The mean durations of hypothermia-induced ventricular fibrillation (VF) in Control, Lidocaine-treated and Bretylium-treated groups.

Group	n	VF durations (sec.)
Control	12	58.75 $\pm$ 2.23
Lidocaine	3	54.67 $\pm$ 4.63 (NS)
Bretylium	3	54.00 $\pm$ 4.75 (NS)

means  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups

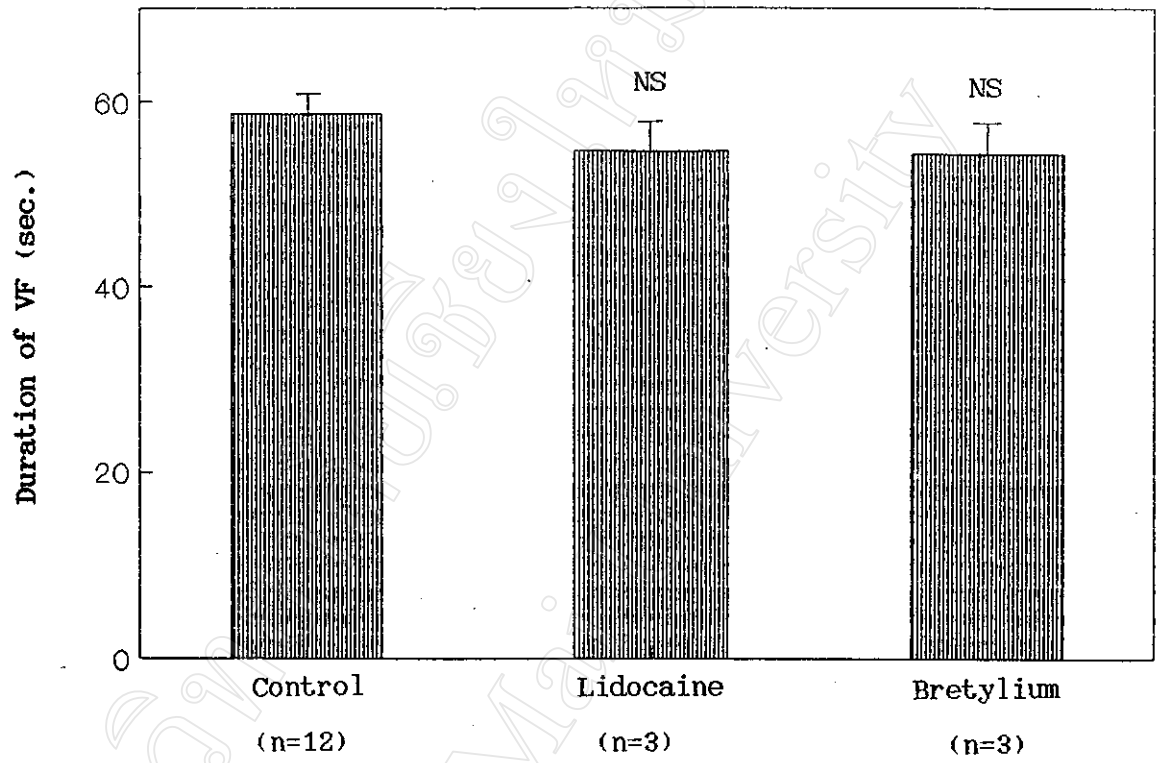


Figure 3. Comparison of the mean ventricular fibrillation durations among control and both of the chemical-treated rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups

### The Body Temperature of Hypothermia-Induced Ventricular Fibrillation

When the body temperature of the animals declined, some of them developed VF spontaneously. In Table 3, the body temperature of VF rats in Control, Lidocaine-treated and Bretylium-treated groups were  $18.1 \pm 0.6$  (n = 12),  $18.7 \pm 0.7$  (n = 3) and  $19.3 \pm 0.6$  (n = 3) °C, respectively. The comparison of the mean body temperatures of the VF animals among three groups are graphically presented in Figure 4. There were no significant differences among all the experimental groups ( $p > 0.05$ ).

### Effects of Hypothermia on Serum Potassium Concentrations in Non-Ventricular Fibrillating (Non-VF) Animals

There were changes in serum potassium concentrations during induction of hypothermia. The mean serum potassium concentrations obtained from animals that had not developed VF of three groups are presented in Table 4. In the Control group, as shown in Figure 5, serum potassium concentrations were progressively decreased from  $3.01 \pm 0.21$  mmol/l at normothermia to  $2.45 \pm 0.18$  mmol/l at 25°C and to  $2.20 \pm 0.17$  mmol/l at 10°C (n = 18). There were significant differences between serum potassium levels at normothermia and 25°C and between the levels at normothermia and 10°C, and also between 25°C and 10°C ( $p < 0.05$ ). In the Lidocaine-treated group, serum potassium concentrations at three hypothermic levels are shown in Figure 6; there were  $2.98 \pm 0.24$ ,  $2.49 \pm 0.26$  and  $2.21 \pm 0.19$  mmol/l at normothermia, at 25°C and at 10°C, respectively (n = 27). Also, significant differences were

Table 3. The mean body temperatures of hypothermia-induced ventricular fibrillation (VF) in Control, Lidocaine-treated and Bretylium-treated groups.

Group	n	Body temperature of VF rats ( $^{\circ}$ C)
Control	12	18.1 $\pm$ 0.6
Lidocaine	3	18.7 $\pm$ 0.7 (NS)
Bretylium	3	19.3 $\pm$ 0.6 (NS)

means  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups



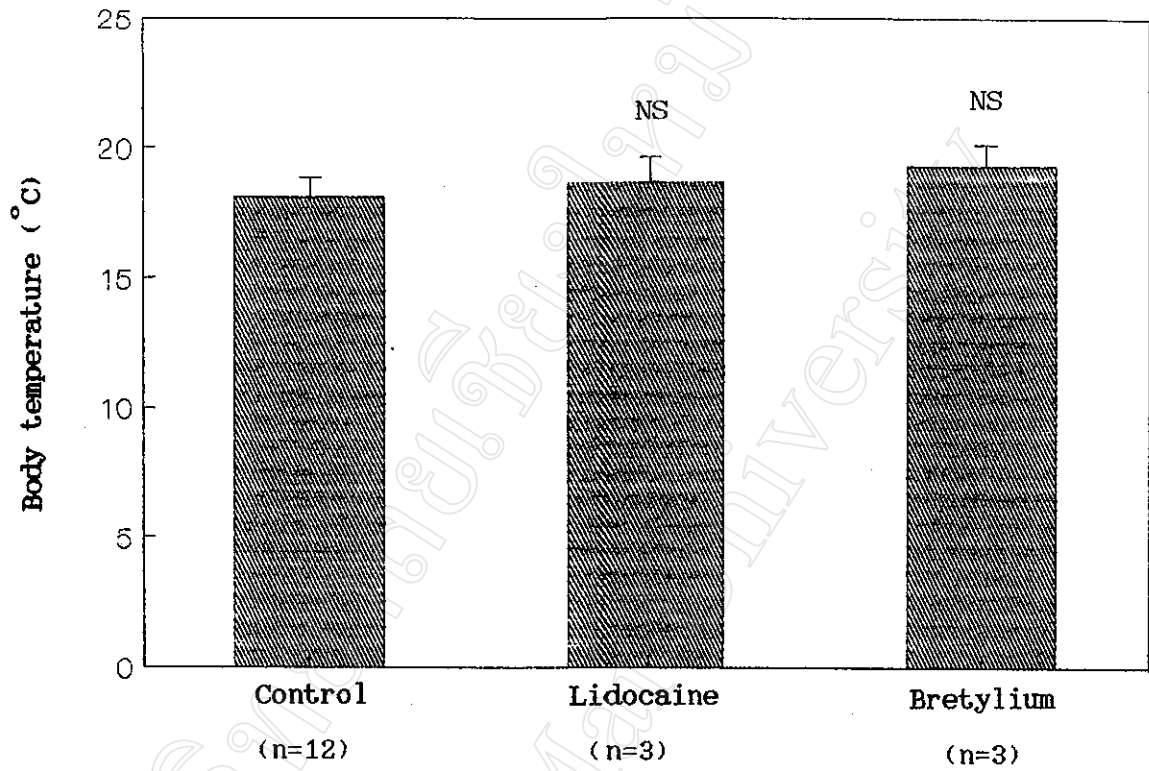


Figure 4. Comparison of the mean body temperature of ventricular fibrillating rats among control and both of the chemical-treated rats.

mean  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups

Table 4. The mean serum potassium concentrations at three levels of body temperature in three groups of non-ventricular fibrillating animals.

