Simultaneous Observations of Changes in Metabolic and Circulatory Parameters during Hypothermia

Eiji Sekino, Akira Takano, Tadao Denbo, Sohei Suzuki and Susumu Ainai

Department of Surgery (Prof. Y. Ishikawa),
Hirosaki University School of Medicine, Hirosaki

Simultaneous observations were made of changes in metabolic and circulatory parameters of the total body, heart and brain under hypothermia. Linear decreases were seen in cardiac output, coronary and cerebral blood flows during hypothermia until the body temperature fell to 30°C, and the rate of each decrease was almost the same. However, our data obtained at body temperature of 25°C showed that the decrease in cardiac output was prominent, compared with that in cerebral and coronary blood flows. That is, the rate of distribution of the blood volume in the coronary and cerebral circulations predominated over that of cardiac output.

This finding suggests that both the brain and heart muscle require relatively large quantities of oxygen even under the condition of hypothermia, and all metabolic and circulatory parameters change in a direction to maintain blood supply to the brain and heart muscle during hypothermia.

The use of hypothermia as well as that of extracorporeal circulation has made a significant contribution to open heart surgery. Indeed, general hypothermia itself has been proved to be useful in some cardiac surgery. Recently, various techniques for producing hypothermia, such as extracorporeal circulation under general hypothermia, perfusion hypothermia, selective hypothermia of the heart, selective brain cooling etc. have been devised. However, practical application of these techniques for producing hypothermia cannot be appreciated unless fundamental physiological behaviors of the organism under hypothermia are understood.

In the present study simultaneous observations were made of changes in metabolism and circulation in the total body, heart and brain during hypothermia.

**Experimental**

1) Experimental animals were dogs weighing 8.5 to 21.0 kg.
2) Endotracheal anesthesia with ether was employed, after intravenous injection of 15 mg/kg pentobarbital. Depth of anesthesia was maintained in the 3rd stage, the 2nd plane.
3) Sampling of cerebral venous blood was performed by means of a polyethylene tube inserted through the sagittal sinus to the confluence sinus.

4) Sampling of coronary venous blood was made by means of a tube inserted through the jugular vein to the coronary sinus.

5) Sampling of mixed venous blood was made by means of a tube inserted through the femoral vein into the vena cava.

6) Blood sampling from, and pressure measurement on, peripheral arteries and veins were made through tubes inserted into the A. profunda femoris and the V. saphena magna, respectively.

7) Hypothermia was induced by using the immersion method in water maintained at a temperature of 4°C–6°C. A thermisiter was inserted in the esophagus for the estimation of body temperature.

**Calculation of parameters**

At body temperatures of 35°C, 30°C and 25°C during the induction of hypothermia, arterial and venous blood samples were drawn through the tubes inserted in the above-mentioned vessels beforehand. Arterial blood pressure was measured with the tube inserted in the femoral artery.

The blood lost at each sampling was substituted by the same amount of exogenous blood.

1) Cardiac output (L/min), \( Q \), was calculated as follows according to Fick's principle:

\[
Q = \frac{\text{Total body oxygen consumption (ml/min)}}{\text{Difference of arterial and venous oxygen content (vol %)}} \times 100
\]

2) Total body oxygen consumption (ml/min), \( V \), was measured by using a Knipping's spirometer connected to an intratracheal tube with a cuff.

3) Peripheral arteriolar resistance (mmHg/ml/min), \( R \), was calculated as follows:

\[
R = \frac{\text{Peripheral arterial pressure (mmHg)}}{\text{Cardiac output (ml/min)}}
\]

4) Cerebral circulating blood volume (ml/100 g brain/min), \( Q_{b} \), was measured by using Scheinberg's modified method. A gas mixture consisting of 15% \( \text{N}_2\text{O} \) and 85% \( \text{O}_2 \) was administered for fifteen minutes by the non-rebreathing method, and during the saturation process, 0.5 ml samples of arterial and venous blood were drawn each minute by syringes. The calculation was as follows:

\[
Q_{b} = \frac{V_{15}}{\int_{0}^{15} (A - V) \, dt}
\]

