〔原著〕

Mixed venous oxygen content estimated from oxygen saturation and heart rate measured for healthy students during a study tour in Colorado

Katsuo UCHIDA

Abstract

Oxygen saturation (SpO_2) and heart rate (HR) were measured for 13 healthy third-grade students (4 males and 9 females ages 20 to 24) of the Physical Therapy Department of Yamagata Prefectural University of Health Sciences, who joined a study tour in Colorado from Sep. 19 to 27, 2012. Means and standard deviations of the SpO_2 values for the 13 students were 98 ± 0.95, 97 ± 1.4, 94 ± 1.9, 93 ± 1.7 and 87 ± 2.8 % at the Narita Airport (altitude 130 m), Denver City (1,609 m), Estes Park (2,499 m), Hidden Valley (2,816 m) and the Alpine Visitor Center (3,595 m), respectively. Averaged HR values simultaneously measured with SpO_2 at the each point were 75 ± 11,78 ± 5.8, 74 ± 7.4, 92 ± 11 and 85 ± 7.6 beats/min. These values except for those at the Narita Airport were measured within 6 hours on the fourth day for staying in Denver. Despite more than 10 % decrease in SpO_2 within 6 hours, no student felt unwell at the height of 3,595 m.

Based on the Fick principle, a correlation of SpO_2 in % with 1/HR in min/beats was described with a regression line that SpO_2 = 2650 (1/HR) + 60.6 with a coefficient of determination 0.600. With the standard oxygen content combined to hemoglobin in arterial blood 20.1 vol% by assuming the normal hemoglobin concentrations for each student, mixed venous oxygen content (C_vO_2) was estimated from the intercept of the regression line as 12.2 vol%. The difference between arterial oxygen content (C_aO_2) obtained from SpO_2 and the estimated C_vO_2 ($C_aO_2 - C_vO_2$) was consistent with those reported by a venous catheter method or a rebreathing method. These results suggest that C_vO_2 can be estimated from a noninvasive method to measure SpO_2 and HR.

Key words : mixed venous oxygen content, oxygen saturation, heart rate, high altitude, Colorado

1. Introduction

Yamagata Prefectural University of Health Sciences (YPUHS) conducted sister-school relationships with the College of Nursing and Physical Therapy Program of University of Colorado (UC) in 2001, and with the Department of Occupational Therapy of Colorado State University (CSU) in 2002. Since then the treaties have been renewed every 5 years. Voluntary

Department of Physical Therapy, Faculty of Health Sciences,
Yamagata Prefectural University of Health Sciences
260 Kamiyanagi, Yamagata, Yamagata, 990-2212, Japan

（受付日 2013. 1. 7，受理日 2013. 2. 1）

Table 1 Year-by-year numbers of participants to the study tour in Colorado. Ratios of the participants to the whole students of each Department of YPUHS are shown in parentheses in %.

Dept.	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
N	16 (29)	19 (34)	14 (22)	15 (23)	14 (23)	14 (23)	12 (20)	19 (26)	8 (13)	13 (21)	18 (31)
PT	10 (48)	9 (47)	7 (30)	16 (70)	12 (57)		11 (55)	13 (62)	11 (50)	14 (61)	13 (59)
OT		6 (32)	4 (18)	5 (25)	10 (50)	7 (37)	4 (20)	6 (32)	12 (55)	4 (18)	6 (26)

N: Nursing Dept. PT: Physical Therapy Dept. OT: Occupational Therapy Dept.
In 2007 study tour of PT Dept was not carried out because of the moving of the Physical Therapy Program of UC to the new campus.

third-grade students in our Nursing, Physical Therapy and Occupational Therapy Departments visit UC or CSU for 9 days in September, when they have no lecture in YPUHS. Table 1 shows the number of students who joined the fall visits by year and by the Departments. The numbers in parentheses are the ratio of the voluntary students to the whole students for each Department.

