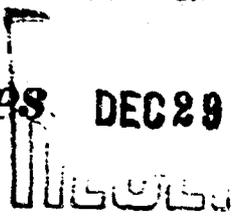


# Acute Altitude Sickness in Females

DEC 29

CHARLES W. HARRIS, M.D., J. L. SHIELDS, Ph.D., and JOHN P. HANNON, Ph.D.



D

AD 644502

An evaluation of symptomatic responses of eight college females to high altitude exposure was conducted at Pikes Peak, Colorado (altitude 14,130 feet). Significant illness occurred during the first four days at altitude, with the predominant complaints being headache, drowsiness, fatigue and insomnia. Only minimal gastrointestinal and cardiorespiratory symptoms were noted. A reduction in blood pressure and elevation of resting pulse and respiratory rate was observed. The electrical activity and x-ray appearance of the heart remained within normal limits during the ten-week stay. Menstrual changes at altitude consisted of decreased flow in five girls. The response of several medications given for the symptoms of altitude sickness was evaluated.

questionnaires. Blood pressure (cuff), heart rate, and respiratory rate were recorded in duplicate each day before arising. Routine electrocardiograms, vectorcardiograms and chest x-rays were taken at altitude, and the effect of altitude on menstrual cycle was also observed.

Several commonly prescribed medications were given for the relief of high altitude symptoms and a gross evaluation of their beneficial effect was conducted. Distribution of the medicines in an experimentally controlled manner was not attempted and the name and dosage of each one used was known to the subject.

Affirmative answers to the medical and psychological symptom questionnaires were scored on a scale of 0-4 representing the degree of discomfort experienced, which varied from minimal to very severe (Table I). Each subject was also required to give an additional comment in her own words regarding each symptom she experienced. This latter information was useful in ascertaining the accuracy of the questionnaire ratings given by the subject. From information obtained in previous high altitude studies, the authors feel that fre-

**M**EDICAL SYMPTOMS encountered during acute high altitude exposure have been recorded for more than 70 years.<sup>1,15,16</sup> More recently, a number of attempts have been made to more accurately describe their nature and severity, as well as the underlying mechanisms responsible for their occurrence.<sup>3,7,15,19,21,27</sup> To date, all of the clinical observations on the symptomatic response of humans to altitude have been obtained from men with the exception of two reports, written prior to 1920, containing comments about Peruvian women at altitude.<sup>1,2</sup> These reports suggest the severity of altitude sickness is less in women than in men. We had the opportunity to observe college females at their annual

TABLE I. HIGH ALTITUDE QUESTIONNAIRE

CLEARINGHOUSE FOR FEDERAL SCIENTIFIC AND TECHNICAL INFORMATION		
Hardcopy	Microfiche	
\$ —	\$ —	5 ppas
ARCHIVE COPY		

1,20

D D C

# Acute Altitude Sickness in Females

DEC 29 1966

CHARLES W. HARRIS, M.D., J. L. SHIELDS, PH.D., and JOHN P. HANNON, PH.D.

AD 644502

An evaluation of symptomatic responses of eight college females to high altitude exposure was conducted at Pikes Peak, Colorado (altitude 14,110 feet). Significant illness occurred during the first four days at altitude, with the predominant complaints being headache, drowsiness, fatigue and insomnia. Only minimal gastrointestinal and cardiorespiratory symptoms were noted. A reduction in blood pressure and elevation of resting pulse and respiratory rate was observed. The electrical activity and x-ray appearance of the heart remained within normal limits during the ten-week stay. Menstrual changes at altitude consisted of decreased flow in five girls. The response of several medications given for the symptoms of altitude sickness was evaluated.

questionnaires. Blood pressure (cuff), heart rate, and respiratory rate were recorded in duplicate each day before arising. Routine electrocardiograms, vectorcardiograms and chest x-rays were taken at altitude, and the effect of altitude on menstrual cycle was also observed.

Several commonly prescribed medications were given for the relief of high altitude symptoms and a gross evaluation of their beneficial effect was conducted. Distribution of the medicines in an experimentally controlled manner was not attempted and the name and dosage of each one used was known to the subject.

