AAL-TDR-61-55

INFLUENCE OF HYPOXIA ON THERMAL HOMEOSTASIS IN MAN

TECHNICAL DOCUMENTARY REPORT AAL-TDR-61-55

June 1962

ARCTIC AEROMEDICAL LABORATORY
AEROSPACE MEDICAL DIVISION
AIR FORCE SYSTEMS COMMAND
FORT WAINWRIGHT, ALASKA

Project 8238-20

(Prepared under Contract AF 41(657)-330 by
Thomas P. K. Lim and Ulrich C. Luft,
Lovelace Foundation for Medical
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Rpt. AAL-TDR-61-55. INFLUENCE OF HYPOXIA ON THERMAL HOMEOSTASIS IN MAN. June 1962. 20p., incl. tables, 12 refs.

Unclassified Report

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1. Anoxia
2. Heat Production (Biology)
3. Exposure
4. Body Temperature
5. Metabolism
6. Circulatory System
7. Respiration
8. Perspiration

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ABSTRACT

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PUBLICATION REVIEW

Horace F. Drury

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Director of Research

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INFLUENCE OF HYPOXIA ON THERMAL HOMEOSTASIS IN MAN

SECTION 1. INTRODUCTION

Our knowledge on hypoxia in relation to homeothermic mechanisms is alarmingly wanting and insufficient. Some of the observations made on body temperature regulation during Alpine expeditions are inherently disconcerting because not only O_2 deficiency but also the cold and possible other stressive environmental factors are operating together under most of these circumstances. On the other hand, the laboratory studies in which the environmental conditions were controlled have produced various refutable data which require much clarification and further study.

It is the purpose of this investigation to examine the extent of disturbance in the thermoregulatory mechanisms of men exposed to mild hypoxia under neutral, cold, and warm environmental conditions. Particular attention has been paid to the behaviors of core and shell temperatures as well as the concomitant alterations of metabolic rate and the cardiovascular parameters under these conditions.

SECTION 2. METHODS

Six healthy male subjects, who have resided in Albuquerque, New Mexico (altitude = 5,300 ft, P_B = 630 mm Hg) from a minimal seven months to a maximal six years, volunteered for the test. Among them four subjects (UL, TL, LK and AD) completed the whole program of neutral, cold, and warm series, while one (JP) of the remaining two subjects participated in the cold and neutral series, and the other (JC) in the warm and neutral series only. At three different environmental conditions of warm (40.5° C, Relative Humidity = 80%), neutral (27.5° C, R.H. = 30%) and cold (4° C, R.H. = 30%) temperatures, the subjects were exposed to a tracheal oxygen tension of approximately P_{IO_2} = 65 mm Hg for two hours. For the control measurement the subject underwent the same procedure at three temperature levels breathing room air. They came to the laboratory after having a light breakfast, and the test was run in the morning hours. The subjects were seminude, wearing only shorts, and rested on a cart, maintaining supine position throughout the test. The physical characteristics of these subjects are shown in Table I.

TABLE I

BIOSTATISTICS OF SIX TEST SUBJECTS

Subject	Age	Sex	Wt(Kg)	Ht(cm)	S.A. (m^2)
UL	50	M	82.8	183	2.01
TL	36	M	70.1	174	1.82
LK	31	M	80.7	188	2.01
AD	26	M	85.7	186	2.06
JP	37	M	84.0	171	1.97
JC	31	M	73.5	176	1.87

Temperature Chamber and Thermometry

To provide a known thermal stress to the subject a temperature chamber was used. It was made of plywood, measuring approximately 3 x 3.5 x 8 feet, and was insulated with Rockwood (Figure 1). The inside temperature of the chamber could be maintained automatically at any desired level within ±1° C over the range of 0 to 50° C. In the cold and neutral series the relative humidity inside the box with a test subject enclosed did not change appreciably, remaining at about 30 per cent, whereas in the warm series it was brought up to 80 per cent initially by a vaporizor and was maintained at this level throughout the test. (The average daytime relative humidity in Albuquerque, New Mexico, in 1959 was 34 per cent, according to U. S. Weather Bureau data.) The fans inside the box distributed the air, temperature and humidity uniformly, the wind velocity at the center of the box being no more than two miles per hour.