Thirteen physical therapy students (4 males, 9 females) joined the study tour in Colorado from Sep. 19 to 27, 2012. I went to Colorado with the students as one of the guiding faculty of the Physical Therapy Department. Using a portable pulse oximeter, oxygen saturation (SpO_2) and heart rate (HR) were measured for the 13 students with informed consents. Measuring points were the Narita Airport, Denver City and three points in the Rocky Mountain National Park, where the altitude was as high as 3,595 m. The Route 34 we passed on a chartered bus and the three points in the Rocky Mountain National Park where SpO_2 and HR were measured are shown in a map[1] of Fig.1.

It is well accepted that SpO_2 decreases and HR increases at high altitudes compared with those at low altitudes[2-6]. Inspired oxygen pressure decreases as the barometric pressure (P_B) is lowered at high altitudes. According to the alveolar gas equation, alveolar O_2 pressure (P_AO_2) can be calculated as[7]

$$P_AO_2 = 0.209\ (P_B - 47) - P_aCO_2/\mathrm{RER} + 0.209\ P_aCO_2 \cdot (1 - \mathrm{RER})/\mathrm{RER} \quad (1)$$

where P_aCO_2 and RER are arterial CO_2 pressure and respiratory exchange ratio, respectively, and 0.209 is the O_2 fraction in the air and 47 saturated water vapor pressure at 37 degrees Celsius. An equation to calculate P_B was shown by West[8, 9]. Once P_AO_2 is calculated from Eq.(1), arterial O_2 content C_aO_2 can be obtained as[7]

$$C_aO_2 = 1.39\ SpO_2 \times Hb/100 + 0.00314\ (P_AO_2 - 5) \quad (2)$$

where SpO_2 is in %, Hb hemoglobin concentration in g/dl, and 1.39 is O_2 quantity combined to hemoglobin

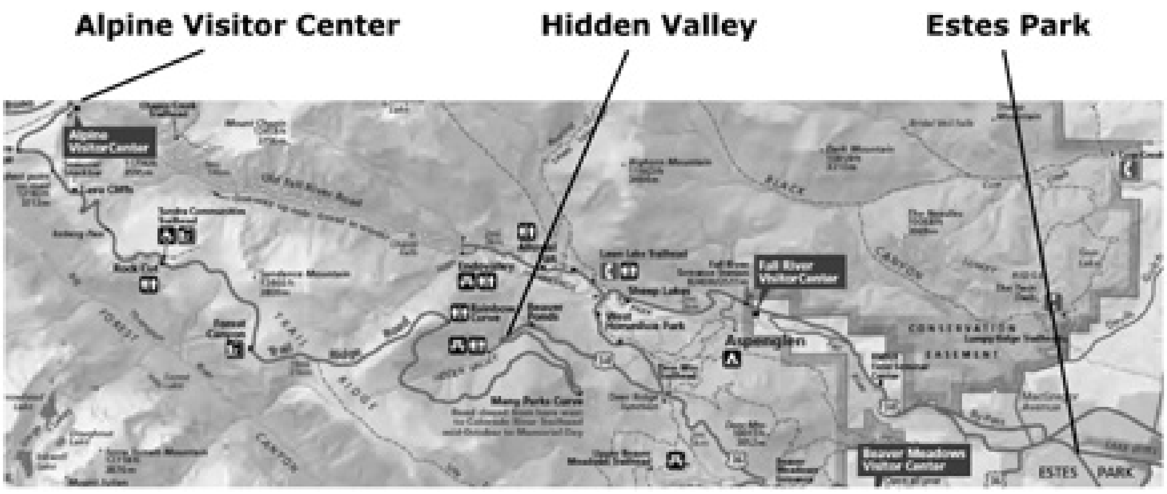

Fig.1 The Alpine Visitor Center (3,595 m) and the other 2 points in the Rocky Mountain National Park where SpO_2 and HR were measured for the 13 students.

in ml/g and 0.00314 the solubility of O_2 in plasma in ml/dl/Torr. The first term in Eq.(2) is chemically combined O_2 to hemoglobin. The second term corresponds to physically dissolved O_2 in plasma with an assumption that alveolar-arterial O_2 gradient is 5 Torr for healthy subjects[10].