Group	n	Serum potassium concentrations (mmol/l)		
		Normothermia	25°C	10°C
Control	18	3.01 ± 0.21	2.45 ± 0.18*	2.20 ± 0.17**+
Lidocaine	27	2.98 ± 0.24	2.49 ± 0.26*	2.21 ± 0.19**+
Bretylum	42	3.05 ± 0.25	2.50 ± 0.31*	2.25 ± 0.22**+

means ± SE.

\* p < 0.05 between Normothermia and 25°C or between Normothermia and 10°C

+ p < 0.05 between 25°C and 10°C

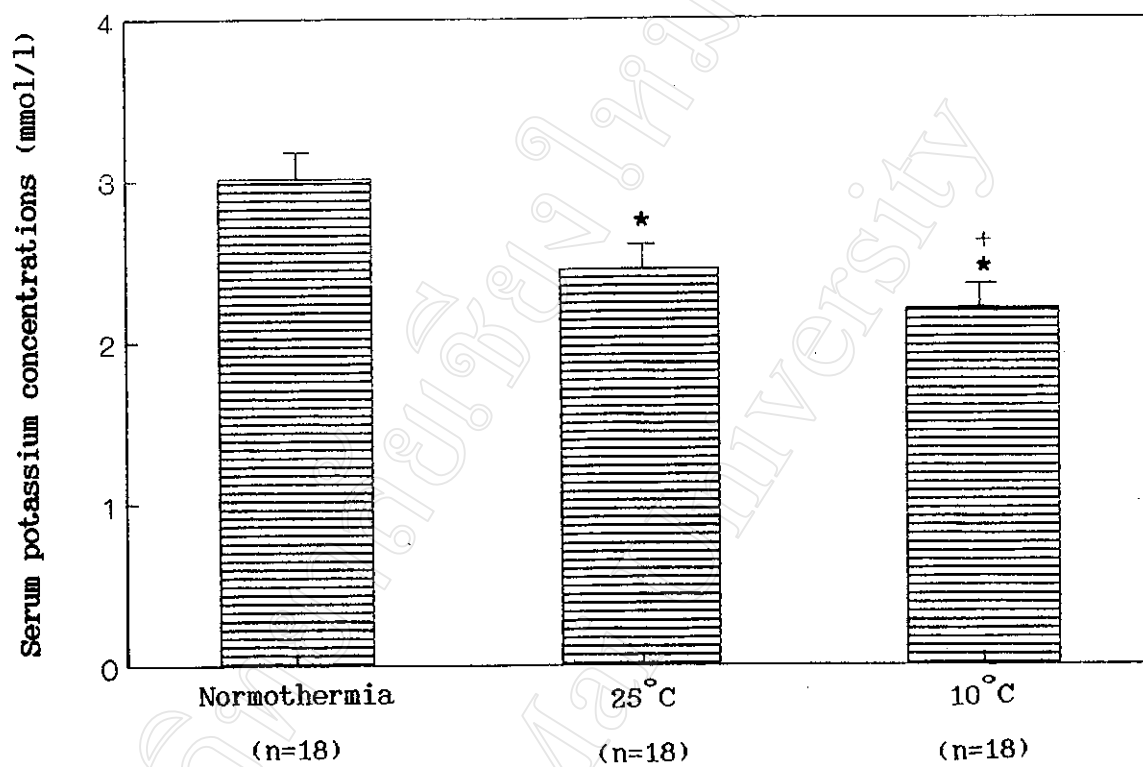


Figure 5. Serum potassium concentrations at three levels of body temperature in non-ventricular fibrillating control rats.

means  $\pm$  SE.

\*  $p < 0.05$  between Normothermia and 25°C or between Normothermia and 10°C

+  $p < 0.05$  between 25°C and 10°C

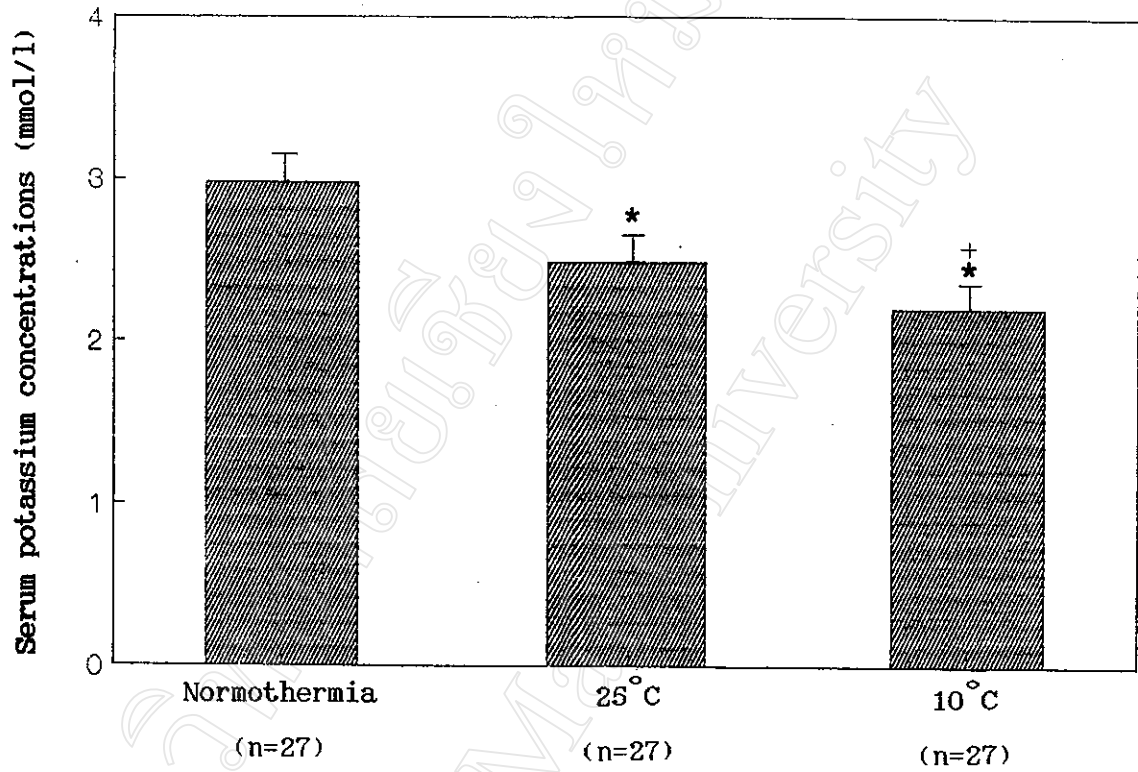


Figure 6. Serum potassium concentrations at three levels of body temperature in non-ventricular fibrillating Lidocaine-treated rats.

means  $\pm$  SE.

\*  $p < 0.05$  between Normothermia and 25°C or between Normothermia and 10°C

+  $p < 0.05$  between 25°C and 10°C

obtained between each of the hypothermic levels as in the Control group ( $p < 0.05$ ). In the animals that received Bretylium before starting the hypothermia procedure ( $n = 42$ ), as seen in Figure 7, serum potassium concentrations were significantly reduced from  $3.05 \pm 0.25$  mmol/l at normothermia to  $2.50 \pm 0.31$  mmol/l at  $25^{\circ}\text{C}$  and to  $2.25 \pm 0.22$  mmol/l at  $10^{\circ}\text{C}$ , respectively ( $p < 0.05$ ). The comparisons of the mean serum potassium concentrations among three experimental groups at normothermia, at  $25^{\circ}\text{C}$  and  $10^{\circ}\text{C}$  are presented in Figure 8, Figure 9 and Figure 10, respectively. There were no significant differences in serum potassium concentrations between and among all groups of animals when compared at the same hypothermic levels ( $p > 0.05$ ). However, it was conclusively found that there was a relationship between body temperature and serum potassium concentrations, implying that hypothermia induced hypokalemia in all groups of animals.