Affirmative answers to the medical and psychological symptom questionnaires were scored on a scale of 0-4 representing the degree of discomfort experienced, which varied from minimal to very severe (Table I). Each subject was also required to give an additional comment in her own words regarding each symptom she experienced. This latter information was useful in ascertaining the accuracy of the questionnaire ratings given by the subject. From information obtained in previous high altitude studies, the authors feel that fre-

**M**EDICAL SYMPTOMS encountered during acute high altitude exposure have been recorded for more than 70 years.<sup>1,15,16</sup> More recently, a number of attempts have been made to more accurately describe their nature and severity, as well as the underlying mechanisms responsible for their occurrence.<sup>3,11,18,19,21,27</sup>

To date, all of the clinical observations on the symptomatic response of humans to altitude have been obtained from men with the exception of two reports, written prior to 1920, containing comments about Peruvian women at altitude.<sup>18,25</sup> These reports suggest the severity of altitude sickness is less in women than in men. We had the opportunity to observe college females at their normal low altitude residence and during a ten-week period of residence at the summit of Pikes Peak, Colorado (altitude 14,110 feet). This report concerns the symptomatology experienced, and certain clinical findings encountered, during their initial period of altitude exposure.

## METHODS

Eight University of Missouri coeds without prior high altitude exposure, were selected on the basis of having a normal medical profile as determined by medical history, physical examination, complete red and white blood cell count, electrocardiogram, chest x-ray, pulmonary function tests and an exercise tolerance test. In addition, the emotional maturity and stability of the girls were grossly evaluated because of the expected stress of isolation inherent in living in a high altitude environment for several weeks.

Clinical observations which were conducted for four days prior to ascent and during the first three weeks at altitude consisted of detailed questioning in the form of oral conferences twice daily and multiple daily

TABLE I. HIGH ALTITUDE QUESTIONNAIRE

Medical Symptoms†	
<i>Cardiorespiratory</i>	<i>General</i>
Chest tightness	*Very fatigued
*Chest pain	*Poor sleep
Palpitations	Change in appetite
*Shortness of breath (rest)	Change in thirst
Shortness of breath (exercise)	<i>Central Nervous System</i>
Irregular breathing	*Headache
Coughing	Visual change
Runny nose	Auditory change
Very dry nose or throat	Change in smell or taste
Sore throat	<i>Urinary</i>
Common cold (with fever)	Oliguria
Cyanoosis of nose or ears	*Dysuria
<i>Gastrointestinal</i>	Nocturia
*Nausea	Hesitancy
*Vomiting	<i>Musculoskeletal</i>
Constipation	*Generalized muscle aches
*Diarrhea	*Joint pain or stiffness
*Stomach cramping	Back or neck stiffness
Increased intestinal gas	
Severe indigestion	
	Psychological Symptoms†
Drowsy	Depressed
Happy	Vigorous
Pleased	Refreshed
Satisfied	Angry
Comfortable	Anxious
Energetic	

From the Physiology Division, U. S. Army Medical Research and Nutrition Laboratory, Fitzsimons General Hospital, Denver, Colorado.

\*When present, these medical symptoms were considered by investigators to be most disabling in terms of daily activity performance.  
†Rated by degree of discomfort (None-Mild-Moderate-Moderately Severe-Severe).

quent and detailed oral and written questioning, conducted in this manner, presents the most useful and accurate picture of high altitude symptomatology. This statistical significance of the questionnaire data was determined by analysis of variance (Figure 1), and by rank order analysis (Figures 2-5).