Oxygen contents in arterial and mixed venous blood are fundamental parameters to combine cardiac output ($\dot{Q}$) and O_2 uptake ($\dot{V}O_2$) based on the Fick principle[11]:

$$\dot{Q} = HR \times SV = \dot{V}O_2 / (C_aO_2 - C_vO_2) \quad , \qquad (3)$$

where SV is stroke volume. C_aO_2 can be calculated from Eq.(2) by using observed SpO_2. On the other hand, mixed venous O_2 content C_vO_2 cannot be estimated nor be measured easily. Wolfel *et al*.[12] measured C_vO_2 at Pikes Peak in the Rocky Mountain National Park using a venous catheter. Although their research is worthy of special mention, such measurements using a venous catheter are invasive to subjects. In this study we introduce a new method to estimate C_vO_2 from SpO_2 and HR, which can be measured noninvasively with a pulse oximeter.

Since the maximum O_2 volume combined with hemoglobin in arterial blood, which corresponds to C_aO_2 with SpO_2 at 100 % in Eq.(2) is 20.1 vol% (ml/dl)[10] with a normal hemoglobin concentration, C_aO_2 can be approximated as

$$C_aO_2 = 0.201\ SpO_2 + 0.00314\ (P_AO_2 - 5) \quad . \qquad (4)$$

Hemoglobin concentration increases at high altitudes after acclimation[13]. In a short time stay at high altitudes as in this study, such changes in hemoglobin concentration can be excluded.

Combining Eq.(3) with Eq.(4), we have

$$\dot{Q} = HR \times SV = 100\ \dot{V}O_2 / \{0.201\ SpO_2 + 0.00314\ (P_AO_2 - 5) - C_vO_2\} \quad , \qquad (5)$$

with $\dot{Q}$ in ml/min, HR beats/min, SV ml, $\dot{V}O_2$ ml/min, SpO_2 % and C_vO_2 is in vol%. From this equation, SpO_2 is expressed as

$$SpO_2 = (100/0.201)\ (\dot{V}O_2/SV)\ (1/HR) + C_vO_2/0.201 - 0.00314\ (P_AO_2 - 5)/0.201 \ . \qquad (6)$$

$\dot{V}O_2/SV$ and C_vO_2 can be estimated from the slope and intercept of a regression line of SpO_2 on 1/HR, respectively.

2. Methods

The mean age of the 13 third-grade students (4 males, 9 females) were 21 (min.20, max.24) years old. The means and standard deviations for their height and body weight were 162.0 ± 9.5 cm and 58.0 ± 7.8 kg. They had no cardio-respiratory diseases. For the healthy 13 students SpO_2 and HR were measured during a study tour in Colorado using a pulse oximeter (PULSOX-2, KONICA MINOLTA) with their informed consents. They put their index or middle fingers into the oximeter for 1 or 2 seconds in a sitting position to measure SpO_2 and HR. The measuring points were the Narita Airport (altitude 130 m), Denver City (1,609 m), Estes Park (2,499 m), Hidden Valley (2,816 m) and at the Alpine Visitor Center (3,595 m). They did not show dyspnea, palpitation, dizziness or staggering.

3. Results

The averaged values for SpO_2 and HR for 13 students are shown in Table 2 with the altitudes of the 5 points where they were measured; Narita Airport, Denver City, Estes Park, Hidden Valley and the Alpine Visitor Center. SpO_2 was significantly reduced and HR increased with increasing altitude as in the earlier

Table 2 Means and standard deviations of SpO_2 and HR observed at the 5 points.

Place	Altitude (m)	P_B (Torr)	SpO_2 (%)	HR (beats/min)
(a) Narita Airport	130	749	98 ± 0.95	75 ± 11
(b) Denver City	1,609	633	97 ± 1.4	78 ± 5.8
(c) Estes Park	2,499	570	94 ± 1.9	74 ± 7.4
(d) Hidden Valley	2,816	549	93 ± 1.7	92 ± 11
(e) Alpine Visitor Center	3,595	500	87 ± 2.8	85 ± 7.6
Statistics $p < 0.05$			(b) > (c)	(a) < (e) (c) < (e)
Statistics $p < 0.001$			(a) > (c) (a),(b) > (d) (a),(b),(c),(d) > (e)	(a),(b),(c) < (d)

P_B was calculated from Eq.(7).