#### **Effects of Hypothermia on Serum Potassium Concentrations in Ventricular Fibrillating (VF) Animals**

The mean serum potassium concentrations in hypothermia-induced VF animals are presented in Table 5. In the Control group ( $n = 12$ ), serum potassium level was significantly decreased from  $3.05 \pm 0.15$  mmol/l at normothermia to  $2.45 \pm 0.16$  mmol/l at  $25^{\circ}\text{C}$  and to  $2.40 \pm 0.16$  mmol/l at the VF-onset ( $p < 0.05$ ). However, there was no significant difference in serum potassium concentrations between the levels at  $25^{\circ}\text{C}$  and those at the VF-onset ( $p > 0.05$ ) (Figure 11). In the Lidocaine-treated group, as shown in Figure 12, serum potassium concentration at normothermia was  $2.93 \pm 0.25$  mmol/l and significantly decreased to  $2.43 \pm 0.20$  mmol/l

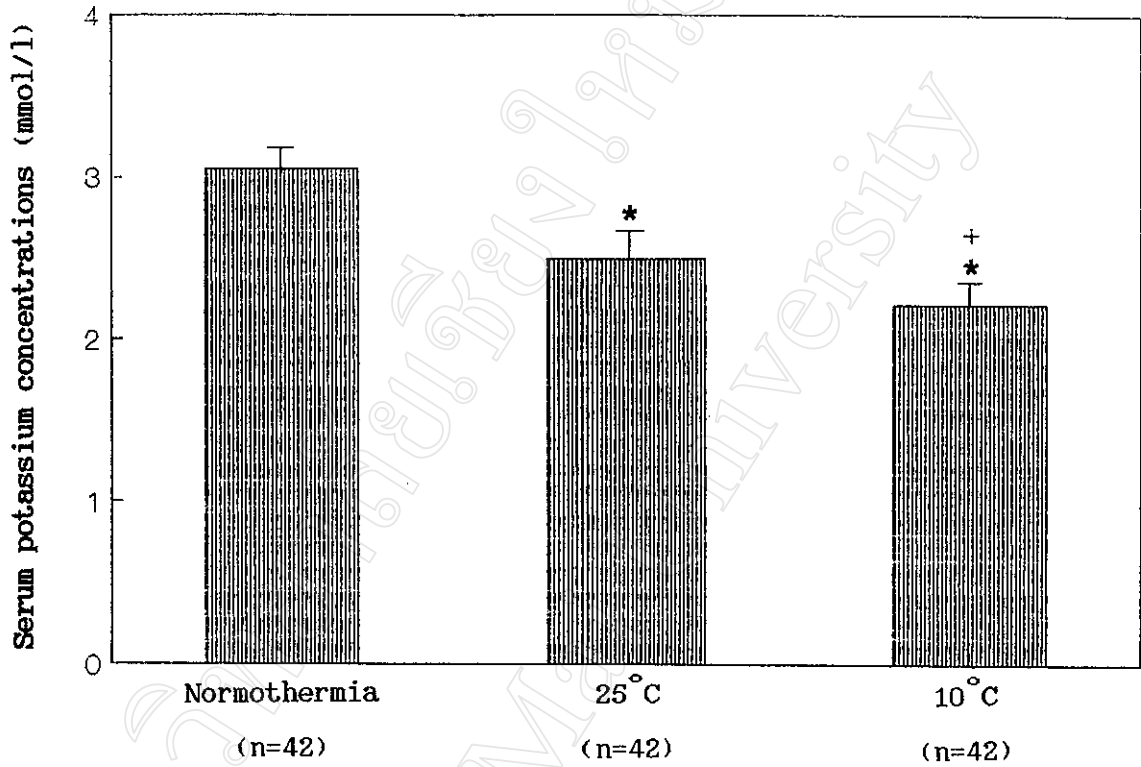


Figure 7. Serum potassium concentrations at three levels of body temperature in non-ventricular fibrillating Bretylium-treated rats.

means  $\pm$  SE.

\*  $p < 0.05$  between Normothermia and 25°C or between Normothermia and 10°C

+  $p < 0.05$  between 25°C and 10°C

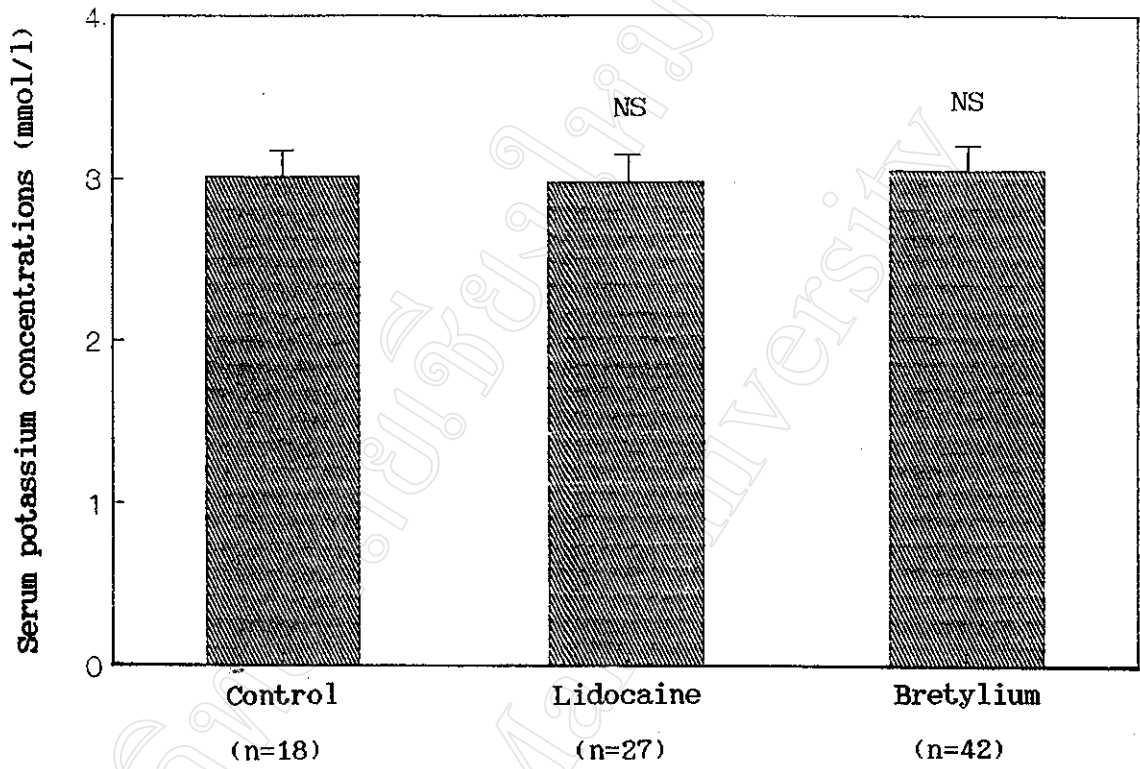


Figure 8. Serum potassium concentrations at Normothermia in non-ventricular fibrillating rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups

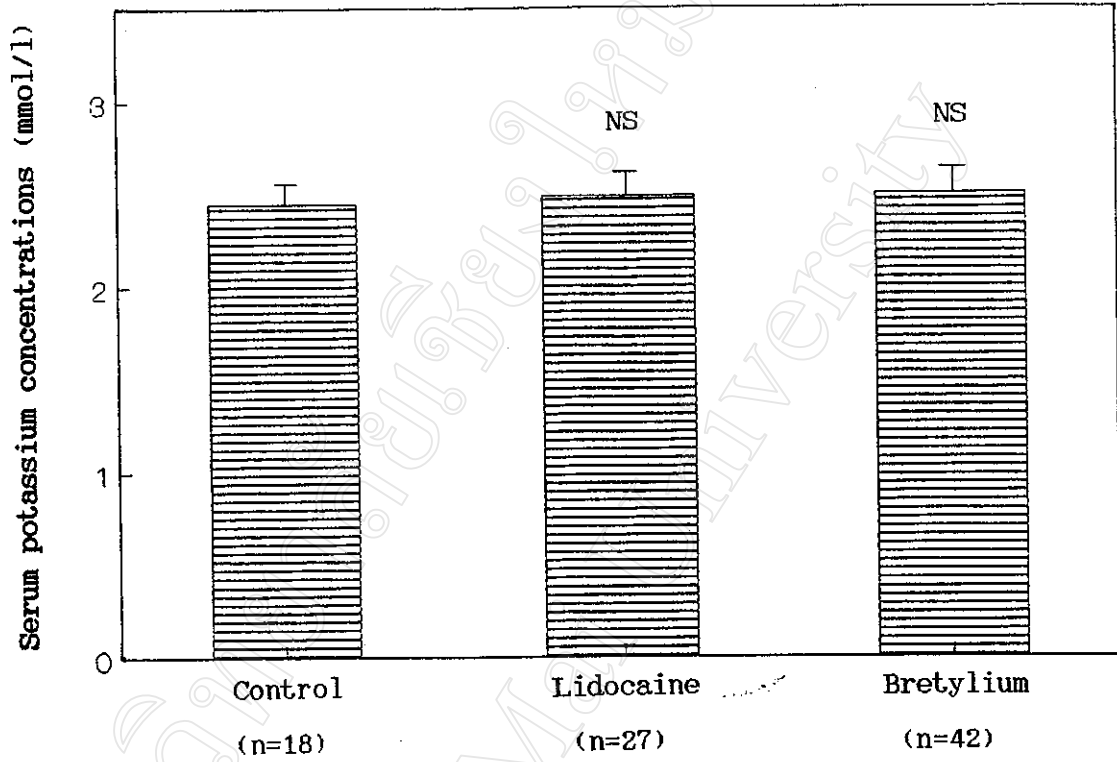


Figure 9. Serum potassium concentrations at 25°C in non-ventricular fibrillating rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups