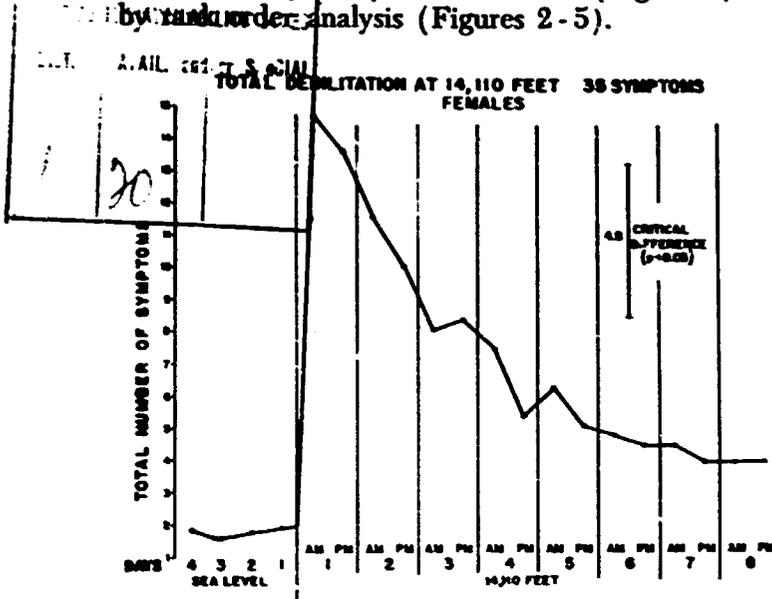


Fig. 1. Illness scale as determined from questionnaires—mean values. Those symptoms designated by an asterisk in table 1 were given a value of 2 in this illustration; all other symptoms have a value of 1.

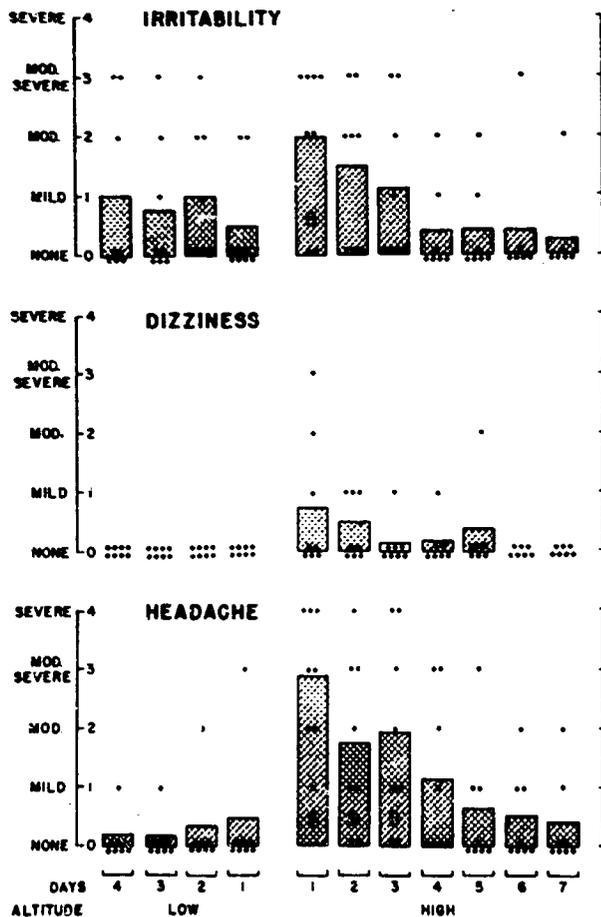


Fig. 2

Figs. 2-5. Degree and duration of symptoms at altitude. Dots represent individual values. Bars show mean values. Low altitude control values obtained during the four days prior to ascent are shown. S = significant ( $P < 0.05$ ) change from low altitude control values.