Table 3　Calculated parameters at the 5 points.

Place	P_AO_2 (Torr)	C_aO_2 (vol%)	$C_aO_2-C_vO_2$ (vol%)	HR×($C_aO_2-C_vO_2$)/100 (min^{-1})
Narita Airport	96.8	20.0	7.8	5.9
Denver City	72.5	19.6	7.4	5.8
Estes Park	59.4	19.1	6.9	5.1
Hidden Valley	55.0	18.7	6.5	6.0
Alpine Visitor Center	44.7	17.5	5.3	4.5

P_AO_2 was calculated from Eq. (1).
C_aO_2 was calculated from Eq. (4).

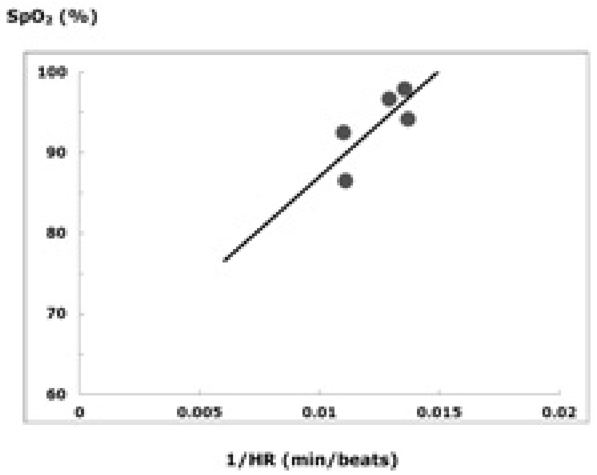

Fig.2　Correlation between the averaged values of SpO_2 and 1/HR measured for the 13 students at the 5 points. The regression line is shown by Eq. (8).

literatures[2-6]. The P_B values in Torr at each altitude were calculated from the following equation[8, 9],

$$P_B = \exp(6.63268 - 0.1112\,h - 0.00149\,h^2), \quad (7)$$

with an altitude h in m.

In Table 3, P_AO_2 were calculated from Eq.(1) with assuming the standard values of P_aCO_2 and RER as 40 Torr and 0.8, respectively, together with the calculated P_B values from Eq.(7) at each altitude. At extremely high altitudes like Mt.Everest[14, 15] or during a long stay at high altitudes like Mt Fuji[16] hyperventilation occurs and P_aCO_2 becomes less than 40 Torr. However, our students kept normal breathing during a short stay at 3,595 m and their P_aCO_2 were thought to remain at 40 Torr.

Correlation between SpO_2 in % and 1/HR in min/beats is shown in Fig.2. The regression line was

$$SpO_2 = 2650\,(1/HR) + 60.6 \quad (8)$$

with a coefficient of determination $R^2 = 0.600$. $\dot{V}O_2/SV$ was obtained as 5.32 from the slope and C_vO_2 as 12.2 vol% from the intercept of the regression line according to Eq.(6) using P_AO_2 in Table 3.

C_aO_2 was calculated from Eq.(4) using the observed SpO_2. C_vO_2 was estimated from the intercept of the regression line in Fig.2 as 12.2 vol% with the P_AO_2 values at each altitude. Then, arterio-venous O_2 content difference $C_aO_2 - C_vO_2$ was calculated as shown in Table 3. Thus obtained $C_aO_2 - C_vO_2$ was multiplied by HR in Table 2 for each altitude. HR ($C_aO_2 - C_vO_2$) is equal to $\dot{V}O_2/SV$ according to Eq.(3).

