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Potentiated Effects of Cold and Low-Pressure in Sheep Pulmonary Hemodynamics

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ABSTRACT

Standing awake sheep, weighing between 25 and 35 kg, were exposed to a simulated altitude of 5,000 m under 20°C room temperature (A group). Other sheep were exposed to the similar altitude under 0°C room temperature (B group). For these, some hemodynamic parameters such as pulmonary artery pressure (P_{PA}), left atrial pressure (P_{LA}) and right atrial pressure (P_{RA}) were obtained. In addition, systemic artery pressure (P_{SA}) and minute cardiac output (CO) were measured. In B group, 20 hrs of cold exposure preceded the experimentation. In both A and B groups CO and P_{PA} increased as the simulated altitude was elevated. By the pretreatment, the initial values of CO and P_{PA} in B became greater than those in A. This tendency was maintained in each stepwise-elevated level. This was thus reflected in the increased right ventricular work rate ($R\dot{V}W$) of B. Consequently, cold and low-pressure applied simultaneously potentiated the $R\dot{V}W$ of B. This would be considered also as the basis for the right ventricular hypertrophy of rats found at high altitudes in winter.

INTRODUCTION

It has been well known that right ventricular hypertrophy develops in high-altitude residents as well as in animals. The chronic exposure to hypoxia, including pulmonary hypertension by pulmonary vasoconstriction, causes right vantricular hypertrophy in a variety of animal species. In the same way, cold acclimation in animals living at high altitude, was

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known to cause cardiac hypertrophy particularly in the right ventricular muscles. Elsewhere, Sakai reported that wild mice (*Apodemus argenteus*) captured at similar altitudes exhibited heavier cardiac weights in winter than those in summer. Although the left (LVW) and the right ventricular weight (RVW) increased simultaneously, the ratio, RVW/LVW became greater by the environmental stimuli, indicating the right-side hypertrophy(Sakai, J.Mamm.Soc.Jap. 6,224,1976).

From this, it was revealed that workload of the heart was imposed especially on the right ventrcle by combined exposures to hypoxia and cold.

In the present study of the sheep, we examined the effects of exposure to simulated altitudes or simultaneous exposure to cold and simulated altitudes on systemic and pulmonary hemodynamics.

MATERIALS AND METHODS

Sheep weighing 25-35 kg were used. The following procedures were done aseptically: Silicon tubes (ID 2 mm) were inserted into the left atrium and the pulmonary artery through a left thoracotomy. An electromagnetic flow probe was placed around the trunk of the pulmonary artery. The tube and electrodes were fixed together at one point of the left chest. The tubes were inserted also into the thoracic aorta through the left carotid and into the right atrium through the right jugular vein. After about one week when the influences of the operational stress seemed to have nearly subsided, we started two types of experiments in the conscious sheep.

Exp. A (n=5) : Sheep were exposed stepwise to simulated altitudes, from 650 m to 5,000 m, at a rate of 500 m / 5 min, in a low pressure chamber under 20°C room temperature.

Exp. B (n=8) : Sheep were exposed to cold (0 ± 1°C) during about 20 hrs, then exposed simultaneously to cold and simulated altitudes.

Left (P_{LA}) and right (P_{RA}) atrial pressures, together with systemic (P_{SA}) and pulmonary (P_{PA}) arterial pressures, were measured using pressure transducers. Cardiac output (CO) was measured by the flowmeter. Heart rate (HR) was measured using a heart rate recorder. Systemic (SVR) and pulmonary (PVR) vascular resistances, right ($R\dot{V}W$) and left ($L\dot{V}W$) ventricular work rates and stroke volume (SV) were calculated by (P_{SA} - P_{RA}) / CO, (P_{PA} - P_{LA}) / CO, P_{PA} x CO, P_{SA} x CO, and CO / HR, respectively.

RESULTS

The results are summarised in Fig.1 - Fig.8 and Table 1.