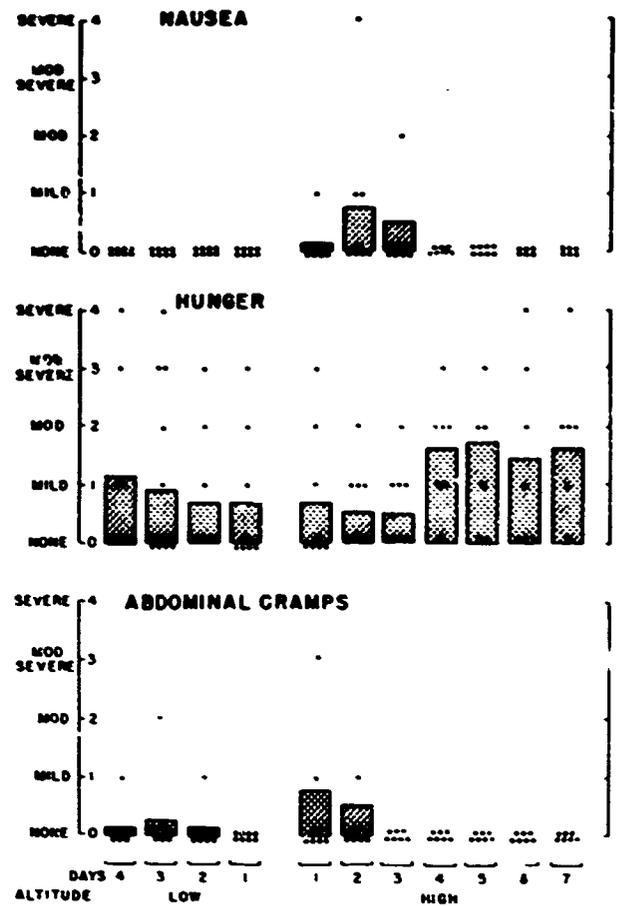


Fig. 3

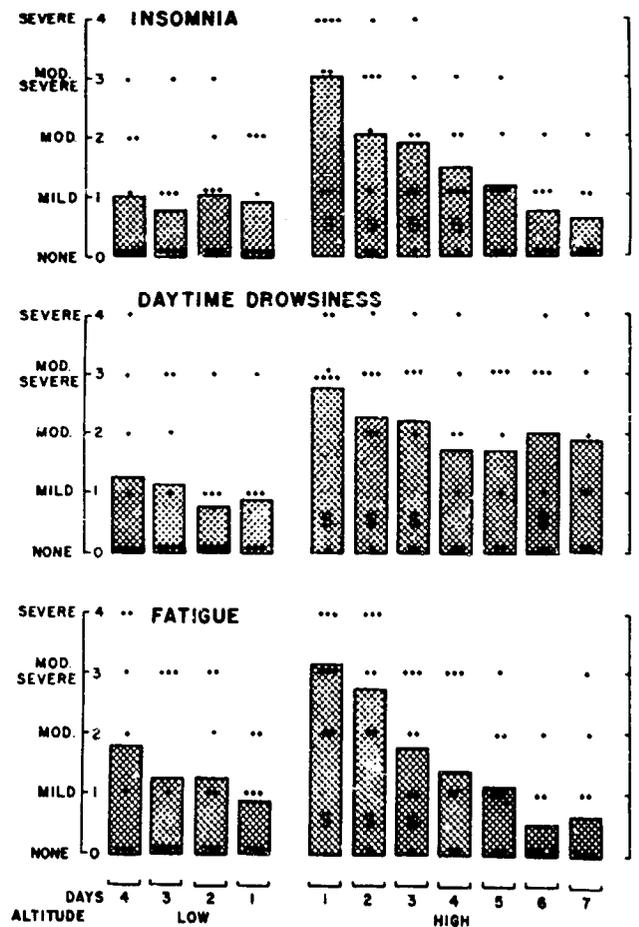


Fig. 4

ACUTE ALTITUDE SICKNESS IN FEMALES—HARRIS, ET AL

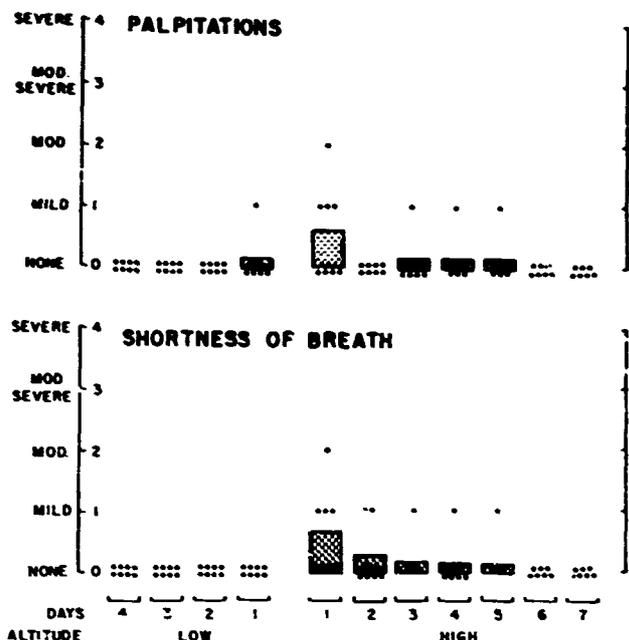


Fig. 5

RESULTS

During the first four days at altitudes there was a period of significant debilitation experienced by the group of eight girls (Figure 1). By the fifth day at altitude there was no difference in the total number of symptoms experienced at altitude when compared to the last four days at sea level. The duration of the illness shown in Figure 1 appears to be somewhat similar to the illness spectrum reported in males exposed to high altitude.<sup>11,14,19,27</sup> The degree and duration of discomfort due to several selected symptoms at altitude is shown in Figures 2-5. Of interest is the frequency and severity of general complaints such as fatigue, drowsiness, headache, irritability and insomnia and the infrequent and minimal difficulty from gastrointestinal and cardiorespiratory symptoms. Headaches were generally frontal or temporal in location and only rarely were experienced posteriorly. Insomnia, which was experienced by all girls during the first four nights at altitude, was associated with Cheyne-Stokes respiration in every case. A gross estimation by the girls of the average period of sleep during the first two nights at altitude was about four hours. Daytime drowsiness seemed most prominent during the morning and in the late afternoon; however, general fatigue and irritability

were unchanged throughout the day. No recognizable pulmonary edema or other serious illnesses occurred.