4. Discussion

To assess the gas exchange in a lung C_vO_2 is one of the most important factors connecting cardiac output and oxygen uptake. Unlike the other fundamental factor C_aO_2, C_vO_2 cannot be easily measured. Therefore, estimation of C_vO_2 is in high relevance to clinical medicine as well as to basic research. At fixed altitudes C_aO_2 slightly increases and C_vO_2 obviously decreases during exercise[17], which cause the extension of $C_aO_2 - C_vO_2$. The slight increase in C_aO_2 is due to the blood concentration by sweating during exercise. We observed $C_aO_2 - C_vO_2$ extension during exercise by a rebreathing method[18]. The $C_aO_2 - C_vO_2$ at rest was 6.8 vol% and that during exercise with $\dot{V}O_2$ at 1,320 ml/min was 10.3 vol%[18]. The $C_aO_2 - C_vO_2$ value in Table 3 at low altitude (Narita Airport) corresponds to that from the rebreathing method at rest[18]. Without exercise C_aO_2 and C_vO_2 remain constant at fixed altitudes.

If the altitude is varied, C_aO_2 will decrease with increasing altitude in accord with the decrease in P_AO_2. In this study without exercise, C_aO_2 decreased with increasing altitude as shown in Table 2, while C_vO_2 was estimated from the correlation between SpO_2 and 1/HR as 12.2 vol%. Since C_vO_2 was obtained from the regression line across the data for the 5 points, thus

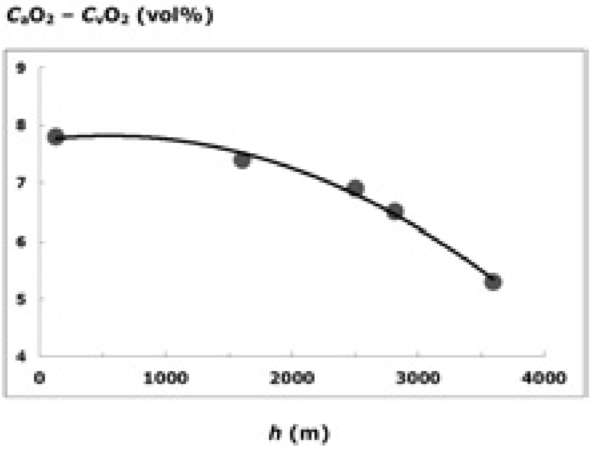

Fig.3 Correlation between the arterio-venous O_2 content difference $C_aO_2 - C_vO_2$ and the altitudes h at the 5 points.The regression line is shown by Eq. (9).

obtained C_vO_2 should be constant regardless of the altitudes. The observed fairly high correlation between SpO_2 and 1/HR suggests that resting C_vO_2 remained unchanged regardless of the altitudes. As shown in Table 3 the $C_aO_2 - C_vO_2$ value at 3,595 m was 5.2 vol%, which was higher than that reported by Wolfel *et al*.[12] 4.0 vol% at Pikes Peak 4,300 m. This difference is probably due to the lower C_aO_2 at the higher altitude. A relation between $C_aO_2 - C_vO_2$ in vol% and altitude h in m is shown in Fig.3 with a regression line as

$$C_aO_2 - C_vO_2 = -0.265 \times 10^{-6} h^2 + 0.289 \times 10^{-3} h + 7.74 \qquad (9)$$

with a coefficient of determination $R^2 = 0.992$. At 4,300 m $C_aO_2 - C_vO_2$ is calculated from this regression line as 4.03 vol%, which is nearly equal to the Wolfel's value[12], indicating that our estimated C_vO_2 is consistent with their observed value.