5) Cerebral oxygen consumption (ml/100 g brain/min), \( V_{v} \), was calculated as follows:
Metabolic and Circulatory Parameters in Hypothermia

\[ V_b = \text{Cerebral circulating blood volume (ml/100 g brain/min)} \times \text{Difference between cerebral arterial and venous oxygen contents (vol %)} \]

6) Cerebral arteriolar resistance (mmHg/ml/100 g brain/min), \( R_b \), was determined as follows:

\[ R_b = \frac{\text{Carotid artery pressure (mmHg)} - \text{Confluence sinus pressure (mmHg)}}{\text{Cerebral circulating blood volume (ml/100 g brain/min)}} \]

7) Coronary circulating blood volume (ml/100 g heart muscle/min), \( Q_h \), was measured by the \( N_2O \) method simultaneously with the measurement of cerebral circulating blood volume.

8) Heart muscle oxygen consumption (ml/100 g heart muscle/min), \( V_h \), was calculated as follows:

\[ V_h = \text{Coronary circulating blood volume (ml/100 g heart muscle/min)} \times \text{Difference between coronary arterial and venous oxygen content (vol %)} \]

9) Coronary arteriolar resistance (mmHg/ml/100 g heart muscle/min), \( R_h \), was obtained as:

\[ R_h = \frac{\text{Aortic pressure (mmHg)} - \text{Coronary sinus pressure (mmHg)}}{\text{Coronary circulating blood volume (ml/100 g heart muscle/min)}} \]

RESULTS

The observations on individual experimental animals are given in Table 1. Table 2 shows the absolute increase or decrease in each recorded parameter at 30°C and 25°C in percentage of its value at 35°C for each animal.

Cardiac output, in ml/kg/min, ranged from 181 to 336 in 8 animals (mean 263) at body temperature of 35°C, from 102 to 227 in 5 animals (mean 175) at 30°C body temperature and from 43 to 131 in 7 animals (mean 76) at 25°C.

Total body oxygen consumption, in ml/kg/min, ranged from 8.0 to 12.6 in 8 animals (mean 10.0) at 35°C, 5.0 to 10.0 in 5 animals (mean 7.0) at 30°C and 2.0 to 4.0 in 7 animals (mean 3.0) at 25°C. The mean total body oxygen consumptions at 30°C and 25°C were 60.1% and 23.1% of that observed at 35°C, respectively.

Peripheral arteriolar resistance tended to increase with deepening hypothermia, at least within our experimental limits of body temperature.

Cerebral circulating blood volumes, in ml/100 g brain/min, ranged from 48 to 94 in 8 animals (mean 66) at 35°C, from 29 to 51 in 5 animals (mean 43) at 30°C and from 21 to 35 in 7 animals (mean 30) at 25°C. The cerebral circulating blood volumes at 30°C and 25°C were 62.1% and 44.7% of that observed at 35°C, respectively.

Cerebral oxygen consumption, in ml/100 g brain/min, ranged from 2.5 to 5.8 in 8 animals (mean 3.6) at 35°C, from 1.4 to 2.6 in 5 animals (mean 1.9) at 30°C.
TABLE 1. Observed values of circulatory and metabolic parameters during hypothermia in individual animals

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<th>V</th>
<th>R</th>
<th>Qb</th>
<th>Vb</th>
<th>Rb</th>
<th>Qh</th>
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Q: Cardiac output (l/min)
V: Total body oxygen consumption (ml/min)
R: Peripheral arteriolar resistance (mmHg/ml/min)
Qb: Cerebral circulating blood volume (ml/100g brain/min)
Vb: Cerebral oxygen consumption (ml/100g brain/min)
Rb: Cerebral arteriolar resistance (mmHg/ml/100g brain/min)
Qh: Coronary circulating blood volume (ml/100 g heart muscle/min)
Vh: Heart muscle oxygen consumption (ml/100 g heart muscle/min)
Rh: Coronary arteriolar resistance (mmHg/ml/100 mg heart muscle/min)

and from 0.9 to 3.4 in 7 animals (mean 1.7) at 25°C. The cerebral oxygen consumptions at 30°C and 25°C were 58.0% and 48.6%, respectively, of that observed at 35°C.