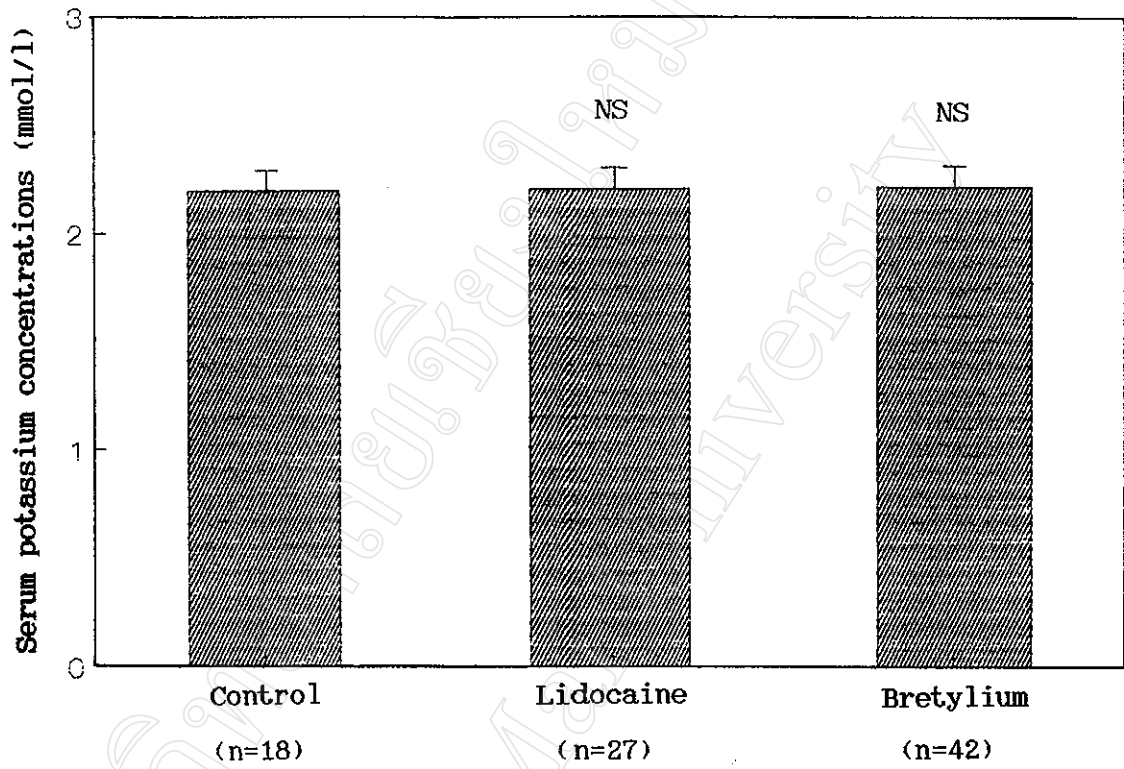


Figure 10. Serum potassium concentrations at 10°C in non-ventricular fibrillating rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups

Table 5. The mean serum potassium concentrations at three levels of body temperature in three groups of ventricular fibrillating animals.

Group	n	Serum potassium concentrations (mmol/l)		
		Normothermia	25°C	VF-onset
Control	12	3.05 ± 0.15	2.45 ± 0.16*	2.40 ± 0.16*
Lidocaine	3	2.93 ± 0.25	2.43 ± 0.20*	2.33 ± 0.20*
Bretylium	3	3.07 ± 0.23	2.51 ± 0.21*	2.37 ± 0.17*

means ± SE.

\* p < 0.05 between Normothermia and 25°C or between Normothermia and VF-onset

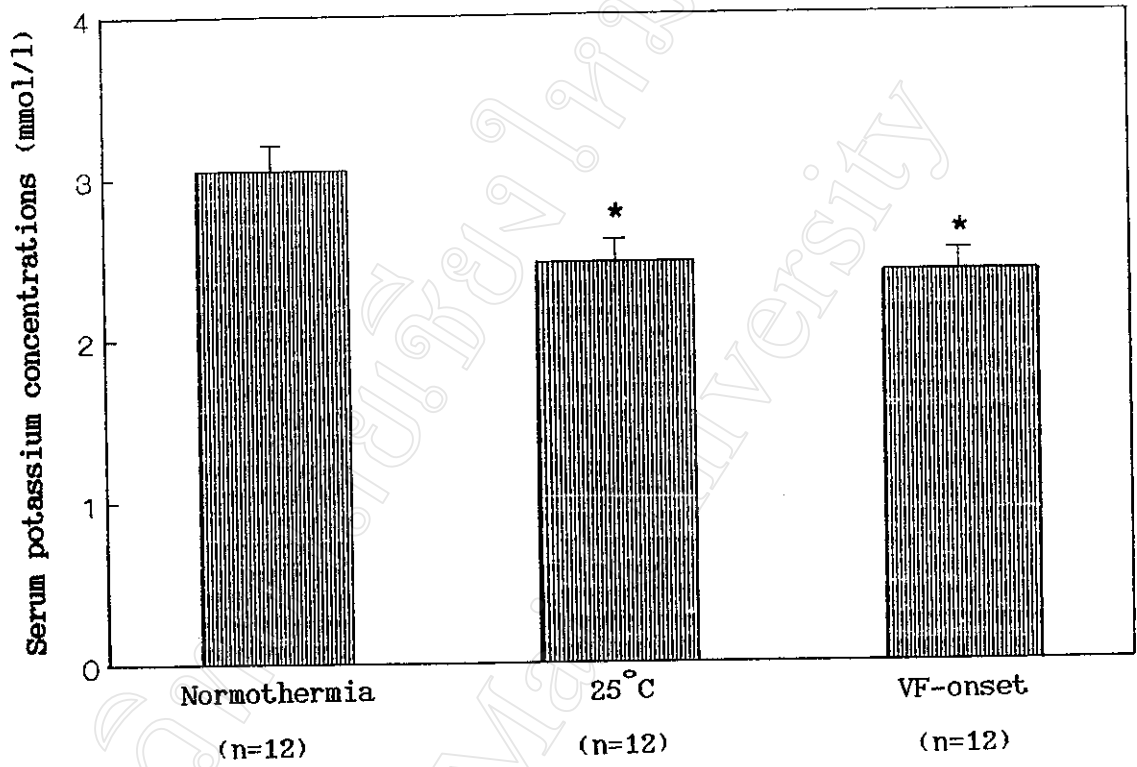


Figure 11. Serum potassium concentrations at three levels of body temperature in ventricular fibrillating control rats.

means  $\pm$  SE.

\*  $p < 0.05$  between Normothermia and 25°C or between Normothermia and VF-onset

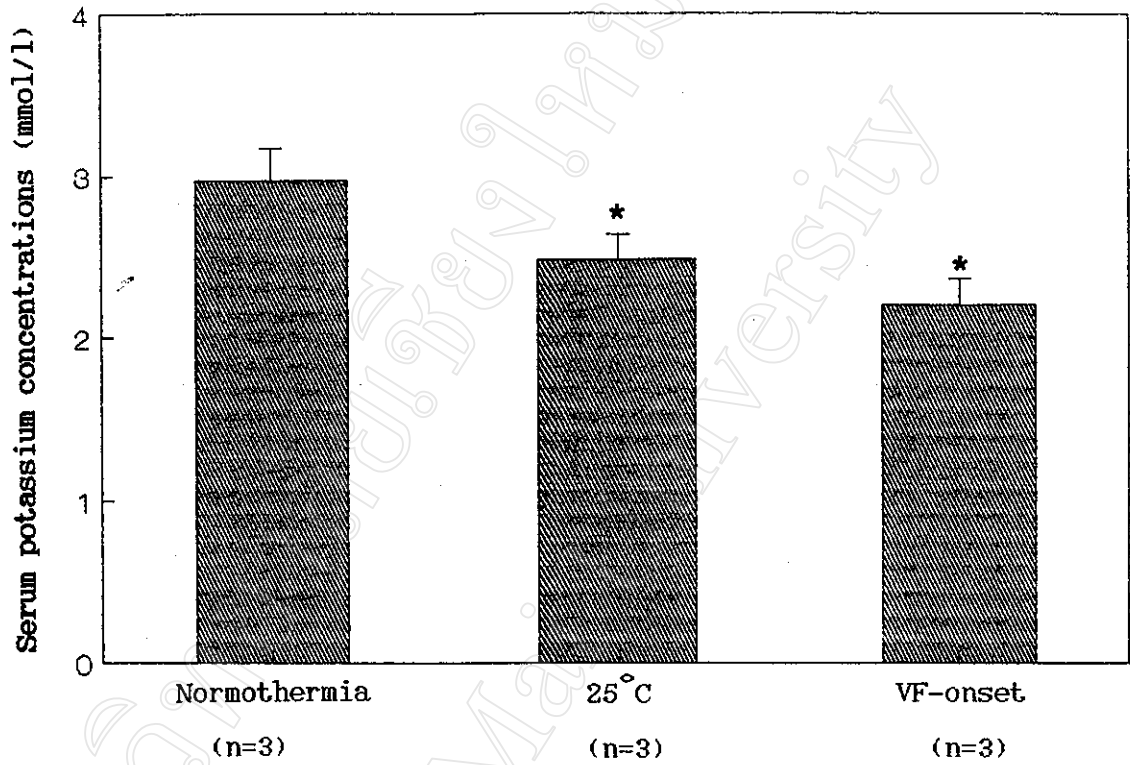


Figure 12. Serum potassium concentrations at three levels of body temperature in ventricular fibrillating Lidocaine-treated rats.

mean  $\pm$  SE.