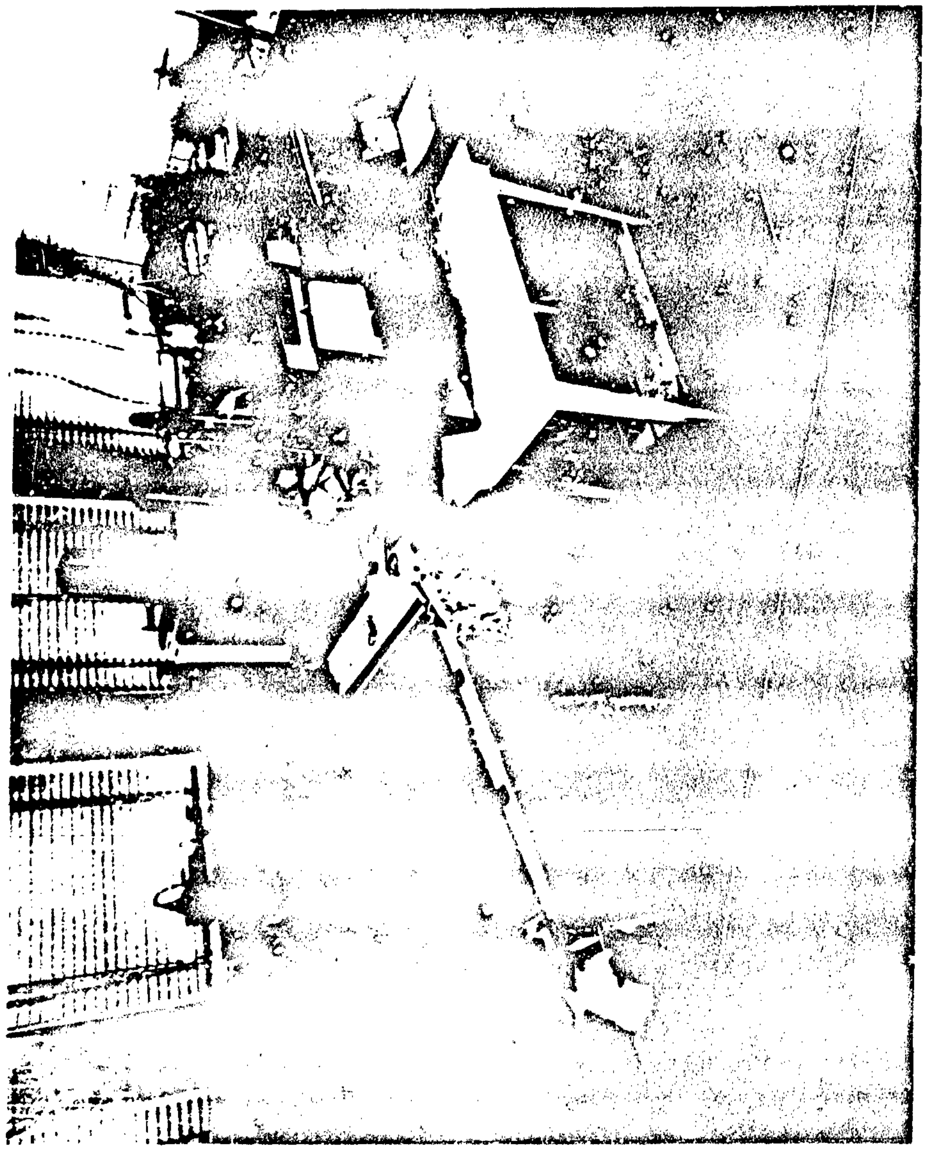


FIGURE 1.

Temperatures were measured by means of copper-constantan (30 gauge) thermocouples connected to the Honeywell automatic temperature recorder. Skin thermocouples were specially constructed, and the seven point system of Hardy and DuBois (1938) was used for computation of mean skin temperature. As core temperature, rectal temperature was monitored at the depth of 10 cm. In addition, whenever it was possible, esophageal temperature was measured in conjunction with rectal temperature.

Induction of Hypoxia

Hypoxia was induced by means of a rebreathing system, which is shown schematically in Figure 2. This system consisted of a spirometer (9 liter capacity), a canister for CO_2 absorption, a large carboy for mixing of expired air, a Beckman O_2 analyzer and another spirometer (4 liter capacity) for O_2 supply. As a subject rebreathed in the closed system the partial pressure of O_2 in the system fell gradually, as monitored continuously by the O_2 analyzer. When P_{O_2} reached a desired level (e.g., 65 mm Hg) the needle valve between the spirometers was opened, introducing 100% O_2 into the system at a rate sufficient to meet the metabolic demand. Once an equilibrium between the metabolic demand and O_2 supply was reached, the spirometer tracing remained horizontal. With this system (shown in Figure 2) it was possible to sustain hypoxic levels within ±3 mm Hg of P_{O_2}. The advantages of using this rebreathing system were that it was readily possible to reach any desired level of hypoxia and that it was much more economical than using commercially available hypoxic gases.

Cardiopulmonary Measurements

In the control studies with room air breathing the expired air was collected in a Douglas bag for three to five minutes at the 30th, 75th, and 120th minute (open-circuit method). The content of the bag was determined by the Scholander gas analyzer, and total ventilation ($\dot{V}_E$), O_2 consumption ($\dot{V}_{O_2}$), CO_2 production ($\dot{V}_{CO_2}$), respiratory gas exchange ratio (RER), and the ventilatory equivalent for O_2 ($V_{E_{O_2}}$) were computed. During the collection of expired gas, respiratory rate (RR) was also counted. In the closed circuit for rebreathing, total ventilation was obtained from the tracings of the spirometer O, and O_2 consumption from the slopes of spirometer L. At the 30th, 75th and 120th minute both inspired and expired airs were sampled simultaneously from the side-arms of C and I for analyses (Figure 2). These analyses served not only for estimation of RER but also as a valuable check for O_2 and CO_2 levels in inspiratory and expiratory sides. The

REBREATHING SYSTEM

A. Beckman oxygen analyzer
B. Aqua pump
C. Side tap for sampling inspiratory gas
D. Three-way stopcock
E. Mouthpiece
F. Rudolph one-way valve
G. Three-way stopcock
H. Carboy (40 liter capacity)
I. Side tap for sampling expiratory gas
J. Carbon dioxide absorber
K. Oxygen tank
L. McKesson spirometer (4 liter capacity)
M. Manual needle valve
N. Flow meter
O. Collins spirometer (9 liter capacity)