Cerebral arteriolar resistance, in mmHg/ml/100 g brain/min, ranged from 1.0 to 1.9 in 8 animals (mean 1.3) at 35°C, 1.6 to 2.5 in 5 animals (mean 1.9) at 30°C and 0.9 to 2.6 in 5 animals (mean 1.8) at 25°C. The mean cerebral arteriolar resistances at 30°C and 25°C were 139.7% and 146.1% of that observed at 35°C, respectively.

Coronary circulating blood volume, in ml/100 g heart muscle/min, ranged
TABLE 2. Change in circulatory and metabolic parameters expressed in percentage of the values obtained at 35°C

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<th>V(%)</th>
<th>R(%)</th>
<th>Qb(%)</th>
<th>Vb(%)</th>
<th>Rh(%)</th>
<th>Qh(%)</th>
<th>Vh(%)</th>
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from 80 to 121 in 8 animals (mean 103) at 35°C, 58 to 85 in 5 animals (mean 71) at 30°C and 38 to 61 in 7 animals (mean 48) at 25°C. The mean coronary circulating blood volumes at 30°C and 25°C were 67.7% and 47.9% of that observed at 35°C, respectively.

Heart muscle oxygen consumption, in ml/100 g heart muscle/min, ranged from 6.3 to 11.5 in 8 animals (mean 8.8) at 35°C, 3.8 to 6.9 in 5 animals (mean 5.3) at 30°C and 2.0 to 5.3 in 7 animals (mean 3.3) at 25°C. The mean heart muscle oxygen consumptions at 30°C and 25°C were 58.2% and 38.9% of that observed at 35°C, respectively.

Coronary arteriolar resistance, in mmHg/ml/100 g heart muscle/min, ranged from 0.5 to 1.0 in 8 animals (mean 0.8) at 35°C, 0.9 to 1.1 in 5 animals (mean 1.0) at 30°C and 0.33 to 1.7 in 7 animals (mean 0.1) at 25°C. The mean coronary arteriolar resistances at 30°C and 25°C were 118.7% and 123.2%, respectively, of that observed at 35°C.

**DISCUSSION**

The purpose of the present study is not to estimate the extent of, but to observe the correlation between, circulatory and metabolic changes during hypothermia.

In Figs. 1 and 2, percentage changes in circulatory parameters, in reference to those at 35°C, are plotted against body temperature. The percent reduction in cerebral and coronary circulating blood volume and in cardiac output is closely
Fig. 1. Percentage reduction in cardiac output, cerebral circulating volume and coronary circulating volume at body temperatures of 30°C and 25°C relative to those at 35°C (see Table 2).

Fig. 2. Percentage changes in cerebral and coronary circulating blood volumes relative to cardiac output at body temperatures of 35°C, 30°C and 25°C.
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parallel to each other as hypothermia progresses at least to 30°C. At between
30°C and 25°C of body temperature, however, the percentage of the decrease in
cardiac output is considerably greater than that in cerebral and coronary
blood flows.

The patterns of decrease in organ blood flow with progressive hypothermia,
at least between 35°C and 30°C of body temperature, are very similar, and all
appear linear. However, in our data at 25°C, the decrease in cardiac output is
prominent compared with that in cerebral or coronary flow and, therefore, the
distribution-rate of coronary and especially cerebral circulating blood volume to
cardiac output is exaggeratedly elevated. This indicates that brain and heart
muscle are receiving a larger blood supply in proportion to cardiac output during
hypothermia than at normal body temperature.

Oxygen consumptions of the total body, brain and heart muscle during
hypothermia show tendencies similar to those observed for circulatory
parameters. Namely, the oxygen consumptions of the total body, brain and heart
muscle decrease as hypothermia progresses. The decrease remains linear
until body temperature is lowered to about 30°C, but below this temperature,
the oxygen consumptions of brain and heart muscle show smaller reductions in
percentage than the oxygen consumption of the total body. This shows that
the brain and heart muscle require comparatively large quantities of oxygen
even in hypothermia.

Cerebral and coronary arteriolar resistances are not so much increased as
peripheral arteriolar resistance in severe hypothermia. This would contribute
much to maintaining a sufficient blood flow to the brain and heart muscle in
hypothermia.

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