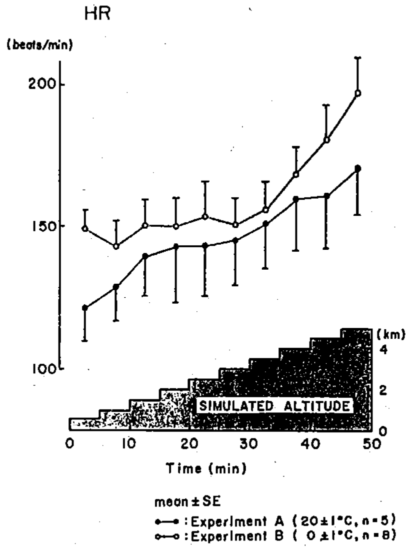

Fig.1 ADDITIVE EFFECT OF COLD EXPOSURE AND SIMULATED ALTITUDE ON HEART RATE (HR) IN CONCIOUS SHEEP.

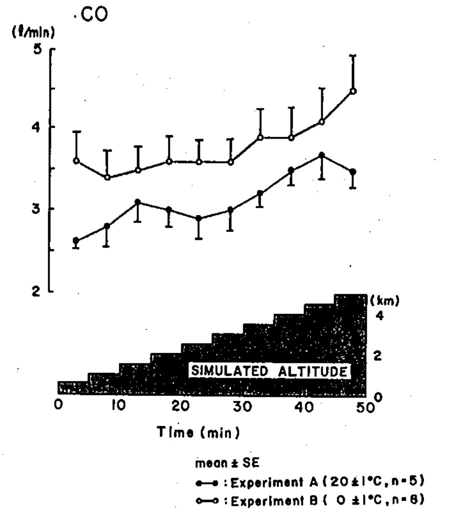

Fig.2 ADDITIVE EFFECT OF COLD EXPOSURE AND SIMULATED ALTITUDE ON CARDIAC OUTPUT (CO) IN CONCIOUS SHEEP.

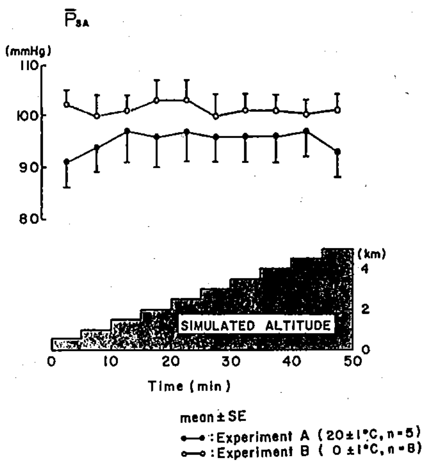

Fig.3 ADDITIVE EFFECT OF COLD EXPOSURE AND SIMULATED ALTITUDE ON MEAN SISTEMIC ARTERIAL PRESSURE ($\bar{P}_{SA}$) IN CONCIOUS SHEEP.

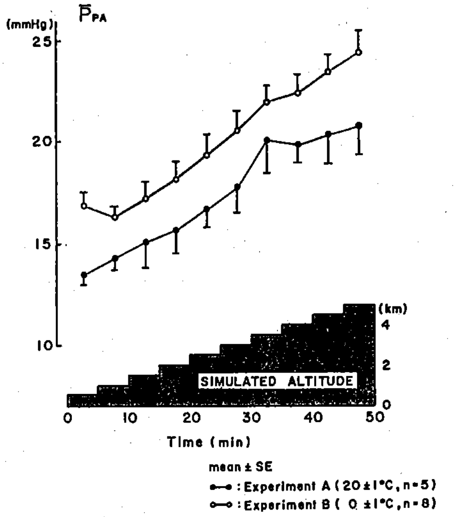

Fig.4 ADDITIVE EFFECT OF COLD EXPOSURE AND SIMULATED ALTITUDE ON MEAN PULMONARY ARTERIAL PRESSURE ($\bar{P}_{PA}$) IN CONCIOUS SHEEP.