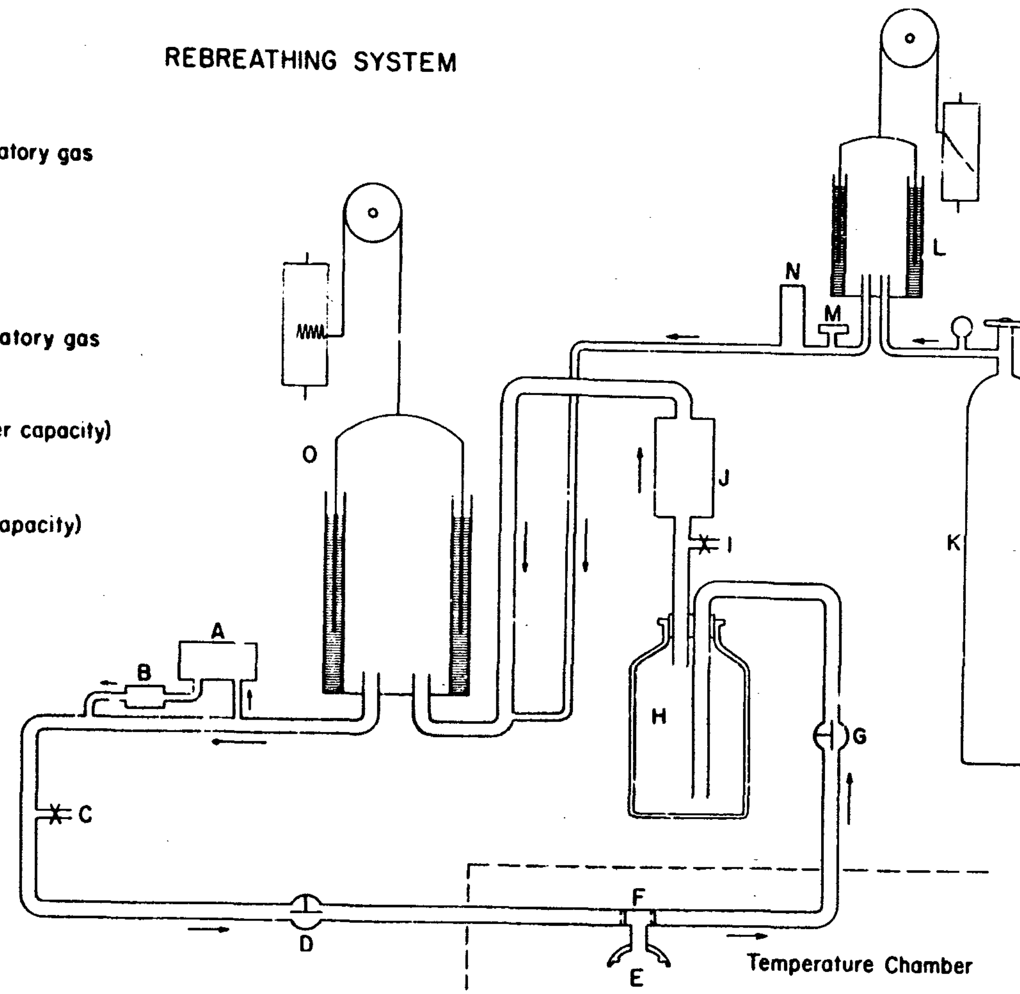


FIGURE 2.

average O_2 and CO_2 contents of inspiratory air during the entire hypoxic series were 10.76% ± 1.18% for O_2 and 0.05% ± 0.02% for CO_2, while the values of expiratory air were 7.43% ± 1.20% for O_2 and 3.15% ± 0.35% for CO_2.

Throughout this study the electrocardiogram was routinely registered by means of a Gilson's polygraph, and blood pressure was determined by auscultation every ten minutes.

Heat Balance

In the calculation of heat balance, heat production was estimated from the O_2 consumption and respiratory gas exchange ratio using Weir's formula (Weir, 1949): $K = 3.9010 + 1.0948 \times R$, where K is the caloric value of 1 liter of O_2 (Kcal) and R is the respiratory gas exchange ratio. Heat debt (or storage) was derived from the following formula (Burton and Edholm, 1955): $\frac{M \times s}{S} \times \frac{d\theta}{dt}$, where M is the gross body weight in kg, s is the specific heat of the human body (employing the value of 0.83), S is the surface area in M^2, and $d\theta/dt$ is the rate of change in mean body temperature in °C/hr. The mean body temperature was estimated from the rectal and mean skin temperatures. In the calculation of heat debt the mean body temperature value of the immediately preceding sample was taken as a base level. The heat debt is positive when heat loss exceeds the heat production (e.g., in the cold) and it is negative when the heat production exceeds heat loss (e.g., in the warm environment).

SECTION 3. RESULTS

Subjective Symptoms

The prevailing symptoms in most of the test subjects following the hypoxic test were headache and malaise which lasted for several hours. The consensus was in preference of cold plus hypoxia test to heat plus hypoxia. Nausea, vomiting, or euphoria were manifested in one of the subjects. The extrasystole and the Cheyne-Stokes type of breathing were common, the latter probably coinciding with sleeping episodes. In the cold series the pain in the toes was a universal complaint with or without hypoxia. In addition, "cold diuresis" was frequently manifested.

Body Temperature

Neither in the neutral nor in the cold series did the hypoxic level of P_{IO_2} = 65 mm Hg cause significant alterations in either core (rectal) or shell (mean skin) temperature when these temperatures were compared to those obtained under similar environmental conditions with room air breathing. In the warm environment, however, the level of core temperature in hypoxia was distinctly higher than that during room air breathing in all subjects. The average data of body temperatures on five subjects in each environment with and without hypoxia are diagrammatically shown in Figures 3, 4, and 5.

In the neutral environment the influence of hypoxia on body temperatures was practically nil, as shown in Figure 3. There appeared no major change in either core or shell temperature, the former remaining at 37° C and the latter at 32.5° C throughout a two-hour period of hypoxia or room air breathing. In the cold environment the vigorous shivering response effectively prevented a fall in core temperature, maintaining the rectal temperature at 37° C (Figure 4). This was the case both with and without hypoxia. On the other hand, shell temperature continued to fall exponentially from 27° C at the onset to 23° C at the end of the test. Although the average curve for mean skin temperature with hypoxia appears slightly higher than that with room air after 40 minutes in the chamber (Figure 4), a statistical evaluation revealed no significant difference between the two curves. The reduction in foot temperature was more drastic, falling from 22° C at the beginning to 11° C at the end of the two-hour sojourn in the box. The rate of fall and the foot temperature level were the same with or without hypoxia. In the warm environment the core temperature continued to climb almost linearly throughout the test (Figure 5) despite the profuse sweating. The most meaningful phenomenon in this environment was the fact that the rectal temperature in hypoxia was significantly higher than that during room air breathing. Meanwhile, it was found that the mean skin temperature in hypoxia was not statistically different from that with room air breathing, although the average value of the former was somewhat higher than that of the latter (Figure 5).