A prompt reduction in systolic and diastolic blood pressure was observed after twenty-four hours of altitude exposure and remained lower than sea level values for about two weeks (Table II). It should be noted that the blood pressure determinations at sea level were made at noon following a short rest, whereas, the altitude values were obtained in the morning before arising. An actual drop in blood pressure at altitude probably occurred, however, as a rebound in blood pressure was noted on the second day at altitude which almost reached sea level values. The expected rise in heart and respiratory rate was also observed (Table II). Chest x-rays, electrocardiograms and vectorcardiograms taken at altitude revealed measurable changes from those taken at sea level, but all remained within normal limits.

Small changes were noted in the average duration and cycle length of menstrual periods at altitude, and a reduction in cycle length was noted for two months after returning to low altitude (Figure 6). A decrease in the amount of menstrual flow was noted by five of the eight girls during the first two months at altitude. Two of these girls considered the reduction to be moderate; however, three girls noted minimal to absent flow. Only minimal changes were noted at altitude in symptoms frequently associated with menstrual periods (Table III).

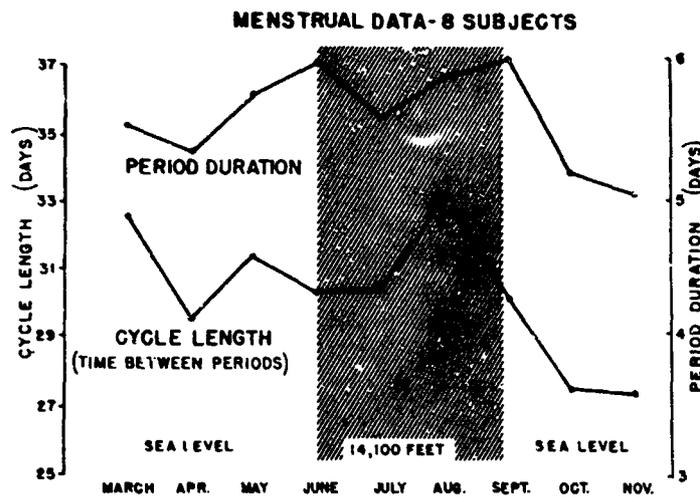


Fig. 6. Menstrual period duration and cycle length—mean values.

TABLE II. AVERAGE BLOOD PRESSURE, PULSE, AND RESPIRATORY RATE\* (8 Subjects)

	Sea Level	Days at Altitude									
		1	2	3†	4†	5†	6	7	9	11	16
Systolic BP	115.2	104.8	112.5	107.8	107.5	108.6	109.4	106.2	105.5	105.8	106.0
Diastolic BP	72.0	67.7	70.0	71.8	71.1	70.3	71.4	69.9	70.0	69.1	69.1
Pulse Rate (min.)	76.1	87.5	88.0	77.5	75.4	74.6	77.6	75.1	69.5	72.0	74.5
Respiratory Rate (min.)	12.0	13.3	14.5	14.5	13.1	14.0	12.8	13.7	13.1	11.2	11.4

\*All measurements at altitude were taken in A.M. before arising. Sea level values were recorded at noon following 20 minutes of rest.