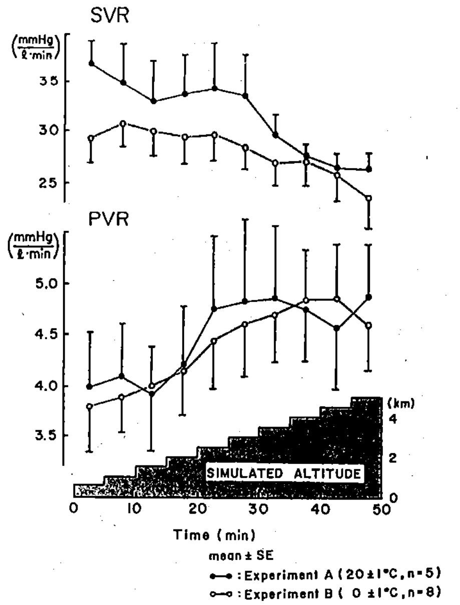

Fig. 5 ADDITIVE EFFECT OF COLD EXPOSURE AND SIMULATED ALTITUDE ON SYSTEMIC VASCULAR RESISTANCE (SVR) AND PULMONARY VASCULAR RESISTANCE (PVR) IN CONCIOUS SHEEP.

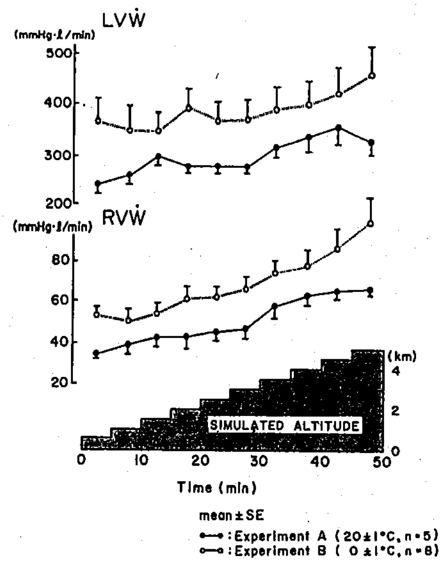

Fig. 6 ADDITIVE EFFECT OF COLD EXPOSURE AND SIMULATED ALTITUDE ON LEFT (LVẆ) AND RIGHT (RVẆ) VENTRICULAR WORK RATES IN CONCIOUS SHEEP.

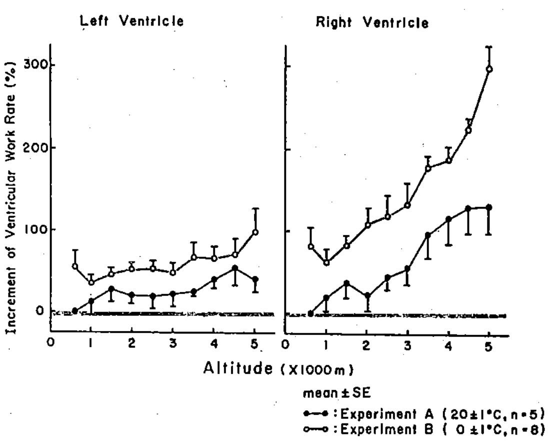

Fig. 7 ADDITIVE EFFECT OF COLD EXPOSURE AND SIMULATED ALTITUDE ON LEFT AND RIGHT VENTRICULAR WORK RATE IN CONCIOUS SHEEP.

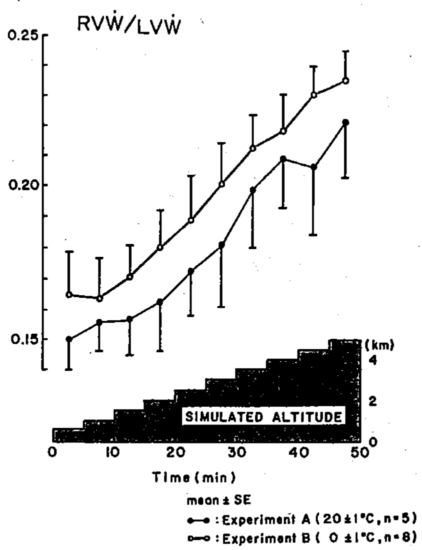

Fig. 8 ADDITIVE EFFECT OF COLD EXPOSURE AND SIMULATED ALTITUDE ON RATIO OF RIGHT TO LEFT VENTRICULAR WORK RATES (RVẆ/LVẆ) IN CONCIOUS SHEEP.