$\dot{V}O_2$/SV was obtained as 5.32 from the slope of the regression line between SpO_2 and 1/HR. The $\dot{V}O_2$/SV value obtained from SpO_2 and HR with the data for across the 5 points also remained unchanged regardless of the altitudes. $\dot{V}O_2$/SV can be written as HR ($C_aO_2 - C_vO_2$) /100 from Eq.(3) with $\dot{V}O_2$ in ml/min., SV ml and $C_aO_2 - C_vO_2$ in vol%. HR ($C_aO_2 - C_vO_2$) /100 are shown in Table 3 at each altitude. The averaged HR ($C_aO_2 - C_vO_2$) /100 for the 5 points is 5.46 which is close to the $\dot{V}O_2$/SV value obtained from the slope of the regression line between SpO_2 and 1/HR. This agreement suggests that $\dot{V}O_2$/SV remains constant regardless of the altitudes. In healthy Japanese young adults $\dot{V}O_2$ is around 200 mL and SV is around 70 mL at rest[19]. Therefore, $\dot{V}O_2$/SV is expected to be nearly 3. The higher observed $\dot{V}O_2$/SV value than the expected value may be caused by higher $\dot{V}O_2$ or lower SV. Wolfel *et al*.[12] reported the increase in $\dot{V}O_2$ and the decrease in SV at rest from sea level to the summit of Pikes Peak at 4,300 m. Although we measured neither $\dot{V}O_2$ nor SV in this study, our higher $\dot{V}O_2$/SV value may be due to the increase in $\dot{V}O_2$ and the decrease in SV at high altitudes.

The obtained $C_aO_2 - C_vO_2$ and $\dot{V}O_2$/SV values were within normal ranges, indicating that respiratory and circulatory functions were well-matched despite the decrease in SpO_2 for our students by more than 10 % within 6 hours.

In conclusion, C_vO_2 and $\dot{V}O_2$/SV can be estimated from the regression line between SpO_2 and 1/HR measured at different altitudes. At low altitudes SpO_2 in healthy subjects is hardly less than 90 % even with severe exercise, and in this sense the application of our noninvasive method to estimate C_vO_2 and $\dot{V}O_2$/SV is limited. However, our method can be used by measuring SpO_2 and HR with inspired gases at various low O_2 concentrations which simulate high altitudes.

Acknowledgements

I am grateful to the thirteen students for the cooperation in the measurements of SpO_2 and HR. I express my gratitude to all of the faculty and staffs of UC, CSU and YPUHS who participate in the sister-school relationships with my sincere wishes for the further development of the relationships. Thanks are also due to Mr.Sam Goodman for searching the altitudes in Colorado.

References

1) Detailed Map of Rocky Mountain National Park. [cited 2012 Dec.29]. Available from: http://www.nps.gov/romo/planyourvisit/upload/parkmap_2011.pdf

2) Noguchi I. SpO_2/pulse rate ratio and the prediction of the general condition —A study during the

mountaineering on the Mt.Damavand (5,671 m, Iran) —. *Jpn J Mount Med*.1993; **13**: 99-106 (in Japanese).

3) Allemann Y, Rotter M, Hutter D, Lipp E, Sartori C, Scherrer U, Seiler C. Impact of acute hypoxic pulmonary hypertension on LV diastolic function in healthy mountaineers at high altitude. *Am J Physiol Heart Circ Physiol*. 2004; **286**: H856-62.

4) Tanobe K, Saito S. Relationship between arterial oxygen saturation and heart rate variability among trekkers at 3456 m. *Jpn J Mount Med*. 2003; **23**: 101-5 (in Japanese).

5) Agostoni P, Swenson ER, Bussotti M, Revera M, Meriggi P, Faini A, Lombardi C, Bilo G, Giuliano A, Bonacina D, Modesti PA, Mancia G, Parati G . High-altitude exposure of three weeks duration increases lung diffusing capacity in humans. *J Appl Physiol*. 2011; **110**: 1564-71.

6) Clarenbach CF, Senn O, Christ AL, Fischler M, Maggiorini M, Bloch KE. Lung function and breathing pattern in subjects developing high altitude pulmonary edema. *PLoS One*, 2012; **7**: 1-6.

7) Grocott MPW, Martin DS, Levett DZH, McMorrow R, Windsor J, Montgomery HE. Arterial blood gases and oxygen content in climbers on Mount Everest. *New Eng J Med*. 2009; **360**: 140-9.

8) West JB, Prediction of barometric pressures at high altitudes with the use of model atmospheres. *J Appl Physiol*. 1996; **81**: 1850-4.

9) West JB, Barometric pressures on Mt.Everest: new data and physiological significance. *J Appl Physiol*. 1999; **86**: 1062-6.

10) Bullock J, Boyle J Ⅲ, Wang MB. Physiology. 4th ed. Baltimore: Lippincott Williams & Wilkins; 2001.