†Measurements based on 7 subjects.

ACUTE ALTITUDE SICKNESS IN FEMALES—HARRIS, ET AL

TABLE III. MENSTRUAL CHANGES AT ALTITUDE\*  
(8 Subjects)

Symptom	Type of Change (No. of girls)		
	Increased	Decreased	Unchanged
Gen. Strength	0	2	5
Flow (amount)	1	5	2
Abdominal cramps	2	1	5
Headache	1	1	6
Nausea	1	1	6
Irritability	2	1	5
Backache	1	0	7

\* Change with respect to the usual degree of menstrual symptomatology.

The subjective responses at altitude to several commonly prescribed symptomatic medications are shown in Table IV. The number of medicines and the number of trials were limited, however, this evaluation revealed the mediocre response of most of the medicines used in reducing acute high altitude symptoms. Salicylates seemed to have a beneficial effect on headache and muscular complaints, but the response of the subjects to other medicines was inconclusive. This limited evaluation demonstrates the need for more detailed investigation concerning the prevention and therapy of acute altitude sickness.

DISCUSSION

Clinical descriptions of acute altitude sickness in males have been available for many years,<sup>3,9,11,25</sup> however, there are relatively few recent descriptions and fewer deliberate clinical studies of this illness.<sup>14,15,19,20,24,27</sup> Almost all reports have noted the predominant symptoms of altitude sickness to be headache, fatigue, breathlessness, and anorexia. Nausea and vomiting are common and insomnia occurs during the first week, in spite of excessive fatigue. Other frequently reported complaints include chest tightness, chest pain, Cheyne-Stokes respiration, sinus pain, lumbar and flank pain, leg cramps, abdominal cramps, increased sensitivity to low temperature and nervous and mental disturbances.<sup>14,27</sup> Changes in mood, in memory and in the ability to perform complex mental tasks and make decisions are examples of the latter. The onset of these difficulties is usually about 8-24 hours after arrival at

altitude and generally continues for the first 3-4 days, but in some cases may continue for several more days.<sup>14,26</sup>

In the present study, significant illness was experienced about 12 hours after arrival at altitude. Symptoms began to subside on the second altitude day and reached control values by the fifth day. As in males, the complaints of headache, drowsiness, fatigue and insomnia were most prominent; however, of particular interest, is the very low incidence of gastrointestinal and cardiorespiratory symptoms. Nausea was noted by only two girls and was associated with vomiting in one. The sensation of hunger, admittedly more difficult to estimate, was only slightly depressed during the second and third day, and in only one case was there an actual loss of appetite. This is in contrast to the frequent and occasionally severe gastrointestinal symptoms usually reported for males and experienced by the male investigators and technicians during this study. Weight loss, which is in part, a reflection of appetite, averaged less than one kg during the first week at altitude; whereas, an average loss of 2.4 kg was noted in eight men of similar age during one week at this altitude.<sup>8</sup>

The sensation of palpitations at rest, shortness of breath, chest tightness and chest pain—fairly common complaints in males—were rarely experienced by the girls. The explanation for these differences in the symptomatic response of females and males to acute altitude exposure is unknown, but this observation would seem to agree with the two available observations recorded more than 45 years ago, regarding altitude sickness in females: "As a rule, females are supposed to suffer less than males"<sup>13</sup> and "I think on the whole that women suffer less than men."<sup>25</sup>

The blood pressure in males during acute altitude exposure has been observed to rise<sup>11</sup> to remain unchanged, or to decline.<sup>11,21</sup> The fall in systolic and diastolic pressure in the study was small and not associated with clinical symptoms or signs of hypotension. This change in blood pressure would coincide with the suspected reduction in peripheral vascular resistance and in blood volume which occurs during early altitude exposure.<sup>2,26</sup> The observed rise in pulse and respiratory rates are of the magnitude observed in males at this altitude.<sup>11,26</sup>