TABLE 1. HEMODYNAMIC RESPONSES TO SIMULATED ALTITUDE EXPOSURE IN CONSCIOUS SHEEP

Simulated altitude (m)	mean pressure (mmHg) Left atrium	Pulmonary artery	Systemic artery	Cardiac output (L/min)	Heart rate (beats/min)	Stroke volume (ml/beat)	Pulmonary vascular resistance (mmHg/L/min)	Systemic vascular resistance (mmHg/L/min)	Right ventricular work rate (mmHg·L/min)	Left ventricular work rate (mmHg·L/min)	Ratio of right to left ventricular work rates (x 10⁻²)
Experiment A : exposed to simulated altitude under 20°C (n=5)											
650	3.2 ±0.5	13.5 ±0.5	91.4 ±4.7	2.59 ±0.07	124 ±10	21.3 ±1.7	3.98 ±0.53	36.9 ±2.4	35.0 ±1.6	238 ±18	14.8 ±0.8
1,000	3.2 ±0.8	14.3 ±0.6	94.1 ±5.0	2.80 ±0.24	129 ±10	22.4 ±3.1	4.13 ±0.51	34.9 ±4.2	40.0 ±4.2	261 ±20	15.6 ±0.8
1,500	3.3 ±0.3	15.0 ±1.2	97.1 ±5.7	3.09 ±0.26	139 ±13	22.8 ±3.4	3.93 ±0.59	32.9 ±4.3	46.3 ±5.5	297 ±19*	15.5 ±1.2
2,000	3.5 ±0.5	15.6 ±1.2	96.1 ±6.1	2.95 ±0.21	143 ±18	22.0 ±3.6	4.18 ±0.59	33.7 ±4.2	46.2 ±6.1	279 ±14	16.3 ±1.5
2,500	3.4 ±0.6	16.6 ±0.9*	97.1 ±6.2	2.90 ±0.26	144 ±16	22.0 ±4.0	4.76 ±0.70	34.4 ±5.0	48.1 ±4.9*	278 ±18	17.3 ±1.4
3,000	3.8 ±0.9	17.6 ±1.3*	96.1 ±5.3	2.98 ±0.24	145 ±15	21.8 ±3.8	4.83 ±0.80	33.5 ±4.3	52.2 ±6.0*	283 ±17	18.6 ±1.9
3,500	4.3 ±1.2	19.9 ±1.6*	96.4 ±5.1	3.28 ±0.17*	152 ±15	22.8 ±3.6	4.85 ±0.71	29.7 ±1.9*	65.4 ±6.6*	316 ±25*	20.9 ±2.2*
4,000	3.4 ±1.1	19.7 ±0.9*	95.7 ±5.5	3.47 ±0.18*	158 ±17	23.3 ±3.5	4.76 ±0.50	27.6 ±1.0*	68.7 ±6.1*	335 ±33*	20.7 ±1.4*
4,500	2.4 ±0.6	20.2 ±1.4*	97.1 ±4.7	3.72 ±0.27*	161 ±17	24.8 ±4.7	4.58 ±0.61	26.4 ±1.5*	80.5 ±12.9*	364 ±37*	21.2 ±1.8*
5,000	3.7 ±0.9	20.6 ±1.4*	92.7 ±4.9	3.48 ±0.20*	168 ±15*	21.9 ±3.1	4.88 ±0.50	26.5 ±1.3*	72.5 ±6.6*	328 ±28*	22.4 ±2.1*
Experiment B : exposed to simulated altitude under 0°C (n=8)											
650	3.9 ±0.7	16.8 ±0.8	101.6 ±3.3	3.63 ±0.34●	149 ± 6●	24.9 ±3.1	3.82 ±0.47	29.2 ±2.3●	55.0 ±4.0●	372 ±42●	16.3 ±0.8
1,000	3.7 ±0.6	16.3 ±0.5●	100.2 ±3.8	3.40 ±0.32	143 ± 9	24.6 ±3.0	3.87 ±0.36	30.7 ±2.5	56.3 ±7.2	346 ±44	16.2 ±0.5
1,500	3.7 ±0.8	17.1 ±0.8●	100.6 ±3.3	3.50 ±0.28	152 ± 8	24.0 ±3.0	4.02 ±0.38	29.9 ±2.7	60.8 ±7.3	353 ±35	17.0 ±1.0
2,000	3.5 ±0.6	18.1 ±0.9	102.7 ±3.5	3.64 ±0.29	151 ± 9	24.4 ±2.8	4.17 ±0.44	29.3 ±2.5	66.7 ±7.7●	387 ±37●	17.4 ±0.8
2,500	3.8 ±0.6	19.2 ±1.0	102.9 ±3.8	3.58 ±0.25	153 ±12	24.0 ±2.8	4.45 ±0.48	29.6 ±2.4	69.1 ±6.8●	371 ±35●	18.9 ±1.4
3,000	4.3 ±0.8	20.5 ±1.0*	100.2 ±3.5	3.64 ±0.28	151 ± 9	24.6 ±3.2	4.62 ±0.49	28.4 ±2.0	75.2 ±7.6*●	367 ±40●	20.5 ±1.4*
3,500	4.5 ±0.9	22.0 ±0.8*	100.7 ±3.1	3.89 ±0.34	156 ± 9	26.4 ±3.8	4.72 ±0.46	27.0 ±2.3	86.6 ±9.8*	395 ±42	21.9 ±1.1*
4,000	4.0 ±0.6	22.2 ±0.9*●	101.1 ±2.8	3.90 ±0.36	168 ± 9	24.1 ±3.2	4.84 ±0.48	27.2 ±2.5	88.0 ±10.1*	398 ±46	22.0 ±1.0*
4,500	4.4 ±0.6	23.3 ±0.9*	99.8 ±3.1	4.11 ±0.42	178 ±12*	23.9 ±3.5	4.87 ±0.51	25.9 ±2.6	97.2 ±11.8*	416 ±53	23.5 ±1.1*
5,000	4.3 ±0.6	24.3 ±1.1*	101.3 ±3.2	4.48 ±0.44	194 ±11*	23.7 ±2.9	4.60 ±0.44	23.6 ±3.3	111.1 ±14.2*●	460 ±57●	24.0 ±1.1*