Metabolism and Respiration

The averaged data on gas exchange and respiration in each of three thermal environments with and without hypoxia are shown in Tables II and III. Although the mean oxygen consumption at neutral temperature with room air breathing was 290 ml/min and that with hypoxia was

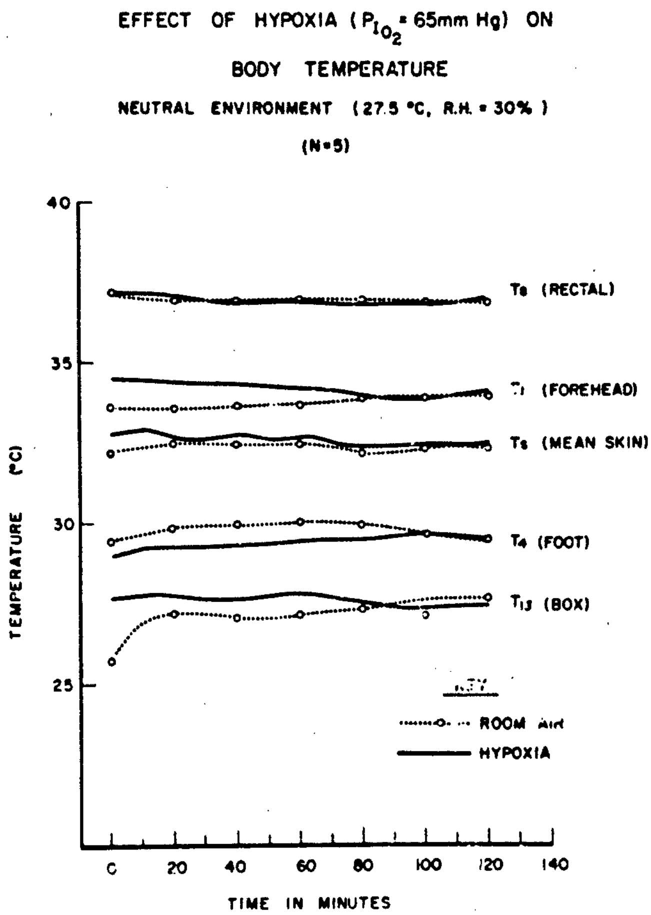
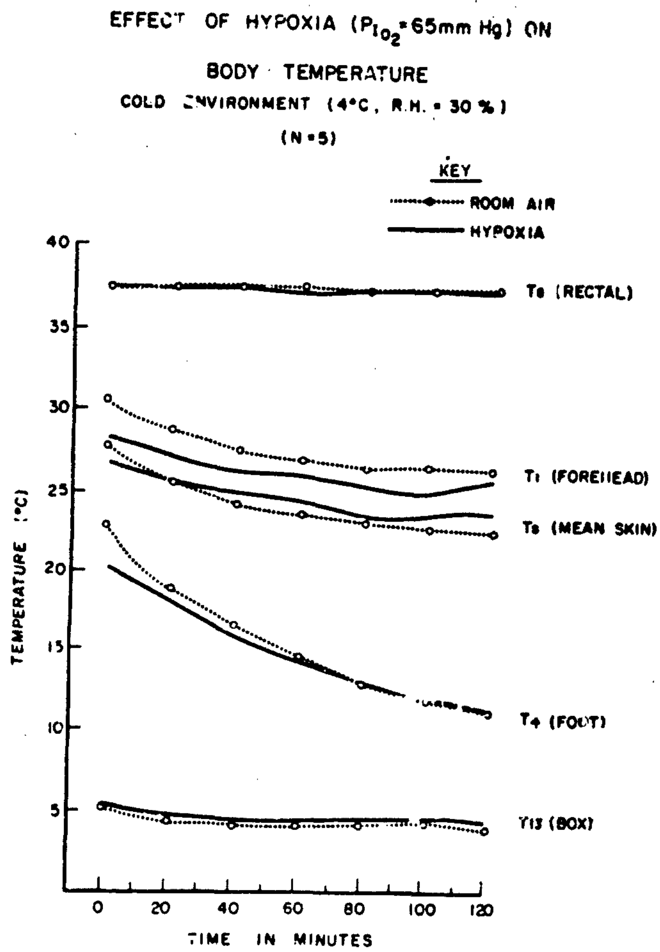
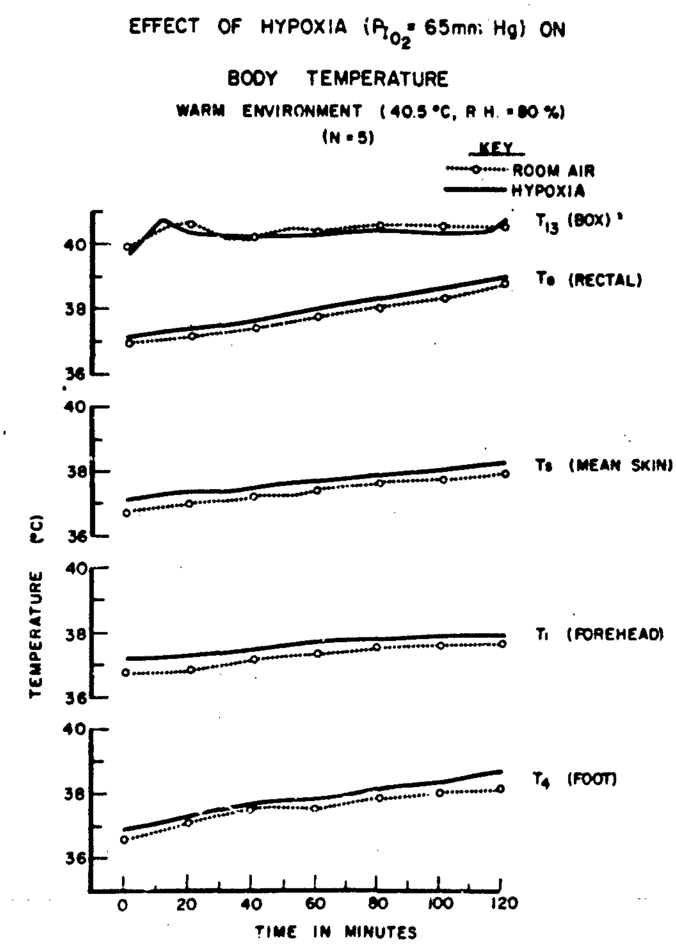