A reduction in the amount of menstrual flow in five

TABLE IV. MEDICATION RESPONSE AT ALTITUDE

Medicine	Complaint	Dosage	No. of Trials	Responses
Acetylsalicylic Acid (Aspirin)	Headaches Muscle Aches	0.6 gms	22	Good—usually relief within 2 hours
Dextro Propoxyphene (Darvon)	Headaches Backaches	65 mg	16	Fair
Acetylsalicylic Acid, Acetophenetidin and Caffeine (APC)	Headaches Muscle Aches	2 tablets	14	Fair
Darvon plus APC	Headaches Muscle Aches	32 mg plus 2 tablets	18	Fair to good
Prochlorperazine (Compazine)	Nausea	10 mg (orally)	3	Fair to poor
Tripelethamine Hcl (Pyribenzamine)	Sinus Fullness or Pain	50 mg	3	Fair
Secobarbital Sodium (Seconal)	Insomnia	0.1 gm	4	Fair to good

girls during the first two months is of some interest. Slight irregularity in the onset of menstrual periods and in the amount of flow is not uncommon in young females under normal circumstances. Whether the diminished flow noted by the girls was related to high altitude exposure per se, or to a generally stressful situation is not known. It may be that the reduced menstrual flow is a physiologic attempt by the body to conserve blood loss and thus help the demand for increased RBC volume. This is only unsubstantiated supposition and it will be necessary to investigate pituitary-ovarian hormonal relationships at altitude before the observed changes are better understood.

There have been many attempts at both preventing and ameliorating the effects of altitude exposure. Studies for this purpose have been conducted using potassium chloride,<sup>11</sup> potassium chlorate,<sup>22</sup> ammonium chloride,<sup>4</sup> epinephrine-like compounds,<sup>17</sup> cobalt-induced polycythemia,<sup>10</sup> packed red cell infusions,<sup>23</sup> carbon dioxide inhalation,<sup>7</sup> amphetamines,<sup>12</sup> codeine,<sup>12</sup> acetazolamide,<sup>6</sup> methylene blue<sup>5</sup> and many other compounds. Apparently only ammonium chloride, potassium chloride, amphetamine, codeine and possibly methylene blue have been administered to subject groups large enough for results to be meaningful. Ammonium chloride, potassium chloride and amphetamine provided very little symptomatic relief, whereas, methylene blue and codeine were possibly of benefit. Aspirin has been shown to be effective for the relief of headaches at altitude<sup>14,19</sup> and was considered to be very beneficial in this study. The rather indefinite response of several other commonly used medicines which were given in this study for the symptoms of headache, muscle aches, nausea, sinus fullness and insomnia (Table 4), suggests that further attempts at reducing high altitude symptoms might best be aimed at preventive rather than suppressive therapy.

## ACKNOWLEDGMENT

The authors wish to express appreciation to the University of Missouri college student subjects for their cooperation; to Dr. Wesley S. Platner, Dept. of Physiology, University of Missouri School of Medicine, for his advice and help and for providing low altitude facilities; to Mr. Bill Carle and The Helen Stewart Company for providing facilities and employment for the subjects at Pikes Peak; and to Miss Barbara Loyd and Mr. William C. Hartner for their help in obtaining this data.