Values are means ± SE. Sheep of experiment B were exposed to cold (0°C) for 20 hrs before this experiment.
*:statistical difference ($p < 0.05$) between control values (650 m) and respective altitude data. ●:statistical difference ($p < 0.05$) between data of A and those of B.

CONCLUSION

Both high-altitude humans and animals tend to exhibit some degree of cardiac hypertrophy especially in th right ventricular muscles. This is advantageous in maintaining the pulmonary circulation normally and is considered to be a sort of morphological adaptation to high-altitude conditions. One of the important factors for the right ventricular hypertrophy would be the increased right ventricular load in the above environmental conditions. So, we attempted to examine the additive effects of cold and low-pressure on systemic and pulmonary hemodynamics in conscious sheep.

When sheep were exposed to cold ($0 \pm 1°C$) during 20 hrs, P_{PA}, P_{SA}, CO, HR, $L\dot{V}W$, $R\dot{V}W$ and $R\dot{V}W/L\dot{V}W$ were increased significantly. P_{LA} and PVR were not altered, and SVR showed a decrease. When they were exposed to simulated altitudes successively from 650m to 5,000m under room temperature (Exp.A), P_{PA}, CO, HR, PVR, $L\dot{V}W$, $R\dot{V}W$ and $R\dot{V}W/L\dot{V}W$ were increased as the simulated altitude was elevated. But, P_{SA} and SV were not altered and SVR showed a decrease. When they were exposed to cold ($0 \pm 1°C$) and simulated altitudes simultaneously (Exp. B), the slopes of the lines plotted for the above parameters versus altitude levels were similar to those in Exp.A. However, the lines for B were located in the higher positions than those for A, especially as for the data of P_{PA}, CO, $R\dot{V}W$ and $R\dot{V}W/L\dot{V}W$.

It is thus emphasized that both cold and hypoxia are very important factors in causing right ventricular hypertrophy at high altitudes.

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