\*  $p < 0.05$  between Normothermia and 25°C or between Normothermia and VF-onset

at 25°C and to  $2.33 \pm 0.20$  mmol/l at the VF-onset ( $n = 3$ ,  $p < 0.05$ ), but there was no difference between the levels at 25°C and those at the VF-onset ( $p > 0.05$ ) as in control animals. Serum potassium concentrations in the Bretylium-treated group compared among three hypothermic levels are shown in Figure 13. They were  $3.07 \pm 0.23$ ,  $2.51 \pm 0.21$  and  $2.37 \pm 0.17$  mmol/l at normothermia, at 25°C and at the VF-onset, respectively ( $n = 3$ ), and significant differences were found between the levels at normothermia and at 25°C, and between normothermia and at the VF-onset ( $p < 0.05$ ). However, between the levels at 25°C and at the VF-onset there was no significant difference ( $p > 0.05$ ). The comparisons of the mean serum potassium concentrations among three experimental groups that developed VF at each hypothermic levels are presented in Figure 14, Figure 15 and Figure 16. There were no significant differences between groups of the animals compared at the same hypothermic level ( $p > 0.05$ ). Nevertheless, it was found that there were the correlations between body temperature and serum potassium concentrations as observed in non-VF animals.

#### **Comparisons of Serum Potassium Concentrations between Non-VF and VF Animals During Hypothermia**

Figure 17, Figure 18 and Figure 19 illustrate serum potassium concentrations at various hypothermic levels of non-VF as compared with those of VF animals in Control, Lidocaine-treated and Bretylium-treated groups. There were no significant differences in serum potassium concentrations between non-VF and VF animals of all experimental groups as presented either at normothermia or at hypothermia of 25°C ( $p > 0.05$ ). Figure 20 and Figure 21 collectively present the serum potassium concen-

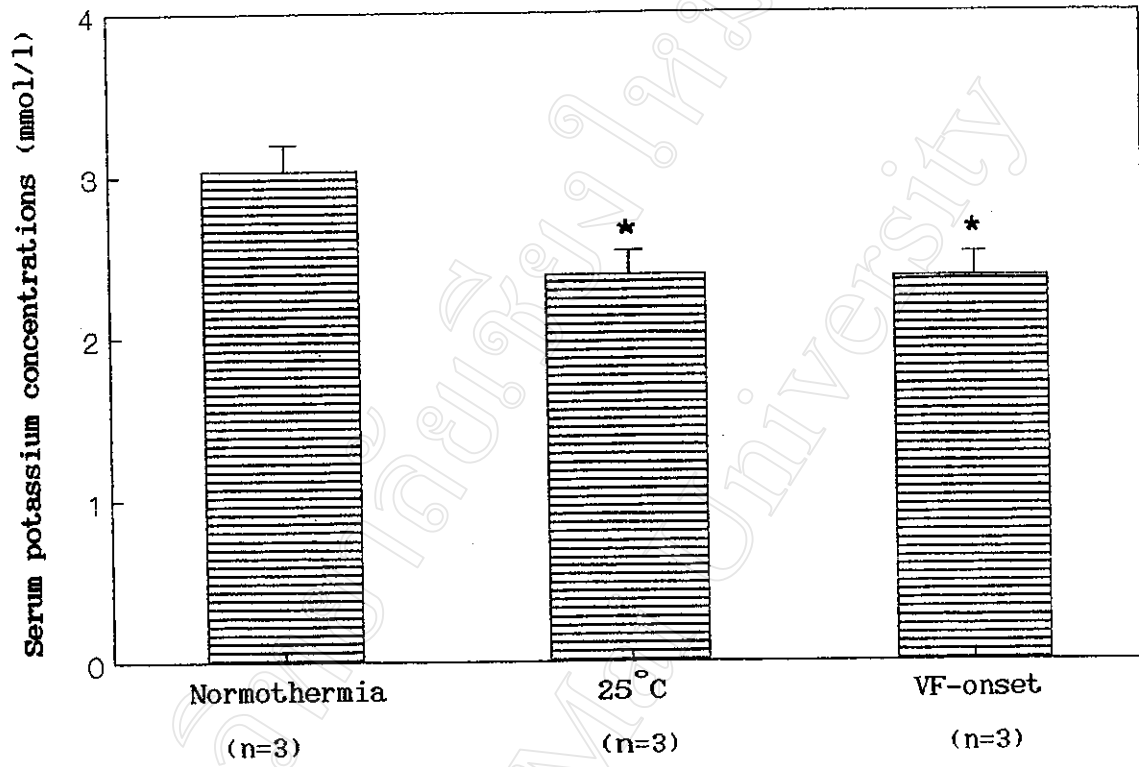


Figure 13. Serum potassium concentrations at three levels of body temperature in ventricular fibrillating Bretylium-treated rats.

means  $\pm$  SE.

\*  $p < 0.05$  between Normothermia and 25°C or between Normothermia and VF-onset

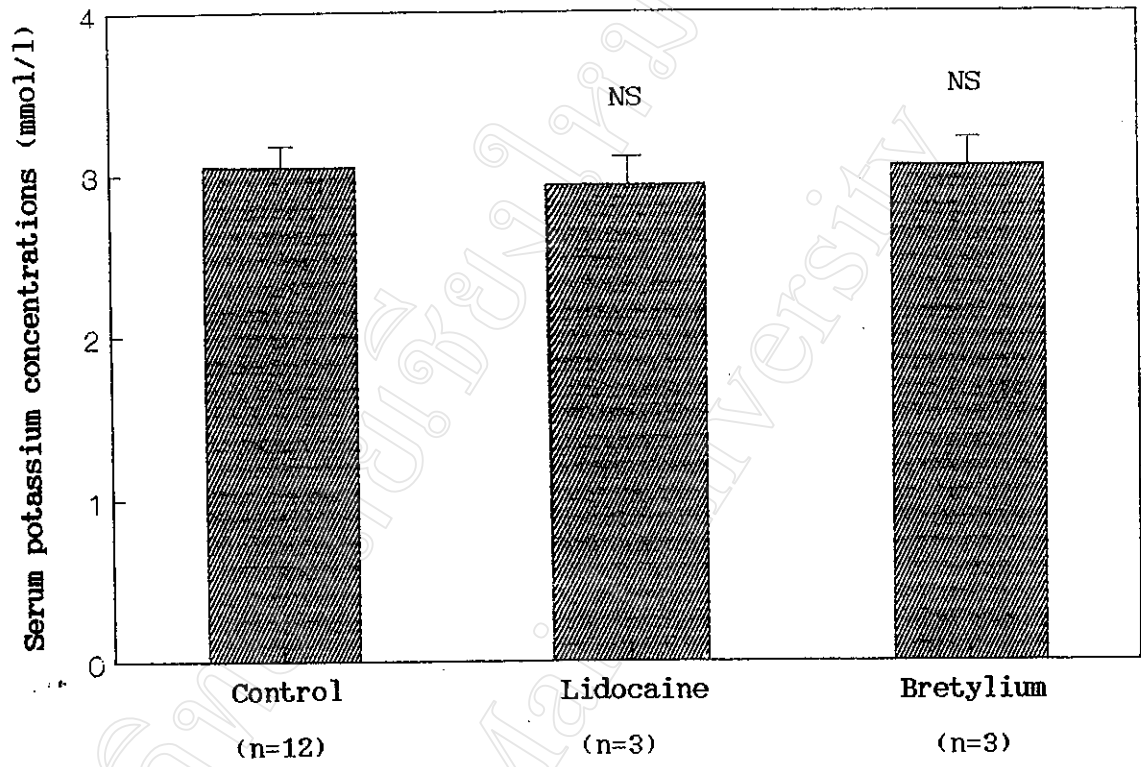


Figure 14. Serum potassium concentrations at Normothermia in ventricular fibrillating rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups

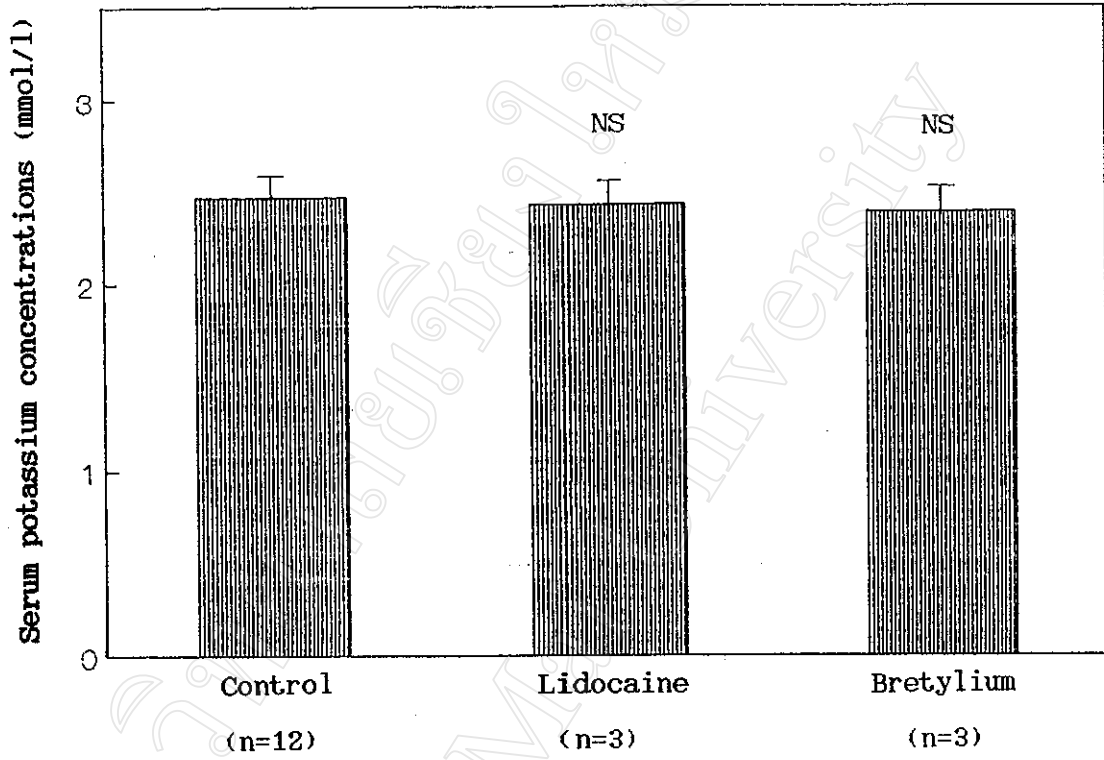


Figure 15. Serum potassium concentrations at 25°C in ventricular fibrillating rats.

mean  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups



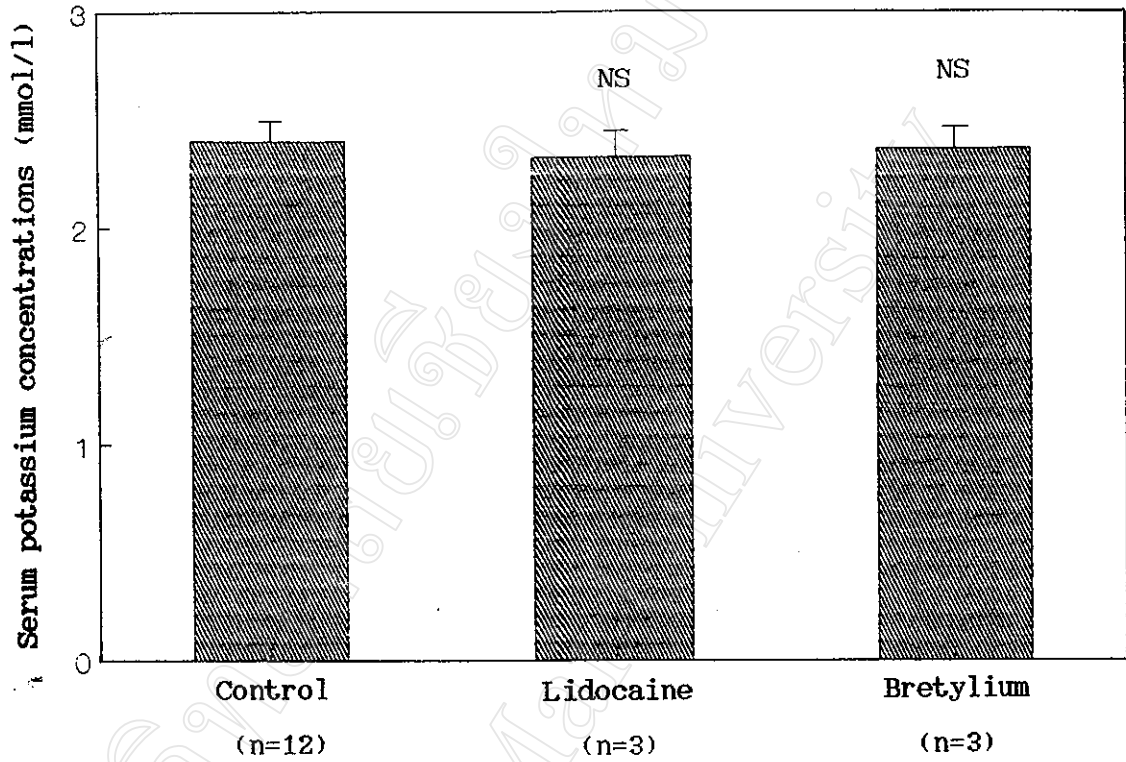


Figure 16. Serum potassium concentrations at the onset of ventricular fibrillation in ventricular fibrillating rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Control and both of the chemical-treated groups

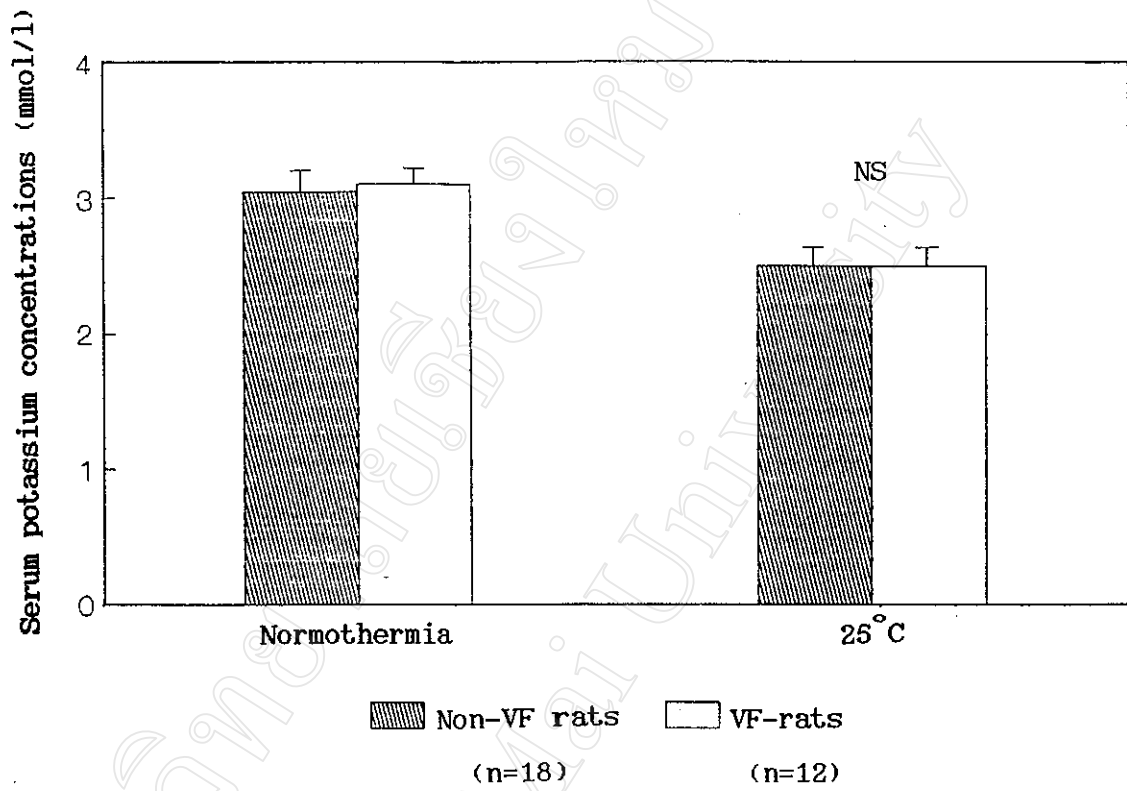


Figure 17. Comparison of the mean serum potassium concentrations at Normothermia and 25°C in control rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Normothermia and 25°C of both non-VF and VF rats