## REFERENCES

- ACOSTA, JOSE: Historia Natural y Moral de las Indias en que se Trata de Cosas Notables del Cielo, de los Clementos, Mentales Plantas y Animals. Barcelona, 1569.
- ASMUSSEN, E., and NIELSEN, M.: Studies on the Initial Increases in O<sub>2</sub>-Capacity of the Blood at Low O<sub>2</sub>-Pressure. *Acta Physiol. Scan.* 9:75-87, 1945.
- BARCROFT, J.: Mountain Sickness. *Nature* 114:90-92, 1924.
- BARRON, E. S. G., DILL, D. B., EDWARDS, H. T., and HURTADO, A.: Acute Mountain Sickness; The Effect of Ammonium Chloride. *J. of Clin. Invest.* 16:541-546, 1937.
- BROOKS, M. M.: Methylene Blue, Antidote to Altitude Sickness. *J. Aviat. Med.*, 19:298-299, 1948.
- CAIN, S. M., and DUNN, J. E.: Increase in Arterial Oxygen Tension at Altitude by Carbonic Anhydrase Inhibition. *J. of Appl. Physiol.* 20:882-884, 1965.
- CHILINS, S. B., HAMLIN, H., and HENDERSON, Y.: Possible Value of Inhalation of Carbon Dioxide in Climbing Great Altitudes. *Nature.* 135:457-458, 1935.
- CONSOLAZIO, C. F.: Observation to be reported.
- COWARD, F. A.: Mountain Sickness as Observed in the Andes. *J. South Carolina Med. Assoc.*, 2:123-125, 1906.
- DORRANCE, S. S., et al.: Effect of Cobalt on Work Performance Under Conditions of Anoxia. *Amer. J. Physiol.* 139:399-405, 1943.
- DOUGLAS, C. G., HALDANE, J. S., HENDERSON, Y., and SCHNEIDER, E. C.: Physiological Observations Made on Pikes Peak with Special Reference to Adaptions to Low Barometric Pressures. *Phil. Trans. Royal Soc. London* 103-B: 185-318, 1913.
- EVANS, W. O.: Personal observations to be reported.
- FITZMAURICE, F. E.: Mountain Sickness in the Andes. *J. Royal Naval Med. Service*, 6:403-407, 1920.
- HALL, W. H., BARILA, T. G., METZGER, E. C. and GUPTA, K. K.: A Clinical Study of Acute Mountain Sickness. *Arch. Environ. Health*, 10:747-753, 1965.
- HEPBURN, M. L.: Mal des Montagnes; or So-Called Mountain Sickness. *St. Bartholomew's Hosp. Reports*, 31:191-219, 1895.
- HEPBURN, M. L.: So-Called Mountain Sickness. *St. Bartholomew's Hosp. J.*, 2:185-187, 1894-1895.
- HERRLIGKOFFER, K. M.: Pervitin in Himalaya. *München Med Wschr* 96 (24): 698, 1954; Abstracted Aerospace Medicine and Biology: Annotated Bibliography, Science and Technology, Division of the Library of Congress, 1954, Vol. 3.
- HOUSTON, C. S.: Some Observations on Acclimatization to High Altitude. *New Eng. J. Med.*, 253:964-968, 1955.
- HULTGREN, H. N., and LUNDBERG, E.: Medical Problems of High Altitude. *Mod. Conc. of Cardiovascular Disease*, 31:719-724, 1962.
- HULTGREN, H., and SPICKORD, W.: Medical Experiences in Peru. *Stanford Med. Bull.*, 18:76-95, 1960.
- KORNER, P. I.: Circulatory Adaptations in Hypoxia. *Physiol. Rev.*, 39:687-730, 1959.
- MORSE, W.: Unrecognized Factor in Altitude Effects. *Sci. Monthly*, 17:108-113, 1923.
- PACE, N., LOZNER, E. L., CONSOLAZIO, W. V., PITTS, G. C., and PECORA, L. J.: The Increase in Hypoxia Tolerance of Normal Men Accompanying the Polycythemia Induced by Transfusion of Erythrocytes. *Amer. J. of Physiology*, 148:152-163, 1947.
- PUGH, L. G.: Physiological and Medical Aspects of Himalayan Scientific and Mountaineering Expedition 1960-61. *Brit. Med. J.*, 2:621-627, 1962.
- RAVENHILL, T. H.: Some Experiences of Mountain Sickness in the Andes. *J. Tropical Med. and Hygiene*, 16:313-320, 1913.
- VOGEL, J. A., HANSEN, J. E., and HARRIS, C. W.: Cardiovascular Responses of Man During Rest, Exhaustive Work and Recovery at Sea Level and 14,100 Feet Altitude. (In preparation)
- WAYNE, H. H.: Clinical Differentiation Between Hypoxia and Hyperventilation. *J. of Aviat. Med.*, 29:307-315, 1958.