11) Fick A. Uber die Messung des Blutquantums in den Herzventrikeln. *Sitzungs Berichte für das Gesellschaftjahr 1870.(Sitzung am Juli 1870) Sitzungs Berichte Physiologishe-Medizinishe Gesellschaft zur Wurzburg* 1870; **16**:1.XVI-VII.

12) Wolfel EE, Selland MA, Cymerman A, Brooks GA, Butterfield GE, Mazzeo RS, Grover RF, Reeves JT. O_2 extraction maintains O_2 uptake during submaximal exercise with β-adrenergic blockade at 4,300 m. *J Appl Physiol*. 1998; **85**: 1092-1102.

13) Villafuerte FC, Cárdenas R, Monge-C C. Optimal hemoglobin concentration and high altitude: a theoretical approach for Andean men at rest. *J Appl Physiol* 2004; **96**: 1581-8.

14) Pugh LGCE, Resting ventilation and alveolar air on mount Everest: with remarks on the relation of barometric pressure to altitude in mountains. *J Physiol*. 1957; **135**: 590-610.

15) West JB. Respiratory and circulatory control at high altitudes. *J Exp Biol*. 1982; **100**: 147-157.

16) Masuda A, Masuyama S. Standard values of SpO_2 and pulse rate on the top of Mt.Fuji 3776 m. *Jpn J Mount Med*. 2007; **27**: 163-7 (in Japanese).

17) Åstrand P, Rodahl K. Textbook of Work Physiology. New York: McGraw-Hill; 1970.

18) Uchida K, Shibuya I, Mochizuki M. Simultaneous measurement of cardiac output and pulmonary diffusing capacity for CO by a rebreathing method. *Jap J Physiol* (successor; *J Physiol Sci*). 1986; **36**: 657-70.

19) Ohno H, Izawa T, Nagasawa J, Fushiki T, Atomi Y, Sato Y, Haga S, Dictionary of exercise physiology and biochemistry, Tokyo, Taisyu-kan, 2001 (in Japanese).

抄　　録

2012 年 9 月 17 日から 26 日にコロラド州での研修に参加した山形県立保健医療大学理学療法学科 3 年の 13 名の健常学生（男性 4 名、女性 9 名）について動脈血酸素飽和度（SpO_2）および心拍数（HR）が測定された。13 名の SpO_2 の平均値および標準偏差は、成田空港（標高 130 m）、デンバー市内（1,609 m）、エステス・パーク（2,499 m）、ヒィデン・バレー（2,816 m）およびアルパイン・ビジター・センター（3,595 m）で、それぞれ 98 ± 0.95、 97 ± 1.4、94 ± 1.9、93 ± 1.7 および 87 ± 2.8％ であった。同時に測定された HR の平均値は、それぞれ 75 ± 11、78 ± 5.8、74 ± 7.4、92 ± 11 および 85 ± 7.6 beats/min であった。これらの値は、成田空港での値を除き、デンバー滞在 4 日目に 6 時間以内に測定されたものである。SpO_2 が短時間に 10％ 以上低下したにもかかわらず標高 3,595 m で気分が悪くなった学生はいなかった。

フィックの原理に基づいて SpO_2（％）と 1/HR（min/beats）の相関を解析し、SpO_2 = 2650（1/HR）＋60.6（決定係数 0.600）の回帰直線を得た。学生たちのヘモグロビン濃度が正常であると仮定し、ヘモグロビンに結合する酸素含量の基準値 20.1 vol％を用いて回帰直線の切片から混合静脈血の酸素含量（C_vO_2）が 12.2 vol％と得られた。SpO_2 から得られた動脈血の酸素含量（C_aO_2）との差 $C_aO_2-C_vO_2$ は、静脈カテーテル法あるいは再呼吸法で得られた文献値と矛盾していなかった。これらの結果は、C_vO_2 が SpO_2 および HR を測定するという非侵襲的方法で推定出来ることを示唆している。

キーワード：混合静脈血酸素含量、動脈血酸素飽和度、心拍数、高地、コロラド