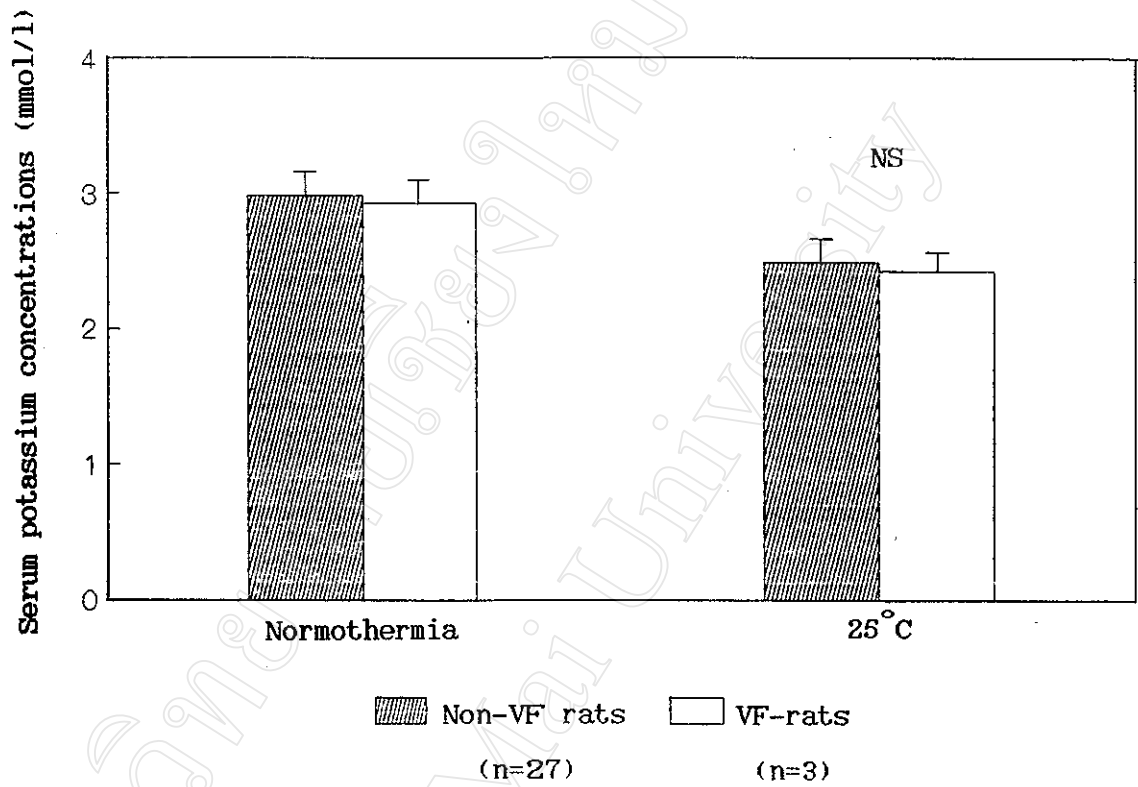


Figure 18. Comparison of the mean serum potassium concentrations at Normothermia and 25°C in Lidocaine-treated rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Normothermia and 25°C of both non-VF and VF rats

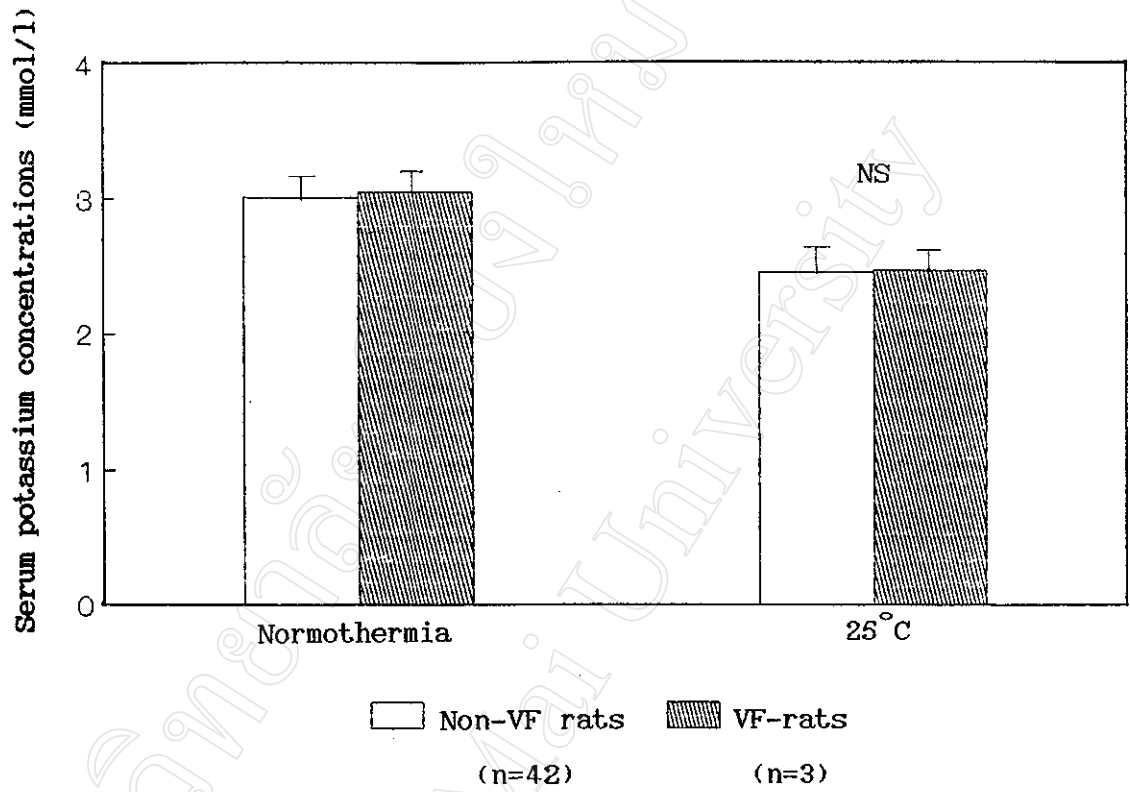


Figure 19. Comparison of the mean serum potassium concentrations at Normothermia and 25°C in Bretylium-treated rats.

means  $\pm$  SE.

NS =  $p > 0.05$  between Normothermia and 25°C of both non-VF and VF rats

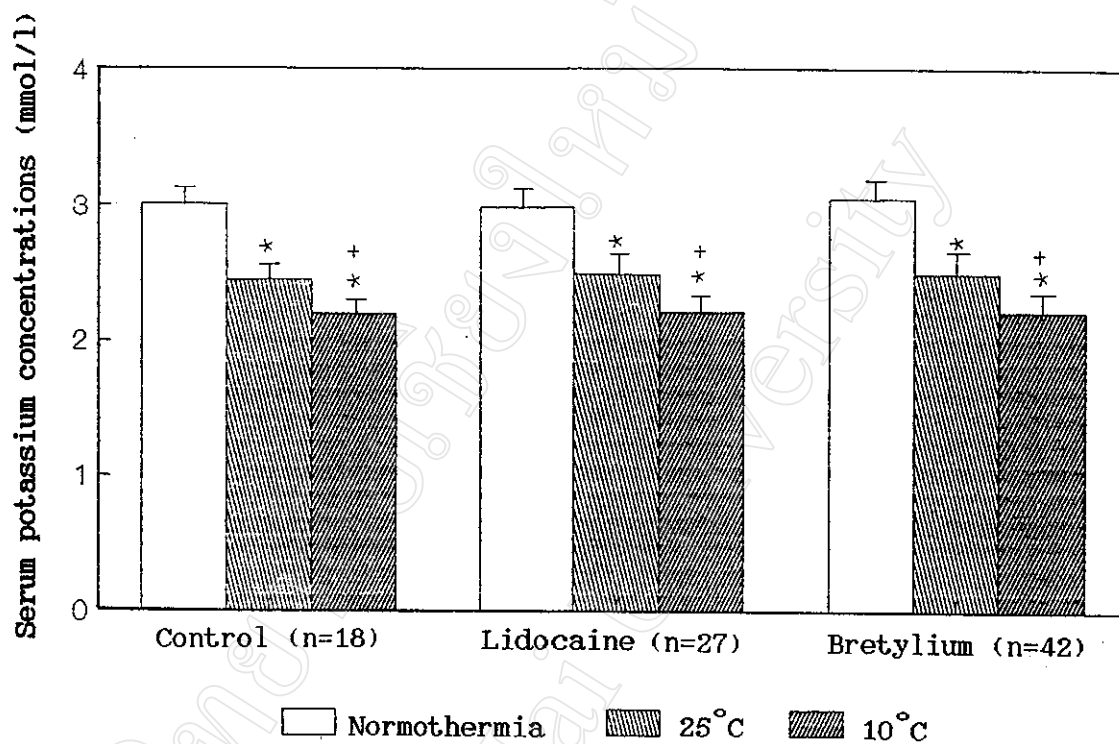


Figure 20. Comparison of the mean serum potassium concentrations at three levels of body temperature among three groups of non-ventricular fibrillating rats.

means  $\pm$  SE.