EFFECT OF HYPOXIA ($P_{I_{O_2}}$ = 65mm Hg) ON
BODY TEMPERATURE
NEUTRAL ENVIRONMENT (27.5 °C, R.H. = 30%)
(N=5)
TEMPERATURE (°C)
40
35
30
25
Tr (RECTAL)
(FOREHEAD)
Ts (MEAN SKIN)
T4 (FOOT)
T13 (BOX)
ROOM AIR
HYPOXIA
C
20
40
60
80
100
120
140
TIME IN MINUTES

FIGURE 3.



EFFECT OF HYPOXIA ($P_{I_{O_2}}$=65mm Hg) ON
BODY TEMPERATURE
COLD ENVIRONMENT (4°C, R.H. = 30 %)
(N=5)
KEY
ROOM AIR
HYPOXIA
40
35
30
25
20
15
10
5
TEMPERATURE (°C)
Tr (RECTAL)
Tf (FOREHEAD)
Ts (MEAN SKIN)
T4 (FOOT)
T13 (BOX)
0
20
40
60
80
100
120
TIME IN MINUTES

FIGURE 4.



EFFECT OF HYPOXIA ($P_{I_{O_2}}$ = 65mm Hg) ON
BODY TEMPERATURE
WARM ENVIRONMENT (40.5 °C, R.H. = 80 %)
(N = 5)
KEY
ROOM AIR
HYPOXIA
T_{13} (BOX)
Tr (RECTAL)
Ts (MEAN SKIN)
Ti (FOREHEAD)
T_4 (FOOT)
TEMPERATURE (°C)
40
38
36
0
20
40
60
80
100
120
TIME IN MINUTES

FIGURE 5.

approximately 310 ml/min, statistical comparisons revealed no meaningful difference between the two data at the 30th and 120th minute samples, with an exception of borderline significance at the 75th minute sample (Table II). This was also true in the warm environment. Oxygen consumption in the cold with or without hypoxia was practically the same throughout the two-hour period. Thus, it may be concluded from these data that at the level of oxygen partial pressure employed in this study, hypoxia exerts virtually no effect on the metabolic rate.

Since the intensity of shivering can be estimated indirectly from the increased amount of oxygen consumed during the involuntary muscular contraction, one of the corollaries of the above finding is that the hypoxic level of $P_{I_{O_2}}$ = 65 mm Hg does not appreciably influence shivering response to cold in men.

Contrary to its effect on metabolic rate, hypoxia caused an increase (30% to 40%) in total ventilation in the neutral environment, this being totally achieved by an increased tidal volume (Table III). Furthermore, the cold stimulus alone brought a considerable increase (120% to 200%) in ventilation with room air breathing. When these ventilatory increments for single stress of hypoxia or cold are examined in conjunction with the observed increase in ventilation during the combined stresses of cold and hypoxia, it is possible to speculate the mode of action of these stimuli on respiration: a simple arithmetic addition of ventilatory increment for single stress of hypoxia and cold indicates approximately 3 to 5 liters/min lower value than the ventilatory increment observed during the combined operation of cold and hypoxia, which fact suggests a synergistic action of these stimuli on respiration rather than an additive one. The increase in total ventilation due to heat stimulus alone was approximately 20% to 40%, and here, again, a synergistic action of heat and hypoxia on respiration is indicated.

Cardiovascular Responses

As a rough estimate of perspiration, gross body weight of the test subject was measured (accuracy: ± 100 g) immediately before and after the warm series. The average weight loss in five subjects following the test was 1.5 ± 0.4 kg with room air breathing and 1.3 ± 0.2 kg with hypoxia, revealing no significant difference in the amount of perspiration with or without hypoxia.

Granting that the alterations in mean skin temperature reflect the peripheral vasomotor activity in general, the behaviors of surface temperature observed in three thermal conditions with and without hypoxia did not disclose any notable effect of hypoxia (Figures 3, 4 and 5). Nonetheless, it was

TABLE II.

METABOLIC RATE IN NEUTRAL, COLD, AND WARM ENVIRONMENT WITH HYPOXIA AND WITH ROOM AIR BREATHING

(n = 5) (Mean Value ± S. D.)