\*  $p < 0.05$  between Normothermia and 25°C or between Normothermia and 10°C

+  $p < 0.05$  between 25°C and 10°C

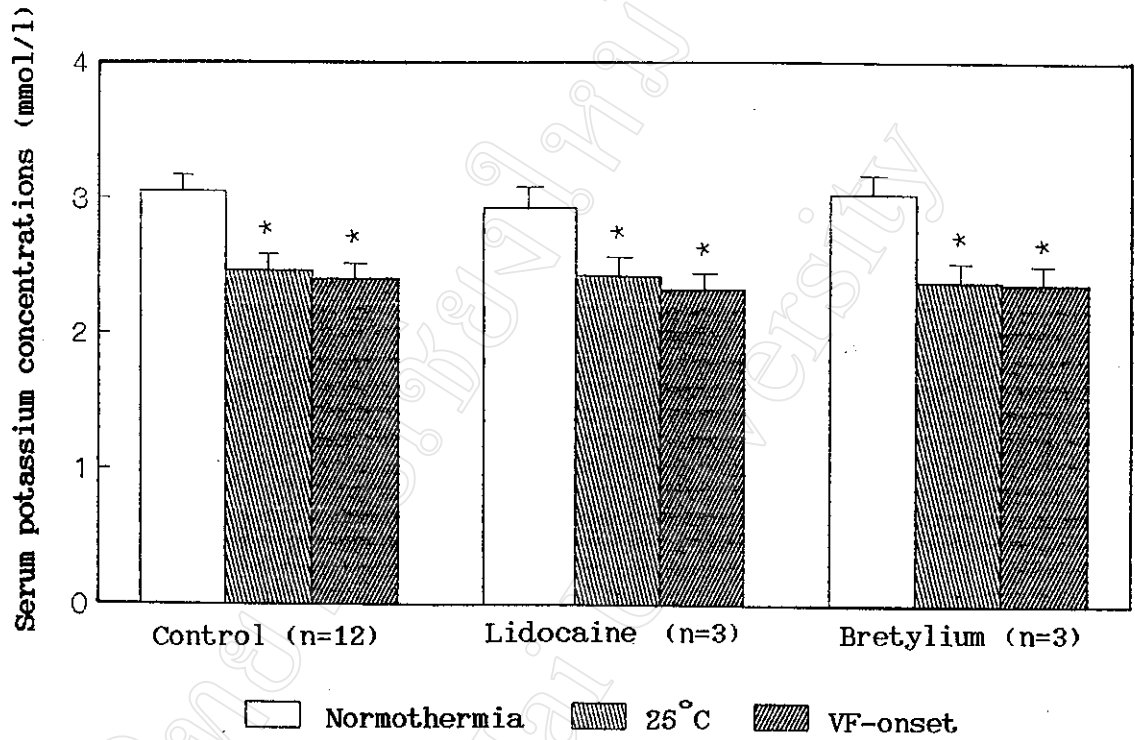


Figure 21. Comparison of the mean serum potassium concentrations at three levels of body temperature among three groups of ventricular fibrillating rats.

means  $\pm$  SE.

\*  $p < 0.05$  between Normothermia and 25°C or between Normothermia and VF-onset

trations of three groups of non-VF and VF animals at various hypothermic levels.

#### **Serum Glucose Concentrations in Hypothermia**

The mean serum glucose concentrations in non-VF animals ( $n = 8$ ) and VF animals ( $n = 2$ ) are presented in Table 6. In non-VF animals, serum glucose levels were  $99.75 \pm 3.11$  mg/dl at normothermia,  $102.75 \pm 2.33$  mg/dl at  $25^{\circ}\text{C}$  and  $103.25 \pm 3.27$  mg/dl at  $10^{\circ}\text{C}$  ( $n = 8$ ). In VF animals, the levels were  $97.5 \pm 4.23$ ,  $103.5 \pm 3.72$  and  $98.5 \pm 5.72$  mg/dl at normothermia,  $25^{\circ}\text{C}$  and at VF-onset, respectively ( $n = 2$ ). There were no significant differences in serum glucose concentrations among the three hypothermic levels both in non-VF and VF animals, as shown in Figure 22 ( $p > 0.05$ ). There were no significant differences in serum glucose levels compared between non-VF and VF animals at normothermia and at  $25^{\circ}\text{C}$  ( $p > 0.05$ ). Serum glucose levels were not compared between non-VF at  $10^{\circ}\text{C}$  and VF animals at VF-onset because of the differences in temperature.

Table 6. The mean serum glucose concentrations at three levels of body temperature.

Body temperature levels	Serum glucose concentrations (mg/dl)	
	Non-VF rats (n = 8)	VF rats (n = 2)
Normothermia	99.75 $\pm$ 3.11	97.5 $\pm$ 4.23 (NS)
25°C	102.75 $\pm$ 2.33	103.5 $\pm$ 3.72 (NS)
10°C or VF onset	103.25 $\pm$ 3.27	98.5 $\pm$ 5.72 (NS)

means  $\pm$  SE.

NS =  $p > 0.05$  between Normothermia and both of the hypothermic levels and between non-VF and VF rats



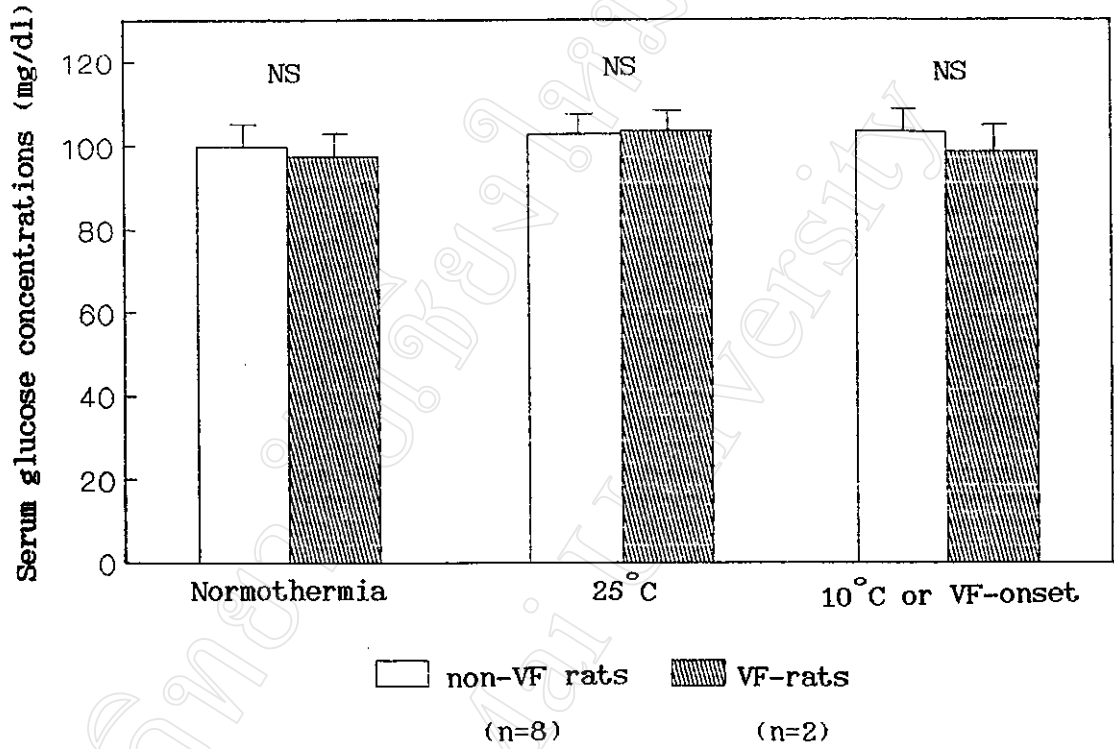


Figure 22. Comparison of the mean serum glucose concentrations at three levels of body temperature between non-ventricular fibrillating and ventricular fibrillating rats.

means  $\pm$  SE.

$p > 0.05$  between Normothermia and both of the hypothermic levels and between non-VF and VF rats