Environments	Time (min.)	$\dot{V}_{O_2}$ ml/min (STPD)	t / p	$\dot{V}_{CO_2}$ ml/min (STPD)	RER
GROUP A (UL, TL, LK, AD, and JP)					
27.5° C + air	30	287 ± 72		238 ± 65	0.82 ± 0.02
"	75	290 ± 32		234 ± 33	0.81 ± 0.05
"	120	290 ± 47		238 ± 51	0.81 ± 0.04
27.5° C + hypoxia	30	312 ± 42	t = 1.16 0.3<p<0.4	266 ± 67	0.82 ± 0.04
"	75	322 ± 39	t = 3.71 0.02<p<0.05	285 ± 103	0.83 ± 0.06
"	120	307 ± 20	t = 0.90 0.4<p<0.5	297 ± 96	0.96 ± 0.28
4° C + air	30	566 ± 132		499 ± 119	0.88 ± 0.04
"	75	755 ± 154		673 ± 139	0.89 ± 0.06
"	120	774 ± 195		687 ± 172	0.89 ± 0.09
4° C + hypoxia	30	646 ± 106	t = 1.14 0.3<p<0.4	620 ± 83	0.94 ± 0.09
"	75	744 ± 110	t = 0.15 0.5<p	648 ± 53	0.90 ± 0.19
"	120	798 ± 52	t = 0.29 0.5<p	685 ± 140	0.85 ± 0.14
GROUP B (UL, TL, LK, AD, and JC)					
27.5° C + air	30	294 ± 73		248 ± 67	0.84 ± 0.01
"	75	288 ± 32		233 ± 32	0.81 ± 0.01
"	120	294 ± 46		238 ± 51	0.80 ± 0.01
27.5° C + hypoxia	30	314 ± 40	t = 0.83 0.4<p<0.5	274 ± 60	0.83 ± 0.12
"	75	315 ± 43	t = 2.24 0.05<p<0.1	285 ± 103	0.87 ± 0.16
"	120	302 ± 21	t = 0.41 0.5<p	288 ± 101	0.96 ± 0.29
40.5° C + air	30	322 ± 48		281 ± 67	0.87 ± 0.08
"	75	344 ± 32		300 ± 48	0.87 ± 0.08
"	120	344 ± 28		296 ± 35	0.86 ± 0.07
40.5° C + hypoxia	30	354 ± 25	t = 1.50 0.2<p<0.3	332 ± 50	0.94 ± 0.10
"	75	383 ± 24	t = 3.60 0.02<p<0.05	310 ± 19	0.81 ± 0.04
"	120	380 ± 42	t = 1.75 0.1<p<0.2	302 ± 38	0.80 ± 0.09

TABLE III

RESPIRATION IN NEUTRAL, COLD, AND WARM ENVIRONMENTS
WITH HYPOXIA AND WITH ROOM AIR BREATHING

(n = 5) (Mean Value ± S.D.)

Environments	Time (min.)	$\dot{V}_E$ l/min (BTPS)	RR	TV ml (BTPS)	$V_{E_{O_2}}$ ($\dot{V}_E/\dot{V}_{O_2}$)
		GROUP A (UL, TL, LK. AD, and JP)			
27.5° C + air	30	8.712 ± 2.440	13.8 ± 2.9	653 ± 236	30.3 ± 2.6
"	75	8.743 ± 1.460	13.0 ± 3.8	708 ± 192	30.1 ± 2.8
"	120	9.144 ± 2.280	12.5 ± 4.2	799 ± 339	31.[illegible] ± 3.2
27.5° C + hypoxia	30	11.457 ± 1.872	10.1 ± 3.4	1,211 ± 360	37.0 ± 6.3
"	75	11.668 ± 3.442	10.6 ± 1.4	1,096 ± 148	35.9 ± 3.3
"	120	12.435 ± 2.602	11.0 ± 2.2	1,156 ± 342	40.2 ± 3.0
4° C + air	30	20.500 ± 8.036	13.8 ± 4.7	1,515 ± 505	35.1 ± 7.2
"	75	26.277 ± 8.948	16.4 ± 5.9	1,643 ± 312	34.5 ± 7.8
"	120	28.203 ± 7.911	16.9 ± 4.7	1,685 ± 258	37.2 ± 9.9
4° C + hypoxia	30	28.719 ± 8.521	14.8 ± 4.0	2,012 ± 589	43.9 ± 7.2
"	75	34.079 ± 5.902	19.1 ± 4.8	1,861 ± 469	46.4 ± 9.7
"	120	34.340 ± 8.508	19.6 ± 6.2	1,831 ± 457	42.9 ± 9.2
		GROUP B (UL, TL, LK, AD, and JC)			
27.5° C + air	30	8.678 ± 2.441	[illegible].3 ± 2.1	726 ± 389	29.4 ± 2.3
"	75	8.311 ± 1.381	[illegible] ± 4.1	761 ± 161	28.8 ± 2.5
"	120	8.901 ± 2.331	10.8 ± 2.1	855 ± 296	29.8 ± 3.2
27.5° C + hypoxia	30	11.133 ± 1.730	9.9 ± 3.2	1,200 ± 369	35.0 ± 3.2
"	75	12.044 ± 2.482	10.8 ± 1.3	1,116 ± 139	38.1 ± 4.4
"	120	12.231 ± 3.452	9.7 ± 5.8	1,251 ± 288	40.2 ± 9.6
40.5° C + air	30	10.192 ± 3.839	12.9 ± 5.8	900 ± 99	30.8 ± 6.5
"	75	11.814 ± 5.105	11.7 ± 4.9	1,111 ± 548	33.9 ± 12.4
"	120	12.187 ± 5.246	14.0 ± 5.5	904 ± 276	34.9 ± 12.0
40.5° C + hypoxia	30	13.774 ± 2.848	14.4 ± 2.5	988 ± 316	42.2 ± 6.8
"	75	15.678 ± 3.444	15.4 ± 5.3	1,093 ± 310	39.8 ± 4.8
"	120	16.270 ± 2.817	16.5 ± 5.8	1,068 ± 300	41.2 ± 5.2

unmistakably clear that both blood pressure and heart rate were greatly disturbed with hypoxia in all three thermal conditions. The changes in blood pressure and heart rate are summarized in Figures 6 and 7, respectively.

In the neutral environment, hypoxia caused no statistically significant change in both systolic and diastolic pressures in comparison to the blood pressures obtained during room air breathing (Figure 6). The heart rate with hypoxia, however, showed universally higher values in all five subjects than that during room air breathing, the amount of increase being 7 to 12 beats/min (Figure 7). Assuming a relatively constant or slightly increased stroke volume, these findings may be interpreted as an indication of increased cardiac output in hypoxia at the neutral temperature, which suggests a reduced total peripheral resistance. In the cold environment the systolic pressure was significantly higher in hypoxia than in room air breathing, while the diastolic pressure was the same in both conditions (Figure 6). The heart rate in hypoxia was again greatly increased without exception, the average heart rate with and without hypoxia being 87 to 99 and 70 to 78 beats/min, respectively (Figure 7). These responses in the cold with hypoxia may be interpreted as an indication of an enhanced cardiac output. However, in view of the concomitant increase in systolic pressure, the change in total peripheral resistance cannot be decided with certainty in this series. The disturbances in the cardiovascular system with hypoxia were best manifested in the warm environment: the heart rate was approximately 20 beats/min higher throughout the two-hour period in hypoxia than in room air breathing (Figure 7). At the same time the diastolic pressure kept falling from 70 to 40 mm Hg in hypoxia, while it was at a steady level of 75 mm Hg in heat alone (Figure 6). This may be interpreted as an indication of a greatly increased cardiac output and a markedly reduced total peripheral resistance in warm environment with hypoxia.

When each increment of heart rate for single stress of hypoxia or cold is added together, the values fall short of the heart rate observed during the combined operation of hypoxia and cold. This difference between the observed and additive value is approximately 8 to 14 beats/min, and this again indicates synergistic action of these stresses on heart rate rather than an additive one. Such a synergism is also shown in the series of heat and hypoxia.

Thermal Balance

The balance sheet of heat exchange and debt in neutral, cold, and warm environments with and without hypoxia is shown in Table IV. In the estimation of heat production, not only O_2 consumption but also other factors such

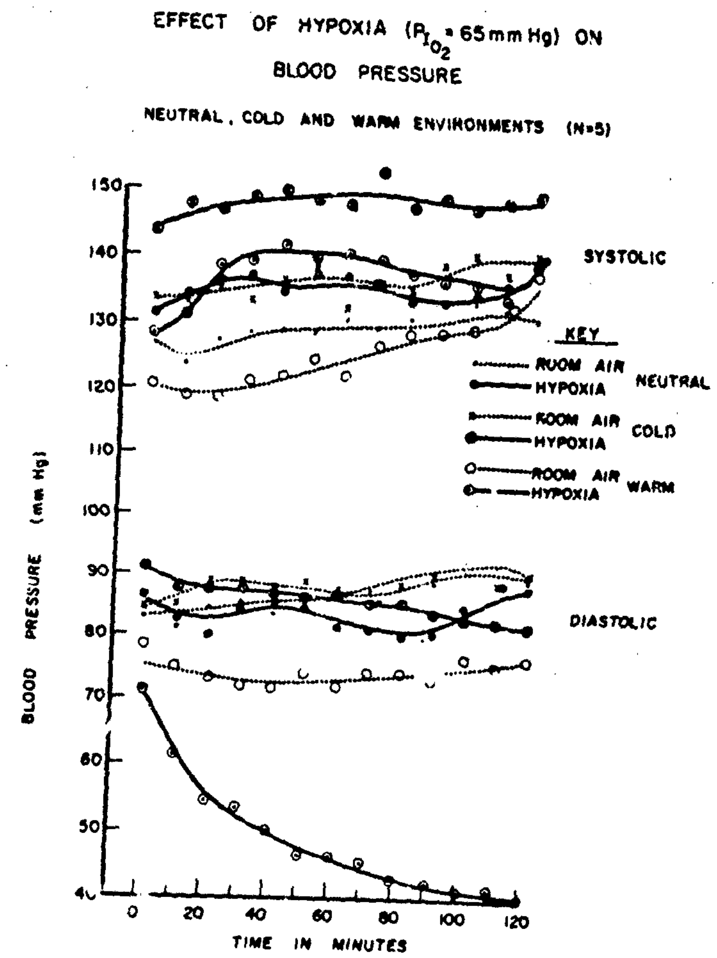

EFFECT OF HYPOXIA ($P_{I_{O_2}}$ = 65 mm Hg) ON
BLOOD PRESSURE
NEUTRAL, COLD AND WARM ENVIRONMENTS (N=5)
SYSTOLIC
DIASTOLIC
KEY
ROOM AIR
HYPOXIA
NEUTRAL
ROOM AIR
HYPOXIA
COLD
ROOM AIR
HYPOXIA
WARM
BLOOD PRESSURE (mm Hg)
TIME IN MINUTES

FIGURE 6.

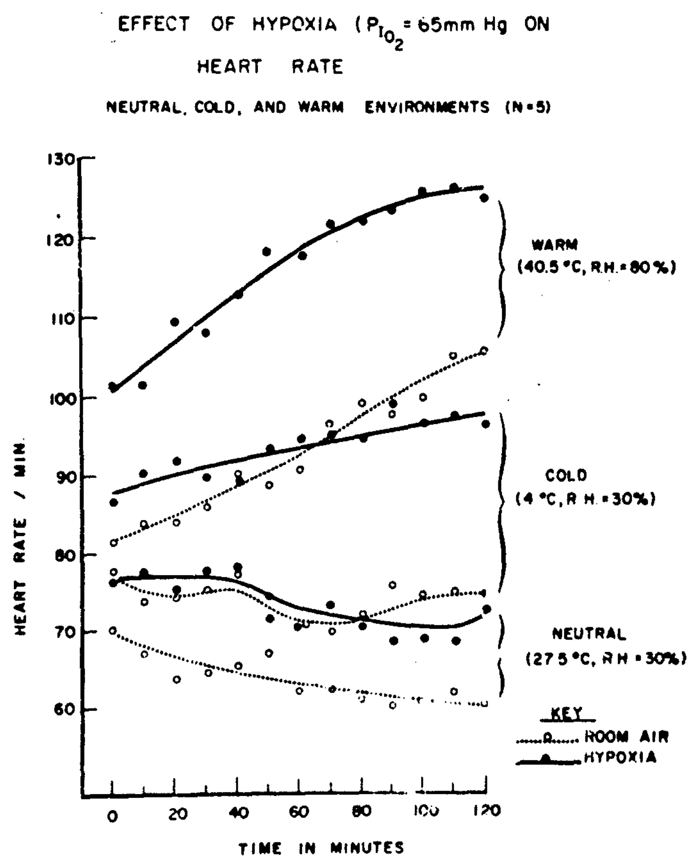

EFFECT OF HYPOXIA ($P_{I_{O_2}}$ = 65mm Hg ON
HEART RATE
NEUTRAL, COLD, AND WARM ENVIRONMENTS (N=5)
HEART RATE / MIN.
TIME IN MINUTES
WARM
(40.5 °C, R.H.=80%)
COLD
(4 °C, R.H.=30%)
NEUTRAL
(27.5 °C, R.H.=30%)
KEY
ROOM AIR
HYPOXIA

FIGURE 7.

TABLE IV

THERMAL BALANCE IN NEUTRAL, COLD, AND WARM ENVIRONMENTS WITH HYPOXIA AND WITH ROOM AIR BREATHING

(n = 5)

	Heat Production (Kcal/m^2/hr)			Heat Debt (Kcal/m^2/hr)			Heat Loss (Kcal/m^2/hr)		
Time (Min)	30	75	120	30	75	120	30	75	120
Environments:									
27.5^o C + air	41.9	42.2	42.2	-	+ 1.8	+ 4.1	-	44.0	46.3
27.5^o C + hypoxia	45.5	47.[illegible]	46.2	-	+ 7.7	- 4.5	-	54.8	41.7
4^o C + air	83.8	112.0	114.8	-	+ 32.2	+ 17.6	-	144.2	132.4
4^o C + hypoxia	96.8	110.5	117.2	-	+ 27.1	+ 4.5	-	137.6	121.7
40.5^o C + air	48.0	51.[illegible]	51.2	-	- 25.4	- 24.9	-	25.9	26.3
40.5^o C + hypoxia	53.6	56.3	55.7	-	- 35.1	- 23.6	-	21.2	32.1

as respiratory gas exchange ratio and surface area are taken into consideration. As it was in O_2 consumption the statistical analyses revealed no significant influence of hypoxia in heat production. The analyses of data on heat debt and heat loss also failed to show any effect of hypoxia on these parameters in man under the experimental conditions.

SECTION 4. DISCUSSION

One of the major objectives of this study was to elucidate the status of systemic peripheral circulation under hypoxia as reflected in the skin temperature. As demonstrated by Wezler and Frank (1948) and also by Marbarger and his associates (1952), the total peripheral resistance decreases during induced hypoxia, suggesting a marked vasodilatory effect of O_2 deficiency in man. In accord with this finding Kottke et al (1948) reported a surprisingly large increase in skin temperature (arm and calf), which amounted to an increase of 2° to 3° C following the exposure to low-oxygen gas mixture (10% O_2) for 90 minutes at 19° C in a subject. Our observations, however, do not confirm this phenomenon of increased skin temperature during hypoxia either in neutral or in adverse temperature zones, but rather agree with those by Brown et al (1952), who could not detect any significant change in skin temperature in ten healthy men during the exposure to 10% O_2 in nitrogen or a simulated altitude of 18, 000 feet in a decompression chamber for a minimum of 90 minutes duration at 10° C. Similarily, Jouck (1944) reported no alteration in skin temperature in five subjects during inhalation of 7.5% to 10.5% O_2 in N_2 at 24° C for 15 minutes. Essentially the same result was obtained by Hülnhagen (1944) in three subjects exposed to 7.5% to 10.5% O_2 in N_2 at various levels of cold temperature ranging from 4° to -12° C for 30 to 60 minutes. Since the total peripheral resistance may be defined as the arithmetic sums of various vascular resistances in parallel, our findings of reduced peripheral resistance without alteration in surface temperature during hypoxia indicate at least two important aspects: a possible preferential vasodilatory action of hypoxia at the vascular beds other than the skin region, and an insignificant role of "physical thermoregulation" in hypoxia.

Contrary to the skin temperature, it has been frequently observed in man that hypoxia causes a marked reduction (0.5° to 1.0° C) in core temperature both in neutral (Jouck, 1914; Frank and Wezler, 1948) and cold (Wezler and Frank, 1948; Kottke et al, 1948; Hulnhagen, 1944) environments, and this phenomenon has been interpreted as an indication of the importance of adequate O_2 tension in maintaining "chemical thermoregulation." For some unknown reason we could not confirm this rather well established phenomenon in either the neutral or the cold environment, as shown in Figures 3 and 4 by the unchanged rectal temperature during hypoxia. Nonetheless, our results are not without confirmatory support: Brown et al (1952) also could not observe any significant influence of hypoxia on core temperature in man at 10° C. The greater elevation of core temperature during hypoxia in the warm environment in our study as opposed to the uneventful behaviors of core temperature in the cold and neutral environments deserves attention and careful interpretation. On the basis of heat balance hypothesis, core temperature may be increased in mammals either by a reduction of heat loss (i. e., disturbance in physical regulation) without change in heat production, by an increased heat production (i. e., disturbance in chemical control) without change in heat loss, or combined disturbances of both heat loss and heat production mechanisms. Unfortunately, our data do not allow a clean-cut differentiation of these possibilities as shown by the quantitative analyses of heat loss and heat production with and without hypoxia. Obviously, a further study is strongly indicated along the line of combined heat and hypoxia series, which promises easier detection of disturbances in peripheral circulation and core temperature.

Our results show an insignificant effect of hypoxia on the heat gain mechanism of shivering, as indicated by the unaltered O_2 consumption or heat production during hypoxia. This is again a sharp contrast to the findings of Kottke and his coworkers (1948), who reported an inhibition of shivering by hypoxia (10% O_2) in all four experiments. In their study, O_2 consumption rose not at all or to a distinctly lesser degree in the cold with hypoxia than in controls (average 12% increase). In relation to the metabolic rate during hypoxia two other studies have to be mentioned: Huckabee (1958) observed no reduction in O_2 uptake in fasting resting subjects given 10% O_2; and Houston and Riley (1947) reported that in acclimatized men, O_2 consumption was unchanged between sea level and 22,000 feet both during rest and during standard work. Our data suggest that the effect of hypoxia on heat loss mechanism of perspiration is also very small.

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